USING ELECTRONIC PATIENT-REPORTED OUTCOMES TO PROMOTE QUALITY OF CARE AND SAFETY IN THE MANAGEMENT OF PATIENTS WITH END STAGE KIDNEY DISEASE REQUIRING TREATMENT WITH HAEMODIALYSIS

by
NICOLA ELIZABETH ANDERSON

A thesis submitted to the University of Birmingham for the degree of
DOCTOR OF PHILOSOPHY

Centre for Patient-Reported Outcome Research (CPROR)
Institute of Applied Health Research
College of Medical and Dental Sciences
University of Birmingham

UNIVERSITY OF
BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

This unpublished thesis/dissertation is copyright of the author and/or third parties. The intellectual property rights of the author or third parties in respect of this work are as defined by The Copyright Designs and Patents Act 1988 or as modified by any successor legislation.

Any use made of information contained in this thesis/dissertation must be in accordance with that legislation and must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the permission of the copyright holder.

Abstract

Patients with Chronic Kidney Disease (CKD), particularly those with end-stage kidney disease (ESKD) undertaking haemodialysis (HD), often experience a high symptom burden and diminished health-related quality of life. Data on these constructs can be collected directly from patients and measured using electronic patient-reported outcomes (ePROs). Responses can be used at an individual level to facilitate optimal care and improve shared decision making; research from other clinical settings suggests ePROs use can improve clinician/patient communication, improve health related quality of life, reduce hospitalisations, and increase overall survival, while demonstrating cost effectiveness. At an aggregate level, these data can be used for audit and benchmarking to improve services. However, ePROs have not been implemented routinely and systematically in kidney care settings.

The overall aim of this thesis was to explore and inform the evidence on how ePROs might be used to promote quality of care and safety in the management of patients with ESKD requiring treatment with HD.

Firstly, a synthesis of current evidence on the use and implementation of PROs for patients with ESKD receiving HD was undertaken; identifying gaps in the evidence base and areas for investigation to deliver a roadmap for increasing the evidence base and introducing ePROs into mainstream HD clinical practice.

Informed by these findings, a qualitative study was conducted, exploring the views, perceptions, and experiences of 22 patients receiving HD and 17 health care

professionals (HCPs) in the HD multi-disciplinary team regarding the collection and use ePROs, in HD settings. This study highlighted the need to measure outcomes important to both patients and clinicians and supported the relevance of patient-reported outcomes included in HD-specific core outcome sets (COS). The study stressed the importance of building an empirical evidence base to support the use of ePROs and discussed key contextual implementation factors, including barriers and facilitators, to successful integration into clinical workflow.

Leading on from this was a study to examine whether currently available patient-reported outcome measures (PROMs) used in HD adequately cover outcomes/domains recommended in HD-specific COS. A systematic search of published literature identified two HD-specific COS designed for use in HD research and routine clinical care and 46 validated PROMs currently being used in HD settings. Following assessment of COS coverage and measure characteristics, options for measure choice were outlined.

Finally, to gain a deeper understanding of how ePROs might be successfully implemented, a mixed methods study was undertaken to comprehensively identify ePRO systems for CKD to explore system characteristics including methods of administration, levels of integration into existing workflow and electronic health records (EHR) and the reporting of ePROs to manage patient safety. Overall, 15 ePRO systems were identified allowing a comprehensive classification of core factors which contribute to successful implementation of ePROs in nephrology, including common facilitators and barriers.

To conclude, this thesis describes the current and potential use of ePROs in CKD, with a focus on use in haemodialysis (HD) populations. It draws together a range of original research, including views on potential measures, existing and emerging ePRO systems and priority areas for future research to outline a roadmap to use ePROs to improve the quality of care delivered to patients with ESKD undergoing HD.

Dedication

To my husband Mark – for your love, encouragement, and wit – I couldn't have done this without you!

To my sons, Tom, Will and Olly – I hope I make you as proud as I am of you!

To my Mom – a source of endless love and support, I know Dad is cheering me on!

Acknowledgments

Thank you to my funder, the National Institute for Health and Care Research (NIHR) for seeing the potential in me as a Nurse Researcher, and to Queen Elizabeth Hospital Kidney Patients Association (QEKPA) and University Hospital Birmingham Charities whose support allowed me to apply for an NIHR Clinical Doctoral Research Fellowship.

Huge thanks to my world-class supervisory team – the amazing Professor Mel Calvert, an endless supply of encouragement, advice and support, thank you for seeing the academic in me and giving me opportunities to grow; to the wonderful Dr Derek Kyte who offered constant sage advice and feedback, I am so grateful for all the help; to the super Professor Paul Cockwell whose passion for nephrology has rubbed off and the fantastic Dr Christel McMullan and Dr Olalekan Aiyegbusi who came as later supervisors but who have been so important to the completion of this thesis.

A special thought and thank you for the redoubtable Sister Mary Dutton, one of a kind, never to be forgotten and most definitely the greatest influence on my nursing career.

Thank you to all the members of CPROR and Renal Research Teams past and present for help, support, and friendship. Thank you, Anita Walker, for all the admin support and the lattes!

Finally, thanks to my friends and family, for their patience, encouragement, and humour – I am truly blessed!

Authorship statement

The research for this thesis was conducted by me (NEA), with guidance from my supervisors: Prof. Melanie Calvert (MC), Dr Derek Kyte (DK), Prof. Paul Cockwell (PC), Dr Olalekan Aiyegbusi (OLA) and Dr Christel McMullan (CM). Specific contributions to each article are detailed below:

Narrative review paper (Chapter 1) – NEA drafted the manuscript. The manuscript was reviewed, edited, and critiqued for intellectual content by MC, DK, PC, and Mary Dutton (MD).

PROM-HD qualitative study (Chapter 3): The study was conceived and designed by NEA, MC, DK, PC, MD. Dr Christel McMullan (CM) reviewed the methodology. NEA undertook patient screening and recruitment, PC checked eligibility. NEA conducted all the interviews. NEA coded and analysed all the transcripts, with secondary coders CM and DK. NEA drafted the initial manuscript which was reviewed, edited, and critiqued for intellectual content by all the authors.

Scoping review (Chapter 4) – The study was designed by NEA, DK, MC, PC, and MD. NEA drafted the protocol manuscript. Benjamin Fletcher (BF) assisted in the screening and selection of eligible studies and data extraction. Mark Anderson (MA) performed independent affinity mapping. NEA drafted the initial manuscript. The manuscript was reviewed, edited, and critiqued for intellectual content by all authors.

Mixed methods review (Chapter 5) - The study was conceived and designed by NEA, DK, MC, PC, CM and OLA. NEA conducted the screening and selection of eligible ePRO systems. NEA drafted protocol and structured survey. NEA conducted all the semi-structured interviews. NEA coded and analysed all the transcripts, with secondary coder CM. NEA drafted the initial manuscript. The manuscript was reviewed, edited, and critiqued for intellectual content by all authors and patient partner, Ravinder Verdi (RV).

Comment paper (Chapter 6) – The paper was conceived and designed by NEA and MC. NEA drafted the initial manuscript which was reviewed, edited, and critiqued for intellectual content by all the authors and patient partner, RV.

Additional study specific Patient and Public Involvement (PPI) activity is outlined in each study chapter.

Table of Contents

Abstract ..... **i**

Dedication ..... **iv**

Acknowledgments ..... **v**

Authorship statement ..... **vi**

List of tables ..... **xiv**

List of figures ..... **xvi**

List of Boxes ..... **xvii**

List of definitions and abbreviations ..... **xviii**

Formatting ..... **xxiv**

Chapter One

1.1 Introduction **2**

1.2 Chronic Kidney Disease **2**

1.3 Patient-Reported Outcomes **9**

1.4 Patient-Reported Outcomes in Nephrology **17**

1.5 Justification for research **17**

Publication 1: The Use of Patient-Reported Outcomes in Patients Treated with Maintenance Hemodialysis: A Perspective **20**

1.6 Thesis aims and structure **21**

Chapter Two

2.1 Introduction.....34

2.2 Research Paradigms.....35

2.3 Patient and public involvement.....39

2.4 Overview of methods.....41

2.5 Review Methods.....43

2.6 Qualitative Methods.....52

Publication 2: Using patient reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. 54

2.7 Mixed Methods including structured survey.....69

2.8 Impact of COVID-19 pandemic.....71

Chapter Three

3.1. Introduction.....81

Publication 3: Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study.....84

3.2 Key findings: 85

Chapter Four

4.1 Introduction.....89

A scoping review of patient-reported outcome measures used in haemodialysis: Are we measuring what matters? 91

4.2 Abstract.....92

4.3 Introduction.....94

4.4 Study Design.....96

4.5 Results.....139

4.6 Discussion.....146

4.7 Conclusion and implications for practice.....153

Chapter Five

5.1. Introduction.....168

Global Use of Electronic Patient-Reported Outcome Systems in Nephrology: A Mixed Methods Study.....171

5.2 Abstract.....172

5.3 Introduction.....175

5.4 Study Design.....177

5.5 Results.....179

5.6 Discussion.....188

Chapter Six

6.1 Introduction..... 222

6.2 Summary of principal findings 222

6.3 Interpretation and implication of findings..... 229

6.4 Recommendations for future research..... 249

6.5 Strengths and limitations of the thesis..... 260

Publication 4: Electronic patient-reported outcomes in chronic kidney disease 265

6.6 Overall Conclusions..... 266

Appendix One

Appendix 1.1: Publication 5 Symptom Burden and Health-Related Quality of Life in Chronic Kidney Disease: A global systematic review and meta-analysis 280

Appendix 1.2: Publication 6: In reply to 'A psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis 281

Appendix 1.3: Search Strategy for narrative review 282

Appendix 1.4: PRISMA diagram for Narrative Review 284

Appendix 1.5: Table 1 Papers discussing implementation of PROMs in HD settings..... 285

Appendix Two

Appendix 2.1: Mixed Methods study protocol 295

Appendix 2.2: Consolidated Framework for Interventional Research (CFIR) Codebook Template..... 326

Appendix Three

Appendix 3.1: PROM-HD Participant Information Sheet – Patient 341

Appendix 3.2 PROM-HD Participant Information Sheet – HCP 348

Appendix 3.3 PROM-HD Exemplar PROMs – KDQOL-SF, KDQOL-36, IPOS-Renal 354

Appendix 3.4 PROM-HD Topic Guide for use with patient participants 375

Appendix 3.5 PROM-HD Topic guide for use with HCP's 377

Appendix 3.6 Patient Data Saturation tables and interview characteristics..... 381

Appendix 3.7 HCP Data Saturation tables and interview characteristics 384

Appendix 3.8 Pre-publication Consolidated Criteria for Reporting Qualitative Studies (COREQ) checklist 387

Appendix Four

Appendix 4.1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews (PRISMA-ScR) Checklist..... 390

Appendix 4.2: Scoping review sample search strategy 394

Appendix Five

Appendix 5.1 Publication 7: Development of an electronic patient reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease 397

Appendix 5.2 Publication 8: Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease 398

Appendix 5.3. Structured Survey (www.smartsurvey.co.uk) includes combined consent sheet v10.06.2021..... 398

Appendix 5.4. Topic Guide for semi-structured interviews v4 11.06.2021 Nephrology ePRO systems review - Topic Guide 413

Appendix 5.5: REC approved invitation email v1 10.06.2021 416

Appendix 5.6: REC approved Participant Information Sheet v3 06.06.2021 417

Appendix Six

Appendix 6.1: Publication 9: Patient reported outcome assessment must be inclusive and equitable..... 422

Appendix 6.2 Publication 10: Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines 423

List of tables

Chapter 1: Introduction		**Page**
Table 1	Core Outcome Sets	16
Table 2	Thesis research objectives	22
Chapter 2: Methodology and Methods		**Page**
Table 1	Overview of thesis methods	41
Table 2	Types of review	44
Table 3 (Table 1 in publication)	Description of questionnaires	Page 3 (publication)
Chapter 3: Qualitative Study		**Page**
Table 1 in publication	Patient participant characteristics	Page 3 (publication)
Table 2 in publication	Healthcare professional – participant characteristics	Page 3 (publication)
Table 3 in publication	Key findings – summary of direct quotes	Page 6-10 (publication)
Chapter 4: Scoping Review		**Page**
Table 1	Core outcome sets	100
Table 2	Study Characteristics	103-112
Table 3	Synopsis of PROM characteristics	113-133

Table 4	Affinity mapping and outcome coverage score	134-138
Chapter 5: Mixed Methods study		Page
Table 1	Overview of ePRO systems	201-206
Table 2	System characteristics	207-208
Table 3	Data collection and assessment	209-210
Table 4	System reporting	211-212

List of figures

Chapter 1: Introduction		Page
Figure 1	Classification of CKD	3
Figure 2	Forest plot of Pooled prevalence of patient-reported symptoms across included studies for patients on dialysis	8
Figure 3 (Fig 1 in publication)	The multiple uses of PROs	Page 402 (publication)
Chapter 2: Methodology and Methods		
Figure 1	Conceptual framework for PRO-integration in clinical care	Page 2 (publication)
Figure 2 (Fig 2 in publication)	Study flow chart diagram	Page 5 (publication)
Chapter 3: Qualitative study		
Figure 1 (Fig 1 in publication)	Conceptual framework and key findings	Page 4 (publication)
Chapter 4: Scoping Review		Page
Figure 1	PRISMA-Scr Diagram	140
Chapter 5: Mixed Methods Study		Page
Figure 1	ePRO systems objectives	213
Figure 2	Conceptual framework and key findings	214
Chapter 6: Discussion		Page
Figure 1	Areas for future research	249

List of Boxes

Chapter 1: Introduction		Page
Box 1	Overview of measurement properties	Page 400 (publication)
Box 2	Examples of renal specific PROs commonly used in HD settings	Page 401 (publication)
Chapter 5: Mixed Methods Study		Page
Box 1	Example illustrative quotes	215-217
Box 2	Key priorities for successful implementation	218-219
Chapter 6: Discussion		**Page**
Box 1	Common barriers and facilitators to ePROs implementation	226

List of definitions and abbreviations

List of abbreviations

AE	Adverse Events
BDI	Beck Depression Inventory
BMI	Body Mass Index
BYOD	Bring your own device
CAPD	Continuous Ambulatory Peritoneal dialysis
CAT	Computer Adaptive Testing
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CFIR	Consolidated Framework for Implementation Research
CI	Chief Investigator
CINAHL+	Cumulative Index to Nursing and Allied Health Literature
CKD	Chronic Kidney Disease
COA	Clinical Outcome Assessment
COMET	Core Outcome Measures in Effectiveness Trials
COREQ	Consolidated criteria for REporting Qualitative research

COS	Core Outcome Set
COSMIN	COnsensus-based Standards for the selection of health Measurement Instruments'
CRF	Chronic Renal Failure
CVI	Content Validity Index
EFA	Exploratory Factor Analysis
eGFR	estimated Glomerular Filtration Rate
EHR	Electronic Health Record
EMBASE	Excerpta Medica Database
EMPATHY	Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care
EPR	Electronic Patient health Record
ePROs	Electronic Patient-Reported Outcomes
ePROMs	Electronic Patient-Reported Outcome Measures
eRAPID	Electronic patient self-Reporting of Adverse events: Patient Information and aDvice
ESRD	End Stage Renal Disease
ESKF	End Stage Kidney Failure
EQ-5D	EuroQol Five Dimension

FACT-G PWB	Functional Assessment of Cancer Therapy – General, Physical Well-being subscale
GCP	Good Clinical Practice
GFI	Goodness-of-Fit Index
HCP	Healthcare Professionals
HD	Haemodialysis
HHD	Home Haemodialysis
HRQOL	Health-Related Quality of Life
ICC	Internal Correlation Coefficient
ICHD	In-centre Haemodialysis
ICHOM	International Consortium for Health Outcomes Measurement
IVRS	Interactive voice response system
KDCS	Kidney Disease Composite Summary
KDIGO	Kidney Disease Improving Global Outcomes
KPIN	Kidney Patent Involvement Network
KRT	Kidney Replacement Therapy
MCS	Mental Composite Summary score

MDT	Multidisciplinary team
MEDLINE	Medical Literature Analysis and Retrieval System Online
MHC	Mental Health Composite
MMR	Mixed Methods Research
mPROM	multi-media patient-reported outcome measure
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NMC	Nursing and Midwifery Council
ONS	Office of National Statistics
PCA	Principal Component Analysis
PCC	Person-centred Care
PCS	Physical Composite Summary score
PD	Peritoneal Dialysis
PHC	Physical Health Composite
PI	Principal Investigator
POR	Patient Orientated Research

PREMs	Patient-Reported Experience Measures
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROs	Patient-Reported Outcomes
PROMs	Patient-Reported Outcome Measures
PROMIS®	Patient Reported Outcomes Measurement Information System
PROSPERO	Prospective register of systematic reviews
QALY	Quality-adjusted life year
REC	Research Ethics Committee
RCT	Randomized Controlled Trial
RMSEA	Root Mean Square Error of Approximation
RRT	Renal Replacement Therapy
SD	Standard Deviation
SE	Standard error
SF	Short Form measure
SF-12	Short-Form Health Survey 12-item questionnaire
SF-36	Short-Form Health Survey 36-item questionnaire
SOPs	Standard Operating Procedures

SONG-HD	the Standardised Outcomes in NephroloGy Haemodialysis initiative
SWIFT	Symptom monitoring WIth Feedback Trial
TA	Thematic Analysis
UHB	University Hospitals Birmingham
UK	United Kingdom
UKKA	United Kingdom Kidney Association
US	United States

Formatting

This thesis was formatted according to the University of Birmingham 'Alternative Format' thesis guidelines, which allows the inclusion of published articles as well as chapters formatted for submission to peer-reviewed journals.

The work presented and discussed within the body of the thesis (4 papers as lead author) and appendices (6 papers as co-author) have been published within 10 peer-reviewed journals. The publications are:

(Chapter 1) Anderson, Nicola Elizabeth et al (2019) **The Use of Patient-Reported Outcomes in Patients Treated with Maintenance Hemodialysis: A Perspective** American Journal of Kidney Diseases, Volume 74, Issue 3, 399 – 406

(Chapter 2) Anderson NE, Calvert M, Cockwell P, et al. (2018) **Using patient reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD)**: **a qualitative study protocol**. BMJ Open; 8:e021532. doi:10.1136/ bmjopen-2018-021532

(Chapter 3) Anderson NE, McMullan C, Calvert M, et al. (2021) **Using patient- reported outcome measures during the management of patients with end- stage kidney disease requiring treatment with haemodialysis (PROM- HD): a qualitative study**. BMJ Open;11:e052629. doi:10.1136/ bmjopen-2021-052629

(Chapter 6) Anderson, N., Kyte, D., McMullan, C. et al. (2022) **Electronic patient-reported outcomes in chronic kidney disease.** Nat Rev Nephrol. https://doi.org/10.1038/s41581-022-00619-3

(Appendix 1.1) Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. (2022) **Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis**. PLoS Med 19(4): e1003954. https://doi.org/10.1371/journal. pmed.1003954

(Appendix 1.2) Anderson, Nicola Elizabeth et al (2019) **In Reply to 'A Psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis'** American Journal of Kidney Diseases, Volume 74, Issue 5, 711 - 712

(Appendix 5.5) Kyte D, Anderson N et al. (2020) **Development of an electronic patient reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease** Journal of Patient-Reported Outcomes https://doi.org/10.1186/s41687-020-00223-8

(Appendix 5.6) Kyte D, Anderson N, Bishop J, et al. (2022) **Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient reported outcome measure in the management of UK patients with advanced chronic kidney disease**. BMJ Open 2022;12:e050610.

(Appendix 6.1) Calvert, M.J., Cruz Rivera, S., Retzer, A. et al. (2022) **Patient reported outcome assessment must be inclusive and equitable.** Nat Med 28, 1120–1124. https://doi.org/10.1038/s41591-022-01781-8

(Appendix 6.2) Cruz Rivera S, Aiyegbusi OL, Ives J, et al. (2022) **Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines**. JAMA;327(19):1910–1919. doi:10.1001/jama.2022.6421

This thesis also includes two chapters prepared for submission to peer-reviewed journals (Chapter 4 and 5). For consistency BMJ Open guidelines were followed https://bmjopen.bmj.com/pages/authors/#submission_guidelines

Please note:

- The page numbers for the articles are not included in the thesis pagination sequence.
- Tables, boxes and figures are presented within the text to ease the reader
- To aid clarity, reference lists are included at the end of each chapter

Excerpts from the University of Birmingham Alternative Format Thesis Guidelines: *"Since the alternative format thesis includes copies or offprints of journal articles, book chapters etc., which already have page numbers, the pages of the publications themselves will not be included in the pagination sequence of the submission."*, *"The incorporation of publication-style chapters in the thesis will inevitably lead to some duplication since each publication-style chapter will have self-contained components that will overlap with parts of the other sections of the thesis…"*

Full 2016-2017 cohort regulations at:

Template for Regulations, Codes of Practice etc (birmingham.ac.uk)

altformatguide.docx (live.com)

Chapter 1:
Introduction and Background

1.1 Introduction

The research within this thesis explores the use of electronic patient-reported outcomes (e-PROs) to promote the quality of care and safety in the management of patients with end-stage kidney disease requiring treatment with haemodialysis. The aim of this chapter is to provide a general introduction and justification for the research, setting out the overall aims and objectives.

1.2 Chronic Kidney Disease

1.2.1 Definition, prevalence, and treatment

Kidney Disease Improving Global Outcomes (KDIGO) is a global organisation created to develop and implement evidence based practice guidelines in kidney disease (1). KIDGO define chronic kidney disease (CKD) as abnormalities of kidney function or structure, that have implications for health, which persist for more than 3 months (2). This definition includes all individuals with markers of kidney damage or those with an estimated Glomerular Filtration Rate (eGFR - a key indicator of kidney function) of ≤ 60 ml/min/1.73m^2 on at least two occasions 90 days apart (with or without markers of kidney damage). CKD is further classified by using eGFR and the level of protein in the urine (Figure 1). This information forms the basis of CKD staging which is useful for planning and managing care and to assist risk stratification (2).

Figure 1: Classification of CKD

Reproduced with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter., Suppl. 2013; 3: 1–150

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Patients with advanced CKD at stages G4 and G5 have severe impairment of kidney function and treatment focuses on preservation of function and managing complications, including increased risk of cardiovascular disease. Patients with an eGFR of <15 ml/min/1.73m^2, or who require some form of dialysis, have CKD stage G5 (2). This is often referred to as end-stage kidney disease (ESKD) but can be termed kidney failure or established renal disease. Patients with ESKD have insufficient kidney function to keep them feeling well and experience a significant symptom burden; an

important predictor of reduced health-related quality of life (HRQOL) (3). Symptoms commonly experienced by patients with advanced CKD include fatigue, pain, sleep problems, itching, nausea and vomiting, cognitive impairment , anxiety and depression (4). Patients with advanced CKD also experience increased risk of hospitalisation and mortality (5). However, both HRQOL and symptoms are often identified by patients with CKD as more important to them than longevity, even though survival rates are poor for those with ESKD even when compared to patients with some cancers (6-8). Patients highlight the importance of life participation and making the most of the life they have left (9). All these factors emphasise the complexity of managing patients with CKD due to symptoms, multiple chronic conditions plus the rate and trajectory of CKD progression which is variable (10).

Patients with ESKD may benefit from kidney replacement therapy (KRT), such as dialysis or a transplant. While pre-emptive transplantation is the gold standard, this is not always possible (11). Guidance from the National Institute for Health and Care Excellence (NICE) recommends starting dialysis when indicated, either by uraemic symptoms or biomedical measures or uncontrollable fluid overload or when eGFR drops to 5-7ml/min^{-1}/1.73m^{-2} in the absence of symptoms (12). The decision on whether or when to start dialysis or the modality of dialysis is not an easy one and decisions should be made jointly between patients (plus or minus discussions with their significant others) and the healthcare team.

Dialysis is a life sustaining treatment that replaces some of the functions of the kidneys when they fail (13). Three KRT modalities are available to patients with ESKD –

haemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation. Conventional HD is usually undertaken 3-4 times weekly for approximately 3-5 hours in-centre at a hospital or a dialysis unit (ICHD) but may be delivered with or without an unpaid caregiver at home (HHD) (14). In simplified terms, during HD blood is removed from the body to perform the dialysis process via a dialysis machine which then returns this blood to the body. This process cannot replicate all the complex functions of the human kidney but can prevent the immediate life-threatening complications of ESKD (11).

Internationally, it is estimated that CKD affects just under 850 million people (15), it is a leading cause of mortality and it is expected to affect increasing numbers of people in the future (16). It is estimated that nearly 4 million people worldwide access HD treatment, while the number actually requiring HD is much higher (17). Globally, HD is the most common form of renal replacement therapy (69%) and also the most common form of dialysis (89%) (17). According to the UK Renal Registry, at the end of 2020, there were 68,249 adult patients receiving HD, a stable prevalence rate to the previous year (18). The fact there was no increase in these numbers is likely due to the COVID-19 pandemic, which saw fewer new HD starters and an increased mortality rate for patients already receiving HD, who were highly vulnerable to the virus (18, 19).

While HD is undoubtedly a lifesaving and life-sustaining healthcare intervention, it is associated with a high resource cost. Healthcare system costs associated with CKD vary across different stages, with ESKD showing the highest costs per stage ($20,110-

$100,593 per patient mean annual health care cost), and with HD being the most expensive form of KRT, particularly when delivered in-centre (20).

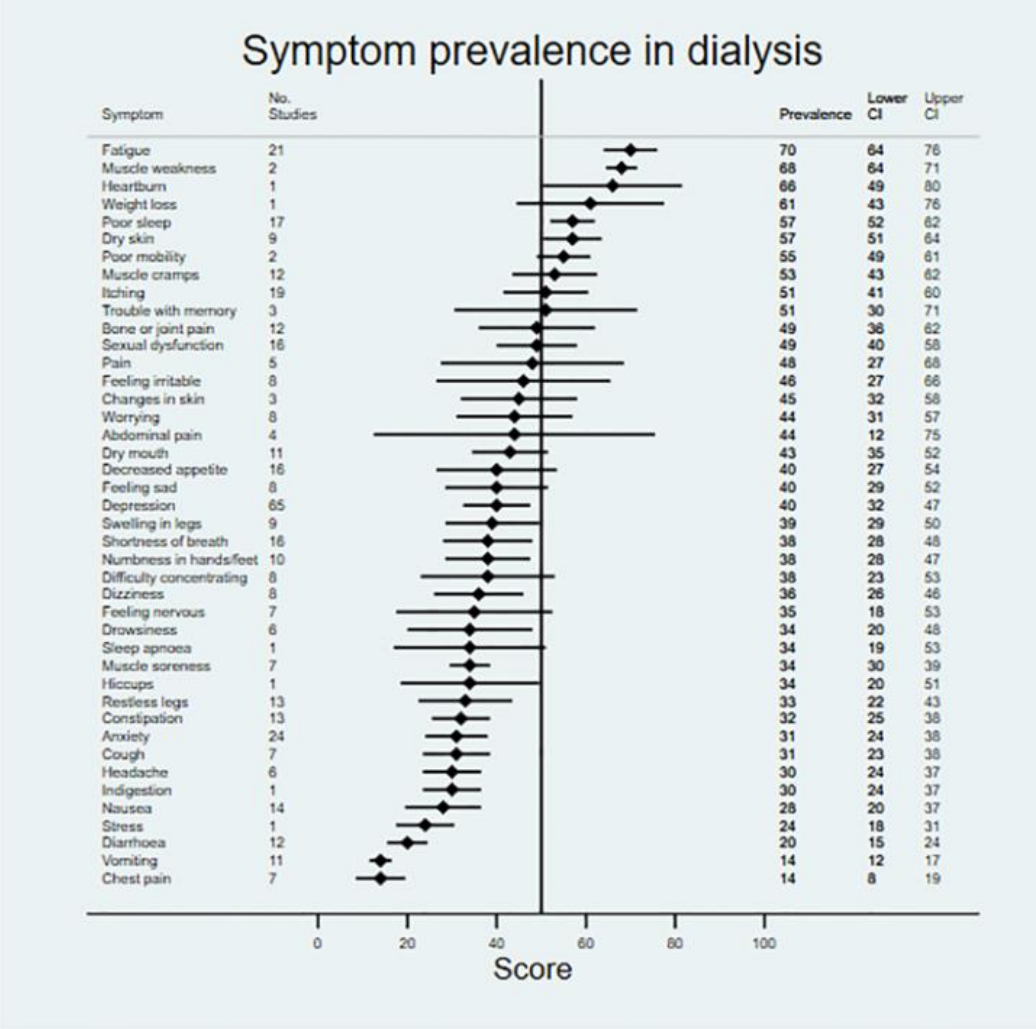
Furthermore, life on HD can be challenging, with many patients reporting a high symptom burden of 11 symptoms on average (21) and poor quality of life due to disease, treatment and co-morbidity (22) (23). While the prevalent symptom profile for patients with advanced CKD not on KRT and those undergoing dialysis is similar, depression and anxiety is more common among the dialysis population (23). However, past studies have shown that potentially treatable symptoms in HD are poorly understood and managed, particularly for emotional symptoms (4, 24). Reasons for this may include a lack of routine standardised symptom assessment; with high variability among patients on dialysis for spontaneously reporting their symptoms (25).

This is important as it has been argued that recognition and subsequent treatment of these symptoms may have the greatest impact on HRQOL for patients receiving dialysis other than kidney transplantation (25, 26). Furthermore, HRQOL, is not only an important outcome in itself, it is associated with clinical outcomes such as healthcare utilisation and mortality (27).

A global systematic review and meta-analysis of 449 studies, including 199,147 patients with varying stages of CKD from 62 countries, found that symptom prevalence data was available for 42 symptoms in patients receiving dialysis (see figure 2) (23). A copy of this paper, co-authored by the author of this thesis, is included in Appendix 1.1. Patients receiving dialysis were included in 274 (61%) of reviewed studies; explicitly stated as haemodialysis in 228 and peritoneal dialysis in 118 studies (23).

According to this review the most common symptom experienced by patients on dialysis was fatigue. However, in terms of severity, pain was the most severe symptom, followed by fatigue, dry skin, and bone/joint pain (23). A review undertaken in 2007 by Murtagh et al also found patients on dialysis experience multiple symptoms; with pain, fatigue, pruritus, and constipation in more than 1 in 2 patients (28). There is increasing recognition that CKD symptoms often occur in clusters; a symptom cluster is generally defined as groups of two or more concurrent symptoms that relate to one another and are independent of other symptom clusters (29). Further research is needed on how symptom clusters interrelate. Thus, studies emphasise that patients with ESKD undergoing HD experience a range of debilitating symptoms and have a markedly reduced quality of life even when compared to all other CKD patient groups (5, 23, 26, 28).

Figure 2: Pooled prevalence of patient-reported symptoms across included studies for patients on dialysis



Reproduced from Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. (2022) **Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis**. PLoS Med 19(4): e1003954. https://doi.org/10.1371/journal. pmed.1003954

Symptom assessment and symptom management have been identified as top priorities for research (30, 31). Yet traditionally, hard data on biomedical outcomes, mortality and hospitalisations has been gathered routinely but HRQOL and symptom data has not; even though such constructs are often identified by patients with CKD as more important to them than clinical outcomes such as survival (6) and increased

symptom burden leads to poorer long term outcomes (21, 32). Moreover, studies involving oncology populations or patients reporting respiratory symptoms have demonstrated that clinicians tend to underestimate the incidence, severity, or distress of symptoms experienced and reported by patients (33, 34). Such disparity appears to be consistent, even when symptoms are severe and distressing. Patients also appear to report both symptom frequency and severity earlier than clinicians do (34). This indicates that additional to routine clinical outcomes, data on other outcomes such as symptoms and HRQOL warrant routine and standardised assessment (32).

1.3 Patient-Reported Outcomes

One way to assess and evaluate the patient experience of disease and/or treatments, such as their symptom burden, functional status and HRQOL, is through the measurement of patient-reported outcomes (PROs) (35). A definition of PROs was developed by the US Food and Drug Administration (FDA): PROs are "…any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else." (36). PROs can be measured using validated questionnaires known as patient-reported outcome measures (PROMs). PROs data can be used alongside biomedical and clinician-reported outcomes to gain a more complete and holistic view of the effects and impact of CKD and treatment including HRQOL (37). HRQOL has been defined as 'a multidimensional construct encompassing perceptions of both positive and negative aspects of dimensions, such as physical, emotional, social, and cognitive functions, as well as the

negative aspects of somatic discomfort and other symptoms produced by a disease or its treatment.' (38).

The rapid growth of digital technologies brings the opportunity to systematically collect PROs electronically (39); termed electronic patient-reported outcomes (ePROs) and the associated measures are ePROMs. Electronic data may be collected via various digital devices using web-based systems, such as smart phones, tablets, and computers. Access to a device may often be from a healthcare provider, however there is increasing interest in the 'Bring Your Own Device' (BYOD) model; which affords patients convenience and removes challenges with logistics and inventory management (40). Telephone-based interactive voice response systems (IVRS) many also be used in some settings (41, 42). A study in patients undergoing KRT suggest high satisfaction with the use of a tablet computer to collect ePROs but highlights a correlation between comfort with technology and computer experience (43). There are challenges to use of mobile devices that need to be overcome, such as cost, training, and health data privacy requirements (44). The shift towards models of remote and virtual care for patients with CKD (45, 46), has been accelerated by the emergence of COVID-19 (47) and monitoring of patient symptoms and HRQOL can provide important information to help optimise CKD management (23).

PROMs have traditionally been categorised into generic and disease-specific tools (48, 49). Disease-specific PROMs are designed to identify specific symptoms and the impact on function and other aspects of health of those specific conditions; while generic PROMs offer the opportunity to compare outcomes across various clinical conditions,

but the subsequent trade-off for this breadth is a loss of responsiveness and sensitivity in many patient groups (48). A sub-group of generic measures are preference-based measures, whose scores summarize multiple domains into a single profile score. This score is then converted into an index score (utilities), using an algorithm that has been derived from surveying members of the public on their preferences for different combinations of health states. Utilities range between 0 and 1, where 1 is usually taken to reflect 'perfect health' and 0 'Death', although it is acknowledged that some measures allow a score of less than zero, i.e., a state worse than death. The utility score can be used to calculate a QALY (Quality adjusted life year) (50).The advantage of preference-based measures is their ability to prioritize health interventions by overall impact and to measure changes in health for comparative-effectiveness and cost-effectiveness analyses i.e., in cost-effectiveness studies or health economic evaluations the QALY can be used to quantify effectiveness (51). (52). Examples of preference based measures include the Euroqol EQ-5D, the preferred measurement method to measure HRQOL in adults for economic evaluations in the UK by the National Institute of Clinical Excellence (NICE) (53), and the Short-form six dimension measure (SF-6D), which uses information on patient-reported health from the SF-36 - a commonly used generic health measure used in clinical research (54). Often, clinical studies use a combination of generic and disease-specific PROMs, while disease-specific PROMs are often preferred for the measurement of patient outcomes at individual patient level (48). PROMs can be designed to measure single items or multiple items and the preferences of key stakeholders, including patients, should be balanced in the task of questionnaire selection and type of PRO data to be collected (55).

1.3.1 Application of PROs

Patient-reported outcome data has the potential for multiple uses (35). For individual patient management, data can be used to: (i) tailor and deliver individualised care (56); (ii) support communication and inform shared decision making (57, 58); (iii) screen and monitor for symptoms to assist treatment planning (59, 60); (iv) support early identification of problems and direct to rapid referral pathways (61, 62); (v) inform prognostication and risk stratification (63) and (vi) assist outpatient planning (64). At an aggregate level, PRO data from research can be used to support labelling claims (36), understand treatment or intervention effects (65, 66) and inform clinical guideline development (67). Audit of aggregated PROs can be used for benchmarking and service improvement (35).

Evidence from oncology populations suggest that ePRO monitoring is effective in enhancing patient clinician communication and patient activation (68), although the exact mechanism for this remains unclear (69, 70). Remote weekly collection of ePRO symptom data within an oncology trial of 1191 adults being treated for metastatic cancer (PRO group n=593, control group receiving usual care n= 598) across 52 oncology practices has provisionally shown statistically significant improvements in physical function, symptom control, and HRQOL at 3 months, when compared with usual care (62). These are provisional findings, pending results of the study's primary outcome of survival (62). While other trials have shown ePRO symptom monitoring, even with digitally inexperienced patients, can assist earlier detection of adverse events; reduced use of emergency room (ER) fewer inpatient hospital episodes; and improvements in overall survival (71-74). Furthermore, study findings suggest that

symptom monitoring using PROs during routine cancer treatment could be cost-effective (75, 76). However, a Cochrane review in 2021 on routine provision of feedback from PROMs to healthcare providers and patients in clinical practice noted that it was unclear if improvements in communication, diagnosis and notation, and disease control, and small improvements to QOL were clinically meaningful or sustainable in the long term. They called for more high-quality studies, particularly studies that used cluster designs and allocation concealment (77).

PROMs should be distinguished from patient-reported experience measures (PREMs), which can be used to help clinical services understand how patients experience their kidney care, to demonstrate where improvement is required. An example of a PREM being used in CKD settings is the UK national Kidney PREM, validated in 2017 and administered via the UK Renal Registry. The measure includes 39 questions across 13 themes of patient care, and a further question on overall experience. Themes range from transport and needling to shared decision-making (78).

1.3.2 Core outcome sets and choice of measure

Patient-reported outcomes are one of several important outcomes which can be used in research or routine clinical care. However, currently a wide range of outcomes are used which hampers evidence synthesis and intervention comparison (79). One way to address this is through the use of core outcome sets (COS), which are currently being developed across a range of clinical specialties to help standardise outcome assessment in research and routine clinical care (79). In a research setting, the Core Outcome Measures in Effectiveness Trials (COMET) Initiative have defined a COS as a

consensus-based agreed minimum set of outcomes that should be measured and reported in all clinical trials of a specific disease or trial population: this could be an outcome based on a score obtained through physical examination, a laboratory measurement, or a PRO (80). The COMET Initiative has systematically identified several hundred published COS and lists these on a free, publicly available, searchable database (81). COMET lists one COS study relevant to this thesis: the Standardised Outcomes in NephroloGy Haemodialysis (SONG-HD) initiative (82). Using patient-centred consensus methodology, the SONG-HD researchers have generated a set of outcomes, including PROs, for use in clinical trials (Table 1). The core outcomes that have been identified for use in all HD trials are fatigue, cardiovascular disease, vascular access and mortality (83). The methodology for establishing core outcome domains involved: 1) a systematic review to identify outcomes reported in trials (84); 2) focus groups with nominal group technique involving patients and caregivers to identify, rank, and describe reasons for their choices; (8) 3) stakeholder interviews to elicit perspectives on core outcomes (85); 4) international online Delphi survey to prioritise a list of core outcome domains based on overall agreement (7); and 5) consensus workshop/s with stakeholders to review the core outcome domains and discuss implementation strategies (86). This has been followed by the development of associated PROMs for the most highly prioritised domains, such as the SONG-HD fatigue measure (87).

While the SONG-HD COS was developed for use in research, another COS has been developed primarily for use in values-based routine healthcare. The International Consortium for Health Outcomes Measurement (ICHOM) group has developed a

standard set of CKD outcomes and case-mix variables which they recommend all providers track, allowing global benchmarking (88) (Table 1).

In 2016, The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative collaborated with COMET to develop a guideline on how to select outcome measurement instruments for core outcomes (89). Measurement properties including validity and reliability provide important information about the quality of the measure in the target population (90). The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) taxonomy describes which aspects should be considered to judge the quality of the PROM (91), described in more detail in the published paper included in this chapter (92).

Table 1: Core Outcome Sets (83, 88)

SONG-HD outcomes	Timing and source not specified	
TIER ONE Critically important to all stakeholders	**TIER TWO** Critically important to some stakeholders	**TIER THREE** Important to all or some stakeholders
Fatigue Feeling tired with no energy for weeks, for most of the time	Ability to work	Anxiety/ Stress
CVD Disease of the heart and blood vessels (e.g., heart attack, stroke, blockage of blood vessels)	Ability to travel to go away for holiday/vacation, event, visiting family, work	Bone Health
VA (Problems with fistula, graft, or catheter required for dialysis (e.g., access infections, bleeding, bruising, pain, discomfort, clotting)	Anaemia	Calcium
Mortality No. of people on hemodialysis therapy who have died, risk for death, how long the patient will live	Blood pressure	Cognition
	Depression	Cramps
	Dialysis Adequacy How well the dialysis cleans the blood, clearance, Kt/V	Financial Impact
	Drop in BP	Food Enjoyment
	Hospitalisation	Itching
	Impact on family and friends	Nausea and Vomiting
	Infection/Immunity	Parathyroid Hormone
	Mobility	Phosphate
	Pain	Restless legs syndrome
	Potassium	Sexual function
Key	Target weight	Sleep
Outcome capable of measurement by PROM	Washed out after dialysis	
Clinical outcome	Dialysis Free Time (Time (hours/days) not doing dialysis	

ICHOM Outcomes		
Measure	**Timing**	**Data Source**
Survival	Ongoing	Clinical
Hospitalisation	Annually	Clinical
Cardiovascular events	Annually	Clinical
Vascular Access survival	6 monthly	Clinical
Health-Related Quality-of-Life	Baseline and 6 monthly	Patient-reported
Pain	Baseline and 6 monthly	Patient-reported
Fatigue	Baseline and 6 monthly	Patient-reported
Physical function	Baseline and 6 monthly	Patient-reported
Depression	Baseline and 6 monthly	Patient-reported
Daily activity	Baseline and 6 monthly	Patient-reported

1.4 Patient-Reported Outcomes in Nephrology

Interest in the use and implementation of PROs is ever growing within nephrology, with an acknowledgment of the shift to patient-centred care and the importance of capturing the patients' perception of their experience: their symptoms, goals, and objectives of care (93).

A realist synthesis was recently undertaken to develop a kidney-specific programme theory about the use of PROs in nephrology (94). The authors proposed that PROs in nephrology could be useful if applied in 3 ways: (i) at the individual-level, collecting PRO data at point of care, (ii) using aggregated PRO data at point of care and (iii) in the use of aggregated PRO data by organisations. They postulate that contextual factors, such as the complexity of kidney disease, the likelihood of comorbidities, time factors and administrative constraints in dialysis settings, all influence PROs use in nephrology, but that electronic collection of PROs may facilitate PRO use given these contexts. However, a key finding was that the current state of the evidence-base for using PROs in nephrology is primarily theoretical and that there is an imperative for empirical research to improve the evidence-base of PRO use at all levels of nephrology care.

1.5 Justification for research

1.5.1 Gaps in the evidence

The following pages include the results from a narrative review published by the thesis author (and reproduced with permission) in the American Journal of Kidney Diseases (*Impact factor 11.072)* (AJKD), as a perspectives article, cited as:

Anderson, Nicola Elizabeth et al. (2019) **The Use of Patient-Reported Outcomes in Patients Treated with Maintenance Hemodialysis: A Perspective.** American Journal of Kidney Diseases, Volume 74, Issue 3, 399406

https://doi.org/10.1053/j.ajkd.2019.01.035

This narrative review aimed to discuss the current use of PROs for patients with end-stage kidney disease receiving haemodialysis and to identify a roadmap for increasing the evidence base and introducing PROs into mainstream clinical practice. The paper highlights gaps in the field, and future research priorities.

This paper prompted a letter to the editor on cognitive impairment and its potential to affect the reliability of PRO data. The editors of the American Journal of Kidney Diseases requested a response to this letter which is reproduced in full in Appendix 1.2 and is cited as follows,

Anderson, Nicola Elizabeth et al. (2019) In Reply to 'A Psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis'. American Journal of Kidney Diseases, Volume 74, Issue 5, 711 – 712 https://doi.org/10.1053/j.ajkd.2019.07.009

The search strategy for this narrative review, associated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and Table of included study characteristics are included in Appendices 1.3-1.5.

Dissemination of narrative review findings.

The narrative review reported in Chapter One was presented at the following conferences as outlined in below:

Year	Conference	Location	Presentation type
2018	ISOQOL (International Society for Quality-of-Life Research) 25th Annual Conference	Dublin, Ireland	Poster
2019	World Congress of Nephrology	Melbourne, Australia	Oral (plenary session)
2019	Annual UK PROMs Conference	Leeds, UK	Poster
2019	UK Kidney Week	Brighton, UK	Poster

Publication 1: The Use of Patient-Reported Outcomes in Patients Treated with Maintenance Hemodialysis: A Perspective

The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective

Nicola Elizabeth Anderson, Melanie Calvert, Paul Cockwell, Mary Dutton, and Derek Kyte

There is increasing interest in the integration of patient-reported outcomes (PROs) into health care research and clinical practice for the benefit of patients with end-stage kidney disease receiving hemodialysis. In a research setting, PROs can be used as a patient-centered primary or secondary outcome in clinical studies. In routine care, PRO data may be used to support service delivery through benchmarking and audit or inform and enhance the care of the individual patient by improving patient-clinician communication. Despite evidence demonstrating the potential benefits of PROs and prioritization of these outcomes by patients, their use in kidney disease remains limited. Although there are significant methodological and operational challenges for the widespread integration of PROs, there is now consensus that this area should be at the forefront of clinical research and implementation science. We discuss the current use of PROs for patients with end-stage kidney disease receiving hemodialysis and identify a roadmap for increasing the evidence base and introducing PROs into mainstream clinical practice.

Complete author and article information provided before references.

Am J Kidney Dis. 74(3): 399-406. Published online April 25, 2019.

doi: 10.1053/j.ajkd.2019.01.035

© 2019 by the National Kidney Foundation, Inc.

Introduction

Patients with end-stage kidney disease receiving hemodialysis (HD) often experience extensive physical symptoms[1,2] comparable to patients with advanced cancer[3,4] and report poor health-related quality of life (HRQoL).[3,5,6] This impairment profile is associated with increased hospitalization and mortality rates.[7,8] This population is highly heterogeneous, with varying underlying kidney disease and presentation, often highlighting health disparities across different races, ethnicities, and socioeconomic status.[9]

The success of HD management has traditionally been evaluated through biochemical dialysis-related targets[10] and mortality and survival rates.[11] Similarly, in research settings, mortality is often used as a primary outcome measure, whereas outcomes such as pain, fatigue, and dialysis-free time are not routinely captured despite evidence that such outcomes are prioritized by patients over their own survival.[3,6,10,12,13] One way to capture this information is using patient-reported outcome (PRO) data. Collection of PROs to provide the patient's perspective on his or her health status/symptom burden offers a unique opportunity to identify and address some of the observed health disparities in the end-stage kidney disease population, with consequent implications for health policy change.

The US Food and Drug Administration defines a PRO as "any report coming from patients about a health condition and its treatment, without interpretation of the patient's response by a clinician or anyone else."[14] These data can be gathered using validated instruments, commonly paper or electronic (ePRO) questionnaires. PRO tools may be "generic," measuring HRQoL regardless of the underlying disease process, or "disease-specific," assessing the impact of a specific disease, such as kidney disease, and its associated symptoms and/or treatment.

This article summarizes key aspects of PRO use and implementation in HD research and routine care, highlighting recent developments, gaps in the field, and future research priorities.

PROs in HD Research

High-quality aggregated PRO data collected from clinical trials can be used to inform labeling claims and health policy and may direct individual care by allowing clinicians and patients to select the "best treatment" from the patient's perspective.[15]

Despite this, PRO collection in HD research is uncommon.[16] In a recent review of the Cochrane Database of Systematic Reviews and ClinicalTrials.gov for all studies involving prevalent patients receiving maintenance dialysis, quality of life was reported in just 9% of trials.[17]

Methodological research has highlighted deficiencies in PRO trial design and reporting, including renal trials.[18] When PROs are collected, there is often a lack of detail and consistency regarding choice of measure, with different PROs being used to assess the same domain. This variability may prevent meaningful synthesis of results, hindering uptake in practice. Too often PROs are chosen and written into trial protocols based on familiarity and availability rather than assessed for relevance and appropriateness to the research question.[19]

Optimizing the Use of PROs in HD Research

The first step toward enhancing PRO capture in HD trials is to reach consensus on what domains should be measured.[20,21] This may be achieved through the development of core outcome sets. Led by the Core Outcome Measures in Effectiveness Trials (COMET) initiative, core outcome set development draws on consensus methodology, incorporating patient and public involvement, to agree on standardized outcomes to be measured and

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

reported for all trials within a clinical specialty.[20] This may lead to consistent collection of more meaningful patient-centered outcomes, reducing outcome reporting bias, aiding meta-analysis, and facilitating efficient use of precious health care resources.[20,22-26]

The principal work on core outcome sets within nephrology research is the SONG (Standardized Outcomes in Nephrology) initiative, formed to establish/implement core outcomes across the spectrum of chronic kidney disease (CKD), including HD (SONG-HD).[12,27,28] This initiative has identified a wide range of recommended outcomes, with patient involvement being a fundamental principle. However, further work is now required to identify robust PRO measures capable of capturing data across the spectrum of SONG-HD outcomes in a way that is nonburdensome for patients. Additionally, these measures should enable data collection across all patients receiving HD, including those with different language requirements, low educational attainment, and cognitive impairment or the critically unwell.[27]

PRO Instrument Selection

Having identified outcomes of interest, it is important to carefully select the optimal measurement tool. The Consensus-Based Standards for the Selection of Health Measure Instruments (COSMIN) group provides guidelines to aid PRO measure selection based on a tool's measurement properties; for example, validity, reliability, responsiveness, and interpretability (Box 1).[23,29] Recent systematic reviews have highlighted the need for comprehensive exploration of PROs used in HD,[30-34] and reviews of PROs for fatigue,[35] anemia,[36] and vascular access outcomes in maintenance HD trials[37] are currently taking place as part of the SONG-HD initiative.

Recent research has supported the KDQOL-36 (Kidney Disease Quality of Life 36-Item Survey) and KDQOL-SF (Kidney Disease Quality of Life Short Form) for use within the dialysis population,[32,38] with the longer KDQOL-SF appropriate for research use and the shorter KDQOL-36 of more use in routine clinical settings (Box 2). However, the authors concluded that further validation work is needed for all measures, particularly with English speakers.[32] It is important to note that measures currently recommended for use in HD do not appear to cover all SONG-HD outcomes. Clearly work is still needed to identify/develop PROs to fill these gaps.

PRO Trial Design, Implementation, and Reporting

As with any trial outcome, PROs should be fully integrated into the design and implementation phases according to best practice guidelines such as the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) PRO extension.[39] This checklist details 16 items recommended for inclusion in a trial protocol in which PROs are the primary or secondary end point.[39] Emerging evidence suggests that robust PRO protocol components aid high-quality data collection and subsequent dissemination.[40,41]

However, unfortunately, PRO trial findings have been poorly reported to date, hindering uptake in practice.[18,41] To address this, the CONSORT (Consolidated Standards of Reporting Trials) PRO extension was developed in 2013.[42] Early evidence suggests that PRO reporting may be improved by journal endorsement and author use of CONSORT PROs.[43] It is recommended that HD trialists use these best practice guidelines when incorporating PROs in their research.

Box 1. Overview of Measurement Properties

- Reliability (the extent to which the measure is free from random error)
  - ◇ Reproducibility (test-test reliability): ie, can the measure yield the same results when repeated
  - ◇ Internal consistency: the degree of correlation between different items in the measure
- Validity (the extent to which the measure assesses what it claims to measure)
  - ◇ Criterion validity: ie, how does the measure relate to the gold standard, if available
  - ◇ Content (face) validity: ie, does the measure cover all important dimensions of the health condition being assessed, does the measure appear to assess what it intends to assess
  - ◇ Construct validity: ie, does the measure assess the intended outcome of interest, which is not usually directly observable
  - ◇ Convergent validity: can 2 measures of an outcome that should be theoretically related actually be observed to be related
  - ◇ Discriminant validity: can measures that are theoretically related be observed to be dissimilar
- Responsiveness (can the measure detect change in an outcome over time)
- Interpretability (the degree to which meaning can be assigned to the scores obtained from the outcome measure)

Based on information found in Mokkink et al.[29]

Implementing PROs in Routine Clinical HD Practice

PROs have multiple potential uses (Fig 1). In routine clinical settings, PROs may aid patient-clinician and multidisciplinary team communication, enhance shared decision making,[44] and support symptom monitoring and management,[45] allowing more personalized care. At an aggregate level, PRO data can be used for audit and benchmarking.[46] For example, the US Centers for Medicare & Medicaid Services mandate that HRQoL is assessed annually for patients receiving long-term dialysis.[47]

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

The International Society of Quality of Life Research (ISOQOL) *User's Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice*[21,48] identifies key pathway components for PRO measure integration into routine care.

1. Defining the Goals for PRO Collection

Given the potential multiple uses of PRO collection (Fig 1), it is imperative that the goal for collection is clearly defined.

Research suggests that clinicians routinely underestimate patient symptoms.[2,49] There is increasing evidence that regular ePRO collection, both within and between clinics, can be used to flag poor symptom control and deterioration in functional status. In oncology settings, this has led to improvements in HRQoL, enhanced patient-clinician communication, reduced hospitalization, and increased survival.[45,50-52] In Denmark, the generic PRO system AmbuFlex combines data collected remotely, with PRO-based automated decision algorithms and graphical overviews for symptom monitoring and decision making in 9 diagnostic groups, including CKD.[53] There are many validated symptom assessment tools available for use with patients receiving HD (Box 2).

PROs also have the potential to enhance shared decision making and advance care planning. Findings from the Dialysis Outcomes and Practice Patterns Study (DOPPS) suggest that patient-reported indicators for physical and mental functioning are prognostic markers[54] and that patients with lower PRO scores on the physical and mental components of the KDQOL-36 have higher mortality rates.[7]

2. Selecting Patients, Timing, and Setting of Assessment

Appropriate timing and frequency of PRO assessment in HD is of great importance. A large proportion of patients receiving HD may exhibit cognitive impairment.[55] However, there remains some debate about the exact level of impairment during different phases of the dialysis treatment cycle,[54-56] and further research is required to explore the temporal effects of HD on cognitive status.[57] A recent consensus meeting involving patient representatives concluded that PROs should preferably not be recorded during dialysis,[31] with PRO experts reflecting that responses given during a dialysis session may be sensitive to the current dialysis experience rather than the "usual" HRQoL. However, further qualitative work to elicit and clarify patient and clinician preferences on the timing of PRO completion is required.[58]

Consideration needs to be given to the setting in which the PRO is completed. Patients may prefer to complete PROs at home or at the dialysis unit. Further research on where best to collect this information is required.

Repeated assessments allow clinicians to track disease progression and inform changes in care.[47] Management of patients receiving HD is complicated by multiple comorbid conditions, polypharmacy, and variables associated with the dialysis treatment itself; consequently, patients can experience dramatic changes in their health status.[59] Moreover, patients usually dialyze at least 3 times per week for a number of hours; thus, the additional patient burden of completing PROs should be considered.[60] Frequent collection of scores without associated intervention has been shown to be burdensome to patients, but data for the optimal frequency of collection of HRQoL information from patients with end-stage kidney disease are lacking.[60] PROs need to be sensitive enough to detect patient-important changes and undertaken often enough to

Box 2. Examples of Renal-Specific PROs Commonly Used in HD Settings

KDQOL-36 (Kidney Disease Quality of Life-36)[38]
- A 36-item HRQoL measure designed for patients undergoing dialysis, derived from the KDQOL-SF
- 3 specific dimensions: (1) signs and symptoms, (2) burden of kidney disease, (3) effects of kidney disease and a generic core derived from the SF-12 (physical and mental scales)
- Overall scores range from 0-100, with higher scores indicating better HRQoL

KDQOL-SF (Kidney Disease Quality of Life-SF)[82]
- An 80-item HRQoL measure designed for patients undergoing dialysis that includes the SF-36 as a generic core (physical and mental scales) supplemented with 8 kidney disease–targeted dimensions and 3 additional QoL dimensions
- Scores range from 0-100 for each dimension, with higher scores indicating better HRQoL

IPOS-Renal (Integrated Patient Outcome Scale–Renal)[83,83]
- A short measure (11 questions) combining the most common symptoms that patients with kidney disease experience plus additional items from IPOS on concerns beyond symptoms, such as information needs, practical issues, family anxiety

Edmonton Symptom Assessment System-Revised Renal (ESASr: Renal)[84]
- Modified ESAS to measure symptom burden in patients receiving dialysis
- 10 symptom-specific items, 10 visual analogue scales with a superimposed 0-10 scale: anchor words No at 0 and Severe at 10
- Total score range 0-100, with higher scores indicating greater symptom distress and burden

Dialysis Symptom Index (DSI)[85]
- A 30-item symptom and prevalence assessment index for patients receiving hemodialysis
- Overall scores for symptom burden and total symptom severity are calculated
- Symptoms scored on 5-point Likert scale
- Score range of 0-150, with higher scores indicating greater symptom severity

Abbreviations: HD, hemodialysis; HRQoL, health-related quality of life; PRO, patient-reported outcome; QoL, quality of life; SF-12, 12-Item Short Form Health Survey; SF-36, 36-Item Short Form Health Survey.

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

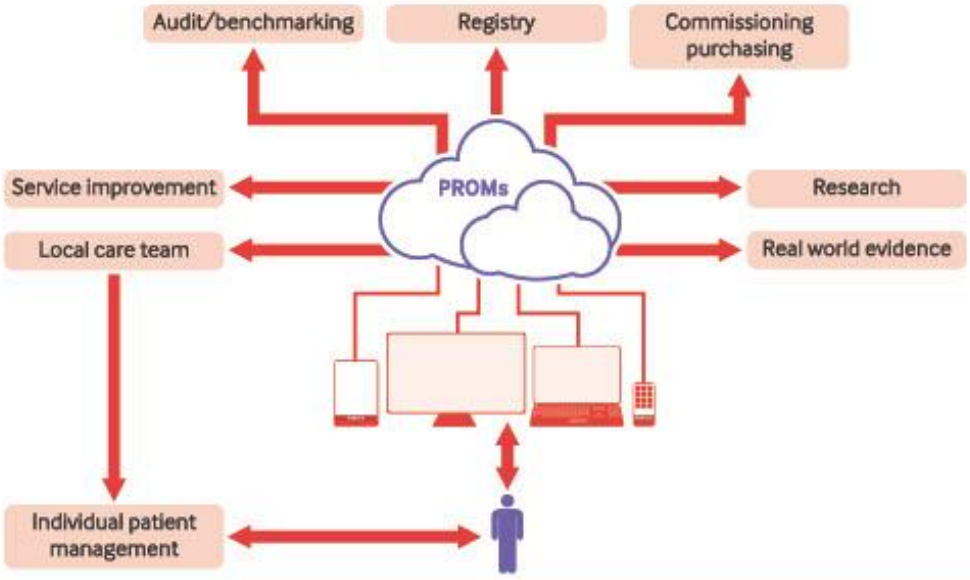


Figure 1. The multiple uses of patient-reported outcomes (PROs). Abbreviation: PROM, PRO measure. Reproduced from Calvert et al.[88]

allow accurate recall. A Danish feasibility study of PRO capture in routine practice reported lower response rates from patients with CKD when compared with other patient groups.[53] This needs further investigation.

3. Determining Which PRO to Use in Routine Care

Recent systematic reviews have highlighted the current PROs most appropriate for use in HD settings,[30,32,33] including PROs that pertain to identified core outcomes such as fatigue.[35] Based on a review of psychometric properties, Peipert et al[38] suggested continued use of the KDQOL-36 for US dialysis center internal quality improvement activity. However, they state that the PRO measure could be modified by inclusion of Patient-Reported Outcomes Measurement Information System (PROMIS) general health items and fine tuning of the kidney disease–targeted scales.[47] The National Institutes of Health PROMIS project uses item response theory and computer adaptive technology to capture global aspects of HRQoL and has been shown to be a potentially valuable tool to assess the impact of CKD in pediatric populations.[61] Computer adaptive technology simplifies PRO completion by selecting questions with patient-specific relevance. This process has a high level of reliability and low burden because patient responses are used to guide subsequent questions.[62]

Further research is required to identify/develop optimum PROs for routine use in HD settings. The cultural appropriateness and cross-cultural reliability of such PROs should be assessed, with issues such as spirituality, which has different resonance for different ethnic groups,[63] being considered. Key to this process is patient involvement in both item generation and selection.[64] While pretesting of PRO translations for comprehension, cultural relevance, and acceptability is common in studies, research such as that conducted by Peipert et al,[65] which examined differential item functioning between black and white patients on the KDQOL-36, is required before measures can be used to make clinical decisions with confidence across subgroups of patients.

The International Consortium on Health Outcomes Measures (ICHOM) has recently published a data collection and reference guide for CKD.[66] This includes the establishment of standard outcome sets for use in routine practice for patients receiving HD, along with recommended generic PRO measures. However, the generic measures chosen by the ICHOM CKD working group have not yet been formally validated in the HD population.

4. Mode of Administration and Scoring

In 2015, as part of the Transforming Participation in CKD (TP-CKD) program,[67] a pilot study was undertaken by the UK Renal Registry involving the collection of patient symptom scores. Patients in 14 renal units were asked to complete the Integrated Patient Outcome Scale for Renal (IPOS-Renal)[68] and the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L).[69] Patients receiving HD were included in the sample. Although adherence was good, the use of paper questionnaires proved logistically complicated, leading to a time lag between completion and feedback. Furthermore, clinical staff reported difficulty using and interpreting the survey results, requiring the organization of on-site workshops to support teams in interpretation and familiarization of the PRO data.[1]

UK and Canadian studies have explored the feasibility of using ePROs in kidney disease, accessed by the patient using electronic devices.[70-73] ePROs offer an avenue for

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

the collection of remote PRO data in real time, allowing health care professionals immediate access to important information to guide care.[73] Pittman et al[70] and Schick-Mazaroff and Molzahn[71-73] have explored the feasibility of ePRO collection. While demonstrating that it was feasible to collect ePRO data in dialysis environments, they found that further research is needed to overcome measurement challenges, including aspects surrounding the responsiveness of the chosen PRO to changes in clinical condition, as well as practical issues such as information technology security and cost.

5. Interpretation and Feedback

The method of PRO data feedback will vary according to the goals of collection; for example, whether aggregate information is required for service improvement or individual-level data are needed to guide care.[74] A recent realist synthesis identified potential tension between these 2 goals and a need for further research on incorporating PRO data into the electronic health record. The authors questioned whether the same PRO could be used for multiple purposes.[75] Individualized PROs that are useful for patient assessment may not be reliable as indicators of service quality and vice versa. For multiplicity of use, all stakeholders should be effectively engaged in future PRO development.[74,76]

Whatever the objective for collection, careful consideration is required to ensure that PRO scores are easily interpretable by all stakeholders. The information should be meaningful and actionable. How the data are visually displayed will affect its use, with studies suggesting that the preferred formats should be as user friendly as possible,[72] highlighting the importance of involving both patients and clinicians in design stages. Pertinent guidance for PRO data feedback is available from ISOQOL and the Patient-Centred Outcomes Research Institute (PCORI),[77] which highlights the importance of training in PRO administration and interpretation as a key methodological consideration.

Increasingly, PRO data collection is being undertaken by renal registries.[1] Breckenridge et al[31] report on a consensus meeting held in 2015 to discuss the routine collection of PRO data within European renal registries. Although agreeing that registries are an ideal way to collect PROs, they identified several challenges around implementation, including resourcing, technological and information governance issues, and maintaining trust in the data. They highlight the need for further research and collaboration to share best practice.

6. Responding to Issues Raised

Tong et al[78] recognized that efforts to integrate PRO use in patients receiving HD may be hindered by issues associated with the range of comorbid conditions and broader HRQoL outcomes experienced by this patient group, who are receiving a technically demanding treatment.

Finkelstein and Finkelstein[59] discussed the challenge of capturing individuals' experiences of dialysis through twice-yearly paper PRO collection within US dialysis centers for performance monitoring and internal quality improvement. They identified issues that included actioning results and noted that clinicians sometimes had difficulty assisting with problems not directly associated with HD. They recommended that while PRO collection should be mandated, given a lack of hard data for optimum methods of implementation, innovative methods should be considered to incorporate PROs into the electronic health records of individual patients.

7. Evaluating the Impact of PRO Intervention on Practice

It is important that the impact of routine PRO collection is assessed to justify their collection and use.[79] The financial and time resource costs associated with administration, interpretation, and staff training,[47] particularly with information technology systems,[73] need to be offset against the potential impact of the intervention. Finkelstein and Finklestein[59] argued that collection of PRO data using standardized questionnaires may not capture the unique experience of the individual, and it is recognized that there are challenges and frustration associated in the uncovering of PROs when little or no effective intervention exists. Further study is required to assess whether PRO collection in such circumstances could have unintended negative consequences, such as promoting false hope or causing distress.

Future Research

Although SONG-HD has identified many outcomes that clearly matter to stakeholders,[12,27,28] they do not map easily to existing measures, so new instruments may be required that efficiently capture all required domains in a nonburdensome way. Innovative means of PRO data capture are required. Platforms that can collect, collate, and feed back PRO data, using the electronic health record/national renal registries, need further investigation and investment. Development of digital systems using item banks and computer adaptive technology algorithms could be one way of lessening the burden and allow PRO data collected at specific times to be used for multiple purposes.[62]

It is important to capture the perspectives of the nephrology multidisciplinary team on feasibility, cost, and patient acceptance of PRO measures. Tong et al[78] have used qualitative methodology to elicit nephrologists' perspectives on defining and applying PROs in HD.[80] Clinicians identified the challenges around the heterogeneity of patient priorities and experiences, limitations of current clinical approaches, and health system–level barriers, including cost and resource constraints. The authors acknowledged that not all clinicians agree that a patient-centered approach to care is better than a disease-

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

orientated approach.[78] Further work is required to ascertain whether these findings are capable of broader transferability.

In terms of overall generalizability, lifestyle outcomes that were given a high priority by patients and caregivers in the SONG-HD initiative were derived from international participants receiving both in-center and home HD.[12,27] However, there will be nuances in the implementation of PROs with subgroups of patients receiving HD. In the United Kingdom, satellite dialysis units may be run by providers independent of the National Health Service (NHS). This means that local considerations need to be made, such as information technology linkage facilities. As recognized by Zbrozek et al,[81] different clinical environments will provide unique and potentially diverse challenges. Therefore, real-world testing is imperative.

Conclusions

Shared decision making and the provision of patient-centered care is crucial for excellence in HD provision. The use of PROs in both research and routine clinical settings may facilitate this. However, successful implementation of PROs requires careful planning and evaluation, and data collection must fit into current research study designs and work flow patterns. Addressing issues required for effective implementation will require input and collaboration from a range of stakeholders, particularly patients.

Article Information

Authors' Full Names and Academic Degrees: Nicola Elizabeth Anderson, MSc, Melanie Calvert, PhD, Paul Cockwell, PhD, Mary Dutton, MSc, and Derek Kyte, PhD.

Authors' Affiliations: Centre for Patient Reported Outcomes Research (NEA, MC, PC, MD, DK) and Institute of Applied Health Research (NEA, MC, PC, DK), University of Birmingham; Research and Development (NEA, MD) and Department of Renal Medicine (NEA, PC, MD), University Hospitals Birmingham NHS Foundation Trust; and NIHR Birmingham Biomedical Research Centre (MC, DK) and NIHR Surgical Reconstruction and Microbiology Research Centre (MC, DK), University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, Birmingham, United Kingdom.

Address for Correspondence: Nicola Elizabeth Anderson, MSc, Centre for Patient Reported Outcomes Research, c/o Room 208 2nd Floor The Learning Centre, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom. E-mail: NEA451@bham.ac.uk

Support: Funding support for the lead author from Queen Elizabeth Hospital Kidney Patients Association. Drs Calvert and Kyte are partially funded by the National Institute for Health Research (NIHR) Birmingham Biomedical Research Centre and the NIHR Surgical Reconstruction and Microbiology Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. Dr Kyte is supported by the NIHR Post-Doctoral Fellowship Scheme, grant PDF-2016-09-009. The funders did not have a role in writing the report or the decision to submit for publication.

Financial Disclosure: Dr Calvert reports receipt of personal fees from Astellas and Takeda and grants from the NIHR, Macmillan Cancer Support, Health Data Research UK, and Innovate UK outside the submitted work. The remaining authors declare that they have no relevant financial interests.

Disclaimer: The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

Peer Review: Received August 3, 2018. Evaluated by 2 external peer reviewers, with direct editorial input from an Associate Editor and a Deputy Editor. Accepted in revised form January 29, 2019.

References

1. van der Veer SN, Aresi G, Gair R. Incorporating patient-reported symptom assessments into routine care for people with chronic kidney disease. *Clin Kidney J*. 2017;10(6):783-787.
2. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. *Adv Chronic Kidney Dis*. 2007;14(1):82-99.
3. Lowney AC, Myles HT, Bristowe K, et al. Understanding what influences the health-related quality of life of hemodialysis patients: a collaborative study in England and Ireland. *J Pain Symptom Manage*. 2015;50(6):778-785.
4. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J Pain Symptom Manage*. 2006;31(1):58-69.
5. Wang R, Tang C, Chen X, et al. Poor sleep and reduced quality of life were associated with symptom distress in patients receiving maintenance hemodialysis. *Health Qual Life Outcomes*. 2016;14(1):125-132.
6. Claxton RN, Blackhall L, Weisbord SD, Holley JL. Undertreatment of symptoms in patients on maintenance hemodialysis. *J Pain Symptom Manage*. 2010;39(2):211-218.
7. Mapes DL, Lopes AA, Satayathum S, et al. Health-related quality of life as a predictor of mortality and hospitalization: the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int*. 2003;64(1):339-349.
8. Brown SA, Tyrer FC, Clarke AL, et al. Symptom burden in patients with chronic kidney disease not requiring renal replacement therapy. *Clin Kidney J*. 2017;10(6):788-796.
9. Nicholas SB, Kalantar-Zadeh K, Norris KC. Socioeconomic disparities in chronic kidney disease. *Adv Chronic Kidney Dis*. 2015;22(1):6-15.
10. Weisbord SD. Patient-centered dialysis care: depression, pain, and quality of life. *Semin Dial*. 2016;29(2):158-164.
11. Aiyegbusi OL, Kyte D, Cockwell P, et al. Using patient-reported outcome measures (PROMs) to promote quality of care and safety in the management of patients with advanced chronic kidney disease (PRO-trACK project): a mixed-methods project protocol. *BMJ Open*. 2017;7(6):e016687.
12. Urquhart-Secord R, Craig JC, Hemmelgarn B, et al. Patient and caregiver priorities for outcomes in hemodialysis: an international nominal group technique study. *Am J Kidney Dis*. 2016;68(3):444-454.
13. Chong K, Unruh M. Why does quality of life remain an under-investigated issue in chronic kidney disease and why is it rarely set as an outcome measure in trials in this population? *Nephrol Dial Transplant*. 2017;32(suppl 2):ii47-ii52.
14. US Department of Health and Human Services Food and Drug Administration. Guidance for industry. Patient reported outcomes measures: use in medical product development to support labeling claims. https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf. 2009. Accessed August 12, 2018.

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

15. Brundage MD, Snyder CF. Patient-reported outcomes in clinical practice: using standards to break down barriers. *Clin Invest*. 2012;2(4):343-346.
16. Tong A, Crowe S, Chando S, et al. Research priorities in CKD: report of a national workshop conducted in Australia. *Am J Kidney Dis*. 2015;66(2):212-222.
17. Sautenet B, Tong A, Williams G, et al. Scope and consistency of outcomes reported in randomized trials conducted in adults receiving hemodialysis: a systematic review. *Am J Kidney Dis*. 2018;72(1):62-74.
18. Kyte D, Duffy H, Fletcher B, et al. Systematic evaluation of the patient-reported outcome (PRO) content of clinical trial protocols. *PLoS One*. 2014;9(10):e110229.
19. Doward LC, Gnanasakthy A, Baker MG. Patient reported outcomes:looking beyond the label claim. *Health Qual Life Outcomes*. 2010;8:89-97.
20. Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: version 1.0. *Trials*. 2017;18(suppl 3):280-320.
21. Snyder CF, Aaronson NK, Choucair AK, et al. Implementing patient-reported outcomes assessment in clinical practice: a review of the options and considerations. *Qual Life Res*. 2012;21(8):1305-1314.
22. Gargon E, Williamson PR, Altman DG, Blazeby JM, Clarke M. The COMET Initiative database: progress and activities from 2011 to 2013. *Trials*. 2014;(15):279-283.
23. Prinsen CA, Vohra S, Rose MR, et al. How to select outcome measurement instruments for outcomes included in a "core outcome set" - a practical guideline. *Trials*. 2016;17(1):449-459.
24. Kirkham JJ, Davis K, Altman DG, et al. Core Outcome Set-STAndards for Development: the COS-STAD recommendations. *PLoS Med*. 2017;14(11):e1002447.
25. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials*. 2012;13:132-140.
26. Macefield RC, Jacobs M, Korfage IJ, et al. Developing core outcome sets: methods for identifying and including patient reported outcomes (PROs). *Trials*. 2014;15:49-61.
27. Evangelidis N, Tong A, Manns B, et al. Developing a set of core outcomes for trials in hemodialysis: an international Delphi survey. *Am J Kidney Dis*. 2017;70(4):464-475.
28. Tong A, Craig JC, Nagler EV, et al; the European Renal Best Practice Advisory Board. Composing a new song for trials: the Standardized Outcomes in Nephrology (SONG) initiative. *Nephrol Dial Transplant*. 2017;32(12):1963-1966.
29. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res*. 2010;19(4):539-549.
30. Gibbons E, Fitzpatrick R. *A Structured Review of Patient Reported Outcome Measures for Adults With Chronic Kidney Disease - A Report*. Oxford, UK: Department of Public Health, University of Oxford; 2010.
31. Breckenridge K, Bekker HL, Gibbons E, et al. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. *Nephrol Dial Transplant*. 2015;30(10):1605-1614.
32. Aiyegbusi OL, Kyte D, Cockwell P, et al. Measurement Properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. *PLoS ONE*. 2017;12(6):1-27. E1079733.
33. Flythe JE, Powell JD, Poulton CJ, et al. Patient-reported outcome instruments for physical symptoms among patients receiving maintenance dialysis: a systematic review. *Am J Kidney Dis*. 2015;66(6):1033-1046.
34. Danquah FVN, Wasserman J, Meininger J, Bergstrom N. Quality of life measures for patients on hemodialysis: a review of psychometric properties. *Nephrol Nurs J*. 2010;37(3):255-269; quiz 270.
35. Ju A, Unruh ML, Davison SN, et al. Patient-reported outcome measures for fatigue in patients on hemodialysis: a systematic review. *Am J Kidney Dis*. 2018;71(3):327-343.
36. Vanya M, Patel C, Paoli CJ, Lin J, Howard K. Patient reported outcomes in end stage renal disease (ESRD) anemia a comprehensive review [abstract]. *Value Health*. 2014;17(3):A232.
37. Viecelli AK, O'Lone E, Sautenet B, et al. Vascular Access Outcomes Reported in Maintenance Hemodialysis Trials: A Systematic Review. *Am J Kidney Dis*. 2018;71(3):382-391.
38. Peipert JD, Bentler PM, Klicko K, Hays RD. Psychometric properties of the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) in the United States. *Am J Kidney Dis*. 2018;71(4):461-468.
39. Calvert M, Kyte D, Mercieca-Bebber R, et al. Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: the SPIRIT-PRO extension. *JAMA*. 2018;319(5):483-494.
40. Kyte DG, Retzer A, Keeley T, Ahmed K, et al. Systematic evaluation pf patient-reported outcome (PRO) protocol content and reporting in cancer clinical trials: the EPiC study. *Qual Life Res*. 2017;26(suppl). 1:55-56.
41. Ahmed K, Kyte D, Keeley T, et al. Systematic evaluation of patient-reported outcome (PRO) protocol content and reporting in UK cancer clinical trials: the EPiC study protocol. *BMJ Open*. 2016;6(9):e012863.
42. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. *JAMA*. 2013;309(8):814-822.
43. Mercieca-Bebber R, Rouette J, Calvert M, et al. Preliminary evidence on the uptake, use and benefits of the CONSORT-PRO extension. *Qual Life Res*. 2017;26(6):1427-1437.
44. Velikova G, Booth L, Smith AB, et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. *J Clin Oncol*. 2004;22(4):714-724.
45. Basch E, Deal AM, Kris MG, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J Clin Oncol*. 2016;34(6):557-565.
46. Hjollund NH, Larsen LP, Biering K, Johnsen SP, Riiskjaer E, Schougaard LM. Use of patient-reported outcome (PRO) measures at group and patient levels: experiences from the generic integrated PRO system, WestChronic. *Interact J Med Res*. 2014;3(1):e5.
47. Peipert JD, Hays RD. Methodological considerations in using patient reported measures in dialysis clinics. *J Patient Rep Outcomes*. 2017;1(11).
48. **Aaronsen N, Elliot T, Greenhalgh J, et al. *User's Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice*. Version 2. Milwaukee, WI: International Society of Quality of Life Research; 2015.**
49. Basch E, Abernethy AP. Supporting clinical practice decisions with real-time patient-reported outcomes. *J Clin Oncol*. 2011;29(8):954-956.
50. Basch E. PRO's - harnessing patient voices to improve clinical care. *N Engl J Med*. 2017;376(2):105-108.
51. Basch E, Deal AM, Dueck AC, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA*. 2017;318(2):197-198.
52. Kotronoulas G, Kearney N, Maguire R, et al. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

health service outcomes in cancer care? A systematic review of controlled trials. *J Clin Oncol*. 2014;32(14):1480-1501.
53. Schougaard LM, Larsen LP, Jessen A, et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow up in chronic and malignant diseases. *Qual Life Res*. 2016;25(3):525-534.
54. Port FK, Morgenstern H, Bieber BA, et al. Understanding associations of hemodialysis practices with clinical and patient-reported outcomes: examples from the DOPPS. *Nephrol Dial Transplant*. 2017;32(suppl 2):ii106-ii112.
55. Tholen S, Schmaderer C, Kusmenkov E, et al. Variability of cognitive performance during hemodialysis: standardization of cognitive assessment. *Dement Geriatr Cogn Disord*. 2014;38(1-2):31-38.
56. Williams MA, Sklar AH, Burright RG, Donovick PJ. Temporal effects of dialysis on cognitive functioning in patients with ESRD. *Am J Kidney Dis*. 2004;43(4):705-711.
57. Drew DA, Tighiouart H, Scott TM, et al. Cognitive performance before and during hemodialysis: a randomized cross-over trial. *Nephron Clin Pract*. 2013;124(3-4):151-158.
58. Anderson NE, Calvert M, Cockwell P, Dutton M, Aiyegbusi OL, Kyte D. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. *BMJ Open*. 2018;8(10):e021532.
59. Finkelstein FO, Finkelstein SH. Time to rethink our approach to patient-reported outcome measures for ESRD. *Clin J Am Soc Nephrol*. 2017;12(11):1885-1888.
60. Chen SS, Al Mawed S, Unruh M. Health-related quality of life in end-stage renal disease patients: how often should we ask and what do we do with the answer? *Blood Purif*. 2016;41(1-3):218-224.
61. Selewski DT, Massengill SF, Troost JP, et al. Gaining the Patient Reported Outcomes Measurement Information System (PROMIS) perspective in chronic kidney disease: a Midwest Pediatric Nephrology Consortium study. *Pediatr Nephrol*. 2014;29(12):2347-2356.
62. Smits N, Paap MCS, Bohnke JR. Some recommendations for developing multidimensional computerized adaptive tests for patient-reported outcomes. *Qual Life Res*. 2018;27(4):1055-1063.
63. Kimmel PL, Cohen SD, Weisbord SD. Quality of life in patients with end-stage renal disease treated with hemodialysis: survival is not enough! *J Nephrol*. 2008;21(suppl 13):S54-S58.
64. **Aiyegbusi OL, Kyte D, Cockwell P, et al. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: a systematic review. *PLoS One*. 12(6):e0179733.**
65. Peipert JD, Bentler P, Klicko K, Hays RD. Negligible impact of differential item functioning between black and white dialysis patients on the Kidney Disease Quality of Life 36-Item Short Form Survey (KDQOL™-36). *Qual Life Res*. 2018;27(10):2699-2707.
66. **International Consortium for Health Outcomes Measurement (ICHOM). Chronic Kidney Disease Data Collection Reference Guide. Version 1.0.0. 2017. https://ichom.org/files/medical-conditions/chronic-kidney-disease/chronic-kidney-disease-reference-guide.pdf. Accessed April 4, 2019.**
67. **UK Renal Registry. Valuing individuals - transforming participation in chronic kidney disease (CKD) programme: project initiation document. 2015. https://www.thinkkidneys.nhs.uk/ckd/wp-content/uploads/sites/4/2015/05/TP-CKD-PID-final.pdf. Accessed August 12, 2018.**
68. **Renal PCOSI. IPOS-Renal 2017. https://pos-pal.org/maix/ipos-renal-in-english.php. Accessed August 12, 2018.**
69. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727-1736.
70. Pittman ZC, John SG, McIntyre CW. Collection of daily patient reported outcomes is feasible and demonstrates differential patient experience in chronic kidney disease. *Hemodial Int*. 2017;21(2):265-273.
71. Schick-Makaroff K, Molzahn A. Brief communication: patient satisfaction with the use of tablet computers: a pilot study in two outpatient home dialysis clinics. *Can J Kidney Health Dis*. 2014;1:22-28.
72. Schick-Makaroff K, Molzahn AE. Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. *BMC Health Serv Res*. 2017;17(1):439.
73. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. *Health Qual Life Outcomes*. 2015;13:2-8.
74. Greenhalgh J, Pawson R, Wright J, et al. Functionality and feedback: a protocol for a realist synthesis of the collation, interpretation and utilisation of PROMs data to improve patient care. *BMJ Open*. 2014;4(7):e005601.
75. Greenhalgh J, Gooding K, Gibbons E, et al. How do patient reported outcome measures (PROMs) support clinician-patient communication and patient care? A realist synthesis. *J Patient Rep Outcomes*. 2018;2(42).
76. Greenhalgh J, Dalkin S, Gooding K, et al. Functionality and feedback: a realist synthesis of the collation, interpretation and utilisation of patient-reported outcome measures data to improve patient care. *Health Serv Delivery Res*. 2017;5(2):1-280.
77. Basch E, Snyder C. Overcoming barriers to integrating patient-reported outcomes in clinical practice and electronic health records. *Ann Oncol*. 2017;28(10):2332-2333.
78. Tong A, Winkelmayer WC, Wheeler DC, et al. Nephrologists' perspectives on defining and applying patient-centered outcomes in hemodialysis. *Clin J Am Soc Nephrol*. 2017;12(3):454-466.
79. Valderas JM, Kotzeva A, Espallargues M, et al. The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. *Qual Life Res*. 2008;17(2):179-193.
80. Bowling CB, Plantinga LC. When all you have is a hammer: the need for tools to define and apply patient-centered outcomes in hemodialysis. *Clin J Am Soc Nephrol*. 2017;12(3):382-384.
81. Zbrozek A, Hebert J, Gogates G, et al. Validation of electronic systems to collect patient-reported outcome (PRO) data-recommendations for clinical trial teams: report of the ISPOR ePRO systems validation good research practices task force. *Value Health*. 2013;16(4):480-489.
82. Hays RD, Kallich JD, Mapes DL, et al. *Kidney Disease Quality of Life Short Form (KDQOL-SF™) Version 1.3: A Manual for Use and Scoring. Contract No.: P-7994*. Santa Monica, CA: Rand; 1995.
83. Raj R, Ahuja K, Frandsen M, Murtagh FEM, Jose M. Validation of the IPOS-Renal Symptom Survey in advanced kidney disease: a cross-sectional study. *J Pain Symptom Manage*. 2018;56(2):281-287.
84. Davison SN, Jhangri GS, Johnson JA. Longitudinal validation of a modified Edmonton symptom assessment system (ESAS) in haemodialysis patients. *Nephrol Dial Transplant*. 2006;21(11):3189-3195.
85. Weisbord SD, Fried LF, Arnold RM, et al. Development of a symptom assessment instrument for chronic hemodialysis patients: the Dialysis Symptom Index. *J Pain Symptom Manage*. 2004;27(3):226-240.
86. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. *BMJ*. 2019;364:k5267.

Downloaded for Nicola Anderson (nicola.anderson@uhb.nhs.uk) at University Hospitals Birmingham NHS Foundation Trust from ClinicalKey.com by Elsevier on September 06, 2022. For personal use only. No other uses without permission. Copyright ©2022. Elsevier Inc. All rights reserved.

As outlined in the Perspectives paper (92), there remain several areas in need of further research: (i) the capture of the perspectives of patients and the nephrology multidisciplinary team (MDT) on feasibility and acceptance of PROs use and key implementation factors; (ii) whether current validated measures are able to efficiently capture COS-endorsed outcomes identified as important to patients and; (iii) research on innovative forms of PRO data capture, with the development of systems able to collect, collate, and feedback PRO data, using the electronic health record/national renal registries.

1.6 Thesis aims and structure

1.6.1 Aim of thesis

The overall aim of this thesis is to explore and inform the evidence on how ePROs might be used to promote quality of care and safety in the management of patients with end stage kidney disease requiring treatment with Haemodialysis.

1.6.2 Objectives

This thesis describes a programme of research which addresses the research gaps highlighted in the narrative review and outlined in Table 2 below. This PhD was funded by a Health Education England and National Institute for Health and Care Research Integrated Clinical Academic Programme Doctoral Fellowship grant (HEE NIHR ICA): Reference No: ICA-CDRF-2018-04-ST2-027). The views expressed are those of the author and not necessarily those of the NHS, the National Institute for Health and Care Research (NIHR) or the Department of Health.

Table 2: Thesis Research Objectives

Knowledge gap and research question	Research objective
Chapter 1 **What is the evidence on the current use and benefit of ePROs in patients with ESKD requiring treatment with HD and why should we consider their use?**	Synthesis of current evidence on the use and implementation of ePROs for patients with end-stage kidney disease receiving haemodialysis. To identify a roadmap for increasing the evidence base and introducing ePROs into mainstream clinical practice
Chapter 3 **What is the methodological basis for the use of routine PROMs assessment, particularly using ePROs, within clinical and research settings?**	To explore the views, perceptions and experiences of patients receiving HD and health care professionals (HCPs) in the HD multi-disciplinary team regarding the collection and use of PROMs, particularly ePROs, in HD settings, to maximise the potential of ePROs use in the management of the care of patients requiring RRT with HD.
Chapter 4 **To support clinicians in the process of PROM selection, aimed at enhancing the management of patients undergoing HD; which ePROMs should we be using to measure those outcomes that matter most to key stakeholders, especially patients?**	To explore whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS. The study objectives were to: (1) conduct a systematic search of published literature for COS and validated PROMs used in HD settings; (2) summarise PROM characteristics and affinity map PROMs items/domains against recommended outcomes in available COS.
Chapter 5 **How do we successfully implement ePROs in nephrology and what are the core factors which contribute to effective implementation, including common facilitators and barriers?**	To comprehensively identify ePRO systems for CKD, including those under development, to explore system characteristics including methods of administration, levels of integration into existing workflow and electronic health records (EHR) and the reporting of ePROs to manage patient safety. The overall aim being to provide a comprehensive classification of core factors which contribute to successful implementation of ePROs in nephrology, including common facilitators and barriers.

1.6.3 Structure of thesis

Chapter 1 introduces the thesis, defining and describing CKD, ESKD and ePROs. It includes a narrative review (published in the American Journal of Kidney Diseases in 2019 (92)) and summarises key aspects of PRO use and implementation in HD research and routine care, highlighting recent developments, gaps in the field, and future research priorities.

Chapter 2 presents the overall methodology for this PhD research, including an overview of the mixed methods research process including researcher reflexivity and patient and public involvement.

Chapter 3 presents the protocol and findings for a qualitative study exploring the methodological basis for routine ePROs assessment to maximise the potential of PRO use, through exploration of the experiences, views and perceptions of patients and healthcare professionals (HCPs) on implementation and use of PROs in HD settings. The protocol paper was published in BMJ Open in 2018 (95) and the study findings paper in 2021 (96).

Chapter 4 presents a scoping review which focuses on whether currently available PROMs adequately cover all outcomes/domains that have been recommended in HD-specific COS. An increased understanding of COS and PROM alignment would assist clinicians in the process of PROM selection, aimed at supporting the management of patients undergoing HD. This study has been written up for submission to a peer reviewed journal for publication.

Chapter 5 reports a mixed methods study which comprehensively identifies existing and developing ePROs system from around the world which were designed specifically for use in kidney care, ascertaining their key characteristics and the factors for successful implementation. A paper based on this study is currently under review with a peer-reviewed journal.

Finally, Chapter 6 discusses the principal findings of this PhD research, considers the interpretation and implications, highlighting the strengths and limitations of the thesis and outlines suggestions for future research with final conclusions.

References

1. KDIGO (Kidney Disease Improving Global Outcomes). KDIGO WEBSITE [Website]. 2022 [cited 2022 12 Nov]. Available from: https://kdigo.org/.
2. KDIGO. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements. 2013;3(1).
3. Davison SN, Jhangri GS, Johnson JA. Longitudinal validation of a modified Edmonton symptom assessment system (ESAS) in haemodialysis patients. Nephrology Dialysis Transplantation. 2006;21(11):3189-95.
4. Metzger M, Abdel-Rahman EM, Boykin H, Song MK. A Narrative Review of Management Strategies for Common Symptoms in Advanced CKD. Kidney Int Rep. 2021;6(4):894-904.
5. Oh TR, Choi, H. S.,Kim, C. S., Bae, E. H.,Oh, Y. K., Kim, Y. S., Choi, K. H., Kim, S. W., Ma, S. K. Association between health related quality of life and progression of chronic kidney disease. Sci Rep. 2019;9(1):19595.
6. Morton RL, Tong A, Howard K, Snelling P, Webster AC. The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies. BMJ. 2010;340:c112.
7. Evangelidis N, Tong A, Manns B, Hemmelgarn B, Wheeler DC, Tugwell P, et al. Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi Survey. American Journal of Kidney Diseases. 2017;70(4):464-75.
8. Urquhart-Secord R, Craig JC, Hemmelgarn B, Tam-Tham H, Manns B, Howell M, et al. Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study. Am J Kidney Dis. 2016;68(3):444-54.
9. Gonzalez AM, Gutman T, Lopez-Vargas P, Anumudu S, Arce CM, Craig JC, et al. Patient and Caregiver Priorities for Outcomes in CKD: A Multinational Nominal Group Technique Study. Am J Kidney Dis. 2020;76(5):679-89.
10. Eckardt KU, Bansal N, Coresh J, Evans M, Grams ME, Herzog CA, et al. Improving the prognosis of patients with severely decreased glomerular filtration rate (CKD G4+): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2018;93(6):1281-92.
11. Thomas N. Renal Nursing: Care and management of people with kidney disease. In: Thomas N, editor. 5th Edition ed. Oxford: John Wiley & Sons; 2019.
12. National Institute for Health and Care Excellence. Renal Replacement Therapy NICE Clinical Guidelines NG107. In: NICE, editor. London2018.
13. Fielding C, Bramley L, Stalker C, Brand S, Toft S, Buchanan H. Patients' experiences of cannulation of arteriovenous access for haemodialysis: A qualitative systematic review. J Vasc Access. 2022:11297298211067630.
14. National Kidney Foundation. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.
15. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Nephrol Dial Transplant. 2019;34(11):1803-5.
16. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney International Supplements. 2022;12(1):7-11.

17. Bello AK, Okpechi IG, Osman MA, Cho Y, Htay H, Jha V, et al. Epidemiology of haemodialysis outcomes. Nat Rev Nephrol. 2022;18:378–95.
18. UK Renal Registry. UK Renal Registry 24th Annual Report – data to 31/12/2020 Bristol, UK2022 [Available from: https://ukkidney.org/audit-research/annual-report.
19. Jager KJ, Kramer A, Chesnaye NC, Couchoud C, Sanchez-Alvarez JE, Garneata L, et al. Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. Kidney Int. 2020;98(6):1540-8.
20. Elshahat S, Cockwell P, Maxwell AP, Griffin M, O'Brien T, O'Neill C. The impact of chronic kidney disease on developed countries from a health economics perspective: A systematic scoping review. PLoS One. 2020;15(3):e0230512.
21. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. Clinical Journal of The American Society of Nephrology: CJASN. 2009;4(6):1057-64.
22. Ng MSN, Wong CL, Ho EHS, Hui YH, Miaskowski C, So WKW. Burden of living with multiple concurrent symptoms in patients with end-stage renal disease. Journal of Clinical Nursing. 2020;29(13-14):2589-601.
23. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954.
24. Claxton R N BL, Weisbord S D, Holley J L. Undertreatment of symptoms in patients on maintenance hemodialysis. Journal of Pain & Symptom Management. 2010;39(2):211-8.
25. Flythe JE, Dorough A, Narendra JH, Forfang D, Hartwell L, Abdel-Rahman E. Perspectives on symptom experiences and symptom reporting among individuals on hemodialysis. Nephrol Dial Transplant. 2018;33(10):1842-52.
26. Almutary H, Bonner, A, Douglas, C. Symptom burden in Chronic Kidney Disease: a review of recent literature. Journal of Renal Care. 2013;39(3):140-50.
27. Tang E, Bansal A, Novak M, Mucsi I. Patient-Reported Outcomes in Patients with Chronic Kidney Disease and Kidney Transplant-Part 1. Front Med (Lausanne). 2017;4:254.
28. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. Adv Chronic Kidney Dis. 2007;14(1):82-99.
29. Lockwood MB, Lash JP, Pauls H, Chung SY, Samra M, Ryan C, et al. Physical Symptom Cluster Subgroups in Chronic Kidney Disease. Nursing Research. 2020;69(2):100-8.
30. Kalfoss M, Schick-Makaroff K, Molzahn AE. Living with Chronic Kidney Disease: Illness Perceptions, Symptoms, Coping, and Quality of Life. Nephrology Nursing Journal. 2019;46(3):277-90.
31. Manns B, Hemmelgarn B, Lillie E, Dip SC, Cyr A, Gladish M, et al. Setting research priorities for patients on or nearing dialysis. Clin J Am Soc Nephrol. 2014;9(10):1813-21.
32. Almutary H, Bonner, A, Douglas, C. Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced CKD stage and dialysis modality. Journal of Renal Care. 2016;42(Issue 2):73-82.

33. Pakhomov SV JS, Chute CG, Roger VL. Agreement between patient-reported symptoms and their documentation in the medical record. Am J Manag Care. 2008;14:530-9.
34. Xiao C, Polomano R, Bruner DW. Comparison between patient-reported and clinician-observed symptoms in oncology. Cancer Nurs. 2013;36(6):E1-E16.
35. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. BMJ. 2019;364:k5267.
36. U.S. Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. In: U.S. Department of Health and Human Services, editor. Rockville, MD2009.
37. Aiyegbusi OL, Kyte D, Cockwell P, Anderson N, Calvert M. A patient-centred approach to measuring quality in kidney care: patient-reported outcome measures and patient-reported experience measures. Curr Opin Nephrol Hypertens. 2017;26(6):442-9.
38. Osoba D. Lessons learned from measuring health-related quality of life in oncology. J Clin Oncol. 1994;12(3):608-16.
39. Meirte J, Hellemans N, Anthonissen M, Denteneer L, Maertens K, Moortgat P, et al. Benefits and Disadvantages of Electronic Patient-reported Outcome Measures: Systematic Review. JMIR Perioper Med. 2020;3(1):e15588.
40. Thukral A, Linsmeier K, Fowler B, Bhardwaj S. Bring Your Own Device: A Practical Framework to Leverage in the Electronic Patient-reported Outcomes Data Collection in Clinical Trials. Journal of the Society for Clinical Data Management. 2022;1(4).
41. Aiyegbusi OL, Nair D, Peipert JD, Schick-Makaroff K, Mucsi I. A narrative review of current evidence supporting the implementation of electronic patient-reported outcome measures in the management of chronic diseases. Therapeutic Advances in Chronic Disease. 2021;12.
42. Coons SJ, Eremenco S, Lundy JJ, O'Donohoe P, O'Gorman H, Malizia W. Capturing Patient-Reported Outcome (PRO) Data Electronically: The Past, Present, and Promise of ePRO Measurement in Clinical Trials. Patient. 2015;8(4):301-9.
43. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).
44. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. Health & Quality of Life Outcomes. 2015;13:2.
45. Hull SA, Rajabzadeh V, Thomas N, Hoong S, Dreyer G, Rainey H, et al. Do virtual renal clinics improve access to kidney care? A preliminary impact evaluation of a virtual clinic in East London. BMC Nephrol. 2020;21(1):10.
46. Harnett P, Jones M, Almond M, Ballasubramaniam G, Kunnath V. A virtual clinic to improve long-term outcomes in chronic kidney disease. Clin Med (Lond). 2018;18(5):356-63.
47. Vas V, North S, Rua T, Chilton D, Cashman M, Malhotra B, et al. Delivering outpatient virtual clinics during the COVID-19 pandemic: early evaluation of clinicians' experiences. BMJ Open Qual. 2022;11(1).

48. Weldring T, Smith SM. Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Health Serv Insights. 2013;6:61-8.
49. Black N. Patient reported outcome measures could help transform healthcare. BMJ. 2013;346:f167.
50. York Health Economics Consortium. Preference based measures [online] York2016 [Available from: https://yhec.co.uk/glossary/preference-based-measures/.
51. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. Br Med Bull. 2010;96:5-21.
52. Zhang J, Dewitt B, Tang E, Breitner D, Saqib M, Li D, et al. Evaluation of PROMIS Preference Scoring System (PROPr) in Patients Undergoing Hemodialysis or Kidney Transplant. Clin J Am Soc Nephrol. 2021;16(9):1328-36.
53. Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: Past, Present and Future. Appl Health Econ Health Policy. 2017;15(2):127-37.
54. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ. 2002;21(2):271-92.
55. Snyder CF, Aaronson NK, Choucair AK, Elliott TE, Greenhalgh J, Halyard MY, et al. Implementing patient-reported outcomes assessment in clinical practice: a review of the options and considerations. Qual Life Res. 2012;21(8):1305-14.
56. Kyte D, Anderson N, Bishop J, Bissell A, Brettell E, Calvert M, et al. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease. BMJ Open. 2022;12(3):e050610.
57. Detmar S B MMJ, Schornhagel J H. Health-Related Quality of Life Assessments and Patient-Physician Communication: A Randomised Controlled Trial. JAMA. 2002;288(23):3027-34.
58. Joeris A, Zhu TY, Lambert S, Wood A, Jayakumar P. Real-world patient data: Can they support decision making and patient engagement? Injury. 2021;21:1383.
59. Collister D, Bangdiwala S, Walsh M, Mian R, Lee SF, Furukawa TA, et al. Patient reported outcome measures in clinical trials should be initially analyzed as continuous outcomes for statistical significance and responder analyses should be reserved as secondary analyses. Journal of Clinical Epidemiology. 2021;134:95-102.
60. Collister D, Rodrigues JC, Mazzetti A, Salisbury K, Morosin L, Rabbat C, et al. Single Questions for the Screening of Anxiety and Depression in Hemodialysis. Canadian Journal of Kidney Health & Disease. 2019;6:2054358118825441.
61. Kyte D, Anderson N, Auti R, Aiyegbusi OL, Bishop J, Bissell A, et al. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. J Patient Rep Outcomes. 2020;4(1):55.
62. Basch E, Schrag D, Henson S, Jansen J, Ginos B, Stover AM, et al. Effect of Electronic Symptom Monitoring on Patient-Reported Outcomes Among Patients With Metastatic Cancer. Jama. 2022;327(74):2413-22.
63. Jesky MD, Dutton M, Dasgupta I, Yadav P, Ng KP, Fenton A, et al. Health-Related Quality of Life Impacts Mortality but Not Progression to End-Stage Renal Disease in Pre-Dialysis Chronic Kidney Disease: A Prospective Observational Study. PLoS One. 2016;11(11):e0165675.

64. Schougaard L M LLP, Jessen A et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow up in chronic and malignant diseases. Qual Life Res. 2016;25(3):525-34.
65. Worboys HM, Cooper NJ, Burton JO, Young HML, Waheed G, Fotheringham J, et al. Measuring Quality of Life in Trials Including Patients on Hemodialysis: Methodological Issues Surrounding use of the Kidney Disease Quality of Life Questionnaire. A Systematic Review. Nephrol Dial Transplant. 2022;37(12):2538-54.
66. Weinfurt KP, Reeve BB. Patient-Reported Outcome Measures in Clinical Research. JAMA. 2022;328(5):472-3.
67. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129-200.
68. Basch E, Stover AM, Schrag D, Chung A, Jansen J, Henson S, et al. Clinical Utility and User Perceptions of a Digital System for Electronic Patient-Reported Symptom Monitoring During Routine Cancer Care: Findings From the PRO-TECT Trial. JCO Clinical Cancer Informatics. 2020(4):947-57.
69. Greenhalgh J, Gooding K, Gibbons E, Dalkin S, Wright J, Valderas J, et al. How do patient reported outcome measures (PROMs) support clinician-patient communication and patient care? A realist synthesis. Journal of Patient-Reported Outcomes. 2018;2(42).
70. Yang LY, Manhas DS, Howard AF, Olson RA. Patient-reported outcome use in oncology: a systematic review of the impact on patient-clinician communication. Support Care Cancer. 2018;26(1):41-60.
71. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA. 2017;318(2):197-8.
72. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J Clin Oncol. 2016;34(6):557-65.
73. Denis F, Basch EM, Lethrosne C, Pourel N, Molinier O, Pointreau Y, et al. Randomized trial comparing a web-mediated follow-up via patient-reported outcomes (PRO) vs. routine surveillance in lung cancer patients: Final results. Journal of Clinical Oncology. 2018;36(15_suppl):6500.
74. Denis F, Lethrosne C, Pourel N, Molinier O, Pointreau Y, Domont J, et al. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. J Natl Cancer Inst. 2017;109(9).
75. Nixon NA, Spackman E, Clement F, Verma S, Manns B. Cost-effectiveness of symptom monitoring with patient-reported outcomes during routine cancer treatment. Journal of Cancer Policy. 2018;15:32-6.
76. Lizée TB, Ethan ; Trémolières, Pierre ; Voog, Eric ; Domont, Julien ; Peyraga, Guillaume ; Urban, Thierry ; Bennouna, Jaafar ; Septans, Anne-Lise ; Balavoine, Magali ; Detournay, Bruno ; Denis, Fabrice. Cost-Effectiveness of Web-Based Patient-Reported

Outcome Surveillance in Patients With Lung Cancer. Journal of Thoracic Oncology. 2019;14(6):1012-21.
77. Gibbons C, Porter I, Goncalves-Bradley DC, Stoilov S, Ricci-Cabello I, Tsangaris E, et al. Routine provision of feedback from patient-reported outcome measurements to healthcare providers and patients in clinical practice. Cochrane Database Syst Rev. 2021;10:CD011589.
78. UK Renal Registry UK Renal Association and UK Kidney Care. Patient Reported Experience of Kidney Care in the UK 2021 2021 [Available from: https://ukkidney.org/kidney-patient-reported-experience-measure.
79. Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, et al. Developing core outcome sets for clinical trials: issues to consider. Trials. 2012;13(1):132.
80. Kirkham JJ, Davis K, Altman DG, Blazeby JM, Clarke M, Tunis S, et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. PLoS Med. 2017;14(11):e1002447.
81. Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(Suppl 3):280.
82. Tong A, Craig JC, Nagler EV, Van Biesen W, Committee SE, the European Renal Best Practice Advisory B, et al. Composing a new song for trials: the Standardized Outcomes in Nephrology (SONG) initiative. Nephrol Dial Transplant. 2017;32(12):1963-6.
83. Standardised Outcomes in Nephrology Haemodiaysis SONG HD. The SONG Handbook Sydney, Australia2017 [updated 18th Dec 2021. Available from: https://songinitiative.org/reports-and-publications/.
84. Sautenet B, Tong A, Williams G, Hemmelgarn BR, Manns B, Wheeler DC, et al. Scope and Consistency of Outcomes Reported in Randomized Trials Conducted in Adults Receiving Hemodialysis: A Systematic Review. Am J Kidney Dis. 2018;72(1):62-74.
85. Tong A, Crowe S, Gill JS, Harris T, Hemmelgarn BR, Manns B, et al. Clinicians' and researchers' perspectives on establishing and implementing core outcomes in haemodialysis: semistructured interview study. BMJ Open. 2018;8(4):e021198.
86. Tong A, Manns B, Hemmelgarn B, Wheeler DC, Evangelidis N, Tugwell P, et al. Establishing Core Outcome Domains in Hemodialysis: Report of the Standardized Outcomes in Nephrology-Hemodialysis (SONG-HD) Consensus Workshop. Am J Kidney Dis. 2017;69(1):97-107.
87. Ju A, Unruh M, Davison S, Dapueto J, Dew MA, Fluck R, et al. Establishing a Core Outcome Measure for Fatigue in Patients on Hemodialysis: A Standardized Outcomes in Nephrology–Hemodialysis (SONG-HD) Consensus Workshop Report. American Journal of Kidney Diseases. 2018;72(1):104-12.
88. International Consortium for Health Outcomes Measurement (ICHOM). Measuring results that matter: Chronic Kidney Disease. Data Collection Reference Guide 2022 [updated 1 April, 2022. Available from: https://connect.ichom.org/wp-content/uploads/2022/08/06-Chronic-Kidney-Disease-Reference-Guide-V4.0_01.04.2022.pdf.

89. Prinsen CA, Vohra S, Rose MR, Boers M, Tugwell P, Clarke M, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" - a practical guideline. Trials. 2016;17(1):449.
90. van der Willik EM, Terwee CB, Bos WJW, Hemmelder MH, Jager KJ, Zoccali C, et al. Patient-reported outcome measures (PROMs): making sense of individual PROM scores and changes in PROM scores over time. Nephrology (Carlton). 2021;26(5):391-9.
91. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. J Clin Epidemiol. 2010;63(7):737-45.
92. Anderson NE, Calvert M, Cockwell P, Dutton M, Kyte D. The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective. Am J Kidney Dis. 2019;74(3):399-406.
93. Finkelstein FO, Finkelstein SH. Time to Rethink Our Approach to Patient-Reported Outcome Measures for ESRD. Clin J Am Soc Nephrol. 2017;12(11):1885-8.
94. Schick-Makaroff K, Levay A, Thompson S, Flynn R, Sawatzky R, Thummapol O, et al. An Evidence-Based Theory About PRO Use in Kidney Care: A Realist Synthesis. Patient. 2022;15(1):21-38.
95. Anderson NE, Calvert M, Cockwell P, Dutton M, Aiyegbusi OL, Kyte D. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. BMJ Open. 2018;8(10):e021532.
96. Anderson NE, McMullan C, Calvert M, Dutton M, Cockwell P, Aiyegbusi OL, et al. Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. BMJ Open. 2021;11(8):e052629.

Appendices for Chapter 1:

Appendix 1.1 Link to publication: Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. (2022) Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med 19(4): e1003954. https://doi.org/10.1371/journal.pmed.1003954

Appendix 1.2 Link to publication: Anderson, Nicola Elizabeth et al. (2019) In Reply to 'A Psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis'. American Journal of Kidney Diseases, Volume 74, Issue 5, 711 – 712 https://doi.org/10.1053/j.ajkd.2019.07.009

Appendix 1.3 Search strategy for narrative review

Appendix 1.4 PRISMA diagram for narrative review

Appendix 1.5 Table of characteristics of studies using PROs in HD

Chapter 2
Methodology and Methods

2.1 Introduction

The overall aim of this thesis was to explore and inform the evidence on how ePROs might be used to promote quality of care and safety in the management of patients with End Stage Kidney Disease (ESKD) requiring treatment with Haemodialysis (HD).

Key objectives to meet this aim were: (i) to investigate the current evidence on the use and implementation of ePROs for patients with ESKD receiving HD. To identify a roadmap for increasing the evidence base and introducing ePROs into mainstream clinical practice, (ii) to explore the views, perceptions and experiences of patients receiving HD and health care professionals (HCPs) in the HD multi-disciplinary team regarding the collection and use of PROMs, particularly ePROs, in HD settings; to maximise the potential of ePROs use in the management of the care of patients requiring renal replacement therapy (RRT) with HD, (iii) to explore whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS, and (iv) to comprehensively identify existing ePRO systems, and those in development, for use in nephrology settings globally, ascertaining key characteristics and factors for successful implementation.

This chapter outlines how a strategy capable of meeting this aim, and objectives was developed, including contemplation of appropriate methodology, associated methods and key concepts such as patient-centred care. Choices around methodology and approach are not made within a void and the philosophical perspectives and practicalities to support and justify decisions are discussed.

2.2 Research Paradigms

Allemang et al (2022) define a research paradigm as 'a theoretical framework comprised of a set of beliefs and values, which guides how research is conducted and knowledge conceptualized within scientific communities' (1). These beliefs and values systems are informed by meta-theoretical assumptions of *ontology* (nature of reality: theories of what exists/is real) and *epistemology* (nature of knowledge; what it is possible to know and ways to acquire knowledge) (2).

The literature on research paradigms is complex and a detailed explanation of the shifting and changing landscape (3) is beyond the scope of this thesis. However, put simply, they range from positivist and post-positivist approaches which assert that a single objective reality exists, independent of human behaviour, which can be observed empirically and explained with logical reasoning, to interpretivist/constructivist orientations which maintain that multiple realities exist that are socially constructed and constantly changing (4, 5). The philosophical underpinnings of the paradigm are reflected in the methodology, which is the plan of action which lies behind the choice and use of particular methods (2). Methods are the techniques used to acquire and analyse data to create knowledge (6, 7). Post-positivist approaches are often associated with quantitative methods, centring on concepts of generalisability, reliability and replicability (7). In contrast, constructivist researchers favour qualitative methods which explore individual perspectives to generate patterns and understandings of experiences, with study findings being the 'creation of the process of interaction' (8).

2.2.1 Pragmatism and mixed methods research

Pragmatism as a research paradigm claims to reconcile these differences in philosophical underpinnings and resultant methods and is based upon the premise of utilizing the best methodological approach to examine the research question being investigated (9), allowing for the use of multiple sources of data and knowledge to answer research problems and supporting studies which combine quantitative and qualitative research methods (10). This lends to its appropriateness for mixed methods research (MMR), whereby quantitative and qualitative data are collected and integrated within a single study, and multiple methods research, which uses multiple forms of quantitative or qualitative data approaches across a programme of study (1, 11). In the last decade, MMR has grown 10-fold in nephrology research (12), and similarly in the field of health outcomes research. The mixed methods approach has been recognised as central for instrument development and/or evaluation, allowing the research question to be explored from different perspectives (13). This can include the patient perspective which has traditionally been under-represented, with one study indicating that only 11% of PROMs have been developed by actually asking patients which outcomes are important to measure (14). Furthermore, multiple and MMR offers an opportunity for skills enhancement, an important consideration in the context of a PhD thesis, with practical application of differing skills through research training and experience.

2.2.2 Person-centered care and patient-orientated research

The delivery of person-centered care (PCC), whereby the patient is acknowledged as having needs whilst also being recognized as a capable and resourceful partner with expert knowledge about their everyday life, goals, and motivation, is now an imperative in modern healthcare environments (15). The Nursing and Midwifery Council (NMC) which regulates the nursing profession in the UK, and of which the author is a registrant, explicitly states that there is an expectation that members deliver PCC (16).

The literature demonstrates confusion regarding the concepts of person- and patient-centered care, perhaps with the goal of care being where the concepts differ (17): the goal of patient-centered care is a functional life with a focus on reduction of suffering, while the goal of person-centered care is a meaningful life; with a broadened perspective on the whole life of the patient (17). An overview of reviews on PCC identified three key attributes: being unique; being heard; and shared responsibility (18), and the authors felt these attributes could be translated into practice by getting to know the patient, building shared understandings and creating opportunities for patients to act; with PROs being capable of measuring the effects of PCC (18).

The philosophy behind PCC and associated concepts such as shared decision making is reflected in the primary objectives of patient-orientated research (19). Involving patients in the design and implementation of trials within nephrology is widely recognized (19), with funders, regulatory agencies, consumer organizations and kidney charities strongly advocating for patient involvement in developing, testing and

selecting patient-reported outcomes for kidney trials (20). Allemang et al (2022) have explored how patient-orientated mixed methods research aligns with the paradigm of pragmatism, and suggest the two are connected by demonstrating core concepts of democratic values, collaborative approaches and the pursuit of social justice (1).

It can be argued that this thesis uses multiple methods overall, with each study chapter able to stand alone, with findings that are integrated and interpreted in the Chapter 6 discussion. However, the study reported in Chapter 5 used a mixed methods design. The approach of a structured survey and in-depth follow up interviews to explore the key characteristics of renal ePROs systems and important implementation factors allowed greater insight into how ePROs systems might be optimised in nephrology than could be gained from survey data alone. This study design can be described as explanatory sequential, i.e. the quantitative phase is followed by the collection of qualitative data that aims to explain or improve understanding of the opening quantitative findings (12). This differs from exploratory sequential analyses often used to develop and validate PROMs, where the first phase of study is hypothesis generating using qualitative methods followed by a quantitative phase involving the development and assessment of a quantitative tool using the qualitative findings (12, 21). Throughout the thesis, an effort has been made to undertake patient-orientated research by involving patients in aspects of prioritisation, planning, implementation and reporting of studies.

2.3 Patient and public involvement

Public involvement in research is defined in the UK Standards for public involvement as "Research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them' (22). High quality non-tokenistic patient and public involvement (PPI) can make a real difference to research and consequently healthcare: from planning through to implementation of study findings PPI can ensure that the evidence generated aligns with patient priorities and maximizes the chance of successful study completion and uptake of results; thereby reducing research waste (23). However, even in the field of PROMs, where the capture of the patient's perspective is essential, a scoping review found that in only 6.7% of reviewed studies patients were involved in all three described phases of new measure development: determination of important outcomes, item development and assessment of face validity and usability (14). Furthermore, there was no involvement from patients at all in 25.9% of PROM development studies (14). To combat such findings, it is now a requirement and priority of many research funding bodies that PPI be considered and undertaken at all stages of the research cycle (24). In 2015, it was suggested that a framework or toolkit of how to embed PPI within PROs research with mechanisms to rigorously evaluate the impact of PPI was required (25). While such a framework remains outstanding, user-friendly tools have been developed to support the involvement of patient partners in making informed contributions to the development of PRO aspects of clinical trial protocols (26), in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)-PRO Extension guidelines (27).

This PhD thesis is being undertaken with the support of the local NHS Trust Kidney Patients Association (QEKPA), who identified research on PROMs as a high priority and provided initial funding to support preparation for an application to HEE/NIHR ICA programme. Patient partners undergoing HD were involved in the design of the PhD plan using a Research Design Service Patient Involvement Grant (Ref 2366). Patients have been involved throughout each of the studies, as reported in each chapter, including co-production and co-authorship of final manuscripts prepared for publication. Purposeful PPI during this PhD has not been without challenges. Face to face PPI activity has been curtailed during the COVID-19 pandemic due to shielding requirements and while digital engagement has been undertaken, it has been harder to create and maintain relationships than had been envisaged. To reduce the potential burden to individual local patient partners, the UK-wide Kidney Patients Involvement Network (www.kpin.org.uk) has been used as a resource for review and to offer the patient perspective on content, readability and relevance.

2.4 Overview of methods

In line with the underlying philosophy of pragmatism and associated concepts of person-centred care and patient-orientated research, choice of method was led by the research objectives and associated question. Table 1 gives an overview of the thesis questions, objectives, and methods. The methods will be described further in the following sections of this chapter.

Table 1: Overview of thesis methods

Knowledge gap and research question	Research objective	Method
What is the evidence on the current use and benefit of ePROs in patients with ESKD requiring treatment with HD and why should we consider their use?	Synthesis of current evidence on the use and implementation of ePROs for patients with end-stage kidney disease receiving haemodialysis. To identify a roadmap for increasing the evidence base and introducing ePROs into mainstream clinical practice	Narrative review (Chapter 1)
What is the methodological basis for the use of routine PROMs assessment, particularly using ePROs, within clinical and research settings?	To explore the views, perceptions and experiences of patients receiving HD and health care professionals (HCPs) in the HD multi-disciplinary team regarding the collection and use of ePROMs, particularly ePROs, in HD settings, to maximise the potential of ePROs use in the management of the care of patients requiring RRT with HD.	Qualitative methods – semi-structured interviews with patients receiving renal replacement by HD and Health Care Professionals (HCPs) in the HD multi-disciplinary team (Chapter 3)

Which ePROMs should we be using to measure those outcomes that matter most to key stakeholders, especially patients?	To explore whether currently available ePROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS. The study objectives were to: (1) conduct a systematic search of published literature for COS and validated PROMs used in HD settings; (2) summarise PROM characteristics and affinity map PROMs items/domains against recommended outcomes in available COS.	Scoping review with affinity mapping (Chapter 4)
How do we successfully implement ePROs in nephrology and what are the core factors which contribute to effective implementation, including common facilitators and barriers?	To comprehensively identify ePRO systems for CKD, including those under development, in order to explore system characteristics including methods of administration, levels of integration into existing workflow and electronic health records (EHR) and the reporting of ePROs to manage patient safety. The overall aim being to provide a comprehensive classification of core factors which contribute to successful implementation of ePROs in nephrology, including common facilitators and barriers.	Mixed methods study: Rapid scoping review followed by structured survey and optional follow up semi-structured interviews (Chapter 5)

2.5 Review Methods

Due to the increase of primary research in evidence-based healthcare, the methodology of reviews has advanced, with new approaches to evidence synthesis based on the review questions and objectives, and over 25 different forms of knowledge synthesis method have been reported in the literature (28). Table 2 outlines the key differences in method for five types of review which were either used or considered for use within this thesis, including their overall strengths and limitations.

Table 2: Types of review

	Narrative Review (Traditional/Expert review) (Chapter One)	Rapid Review (Chapter five)	Mapping Review	Scoping Review (Chapter four)	Systematic Review (SR)
Purpose and use	To objectively report the current knowledge on given topic to give broad overview	Used to provide evidence summary in timely fashion at reduced cost	Broad objective to identify where the evidence is located rather than what the evidence is To inform research priorities and research funding	Broad objective about what the evidence or the methods used in a research area is To inform research and policy	Clearly defined, focused aim about a given question/topic To inform policy and practice
A priori protocol	No – but ideally others need to be able to understand, follow how research was selected	Possibly – can follow similar steps to systematic reviews; however, steps may be omitted, modified, or simplified to expedite process. SelecTing Approaches for Rapid Reviews (STARR) is a decision tool that offers researchers guidance on planning a rapid review (29)	No (but recommended)	Yes	Yes – deviations from protocol must be reported and explained
Prospero registration	No	No	No	No	Yes

	Narrative Review (Traditional/Expert review) (Chapter One)	Rapid Review (Chapter five)	Mapping Review	Scoping Review (Chapter four)	Systematic Review (SR)
Scope	1. Critiques and summarises a body of literature 2.Draws conclusions about a topic 3. Demonstrate evidence gaps or inconsistencies in literature and need for new research	1. Provide rapid-turnaround evidence for decision-makers who need guidance in fast-paced contexts	1. To describe the nature, characteristics of research in a particular area or field. 2. To examine the volume of research in a particular area 3. To inform research design. 4. to set agenda for future research 5. To identify and analyse knowledge gaps	1. To identify the types of available evidence in a particular area field (scope and gaps). 2. To explain key concepts/ definitions in the literature. 3. To investigate how research is conducted on a certain topic. 4. To identify key characteristics or factors related to a concept. 5. As a precursor to a systematic review. 6. Identify and analyse knowledge gaps	1. Identify the international evidence 2. Identify current practice/ address any variation/identify new practices. 3. Recognize and inform areas for future research. 4.Investigate conflicting results 5. Generate statements to guide decision-making
Inclusion criteria – screening and selection	Not usually set – usually Purposive sampling and selection	Yes - Follows the PICO format. P=Participant, I=Intervention, C =comparator, O=outcomes	Yes - Follows the PICO format. P=Participant, I=Intervention, C =comparator, O=outcomes	Yes - Completeness of search may be determined by time/scope constraints Follows the PCC format P=Participants, C=Concept, C=context	Yes exhaustive, unbiased, comprehensive – more than one reviewer Predefined selection criteria based on hypothesis/research question. Follows the PICO format (P=Participant, I=Intervention, C=comparator, O=outcomes) or other formats depending on the research question

	Narrative Review (Traditional/Expert review) (Chapter One)	Rapid Review (Chapter five)	Mapping Review	Scoping Review (Chapter four)	Systematic Review (SR)
Searching – explicit, transparent, peer-reviewed search strategy	No - Method not usually specified	Tailored to timeframe, resources, needs	Comprehensive and systematic: Includes searching grey literature. Hand searching is not usually undertaken	Yes - Comprehensive and systematic: It includes hand searching and other grey literature depends on the research question	Yes - Comprehensive and systematic: It includes various types of evidence to capture all the available evidence related to a particular topic. Hand searching is recommended
Data extraction using forms	No - Method of synthesis not usually specified	Tailored to timeframe, resources, needs	Limited coding of studies and intervention characteristics	Yes	Yes
Data charting	Descriptive	Tailored to timeframe, resources, needs	The use of published frameworks to guide data mapping	Data charting can be inductive or deductive	Depending on the research question
Synthesis of individual studies and 'summary of findings'	No	Tailored to timeframe, resources, needs	No	No	Yes – may include meta-analysis or meta-synthesis
Assessment of quality	No formal assessment of quality required but SANRA, the Scale for the Assessment of Narrative Review Articles, a brief critical appraisal tool for the assessment of non-systematic articles has been developed (30).	No formal assessment of quality: reviewers may decide to assess and report the risk of bias in scoping reviews. No specific critical appraisal tool available	No formal assessment of quality	No formal assessment of quality: reviewers may decide to assess and report the risk of bias in scoping reviews.	Critical appraisal of methodological quality of included studies on basis of strict criteria: grading of quality by appropriate critical appraisal tool: will inform inclusion

	Narrative Review (Traditional/Expert review) (Chapter One)	Rapid Review (Chapter five)	Mapping Review	Scoping Review (Chapter four)	Systematic Review (SR)
Reporting Guidelines	No formal guidelines	No formal guidelines – but should demonstrate transparency in abbreviations to SR process	Graphical representation of map availability of evidence. Descriptive overview of map. Can use PRISMA-ScR	PRISMA-ScR	Systematic reporting of evidence. PRISMA 2020
Strengths	Allows wider scope than SR.	Ideal when dealing with time and funding constraints, good for urgent decision making, can be 'converted' to full SR at later stage	Focused on visual synthesis of data so ideal when there is a lot of diverse research evidence	Useful guide to further research Can be highly resource intensive due to volume of literature and depth of data extraction and coding	High quality trust-worthy evidence, methodological rigorous, transparent, and reduced risk of bias, reproducible, capable of being updated
limitations	Potential author bias, not reproducible, not able to be updated	Risk that evidence is missed or poorly synthesised, appraised	Potential lack of depth of detail, no assessment of risk of bias or assessment of methodological quality	Likely no assessment of risk of bias or assessment of methodological quality	Time and resource intensive, not good for urgent decision making

Table 1 References
(31-37)

2.5.1 Narrative review

Chapter 1 presents findings from a narrative review of the literature on ePROs use and implementation in HD settings. A narrative review can be undertaken to describe and discuss the current evidence and literature on a specific topic or theme, providing both underlying theory and context (36). Authors of a narrative review have wide discretion in how they undertake the review process, as seen in Table 2. An acknowledged limitation of this approach is the lack of quality review of the included papers and the possibility that relevant papers may be missed (38). Whilst more time-consuming, a full systematic review (SR) which uses an explicit, rigorous methodological approach reduces the risk of researcher bias and limits subjectivity (38). A full SR is considered highest in the hierarchy of evidence for evaluating healthcare interventions, by not undertaking methodological trade-offs seen in other forms of review (see Table 2) (39). However, Greenhalgh et al (2018) argue that such a view is erroneous and that while a SR addresses a narrowly focused question and summarizes the data, a narrative review serves a different purpose by deepening the understanding of a topic by providing interpretation and critique (40).

Since a SR does not lend itself well to a broad topic area and as the aim of evidence synthesis in Chapter 1 was to give a comprehensive overview of the current literature and evidence regarding the use and implementation of ePROs within HD settings, a narrative review approach was taken. In order to improve the reliability of the findings of this narrative review, details of the search strategy and data extraction tables showing the key characteristics of included papers are presented (see Appendices 1.3

and 1.5); as suggested by the developers of the Scale for the Assessment of Narrative Review Articles (SANRA) (30). A perspectives article (41) published in the American Journal of Kidney Diseases based upon the findings of this review is reproduced in Chapter 1 (page 20). The narrative review was performed primarily to demonstrate the gaps in evidence, allowing this thesis to be positioned in the context of previous findings (32, 41).

2.5.2 Scoping Review

Chapter 4 presents a study using scoping review methods which were employed systematically to map evidence on currently available HD PROM content and HD-specific core outcome set alignment to identify gaps in outcome measurement.

Scoping reviews are effective in synthesising research evidence and are often used to map existing findings in a given field in terms of its nature, features, and volume (42). Consequently, scoping reviews have also been called 'mapping' reviews (42, 43), and such methodology can be used for exploration; to clarify definitions, scope of literature and conceptual boundaries of a chosen topic including knowledge gaps (33, 44). However, as review and evidence synthesis methodology has expanded, the taxonomy has become more clearly defined. Khalil & Tricco (2022) distinguish scoping and mapping reviews, citing several differences, including protocol development, scope, inclusion criteria, data extraction, reporting, and use (37). For broader research questions without the need for an in-depth analysis of the collected evidence, a mapping review is recommended by methodologists in evidence synthesis (37). They also suggest mapping reviews are appropriate for questions of effectiveness, while

scoping reviews are best used to map a concept of interest relevant to a particular population and setting (37). Furthermore, scoping reviews may be undertaken to determine the value and probable scope of a full systematic review, they can also be used to summarize and disseminate research findings, to identify research gaps, and to make recommendations for future research (44).

A distinction between scoping reviews and systematic reviews is that unlike a systematic review, a formal assessment of methodological quality of the included studies is generally not performed nor required for a scoping review (45).

Given the breadth of the research question and the depth of analysis required, systematic and mapping review approaches were rejected in favour of a study using scoping review methods which were employed systematically to collect, synthesise, and chart evidence on currently available HD PROM content against HD-specific core outcome sets to assess alignment and to identify gaps in outcome measurement.

There is now considerable guidance available on the indicators and methods for scoping reviews that promote transparent and trustworthy results (33). From the original framework developed by Arskey and O'Malley in 2005 (42), scoping review methodology has been refined with guidance on method now available from the Joanna Briggs Institute Collaborative (JBIC) (46) and a checklist developed specifically for reporting scoping reporting, the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) (47).

The scoping review reported in Chapter 4 was conducted and reported according to a registered protocol: Review Registry 1269 Browse the Registry - Research Registry and the PRISMA-ScR checklist (47) associated with this study is included in Appendix 4.1.

2.5.3 Rapid Review

The final review type utilised in this thesis is the rapid review. Chapter 5 reports a mixed methods study on the global use of ePROs systems in nephrology. The protocol for this mixed methods study was submitted to the University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee ref: ERN_21-0495 and is reproduced in Appendix 2.1. This protocol paper sets out the rationale and background for this study, outlining the theoretical framework and research design including study methods (setting, recruitment, ethical and regulation considerations, as well as the dissemination plan). Part one of this mixed methods study involved a rapid scoping review to identify ePRO systems that are being used or developed for use in nephrology practice settings, which assess PROs electronically and summarise kidney patients' responses to their care provider. This allowed identification of key system developers who carried responsibility for aspects of design, development, or implementation of these eligible ePRO systems.

A rapid review is a form of knowledge synthesis where aspects of the full SR process are simplified or omitted to produce information in a quick time-frame (48), and the approach has largely emerged as a method for delivering timely evidence at reduced cost (35) (Table 2). It has been argued that rapid reviews are not a method of evidence synthesis, but an approach, and that other types of evidence synthesis can be

completed rapidly (35). Consequently, there is increasing study of the impact on the validity of results when elements of the traditional systematic review process are left out or truncated (35).

Rapid scoping review methods were used in this study due to time factors and the purpose of the review: to swiftly scope the evidence base to identify eligible ePROs systems and corresponding developers for later parts of the mixed methods study. Systems were identified through publications including conference abstracts and grey literature using 'pearl-growing/snowballing' methodology (pursuing references of references) (49-51) and by consulting experts in the field of nephrology ePROs systems. The results of this review were also used to identify key system characteristics and clinical implementation fields, (e.g., administration of PRO assessments/level of automation, integration into existing systems and reporting of responses) to create a structured survey form that could be sent to eligible ePROs systems developers, described later in this chapter.

2.6 Qualitative Methods

2.6.1 PROM-HD Qualitative study

A qualitative study exploring the views, perceptions and experiences of patients receiving HD and HCPs in the HD multidisciplinary team regarding the collection and use of ePROs was undertaken. The protocol outlining the research design for this study (cited below) was accepted for publication in BMJ Open . This protocol paper is presented next in this chapter, followed by expansions on the study methods, the

choice and method of analysis and the utilised framework. The overall findings for this study are presented in Chapter 3.

Qualitative study protocol Publication

The study protocol was accepted for open access publication as:

Anderson NE, Calvert M, Cockwell P, et al. **Using patient reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol.** BMJ Open 2018;8:e021532. doi:10.1136/ bmjopen-2018-021532 DOI: 10.1136/bmjopen-2018-021532

The study protocol was presented at the following conferences as outlined below:

Year	Conference	Location	Presentation type
2017	University Hospitals Birmingham Celebrating Multidisciplinary Research	Birmingham, UK	Poster
2017	UK Kidney Week	Liverpool, UK	Poster
2017	ISOQOL (International Society for Quality-of-Life Research) 24th Annual Conference	Philadelphia, USA	Poster
2017	Patient Reported Outcome Measure's (PROMs) Conference Oxford 2017: Advances in Patient Reported Outcomes Research	Oxford, UK	Poster

Publication 2: Using patient reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol.

BMJ Open

Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol

Nicola Elzabeth Anderson,[1,2] Melanie Calvert,[1] Paul Cockwell,[1,2] Mary Dutton,[1,2] Olalekan Lee Aiyegbusi,[1] Derek Kyte[1]

To cite: Anderson NE, Calvert M, Cockwell P, *et al*. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. *BMJ Open* 2018;8:e021532. doi:10.1136/bmjopen-2018-021532

► Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-021532).

Received 8 January 2018
Revised 24 July 2018
Accepted 22 August 2018

Check for updates

© Author(s) (or their employer(s)) 2018. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

[1]Centre for Patient Reported Outcomes Research, University of Birmingham, Birmingham, UK
[2]Department of Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital, Birmingham, UK

Correspondence to
Dr Derek Kyte;
d.g.kyte@bham.ac.uk

ABSTRACT

Introduction Patients undergoing haemodialysis (HD) for end-stage kidney disease often report a poor quality of life (QoL) and identify that improving QoL has a higher priority for them than improvements in long-term survival. Research suggests that regular collection and usage of patient-reported outcome measures (PROMs) in patients with chronic conditions may reduce hospitalisation, improve QoL and overall survival. In the UK, despite increased use within research settings, PROMs have not been introduced into the routine clinical care for patients undergoing HD. We report the protocol for 'Using patient reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK—PROM-HD'. The study aim is to investigate the methodological basis for the use of routine PROMs assessment, particularly using electronic formats (ePROMs) within clinical and research settings, to maximise the potential of PROM use in the management of the care of this patient group.

Methods and analysis The project will use qualitative methodology to explore, by thematic analysis, the views, perceptions and experiences of patients receiving HD and members of the HD multidisciplinary team regarding the collection and use of PROMs in routine clinical care, particularly ePROMs. This will involve interviews with up to 30 patients or until saturation is achieved and three focus group sessions with approximately 18 members of the clinical team delivering care to this patient group, which will be interpreted broadly to include both professional and non-professional staff.

Strengths and limitations of this study

- The use of semistructured interviews and focus groups allows a detailed and in-depth examination of the issues surrounding the use and implementation of renal patient-reported outcome measures to promote high-quality care in haemodialysis settings.
- The iterative approach allows the data collection tools to develop and expand as new information emerges, and as the data are based on human experience, it is powerful and possibly more compelling than quantitative data on this topic.
- The qualitative data arising from this study are unlikely to be generalisable, but will inform future planned research in this area.
- The role of the researcher within the process can affect participant responses.

INTRODUCTION

The number of patients with end-stage kidney diseases that are being treated with renal replacement therapy (RRT) by dialysis or transplantation continues to grow. In the UK, in December 2015, 61 256 patients were receiving RRT, with haemodialysis (HD) being used as the treatment modality for 41%[1]: of these 25 114 patients, the large majority receive in-centre HD (17.8% hospital, 21.2% satellite), 2% receive home HD.[1]

Patients receiving maintenance HD often experience a significant symptom burden associated with their renal failure, both physical and mental,[2–5] and outcomes in terms of quality of life (QoL) and survival remain poor, even when compared with oncology patients.[6 7] Traditionally reported outcomes such as mortality and progression of kidney disease to end-stage kidney disease are established indicators of health,[8] but it is increasingly recognised that these 'hard' outcomes

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

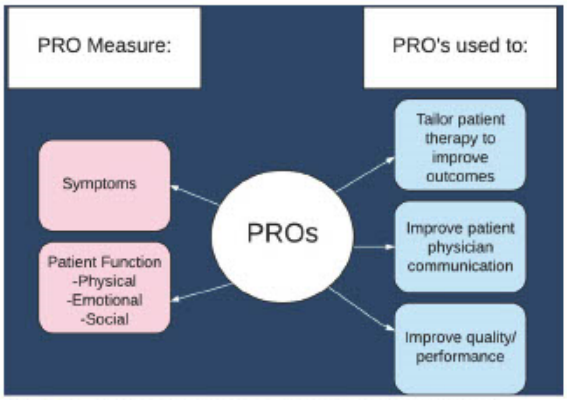


Figure 1 Conceptual framework for patient-reported outcome (PRO) integration in clinical care taken from Dobrozsi and Panepinto.[21]

do not adequately capture patients' overall QOL and may underestimate symptom burden.[8 9] While biomedical outcomes, such as blood results, are often collected and reported during renal care and research, those outcomes which focus on well-being and QoL are often deemed more important by patients.[10 11] Failure to address what matters to patients means symptoms and physical problems can go undetected and therefore untreated,[2 12 13] especially in-between clinic visits,[9] and this leads to further suffering. Furthermore, patients approaching end-stage kidney disease may be willing to trade considerable life expectancy to reduce the burdens and restrictions associated with dialysis affecting QoL.[14 15]

UK health policy holds patient-centred care and shared decision making as a key tenet.[16] Patient-centred care emphasises, and aligns treatment decisions with, patients' preferences, values and goals.[17] This involves a change in the philosophy of care from a traditionally passive patient role to one where patients are actively involved in care planning and problem solving.[18] With increased prominence being given to patient-centred care and shared decision making, the collection of QoL data and other patient-reported outcomes (PROs) are becoming progressively more important.

PROs are defined as 'any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else'.[19] Such PROs are most often collected using PRO measures (PROMs), self-completed questionnaires commonly collating data on general QoL and health-related QoL (HRQoL) as well as physical, emotional and social function, signs or symptoms, from the patients' own point of view.[20] Evidence drawn from oncology studies suggests that PROMs can offer a standardised approach to measuring QoL and symptom burden, augmenting clinician understanding of the patient's health status and leading to overall improvements in patient care.[21] The mode of administration of PROMs has traditionally been in paper format, but increasingly they are being completed electronically using various digital platforms (ePROMs).

Figure 1 outlines a conceptual framework for PRO integration in clinical care taken from Dobrozsi and Panepinto.[21]

While the use of PROMs in routine nephrology practice is currently limited, their use in research as measures of clinical or treatment effectiveness is more widespread.[8] However, there is no consensus on which PROMs to use or their implementation. As part of the international Standardised Outcomes in Nephrology Initiative—Haemodialysis (SONG-HD), major stakeholders have been consulted to help develop a core outcome set that reflects the priorities of patients, carers and clinicians for use in research trials involving HD.[7 22] Patients and carers placed the highest value on outcomes which allowed them to maintain their daily well-being and lifestyle. These included the ability to travel, dialysis-free time and dialysis adequacy, which was conceptualised broadly as dialysis that is adequate for enabling patients to feel well, rather than attributable to a biochemical value.[7]

Initial feedback on the routine use of ePROMs received from the USA has focused on some of the perceived and experienced challenges in their use, such as increased time for completion and IT difficulties. However, with increased usage, evidence suggests PRO collection may not only enhance clinical care from the patients' perspective but may also improve physician satisfaction levels and prevent burnout. This is achieved by improvements in patient–clinician communication, which may increase workflow efficiency.[23]

While there is evidence to support the use of PROMs and particularly ePROMs in the management of patients diagnosed with other conditions, such as cancer,[24–28] the evidence for the use and implementation of PROMs in the management of patients with end-stage kidney disease requiring treatment with HD is currently limited. However, although use of PROMs in nephrology research studies is increasingly common, standardisation in terms of how measures are chosen, implemented and reported is lacking. To help address these issues, this study aims to provide a rigorous exploration of the acceptability and operational feasibility of the collection of routine ePROM data with patients undergoing HD, for potential use in clinical and research settings.

Overall study aim

To explore the feasibility and acceptability of using routine PROM assessment, in both clinical and research settings, in order to aid the management of patients with established renal failure undergoing HD.

Key objectives and key associated questions

1. To investigate the need for PROM use with patients and clinicians in HD settings.
   - Do patients and clinicians feel PROM use would be beneficial? If so, how might their use alter practice and delivery of care?

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

- Would answers to questions differ if PROMs are collected in a research setting, rather than for routine clinical practice?

2. To explore the practicalities associated with PROM implementation in HD settings.
   - To assess the optimal timing of collection, that is, before or during dialysis sessions, from the patient and clinician perspective.
   - To consider the optimal frequency of collection and to determine the average length of time required or that patients are prepared to spend on completion, from the patient and clinician perspective.
   - To gauge the best setting for completion, that is, home or clinical area, from the patient and clinician perspective.
   - To determine patients' ability to self-complete a questionnaire successfully and, if not, how much assistance they would require.
   - To examine the feasibility of PROM collection in different patient groups (eg, older patients, patients of non-white ethnicity).
   - To ascertain the most effective mode of administration for collection of PRO data, that is, in paper or electronic formats, such as mobile application or telephone recognition systems, in terms of usability and preferences for patients and clinicians.
   - To explore the likely factors (barriers and facilitators) that may improve or discourage the completion of PROMs by patients and clinicians.
3. To explore the practicalities associated with PROM feedback in HD settings.
   - To explore how patients would like to receive feedback from the clinical team regarding PRO data.
   - To determine clinicians preferred method of displaying PRO data and the optimum way of providing patient feedback.
4. To explore the use of existing PROMs with patients in HD settings.
   - To explore and determine whether existing validated PRO measurement tools for example, Kidney Disease Quality of Life-Short Form survey (KDQOL-SF), Kidney Disease Quality of Life-36-item survey (KDQOL-36), Integrated Palliative care Outcome Scale-Renal (IPOS-Renal) (see table 1) would be acceptable to patients undergoing HD and members of the renal multidisciplinary team (MDT) working within the HD setting for the routine monitoring of patient's health status.
   - To evaluate the selected PRO questionnaires in terms of the relevance of their items and discuss any potentially missing items with patient and clinician participants.

METHODS AND ANALYSIS

Project design

This project will use qualitative methods, including semi-structured interviews and focus groups, to explore the experiences and perceptions of patients undergoing HD and of clinicians within the MDT caring for these patients.

Project setting

University Hospitals Birmingham NHS Foundation Trust will be the host site for this project. Patients who are established on HD and are being treated within hospital and associated satellite dialysis units will be invited to participate in semistructured interviews to explore their views and perceptions on the routine use of PROMs. Members of the MDT caring for this patient group will be asked to participate in focus group sessions to explore their views on the use, administration and feedback of PROM data.

Project participants

Participants taking part in the patient interviews must be aged ≥18 years old, be able to give valid informed consent and be conversant in everyday English. Only patients who have been established on HD ≥3 months will be interviewed, allowing adjustment to specific issues associated with commencement of dialysis. Patients with an active intercurrent medical problem, which means they require enhanced routine clinical care, will be excluded from the study, such as patients who have experienced

Table 1 Description of questionnaires

Measure	Description
Kidney Disease Quality of life-36 (KDQOL-36)	A 36-item health-related quality of life (HRQoL) measure designed for patients undergoing dialysis, derived from the KDQOL-SF. Three specific dimensions: (1) signs and symptoms, (2) burden of kidney disease and (3) effects of kidney disease and a generic core derived from the SF-12 (physical and mental scales). Overall scores range from 0 to 100, with higher scores indicating better HRQoL[52–55]
Kidney Disease Quality of life-SF (KDQOL-SF)	An 80-item HRQoL measure designed for patients undergoing dialysis which includes the SF-36 as a generic core (physical and mental scales) supplemented with eight kidney disease-targeted dimensions and three additional QoL dimensions. Scores range from 0 to 100 for each dimension with higher scores indicating better HRQoL[52 56 57]
Integrated Patient Outcome Scale-Renal (IPOS-Renal)	IPOS-Renal is a short measure (11 questions), combining the most common symptoms renal patients experience plus additional items from IPOS on concerns beyond symptoms, such as information needs, practical issues, family anxiety[33]

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

a recent episode of acute kidney injury (within the last 3 months) or have a terminal illness that in the opinion of the consultant responsible for routine clinical care is likely to lead to the death of the patients within 6 months of study participation.

Purposive sampling will be undertaken. Participants will be selected for characteristics of relevance to the research questions. For example, sampling by ethnicity, age, gender and dialysis vintage will be conducted to elicit diverse experiences of the phenomenon of interest, PROM use in patients receiving HD (maximum variation sampling). Every effort will be made to recruit participants from minority ethnic groups to reflect the broad ethnic diversity within a large geographical dialysis catchment area that includes both rural and urban populations. Recruitment from more than one satellite HD unit will ensure that the study reflects the diversity which exists within the patient population. Data on participant characteristics will be collected as the study progresses in order to monitor sample diversity.

Participants invited to take part in MDT focus groups must be aged ≥18 years old, be able to give consent and be a member of the MDT involved in the care of patients undergoing HD at the host site or an associated satellite HD unit. The MDT is viewed broadly; therefore, we will interview staff with and without membership of professional bodies and could include doctors, nurses, dietitians, physiotherapists, psychologists, healthcare assistants (HCAs) and unit housekeepers. While a highly technical clinical specialty, the role of renal HCAs continues to expand, and non- professional staff often foster unique and close relationships with patients. In other specialities, HCAs are being directly involved in the assessment of outcomes,[29] and anecdotally, it is often stated that patients will share more, in terms of their experience of living with dialysis treatment, than with their nurses and doctors. Therefore, the views on the collection and implementation of renal PROMS by non-professional members of the MDT will be sought.

Based on experience from previous similar qualitative studies conducted by the research team, recruitment will continue until a target sample size of up to 30 patient participants is attained or until saturation is achieved. Saturation can be described as existing when no new codes, themes or categories are emerging from the data and the relationships between them can be explained.[29]

We aim to include up to 18 MDT participants in three focus groups (six participants in each group) and, if necessary, follow-up interviews will be conducted, depending on emerging data. The focus group sample size has also been derived from prior experience of such studies by the research team, and recruitment will continue until saturation is reached.

It is recognised that travel to and from dialysis units is a significant issue for patients receiving HD. If travel associated with routine HD appointments is disrupted or likely to be disrupted, reasonable travel expenses, that is, taxi fare to/from their home address, will be offered so that there is as little inconvenience as possible for the patient. Likewise, if focus groups are scheduled outside of staff members working hours, reasonable travel expenses will be made available.

Recruitment methods

A member of the renal research team will screen for potentially eligible patients using an in-house electronic patient records system at the host site, in collaboration with members of the dialysis care team. Eligibility will be confirmed by a clinician who is on the study delegation log. Eligible patients will be sent a study-specific participant information sheet, which will be discussed further in clinic or prior to a dialysis session with a member of the research team, where willingness to participate can be ascertained. Ethical approval to post information to patients following screening but prior to consent has been obtained.

Members of the MDT will be approached about study participation, and if interested will be provided with a focus group information sheet. Those who would like to participate will be consented and invited to attend a focus group at a mutually convenient time.

Prior to interview or focus group attendance, participants will be sent copies of selected validated PROMs (KDQOL-36, KDQOL-SF and IPOS-Renal, see table 1) with instructions to read and review the contents so that they are familiar with the form and types of content PROMs can take. However, they will be advised that they do not need to complete these PROMs, and these are samples to assist discussion only.

Recent systematic reviews[30 31] have assessed the quality of the measurement properties of existing PROMs and they recommend the KDQOL-36 for routine clinical practice and the slightly longer KDQOL-SF for clinical trials/research purposes in dialysis patients.[30]

The UK Renal Registry, in response to the growing interest in PROMs by the renal community and as part of the 'Valuing Individuals' and 'Transforming Participation in Chronic Kidney Disease (TP-CKD)' programmes has begun piloting the collection of PROM data in the form of the generic EuroQol five dimension scale 5-level version (EQ-5D-5L) and the disease-specific Palliative care Outcome Scale - Symptoms - Renal (POS-S-Renal) questionnaires.[32] The Palliative care Outcome Scale - Renal (IPOS-Renal) is a short measure that has been adapted from the POS-S-Renal and combines the most common symptoms experienced by renal patients with issues such as information needs, practical concerns, anxiety or low mood, family anxieties and overall feeling of being at peace. IPOS has been validated in a mixed population of those with cancer and non-cancer diagnosis, including renal patients, and shows good content and construct validity, reliability and responsiveness to change.[33]

The IPOS-Renal has been identified by the Renal Research Patient Advisory Group as brief and understandable and is currently undergoing content validation along with the KDQOL-36 in the local renal population

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

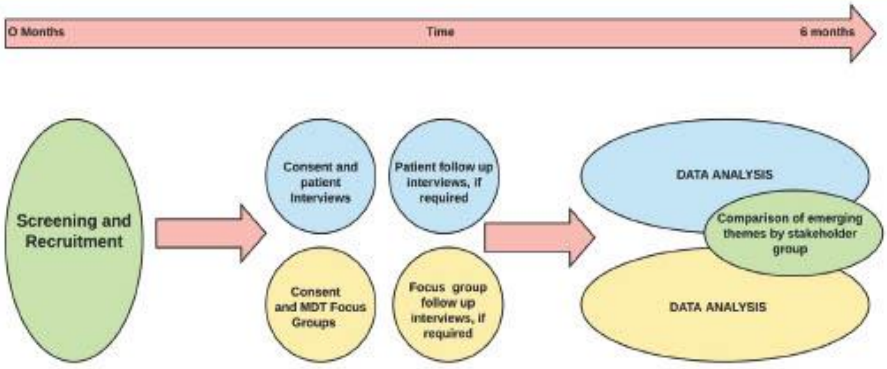


Figure 2 Study flow chart diagram. MDT, multidisciplinary team.

as part of the Using Patient-Reported Outcome Measures to promote quality of care and safety in the management of patients with Advanced Chronic Kidney disease (PRO-TRACK) project.[30] Therefore, the KDQOL-36, KDQOL-SF and IPOS-Renal were selected as the PROMs that will be shown and discussed with patients and members of the MDT in this qualitative study. There is no charge for use from the developers for the KDQOL or IPOS-Renal. As the KDQOL-36 is a subset of the KDQOL-SF, patients will be asked to consider if the shorter PROM is adequate to assess the outcomes which matter most, compared with the broader, but longer and hence more time consuming to complete KDQOL-SF.

Data collection

The guiding qualitative research methodology chosen for this study is thematic analysis, as defined by Braun and Clarke.[34 35] Thematic analysis is a method for identifying, analysing and reporting patterns (themes) within data. It minimally organises and describes the data set in rich detail, also allowing interpretation of various aspects of the research topic.[35] Patients will be interviewed face-to-face, or by telephone, to explore their experiences, perceptions and views of PROMs. The purpose of the focus groups will be to consider the content of selected questionnaires in current use with patients receiving HD and to discuss the various issues that relate to their use and administration. Face-to face or telephone interviews with selected staff may be conducted to explore their views further.

A topic guide will be used to structure the interviews so that all perceived relevant topics are discussed. However, there will be scope to digress from the guide if new and relevant topics are raised by participants. Analysis of transcripts will be conducted alongside data collection; this analysis may shape iterative adjustments to the topic guide to ensure all new and emerging topics are fully explored.

Figure 2 demonstrates the participant pathway through the study.

Data analysis

Analysis of the transcript data will be conducted using the Nvivo V.11 software package by QSR International. Thematic analysis of the data will be conducted following the six-phase guide described by Braun and Clarke.[34 35] The project team will randomly review a sample of coded transcripts for verification purposes. Data analysis will be carried out simultaneously with data collection and both will continue until no new themes emerge from the further analysis, that is, data saturation has been reached.[36] Patient and MDT data will be initially analysed separately and then compared for recurrent or unique themes. Respondent validation also termed 'member checking' will be undertaken, whereby a summary of the main points arising from the interview will be sent to each participant for comments to explore the credibility of the results.[37] In order to minimise the challenges associated with member checking, such as disagreement and distress, we will follow synthesised member-checking processes outlined by Birt *et al*.[37]

Study withdrawal

Study participants who are interviewed will be informed that they have the right to freely withdraw from the study, for any reason, at any time prior to their data being integrated into the data set (ie, within 5 working days following their interview). MDT study participants will be informed that they have the right to withdraw from the study, for any reason, before the focus group session. Participants will be reminded at the start of a session that, as the focus groups are audio recorded, it will not be possible to remove any of their subsequent data once the session has commenced due to the nature of evolving group discussion. It will be made clear to participants that they will not be required to supply a reason for their withdrawal and the decision will have no effect on either their care or terms of employment.

Patient involvement

The study protocol was developed in collaboration with members of the Renal Research Patients Advisory Group, Centre for Patient-Reported Outcomes Research, University of Birmingham and selected HD patients who gave comments and suggestions during the development of this project.

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

DISCUSSION

The collection of symptom and QoL data through simple but validated questionnaires can potentially address the problems of underassessing symptom and QoL issues; recent studies suggested that ePROM collection may be sensitive enough to detect clinically relevant changes and could be used to provide 'early warning' prompts for intervention,[38] enhancing and promoting patient engagement and activation in their treatment.[39 40] The use of ePROMs allows QoL and symptom data to be collected remotely and assessed and acted on in 'real time',[30] with research demonstrating that patient reporting may detect potentially serious adverse event symptoms earlier than traditional clinician reporting.[41]

Furthermore, the use of PROMs has demonstrated substantial improvement in the recognition of problems which are traditionally underestimated by clinicians such as fatigue, pain, emotional and social health when compared with control groups.[42] There is increasing evidence within oncology settings that the collection and feedback of PROMs can improve QoL, enrich the communication between clinician and patient and reduce hospitalisations and may improve overall survival.[27 28 43]

The adequacy of a PROM depends on its characteristics and measurement properties; to be effective, a PROM must demonstrate reliability, construct and content validity and ability to detect change.[30] However, to successfully implement the use of selected validated PROMs for routine monitoring of health status, it is important to consider a wide range of operational issues from both patient and clinician perspectives. These include: the optimal timing/frequency of PROM data collection, the feasibility of PROM collection in different patient groups (older patients, patients of non-white ethnicity) and the most effective mode of administration for collection of PROMs, that is, paper, electronic formats or telephone recognition systems.

It is important to consider appropriate recall period, and the need to be sure that the patient understands what is meant by the recall period. PRO instruments that cause patients to rely on their memory, that is, they need to recall over a long period of time or which compare their current state with an earlier period, or average their response over time, can possibly undermine content validity. Response is likely to be influenced by the patient's state at the time of recall,[19] a factor which must be considered for patients who receive HD.

Results obtained using PROMs can vary according to the instructions given to patients or the training given to the interviewer or persons supervising PRO data collection during a clinical trial.[19] There is every reason to assume this is true for PRO data collected outside trial settings, so it is important to consider how PROMs are presented and how clinicians are prepared in terms of delivery and feedback mechanisms.

What degree of respondent burden are HD patients prepared to tolerate? This will be affected by the length and regularity of proposed measures,[44] formatting of the PROM and questions that patients may feel unwilling or uncomfortable in answering; note there is always the proviso that patients may refuse to answer any questions, if they wish. Research suggests that patients with lower cognitive function are more likely to report higher response burden when completing PRO measures,[45] and since we know that HD effects cognitive performance,[46] it is important that burden is considered in this clinical setting.

Consideration needs to be given to the availability of privacy in the setting where the PROM is completed (eg, providing a private space for patients to complete or ask for assistance in completing questionnaires containing sensitive information about their sexual activity or substance abuse history, if required).

Most importantly, the timing of measurement needs to be considered, that is, 'when' in terms of a patient's dialysis regimen. Up to 70% of HD patients over 54 years of age may demonstrate cognitive impairment and it has been hypothesised that cognitive performance will be further impacted by the time point and place of testing.[46] Such fluctuations may be relevant to PROM data collection. Data from a recent consensus meeting[39] suggest PROs should preferably not be recorded during dialysis.

A shift from paper PRO collection to ePROMs is already evident in other settings.[47] The use of ePROM capture and feedback needs to be investigated within the HD environment. Many HD satellite units are jointly run across the National Health Service and private sector, with established Electronic Patient Records (EPR) systems that could be used to incorporate PROs into their 'big data' collection. Small studies of home HD and Peritoneal Dialysis (PD) patients suggest that satisfaction with the use of tablet computers is high, even with those unused to this technology[48] but the researchers identified challenges in the form of logistics of technology, security, institutional and financial support and electronic design.[49] Such issues will be further explored. However, while qualitative methodology will allow exploration of preferences regarding mode of administration and issues around technical usability, it is noted that such methodology will not explore differences in scores or reliability by mode.

It is important that feedback mechanisms are also considered. Inadequate feedback means that outcomes reporting will not lead to improvements in patient care. By facilitating identification of HRQoL concerns and providing a structured way to discuss these, more clinical actions are then taken in response to these identified needs leading to more responsive and holistic care.[50] There is limited evidence on the feedback of PROMs data to MDTs rather than individual doctors and nurses. Modern healthcare means it is unlikely that you will see the same clinician in a healthcare outpatient setting, although it is arguable that regular dialysis sessions do offer a degree of continuity compared with other specialities. However, it is suggested that PROMs can further facilitate MDT decision-making by focusing the team on aspects of care central to the patient.[51] This aspect of

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

PROM use will be explored further during the MDT focus group sessions.

It is important to consider how operational issues may differ in a research setting: would patients and clinicians be prepared to undertake a more burdensome regime of PRO data collection and how would feedback mechanisms and electronic symptom alerts to identify adverse events be managed? While the focus of this study is around views and perceptions on the acceptability and feasibility of routine collection of PROMs in a clinical setting, it is important that any nuances around collection in a research setting be gathered.

While the evidence for PRO data collection is becoming clearer, challenges remain, in the form of how the data are collected, interpreted and fed back to patients, both within and without research settings. The collection of PRO data may involve a shift in workflow, with QoL and symptom data potentially being reported in 'real-time' by patients into their electronic records. There needs to be effective mechanisms to respond to these data that are not excessively costly or time-consuming.[43] The key to successful implementation is 'buy-in' from patients and clinicians and this requires collaboration with all stakeholders.

The results from this study will be used to inform further research on the implementation of PROMs in research and clinical settings, allowing extrapolation to other dialysis modalities. As a form of preliminary exploration, qualitative research is invaluable in shaping the development of an intervention by exploring its feasibility, acceptability and appropriateness. It is hoped this project will contribute to the development and implementation of PROMs that could enhance QoL assessment and hence improve overall QoL for individual patients requiring HD as well as improving service delivery and patient care.

ETHICS AND DISSEMINATION

This project was approved. It is planned that project findings will be presented at conferences and submitted for dissemination via peer-reviewed open access publications. Participants will be sent a summary of study findings, if they wish.

Acknowledgements The authors would like to thank all members of the Renal Research Patients Advisory Group (RRPAG), Centre for Patient-Reported Outcomes Research (CPROR), University of Birmingham and selected haemodialysis patients for comments and suggestions during the development of this project.

Contributors DK is the guarantor for this project. The project was conceived by DK, MC, PC, MD and NEA. NEA drafted the protocol manuscript. The manuscript was reviewed by DK, MC, PC, MD and OLA. The final draft was approved by all authors.

Funding This project is funded by the Queen Elizabeth Kidney Patients Association (QEKPA): an independent charity working to provide patients with information and support with renal matters.

Disclaimer The views expressed are the author's own and not an official position of the institution or funder. The researchers are independent from the funders.

Competing interests None declared.

Patient consent Not required.

Ethics approval The Gwasanaeth Moeseg Ymchwil (Wales 7) REC(17/WA/0281) following proportionate review and Health ResearchAuthority approval on 16 October 2017.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES

1. MacNeill SJ, Ford D. UK renal registry 19th annual report: chapter 2 UK renal replacement therapy prevalence in 2015: national and centre-specific analyses. *Nephron* 2017;137(Suppl 1):45–72.
2. Scherer JS, Combs SA, Brennan F, *et al*. Sleep disorders, restless legs syndrome, and uremic pruritus: diagnosis and treatment of common symptoms in dialysis patients. *Am J Kidney Dis* 2017;69:117–28.
3. Lowney AC, Myles HT, Bristowe K, *et al*. Understanding what influences the health-related quality of life of hemodialysis patients: a collaborative study in England and Ireland. *J Pain Symptom Manage* 2015;50:778–85.
4. Kraus MA, Fluck RJ, Weinhandl ED, *et al*. Intensive hemodialysis and health-related quality of life. *Am J Kidney Dis* 2016;68:S33–S42.
5. Theofilou P. Quality of life in patients undergoing hemodialysis or peritoneal dialysis treatment. *J Clin Med Res* 2011;3:132–8.
6. Wyld M, Morton RL, Hayen A, *et al*. A systematic review and meta-analysis of utility-based quality of life in chronic kidney disease treatments. *PLoS Med* 2012;9:e1001307.
7. Evangelidis N, Tong A, Manns B, *et al*. Developing a set of core outcomes for trials in hemodialysis: an international delphi survey. *Am J Kidney Dis* 2017;70:464–75.
8. Aiyegbusi OL, Kyte D, Cockwell P, *et al*. A patient-centred approach to measuring quality in kidney care: patient-reported outcome measures and patient-reported experience measures. *Curr Opin Nephrol Hypertens* 2017;26:442–9.
9. Pakhomov SV, Jacobsen SJ, Chute CG, *et al*. Agreement between patient-reported symptoms and their documentation in the medical record. *Am J Manag Care* 2008;14:530–9.
10. Nissenson AR. Improving outcomes for ESRD patients: shifting the quality paradigm. *Clin J Am Soc Nephrol* 2014;9:430–4.
11. Moss AH, Davison SN. How the ESRD quality incentive program could potentially improve quality of life for patients on dialysis. *Clin J Am Soc Nephrol* 2015;10:888–93.
12. Weisbord SD, Fried LF, Mor MK, *et al*. Renal provider recognition of symptoms in patients on maintenance hemodialysis. *Clin J Am Soc Nephrol* 2007;2:960–7.
13. Claxton RN, Blackhall L, Weisbord SD, *et al*. Undertreatment of symptoms in patients on maintenance hemodialysis. *J Pain Symptom Manage* 2010;39:211–8.
14. Morton RL, Tong A, Howard K, *et al*. The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies. *BMJ* 2010;340:c112.
15. Morton RL, Snelling P, Webster AC, *et al*. Factors influencing patient choice of dialysis versus conservative care to treat end-stage kidney disease. *CMAJ* 2012;184:E277–E283.
16. Richards T, Coulter A, Wicks P. Time to deliver patient centred care. *BMJ* 2015;350:h530.
17. Davison SN, Levin A, Moss AH, *et al*. Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care. *Kidney Int* 2015;88:447–59.
18. Coates V. Role of nurses in supporting patients to self-manage chronic conditions. *Nurs Stand* 2017;31:42–6.
19. Food and Drug Administration, 2009. Guidance for industry. Patient reported outcomes measaures_ Use in medical product development to support labelling claims. https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf (accessed Dec 2017).
20. Hjollund NH, Larsen LP, Biering K, *et al*. Use of Patient-Reported Outcome (PRO) measures at group and patient levels: experiences from the generic integrated PRO System, WestChronic. *Interact J Med Res* 2014;3:e5.
21. Dobrozsi S, Panepinto J. Patient-reported outcomes in clinical practice. *Hematology Am Soc Hematol Educ Program* 2015;2015:501–6.

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

22. Urquhart-Secord R, Craig JC, Hemmelgarn B, *et al*. Patient and caregiver priorities for outcomes in hemodialysis: an international nominal group technique study. *Am J Kidney Dis* 2016;68:444–54.
23. Rotenstein LS, Huckman RS, Wagle NW. Making patients and doctors happier - the potential of patient-reported outcomes. *N Engl J Med* 2017;377:1309–12.
24. Jensen RE, Snyder CF, Abernethy AP, *et al*. Review of electronic patient-reported outcomes systems used in cancer clinical care. *J Oncol Pract* 2014;10:e215–e222.
25. Bennett AV, Jensen RE, Basch E. Electronic patient-reported outcome systems in oncology clinical practice. *CA Cancer J Clin* 2012;62:337–47.
26. Basch E, Snyder C. Overcoming barriers to integrating patient-reported outcomes in clinical practice and electronic health records. *Ann Oncol* 2017;28:2332–3.
27. Basch E, Deal AM, Kris MG, *et al*. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. *J Clin Oncol* 2016;34:557–65.
28. Basch E, Deal AM, Dueck AC, *et al*. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA* 2017;318:197–8.
29. Seale C. *The quality of qualitative research*. London: Sage Publications, 2000.
30. Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Using Patient-Reported Outcome Measures (PROMs) to promote quality of care and safety in the management of patients with Advanced Chronic Kidney disease (PRO-trACK project): a mixed-methods project protocol. *BMJ Open* 2017;7:e016687.
31. Gibbons E, Fitzpatrick R. *A structured review of patient reported outcome measures for adults with CKD*. Oxford: University of Oxford, 2010.
32. (Undated) URRU. Overview of site and work Undated. https://www.england.nhs.uk/wp-content/uploads/2016/07/pa-uk-renal-registry.pdf
33. Palliative Care Outcome Scale, 2017. IPOS-Renal. https://pos-pal.org/maix/ipos-renal-in-english.php
34. Braun V, Clarke V. *Succesful qualitative research*. London: Sage Publications, 2013.
35. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3:77–101.
36. Fusch P, Ness L. Are we there yet? Data saturation in qualitative research. *The Qualitative Report* 2015;20:1408–16.
37. Birt L, Scott S, Cavers D, *et al*. Member Checking: A Tool to Enhance Trustworthiness or Merely a Nod to Validation? *Qual Health Res* 2016. doi: 10.1177/1049732316654870. [Epub ahead of print 22 Jun 2016].
38. Pittman ZC, John SG, McIntyre CW. Collection of daily patient reported outcomes is feasible and demonstrates differential patient experience in chronic kidney disease. *Hemodial Int* 2017;21:265–73.
39. Breckenridge K, Bekker HL, Gibbons E, *et al*. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. *Nephrol Dial Transplant* 2015;30:1605–14.
40. Schougaard LM, Larsen LP, Jessen A, *et al*. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow-up in chronic and malignant diseases. *Qual Life Res* 2016;25:525–34.
41. Basch E, Bennett A, Pietanza MC. Use of patient-reported outcomes to improve the predictive accuracy of clinician-reported adverse events. *J Natl Cancer Inst* 2011;103:1808–10.
42. Detmar SB, Muller MJ, Schornagel JH, *et al*. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. *JAMA* 2002;288:3027–34.
43. Basch E. PRO's - Harnessing patient voices to improve clinical care. *N Engl J Med* 2017;376:105–8.
44. Senders A, Hanes D, Bourdette D, *et al*. Reducing survey burden: feasibility and validity of PROMIS measures in multiple sclerosis. *Mult Scler* 2014;20:1102–11.
45. Atkinson TM, Schwartz CE, Goldstein L, *et al*. How much is too much? predictors of patient response burden in the completion of patient-reported outcome assessments. *Quality of Life Research* 2017;26(Suppl 1):47–8.
46. Tholen S, Schmaderer C, Kusmenkov E, *et al*. Variability of cognitive performance during hemodialysis: standardization of cognitive assessment. *Dement Geriatr Cogn Disord* 2014;38:31–8.
47. eRAPID, 2017. eRAPID Towards safer delivery and monitoring of cancer treatments. Electronic patient self-Reporting of Adverse-events (AE): Patient Information and aDvice. http://pogweb.org/index.php/erapid/
48. Schick-Makaroff K, Molzahn A. Brief communication: patient satisfaction with the use of tablet computers: a pilot study in two outpatient home dialysis clinics. *Can J Kidney Health Dis* 2014;1:22.
49. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. *Health Qual Life Outcomes* 2015;13:2.
50. Etkind SN, Daveson BA, Kwok W, *et al*. Capture, transfer, and feedback of patient-centered outcomes data in palliative care populations: does it make a difference? A systematic review. *J Pain Symptom Manage* 2015;49:611–24.
51. Greenhalgh J. The applications of PROs in clinical practice: what are they, do they work, and why? *Qual Life Res* 2009;18:115–23.
52. Peipert JD, Hays RD. Methodological considerations in using patient reported measures in dialysis clinics. *J Patient Rep Outcomes* 2017;1.
53. Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: a systematic review protocol. *BMJ Open* 2016;6:e012014.
54. Peipert JD, Bentler PM, Klicko K, *et al*. Psychometric properties of the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) in the United States. *Am J Kidney Dis* 2018;71.
55. Peipert JD, Bentler P, Klicko K, *et al*. Negligible impact of differential item functioning between Black and White dialysis patients on the Kidney Disease Quality of Life 36-item short form survey (KDQOL-36). *Qual Life Res* 2018:2699–707.
56. Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. *PLoS One* 2017;12:e0179733.
57. Hays RD, Kallich JD, Mapes DL, *et al*. *Kidney Disease Quality of Life Short Form (KDQOL-SFTM) Version 1.3: A manual for use and scoring*. Santa Monica, CA: Rand, 1995. Contract No.: P-7994.

BMJ Open: first published as 10.1136/bmjopen-2018-021532 on 28 October 2018. Downloaded from http://bmjopen.bmj.com/ on 10 January 2019 by guest. Protected by copyright.

2.6.2 Data Collection

In the preceding PROM-HD qualitative study protocol, it was originally conceived that semi-structured interviews would be undertaken with patient participants and focus groups with HCPs, to explore their views and experiences on the use, administration and feedback of PRO data (52). Semi-structured interviews can support in-depth exploration of experiential data, using a piloted topic guide which evolves iteratively (53). While potentially time consuming and costly, such interviews allow one-to-one discussion and clarification to collect 'rich' and detailed data on participant experiences; they allow the participant to raise unanticipated issues through the use of open-ended questions (53). Discussion in a focus group allows data to be collected from multiple participants at the same time; with discussion guided ideally by an experienced moderator (54). Social interaction means participants can also pose questions, challenge and agree with points of view, within the boundaries of agreed ground-rules (53, 55). It is important to assess the potential relative contribution that different participants might make to the overall discussion and the factors likely to impact upon levels of participation (54). While being ideal for interaction and meaning-making, it is recognised that focus groups can be logistically difficult (hard to recruit to and organise) and are not an ideal method to use with 'time poor' people in terms managing recruitment (53). This proved to be the case with HCPs. Furthermore, it was quickly recognised that given the disparity demonstrated in previous experience and knowledge about PROs among members of the multi-disciplinary team during consenting processes, there was a danger of one group (medical doctors) dominating

discussion, which would include nursing colleagues. For these reasons a protocol amendment was sought and approved to conduct semi-structured interviews with HCPs.

2.6.3 Codebook Thematic Analysis

Having felt most closely aligned with the pragmatic paradigm as an approach to guide and conduct this thesis, Codebook thematic analysis was deemed a good overall fit for the qualitative analytic method for both the qualitative study (Chapter 3) and the qualitative component of the mixed methods study (Chapter 5). Thematic analysis (TA) has been promoted by its developers as offering theoretical flexibility and, it has been suggested as a foundational method for those new to qualitative analysis (56). Braun and Clarke published their seminal paper on TA in 2006, describing their 6-step guide: (i) familiarisation with the data; (ii) generating initial codes; (iii) searching for themes; (iv) reviewing themes; (v) defining and naming themes; and (vi) producing the report (56). Braun and Clarke have clarified their approach to TA in later years, highlighting the diversity in TA approaches (57). They describe TA as a spectrum of methods, with interpretivist values at one end and (post) positivist assumptions at the other (57). This continuum shifts from *reflexive TA,* through *Codebook TA* to *Coding reliability* approaches. In reflexive TA, the coding structure is described as unstructured and organic with theme development requiring the researcher to reflect on how their subjective assumptions might affect the coding process during the 6-step process described above. Whereas, in coding reliability approaches, themes may be seen more as topic summaries and multiple coders engage independently with the coding

process, which is highly structured using a coding frame or codebook and final coding is achieved through consensus (3, 57). Sitting on the spectrum between these approaches is Codebook TA; within this method the codebook is not used to increase the reliability of coding but to chart the developing analysis (3, 57). In this method more than one coder can participate, not to ensure accuracy of coding, but to discuss and compare codes to refine the coding system. Measures of inter-coder reliability are not recommended for this form of TA (3). The Codebook TA approach of framework analysis was chosen to analyse the semi-structured interview data as although it sits largely within the qualitative paradigm, it allows pragmatic compromises (58).

A transcription company was used to save time and had been built into the costing model for the PhD. However, time was spent checking the transcripts against the original recordings and this assisted with familiarisation of the data set, in line with the 6-step guidance described by Braun and Clarke (56). The domains from the Consolidated Framework for Interventional Research (CFIR) (59), discussed in detail below, were used to form the codebook for studies reported in chapter 3 and 5. Since coding was being undertaken for a specific research question (which maps onto the more theoretical approach of codebook TA), a theoretical deductive approach was taken as a starting point and domains from the CFIR were used to create the codebook. Overall, there was a tendency to take a semantic approach and not look beyond what the participant was saying. As such, some of the created themes are arguably 'topic summaries', whereby the different and recurrent responses and meanings around a topic that are relevant to the research question are summarised and reported rather than a shared meaning or idea (3), such an approach would be

incompatible with reflexive TA but can be justified in codebook TA where themes are conceptualised as analytical 'inputs' developed early in the process (58). However, later stages of engagement with the data shifted to a more inductive approach and there was a need to be mindful of the impact of the researcher on meaning-making (see reflexivity section below). Care was taken not to over-interpret the data in order to 'shoe-horn' data into the coding framework. The process of TA was not a linear movement across the 6 phases: since a codebook was used, steps 3-5 were particularly iterative. Thematic notes were created to help make sense of the data and to assist in the overall conceptualisation of data patterns: the interaction of codes, topic summaries and potential themes.

In preparing the study for publication it was noted that while the themes which were created were an accurate reflection of the content of the entire data set, it was acknowledged that in such an analysis, there is a risk some depth and complexity is necessarily lost, but an effort to a provide a rich overall description relevant to the research question was made.

2.6.4 Consolidated Framework for Implementation Research

There is a need to understand how and why implementation of ePROs would succeed or fail, by being cognizant of the complexity of the intervention but also the system/setting it sits within (60). To be effective, an intervention needs to translate into improved patient care and associated outcomes, thereby assisting sustainability and allowing transfer into other care settings. Use of an implementation framework can support identification of factors to support this. There are a wide number of

implementation theories to promote effective implementation, covering a number of domains and constructs, with a range of terminology and definitions (61). Conceptual determinant frameworks provide a frame of reference for organising thinking; by pointing to factors believed or found to influence implementation outcomes, such as the Consolidated Framework for Implementation Research (CFIR) (59, 62). Likewise, process frameworks provide practical guidance in the planning and execution, i.e., Knowledge to Action framework (63), while evaluation frameworks guide identification of outcomes that can be used to assess implementation efforts, i.e., RE-AIM (Reach, Effectiveness, Adoption, Implementation Maintenance) (64, 65).

The CFIR 2009 is a framework that can be used alone or with a process model to guide how implementation is planned, organised and scheduled (66); offering an overarching typology 'to promote implantation theory development and verification about what works where and why across multiple contexts' (59). As a 'determinant framework' the overall aim of the CFIR 2009 is to understand and define conceptual constructs that may influence (i.e. moderators) implementation outcomes (64). The CFIR 2009 explores 39 concepts across five major domains namely: intervention characteristics; outer setting (the socio-economic and political context in which the organisation is situated); inner setting (the structural, political, and cultural contexts for the implementation process); characteristics of the individuals involved; and the process of implementation (59). See Appendix 2.2 for a copy of the CFIR 2009 template codebook with definitions of domains and constructs.

Using the framework in the pre-implementation and planning phase allows early identification of potential barriers and facilitators, generating findings to inform implementation/pilot strategies in order to optimise an intervention's viability (67). The CFIR 2009 has been heavily used before as a theoretical framework for both guiding and evaluating implementation processes but more importantly it has been used to identify facilitators and barriers to implementing PROs in organisations (66-68).

There are over 60 conceptual implementation frameworks in existence, all with varying degrees of construct flexibility, at differing stages of the continuum from dissemination to implementation, working at different levels (system, community, organization, and individual) (69). It may have been possible to combine frameworks to address different purposes; to describe and guide the intervention process, to identify the determinants of implementation and evaluation of an intervention (70). However, this could have introduced additional complexity and possible research redundancy (70). To a novice qualitative researcher, the CFIR is a meta-theoretical, multi-level framework which offers flexibility and support in relation to operationalisability: the CFIR 2009 has a technical assistance website (www.cfirguide.org) which offers resources including coding templates, interview topic guides and training resources. The CFIR was used to guide data collection (in mixed methods review see Chapter 5) and data analysis/interpretation of qualitative data (Chapters 3 and 5).

In 2022, since the qualitative analysis phases of this thesis using the CFIR 2009 as the basis for the coding framework were completed, the developer and colleagues of the

CFIR 2009 have prepared an updated CFIR, version 2.0, termed the CFIR 2022 (71). The updated CFIR 2022 now contains 48 constructs and 19 sub-constructs across 5 domains (with one domain including two subdomains) (71). Analysis of a survey for users of the original CFIR, found users thought it was applicable across settings (67%) and innovations (81%), and useful for reporting determinants (77%) and designing implementation strategies (65%), however 58% of survey respondents felt the CFIR 2009 was overly complicated and the large number of constructs/domains needed revising or relocating (71). The developers of the CFIR have acknowledged that responses to questions regarding CFIR constructs will necessarily be both objective observations and subjective perceptions of reality dependent on the experiences of individuals that have influence and/or power over the outcome of implementation efforts (71). Constructs and sub-constructs have been added to address missing themes and there has been further development and clarification of domains, and language has been refined to increase applicability of the CFIR i.e., using the term 'innovation' rather than 'intervention' (71). All references to stakeholders have been removed and the CFIR now refers to people who "have influence and/or power over the outcome of implementation efforts" (71). Some users had questioned the inclusion of the 'Implementation Process Domain' in the CFIR 2009 because it included strategies not contextual factors (71). Indeed, this domain was hardest to code against in the study reported in Chapter 3, as the intervention (ePROs) being discussed was hypothetical in the setting where the study took place. It has been recognised within the literature that poor distinction between innovation and implementation strategy can increase the complexity of accurate implementation outcomes attribution (71, 72).

To avoid any confusion, the CFIR 2022 encourages users to describe their overall approach or implementation process framework and use a reporting guideline for the innovation to help distinguish the innovation from the implementation Process (71).

Framework-level guidance encourages users to operationalize the CFIR for their project; adapting language so it is conceptualised to the setting, as well as including additional constructs as needed to capture salient themes (71). While codebook thematic analysis methods used deductive analysis using the CFIR as a framework for the analysis codebook, inductive analysis was also undertaken to create sub-constructs: such an approach has therefore been confirmed as consistent with the revised CFIR guidance (71) .

Detailed guidance on applying and operationalizing the CFIR 2022 is to be provided, presumably with associated updates to the online resources, in addition to the proposed CFIR outcomes addendum which will offer clear conceptual distinctions between types of outcomes for use with the CFIR (73). The proposed addendum clarifies that data collection on CFIR constructs should be from those participants who have power and/or influence over implementation outcomes and that data collection from those not involved in implementation should be a source of information for innovation determinants and outcomes (73) . Future projects will need to use this revised CFIR 2022 framework, but the developers have been careful to ensure that new updates to constructs can be mapped back to the CFIR 2009 to ensure longitudinal consistency (71) .

2.6.5 Concept of saturation and sample size

It was stated within the PROM-HD qualitative study protocol that recruitment would continue until a target sample of 30 participants was reached or once saturation were achieved (52). Saturation has been described as 'data adequacy' – the point when no new information is obtained from additional qualitative data (74). However, there are no standard tests for estimating or proving an adequate sample size for reaching saturation (75), and depending on the philosophical assumptions underpinning your study, some qualitative researchers question whether saturation to inform sample size is a useful concept (76). Braun and Clarke see 'saturation' and efforts to operationalize this concept as consistent with post-positivist coding reliability types of TA, and not coherent with reflexive TA where the decision to stop data collection is subjective and cannot be wholly determined in advance (76). Since Codebook TA was adopted, using a structured coding framework (CFIR) which was determined prior to commencement of analysis (57), it was decided that the concept of 'code' saturation, as opposed to 'thematic' saturation, would be documented using data saturation tables (see Appendices 3.6 and 3.7) (75). The saturation tables demonstrate this by charting the code frequency (prevalence) and the first time the code was applied or created. While such methods do not meaningfully contribute to the assessment of saturation per se (they focus on breadth of information rather than depth) (75), they do provide useful information regarding the consistency of concept appearance across interviews and help identify infrequently identified concepts (75). However, data saturation tables were created retrospectively to demonstrate saturation and therefore did not inform

the predicted sample size; to do so would have required an iterative process of data collection and analysis (75), which was not undertaken in this study.

Concepts such as 'information power' are being suggested in place of saturation (77, 78). Malterud et al 2016 propose that the more relevant information the sample holds, the lower the number of participants required in the sample – inferring adequate information power (78). They expand on this, stating that sample sizes for qualitative studies depend on five key dimensions: (i) study aim, (ii) sample specificity, (iii) established theory, (iv) the quality of dialogue, and (v) analysis strategy. They argue that theoretically informed studies with narrow aims, highly specific types of participant, rich interview dialogue that require longitudinal in-depth exploration rather than cross-case analyses, will need fewer participants (78).

Such dimensions could be applied to the mixed methods study reported in Chapter 5, where a very specific population sample was set, based upon identification as a nephrology-specific ePROs developer; all of whom were approached to take part in a structured survey and follow-up interview. In this case it is argued the mixed methods study sample size was sufficient to allow transferability of findings to other CKD contexts, and appropriate i.e., able to answer the research questions.

2.6.6 Reflexivity

Potential bias or subjectivity as it is increasingly referred to (3) can be introduced by the researcher through their past experiences and influences, and should be considered regardless of research design, but particularly when using qualitative

research methods (79). The researcher is seen as an instrument actively having a role upon the design, collection, analysis and interpretation of data (80). The concept of Reflexivity (to reflect on the effect of the personality or sheer presence of the researcher on what is being studied) and the ability to reflect on potential disparities in the power relationship between interviewer and interviewee should be considered (79, 80).

Therefore, I needed to speculate on ways I might influence the study process and findings and how I might recognise and thus use my subjectivity in a positive way. This thesis forms the academic component of a clinical academic doctoral research fellowship. There was an experience/knowledge imbalance between my roles as a senior clinical research nurse and that of early career academic researcher that needed to be negotiated. I felt that I held both insider and outsider roles as a clinical academic seen as an insider by some clinical colleagues with whom I had worked in a clinical research context, but also as an outsider, functioning outside the clinical 'frontline' in the eyes of both clinicians and patients (81, 82). I was cognizant that an awareness of these differing roles had the potential to work positively and negatively – 'insider' status could be used as a strategy for building rapport but could also stop interactions being open and honest if participants questioned my independence from the data or clinical setting.

I used various mechanisms to regulate my potential influence over the research process. I undertook informal peer debriefing with other clinical nurse academics but noted that future projects might benefit from more formalised debriefing using

impartial peers. I kept a reflexive journal throughout the PhD journey to record immediate thoughts and ideas about all aspects of the research pathway, but particularly the coding and theme development process. Revisiting this journal has helped me see the development of my thought processes. I considered how notions of 'imposter syndrome' (a psychological term that refers to a pattern of behaviour where someone, regardless of previous objective successes, doubts their abilities and feels a persistent anxiety of being exposed as incapable or a fraud (83)) affected my interactions with clinical colleagues and ePROs experts.

I reflected on past experiences that meant certain aspects of the data resonated loudly, where fixed ideas and subjectivities might have arisen and why this might matter. For example, reflecting on my own thoughts about what I think it must be like living with ESKD and needing dialysis and the potential of imposing my values on others, or recognising my own frustrations on wanting to provide person-centred care but feeling I work within a system that won't support this. Reflections included how I have felt about the research process: the early confusion over theoretical assumptions and not knowing where to start with initial qualitative data analysis. Memo writing and the taking of field notes was useful in documenting the emergence of ideas that could then be contextualised.

Reflections on interactions with patients

Scholars agree that safe spaces for conversation should be created, but there is disagreement on how this achieved; some argue a need for interpersonal connection,

while others suggest self-disclosure can create distance by making the interviewer seem more knowledgeable that the interviewee (68).

During the qualitative study presented in Chapter 3, I decided to disclose early during the consent process that I was a nurse by background, but I was very clear about my scope of practice, confidentiality, and links with clinical team i.e., I was not part of the direct care team. My background did not seem to be an issue for patients; indeed, the majority were candid about their experiences on HD. However, some were keen to say how happy they were with their care, perhaps demonstrating anxiety that I might report back to clinical staff. I believe my clinical background helped build rapport due to common language and understanding of systems, but I was aware that some patients might hold back, although this was not obvious with some patients clearly expressing negative experiences. To maintain rapport, it was necessary to engage on topics well beyond the interview guide and I needed to develop techniques to steer the interview back without shutting down conversation.

I made the decision to not wear a uniform during any interactions with clinical staff or patient participants in semi-structured interviews: thus, emphasising my role as PhD researcher, not a nurse. Patient participants had not seen me active in my nurse role, but I was aware I needed to take care not to slip into the nurse role, and refrain from history taking or problem solving.

It was important that I respected when and where the interviews took place and offered flexibility, which had a corresponding impact on power dynamics. Some patients were interviewed in their home, with carers or family members present.

Other patients were interviewed in the dialysis unit. I began the PROM-HD qualitative study interviewing patients before dialysis in a private room. This decision affected recruitment, as patients did not want to attend early, have their transport interrupted or spend any more time at the dialysis unit than was necessary. Therefore, following ethical review of an amendment to the protocol on timing of interviews, I switched to interviewing patients at the beginning of dialysis once they were stably connected. Some patients dialyse in open bays so privacy then became an issue and although it was not apparent, this could potentially have affected responses. All patients were consented prior to interview and a check was made that they were happy to proceed in an open bay, if that is where they routinely dialysed.

Reflections on interactions with clinicians

I had a previous working relationship with several of the medical doctor participants, who had been in positions of power relative to myself (i.e., Principal Investigators in clinical research studies). It was important to outline my current role, as a PhD student undertaking a thesis, and interviews were conducted in non-uniform. Interviews took place in offices at the interviewee's place of work. Again, I feel I held an insider/outsider status, but I believe participants were frank and candid. As outlined earlier in this chapter, I had originally planned focus groups with HCPs but switched to individual interviews. Within the multi-disciplinary team the nursing voice has traditionally required strengthening, with its absence attributed to factors such as lack of confidence about being listened to and valued (84). Given the disparity in previous experience and exposure to PROs use between professional groups, it was hoped that

individual interviews increased nurse and other non-medical HCP engagement, as interviewees included an administrator and healthcare assistant.

Reflections on interactions with ePRO system developers

In the ePROs systems mixed methods study reported in Chapter 5, international interview participants were experts in the field of PROs and ePROs implementation. Due to the pandemic, restrictions on travel, environmental considerations and cost factors, the interviews were conducted remotely by video-conferencing platform. Online interviewing via videoconferencing software offers advantages and disadvantages. Interviews can be undertaken quickly and conveniently without the need or expense of travel (85), however, the building of rapport is more challenging (85). Yet although there was a knowledge/experience imbalance, I felt it was countered by shared interests, beliefs, and values around the potential of PROs data. Furthermore, the fact that participants were all active senior researchers assisted conversations about the research purpose, consent, confidentiality and how information would be used.

Reflections on process overall

Overall, the process of reflexivity gave space to consider not only the effect of oneself on the research process and findings but also the personal growth that takes place during the PhD journey.

2.7 Mixed Methods including structured survey

The survey reported in Chapter 5 was administered electronically using 2022

SmartSurvey™ Online Survey Software and Questionnaire Tool - SmartSurvey) and distributed by email to ePRO system developers. This survey focused on system design and software features, integration of e-PRO collection and reporting into nephrology clinical care. Additionally, data on other critical elements, such as PRO instruments used, and analytic approaches were collected via a mix of multiple-choice questions and free text responses (see Appendix 5.3). The survey was constructed to allow respondents to skip questions or include 'rather not say' in a free text option, to avoid disclosing proprietary information and breaching copyright or non-disclosure agreements. Surveys are a cost efficient study design, made even more attractive by software packages such as Smart-Survey, which offer accessible, flexible design systems capable of skip logic, piping and branching to tailor survey content to individual participants (86). Respondents may be willing to share more information via survey than in an interview, however online surveys have an average response rate of 20-30% and the characteristics of respondents might be different to non-respondents leading to non-response bias (86). Response rates have been shown to increase if there are clear instructions, surveys are concise and easy to complete, there are incentives or rewards for participating, content is of relevance to participants and reminders are sent (86-88). For these reasons vouchers as reimbursement for time spent, email reminders and a save and complete later function were used to support response rate, which was 66% (10 responses/15 invites). To counter the potential for missing information within the survey, respondents were asked if they would take part in an option follow up interview to clarify and probe survey responses, 70% (n=10) of survey respondents agreed. Pilot testing of the survey was undertaken prior to launch,

to assess comprehensibility, face validity, respondent burden, relevance, layout, and accuracy of skip logic. Personal identifiable information from surveys and follow up interview transcripts was anonymised, but institution and system identifiers were included in study write up. To mitigate for this, participants were given an opportunity to review any interview transcript and to redact any information they wished.

2.8 Impact of COVID-19 pandemic

This thesis has been prepared in the context of an international pandemic and has been both indirectly and directly affected. The COVID-19 pandemic has had a significant impact on healthcare in the UK. Along with many changes, digital methods of healthcare delivery were rapidly expedited, with quick transfer to remote consultations, virtual wards and remote follow up to minimise interactions, potential virus transmission and maximise a limited workforce (89). Patients have demonstrated willingness and the ability to use new ways of communicating and interacting with health services, suggesting that remote consultations saved time and money and were less burdensome (90). Electronic PROs have the potential to support these new ways of working (91); further increasing the need for further research in this field.

The COVID-19 pandemic has directly affected the thesis in the following ways: firstly, the author undertook two leaves of absence (April-June 2022 and Jan-Mar 2021) to allow a return to full-time clinical working, as a senior clinical research nurse, supporting delivery of COVID research studies. Secondly, a change to the original thesis design was made. Originally it was planned to determine the utility of using

established electronic platforms currently collecting data in routine clinical care in the UK to collect ePROs. This was to be conducted by undertaking usability testing of existing PROMs identified in the scoping review (Chapter 4), via such an established electronic platform. However, many staff were redeployed to pandemic response activity, including IT/informatics staff, who would have been required for platform adaption for any usability testing study. Furthermore, due to their vulnerability to the virus, access to patients undergoing HD was restricted, affecting any recruitment plans and face to face research that was not COVID-19 related. Given these challenges and the emerging body of evidence on ePROs usability testing in CKD (92-95) it was decided on pragmatic grounds, to undertake a mixed methods review exploring current and developing ePRO systems being used in nephrology globally (Chapter 5). This is the first time such a review has been undertaken in CKD and findings will inform future implementation strategies.

References

1. Allemang B, Sitter K, Dimitropoulos G. Pragmatism as a paradigm for patient-oriented research. Health Expect. 2022;25(1):38-47.
2. Scotland J. Exploring the Philosophical Underpinnings of Research: Relating Ontology and Epistemology to the Methodology and Methods of the Scientific, Interpretive, and Critical Research Paradigms. English Language Teaching. 2012;5(9).
3. Braun V, Clarke, V,. Thematic Analysis: a practical guide. First Edition ed: Sage Publications Ltd; 2022.
4. Guba E, G & Lincoln, Y, S. Competing Paradigms in Qualitative Research. In: Lincoln NKDYS, editor. Handbook of qualitative research. Thousand Oaks, CA: SAGE; 1994. p. 105-17.
5. Petty NJ, Thomson OP, Stew G. Ready for a paradigm shift? Part 1: introducing the philosophy of qualitative research. Man Ther. 2012;17(4):267-74.
6. Petty NJ, Thomson OP, Stew G. Ready for a paradigm shift? Part 2: introducing qualitative research methodologies and methods. Man Ther. 2012;17(5):378-84.
7. Carter SM, Little M. Justifying Knowledge, Justifying Method, Taking Action: Epistemologies, Methodologies, and Methods in Qualitative Research. Qualitative Health Research. 2007;17(10):1316-28.
8. Appleton JV, King L. Journeying from the philosophical contemplation of constructivism to the methodological pragmatics of health services research. Journal of Advanced Nursing. 2002;40(6):641-8.
9. Kaushik V, Walsh CA. Pragmatism as a Research Paradigm and Its Implications for Social Work Research. Social Sciences. 2019;8(9).
10. Morgan DL. Paradigms Lost and Pragmatism Regained:Methodological Implications of Combining Qualitative and Quantitative Methods. Journal of Mixed Methods Research. 2007;1(1):48-76.
11. Fetters MD, Molina-Azorin JF. The Journal of Mixed Methods Research Starts a New Decade. Journal of Mixed Methods Research. 2016;11(1):3-10.
12. Bailey PK, Hole BD, Plumb LA, Caskey FJ. Mixed-methods research in nephrology. Kidney International. 2022;101(5):895-905.
13. Regnault A, Willgoss T, Barbic S, International Society for Quality of Life Research Mixed Methods Special Interest G. Towards the use of mixed methods inquiry as best practice in health outcomes research. J Patient Rep Outcomes. 2017;2(1):19.
14. Wiering B, de Boer D, Delnoij D. Patient involvement in the development of patient-reported outcome measures: a scoping review. Health Expect. 2017;20(1):11-23.
15. Britten N, Ekman I, Naldemirci O, Javinger M, Hedman H, Wolf A. Learning from Gothenburg model of person centred healthcare. BMJ. 2020;370:m2738.
16. Nursing and Midwifery Council. NMC launches new equality, diversity and inclusion plan for 2022-2025 [Webpage]. NMC; 2022 [Available from: https://www.nmc.org.uk/news/news-and-updates/nmc-launches-new-equality-diversity-and-inclusion-plan-for-2022-2025/.
17. Hakansson Eklund J, Holmstrom IK, Kumlin T, Kaminsky E, Skoglund K, Hoglander J, et al. "Same same or different?" A review of reviews of person-centered and patient-centered care. Patient Educ Couns. 2019;102(1):3-11.
18. Feldthusen C, Forsgren E, Wallström S, Jakobsson Ung E, Öhlén J. Person-centeredness and person-centred care in practice: an overview of reviews. International Journal of Integrated Care. 2022;22(S1).

19. Tong A, Scholes-Robertson N, Hawley C, Viecelli AK, Carter SA, Levin A, et al. Patient-centred clinical trial design. Nature Reviews Nephrology. 2022;18(8):514-23.
20. Hurst FP, Chianchiano D, Upchurch L, Fisher BR, Flythe JE, Castillo Lee C, et al. Stimulating Patient Engagement in Medical Device Development in Kidney Disease: A Report of a Kidney Health Initiative Workshop. American Journal of Kidney Diseases. 2017;70(4):561-9.
21. Rothrock NE, Kaiser KA, Cella D. Developing a valid patient-reported outcome measure. Clin Pharmacol Ther. 2011;90(5):737-42.
22. UK Standards for Public Involvement. UK Standards for public involvement 2022 [Available from: https://sites.google.com/nihr.ac.uk/pi-standards/standards.
23. Banerjee D, Lowe-Jones R, Damster S, Thomas N, Scholes-Robertson N, Tong A, et al. International perspectives on patient involvement in clinical trials in nephrology. Kidney Int. 2020;98(3):566-71.
24. Blackburn S, McLachlan S, Jowett S, Kinghorn P, Gill P, Higginbottom A, et al. The extent, quality and impact of patient and public involvement in primary care research: a mixed methods study. Res Involv Engagem. 2018;4:16.
25. Haywood K, Brett J, Salek S, Marlett N, Penman C, Shklarov S, et al. Patient and public engagement in health-related quality of life and patient-reported outcomes research: what is important and why should we care? Findings from the first ISOQOL patient engagement symposium. Qual Life Res. 2015;24(5):1069-76.
26. Cruz Rivera S, Stephens R, Mercieca-Bebber R, Retzer A, Rutherford C, Price G, et al. 'Give Us The Tools!': development of knowledge transfer tools to support the involvement of patient partners in the development of clinical trial protocols with patient-reported outcomes (PROs), in accordance with SPIRIT-PRO Extension. BMJ Open. 2021;11(6):e046450.
27. Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan AW, King MT, et al. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension. JAMA. 2018;319(5):483-94.
28. Tricco AC, Soobiah C, Antony J, Cogo E, MacDonald H, Lillie E, et al. A scoping review identifies multiple emerging knowledge synthesis methods, but few studies operationalize the method. J Clin Epidemiol. 2016;73:19-28.
29. Pandor A, Kaltenthaler E, Cooper K, James MM-S, Wong R. SelecTing Approaches for Rapid Reviews (STARR) Decision Tool University of Sheffield2019 [Available from: https://doi.org/10.15131/shef.data.7970894.v1.
30. Baethge C, Goldbeck-Wood S, Mertens S. SANRA-a scale for the quality assessment of narrative review articles. Res Integr Peer Rev. 2019;4:5.
31. Pae CU. Why Systematic Review rather than Narrative Review? Psychiatry Investig. 2015;12(3):417-9.
32. Baker JD. The Purpose, Process, and Methods of Writing a Literature Review. AORN J. 2016;103(3):265-9.
33. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol. 2018;18(1):143.
34. Munn Z, Pollock D, Khalil H, Alexander L, McLnerney P, Godfrey CM, et al. What are scoping reviews? Providing a formal definition of scoping reviews as a type of evidence synthesis. JBI Evid Synth. 2022;20(4):950-2.
35. Tricco AC, Khalil H, Holly C, Feyissa G, Godfrey C, Evans C, et al. Rapid reviews and the methodological rigor of evidence synthesis: a JBI position statement. JBI Evid Synth. 2022;20(4):944-9.
36. Henry BM, Skinningsrud B, Vikse J, Pekala PA, Walocha JA, Loukas M, et al. Systematic reviews versus narrative reviews in clinical anatomy: Methodological approaches in the era of evidence-based anatomy. Clin Anat. 2018;31(3):364-7.

37. Khalil H, Tricco AC. Differentiating between mapping reviews and scoping reviews in the evidence synthesis ecosystem. J Clin Epidemiol. 2022;149:175-82.
38. Chandler J CM, Thomas J, Higgins JPT, Deeks JJ, Clarke MJ. Cochrane Handbook for Systematic Reviews of Interventions Version 6.3: Cochrane; 2022 [Available from: www.training.cochrane.org/handbook.
39. Evans D. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. Journal of Clinical Nursing. 2003;12(1):77-84.
40. Greenhalgh T, Thorne S, Malterud K. Time to challenge the spurious hierarchy of systematic over narrative reviews? Eur J Clin Invest. 2018;48(6):e12931.
41. Anderson NE, Calvert M, Cockwell P, Dutton M, Kyte D. The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective. Am J Kidney Dis. 2019;74(3):399-406.
42. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology. 2005;8(1):19-32.
43. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. 2015;13(3):141-6.
44. Davis K, Drey N, Gould D. What are scoping studies? A review of the nursing literature. Int J Nurs Stud. 2009;46(10):1386-400.
45. Peters MDJ, Marnie, C., Tricco, A. C., Pollock, D., Munn, Z., Alexander, L., McInerney, P., Godfrey, C. M., Khalil, H. Updated methodological guidance for the conduct of scoping reviews. JBI Evidence Synthesis. 2020;18(10):2119-26.
46. Peters MDJ, Godfrey C, McInerney P, Khalil H, Larsen P, Marnie C, et al. Best practice guidance and reporting items for the development of scoping review protocols. JBI Evid Synth. 2022;20(4):953-68.
47. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.
48. Tricco AC, Antony J, Zarin W, Strifler L, Ghassemi M, Ivory J, et al. A scoping review of rapid review methods. BMC Med. 2015;13:224.
49. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. BMJ. 2005;331(7524):1064-5.
50. Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. Cochrane Database Syst Rev. 2011(8):MR000026.
51. Lefebvre C, Glanville J, Wieland LS, Coles B, Weightman AL. Methodological developments in searching for studies for systematic reviews: past, present and future? Syst Rev. 2013;2:78.
52. Anderson NE, Calvert M, Cockwell P, Dutton M, Aiyegbusi OL, Kyte D. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. BMJ Open. 2018;8(10):e021532.
53. Braun V, Clarke, V. Succesful Qualitative Research. London: Sage Publications; 2013.
54. Parker A, Tritter J. Focus group method and methodology: current practice and recent debate. International Journal of Research & Method in Education. 2006;29(1):23-37.
55. Seale C. Researching Society and Culture. Seale C, editor. London: SAGE Publications; 2004.
56. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
57. Braun V, Clarke V. Can I use TA? Should I use TA? Should I not use TA? Comparing reflexive thematic analysis and other pattern-based qualitative analytic approaches. Counselling & Psychotherapy Research. 2021;21(2):37-47.

58. Braun V, Clarke,V. One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qualitative Research in Psychology. 2020:1-25.
59. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
60. Greenhalgh T, Papoutsi C. Studying complexity in health services research: desperately seeking an overdue paradigm shift. BMC Med. 2018;16(1):95.
61. Field BB, A. Illott, I. Gerrish, K. Using the Knowledge to action framework in practice: a citation analysis and systematic review. Implementation Science. 2014;9(172).
62. Nilsen P. Making sense of implementation theories, models and frameworks. Implement Sci. 2015;10:53.
63. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Prof. 2006;26(1):13-24.
64. Damschroder LJ. Clarity out of chaos: Use of theory in implementation research. Psychiatry Res. 2020;283:112461.
65. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health. 1999;89(9):1322-7.
66. Foster A, Croot L, Brazier J, Harris J, O'Cathain A. The facilitators and barriers to implementing patient reported outcome measures in organisations delivering health related services: a systematic review of reviews. Journal of Patient-Reported Outcomes. 2018;2(1).
67. Litchfield I, Greenfield S, Turner G, Finnikin S, Calvert M. Implementing PROMs in routine clinical care: a qualitative exploration of GP perspectives. BJGP Open. 2021;5(1):bjgpopen20X101135.
68. van Oers HAT, L. Schepers, S. A. Grootenhuis, M. A. Haverman, L. Isoqol PROMs PREMs in Clinical Practice Implementation Science Group,. A retrospective assessment of the KLIK PROM portal implementation using the Consolidated Framework for Implementation Research (CFIR). Qual Life Res. 2020;30(11):3049-61.
69. Tabak RG, Khoong EC, Chambers DA, Brownson RC. Bridging research and practice: models for dissemination and implementation research. Am J Prev Med. 2012;43(3):337-50.
70. Birken SA, Powell BJ, Presseau J, Kirk MA, Lorencatto F, Gould NJ, et al. Combined use of the Consolidated Framework for Implementation Research (CFIR) and the Theoretical Domains Framework (TDF): a systematic review. Implement Sci. 2017;12(1):2.
71. Damschroder LJ, Reardon CM, Widerquist MAO, Lowery J. The updated Consolidated Framework for Implementation Research based on user feedback. Implement Sci. 2022;17(1):75.
72. Pinnock H, Barwick M, Carpenter CR, Eldridge S, Grandes G, Griffiths CJ, et al. Standards for Reporting Implementation Studies (StaRI) Statement. BMJ. 2017;356:i6795.
73. Damschroder LJ, Reardon CM, Opra Widerquist MA, Lowery J. Conceptualizing outcomes for use with the Consolidated Framework for Implementation Research (CFIR): the CFIR Outcomes Addendum. Implement Sci. 2022;17(1):7.
74. Morse JM. The Significance of Saturation. Qualitative Health Research. 1995;5(2):147-9.
75. Kerr CN, A. Wild, D. Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. Expert Review of Pharmacoeconomics & Outcomes Research. 2010;10(3):269-81.
76. Braun V, Clarke V. To saturate or not to saturate? Questioning data saturation as a useful concept for thematic analysis and sample-size rationales. Qualitative Research in Sport, Exercise and Health. 2019:1-16.

77. Varpio L, Ajjawi R, Monrouxe LV, O'Brien BC, Rees CE. Shedding the cobra effect: problematising thematic emergence, triangulation, saturation and member checking. Med Educ. 2017;51(1):40-50.
78. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qual Health Res. 2016;26(13):1753-60.
79. Roller MR. Research Design Review 2009-2022 [Internet]. Roller M, editor2022. [cited 2022]. Available from: https://researchdesignreview.com/2020/05/28/reflexivity-10-articles-role-reflection-qualitative-research/.
80. Pezalla AE, Pettigrew J, Miller-Day M. Researching the researcher-as-instrument: an exercise in interviewer self-reflexivity. Qualitative Research. 2012;12(2):165-85.
81. Dwyer SC, Buckle JL. The Space Between: On Being an Insider-Outsider in Qualitative Research. International Journal of Qualitative Methods. 2009;8(1):54-63.
82. Hayfield N, Huxley C. Insider and Outsider Perspectives: Reflections on Researcher Identities in Research with Lesbian and Bisexual Women. Qualitative Research in Psychology. 2015;12(2):91-106.
83. Mullangi S, Jagsi R. Imposter Syndrome: Treat the Cause, Not the Symptom. JAMA. 2019;322 5:403-4.
84. Lavender V. Finding our voice in the MDT. Br J Nurs. 2017;26(4):S3.
85. Engward H, Goldspink S, Iancu M, Kersey T, Wood A. Togetherness in Separation: Practical Considerations for Doing Remote Qualitative Interviews Ethically. International Journal of Qualitative Methods. 2022;21.
86. Safdar N, Abbo LM, Knobloch MJ, Seo SK. Research Methods in Healthcare Epidemiology: Survey and Qualitative Research. Infect Control Hosp Epidemiol. 2016;37(11):1272-7.
87. Funkhouser E, Vellala K, Baltuck C, Cacciato R, Durand E, McEdward D, et al. Survey Methods to Optimize Response Rate in the National Dental Practice-Based Research Network. Eval Health Prof. 2017;40(3):332-58.
88. Fan W, Yan Z. Factors affecting response rates of the web survey: A systematic review. Computers in Human Behavior. 2010;26(2):132-9.
89. British Medical Association. BMA COVID Review 3: Delivery of healthcare during pandemic: BMA; 2022 [updated 3 June 2022. Available from: https://www.bma.org.uk/media/5816/bma-covid-review-report-3-june-2022.pdf.
90. Damery S JJ, O'Connell Francischetto E, Jolly K, Lilford R, Ferguson J. Remote Consultations Versus Standard Face-to-Face Appointments for Liver Transplant Patients in Routine Hospital Care: Feasibility Randomized Controlled Trial of myVideoClinic. Journal Med Internet Res. 2021;23(e19232).
91. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. BMJ. 2019;364:k5267.
92. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Slade A, et al. Using Patient-Reported Outcome Measures (PROMs) to promote quality of care and safety in the management of patients with Advanced Chronic Kidney disease (PRO-trACK project): a mixed-methods project protocol. BMJ Open. 2017;7(6):e016687.
93. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Walmsley-Allen N, et al. Development and usability testing of an electronic patient-reported outcome measure (ePROM) system for patients with advanced chronic kidney disease. Computers in Biology & Medicine.101:120-7.
94. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).

95. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. Health & Quality of Life Outcomes. 2015;13:2.

Appendices for Chapter 2:

Appendix 2.1 Mixed Methods study protocol: Using electronic Patient-Reported Outcome Measures (ePROs) to promote quality of care and safety in the management of patients with End Stage Kidney Disease: Review of Electronic Patient-Reported Outcomes Systems used in Nephrology settings

Appendix 2.2 Consolidated Framework for Interventional Research (CFIR) Codebook Template.

Reproduced with permission from: Consolidated Framework for Implementation Research (CFIR) Website. *CFIR Constructs table* Available from https://cfirguide.org/constructs/ [last accessed 13 Nov 2022]

Chapter 3: Using patient-reported Outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study

Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study

3.1. Introduction

Patients undergoing HD often report a high symptom burden and reduced HRQOL (1, 2), and studies demonstrate how the concepts of quality of life, physical-well-being and social support are closely entwined for patients undergoing HD (3). However, such data are not collected routinely in the UK. Systematic collection and use of PROs, including those collected electronically, may help support tailored healthcare and improve overall outcomes by recognising these unique values in regards to quality of life, where life is reliant on dialysis (4). This chapter reports a qualitative study which explored the experiences, views and perceptions of patients and HCPs on the collection and use of PROs in HD settings. This further informs a growing body of evidence on the perspectives of patients and clinicians on the use of ePROs in the management of CKD (5-9). Findings from this study will inform future implementation, through an increased understanding of the barriers and facilitators to routine and systematic use of ePROs, including key perspectives on practical factors such as timing, setting, mode, frequency, and reporting of ePRO data collection.

References

1. Almutary H, Bonner, A, Douglas, C. Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced CKD stage and dialysis modality. Journal of Renal Care. 2016;42(Issue 2):73-82.
2. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954.
3. Hall RK, Cary MP, Jr., Washington TR, Colon-Emeric CS. Quality of life in older adults receiving hemodialysis: a qualitative study. Qual Life Res. 2020;29(3):655-63.
4. Finkelstein FO, Finkelstein SH. Time to Rethink Our Approach to Patient-Reported Outcome Measures for ESRD. Clin J Am Soc Nephrol. 2017;12(11):1885-8.
5. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Walmsley-Allen N, et al. Patient and Clinician Perspectives on Electronic Patient-Reported Outcome Measures in the Management of Advanced CKD: A Qualitative Study. Am J Kidney Dis. 2019;74(2):167-78.
6. Tong A, Crowe S, Gill JS, Harris T, Hemmelgarn BR, Manns B, et al. Clinicians' and researchers' perspectives on establishing and implementing core outcomes in haemodialysis: semistructured interview study. BMJ Open.8(4):e021198.
7. Viecelli AK, Duncanson E, Bennett PN, D'Antoine M, Dansie K, Handke W, et al. Perspectives of Patients, Nurses, and Nephrologists About Electronic Symptom Monitoring With Feedback in Hemodialysis Care. Am J Kidney Dis. 2022;80(2):215-26.
8. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. Burden of mental health symptoms and perceptions of their management in in-centre hemodialysis care: a mixed methods study. J Patient Rep Outcomes. 2021;5(1):111.
9. van der Willik EM, Milders J, Bart JAJ, Bos WJW, van Ittersum FJ, Ten Dam M, et al. Discussing results of patient-reported outcome measures (PROMs) between patients and healthcare professionals in routine dialysis care: a qualitative study. BMJ Open. 2022;12(11):e067044.

Publication 3: Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study

The study results were accepted for open access publication as:

Anderson NE, McMullan C, Calvert M, et al. **Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study**. BMJ Open 2021;11:e052629. doi:10.1136/bmjopen-2021-052629

http://dx.doi.org/10.1136/bmjopen-2021-052629

The study findings were presented at the following conferences as outlined in below:

Year	Conference	Location	Presentation type
2020	UK Kidney Week	Online conference	Poster
2020	ISOQOL (International Society for Quality-of-Life Research) 27th Annual Conference	Online conference	Oral

Publication 3: Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study

BMJ Open

Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study

Nicola Elzabeth Anderson [1,2,3] Christel McMullan [3,4] Melanie Calvert [3,4,5,6,7] Mary Dutton,[1,2,3] Paul Cockwell,[2,3] Olalekan L Aiyegbusi,[3,5,6,7] Derek Kyte [3,8]

To cite: Anderson NE, McMullan C, Calvert M, *et al*. Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. *BMJ Open* 2021;**11**:e052629. doi:10.1136/bmjopen-2021-052629

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-052629).

Received 27 April 2021
Accepted 06 July 2021

Check for updates

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to
Mrs Nicola Elzabeth Anderson; NEA451@bham.ac.uk

ABSTRACT

Objectives Patients undergoing haemodialysis report elevated symptoms and reduced health-related quality of life, and often prioritise improvements in psychosocial well-being over long-term survival. Systematic collection and use of patient-reported outcomes (PROs) may help support tailored healthcare and improve outcomes. This study investigates the methodological basis for routine PRO assessment, particularly using electronic formats (ePROs), to maximise the potential of PRO use, through exploration of the experiences, views and perceptions of patients and healthcare professionals (HCPs) on implementation and use of PROs in haemodialysis settings.

Study design Qualitative study.

Setting and participants Semistructured interviews with 22 patients undergoing haemodialysis, and 17 HCPs in the UK.

Analytical approach Transcripts were analysed deductively using the Consolidated Framework for Implementation Research (CFIR) and inductively using thematic analysis.

Results For effective implementation, the potential value of PROs needs to be demonstrated empirically to stakeholders. Any intervention must remain flexible enough for individual and aggregate use, measuring outcomes that matter to patients and clinicians, while maintaining operational simplicity. Any implementation must sit within a wider framework of education and support for both patients and clinicians who demonstrate varying previous experience of using PROs and often confuse related concepts. Implementation plans must recognise the multidimensionality of end-stage kidney disease and treatment by haemodialysis, while acknowledging the associated challenges of delivering care in a highly specialised environment. To support implementation, careful consideration needs to be given to barriers and facilitators including effective leadership, the role of champions, effective launch and ongoing evaluation.

Conclusions Using the CFIR to explore the experiences, views and perceptions of key stakeholders, this study identified key factors at organisational and individual levels which could assist effective implementation of ePROs in haemodialysis settings. Further research will be required to evaluate subsequent ePRO interventions to demonstrate the impact and benefit to the dialysis community.

Strengths and limitations of this study

- Qualitative methods yield rich data with face-to-face semistructured interviews allowing the interviewer to monitor non-verbal communications and clarify ambiguous responses.
- This study involved explorations of a prospective intervention, meaning some participants were unfamiliar with key concepts. Preinterview materials were shared to support and inform discussion and participation.
- The role of the researchers was carefully considered to acknowledge and minimise bias associated with beliefs and values. Steps were taken to mitigate risks, including use of reflective diaries, participant checking and multiple researchers involved in the coding process.
- While purposive sampling methods led to a diverse sample of participants, it is acknowledged that the sample did not include non-English speakers or carers. Further research is required.
- Data were collected before the coronavirus pandemic. The healthcare delivery landscape in the UK has changed, and it is possible that some attitudes and beliefs particularly around digital data capture may have evolved.

INTRODUCTION

The prevalence of end-stage kidney disease (ESKD) requiring treatment with renal replacement therapies such as haemodialysis (HD) continues to rise worldwide.[1] Both underlying disease and treatment are associated with a high symptom burden and reduced health-related quality of life (HRQoL).[2 3] Historically, outcomes such as mortality and

dialysis adequacy based on biomedical parameters have been used to inform the management of dialysis services and individual care.[4] However, there is now a body of established research[5–10] demonstrating the importance of also capturing patient-reported outcomes (PROs). PRO measures capture data directly from patients on how they feel or function, without requiring interpretation from others, using standardised symptom and/or QoL questionnaires,[11] and are often in electronic format (ePROs).

However, while patient-reported experience measures (PREMs), which allow patients to self-report their experience of receiving healthcare, have been collected since 2017,[12] PROs are still not routinely and systematically collected to manage individual patient care in the UK: meaning that many patients and some members of the multidisciplinary team caring for them are inexperienced in PROs and related concepts.

Yet the international body of evidence exploring the use of PROs in nephrology settings is growing,[13–22] demonstrating acceptability and feasibility of ePRO capture[23–25] and how ePROs can support the delivery of patient-centred care.[26 27] However, the overall impact and benefit of PRO use in dialysis care is yet to be established.[28] In comparison, PRO research in oncology has shown defined benefits ranging from improved QoL and reduction in hospitalisations to overall survival[29] and even cost-effectiveness.[30]

In November 2020, an online UK Summit led by the UK Renal Association, entitled 'ePROs for the Kidney Patient Community', was held to create a comprehensive, UK-wide roadmap to facilitate and optimise the collection and use of ePROs for the benefit of people with chronic kidney disease (CKD). This summit highlighted the importance of key stakeholder engagement, including patients and front-line clinicians, early and at all stages of design and implementation.[31]

To inform and direct future research plans, this study aimed to investigate the methodological basis for routine PRO assessment through exploration of the experiences, views and perceptions of patients and healthcare professionals (HCPs) on implementation and use of PROs, particularly ePROs, in HD settings.

METHODS

Design

The qualitative research question: 'What are the experiences, views and perceptions of patients undergoing HD on the implementation and use of ePROs in routine care and research settings?'

Epistemologically, pragmatism, which is set within a paradigm of enquiry processes and research practicality,[32] provides the philosophical framework to answer this question. A core assumption of pragmatism is that research should proceed from a wish to produce actionable knowledge[33]; allowing the researcher to select the research design and the methodology deemed most appropriate.[34] These foundations led to the decision to use the Consolidated Framework for Implementation Research[35] to offer a theoretical perspective and a qualitative descriptive (QD) methodology.[36–38] This is particularly useful for healthcare studies focused on discovering the who, what and where of events or experiences and gaining understanding of inadequately understood phenomenon. Kim *et al*[38] describe QD as the 'label of choice' when an unambiguous description of a phenomenon is desired or information is sought to develop and refine questionnaires or interventions.[39] This choice of methodology led to the utilisation of the following methods.

Participant selection

Participants included adults (≥18 years), receiving HD (in centre or at home), able to provide valid informed consent and converse in everyday English. Patients were excluded if they were not deemed established on HD or had been undergoing HD <3 months, or if they had an active intercurrent medical problem requiring enhanced routine clinical care.[40] Participants were identified and recruited between July 2018 and November 2019 by the lead author. Eligible patients were primarily approached face to face in the dialysis unit; patients dialysing in centre were approached before dialysis session and patients who dialysed at home (home haemodialysis (HHD)) were approached when they attended for clinic. Purposive sampling was undertaken to achieve maximum variation across age, gender, ethnicity, time on dialysis and comorbidities.[41] HCPs were recruited from the broader renal team, and initially contacted by email by the lead author; they included healthcare and administrative assistants.[40]

Setting

Data were collected from 22 patients undergoing HD and 17 HCPs in the UK (see tables 1 and 2). All participants were being treated via, or working at, a large regional hospital. To accurately reflect the diversity within the dialysis population, patients being treated in centre (n=15) were recruited from two satellite units as well as seven patients choosing to dialyse at home. Non-medical members of the multidisciplinary team were targeted from these two units, one in a city and one serving mainly rural communities. All HCPs currently working in the home setting (n=5) had extensive previous experience of in-centre dialysis delivery.

Data collection

All consenting participants took part in an audio-recorded semistructured interview with the lead author, either face to face or by telephone. Ethical approval was gained for follow-up interviews, but none were required. Patient interviews were conducted at the dialysis unit for those dialysing in centre (n=15) and at home for the HHD group (n=7). Since these interviews were conducted in patient homes, family members were sometimes present at the request of the patient, but did not take an active role in the interview. HCPs were interviewed in a private room at their workplace. Topic guides were used to steer

Table 1 Patient participant characteristics

Variable	Count (%)
Age	
<40	2/22 (9)
40–49	3/22 (13)
50–59	5/22 (23)
60–69	3/22 (14)
70–79	6/22 (27)
>80	3/22 (13)
Gender	
Male	12/22 (55)
Female	10/22 (45)
Ethnicity	
White British	16/22 (73)
Black British	4/22 (18)
Asian/Asian British	2/22 (9)
In-centre dialysis	15/22 (68)
Morning sessions	12/15 (80)
Home HD	7/22 (32)
Current vascular access	
Arteriovenous fistula	19/22 (86)
Arteriovenous graft	0/22 (0)
Central venous catheter	3/22 (14)
Charlson Comorbidity Score	
<2	1 (4)
3–4	5 (23)
5–6	4 (18)
7–8	6 (27)
9–10	5 (23)
11–12	1 (4)
13+	0 (0)
Time since dialysis commencement (years)	
≤5	11/22 (50)
6–10	5/22 (23)
11–15	3/22 (14)
16–20	1/22 (4.5)
>20	2/22 (9)

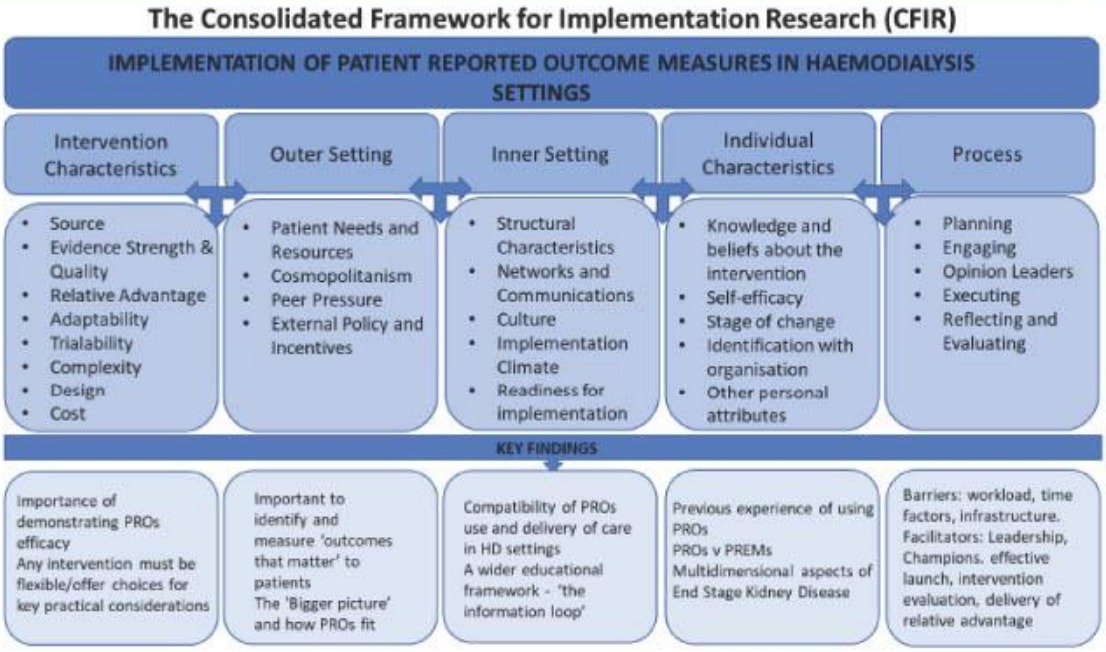
Charlson Comorbidity Index (CCI)[65] quantifies an individual's burden of disease and corresponding 1-year mortality risk. The index adjusts for 17 comorbidities, each one classified with a validated score of 1–6 points, based on the adjusted relative risk of 1-year mortality. The final total score is used to calculate the probability of survival. The index is being used in this context to demonstrate the overall disease burden of the population under study.
n=22.
HD, haemodialysis.

Table 2 Healthcare professional participant characteristics

Variable	Count (%)
Gender	
Male	5/17 (29)
Female	12/17 (71)
Ethnicity (Office of National Statistics categories)	
White British	9/17 (53)
Other white background	2/17 (12)
Black British	1/17 (6)
Asian/Asian British	1/17 (6)
Any other Asian background	2/17 (12)
Black African	1/17 (6)
White and Black Caribbean	1/17 (6)
Role	
Consultant nephrologist	5/17 (29)
Consultant surgeon	1/17 (6)
Registered nurse	9/17 (53)
Non-registered healthcare assistant	1/17 (6)
Administrative assistant	1/17 (6)
Time working across HD setting (years)	
≤5	1/17 (6)
6–10	4/17 (24)
11–15	3/17 (18)
16–20	2/17 (12)
>20	7/17 (41)

n=17.
HD, haemodialysis.

and support the interview process (see online supplemental files 1 and 2). These guides were piloted with one participant from each group and then refined iteratively during the collection phase in response to initial findings. Field notes and in-depth memos were created after each interaction. Since PROs are not routinely collected in the UK, including the hospital trust where this research was undertaken, it was recognised preinterview information was required to aid the quality of discussion around PROs and future implementation. Therefore, participants were provided with a diagram of a core outcome set selected specifically for use in HD trials, to illustrate the position of PROs in outcome measurement[42] and example PROs from a recent systematic review and supported by our local renal public and patient involvement group: Kidney Disease Quality of Life Short Form,[43] Kidney Disease Quality of Life 36[44] and Integrated Patient Outcome Scale-Renal.[45] Patients in all UK renal units are invited to complete the annual renal PREM to report their experience of kidney care. This report demonstrates variation in experience across centres and can be used to drive organisational change and improvement[19]; some patient



1. Adapted from Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.

Figure 1 Conceptual framework and key findings (adapted from Damschroder *et al*[35]). HD, haemodialysis; PREM, patient-reported experience measure; PRO, patient-reported outcome.

participants indicated they had completed the annual PREM.

Analysis

Using codebook thematic analysis,[46] a coding framework, drawing on the Consolidated Framework for Implementation Research (CFIR),[35] was used to deductively analyse transcripts, with further new subthemes developed inductively through data engagement and the analytical process.

The CFIR is a widely used conceptual framework developed to guide systematic assessment of factors that might influence implementation and effectiveness, including assessing potential barriers and facilitators in preparation for implementing an innovation (see figure 1).[35 47] Primary data analysis was conducted by the lead author, with two investigators (CMcM, DK) reviewing coding for consistency and appropriateness. As the lead author was a renal research nurse conducting this research as part of a Clinical Doctoral Research Fellowship, she was known to some HCP participants. This information was declared and discussed during the valid informed consent process. Additionally, a reflective research diary, memo writing and discussion with the study management team were used to try to minimise the influence of prior relationships on analysis. Data analysis was supported by qualitative data analysis software—QSR NVivo V.12. Participant verification,[48] to check that the transcript correctly documented the discussion, was undertaken on one transcript from each group—no discrepant comments were reported. Data collection and analysis continued until saturation was achieved, that is, no new information pertinent to the research question was being generated by further interviews (see online supplemental tables 1 and 2).[49]

Patient and public involvement

Research on the use and implementation of PROs in nephrology settings was prioritised by the local kidney patients charity. An existing patient and public involvement (PPI) group was used and a study-specific PPI group was convened to help develop the research question, design this study and the associated fellowship application. Patients were consulted on the study documentation, including topic guides and example materials (see online supplemental files 1 and 2). A summary of study findings will be made available for study participants.

RESULTS

Participant characteristics

Participant characteristics are summarised in tables 1 and 2.

The patient sample was broadly representative of prevalent HD population in the UK.[50]

Data saturation was deemed achieved after interviewing 16 HCPs and 15 patients (see online supplemental tables 1 and 2 for further detail).

Key findings

Analysis identified the following themes, which are presented in line with the CFIR key domains. Although presented in a linear fashion, the five domains and their respective constructs cannot be considered in isolation, all interact to effect implementation.

Figure 1 shows the conceptual framework and associated findings. Illustrative quotations are provided in table 3.

Intervention characteristics: factors associated with design and quality of the intervention, including how intervention is perceived

The importance of demonstrating PRO efficacy and impact

Both patients and HCP participants felt that PROs could support the delivery of person-centred care through shared decision-making and management in dialysis settings. However, HCP interviewees highlighted the key challenge was not the physical collection of PROs, but how the data were then used to improve outcomes. For patients, it was key that any time spent completing questionnaires should be rewarded with review and appropriate action, that is, not a 'tick-box' exercise.

HCPs, particularly nephrologists, extolled the importance of PROs in research settings.

Intervention flexibility

The topic guide initiated discussions with participants on key practical considerations, including frequency (of PRO completion), optimal timing (around dialysis), preferred setting (home or in centre), favoured mode of administration (electronic or paper versions) and interpretation and feedback of the responses.

It was clear from the patients that a fixed means of implementing PROs would not meet the requirements of this heterogeneous group. Any system would need to be flexible while maintaining maximum simplicity. Most patients felt they could complete electronic measures if required, but some strongly favoured paper options. Most interviewees stated that self-completion was possible but felt some would need physical or emotional support from carers. A few patients indicated a desire for assistance with information technology (IT) aspects until they became familiar. Several patients alluded to the need to 'compartmentalise' their dialysis by conducting all dialysis-related activity in centre or by having discrete facilities and times for dialysis if being treated at home; suggesting that PRO completion would need to be undertaken at defined times/settings within their schedule. Others were less concerned about daily reminders of their disease and management, so were open to completion timings/settings that were more variable.

HCPs discussed the promise of electronic capture to support enhanced management of chronic symptoms, but some expressed concerns about potentially missing acute signs and effectiveness of associated safety reporting and actions. Two HHD patients foresaw the potential benefits of automated safety alerts associated with electronic capture. However, one patient noted that it was important that any automated information or self-help advice should not conflict with information given face to face by the doctor.

Participants were asked for their perspectives on computer adaptive technology, a type of assessment in which questions are generated specifically for each individual, using item response theory. This was a new concept to nearly all participants, but most quickly grasped the underlying theory after a short explanation and were supportive of the idea, recognising the potential to stop redundant questions and save time. (See table 4 for overview of practical considerations.)

Outer setting: the wider societal, economic and organisational contexts in which the stakeholders and organisation implementing the intervention reside

Identifying outcomes that matter

There was a general agreement among all participants that it was important to ensure measurement of 'what outcomes matter most' to patients.[51] There was a broad agreement from patients that the example PROs they had been provided with were comprehensive in covering the key symptoms facing patients undertaking HD. Furthermore, they agreed with findings from the Standardised Outcomes in Nephrology (Haemodialysis) initiative (SONG-HD) [42] that fluctuations in HRQoL mattered more, to them, than biomedical outcomes. The importance of these outcomes was acknowledged by the HCPs, but it was felt that deep exploration of some PRO data fell outside the remit of the nephrologist or dialysis nurse and there was anxiety about acting outside their competency and the associated risks of litigation.

The 'Bigger Picture'

Several patients highlighted problems with continuity of care and lack of cohesion between primary care and their dialysis provision. One HHD patient felt the use of PROs could assist uptake of home therapies by demonstrating better overall outcomes/HRQoL for patients managing their own dialysis. Participants in both groups reflected that PROs could help support shared decision-making by targeting and prioritising discussions according to the patient's agenda.

Inner setting: the structural and cultural contexts around where the implementation will take place

Compatibility of PRO use and approaches to care in HD settings

Discussing potential implementation and how participants perceive the current situation as needing change, patients and staff alike discussed the approaches to care within dialysis settings. Patients clearly described a 'task orientated' style of care in centre, with a focus on practically administering HD, versus a more patient-centred model discussed by those dialysing at home. HHD patients dialysing themselves felt they had developed a level of expertise and the increased 'control' had improved their HRQoL. They indicated current communication pathways were effective and that the HHD team was responsive

Table 3 Key findings—summary of direct quotes

Key finding	Illustrative quotation	
1. Intervention characteristics	**Patient participants**	**HCP participants**
The importance of demonstrating efficacy/benefit	*'If they haven't got a point for collecting them that isn't going to be actioned or put into a specific piece of research, then they shouldn't be there… 'Yes, it makes you unwilling to invest your own time in something that you hadn't seen any benefit from in the past…. If it's just a box ticking exercise for your unit or whatever, to say that I've complied with some directive and nothing is going to change, then why would you'.'* Patient JI18	*'one is convincing those patients and doctors and nurses that it's [PROs] actually of use to man or beast. I think that is going to be the main barrier.'* HCP11
The intervention must be flexible/ offer choices		*'I think if you could then see that it changed a consultation that meant that you went, 'Oh, I didn't know you were having that issue; I can do something about that'. The difficulty is if they then, it drives a lot of conversations that, you know, saying, 'Yeah, can't really do anything about then', and then everybody may well think well this hasn't changed anything so, you know, is it making you feel better writing it down? Don't know really. So if there's not an outcome difference to it then it just becomes a kind of form-filling exercise but there's not obviously a benefit.'* HCP16
Practical considerations	*'Yeah, but certainly filling it in is not an issue, I think discussing it and whether somebody has their partner with them or carer or whatever, I think it's something you should offer them and it's for them to make up their mind.'* Patient MN07	
	See table 4 for key findings and illustrative direct quotes.	*'I guess we have to give the option to the patient whether and how they want to fill this in or not because some patients may not want to fill it in. And I can think of a few patients on my dialysis unit that probably would not want to fill this in.'* HCP14
2. Outer setting		
Identifying and measuring outcomes that matter	*'I need to go out. I need to keep this going. I need to keep feeling that I'm worth something by bringing home a wage and working.'* Patient YZ13	*'Yes, definitely. We see that all the time don't we? I mean you know, we see that all the time. I mean that's the battle, to get people to dialyse three times a week rather than twice a week [yeah, yeah]. So you know, I'm having this battle with a man in XUnit at the moment who's decided to go and dialyse twice a week and he tried it for a few weeks. And he said, 'Oh, I feel perfectly well. So I'm just going to carry on dialysing twice a week' and I said, 'Well, that's not the point' [laughs] [absolutely]. And he said, 'Yeah, but I feel fine. I get more time, I get more spare time'.'* HCP13
How PROs fit into the 'Bigger Picture'	*'It does really knock the quality of life, some people tend to be more worried about the quantity of life but I'm interested in the quality of life because not having quality of life, I can understand why some people do commit suicide, there's no quality.'* Patient ST10	
	Continuity of care and communication with primary care: *' Yeah, the other thing I find with my GP for example, now she rang me, I have monthly blood test here and every 12 months you go to the GP and I go to the diabetic clinic, my diabetes is good… so the doctor (GP) rang up and said, I think you're anaemic, I said well I've had these blood tests at the dialysis centre and nobody phoned up that I was anaemic….'* Patient ST10	*'I think so, I think it [useful for GP's to be able to see the patients results, answers to some of these questions] would because most of this is in the community so it would be very, very useful for the GP's to be able to access all the information.'* HCP04
3. Inner setting		
Compatibility of PROs and approaches to delivery of care in HD settings	Task-centred care versus patient-centred care: *'yes, you might be surrounded by them [unit staff] but they might not be asking questions, you might not feel you can ask questions. There might be aspects that you might not necessarily think it is worthwhile asking.'* Patient JI18	Task-centred care versus patient-centred care: *'we don't always see the bigger picture, we're so focused on getting that needle in to get dialysis, that we forget, oh my god, there's a person on the end of that arm….'* HCP12
		'in-centre, it's looking at the patient, home haemo it's looking at the person.' HCP08
		'I think the nurses have got time to get to know the patients to a certain extent as far as medically, their medication is involved. You know, how poorly they are, obviously what they need. Unfortunately, I don't think they have time to carry that a bit further….' HCP02

Continued

Table 3 Continued

Key finding	Illustrative quotation	
PROs as part of a wider educational framework—'the information loop'	Health literacy of patients: *'Talking about monthly QA reports—'…and we all get these, telling us about our potassium, and somebody says to me, do you understand them? I say, I haven't got a clue, he says nor me, I says, all I know, when I go in there, they tell me that's okay, that's okay, that's okay, I said but I haven't got a clue'.'* Patient BA14	Implementation must be part of a wider framework of training, education and support: *'this will be exciting if implemented correctly, but there's a whole massive amount of work, it's not just this, it's everything else around it yeah, I think so.'* HCP17 Staff education requirements: *'So I guess education would be vital, but they're about communication skills, they're about learning what matters in chronic disease management. And it would also be about, because that's burdensome, it's hugely draining to do it day in day out with a similar group of people. And you would need to put in support, raising the education for them is one, raising awareness. But I also think if you are hearing people's symptoms, which are as I say some of them you can't resolve and you're hearing them day in day out, you need somewhere to offload to as well. So it's like, but building a good structure around what's needed. But that doesn't mean don't talk about them.'* HCP05
4. Characteristics of individuals		
Previous experience of using PROs Concept of PROs versus PREMs	Have you ever completed anything like these questionnaires before? *'No I don't think so.'* Patient UV11, Patient BA14 *'No I haven't.'* Patient WX12 *'I think I have, but I can't remember, it must have been some time ago…I don't think there were as many questions as that one.'* (KDQOL-SF) Patient DC15	*'I mean I've used them in various research projects…And that's one of the reasons why I haven't routinely used them in clinical practice because I think they're fine for research, but I haven't found one that's hugely clinically, that I feel I'd really want to use.'* HCP06 *'[PROMs & PREMs] I get confused and I think there's crossover and I find it quite difficult to draw a line between experience and outcome. Because for example, the experience of a patient. So, tiredness for example can be strongly affected by a patient experience. So, you have travelled six hours to get there or waited for your transport, your experience, it affects your tiredness which is—I think—I'm not sure always it's a useful distinction.'* HCP12
Multidimensionality of ESKD and consequent challenges	Interviewer: *Have you been asked to complete anything like that [exemplar PROs] before?* Patient MN20: *I've done questionnaires before, I think.* Interviewer: *Have you? What kind of questions did they ask? Were they similar ones?* Patient MN20: *Most of them have been in here about the staff and stuff about dialysis and how long I've been on it. It was similar.* *'…obviously the doctors can't cure that, they can't cure that, they can only cure your medical condition, they can't cure your mental condition so that's for you, but they can make it as well, so they give you the positivity to carry on.'* Patient BA14 *'…it's most of the time that I get anxious with social situations because of my other medical problems. It's not just about my kidney problems and then dealing with the social aspect. It's my kidney problems, plus my other medical problems and then the social situation. I have to deal with my other medical problems before I can even contemplate going out with family or friends…or shopping and things like that.'* Patient WX12 *'The main problem? [with dialysis] Social life. Absolutely. It's not just my social life; it's the wife's social life as well. She's like a nurse to me really. Without wife, I don't know where I'd be. I've got two lads but you can't rely on them to be here.'* Patient YZ13	Interviewer: *Yeah. So do you think we should be measuring them (PROMs and PREMs) at the same time?* HCP16: *I think that they should be part of the same thing. I think that they should be seen so that we can pick apart whether people are happy with the service that they're getting but also how that interplays with their health and their feelings and their symptoms so I think the two things overlap.* *'If we can't do much about it, then it's not our problem, sort of thing. That's one of those barriers; I think there's the worry that it uncovers things that are uncomfortable to talk about….'* HCP15 *'Acknowledgement that there are aspects of care that do not fall within doctors 'remit' 'things that aren't necessarily medical, that may relate to social services or other things that are driving a symptom or feeling that relates more to social care, to a dietitian or other members of the team….'.'* HCP16
5. Process of implementation		

Continued

Table 3 Continued

Key finding	Illustrative quotation	
Supporting the process of implementation	Importance of leadership and champions: *'Yeah, Yeah, I've helped a lot of people. When I used to go to look at their machines, because they send me first to look at the room and whether it can be done, they didn't even know I was on dialysis. They'd look at me and say 'you seem to know a lot about this'. I said, 'yeah, because I'm a dialysis patient'.'* Patient YZ13	Importance of leadership and champions: *'Time, resources, you know, if someone's not here, say, if it was me implementing it, if I'm not here, I'm thinking, will it get done? It's as simple as that.'* HCP17
Barriers to effective implementation: time/attitude/IT problems	*'They [Doctors] haven't got time anymore. We all know that, but it's nice to not be rushed along and ignored.'* Patient MN20 *'It does annoy me when we have problems with logging in and passwords.'* Patient WX12	*'You might need to bring somebody else in from outside, yeah but that runs its own complications so what's the answer, a patient representative might be an answer, somebody who knows dialysis.'* HCP17
Facilitators to effective implementation: how PROs might deliver a relative advantage over current systems of care delivery	Acts as a communication tool: *'Yeah, yeah, you know, if you had a form to fill in, you're divorced from it because obviously within our human nature we always, we don't want to look vulnerable, we don't want to look vulnerable, right, so therefore, if the doctors say, you might be feeling sick, and you think, well I only get it now and again, to yourself, this is, so you don't mention it but if you mentioned it, he or she can make a diagnosis on that,....'* Patient BA14	Bottom-up approach: *'Often there are new things that are introduced and when you've just got to do it attitude. Now that just gets peoples backs up to start with...have a proper process in place to prepare people.'* HCP07 *'So it has to be easy access for the patient. It's pointless having something they can't actually get to and that's scary or frustrating to get onto, to log on or something, yeah.'* HCP05
	'I couldn't seem to settle in, i.e. couldn't communicate with the nurses, me as a person, I don't communicate very well.' Patient QR09	Could reduce workload: *'I find it really interesting how people would say that this is an increase in workload, when actually this is things that you need to be looking at anyway. For me this is nothing out of what I'm already looking at in every patient and of course it will be an increase in workload if you don't look at them.'* HCP17
	Help target the consultation: save time. *'Probably save your doctor from doing some of the work as well...As I say, if I'm not giving information that I need, we're not getting anywhere, are we?'* Patient AB01	Potentially time saving: *'I think the PROMs, certainly one is useful when they fill them in but quite often they haven't filled them in and it's then sometimes difficult to ascertain have they not filled them in because they have got symptoms but they just aren't necessarily engaging or thinking oh therefore I will fill this in or whether they haven't filled it in 'cause they're fine. But then at the same time it's quite easy to ask a patient and say, 'Have you not filled this in?', because actually they're fine and then they'll say, 'Yes, I'm fine. There's nothing to worry about', sort of thing and then in a way you can think well I can, I don't necessarily need to give you targeted questions 'cause you've already got the opportunity to do that. Sometimes it then speeds things up.'* HCP06
	Help deliver person-centred care. *'If we've got monthly bloods and we've got the information on that at the same time, they can look at that [ePRO] instead of looking at the computer and seeing what's really going on with that person....'* Patient AB01	
	'Even if that doctor is reading that one-on-one, he can look at this...even if it's on a computer, he can look at it and say, 'He's got a problem with that area. Let's go and deal with that'.' Patient AB01	
	'These questionnaires are good as well because a couple of symptoms cropped up that I do get but that I forgot is related to everything. I thought, 'Oh, that's why I get that then. Oh, that's why I get that'.' Patient WX12	

ESKD, end-stage kidney disease; GP, general practitioner; HCP, healthcare professional; HD, haemodialysis; IT, information technology; KDQOL-SF, Kidney Disease Quality of Life Short Form; PREM, patient-reported experience measure; PRO, patient-reported outcome; PROM, patient-reported outcome measure.

Table 4 Practical considerations and illustrative direct quotes

Practical considerations	Key findings	
	Patient participants	**HCP participants**
Frequency (to allow for accurate recall)	Wide variation of responses from 1 week to 12 months. Agreement that it needed to match recall while allowing for treatment responses. Several patients would complete as frequently as asked—demonstrating no preference.	Wide variation of responses from, as required to 12 months. Focus on practicality, that is, how often they thought patients would complete and time burden rather than sensitivity to changes and recall. Before routine clinic visit was a popular response.
Timing (in relation to dialysis cycle)	Some patients wanted to complete during dialysis but noted this could be practically difficult, particularly if their access was in dominant arm. Most did not want to complete immediately after dialysis, the majority requiring some recovery time.	*'Horses for courses' HCP11* meaning that people are different and will need different things. In terms of timing, some will need a short amount of time to complete, others will need longer. Options, in centre before or during session or patient's choice at home (need time frame for completion? ie, within 5-day window). General agreement that straight after dialysis patients are very fatigued, so not optimum time for completion. Effects of cognitive status on concentration levels—ability to partially complete and come back later, recall bias will be relevant. Need to consider are you asking about today, last 2 weeks, last month, when designing a tool.
Setting of completion (home/in centre)	Some favoured completion in centre, others preferred to complete at home, particularly if carer assistance required.	Patients needed options (home/unit)—some patients need assistance so carers could help (unlikely nurses would have time). It was suggested better returns if encouraged to complete at unit: at home patients are 'distracted by life'. *'Will responses be different if completing at home—does that matter? 'either way, you're gonna get the reality of their life, so perhaps it doesn't matter'.'* HCP05 Lack of privacy in centre noted by number of respondents.
Mode of capture	Varied responses—digital, paper or no preference. Proponents of digital capture displayed no obvious preference for choice of device. Only one patient had no access to a digital device at home. Preference for paper often reflected lack of confidence in ability to complete digitally, a number said they would need assistance to complete electronically. *'I feel like my confidence is down and that needs to build back up again before I use the computer.'* Patient CD02	Advantages of electronic collection raised (real-time review, less admin, less likely to lose returns, easier to track responses, to review responses/feedback) but option of paper needs to be available, as some patients would be unable to complete digitally, and who would provide this assistance? Some pondered that current digital resources, that is, PatientView, are not widely used. IT systems require resource for infrastructure, upkeep and training.
Readability	No jargon or medical terms—got to be easy to read and understand. Guidance around more complex constructs. Availability of measure in other languages. *'You may find you need to print them in their own Urdu or whatever, so that they do understand them. And that has to be very careful that the question doesn't get lost in the translation.'* Patient MN07	Simple and clear rating scales for staff undertaking interpretation. Need to be culturally sensitive/valid and available in languages other than English.

Continued

Table 4 Continued

Practical considerations	Key findings	
	Patient participants	**HCP participants**
Length of questionnaire	Generally, length was not an issue, provided patients could see a purpose to completion. There was a dislike of repetitive questions. Potential time burden of lengthy questionnaires, seen as an inconvenience for carers. *'So the other question I was going to ask was were you put off by the length of some of those questionnaires?'* Interviewee: *'No I wasn't, no, you know I'd put aside the time to do it so no I wasn't, I could see the point of them.'* Patient UV11	Consensus that the shorter the questionnaire, the better. Some commented that current validated PROs were much too lengthy.
Form of feedback	No overall preference: could be letter, email or discussion. Most happy to use graphical data. However, it is important that timely feedback given and PRO completion *'not just a tick box exercise'*. Some patients wanted carers involved in feedback process. *'Because I don't do emails and sometimes my eyesight, I can't able to read. Yeah. I prefer in person.'* Patient GH04 The need for timely feedback was made: Interviewer: *So you'd want to see some sort of feedback within two weeks*. Interviewee: *'Two weeks and they sort it out. Not leave it for months and months and years and years, no good at all.'* Patient KL06 *'As well as giving helpful information to help you manage your condition, it would also be useful to have information about what causes certain things in order to put your mind at rest, if you know what I mean?'* Patient CD02	Consensus that electronic feedback is ideal. Responses outlined in letter to patient or face to face in clinic to allow 'probing'—but this requires resource. Agreement that longitudinal data would be advantageous to see trends—preference for graphical rather than tabular form—but scales need to be well thought through, 0–3 not considered 'sensitive' enough to be able to show changes—preference for EQ-5D thermometer scale… *'but a 'Blunt tool'—good clinician should pick up sensitive changes before PROs would.'* HCP11 No time to read lots of free text.
Setting of feedback	Currently most consultations take place while the patient is dialysing. Patients gave mixed responses to the wish to be seen in private, most did not want additional or extended visits at the dialysis unit and seemed resigned to being seen in open bays.	If medical staff were providing feedback in person, pragmatically best to do this in clinic, it was acknowledged this feedback can take place at the bedside during dialysis but participants noted this may affect the quality and content of the discussion.
Who provides feedback	No overall preference, but one patient felt more comfortable talking to nursing staff.	Variation on responses—some thought medical staff (but concerns raised around time and workload), others thought nurses (some anxiety regarding time constraints and knowledge/experience of junior nursing staff to know how to manage symptoms or issues raised by PROs). *'Need clear process for review and feedback—'can't have 6 nurses going back to patient to discuss responses'.'* HCP16

EQ-5D, EuroQol-5 Dimension; HCP, healthcare professional; IT, information technology; PRO, patient-related outcome.

and holistic in their approach to care. Analysis of patient and HCP data suggested that time constraints were the major reason for a task-based approach in centre with both patients and staff exhibiting a desire to complete dialysis sessions with as little impediment as possible. Correspondingly, most in-centre patients did not feel staff had time to have long discussions and some suggested PROs might help rectify this. There was no discernible variation in the views of the HHD cohort on the practicalities of PRO collection.

Part of a wider framework: the 'information loop', the role of PROs in addressing training needs and health literacy

HCP data analysis highlighted the importance of education, training and support for successful implementation. It was indicated that while medical staff needed training in PRO interpretation, such as rating scales, nurses might need a broader programme on use of PROs as well as associated chronic disease management. There was disparity indicated in the health literacy of the patient group; some HHD patients appeared expert in their illness and treatment, while some in-centre patients appeared less confident in their knowledge.

Characteristics of individuals: factors associated with individuals involved in implementation

Previous experience of using PROs

Patients expressed an overall lack of awareness and experience of PROs. Many had completed annual PREMs but highlighted a lack of feedback or action. Some patients expressed general anxiety about questionnaire completion, linked to their experience of externally administered questionnaires for other agencies: for example, Personal Independence Payment surveys assessing entitlement to extra costs associated with long-term ill health or disability. When reviewing the example PROs, it was noted that some patients, particularly those from minority ethnic backgrounds, flagged the potential difficulty around asking about sensitive issues such as sexual function. While the participants themselves were happy to discuss such issues, they recognised that not all patients might be.

All nephrologists interviewed had experience of using PROs in research settings, but none had regularly and systematically collected PROs in routine care. PRO use in any setting was largely a new concept for nursing staff.

There was a confusion around the concepts of PROs versus PREMs, expressed by both patients and HCPs. Participants found it hard to distinguish experience of care from outcomes and used terms interchangeably.

Multidimensional aspects of ESKD and consequent challenges

Many of the patients in the study had multiple comorbidities and associated symptoms, reflective of the wider HD population. Patients indicated that it was often hard to know which symptoms related to their ESKD and/or treatment, and which were associated with other diseases or advancing age; leading to anxiety about what to raise during a consultation. It was suggested that PRO data review and feedback gave a chance to discuss symptoms and potential causes, thereby potentially providing reassurance. However, some clinicians thought it was outside their role to manage non-nephrology-related outcomes presented by PROs and that it would be difficult to disentangle several, possibly unrelated, symptoms. They feared focusing on symptoms that were not currently being experienced or intractable could cause frustration or anxiety for themselves and the patients. Some patients gave a contrasting opinion, revealing the chance to be heard, even without a solution, was often sufficient to maintain the patient–clinician relationship. There was also concern that an over-reliance on PROs could result in a distraction from other important clinical issues.

The experience of life on dialysis was highly varied, with some participants exhibiting signs of depression, anger or acceptance, as well as reporting multiple symptoms.

The process of implementation

Supporting the process of implementation

The analysis identified leadership, the identification of champions and a 'bottom up' approach to communication and shared solutions among both patients and clinicians as key factors supporting implementation. All participants emphasised the importance of support during completion; however, patients highlighted this need not always be delivered by healthcare staff. Peer-to-peer support and non-clinical champions, that is, administrative staff, might assist. HCPs felt a comprehensive launch was important and that individual roles should be clear. They reflected that senior members of the clinical team would be opinion leaders, and any change agents would need to understand the dialysis setting. Evaluation and reflection were important process components to recognise and deal with any unintended consequences.

Overarching themes: barriers and facilitators to effective implementation

Across all CFIR constructs, analysis identified potential barriers and facilitators to the introduction of PROs.

Potential barriers

Nephrologists cited a lack of evidence base supporting the use of PROs in routine kidney care and were concerned regarding the risk of overmedicalising the patient experience. There were perceived time barriers for staff, that is, workflow interruptions, additional obligations caused by PROs; with nurses perceiving quality time with patients in centre as limited. HCP participants argued that nursing documentation had lessened available time, as it often required recording on digital devices away from the bedside. They feared patients were being overburdened by questionnaires, particularly the less health literate.

In contrast, patients were often already aware of the complications associated with ESKD and HD. Many had achieved a degree of acceptance and some were reassured that the symptoms were expected and not something new

to deal with. Frustration would only arise if, having taken time to complete the questionnaires, no action was taken. Both groups agreed that IT issues, that is, inability to log in, no Wi-Fi, could be a barrier.

Potential facilitators

Several HCPs considered how PROs might work to deliver a relative advantage over current systems to support more patient-centred care. Participants felt PROs could be a communication tool—acting like a 'tin opener'; but requiring that responses be carefully probed, highlighting that this required appropriate skills and training. Others saw the measures as an aide-mémoire which could help target the consultation and even save time; as could the possibility of remote management of care using ePROs. Perhaps, most importantly, PROs were seen by both patients and HCPs as a way to get to know the patients and hence deliver more meaningful care.

DISCUSSION

There is a growing body of published, peer-reviewed literature exploring the experiences of both kidney patients and multidisciplinary kidney HCPs with ePROs.[13 17 23 26 27 52] Previous studies have included non-dialysis-dependent CKD and peritoneal dialysis populations,[17 23 27] evaluating existing ePROs and associated delivery systems. This paper adds to the corpus by using semistructured interviews to gain rich data to inform and optimise future ePRO implementation in an HD population naïve to ePRO collection and clinicians unused to routine and systematic ePRO use.

The key findings of this study are that while patients and HCPs support the concept of PROs, further evidence of their potential benefit is required for effective implementation. It emphasises that any system should be flexible and measure what matters most to patients. Most importantly, the data collected should be acted on. There was a general lack of awareness and experience of PROs particularly among patients and nurses, with concern among the HCPs that PRO capture may highlight issues they might have neither the experience nor resources to manage. Therefore, a comprehensive implementation strategy is required to support any delivery, which involves strong leadership, patient and clinician involvement and ongoing training.

This study highlighted the importance of getting 'buy in', that is, gaining acceptability, from these stakeholders. This could be achieved by demonstrating evidence on their potential benefits thereby increasing trust to warrant practice change. Clinicians particularly questioned whether positive effects on survival, reported QoL, patient–clinician communications and cost efficiencies demonstrated in oncology[29 53–55] could be replicated in HD settings.

The body of evidence around ePROs in nephrology is emerging. Studies from North America demonstrate the feasibility of electronic capture of PROs in HD[19 24] and an Australian pilot study is currently exploring the feasibility and acceptability of ePRO capture and feedback among patients receiving HD in the Symptom Monitoring With Feedback Trial.[20] In advanced CKD populations, the Renal Electronic Patient Reported Outcome Measures (RePROM) study is piloting the use of an ePRO for remote symptom monitoring in the UK,[56] while the AmbuFlex telePRO system is used to manage renal follow-up in Denmark.[25] Aiyegbusi *et al*[17] explored key stakeholder perspectives on the use of PROs in these predialysis patients and their findings are consistent with this study, particularly regarding potential benefits and administrative aspects; suggesting PRO data collection early in the patient pathway can be instituted and continue as illness advances through to renal replacement therapy or even conservative care.

A review and synthesis of evidence is currently being undertaken to investigate how PROs might work to enhance patient-centred care in renal settings, to offer strategy and guidance at individual and aggregate levels of decision-making.[57] For effective multiple uses of data, implementation needs to be viewed within the context of complex data linkage and accessibility issues. Studies in the UK and Australia are currently exploring and testing such linkage of symptoms and QoL data to the Australia and New Zealand Dialysis and Transplant Registry and UK Renal Registry.[20 22 58]

However, the purpose of data collection must be clear. Participants in this study confused the concepts of PROs versus PREMs, understandable given that experience of undertaking HD is intricately linked to both HRQoL and symptoms. The integrated use of both measures, side by side, warrants further investigation. Anxieties about purpose and data sharing could affect patient engagement; clear communication of roles and expectations should be undertaken.

While guidance exists on what outcomes to measure in research[5 6] and routine practice[9] this has not necessarily been centred on routine capture and feedback to guide individual care. Consequently, it is not clear which measure(s) should be used to capture data in a non-burdensome way, while providing sufficient measurement properties to support both single patient monitoring and aggregation of data where required, meaning further enquiry is needed.

The general lack of awareness and experience of PROs and concern that PRO capture may highlight issues that HCPs should not or cannot deal with, leads to a significant finding that PRO implementation must sit within a broader educational framework. PROs could be used to support wider initiatives and training, especially in the nursing group, who can then cascade information and self-management skills to patients, thereby increasing overall patient health literacy. This could be considered as closing an 'information loop'. There is already evidence that patient education is associated with better patient outcomes[59] and new strategies and quality improvement programmes exist such as Shared HD, a UK programme

aiming to support patients receiving in-centre HD to be more independent and confident in participating in aspects of their own care.[60] Potential barriers are cost and resources, but increasingly, accredited online learning facilities are available. However, it is acknowledged, staff in this study indicated a preference for face-to-face training. Education and training on PROs would be needed for all stakeholders.

This study identified time and workflow interruptions as key barriers to implementation. Rotenstein *et al*[61] found that following initiation of routine PRO collection in surgical settings, such concerns shifted as clinicians became comfortable with new processes. There was even a suggestion that PROs could enhance physician satisfaction and prevent 'burnout'.[61] Tong *et al*[62] interviewed the nephrologists, who also identified resource constraints and uncertainties in how to prioritise, measure and manage a range of competing comorbidities and broader QoL outcomes in a clinical setting that is technically demanding and traditionally focused on biochemical factors; findings mirrored by this study. Such anxieties will need addressing.

During the SARS-CoV-2 pandemic, data from the UK Renal Registry showed that patients undergoing HD experience a relative risk of mortality of 45.5% compared with the general population.[62] This vulnerable population has been unable to effectively shield, requiring regular dialysis treatment with associated risks around shared transport and waiting areas. Various strategies have been employed to reduce risks[63] but new ways of care delivery were required. The pandemic has irrevocably changed healthcare, with increased use of virtual services[64] and remote clinic visits. The addition of ePROs to readily available biomedical data means that clinicians could more effectively deliver patient-centred care without the necessity of the patient being physically present. This study also suggests that remote symptom monitoring could offer patients the safety and confidence to dialyse at home and arguably ePROs could assist the HHD service in maintaining its patient-centred approach while serving ever increasing numbers.

There are limitations to this study. Participants needed to be English speakers; this could affect transferability of findings. Views of carers were not specifically sought but their influence and importance were clearly identified by patients, suggesting further research targeting this group is warranted. Critically, data collection took place before SARS-COV-2 pandemic and experiences and perceptions around digital data capture and new approaches to healthcare delivery may well have shifted.

To conclude, the SARs-COV-19 pandemic has caused an irreversible shift in healthcare delivery, with increased use of digital communication and assessment. While the nephrology community, both patients and HCPs, are largely supportive of the concept of ePROs, there remain caveats to their routine and systematic use. Stakeholders need to be convinced by empirical evidence, considering the best available measures and methodological considerations. By exploring the experiences, views and perceptions of major stakeholders, this study identified key factors at organisational and individual levels which would assist effective implementation of ePROs. Further research will then be required to evaluate any subsequent ePRO interventions to empirically demonstrate the impact and benefit of their use to the dialysis community.

Author affiliations
[1]Research and Development, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[2]Department of Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[3]Centre for Patient Reported Outcomes Research, Institute of Applied Health Research, University of Birmingham, Birmingham, UK
[4]NIHR SMRC, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[5]NIHR Birmingham Biomedical Research Centre, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[6]Centre for Regulatory Science and Innovation, Birmingham Health Partners, Birmingham, UK
[7]NIHR Applied Research Collaboration West Midlands, University of Birmingham, Birmingham, UK
[8]School of Allied Health and Community, University of Worcester, Worcester, UK

Twitter Nicola Elzabeth Anderson @neanderson100 and Christel McMullan @christel_uob

Acknowledgements PROM-HD PPI Group, Renal Research Patient Advisory Group, Queen Elizabeth Hospital Kidney Patients Association (QEKPA).

Contributors NEA, CMcM, MC, MD, PC, OLA, DK: substantial contribution to the conception and design of the study. NEA: data collection. NEA, CMcM, DK: analysis and interpretation of data for the work. NEA, CMcM, MC, MD, PC, OLA, DK: drafting and revising the work critically for important intellectual content and final approval of version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding (Nicola Anderson, Clinical Doctoral Research Fellow, Grant Reference ICA-CDRF-2018-04-ST2-027) is funded by Health Education England (HEE) / National Institute for Health Research (NIHR) for this research project.

Disclaimer The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The study sponsor and funders have no role in study design, including collection, management, analysis and interpretation of data; writing of the report and the decision to submit the report for publication.

Competing interests MC is an NIHR senior investigator and receives funding from the NIHR Birmingham Biomedical Research Centre, the NIHR Surgical Reconstruction and Microbiology Research Centre and NIHR Applied Research Collaboration West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, UCB Pharma and GSK. MC has received personal fees from Astellas, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute (PCORI) outside the submitted work. DK reports grants from Macmillan Cancer Support, Innovate UK, the NIHR, NIHR Birmingham Biomedical Research Centre and NIHR SRMRC at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, and personal fees from Merck and GSK outside the submitted work. OLA is funded by the NIHR Birmingham Biomedical Research Centre and declares personal fees from Gilead Sciences and GSK.

Patient consent for publication Not required.

Ethics approval Ethics approval was issued on 13 September 2017 (Ref No: 17/WA/0281) by Wales 7 Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Deidentified data may be available upon reasonable request via the corresponding author (ORCID 0000-0002-0614-3198). Protocol available doi:10.1136/bmjopen-2018-021532.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: https://creativecommons.org/licenses/by/4.0/.

ORCID iDs
Nicola Elizabeth Anderson http://orcid.org/0000-0002-0614-3198
Christel McMullan http://orcid.org/0000-0002-0878-1513
Melanie Calvert http://orcid.org/0000-0002-1856-837X
Derek Kyte http://orcid.org/0000-0002-7679-6741

REFERENCES

1 Bikbov B, Purcell CA, Levey AS, *et al*. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of disease study 2017. *The Lancet* 2020;395:709–33.
2 Almutary H, Bonner A, Douglas C. Symptom burden in chronic kidney disease: a review of recent literature. *J Ren Care* 2013;39:140–50.
3 Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol* 2009;4:1057–64.
4 KDIGO. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney International Supplements* 2013;3:1–150.
5 Evangelidis N, Tong A, Manns B, *et al*. Developing a set of core outcomes for trials in hemodialysis: an international Delphi survey. *American Journal of Kidney Diseases* 2017;70:464–75.
6 Tong A, Manns B, Hemmelgarn B, *et al*. Establishing core outcome domains in hemodialysis: report of the standardized outcomes in Nephrology-Hemodialysis (SONG-HD) consensus workshop. *Am J Kidney Dis* 2017;69:97–107.
7 Viecelli AK, Tong A, O'Lone E, *et al*. Report of the standardized outcomes in nephrology-hemodialysis (SONG-HD) consensus workshop on establishing a core outcome measure for hemodialysis vascular access. *Am J Kidney Dis* 2018;71:Pages 690–700.
8 Urquhart-Secord R, Craig JC, Hemmelgarn B, *et al*. Patient and caregiver priorities for outcomes in hemodialysis: an international nominal group technique study. *Am J Kidney Dis* 2016;68:444–54.
9 Verberne WR, Das-Gupta Z, Allegretti AS, *et al*. Development of an international standard set of value-based outcome measures for patients with chronic kidney disease: a report of the International Consortium for health outcomes measurement (ICHOM) CKD Working group. *Am J Kidney Dis* 2019;73:372–84.
10 International Consortium for Health Outcomes Measurement (ICHOM). Chronic kidney disease: data collection reference guide. ICHOM; 2017 OCT 25th 2017. contract No.: version 1.0, 2021. Available: https://www.ichom.org/wp-content/uploads/2020/02/ICHOM-Chronic-Kidney-Disease-Reference-Guide-20171025-1.00.pdf
11 FDA. Guidance for industry. Patient reported outcomes measures: Use in medical product development to support labeling claims. Docket No:FDA-2006-D-0362, 2009. Available: https://www.fda.gov/media/77832/download
12 UK Renal Assocation & Kidney Care UK. Patient reported experience of kidney care in the UK 2020, 2021. Available: https://www.kidneycareuk.org/news-and-campaigns/prem/#:~:text=PREM%20stands%20for%20Patient%20Reported%20Experience%20Measures.%20The,improvement%20can%20be%20made%20from%20a%20patient%20perspective
13 Smith V, Wise K. Evaluating nurses' action outcomes and exploring their perspectives of implementing the POS-S (Renal) assessment tool for haemodialysis patients. *Renal Society of Australasia Journal* 2017;13:14–21.
14 Schick-Makaroff K, Mharapara P. Use of electronic patient-reported outcomes in the care of patients with kidney failure. *Nephrol Nurs J* 2020;47:465–72.
15 Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Using patient-reported outcome measures (PROMs) to promote quality of care and safety in the management of patients with advanced chronic kidney disease (PRO-trACK project): a mixed-methods project protocol. *BMJ Open* 2017;7:e016687.
16 Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Development and usability testing of an electronic patient-reported outcome measure (ePROM) system for patients with advanced chronic kidney disease. *Comput Biol Med* 2018;101:120–7.
17 Aiyegbusi OL, Kyte D, Cockwell P, *et al*. Patient and clinician perspectives on electronic patient-reported outcome measures in the management of advanced CKD: a qualitative study. *Am J Kidney Dis* 2019;74:pages 167–78.
18 Kyte D, Anderson N, Auti R, *et al*. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. *J Patient Rep Outcomes* 2020;4:55.
19 Gabbard J, McLouth CJ, Brenes G, *et al*. Rapid electronic capturing of patient-reported outcome measures in older adults with end-stage renal disease: a feasibility study. *Am J Hosp Palliat Care* 2021;38:432-440.
20 Viecelli A, Dansie K, McDonald S, *et al*. Symptom monitoring with feedback trial (swift) pilot to explore the feasibility and acceptability of electronic patient reported outcome measures (e-proms) data capture and feedback. *Nephrology Dialysis Transplantation* 2020;35:iii137.
21 Breckenridge K, Bekker HL, Gibbons E, *et al*. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. *Nephrol Dial Transplant* 2015;30:1605–14.
22 Van Der Veer SN, Ercia A, Caskey FJ, *et al*. Developing an intervention to implement electronic patient-reported outcomes in renal services in the UK. *Stud Health Technol Inform* 2020;270:936–40.
23 Schick-Makaroff K, Molzahn AE. Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. *BMC Health Serv Res* 2017;17:439.
24 Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. *Health Qual Life Outcomes* 2015;13:2.
25 Schougaard LMV, Larsen LP, Jessen A, *et al*. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow-up in chronic and malignant diseases. *Qual Life Res* 2016;25:525–34.
26 Trillingsgaard C NBK, Hjollund NH, Lomborg K. Use of patient-reported outcomes in outpatient settings as a means of patient involvement and self-management support - a qualitative study of the patient perspective. *European Journal for Patient-Centred Healthcare* 2016;4:359–67.
27 Schick-Makaroff K, Tate K, Molzahn A. Use of electronic patient reported outcomes in clinical nephrology practice: a qualitative pilot study. *Can J Kidney Health Dis* 2019;6:2054358119879451.
28 Yang Y, Chen H, Qazi H, *et al*. Intervention and evaluation of mobile health technologies in management of patients undergoing chronic dialysis: Scoping review. *JMIR Mhealth Uhealth* 2020;8:e15549.
29 Basch E, Deal AM, Dueck AC, *et al*. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA* 2017;318:197–8.
30 Lizée T, Basch E, Trémolières P, *et al*. Cost-Effectiveness of web-based patient-reported outcome surveillance in patients with lung cancer. *J Thorac Oncol* 2019;14:1012–21.
31 UK Renal Association. Electronic patient-reported outcomes (ePROs) for the kidney patient community 2020. available at. Available: https://wwwyoutubecom/watch?v=iQ0mOVee_dg&feature=youtube
32 Kelly LM, Cordeiro M. Three principles of pragmatism for research on organizational processes. *Method Innov* 2020;13:2059799120937242.
33 Yvonne Feilzer M, Feilzer YM. Doing mixed methods research Pragmatically: implications for the rediscovery of pragmatism as a research paradigm. *J Mix Methods Res* 2010;4:6–16.
34 Kaushik V, Walsh CA. Pragmatism as a research paradigm and its implications for social work research. *Soc Sci* 2019;8:255.
35 Damschroder LJ, Aron DC, Keith RE, *et al*. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009;4:50.
36 Sandelowski M. Whatever happened to qualitative description? *Res Nurs Health* 2000;23:334–40.
37 Sandelowski M. What's in a name? qualitative description revisited. *Res Nurs Health* 2010;33:77–84.

38 Kim H, Sefcik JS, Bradway C. Characteristics of qualitative descriptive studies: a systematic review. *Res Nurs Health* 2017;40:23–42.
39 Neergaard MA, Olesen F, Andersen RS, *et al*. Qualitative description - the poor cousin of health research? *BMC Med Res Methodol* 2009;9:52.
40 Anderson NE, Calvert M, Cockwell P, *et al*. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. *BMJ Open* 2018;8:e021532.
41 Etikan I. Comparison of convenience sampling and purposive sampling. *American Journal of Theoretical and Applied Statistics* 2016;5:1.
42 Standardised Outcomes in Nephrology (SONG). The song Handbook. Version 1. Sydney, Australia, 2017. Available: songinitiative.org/reports-and-publications/
43 Hays R D KJD, Mapes DL, Coons SJ, *et al*. *Kidney disease quality of life short form (KDQOL-SF): a manual for use and scoring. in: Rand, editor*. Santa Monica, CA: Rand, 1997. https://www.rand.org/content/dam/rand/pubs/papers/2006/P7994.pdf
44 Hays RD, Kallich JD, Mapes DL, *et al*. Development of the kidney disease quality of life (KDQOL) instrument. *Qual Life Res* 1994;3:329–38.
45 Pos-pal.org. Pos palliative care outcome scale, 2017. Available: https://pos-pal.org/maix/ipos-renal-in-english.php
46 Braun V, Clarke V. Can I use TA? Should I use TA? Should I *not* use TA? Comparing reflexive thematic analysis and other pattern-based qualitative analytic approaches. *Couns Psychother Res* 2021;21:37–47.
47 van Oers HA, Teela L, Schepers SA, *et al*. A retrospective assessment of the KLIK PROM portal implementation using the consolidated framework for implementation research (CFIR). *Qual Life Res* 2020;2.
48 Birt L, Scott S, Cavers D, *et al*. Member checking: a tool to enhance Trustworthiness or merely a NOD to validation? *Qual Health Res* 2016;26:1802-1811.
49 Kerr C, Nixon A, Wild D. Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. *Expert Rev Pharmacoecon Outcomes Res* 2010;10:269–81.
50 UK Renal Registry. Uk renal registry 22nd annual report – data to 31/12/2018,. Bristol, United Kingdom, 2020. Available: https://renal.org/audit-research/22nd-annual-report-data-31122018
51 Coulter A. Measuring what matters to patients. *BMJ* 2017;356:j816.
52 Tong A, Winkelmayer WC, Wheeler DC, *et al*. Nephrologists' perspectives on defining and applying patient-centered outcomes in hemodialysis. *Clin J Am Soc Nephrol* 2017;12:454–66.
53 Denis F, Basch EM, Lethrosne C, *et al*. Randomized trial comparing a web-mediated follow-up via patient-reported outcomes (pro) vs. routine surveillance in lung cancer patients: final results. *Journal of Clinical Oncology* 2018;36:6500.
54 Denis F, Basch E, Septans A-L, *et al*. Two-Year survival comparing web-based symptom monitoring vs routine surveillance following treatment for lung cancer. *JAMA* 2019;321:306–7.
55 Greenhalgh J, Abhyankar P, McCluskey S, Takeuchi E, *et al*. How do doctors refer to patient-reported outcome measures (PROMs) in oncology consultations? *Qual Life Res* 2013;22:939–50.
56 Kyte D, Bishop J, Brettell E, *et al*. Use of an electronic patient-reported outcome measure in the management of patients with advanced chronic kidney disease: the RePROM pilot trial protocol. *BMJ Open* 2018;8:e026080.
57 Schick-Makaroff K, Thummapol O, Thompson S, *et al*. Strategies for incorporating patient-reported outcomes in the care of people with chronic kidney disease (pro kidney): a protocol for a realist synthesis. *Syst Rev* 2019;8:20.
58 Morton RL, Lioufas N, Dansie K. Patient reported outcome measures in Australian and New Zealand renal units: an anzdata survey of current practice. *Nephrology* 2019;23:32.
59 Narva AS, Norton JM, Boulware LE. Educating patients about CKD: the path to self-management and patient-centered care. *Clin J Am Soc Nephrol* 2016;11:694–703.
60 Wilkie M, Barnes T. Shared hemodialysis care: increasing patient involvement in center-based dialysis. *Clin J Am Soc Nephrol* 2019;14:1402–4.
61 Rotenstein LS, Huckman RS, Wagle NW. Making patients and doctors Happier — the potential of patient-reported outcomes. *N Engl J Med Overseas Ed* 2017;377:1309–12.
62 Savino M, Casula A, Santhakumaran S, *et al*. Sociodemographic features and mortality of individuals on haemodialysis treatment who test positive for SARS-CoV-2: a UK renal registry data analysis. *PLoS One* 2020;15:e0241263.
63 Roper T, Kumar N, Lewis-Morris T, *et al*. Delivering dialysis during the COVID-19 outbreak: strategies and outcomes. *Kidney Int Rep* 2020;5:1090–4.
64 Hull SA, Rajabzadeh V, Thomas N, *et al*. Do virtual renal clinics improve access to kidney care? A preliminary impact evaluation of a virtual clinic in East London. *BMC Nephrol* 2020;21:10.
65 Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.

3.2 Key findings:

Chapter 3 reports a qualitative study which explored the experiences and perceptions of patients and healthcare professionals (HCPs) on the collection and use of PROs in HD settings. Semi-structured interviews highlighted the importance of measuring outcomes that matter to patients and clinicians, and participants broadly agreed that the SONG-HD COS was relevant and comprehensive. It was identified that further evidence on measure selection to capture PRO data in a non-burdensome way was required. Chapter 4 aims to further investigate issues of measure selection and the importance of measuring outcomes of relevance to the HD population by reporting a study which explored whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS: along with data on key PROM characteristics.

Findings from this chapter also highlight the value of empirical evidence to demonstrate the potential benefits of PROs to gain 'buy-in' from clinicians, particularly from doctors. Patients indicated that they needed to know the purpose of PROs data collection, to be reassured that they were not taking part in a 'tick-box' exercise. Participants indicated that ePRO systems needed to be operationally flexible for routine functioning to assess individual patient data and collate real-world data for aggregate use. Additionally, any implementation must sit within a wider framework of education and support. Participants felt careful consideration needed to be given to barriers and facilitators of ePROs implementation: including effective leadership,

consideration of the role of ‘champions’, effective launch plans and ongoing evaluation. Chapter 5 reports a mixed methods study which comprehensively identifies existing and developing ePROs systems around the world which were designed specifically for use in kidney care in to ascertain their key characteristics and the factors for successful implementation, including barriers and facilitators.

Appendices for Chapter 3:

Appendix 3.1 PROM-HD Participant Information Sheet – Patient

Appendix 3.2 PROM-HD Participant Information Sheet – HCP

Appendix 3.3 PROM-HD Exemplar PROMs – KDQOL-SF, KDQOL-36, IPOS-Renal

Appendix 3.4 PROM-HD Topic Guide for use with patient participants

Appendix 3.5 PROM-HD Topic guide for use with HCP's

Appendix 3.6 Table 1 Patient Data Saturation tables and interview characteristics

Appendix 3.7 Table 2 HCP Data Saturation tables and interview characteristics

Appendix 3.8 Pre-publication Consolidated Criteria for Reporting Qualitative Studies (COREQ) checklist

Chapter 4: A scoping review of patient-reported outcome measures used in haemodialysis: Are we measuring what matters?

A scoping review of patient-reported outcome measures used in haemodialysis: Are we measuring what matters?

4.1 Introduction

While it is evident from the literature and findings from the preceding study that both patients and HCP participants felt that PROs could support the delivery of person-centred care in HD settings, key decisions need to be made before implementation can proceed (1). One of the decisions that can be challenging for proponents of PROs, and particularly those who are unfamiliar with the methodological development of PROMs and their psychometric assessment, is the choice of measure(s). This is exacerbated by the number of PROMs available for use with the HD population (2, 3). When choosing a measure, consideration needs to be given to the outcomes measured, but also practical considerations such as feasibility of administration and ease of interpretation. Findings from chapter 3 highlighted the significance of measuring what matters to patients (4, 5), and patient participants broadly confirmed that the COS as developed by the SONG-HD initiative (6) was relevant and important. Patient participants also stated that generally, length of measure was not an issue, provided there was a clear purpose for completion. However, there was a dislike of repetitive questions, and the potential time burden of lengthy questionnaires was seen as an inconvenience for carers, if completion support was required. HCP participants felt the length of questionnaire was an issue and ideally the shorter the better. They also felt that some of the current validated measures were too long and were consequently burdensome for patients to complete and clinicians to review (4). Given such findings, the aim of

the study presented in this chapter was to explore whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS; along with data on key PROM characteristics such as number of items/domains, scoring, available translations, modes of administration, time to complete, recall period and accessibility and permissions.

An increased understanding of COS and PROM alignment and associated questionnaire characteristics will assist clinicians in the process of PROM selection, aimed at optimising ePROs implementation to support the management of patients undergoing HD.

This chapter is presented in manuscript format in the style of the peer-reviewed journal BMJ Open; however, tables and figures are inserted within the text to facilitate review.

A scoping review of patient-reported outcome measures used in haemodialysis: Are we measuring what matters?

Nicola Anderson MSc, RN Dip HE[1, 2, 3], Ben Fletcher PhD[4], Derek Kyte PhD[1, 5], Mark Anderson PhD[6], Christel McMullan PhD[1, 7,8],
Paul Cockwell PhD[1 9], Olalekan L Aiyegbusi PhD [1, 2, 8, 10, 11] Melanie Calvert PhD[1, 2, 7, 8,10, 11]

[1] Centre for Patient Reported Outcomes Research, Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom
[2] Birmingham Health Partners Centre for Regulatory Science and Innovation
[3]Research and Development, University Hospitals Birmingham NHS Foundation Trust
[4] National Institute for Health and Care Excellence (NICE)
[5] School of Allied Health and Community, University of Worcester, Worcester, UK
[6] Sandwell and West Birmingham NHS Trust
[7] NIHR SRMRC, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, UK
[8]NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics
[9] Department of Nephrology, University Hospitals Birmingham NHS Foundation Trust
[10] NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, UK
[11] NIHR Applied Research Collaboration West Midlands, University of Birmingham
Corresponding author: Nicola Anderson [redacted]

Funding Statement
This presentation refers to independent research funded by the National Institute of Health Research (NIHR) under its Clinical Doctoral Research Fellowship Programme (Grant Reference ICA-CDRF-2018-04-ST2-027)

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The study sponsor and funders have no role in study design, including collection, management, analysis and interpretation of data; writing of the report and the decision to submit the report for publication.

4.2 Abstract

Patients undergoing haemodialysis (HD) often experience significant symptom burden and reduced health-related quality-of-life (HRQOL). This was recognised in core outcome set (COS) development, outlining the minimum set of outcomes that should be measured and reported in clinical trials and routine care. Internationally endorsed HD COS prioritise the measurement of symptom burden and HRQOL, using robust patient-reported outcome measures (PROMs). However, it is unclear if currently available PROMs adequately cover all recommended outcomes. An increased understanding of alignment between recommended outcomes and available measures will support clinicians in the process of PROM selection, aimed at enhancing the management of patients undergoing HD.

4.2.1 Objectives

To explore whether PROMs adequately cover outcomes recommended in HD-specific COS; by (1) conducting a systematic search of published literature for COS and validated PROMs used in HD settings and (2) summarising PROM characteristics and affinity mapping PROMs items against recommended outcomes in available COS.

4.2.2 Design

Scoping review

4.2.3 Setting and Participants

Adults with end stage kidney disease undergoing haemodialysis.

4.2.4 Results

This review was unable to identify one measure covering all COS outcomes. Those involved in measure selection currently have three options, to use (i) a single well investigated, easily accessible measure i.e., KDQOL-SF (80 items) offering a good assessment of overall HRQOL and the effects of living with kidney disease, while noting the KDQOL-SF is lengthy and this could lead to reduced compliance, or (ii) a shorter measure such as the KDQOL-36 (36 items), accepting reduced outcome coverage. or (iii) a combination of shorter measures to maximise coverage in as few items as possible. However, this may lead to item overlap and repetition, plus burden associated with differing instructions, recall times and response options.

4.2.5 Conclusion

Research should focus on optimising existing measures, or utilising new technologies such as computer adaptive testing, to improve COS coverage and reduce questionnaire burden.

4.2.6 Strengths and Limitations

- This review provides the first comprehensive affinity mapping of PROMs with international core outcome sets developed for research and routine care of patients undergoing HD.
- Detailed charting of core outcome set and PROM characteristics, and affinity mapping verified by more than one researcher to maintain data integrity.
- This review used a comprehensive, previously tested and reported search strategy.

- Searches were limited to English Language.
- Following latest guidance on scoping review methodology, an assessment of the methodological quality of included studies has not been undertaken.

4.3 Introduction

Chronic kidney disease (CKD) is a progressive condition currently affecting an estimated 843.6 million people worldwide (7, 8). For patients experiencing end stage kidney disease (ESKD) and able to access treatment, haemodialysis (HD) is the most common form of kidney replacement therapy (KRT) (9). Patients undergoing HD experience high levels of co-morbidity and significant symptom burden, which along with factors such as lifestyle and dietary modifications due to disease and treatment, can lead to significant reductions in health-related quality-of-life (HRQOL) (3, 10, 11).

Measuring such outcomes for these individuals is an important priority, as it may support more patient-centred care (12). Traditionally, measurement in both HD trials and routine care has focused on biomedical outcomes, such as blood results, which patients often report have little meaning for their daily lives (6). While patients value long life, many regard symptom reduction, maximising function and improving psychosocial status as more important than longevity (12, 13).

Patient-Reported Outcome Measures (PROMs) are standardised questionnaires used to assess outcomes such as symptoms, HRQOL, functional status, and other aspects of psychological, social, and spiritual well-being directly from patients, without requiring interpretation from others (14). Such data can be used for multiple applications;

individually to tailor care to patient needs, or at an aggregate level for audit and benchmarking to improve overall kidney patient care (15, 16).

There are a large number of PROMs available for use in adults with pre-KRT CKD and those who are dialysis-dependent or have a kidney transplant (1). There are also a wide range of symptoms experienced by patients with CKD that may be amenable to measurement using PROMs (3). As a result, it can be challenging for clinicians to choose the most appropriate PROM(s). This problem has been highlighted in a recent systematic review of symptom burden and HRQOL, which included studies involving 199,147 participants from 62 countries (3). The review identified 68 symptoms that were prevalent in CKD, that were measured using more than 50 PROMs across the literature and the use of so many different PROMs may seriously hinder evidence synthesis (3).

It is for this reason that there has been considerable investment in the development of core outcome sets (COS) for use in nephrology (6, 17). COS are an agreed, standardised set of outcomes that represent the minimum that should be measured and reported in all clinical trials of a specific condition, and this consistency of measures should facilitate both comparison and combination of results thereby reducing research waste (18). COS are also suitable for use in routine care, clinical audit and other research (19). Core outcomes that are of relevance to all key stakeholders i.e., patients, carers and healthcare professionals, are agreed using consensus methodology (19). COS developers should involve those interested parties who have experienced or are affected by the condition (e.g., patients, family members, and carers) (20).

To date, however, there has been no research to explore whether currently available PROMs adequately cover all outcomes/domains that have been recommended in HD-specific COS. An increased understanding of COS and PROM alignment, along with key measure characteristics, would assist clinicians in the process of PROM selection, aimed at supporting the management of patients undergoing HD.

Therefore, the primary aim of this study was to conduct a scoping review to explore whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS. The study objectives were to: (1) conduct a systematic search of published literature for COS and validated PROMs used in HD settings; (2) summarise PROM characteristics and map PROMs items/domains against available COS.

4.4 Study Design

Scoping reviews are effective in synthesizing research evidence and are often used to map existing findings in a given field in terms of its nature, features, and volume (21) therefore scoping review methodology was chosen as an effective means to underpin evidence synthesis (22). This scoping review was conducted and reported according to a registered protocol: Review Registry 1269 https://www.researchregistry.com/browse-theregistry#registryofsystematicreviewsmetaanalyses/registryofsystematicreviewsmeta-analysesdetails/61b5c2584c1323001f3b011f/ and reported using the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) checklist (see Appendix 4.1) (23).

4.4.1 Search strategy

The Core Outcome Measures in Effectiveness Trials (COMET) database and the International Consortium for Health Outcomes Measurement (ICHOM) website (www.ichom.org) were searched for core outcome sets relevant to HD populations (17). Results were filtered for English language only papers. A manual search of reference lists and citations of selected papers was also carried out. The search strategy to identify validated PROMs being used in HD settings was based upon that developed and reported in a systematic review by Aiyegbusi et al 2017 (2); which was used as an index paper for this study (See Appendix 4.2 for sample search strategy). Additional searching was limited to the time since the searches for this comprehensive published review were undertaken. Therefore, relevant databases including MEDLINE, EMBASE, PsycINFO and CINAHL Plus and the first five pages of Google Scholar were systematically searched from 21st December 2015 to 16th Nov 2021. The Aiyegbusi et al (2017) review identified 14 PROMs used within HD populations (2) and these measures were included in the evidence synthesis. Search records were downloaded into Endnote X9, and duplicates removed.

4.4.2 Setting & Study Population

Adults with end stage kidney disease undergoing haemodialysis.

4.4.3 Screening process

All titles and abstracts were screened independently by two reviewers (NEA and BF). Rayyan Intelligent Systematic software was used to manage the selection and screening process (24). Full-text articles were obtained for all studies which potentially met the eligibility criteria and were independently reviewed (NEA and BF). Disagreements regarding eligibility were resolved through discussion.

4.4.4 Selection of core outcome sets and studies

Core outcome sets were included if they established core outcomes relevant to adult patients with ESKD requiring treatment with HD. Core outcome sets developed for clinical trials, research or routine practice were included. Core outcome sets which focused on children, other kidney replacement modalities such as peritoneal dialysis or transplantation and kidney disease subtype specific COS were excluded. Only core outcomes that could be measured using a PROM were included in the analysis (see Table 1).

Studies were included if they: (1) focused on PROMs used specifically for measuring HRQOL and/or symptoms (the constructs of interest) in the study population; and (2) reported either the development of the PROM and/or an evaluation of one or more psychometric properties. Articles clinical trial reports, editorials, reviews, and conference abstracts were excluded. In addition, studies that focussed on clinician-assessed instruments, patient experience, satisfaction or activation measures were also excluded. PROMs developed for use in patients with acute kidney injury or in

patients below 18 years of age were excluded, as they were beyond the scope of this review. Studies and associated measures unavailable in English were not included.

Table 1: Core Outcome Sets (6, 17)

SONG HD Core Domains **TIER ONE** Critically Important to all stakeholders	**TIER TWO** Critically important to some stakeholders	**TIER THREE** Important to all or some stakeholders
Fatigue Feeling tired with no energy for weeks, for most of the time	Ability to work	Anxiety/ Stress
CVD disease of the heart and blood vessels (e.g., heart attack, stroke, blockage of blood vessels)	Ability to travel to go away for holiday/vacation, event, visiting family, work	Bone Health
VA (Problems with fistula, graft, or catheter required for dialysis (e.g., access infections, bleeding, bruising, pain, discomfort, clotting)	Anaemia	Calcium
Mortality No. of people on hemodialysis therapy who have died, risk for death, how long the patient will live	Blood pressure	Cognition
	Depression	Cramps
	Dialysis Adequacy How well the dialysis cleans the blood, clearance, Kt/V	Financial Impact
	Drop in BP	Food Enjoyment
	Hospitalisation	Itching
	Impact on family and friends	Nausea and Vomiting
	Infection/Immunity	Parathyroid Hormone
	Mobility	Phosphate
	Pain	Restless legs syndrome
	Potassium	Sexual function
	Target weight	Sleep
	Washed out after dialysis	
	Dialysis Free Time (Time (hours/days) not doing dialysis	

ICHOM PROM domains
Health-Related Quality-of-Life
Pain
Fatigue
Physical function
Depression
Daily activity

Key
Outcome capable of measurement by PROM
Clinical outcome

4.4.5 Data Charting and extraction

Data from studies and associated PROMs were charted by NEA using piloted data charting forms. As per the protocol, 20% of data extracted from studies was checked by BF. Any discrepancies were resolved through discussion. (See table 2). Relevant study investigators were contacted for unreported data or additional details. The term 'not reported' was used when information was unobtainable.

4.4.6 Analytical Approach and Data Synthesis

A descriptive tabular and narrative synthesis was conducted of key study, COS, and PROM characteristics (see tables 1-3). Affinity mapping was used to undertake an analysis of outcome domains assessed by the identified measures to highlight gaps (25). Affinity mapping involves grouping similar items or domains from the PROMs into clusters and then charting single items or clusters under relevant outcomes. The mapped items/domain are said to have a "mutual affinity" with the relevant outcome. Affinity mapping is an inductive process designed to obtain agreement that items sharing a common meaning or definition belong in the same outcome group (25). Affinity mapping was undertaken by NEA and checked independently by MA; any disagreement was reached by agreement. A comments log was maintained during mapping to ensure consistency i.e., items referring to 'tiredness' were mapped to the outcome 'fatigue'. Affinity mapping data is presented in text and table format, including descriptive statistics (percentages) (Table 4). For each core outcome assessed by a PROM item or domain, a score of 1 was given; partial coverage was given a score

of 0.5. For each PROM, coverage could be scored from 0 (no COS PROs assessed by the measurement tool) to 20 (all COS PROs assessed). This score was converted to a percentage i.e., the higher the percentage, the more outcomes measured (see Table 4).

Table 2 Study Characteristics

Study Identifiers	Country	Language of study	Study design	Study population /setting	Study measure	Application of PROs	Sample size (n)	Mean age	Duration of HD (mean)
							(% females)		
(001) Elamin 2019 (26)	Sudan	Arabic	Cross cultural validation study	Adult patients undergoing HD or transplant	KDQOL-36	Not reported	test-retest reliability 10 HD patients, testing other measurement properties 62 HD patients/82 transplant patients	Not reported	Not reported
(005) Bautovich et al 2018 (27)	Australia	English	Evaluation of measurement properties	Adult patients undergoing HD	Beck Depression Inventory, Cognitive Depression Index	clinical practice	n=45 (42%)	65-74	1241 days
(007) Nochaiwong et al 2018 (28)	Thailand	Thai	Cross sectional study	Adult patients undergoing HD with Uraemic Pruritis	UP-Dial	clinical practice	n = 258 (39.5%) PD 76% HD 24% subgroup analysis demonstrated no sig dif for PD/HD groups	59.2 years	> 3 months median not reported

(010) Goh 2019 (29)	Malaysia	Malay	Cross cultural adaption/ validation study	CKD patients stages 1-3A and HD patients, tertiary hospital and HD centres	KDQOL-36	Not reported	HD patients n=90 CKD stages 1-3A n=91 (37.8%)	50.5 years	36 months
(014) Flythe 2019 (30)	United States of America	English	Development and validation of new measure	Adult HD patients receiving in-centre dialysis.	SMaART-HD	for clinical practice and research use	n = 42 (54.8%) patients in concept elicitation interviews + n = 52 (44.2%) patients in cognitive interviews	Concept elicitation interviews 57.3 ± 13 years. Cognitive interviews 58.5 ± 12 years	> 6 months
(019) Schouten 2019 (31)	The Netherlands	Dutch, English, Turkish, Moroccan Arabic translations .	Observational retrospective cohort study	Dialysis centres n=11	Beck Depression Inventory	Clinical practice and research	n=687 inc HD (88%) and PD (12%) (38% female overall)	64 years	At least 90 days
(027) Finkelstein 2018 (32)	United States of America	English	Evaluation of measurement properties	HD/PD patients on a clinical trial	SF-36, FACT-An	Research	HD and PD patients n=59 (47.5%) Paper does not state how many patients received HD.	50 years	2 weeks - 4 months (new dialysis patients)

(028) Picariello 2016 (33)	United Kingdom	English	Evaluation of measurement properties	Adult patients undergoing HD	Chalder Fatigue Q'naire	Research	n=174 HD patients (36.8%)	58.9 years	50.6 months
(031) Peipert 2018 (34)	United States of America	English	Evaluation of measurement properties	Adult patients undergoing HD	KDQOL-36	Clinical practice and Research	n = 39,843 patients 84% HD, 14% PD, 2% other (not stated)	66 years (18–100) white pts 59 years (18–97) Black pts	Not reported
(032) Rodakowska 2020 (35)	Poland	Polish	Cross sectional study	Adult patients undergoing HD	OHIP-14, GOHAI	Clinical practice and research	n=72 (60.7%)	63.2±15.2 years	43.8 months.
(034) van der Willik 2019 (36)	The Netherlands	Dutch English	Four phase mixed methods study	Patients with advanced CKD stages 4-5, including patients with ESKD receiving dialysis (HD/PD) and transplant.	Dialysis Symptom Index, IPOS-Renal	Clinical practice	Phase 2 n=13/18 patients on HD Phase 4 n=17/151 patients on HD	Phase 2: 20-83 years (50%) Phase 4 not reported	Not reported
(038) Dang et al 2016 (37)	Vietnam	Vietnamese	Cross cultural validation study - methodological study	Adult patients undergoing HD, national hospital dialysis units	HSS-V (Modified HSS)	Clinical Practice and research	n=180 (43.3%)	45.5 ± 14.9 years (range: 21 to 79 years)	Mean ± SD = 5.7 ± 3.3 years) range: 0.3-19 years
(039) Sharif et al 2020 (38)	Iran	Farsi	Cross cultural validation study - methodological study	Adult patients undergoing HD	Death Anxiety Scale	Clinical practice	N=507 (51.7%) (n=10 HD patients assessed content validity)	38.90 years SD 13.48.	Not reported

(040) Chao et al 2016 (39)	Taiwan	Taiwanese-Chinese	Cross cultural validation study - methodological study	CKD stages 1-5 including HD and PD patients	KDQOL-36	Clinical practice /Research	n=428 Participant totals in CKD Stages 1:16 (4%), 2: 36 (8%), 3: 153 (36%), 4: 130 (30%), 5: 93 (22%) Females: 41%	62.0 years (SD = 12.3 years)	Not reported
(045) Chilcot et al 2018 (40)	United Kingdom	English	Evaluation of measurement properties	Adult patients undergoing HD	PHQ-ADS	Clinical Practice /Research	n=182 (44%)	54.9 years SD (16.9)	Not reported
(046) Collister et al 2019 (41)	Canada	English	Cross sectional cohort study	Adult patients undergoing HD, tertiary and community HD Units	ESAS RLS (based on ESASr-Renal), IRLS, Single Qu to diagnose RLS	Clinical practice	n=50 (48%)	64 (SD = 12.4) years	at least the last 90 days
(047) Chilcot et al 2018 (42)	United Kingdom	English	Evaluation of measurement properties	Adult patients undergoing HD	BDI-II, PHQ-9	Clinical practice /research	n=709 (36.7%)	64.1 (SD 16.4) years.	Median dialysis vintage of 33 months (inter quartile range=59)
(049) Collister et al 2019 (43)	Canada	English	Cross sectional study	Adult patients receiving HD at tertiary/ community dialysis units	ESASr (HADs used as reference standard)	Clinical practice	n=50 (48%)	64 (SD = 12.4) years	For at least 90 days before study entry

(050) Gutierrez-Sanchez et al 2016 (44)	Spain	Spanish	Cross cultural validation study - methodological study	Adult patients with ACKD receiving dialysis or renal conservative management (without dialysis)	POS-S-Renal	Clinical practice and research	n=30 (cross cultural adaption study) n=61/200 HD patients validation study (42.6%)	59.15 years (±15.4)	Not reported
(052) Biniaz et al 2019 (45)	Iran	Not reported	Development study - mixed method sequential exploratory design	Adult patients undergoing HD in public, private and charity HD units	Subjective Adequacy Questionnaire - SHAMQ	Clinical Practice	n=19/25 (Qualitative phase) n=10 testing face validity n=538 validation study	Not reported	Not reported
(055) Hadjiioannou et al 2020 (46)	United Kingdom	English	Pragmatic non-randomised controlled trial	40 patients across CKD trajectory	HADS, DASI	Clinical practice	Dialysis n=10	57.1 years for HD patients	> 3 months
(056) Dehesa-Lopezet al 2017 (47)	Mexico	Spanish	Cross cultural validation study - methodological study	Adult patients undergoing HD	KDQOL-36	Clinical practice and research	n=194 (55.4%)	54 ± 16 years	more than 1 month
(057) Lai et al 2017 (48)	China	Chinese, dialect not reported	Cross sectional study	Adult patients undergoing HD, University Hospital HD unit	5-D itching scale	Research	n=409 (47.4%)	63 +/- 13 years	> 3 months median not reported

(059) Prado de Souza & de Souza Orlandi 2019 (49)	Brazil	Brazilian Portuguese	Cross cultural validation study - methodological study	Adult patients undergoing HD	PPHS	Clinical Practice and research	n=20 (45%)	47.9 years	At least 6 months
(060) Cohen et al 2019 (50)	United States of America	English	Retrospective observational study	Mixed modalities including PD	KDQOL-36	Annual HRQOL mandated by the Centers for Medicaid and Medicare Services	n=413,964 (total) HD 358,475 (86.6%), HHD 6596 (1.6%) Nocturnal dialysis 2977 (0.7%) Total sample 44.4% female	61.4years ± 14.9 for total sample	29 months
(064) Kittiskulnam, Sheshadri and Johansen 2019 (51)	United States of America	English	Cross-sectional study	Mixed modality - PD/HD	LoPAQ	Clinical practice and research	n=60 (48 HD/12 PD) (21.7%)	58.0 years (SD±12.7)	3.1 (IQR, 1.1–5.8) years
(067) Raj et al 2018 (52)	Australia	English	Cross sectional Methodological study	Adult patients undergoing RRT (PD/HD) or supportive care. Regional outpatient and dialysis services	IPOS-Renal	Clinical Practice	n=81 (65 HD, 10 PD, 6 Supportive Care) (44%)	64.9 years +/- 13.3	Not reported
(071) Cho, Kin and Shim DSI 2018 (53)	Korea	Korean	Cross cultural validation study methodological study	HD patients	Dialysis Symptom Index	Clinical Practice	n=230 (47.4%)	60.5 years (SD 14 years)	4.2 years (+/- 4.1 years)

(074) Rehman & Khan 2017 (54)	Pakistan	English, Urdu	Cross cultural validation study - methodological study	Adult patients receiving HD, tertiary dialysis units	5 D Itching Scale	Clinical Practice and research	n=50 (36%)	38 years IQR [30.75–52.75]	Not reported
(076) Nordyke et al 2020 (55)	United States of America	English	Development study - qualitative	Adult patients receiving HD with current use of AVF, AVG or CVC, four sites across US	HARQ	Clinical Practice and research	Patient Focus groups n=37 (57%) Patient Cognitive interviews n=17 (53%) HCP interviews n=9	Focus Group: Median age group 55-64 years Cognitive interviews: Median age group 45-54 years	At least 6 months
(099) Schouten et al 2020 (56)	The Netherlands	Dutch, English, Turkish, and Moroccan Arabic translations .	Observational retrospective cohort study	Urban dialysis centres	Beck Anxiety Inventory	Clinical Practice and research	n=687 inc HD (88%) and PD (12%) (38% female overall)	65 +/−SD 15 years	13 months (IQR 4-47) for prevalent group
(100) Prest et al 2020 (57)	United States of America	English	Evaluation of measurement properties	Adult patients undergoing HD, outpatient haemodialysis unit	Nutrition Specific Quality of Life Q'naire (NSQOL)	Clinical Practice	n=27 (37%)	60 years +/- 13	Min of 6 months
(104) Manju et al 2020 (58)	India	Malayalam	Cross-cultural validation - cross sectional study	HD patients	KDQOL-SF	Not stated	n=112 (33.9%)	60.55 years	At least 3 months

(106) Tang et al 2021 (59)	Canada	English	Secondary analysis of data collected in cross sectional study	HD and transplant patients. (456 (49%) KTRs and 475 (51%) patients on maintenance dialysis)	ESASR (PHQ-9 GAD-7 used as reference standard)	Clinical Practice	n=931 (40%)	56 years (SD 16)	93% > 3 years
(107) Richarz et al 2021 (60)	United Kingdom	English	Evaluation of measurement properties - validation study - longitudinal cohort	Adult patients receiving HD with stage 5 CKD who have undergone VA access creation, satellite and in-patient dialysis units	vascular access specific quality of life measure (VASQoL)	Clinical Practice and research	Cognitive interviews n=23 longitudinal cohort study n=101 (45.5%)	58.7 years (±14.1)	607 days (IQR 157–1460)
(108) Ajeebi et al 2020 (61)	Saudi Arabia	Arabic	Cross sectional study	Adult patients undergoing HD	KDQOL-36	Research	n=254 (39%)	58.2 years (SD 18.2)	4.9 years (SD 4.9)
(111) Chen at al 2021 (62)	Taiwan	Mandarin Chinese /Taiwanese	Cross sectional, descriptive study	Adult patients undergoing HD, medical university hospital	HSD-22	Clinical Practice	n=216 EFA (55.6%) (n=20 pilot testing)	63 years ± 12.75	≥ 3 months

(119) Joshwa et al 2020 (63)	United States of America	English	Quantitative, non-experimental, descriptive, correlational, before-after design	Adult patients undergoing HD, large dialysis organisation	Piper Fatigue Scale (PFS-12), (PROMIS) – Fatigue	Clinical Practice	n=86 (41.9%)	61.71 years (SD = 13.81, Median = 63.5	> 3 months
(125) Huang et al 2021 (64)	China	English-Chinese (dialect not reported)	Cross-sectional cross-cultural validation study	Adult patients undergoing HD, outpatient haemodialysis units	Low Physical Activity Questionnaire LoPAQ	Clinical Practice	Validity test n=85 (43.5%), reliability test n=29 (34.5%)	Validity test 62.3 years ± 11.8, reliability test 63.7 years ± 10.7	Validity test = 4.9 years ± 3.7 Reliability test 8.9 years ± 7.0
(126) Salazar-robles et al 2021 (65)	Mexico	English - Spanish	Cross-sectional cross-cultural validation study	HD patients, regional HD Units	Council on Nutrition Appetite Questionnaire (CNAQ)	Clinical Practice	n=242 Validation study (39%)	Range 18-80 years old	At least 3 months
(130) Yoosefinejad et al 2021(66)	Iran	English Persian	Cross-sectional cross-cultural validation study	Adult patients undergoing HD, University affiliated dialysis units	5-D itching scale	Clinical Practice	n=90 (44.4%)	Mean 54.4 years (range 39, Median 58 years)	7.04 ± 3.01 years (Range: 13 years)

(135) Ju et al 2020 (67)	United Kingdom, Australia, and Romania	English	longitudinal cohort study	Adult patients undergoing HD, HD units	Standardized Outcomes in Nephrology-Hemodialysis Fatigue [SONG HD Fatigue measure]	Research	n=485 - Australia (n =106), the United Kingdom (n=303), and Romania (n=76) (40%)	Most of the participants were aged from 51 to 70 years (322; 66%)	majority had been on HD for up to 5 years (405; 84%)

Table 3: Synopsis of PROM characteristics

(references for each PROM next to table 4, *entry on PROQOLID database via https://eprovide.mapi-trust.org/, # PROM identified from Aiyegbusi et al 2017 review (2))

Instrument name	Available validated translations	Instrument Summary Domain/Items	Scoring method	Measure able to produce total/summary score	Mode of admin	Time to complete	Recall period	Accessibility/ Permissions
Generic PROMS								
SF-36v2®* **(Also included in ICHOM set)**	English for the US + 213 translations	Generic measure. SF-36 contains 36 items, 8 domains: Physical functioning (10 items), Role-physical (4 items), Bodily Pain (2 items), General Health (5 items), Vitality (4 items), Social functioning (2 items), Role-emotional (3 items), and Mental Health (5 items) +1 item on Reported Health Transition Responses: Dichotomous Yes/No, Likert scale 3,5 or 6 point	Two Component Summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS), calculated with all scores using the norm-based approach (US population norm mean score for each domain and summary score is 50, with a standard deviation [SD] of 10)	No global score, scores by domain - Physical Component Summary (PCS) and Mental Component Summary (MCS) scores can be calculated (different than the item clusters for the domains) Higher score = better health status Scoring manual available for commercial version (Quality metric)	E-version Interactive Voice Response System (IVR) Telephone-administered Paper and pen Interviewer-administered Self-administered	5-10 mins	The last 4 weeks (standard version) / The last week (acute version)	Commercial version: Fees for commercial use, under agreement or contract contact Quality Metric. (RAND academic version - Free for use in clinical practice and a license is not required - but terms and conditions)

Edmonton Symptom Assessment System revised (ESASr) - ESASr-Renal (MODIFIED for RLS)*#	English + 36 translations	10 items (symptoms - pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, well-being, other problem - Can be modified to include Restless Legs Syndrome single question, RLS defined as 'uncontrollable urge to move your legs')	"The scale for each symptom is anchored by the words `No' and `Severe' at 0 and 10, respectively and the sum of scores range from 0 to 100 with higher scores indicating greater symptom distress and burden"	Global score ranging from 0 to 100, Lower score = better QoL	"Electronic/paper and pen, Preferably Self-administered but also can be Caregiver-administered Proxy-administered Proxy-rated	A few minutes	'Now'	Free access: with appropriate acknowledgement of its source
Nottingham Health Profile *#	English for UK + 28 translations	38 items: 6 Domain(s) Pain (8 items) Physical mobility (8 items) Sleep (5 items) Emotional reactions (9 items) Energy (3 items) Social isolation (5 items)	Response options yes/no. Scores by dimension ranging from 0 to 100, weighting, Lower score = better QoL. Scoring/interpretation/user manual via copyright holder.	Not reported	Self -administered, paper and pen	15 mins	At the moment	Conditions of use: need authors written permission/copyright holder, fees for commercial /Pharmaceutical companies.
SF-12 *#	English for USA + 141 languages	A generic HRQOL questionnaire developed to be a much shorter, yet valid, alternative to the SF-36®. 12 items to measure HRQOL. Domains: Physical functioning (PF) (2 items) Role physical (RP) (2 items) Bodily pain (BP) (1 item) General health (GH) (1 item) Vitality (VT) (1 item) Social functioning (SF) (1 item) Role emotional (RE) (2 items) Mental health (MH) (2 items)	Response options: Yes/No 5 to 6-point Likert Scale, Higher score = better health status, Scoring/interpretation/user manual available	Scores by domains: In SF-12v2® use of norm-based scores rather than 0-100 scores is recommended, Other: Physical Component Summary (PCS) and Mental Component Summary (MCS) scores	Self-administered, interviewer administered E-version, suitable for handheld devices Interactive Voice Response System (IVR) Telephone-administered Paper and pen,	2 mins	The past 4 weeks (standard version) / The past week (acute version)	Not free for use, with fees for commercial/pharmaceutical companies with the signature of a contract/agreement, please contact copyright holder directly
WHOQOL-BREF (Dialysis module- TW version) #	Taiwanese	A 32-item HRQOL measure modified for use in dialysis patients with 4 domains (incorporating 4 dialysis-specific items): (i) physical (ii) psychological (iii) social relationship (iv) environment. The measure also includes two global items (general QOL and general health).	A 5-point Likert scale is used, and higher scores signify higher HRQOL	The score for each domain ranges from 4 to 20. Calculated by multiplying the average scores for all items in the domain by 4. Scoring manual for core WHOQOL-BREF available.	Self or interviewer administered	Not reported	last 2 weeks in core WHOQOL BREF, extended to 1 month in modified version	Contact the authors - WHOQOL group, copyright held by WHO

Quality Life Index 3.0 – QLI #	English + 6 translations	A 68-item QOL measure divided into 2 sections. One section measures satisfaction with various domains of life, while the second measures the importance of the domain to the individual [64]. There are 4 domains: (i) health and functioning (ii) Social and economic (iii) psychological/spiritual (iv) family. Each section has 3 additional dialysis-related items.	Response Options: Likert scale, scoring manual available	Global score and scores by dimension Score Direction: Higher scores show better QoL	Self- administered	10 mins	Not reported	Contact authors for permission to use - copyright in place.
Kidney Disease specific PROMs								
Instrument name	**Available validated translations**	**Instrument Summary Domain/Items**	**Scoring method**	**Measure able to produce total/summary score**	**Mode of admin**	**Time to complete**	**Recall period**	**Accessibility/ Permissions**
KDQOL-SF™ 1.3* # (includes screening item on sexual activity)	English for the US +28 translations	KDQOL-SF, 80 items have two components: Kidney Disease Specific Component and SF-36. 19 domains in total, 43 questions assess 11 kidney disease specific components of QOL and SF-36 questionnaire in which the 36 questions assess the general health related QOL in eight domains.	Scoring rules given in KDQOL-SF™ user's manual. The pre-coded items were transformed into 0-100 scale, with higher score representing better quality of life. Dichotomous Yes/No, 4-to-7-point Likert scale, Other: Numerical Rating Scales ranging from 0 to 10 and 3-pont rating scale	All items in a domain are summed up and averaged to give an average score for each domain which ranges from 0 (worst health) to 100 (best health). Higher score = Better HRQOL, Scoring manual available via website.	Paper and pen Interviewer-administered Self-administered	16 mins	In general, the past four weeks	Available without charge (for non-commercial purposes)

KDQOL-36 *#	English for the US + 41 translations	Based on the KDQOL-SF™. It includes the SF-12 as generic core plus the burden of kidney disease, symptoms/problems of kidney disease, and effects of kidney disease scales from the KDQOL-SF™v1.3.36 items, and two cores: the SF-12 (i.e., generic QOL) and the disease-specific core. The generic core consists of two domains: the physical component summary (PCS) [6 items] and the Mental Component Summary (MCS) [6 items]. The disease-specific core consists of 24 items with 3 domains: symptoms and problems (12 items), burden of kidney disease (4 items) and effects of kidney disease (8 items).	Dichotomous: Yes/No 5-to-6-point Likert type scales ranging from 1 to 5 or 6 Other: 3-point rating scale. The raw scores were transformed according to the RAND scoring manual ranging from 0 to 100, where a higher score indicates better QOL	Global score can be calculated but not recommended by RAND organization Scores by domains Scores by items A stand-alone Excel scoring tool has been developed by RAND organization to help with the scoring of the KDQOL-36™	Paper and pen E-version Interviewer-administered Self-administered	Not reported	In general, / During a typical day/ During the past four weeks	Available without charge (for non-commercial purposes)
POS-S-RENAL (symptom list version 1.0)	English, Spanish	The POS Symptom list (POS-S) comprises 10 symptoms and two open questions. It can be used alongside POS to capture more information about symptoms and is especially useful where a patient has multiple symptoms. POS-S can also be used on its own, if only a symptom assessment is required., POS-S is available as a renal card - this version assesses 17 symptoms, plus open fields to list main symptoms.	Each symptom is scored on a 5-point scale (absent, mild, moderate, severe, and overwhelming) and is scored as 0 if absent, 1 if mild, 2 if moderate, 3 if severe, or 4 if overwhelming.	Guidance on scoring available from website. Can be used to calculate individual item scores and an overall profile score . A total score is calculated by summing the individual scores for each of the 17 symptoms, giving a potential score of between 0 and 68.	Paper. Patient and staff versions	Not reported	Can be used with 3 day or 1 week recall, choice depends on setting and circumstances of use.	Freely available copyrighted instrument - contact authors to discuss use in research and any adaptions.

IPOS-RENAL	English	IPOS-Renal has been developed as a result of demand from clinicians to merge IPOS and POS-S Renal. IPOS-Renal is a short measure (11 questions), combining the most common symptoms renal patients experience plus additional items from IPOS on concerns beyond symptoms, such as information needs, practical issues, family anxiety	Qu 2 addressed 10 specific symptoms, for each you can score on a 5-point Likert type scale 0-4 (Not at all, Slightly, Moderately, Severely, Overwhelmingly Qu 3-9 address psychological, spiritual, communication and practical symptoms and concerns - score on 5-point Likert type scale, text descriptors and direction of options varies.	Guidance on scoring available on website. Can be used to score individual item scores, subscales and an overall IPOS score. Total scores should be reported in addition to individual symptom scores to avoid symptom masking. If any individual item scores are missing, an overall IPOS score cannot be generated.	Paper, Qu in measure on whether patients completed on own, with friend/family or with staff, availability of staff version assessing same domains	7.5 mins (SD 1.8 mins) to complete (Study 34)	Can be used with 3 day or 1 week recall, choice depends on setting and circumstance s of use.	Freely available copyrighted instrument - contact authors to discuss use in research and any adaptions.
CHEQ - CHOICE Health Experience Questionnaire (Choices for Healthy Outcomes in Caring for End-Stage Renal Disease) * #	English + 1 translation Thai	An 83-item (21 domain) HRQOL measure. Designed to complement SF-36 and assess the effectiveness of dialysis modalities and dialysis dose. Comprises of 8 dimensions from SF36 combined with 7 supplementary items and 13 specific dimensions namely: (i) freedom (ii) travel restrictions (iii) cognitive functioning (iv) financial (v) restrictions on diet and fluids (vi) recreation (vii) work (viii) body image (ix) symptoms (x) sleep (xi) sexual functioning (xii) access-related problems (xiii) quality of life. An additional 2 person-specific quality of life item.	Possible scores range from 0 to 100 with higher scores indicating better HRQOL	Produces a profile of scores on specific domains. Additional work is needed to determine whether global summary scores can be generated.	Self or interviewer administered	Approximately 25 mins	General health question: one year ago. Other: typical day, 4-week recall	No information - contact authors

KDQ Kidney Disease # Questionnaire (mini KDQ with 2 less items per domain available)	English + Spanish	A 26-item measure designed to assess the effects of interventions on the QOL of patients undergoing haemodialysis. There are 5 dimensions namely: (i) physical symptoms (ii) fatigue (iii) depression (iv) relationships with others (v) frustration. Note that the physical symptom dimension is patient-specific, thus the symptoms most important to individual patients are identified and used to evaluate the dimension. (Mini KDQ with 2 less items per domain available)	Questions are scored on a 7-point Likert scale and higher scores indicate a lower impact of disease on HRQOL	Score for each domain. No global score.	Self or interviewer administered	10-15 mins	During the previous 2 weeks	Original paper says copy of questionnaire available from authors upon request
Original KDQOL*# +	English	A 134-item for use in kidney disease patients undergoing dialysis. It consists of SF36 dimensions, 11 kidney disease targeted scales (symptom/problems, effects of kidney disease on daily life, burden of kidney disease, cognitive function, work status, sexual function, quality of social interaction, sleep). Also Included were multi-item measures of social support, dialysis staff encouragement and patient satisfaction and an item that assesses change in health over a year (overall health rating)	All scale scores are transformed linearly into 0±100-point scales with higher scores indicating better HRQOL, RAND scoring for SF-36 component.	Score for each domain. No global score.	Self or interviewer administered	about 30 mins to complete	Recall last 30 days	Contact Authors
Modified KDQOL - Development of subscales from the symptoms/ problems and effects of kidney disease scales of the KDQOL (Rao 2000) –		The modified KDQOL is a 55-item QOL measure derived from the KDQOL. 11 subscales [(58)] were identified namely: (i) pain (ii) psychological dependency (iii) cognitive functioning (iv) social functioning (v) dialysis related symptoms (vi) cardiopulmonary symptoms (vii) sleep (viii) energy (ix) cramps (x) diet (xi) appetite. 4 items were ungrouped.	The measure is scored on a 0 to 100 scale with higher scores indicating better HRQOL					

CKD-Symptom Burden Index (Modified DSI) #	Arabic	A 32-item measure of symptom burden. Derived from the DSI. The CKD-SBI was developed for use in patients with CKD stages IV and V. The measure has 4 dimensions namely: (i) prevalence (ii) distress (iii) severity (iv) frequency. Added depression and nocturia plus free field to DSI	Total score ranges from 0 to 100 .All symptom dimensions (frequency, severity and distress) were rated on a 0–10-point scale. The prevalence scale assesses the presence or absence (Yes/No) of each symptom with a higher overall score indicating a higher symptom occurrence. The possible range of prevalence scores is 0-32. Distress, severity and frequency are each measured using a 0 to 10 scale for each of the symptoms. Participants rate the "distress" subscale from none to very much, "severity" from none to very severe, and "frequency" from never to constant	A maximum total score for each of these scales is 320 (range 0-320). The total CKD-SBI score is calculated by summing the scores of each CKD-SBI subscale (prevalence, distress, severity and frequency) and then multiplying the result by 0.1008 (constant number). The total score for the CKD-SBI scale therefore ranges between 0-100, where 100 indicates the highest symptom burden possible.	Self-administered	15-30 mins	Extended from 1 week in the original DSI to 4 weeks to reflect the chronicity of CKD symptoms	No information - contact authors

HD Specific PROMs								
Instrument name	**Available validated translations**	**Instrument Summary Domain/Items**	**Scoring method**	**Measure able to produce total/summary score**	**Mode of admin**	**Time to complete**	**Recall period**	**Accessibility/ Permissions**
DSI Dialysis Symptom Index #	English, Korean, Turkish	A 30-item measure designed to assess symptom prevalence and severity in patients on haemodialysis. 21 items relate to physical symptoms, 9 to emotional symptoms, plus open-ended question to report additional symptoms.	The severity of each symptom is assessed using a 5-point Likert scale, ranging from "not at all bothersome" (0) to "very bothersome" (4).	An overall symptom burden score and a total symptom severity score are calculated: The number (0–30 symptoms) and burden [score ranging from 0 (no symptoms) to 150 (all 30 symptoms are present and are very burdensome)] of symptoms were calculated, with higher scores indicating higher symptom burden.	Paper, Self or interviewer administered	5.4 mins (SD 1.6 mins) to complete (Study 34), 3-10 mins (study 71)	During the past week	Needed written approval from developers to create translation
Modified Haemodialysis Stressor Scale HSS	English, Vietnamese, Chinese	32 item scale two subscales. The first (25 items) encompasses psychosocial stressors such as 'limitation of fluid', 'limitation of physical activity' and 'fear of being alone'. The second (seven items) includes physiological stressors such as 'muscle cramps', 'fatigue' and 'itching'	four-point Likert scale ranging from 0 (not at all) to 3 (a great deal) higher scores representing a higher intensity of stressor	Subscale and total scores. A total stressor score was derived by summing the ratings of all 32 items with a possible range of 0 to 96. The higher the total stressor score was, the greater the degree of stress experienced by patients receiving haemodialysis	Paper	15-20 mins (study 38)	Not specified	Acknowledge original authors
Patient Perceptions of Hemodialysis Scale (PPHS) - modified version	English, Brazilian Portuguese	36 item measure with 5 subscales - emotional well-being, psychosocial distress, nursing support, physician support and physical health	Five-point Likert scale. Items are rated 0 to 4, "with 0 indicating no incidence of the symptom or no satisfaction/concern with the item and 4 indicating that they almost always experience the symptom	Each of the five subscales included in the PPHS were constructed to allow for summative scores reflecting the constructs of interest. A higher mean score represents a more positive outcome in all the subscales	Paper	Nor reported	Not specified	Contact the authors

Hemodialysis Symptom Patient-Reported Outcome Measure - SMarRRT HD	English	14-item PROM intended for use in haemodialysis patents comprising 13 Symptoms (12 specific, 1 write in); time to recovery question	Symptom attributes of severity (5-point Likert scale) none, mild, moderate, severe, very severe	Further work being undertaken in development of measurement scoring by measure developers.	Currently available in paper form but developers are exploring conversion to e-tablet based application	Not reported	Recall period of the "last dialysis treatment" for each item. Frequency not stated.	Contact the authors
Subjective Haemodialysis Adequacy Questionnaire - SHAMQ	Farsi	A 30-item questionnaire with 4 sub scales, physical vitality, spiritual health, sense of well-being, and self-obligation for effective care.	Scoring via a 5-point Likert scale from strongly agree to strongly disagree	No guidance on scoring or interpretation	Unknown	Unknown	No recall period stated. Frequency not stated	Seek permission of authors
Haemodialysis Symptom Distress scale DSM-22	English	HSD scale was composed of five factors with 22 items, including insufficient energy/vitality, cardiac–pulmonary distress, sleep disturbance, musculoskeletal distress, and gastrointestinal distress	Can skip item if symptom not experienced. Qu on occurrence frequency (score 1-4 it rarely happened, it happened occasionally it happened frequently, it happened almost every day) Severity - VAS line 1-10, mild to severe, Degree of disturbance VAS line 1-10, mild to extreme disturbance	No guidance on scoring or interpretation	Self - administered, paper and pen	20-30 mins	Past 3 months	No details: Contact authors
CDQOL Chinese Dialysis Quality of Life Scale #	Cantonese	A 29-item measure designed to measure the QOL of Chinese dialysis patients	Scored on a 5-point Likert scale. Higher scores indicate better quality of life as perceived by the patient	Patients' responses were examined by calculating the average scores of the scales. Item scores were summed and divided by the number of items to get the item average scores or the scale. The higher the score, the better the quality of life perceived by the patient	Self-administered	less than 20 mins	No specific recall period stated	No information - contact authors

Domain specific PROMs								
Instrument name	**Available validated translations**	**Instrument Summary Domain/Items**	**Scoring method**	**Measure able to produce total/summary score**	**Mode of admin**	**Time to complete**	**Recall period**	**Accessibility/ Permissions**
Hospital Anxiety and Depression Scale HADS*	English for the UK + Over 100 other translations available, other existing translations can be obtained from Mapi Research Trust	14 questions and is divided into two sub-scales with 7 representing anxiety (HAD-A) and 7 depression (HAD-D)	4-point Likert/Likert type scale. Scores by domain. Lower score = better QoL. Scoring manual available. For each subscale, a score of 0 to 7 is considered as being in the normal range and a score of 11 or higher indicates a potential mood disorder. Patient can score 0-21 on each subscale	Scores by domain	Self-administered. Paper and Pen, e-version (conditions attached to use)	2-5 mins	In the past week	Need to use under licence and pay users' fee. The use of the questionnaire is licensed by GL Assessment
Beck Depression Inventory II *BDI (Version 2) Cognitive Depression Index (CDI)	English for the US + 73 translations	BDI - 21-items covering construct of psychological functioning including coping. 2 domains - Cognitive-affective, Somatic CDI - variant/subscale of BDI - excludes 6 somatically focused questions (to minimise the confounding effects of these symptoms in patients with comorbid physical health problems)	4-point Likert scale. Each item scored 0-3 allowing summary score to be calculated. High total scores indicate more severe depression. Can use cut off scores to define clinically significant depression. Scoring manual available.	BDI-II is sufficiently unidimensional to warrant the use of a total score (47) Global score ranging 0-63	Interviewer-administered, E-version Paper and pen Self-administered	5-10 mins	previous 2 weeks including day of assessment	Need contract and to pay users fee
Beck Anxiety Inventory *	English for the US + 17 Translations	21 items, Unidimensional - Each item is descriptive of subjective, somatic, or panic-related symptoms of anxiety.	4-point Likert Scale from 0= Not at all to 3= Severely--I could barely stand it. Higher score = Higher anxiety symptoms	Global score ranging 0-63	Paper and pen Self-administered or interviewer administered	5-10 mins	Not specific recall period stated	Need contract and to pay users fee

PHQ-9*	English for the US + 104 translations	The PHQ, a self-administered version of the PRIME-MD, contains the mood (PHQ-9), anxiety, alcohol, eating, and somatoform modules as covered in the original PRIME-MD (Primary Care Evaluation of Mental Disorders (PRIME-MD) 9 items +1 item checking any problems on the questionnaire, Unidimensional	Likert scale format 0-3 - scoring interpretation guide available. 4-point Likert scale ranging from 0 "Not at all" to 3 "Nearly every day" Cut-off scores: 5, 10, 15 and 20 represented mild, moderate, moderately severe, and severe depression, respectively Higher score = More severe depressive symptoms	PHQ-9 sufficiently unidimensional to warrant the use of a total score (47) Global score 0-27,	Interviewer-administered Self-administered E-version Telephone-administered Paper and pen	More than a minute	Over the last 2 weeks	The copyright for the PHQ-9 was formerly held with Pfizer, who provided the educational grant for Drs Spitzer, Williams and Kroenke who originally designed it.[1] This is no longer the case, and no permission is required to reproduce, translate, display or distribute the PHQ-9.
Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS) *	English for the US	PHQ-ADS is a composite measure of depression and anxiety, taken from summing the PHQ-9 and GAD-7 items 16 items	Total scores can range from 0 to 48, with higher scores indicating more distress. 4-point Likert scale ranging from 0 "Not at all" to 3 "Nearly every day" Cut-points of 10, 20 and 30 can be used to indicate mild, moderate, and severe levels of distress. Unidimensional, scoring and interpretation guide available	Global score 0-48, The PHQ-ADS is the sum of the PHQ-9 and GAD-7 scores.	Interviewer-administered Self-administered E-version Telephone-administered Paper and pen	More than a minute	Over the last 2 weeks	Free access

Death Anxiety Scale - Extended DAS-E	Farsi	51 item scale	Likert scale format (scale of 1 to 5, strongly disagree to strongly agree). Five DAS-E questions are scored inversely (Items 2, 3, 6, 7, and 15). Thus, the total potential score ranges from 51 to 255, with a higher score indicating higher levels of DA.	Not reported	Not reported	Not reported	No recall period stated	Not reported - contact the authors
Functional Assessment of Cancer Therapy - Anemia (FACT-An) *	English for the US +57 translations	47 items: 27 item FACT-General (FACT-G) includes four dimensions of well-being: Physical (7 items), Functional (7 items), Social/Family (SWB; 7 items), and Emotional (6 items) The FACT-An also includes 13 fatigue-specific items (the Fatigue Subscale) plus an additional 7 items specific to anemia and unrelated to fatigue. Anemia subscales such as FACT-A Total and the Fatigue and Anemia subscales were of special interest. These last 20 items (13 + 7) combine to form the Anemia subscale.	5-point Likert Scale from 0 (Not at all) to 4 (Very much Higher scores indicate better health status. Higher scores indicate better health status. An important change score estimate of 4 points for the Anemia total score and 3 points for the Fatigue score has previously been reported in patients with cancer. In patients with CKD, a three-point or greater increase was previously identified as a clinically meaningful improvement on the FACT-Fatigue total score (41)	Global and domain scores, some items must be reversed before being added to obtain subscales scores. SAS/SPSS algorithms and manual scoring template available.	Paper and pen E-version Interviewer-administered Self-administered	Approx. 10-15mins	The past 7 days	Need to contact developer

Chalder Fatigue Questionnaire (CFQ)*	English for UK + 9 translations	11 items- loading onto two dimensions of fatigue severity, namely mental fatigue and physical fatigue. Seven items represent physical fatigue (items 1–7) and 4 represent mental fatigue (items 8–11)	Two methods of scoring - 4-point Likert/Likert-type Scale: the Likert scoring system can be used to examine the distribution of scores: 0: 'better than usual', 1: 'no more than usual'. 2: 'worse than usual', 3: 'much worse than usual' where the maximum score possible would be 33 and Other: the bi-modal scoring system from which caseness can be derived: 0,0,1,1 where the maximum possible score would be 11	Global score, Scores by domains, Scores by items, Higher score = Higher Fatigue	Self - administrated, paper and pen	Not reported	The last month	Free of charge as long as the source is acknowledged
Piper Fatigue Scale (PFS)-12	English	12 numerically scaled items that measure four dimensions of fatigue, including behavioural/severity, affective meaning, sensory, and cognitive/mood (Based on 22 item PFS-R)	Each item score can range from 0 to 10 Higher scores on the subscale and the total fatigue scale reflect severe fatigue.	Each dimension score can range from 0 to 30 as a subscale score. A total fatigue score ranges from 0 to 120.	Self - administrated, paper and pen	Not reported	In the past 4 weeks	Contact the authors

PROMIS-CAT-Fatigue* - PROMIS Item Bank v1.0 - Fatigue 2May2017*	47 languages + see website	The PROMIS Fatigue item banks assess a range of self-reported symptoms, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Fatigue is divided into the experience of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental, and social activities. In CAT format, questions are provided to the individual based on responses given. Scoring manual available.	Scores obtained from individual responses are summed into a total	Scores obtained from individual responses are summed into a total also known as the 'raw score,' which is converted to a T-score by the computer. A total score of 50 with a standard deviation of 10 is considered an average score. Higher scores obtained indicate more severe fatigue - reference population = general population	Self - administered, electronic CAT (Computer Adaptive Testing) format - Administration Platforms Assessment Center API (includes REDCap) Epic PROMIS CAT Application NIH Toolbox iPad App PROMIS iPad App also available in short form allowing paper and pen collection	CAT 3-5 mins	CAT Past 7 days	Free to use, see www.healthmeasures.net
SONG-HD Fatigue	English	three items that assess (1) the effect of fatigue on life participation, (2) tiredness, and (3) level of energy.	Four-point Likert scale indicating increasing severity, ranging from zero (not at all) to three (severely)	Overall score for fatigue is obtained by summing the responses across the three questions, resulting in a scale ranging from zero (no fatigue) to nine (maximum fatigue)	Self - administered, paper and pen	No information	Past week	Contact the authors
Oral Health Impact Scale Short Form (OHIP-14) *	English for Australia + 23 translations	14 items: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap.	5-point Likert scale (0 – never, 4 – always), OHIP-14 scale ranged from 0 to 56 Higher scores indicated poorer OHRQOL, weighting used in scoring.	Global score ranging from 0 to 100 scores by dimension Scoring manual available	Self - administered, paper and pen	17 mins	One year time reference	Free access, contact the author

Geriatric/General Oral Health Assessment Index (GOHAI)*	English for the US + 12 translations	12 item GOHAI measure evaluates three dimensions of OHRQOL: 1) physical function including eating, speech and swallowing; 2) psychosocial function including worry or concern about oral health, dissatisfaction with appearance, self- consciousness about oral health and avoidance of social contacts because of oral problems and 3) pain or dis- comfort including the use of medication to relieve pain or discomfort from the mouth. Nine negative questions and three positive questions	Five response categories for each question and a score has been assigned for each response category (l = always, 2 = often, 3 = sometimes, 4 = seldom, and 5 = never). Scores from the positively worded questions were reversed during data processing so that the directions of all responses were the same. The GOHAI score was computed by adding up the scores of the responses to the 12 questions	Global score - Additive (ADD) scores for the GOHAI were obtained by summing the response codes for the 12 items after reversing the coding of the three positively worded items 0-60 with higher score indicating better oral health.	Self-administrated, paper and pen	Not reported	Last 3 months	Contact the authors - measure copyrighted
IRLS - International Restless Legs Syndrome Study Group Rating Scale*	English for the US + 12 translations	10 question scale: Symptom severity (6 items) Impact on daily living (3 items) Item 3 (relief) is measuring a distinct concept. It does not belong to any of the two subscales	5-point Likert scale from 4 very severe to 0 none. Lower score = better QoL, scoring manual available.	Global score ranging from 0 to 40 Scores by dimension: Symptom severity subscale: 0-24 Impact on daily living subscale: 0-12	Paper and Pen, interviewer administered, Self-report with aid of a trained staff member	10 mins	In the past week	Use under a licence, fees may apply for funded academic users, healthcare organisations, commercial users and IT companies

Council on Nutrition Appetite Questionnaire (CNAQ)*	English for the US + 1 Translation	8 items, single domain, to assess appetite and predict weight loss.	Responses are scored by using a 5-point (A to E), verbally labelled, Likert-type scale	The total CNAQ score is the sum of scores on the 8 items, with lower scores indicating deterioration in appetite. Possible scores range from 8 (worst) to 40 (best) CNAQ score 28 indicates significant risk of at least 5% weight loss within six months.	Pen and paper, self-administered	Takes approx. 3 mins to complete	Immediate recall	Contact the authors
Nutrition-Specific Quality of Life Questionnaire - NSQOL	English	15 questions that assess factors which may affect nutrition quality of life in a patient receiving MHD. The ADAT (Appetite and Diet Assessment Tool) and the FED (Food Enjoyment in Dialysis) questionnaire were combined to create the NSQOL instrument			Interviewer administered, self-administered, Paper and pen	Quick to administer' Prest et al 2020	Mixed recall: Since starting dialysis, Past 4 weeks, over past 7 days, days on/off dialysis	Contact the authors

5D Itching Scale *	English for US + 25 translations	5 dimensions, 8 items - Duration (1 item), Degree (1 item), Direction (1 item), Disability (4 items), Distribution (1 item)	5-point Likert/Likert-type Scale from 1 (less severe symptoms or impairments) to 5 (more severe symptoms or impairments). For 3 items of the Disability domain (Leisure/Social, Housework/Errands, Work/School), an N/A box can be chosen Other: patients have to indicate itch location by choosing among a list of 15 body parts and 1 point of contact with clothing or bandages (or the one closest anatomically if a body part is not listed)	The scores of each of the five domains are achieved separately and then summed together to obtain a total 5-D score. 5-D, Global Scores can potentially range between 5 (no pruritus) and 25 (most severe pruritus) Scores by domains: Single-item domain scores (Duration, Degree, Direction) ranged from 1 to 5. For the Disability domain score, the highest item score (range 1-5) is chosen among the 4 items. For the Distribution domain score, the sum of all affected body parts (range 0-16) is sorted into 5 scores: 1 (=sum of 0-2), 2 (=sum of 3-5), 3 (=sum of 6-10), 4 (=sum of 11-13) and 5 (=sum of 14-16) Higher score = More severe pruritus	Interviewer-administered According to authors, the instrument could be easily self-administered but they did not test this mode of administration in the development and validation study Telephone-administered Paper and pen	Less than 5 mins	Past 2 weeks	Free of charge
011 Uremic Pruritus in Dialysis Patients (UP-Dial) scale	Thai, English version non validated	The UP-Dial, a 14-item multidimensional scale for the assessment of UP that encompassed three domains: signs and symptoms (seven items), psychosocial (four items) and sleep (three items).	Each item is scored on a five-point response scale (0–4) and added to give a summary score from zero to 56. The higher scores indicate greater severity and burden of UP.	Summary score ranging 0-56, but can also use domain scores	Pen and paper, self-administered, interviewer administered	Average completion time of 10–15 min	Last 2 weeks	Contact the authors

Duke Activity Status Index (DASI)*	Original English for US + 4 translations	12 questions: Domains - Personal care (1 item) Ambulation (4 item) Household tasks (4 items) Sexual function (1 item) Recreation (2 items)	4-point Likert scale with weighting. Positive responses are summed to get a total score, which ranges from 0 to 58.2. Higher scores indicate higher functional capacity	Global score	Pen and Paper, Interviewer-administered Self-administered	5 mins	Not specified	Free of charge for academic use in small projects, especially by trainees or junior investigators, with fees for commercial/pharmaceutical companies
Low Physical Activity Questionnaire (LoPAQ)	English, Chinese	11 questions, with sub questions.	Each Qu answered yes/no, with average time recorded	Quantifies kilo calories of total leisure-time physical activity and time spent sitting	Pen and Paper, Interviewer-administered Self-administered	10 minutes (including instruction time)	Last week, past 7 days	Contact the authors
Vascular access-specific health-related quality of life impacts among hemodialysis patients HARQ	English	draft measure has 12 question groups (based on recall period) representing a total of 47 items in 6 domains. - six domains: symptoms, physical functioning, emotional impacts, social and role functioning, sleep, and care-related burdens. Items are derived from KDQOL-36, VAQ, CHEQ, PROMIS Physical Function item bank, and Neuro-QOL as item sources	All items used 5-point polytomous response scales, with the exception of one global pain question using a scale from 1 to 10. Recall periods in the original instruments were used.	Not reported	Pen and paper, Self-administered	Not reported	Last 7 days, during the last 4 weeks	Contact the authors
VasQOL	English, additional translations planned	11 items- 3 domains physical, VA functioning and capabilities.	Score from 0-10 Not satisfied at all to completely satisfied, no interference to significantly interfered. In v2.0 score reduced from 0-7.	Not reported	Electronic or paper	Not reported	The Last week. A separate VASQOL should be completed for each functioning vascular access	Contact the authors

ICHOM Measures	Available translations include	Instrument Summary Domain/Items	Scoring method	Measure able to produce total/summary score	Mode of admin	Time to complete	Recall period	Accessibility /permissions
The Optum™ SF-36v2® Health Survey *The SF-36 and RAND-36 include the same set of items that were developed in the Medical Outcomes Study. Scoring of the general health and pain scales is different between the versions. *	English for the USA + 213 translations	36 items: Domains Physical Functioning (PF) (10 items) Role-Physical (RP) (4 items) Bodily Pain (BP) (2 items) General Health (GH) (5 items) Vitality (VT) (4 items) Social Functioning (SF) (2 items) Role-Emotional (RE) (3 items) Mental Health (MH) (5 items) +1 item on Reported Health Transition	Scoring Response Options: Dichotomous: Yes/No 3-, 5- or 6-point Likert Scale Higher score = better health status	The scoring guide for the SF36v2 is only available upon a license agreement being made. Software to aid scoring available. Scores by domains: In SF-36v2® use of norm-based scores rather than 0-100 scores is recommended. Physical Component Summary (PCS) and Mental Component Summary (MCS) scores can be calculated (different than the item clusters for the domains)	Interviewer-administered Self-administered Data collection mode E-version Interactive Voice Response System (IVR) Telephone-administered Paper and pen Also suited for handheld device administration	5-10 mins	4-week, 1-week, 24-hour	The SF-36v2 Health Survey requires a license agreement prior to the use or reproduction of the tool. Information on how to obtain a license can be found here: https://www.qualitymetric.com/
RAND 36-Item Short-Form Questionnaire (SF-36) *The SF-36 and RAND-36 include same set of items that developed in the Medical Outcomes Study. Scoring of the general health and pain scales is different between the versions.	English (no of translations unknown)	36 items: Domains Physical Functioning (PF) (10 items) Role-Physical (RP) (4 items) Bodily Pain (BP) (2 items) General Health (GH) (5 items) Vitality (VT) (4 items) Social Functioning (SF) (2 items) Role-Emotional (RE) (3 items) Mental Health (MH) (5 items) +1 item on Reported Health Transition	Scoring Response Options: Dichotomous: Yes/No 3-, 5- or 6-point Likert Scale Higher score = better health status	Scoring guide available: After standardizing the 8 scales to z-scores based on means and standard deviations for the general US population, aggregate physical and mental component summary scales are calculated by adding the eight differentially weighted scales. Finally, each component score is transformed to a normalized T-score with a mean of 50 and a standard deviation of 10.	Self-reporting Administration by a trained interviewer in person or over the telephone	5-10 mins	Standard (4-week) version or Acute (1-week) version	Free for use in clinical practice and a license is not required - but terms and conditions

PROMIS-Global Health*	English for the USA + 29 translations	10 items: Domain(s) covered by the questionnaire Physical Health (4 items) Mental Health (4 items) + 2 single items about social roles and General Health	Response options: 5-point Likert/Likert-type Scale ranging from 1: "Poor/Not at all/Always/Very severe" to 5: "Excellent/Completely/Never/None" and Numerical Rating Scale ranging from 0: "No pain" to 10: "Worst imaginable pain"	Scoring guide available via HealthMeasures website: Scores by domains: the Physical Health and Mental Health scores HealthMeasures Scoring Service Integrated in Data Collection Tool Measure-Specific Scoring Guide Scores by items, no global score. Weighting, Lower score = Worse health status	Self-administered Paper and pen E-version Epic PROMIS CAT Application NIH Toolbox iPad App PROMIS iPad App	2 mins	Recall: Depends on the item: in general, or in the past 7 days	Free to use for non-commercial purposes and in clinical practice without a license. PROMIS measures are copyrighted. Commercial users must seek permission to use, reproduce, or distribute measures. Integration into proprietary technology requires written permission. Please read the PROMIS Terms and Conditions of Use for more information

PROMiS-29 v2.1* developers recommend to only use the latest version of the instrument:	English for the USA + 57 translations	29 items: Domain(s) covered by the questionnaire Physical Function (4 items) Anxiety (4 items) Depression (4 items) Fatigue (4 items) Sleep Disturbance (4 items) Ability to Participate in Social Roles and Activities (4 items) Pain Interference (4 items) + 1 single item assessing pain intensity	Scoring options: 5-point Likert/Likert-type Scale ranging from 1 to 5 and Numerical Rating Scale ranging from 0: "No pain" to 10: "Worst pain imaginable"	Scoring guide available via HealthMeasures website: Scores by domains with a conversion of the raw score into a standardized T-score with a mean of 50 and a standard deviation (SD) of 10, No weighting. Higher score = Better health status HealthMeasures Scoring Service Integrated in Data Collection Tool Measure-Specific Scoring Guide	Self-administered Paper and pen E-version: Assessment Center API (includes REDCap) NIH Toolbox iPad App PROMIS iPad App	Not reported	The past 7 days except for Physical Function which has no timeframe specified	Free to use for non-commercial purposes and in clinical practice without a license. PROMIS measures are copyrighted. Commercial users must seek permission to use, reproduce, or distribute measures. Integration into proprietary technology requires written permission. Please read the PROMIS Terms and Conditions of Use

Table 4: Affinity mapping and outcome coverage score

Instrument name		CHEQ – CHOICE	Original KDQOL	KDQOL–SF™ 1.3	KDQOL–36	Modified HD Stressor Scale HSS	IPOS–RENAL	CKD–Symptom Burden Index (Modified DSI)	Dialysis Symptom Index (DSI)	FACT–AN	WHOQOL–BREF (Dialysis module TW)	Nottingham Health Profile	POS–S–RENAL (symptom list version 1.0)
Number of items		83	134	80	36	32	11	32	30	47	32	38	17
Tier One outcomes	Fatigue												
	Vascular Access												
Tier Two outcomes	Ability to work												
	Ability to travel												
	Depression												
	Dialysis free time												
	Impact on family and friends												
	Mobility												
	Pain												
	Washed out after dialysis												
Tier Three outcomes	Anxiety/ Stress												
	Cognition												
	Cramps												
	Financial Impact												
	Food Enjoyment												
	Itching												
	Nausea and Vomiting												
	Restless legs syndrome												
	Sexual function												
	Sleep												
Tier 1 Total 2/2	Coverage	2/2 (100%)	2/2 (100%)	2/2 (100%)	2/2 (100%)	2/2 (100%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)
Tier 2 Total 8/8		6.5/8 (81.25%)	7/8 (87.5%)	7/8 (87.5%)	7/8 (87.5%	4.5/8 (56.25%)	4.5/8 (56.25%)	2/8 (25%)	1/8 (12.5%)	5/8 (62.5%)	4.5/8 (56.25%)	6/8 (75%)	3/8 (37.5%)
Tier 3 Total 10/10		10/10 (100%)	9/10 (90%)	9/10 (90%)	6/10 (60%)	7/10 (70%)	7/10 (70%)	9/10 (90%)	9/10 (90%)	5/10 (50%)	5/10 (50%)	3/10 (30%)	6/10 (60%)
Total = 20/20		18.5/20 (92.5%)	18/20 (90%)	18/20 (90%)	15/20 (75%)	13.5/20 (67.5%)	12.5/20 (62.5%) *free fields	12/20 (60%) *free fields	11/20 (55%)	11/20 (55%)	10.5/20 (52.5%)	10/20 (50%)	10/20 (50%) *free fields

Instrument name		ESASr-Renal (MODIFIED for RLS)	HD Symptom Distress scale DSM-22	CDQOL Chinese Dialysis Quality of Life Scale	PROMIS-29 v2.1	PROMIS-Global Health	SF-36 Rand	SF-36v2®	Patient Perception of HD Scale (PPHS) – modified version	SF-12	Quality Life Index 3.0 – QLI	BDI II	PHQ-ADS	PHQ-9
Number of items		12 +	22	29	29	10	36	36	36	12	68	21	16	9
Tier One outcomes	Fatigue													
	Vascular Access													
Tier Two outcomes	Ability to work													
	Ability to travel													
	Depression													
	Dialysis free time													
	Impact on family and friends													
	Mobility													
	Pain													
	Washed out after dialysis													
Tier Three outcomes	Anxiety/ Stress													
	Cognition													
	Cramps													
	Financial Impact													
	Food Enjoyment													
	Itching													
	Nausea and Vomiting													
	Restless legs syndrome													
	Sexual function													
	Sleep													
Tier 1 Total 2/2	Coverage	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)	1/2 (50%)
Tier 2 Total 8/8		2/8 (25%)	1/8 (12.5%)	3.5/8 (43.75%)	5/8 (62.5%)	5/8 (62.5%)	5/8 (62.5%)	5/8 (62.5%)	4/8 (50%)	5/8 (62.5%)	3/8 (37.5)	1/8 (12.5%)	1/8 (1.25%)	1/8 (25%)
Tier 3 Total 10/10		6/10 (60%)	7/10 (70%)	3.5/10 (35%)	2/10 (20%)	2.5/10 (25%)	1/10 (10%)	1/10 (10%)	2/10 (20%)	1/10 (10%)	3/10 (30%)	4/10 (40%)	4/10 (40%)	3/10 (30%)
Total = 20/20		9/20 (45%) *free fields	9/20 (45%)* free fields	8/20 (40%)	8/20 (40%)	7.5/20 (37.5%)	7/20 (35%)	7/20 (35%)	7/20 (35%)	7/20 (35%)	7/20 (35%)	6/20 (30%)	6/20 (30%)	5/20 (25%)

Instrument name		SHAMQ	HARQ	IRLS	UP-Dial scale	PROMIS-CAT-Fatigue	Chalder Fatigue Questionnaire (CFQ)	Oral Health Impact scale Short Form(OHIP-14)	KDQ Kidney Disease Questionnaire	Piper Fatigue Scale (PFS)-12	Geriatric/General Oral Health Assessment Index (GOHAI)	VasQOL	Low Physical Activity Questionnaire (LoPAQ)	Duke Activity Status Index (DASI)
Number of items		30	47	10	14	CAT	11	14	26	12	12	11	11	12
Tier One outcomes	Fatigue													
	Vascular Access													
Tier Two outcomes	Ability to work													
	Ability to travel													
	Depression													
	Dialysis free time													
	Impact on family and friends													
	Mobility													
	Pain													
	Washed out after dialysis													
Tier Three outcomes	Anxiety/ Stress													
	Cognition													
	Cramps													
	Financial Impact													
	Food Enjoyment													
	Itching													
	Nausea and Vomiting													
	Restless legs syndrome													
	Sexual function													
	Sleep													
Tier 1 Total 2/2	Coverage	0/2 (0%)	1/2 (50%)	0.5/2 (25%)	0/2 (0%)	1/2 (50%)	1/2 (50%)	0/2 (0%)	1/2 (50%)	1/2 (50%)	0/2 (0%)	1/2 (50%)	0/2 (0%)	0/2 (0%)
Tier 2 Total 8/8		1/8 (12.5%)	2/8 (25%)	1.5/8 (18.75%)	1/8 (12.5%)	1.5/8 (18.75%)	1/8 (12.5%)	2/8 (25%)	2.5/8 (31.25%)	0.5/8 (6.25%)	1/8 (12.5%)	1/8 (12.5%)	1.5/8 (18.75%)	1.5/8 (18.75%)
Tier 3 Total 10/10		3.5/10 (35%)	1.5/10 (15%)	2/10 (20%)	3/10 (30%)	1/10 (10%)	1.5/10 (15%)	1.5/10 (15%)	0/10 (0%)	1.5/10 (15%)	1.5/10 (15%)	0.5/10 (5%)	1/10 (10%)	1/10 (10%)
Total = 20/20		4.5/20 (22.5%)	4.5/20 (22.5%)	4/20 (20%)	4/20 (20%)	3.5/20 (22.5%)	3.5/20 (17.5%)	3.5/20 (17.5%)	3.5/20 (17.5%) *6 free fields	3/20 (15%)	2.5/20 (12.5%)	2.5/20 (12.5%)	2.5/20 (12.5%)	2.5/20 (12.5%)

Instrument name		5D Itching Scale	Council on Nutrition Appetite Questionnaire (CNAQ)	Hospital Anxiety and Depression Scale HADS	SONG-HD Fatigue	Beck Anxiety Inventory	Nutrition-Specific Quality of Life Questionnaire – NSQOL	Death Anxiety Scale – Extended DAS-E	HD Symptom PROM-SMarRRT HD
Number of items		8	8	14	3	21	15	51	
Tier One outcomes	Fatigue								
	Vascular Access								
Tier Two outcomes	Ability to work								
	Ability to travel								
	Depression								
	Dialysis free time								
	Impact on family and friends								
	Mobility								
	Pain								
	Washed out after dialysis								
Tier Three outcomes	Anxiety/ Stress								
	Cognition								
	Cramps								
	Financial Impact								
	Food Enjoyment								
	Itching								
	Nausea and Vomiting								
	Restless legs syndrome								
	Sexual function								
	Sleep								
Tier 1 Total 2/2	Coverage	0/2 (0%)	0/2 (0%)	0/2 (0%)	1/2 (50%)	0/2 (0%)	0/2 (0%)	0/2 (0%)	
Tier 2 Total 8/8		0.5/8 (6.25%)	0.5/8 (6.25%)	1/8 (12.5%)	0/8 (0%)	0/8 (0%)	0/8 (0%)	0/8 (0%)	
Tier 3 Total 10/10		1.5/10 (15%)	1.5/10 (15%)	1/10 (10%)	0/10 (0%)	1/10 (10%)	1/10 (10%)	1/10 (10%)	
Total = 20/20		2/20 (10%)	2/20 (10%)	2/20 (10%)	1/20 (5%)	1/20 (5%)	1/20 (5%)	1/20 (5%)	

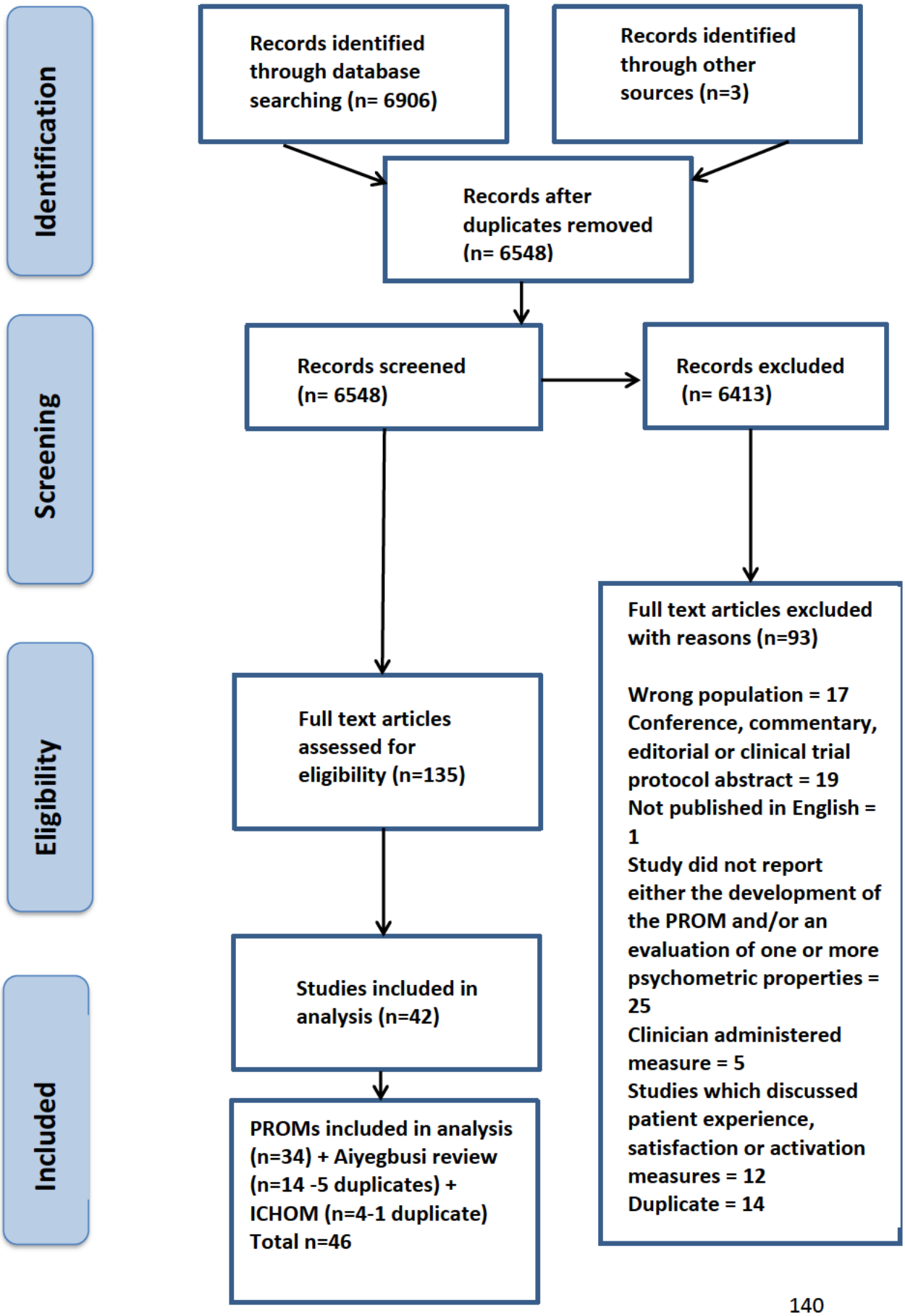
References for Table 3 and 4:

BDI II (27, 31, 42), Beck Anxiety Inventory (56, 68), Chinese Dialysis Quality of Life scale (CDQOL) (69), CFQ (33, 70), The CHOICE Health experience questionnaire (CHEQ) (71, 72), CNAQ (65, 73), CKD Symptom Burden Index (74), DSI (53, 75-77), DASI (46, 78), Death Anxiety Scale – Extended (DAS-E) (38), Functional Assessment of cancer therapy Anaemia (FACT-An) (32, 79), GOHAI (35, 80, 81), HADS (43, 46), HARQ (55), HD Symptom Distress Scale DSM-22 (62), IPOS-Renal (52), , IRLS (41), 5D-itch scale (48, 82), KDQ (83), Kidney Disease Quality-of-Life Instrument KDQOL-SFTM v1.3 (58, 84), Original KDQOL (85), Modified KDQOL (25), KDQOL-36TM (39, 86), LOPAQ (51, 64), Modified ESAS –renal (41, 43, 59, 87), Modified Haemodialysis Stressor scale (HSS) (37, 88, 89), Nottingham Health Profile (90, 91), NSQOL (57, 92), OHIP-14 (35, 93), PFS (63, 94), PHQ-9 (42, 95), PHQ-ADS (40, 96), POS-S-Renal (44), PPHS (49, 97), PROMIS v29 v2.1 (98), PROMIS CAT-Fatigue (63, 99), PROMIS Global Health (100), QLI 3.0 (101), SF-36 RAND version (102), SF-36 (32), SF-12 (103), SHAMQ (45), SONG-HD Fatigue measure (67), SMaRRT HDTM (30), UP-Dial (28, 104),VASQOL (60), WHO-BREF (Dialysis module) (105)

4.5 Results

The searches identified two core outcome sets for use in HD populations (6, 17) and 6,548 records from the PROM literature search after deduplication. This included three additional articles identified by citation searching. Following title and abstract screening, 135 full text articles were acquired. Ninety-three articles were excluded following full text review against the inclusion and exclusion criteria. Forty-two studies were included in the final syntheses, describing 34 PROMs, plus 14 PROMs previously evaluated for use in HD settings by Aiyegbusi et al 2017 (2) and a further four measures recommended for use by ICHOM COS developers (17).Following the removal of six duplicates, 46 PROMs were included for evidence synthesis (see PRISMA-ScR diagram Figure 1).

Figure 1: PRISMA-ScR diagram



4.5.1 Core Outcome Sets

Table 1 outlines the two COS identified for use in HD settings and highlights their PRO components. The COS included the Standardised Outcomes in Nephrology Initiative (SONG-HD) (106-108) and International Consortium for Health Outcomes Measurement (ICHOM) (109).

The SONG-HD outcomes were developed based on the shared priorities of relevant stakeholders, including patients and carers (106, 108). The initiative categorised three tiers of outcomes, based on the level of assessed importance (see table 1).

The need to measure outcomes that matter to both patients and clinicians was also highlighted by ICHOM in line with the paradigm shifts towards values-based care and shared decision-making as strategies for improving healthcare quality (109). The ICHOM group prioritized six patient-reported outcome domains for HRQOL: general HRQOL, pain, fatigue, physical function, depression, and daily activity, targeted for clinical use ICHOM (109) (see table 1).

Both initiatives made recommendations for outcome measures (17, 67, 110). Following exploration of available PROMs, ICHOM opted to use generic measures, reasoning that such tools could be used across treatment modalities and were capable of capturing the burden of multiple long-term conditions. They recommended four measures for use, the Optum™ SF-36v2® or the Short-Form Questionnaire (SF-36) RAND-36 or a combination of the Patient-Reported Outcomes Measurement Information System (PROMIS)-Global Health and PROMIS-29 (17): suggesting baseline (start of HD) and 6-

monthly assessment. The SONG-HD developers took a different approach. Mortality, cardiovascular disease, fatigue and vascular access were identified as tier one outcomes deemed critically important to all stakeholder groups, requiring measurement in all trials. Following research to identify suitable tools to assess fatigue (111), they decided to develop a new measure (67, 112, 113). The SONG-HD fatigue measure is currently being validated as part of the Symptom monitoring with feedback trial (SWIFT) study (114). Vascular access outcome measures are under investigation (115).

4.5.2 Characteristics of included PROM studies

Table 2 summarises the characteristics of the included studies.

4.5.3 Patient-Reported Outcome Measures

Table 3 presents a synopsis of the identified PROMs and their key characteristics.

A total of 34 PROMs were identified from the 42 publications: 10 disease-specific measures including six questionnaires specific to HD, three generic and 21 domain specific PROMs. The domain specific PROMs covered eight domains and subdomains: anxiety and depression, fatigue, oral health, appetite and nutrition, itching, physical activity, vascular access and restless legs syndrome (see Table 3). One PROM could not be mapped against core outcomes, the Symptom Monitoring on Renal Replacement Therapy-Hemodialysis questionnaire (SMaRRT-HD™) (30) as a copy of the measure or clear item descriptions could not be obtained. An additional three measures recommended by ICHOM developers (the SF-36 was also identified in the literature

search), and nine PROMs identified by Aiyegbusi et al 2017 (2) in a recent systematic review exploring PROMs used in HD settings were included in the affinity mapping exercise.

The measures demonstrated high levels of variation in terms of length, mode of administration, availability of guidance around delivery and interpretation, language availability, proxy/interviewer administration and recall periods. Several PROMs had their own website entries with details on development, quality assessment, scoring and interpretation. However, many measures had no associated resources and no clear pathway on permissions for use or modification.

Many identified PROMs could be administered by paper or electronically. Three generic PROMIS measures (PROMIS Global Health Scale and PROMIS-29, and the PROMIS-CAT-Fatigue) were currently being used in HD settings and were available as short form questionnaires, but additionally form part of an extensive item bank that could be assessed via computer adaptive test.

4.5.4 Affinity mapping: outcome coverage

Table 4 uses colour coding to visually display the coverage of the identified PROMs against each of the core outcomes in terms of SONG-HD tier and total percentages. The key finding was that no identified PROM covered all COS-endorsed outcomes. The majority of PROMs included in the analysis (72% 33/46) measured less than half of COS-endorsed outcomes. However, there were four PROMs (9%), each one of which covered $\geq$ 75% of COS-endorsed outcomes (see Table 4). The CHEQ - CHOICE Health

Experience Questionnaire (Choices for Healthy Outcomes in Caring for End-Stage Renal Disease) (72) demonstrated highest overall COS outcome coverage (92.5%). This is an 83-item measure, designed to complement the SF-36 (36 items). The other three measures belong to the family of KDQOL instruments. The legacy long form of the KDQOL™ (134 items) which takes 30 mins to complete was developed in 1994 (85). Followed by the development of a short form which includes the SF-36 as a generic core; the KDQOL-SF v1.3 (80 items) can be completed in approximately 16 mins (84). Finally, the KDQOL-36 (36 items) which is even shorter, utilising the SF-12 to capture generic HRQOL (116). Rao et al (2000) developed subscales from the 55 items comprising the Symptoms/Problems and Effects of Kidney Disease scales of the original KDQOL, demonstrating that the symptoms/problems and the effects of kidney disease subscales of the KDQOL could potentially be used as standalone tools (25). The original KDQOL (85) and the shorter KDQOL-SF (84) offer total coverage of 90%, with both measures lacking an item specifically on restless legs syndrome (RLS) and including some items which could partially measure recommended outcomes 'dialysis-free time' and 'washed out after dialysis'. The outcome 'dialysis-free time' was defined by the SONG-HD developers as 'Time (hours/days) not doing dialysis' (106) and this outcome was only deemed fully covered if time on/off treatment were calculated. The shorter KDQOL-36 had 75% coverage, lacking items to measure outcomes including RLS, cognition and sleep. One of the shortest measures is the Integrated Patient Outcomes Scale- (IPOS) Renal which has 11 items for use by people with advanced kidney disease including those requiring HD to assess care needs. Questions cover symptoms (like pain and itch) plus other constructs (like practical problems resulting from their CKD).

There is also a staff version, for use when people are too unwell to complete for themselves (52).

The CHEQ-Choice and KDQOL measures were developed to measure both HRQOL, aspects of functional status, and symptoms. Several of the other identified measures are being used to measure symptoms only. There was little consistency across these measures, some measured multiple symptoms (e.g., DSI, IPOS-Renal), others addressed a single symptom (e.g., Piper fatigue Scale, Chalder Fatigue Questionnaire: fatigue) or symptom subdomains (e.g., HADS: Anxiety and Depression). Several measures had free text fields to add specific symptoms (see Table 4), such as the Kidney Disease Questionnaire (KDQ) which was developed for use in trials to assess interventions and does not list symptoms, but asks patients to specify physical symptoms that are most important to them (83). The best fit symptom only measures were the Dialysis Symptom Index (76) and the CKD Symptom Burden Index (a modified version of the DSI in Farsi/English, with an item on depression) (74).

The COS-endorsed outcome with the poorest PROM coverage was 'washed out after dialysis'; only measured by HD specific tools: the Patient Perceptions of Hemodialysis Scale (PPHS) (97) and the Subjective Haemodialysis Adequacy Questionnaire (SHAMQ) (45). The KDQOL-SF and KDQOL-36 partially measure this construct with an item on 'washed out or drained' but make no direct reference to dialysis (39, 84). The HD specific measure which offered the best overall outcome assessment (67.5%) was the Modified Haemodialysis Stressor Scale (HSS) (37). However, domains on depression,

pain, washed out after dialysis and cognition and presence, severity or impact of RLS were not measured.

Predictably, the measures with the least outcome coverage were the domain specific questionnaires. However, importantly, many of these tools assessed the impact of particular symptoms or aspects of HD treatment upon overall HRQOL e.g., vascular access specific quality of life measure (VASQoL) (60) and the hemodialysis access-related QOL (HARQ) instrument. (55).

The generic PROMIS and SF-36 instruments recommended by ICHOM developers are widely used and have good accessibility. However, these tools offered a total outcome assessment of 35-40%, suggesting they would need supplementation with other measures to capture the full experience of life on dialysis.

4.6 Discussion

This review provides the first comprehensive affinity mapping of PROMs with international core outcome sets developed for research and routine care of patients undergoing HD.

Table 2 summarises the characteristics of the included studies, which demonstrated the different applications of PROMs. For example, to manage individual care they could be used as overall symptom assessment tools (52), as screening aids for specific symptoms (59) or to assess the impact of a particular aspect of HD, such as vascular access (55, 60). At aggregate levels, the SF-36 is used in the United States for

mandatory annual assessment of HRQOL by the Centers for Medicare and Medicaid Services as part of its conditions for coverage for ESKD facilities (22)

The findings highlighted two COS and 46 PROMs relevant for HD setting. Affinity mapping of the included PROMs against recommended COS PROs suggests there was no single measure which covered all outcomes. Four measures (9%) individually had items which assessed ≥ 75% of COS-endorsed outcomes; however, most PROMs measured less than 50% of these outcomes. This makes it challenging to measure patient-important outcomes without asking individuals to complete multiple measures; potentially leading to unnecessary questionnaire burden and impacting compliance.

Of the four candidate measures that offered the highest coverage, the CHEQ-CHOICE, which was developed in 2001 (72), has excellent coverage (92.5%) but does not appear to have been highly utilised in research or practice, possibly due to its length (83 items). Similarly, despite the good psychometric performance of the original KDQOL™, (90% coverage) investigators have been reluctant to use it because of the length at 134 items (44).

This review suggests that of the current validated measures, the KDQOL measures (KDQOL-SF or KDQOL-36) offer good assessment of core outcomes (90% and 75% respectively), in addition to having good accessibility and support on interpretation via supporting websites (Kidney Disease Quality of Life Instrument (KDQOL) | RAND). However, to cover all recommended outcomes, clinicians would still need to supplement either the KDQOL-SF or the KDQOL-36 to cover all COS-endorsed

outcomes. This review suggests that use of the KDQOL-36 (36 items) plus IPOS-Renal (11 items) plus a cognitive screening tool could offer the 'best' combination of current measures while offering greatest coverage of COS-endorsed outcomes with fewest items.

However, the use of a suite of complete or partial measures creates challenges, particularly in terms of validity and interpretation of scores. To enable comparisons among PROMs, measures of the same outcome domain can sometimes be translated into a common metric, developed by PROsetta Stone (www.prosettastone.org). However, when using more than one whole measure, if there is duplication across measures this may lead to burdensome completion schedules and could lead to inconsistency i.e., patient completes measures covering same construct differently, particularly if completing at different times with different recall periods

Furthermore, the ICHOM group declined to recommend the KDQOL measures: stating that the KDQOL-SF contained substantially more questions than strictly needed to measure the six standard set domains, while the KDQOL-36 provided only two summary scores on physical and mental health (109). Questionnaire length and the associated time burden has been an issue for clinicians in their hesitance to use PROMs, and while patients indicate that length is not a barrier provided their submitted data is used for a stated purpose (4), it is an important factor to consider when choosing a measure, as respondent burden can contribute to overall poor compliance (117).

The use of the KDQOL suite of measures does align with findings from a systematic review exploring measurement properties of PROMs used in adults with CKD which found evidence to support the use of either the KDQOL-SF and the KDQOL-36 in dialysis patients (2). The measures offered the advantage of a generic core (SF-36 or SF-12 respectively) but with a kidney disease specific component. While generic HRQOL components attribute certain health-related outcomes to general health status, disease specific measures attribute symptoms/outcomes to a specific disease. Additionally, although the SF36/12 were not specifically developed for use in health economic evaluation, the SF-6D provides a means for using these measures when exploring cost-effectiveness of interventions (118, 119). Disease specific attribution is important because it shifts focus to that disease as opposed to other diseases, or to health in general and has been shown to give a better signal about changes in patient quality of life that may be attributed to the disease and symptoms (120). Attribution is important in this population due to the highly technical care environment and the need to collect responses that clinicians can action within their workflow (121).

The large number of available PROMs confirms findings from other studies. A global systematic review exploring symptom burden and HRQOL in CKD found that more than 50 PROMs covered 68 different symptoms reported by patients (3) and perceived gaps in outcome capture commonly leads researchers to develop new tools, sometimes ignoring legacy measures which could be adapted or modified. Cohen et al (2019) suggest that the KDQOL-36 may not address factors, particularly symptoms, which are most important to patients in a contemporary setting, given the substantial

improvements in dialysis delivery and other aspects of ESKD management (50), indicating that regular review and revision of even well used instruments is required.

This review underlines the variety of PROMs development reasons and usage; from evaluating effectiveness of dialysis modality (CHOICE CHEQ measure) (72), for use in research (KDQ, SONG Fatigue measure) (67, 83) to symptom control (DSI) (75) and screening (BDI) (27). Whilst it is ideal to have a tool that has more than one purpose, this might not be possible (15). It can be argued that a single PROM cannot complete multiple functions adequately, and it might be better to have a suite of available measures. A domain specific PROM might be more useful for screening or could be used as a secondary adjunctive PROM following use of a multidimensional generic or disease specific measure. If focus is upon a particular aspect of HD care such as vascular access, a domain specific PROM such as the HARQ (55) or the VASQoL (60) should be considered. Those taking a pragmatic approach about the need to collect actionable PRO data within current clinical systems might choose to focus on symptoms rather than other aspects of HRQOL, and choose to use an instrument such as Dialysis Symptom Index (DSI) (75) or the CKD Symptom Burden Index (74). Both these measures have been previously highlighted as having the most comprehensive symptom coverage when compared to other measures (3) .

Decisions relating to PROM choice should involve meaningful patient and public involvement, to ensure key outcomes that are important to your patient population are assessed. Outcomes relating to religion and spirituality are missing from the identified COS but are very relevant to certain groups (122). Other important factors to

consider include accessibility and permissions. Legacy measures can be hard to access, with no clear permissions pathway. Candidate measures that have been well investigated and offer online resources (interpretation guidelines, scoring manual, and evidence of psychometric properties) will aid implementation plans.

A possible solution to length and coverage issues is the use of item banks and Computer Adaptive Testing (CAT) (123). CAT methodology has its psychometric basis in Item Response Theory (IRT) and reduces the overall questionnaire burden by refining the number of questions needed in a survey by not asking inappropriate or redundant items given the respondent's level of health (123). Ware et al (2019) have developed a CKD health-related QOL item bank and evaluated an approach to measuring CKD specific QOL impact using a single summary score, with the approach reducing respondent burden by measuring CKD-specific QOL with either a six-item static survey or a three- to six item CAT. (123), Overall, compared with the KDQOL-36, the new summary approach performed better across multiple tests of validity, and CAT surveys were more efficient than static surveys in measuring the impact of CKD on QOL (123). The PROMIS Global Health and PROMIS-29 HRQOL measures, recommended for use by ICHOM, can also be delivered using CAT. ICHOM developers could not achieve a consensus on a single measure for use, determining that recommendations should be kept under review with each revision of the standard set (109), presumably as new measures emerge, psychometric properties of these and legacy measures are tested and new measurement approaches are established.

4.6.1 Limitations

Scoping reviews are designed to provide an overview of the existing evidence base regardless of quality, and assessment of the methodological quality of included studies was not a requirement (124-127).

The comprehensive systematic review conducted in the target population by Aiyegbusi et al 2017 (2) evaluated the psychometric properties of 14 HD measures and the PROQOLID^{TM} database, an online database designed to assist in the search and evaluation of clinical outcome assessments, has full and partial entries for 54% of included PROMs (128) but full assessment of the measurement properties of all 46 identified PROMs was deemed outside the scope of this review. For benefit to be derived from using PROMs it is important that they are well validated; ensuring that they measure what they are supposed to, produce consistent results, and capture all aspects of the construct(s) under investigation. Further research is required to investigate which of the included PROMs display evidence of adequate measurement properties.

The SONG-HD outcomes that were not deemed critically important to all stakeholder groups have not been strictly defined (106) (see Table One). This means that a degree of interpretation was used to assess outcome and domain coverage by items within the reviewed PROMs. To combat this, two researchers (NEA and MA) undertook the affinity mapping process, with any disagreements resolved by consensus.

4.7 Conclusion and implications for practice

PROMs effectively capture the patient voice and can help deliver a personalized approach to care, but only if they measure those outcomes that have been identified as important to patients and clinicians.

This review was unable to identify a single measure that covers all COS outcomes. However, measure choice will be heavily influenced by the purpose of use, preferences of the target population and ease of accessibility and interpretation. Those involved in measure selection must balance practicality with precision when using scores to manage individual patient care or for research (123). There are currently three options; (i) use a single comprehensive measure such as the KDQOL-SF which offers a good assessment of overall HRQOL and the effects of living with kidney disease. However, while easily accessible and well investigated, it is lengthy and this could lead to reduced compliance, especially overtime, or (ii) use a shorter measure such as the KDQOL-36, and accept reduced outcome coverage, or (iii) use a combination of shorter measures to maximise coverage in as few items as possible. However, this may lead to item overlap and repetition, and burden associated with differing instructions, recall times and response options for both respondents and HCPs giving feedback (117).

To conclude, to fully capture the patient experience and offer data capable of use at individual and aggregate levels, clinicians might need to draw on a suite of measures. To reduce burden, ideally these measures wouldn't overlap, would have good measurement properties, be easy for patients to complete and straightforward for

clinicians to interpret and use. It is proposed future research should not focus on endless development of new tools, but place emphasis on optimising, refining, and evaluating current measures to these ends, through further study of psychometric properties, effective interpretation, new administration technologies and measurement advances.

Acknowledgements

Mary Dutton MSc. RN.

Competing interests

NEA receives funding from the National Institute of Health and Care Research (NIHR) under its Clinical Doctoral Research Fellowship Programme (Grant Reference ICA-CDRF-2018-04-ST2-027) and declares personal fees from GlaxoSmithKline (GSK) outside the submitted work.

MC is a NIHR Senior Investigator and receives funding from the NIHR Birmingham Biomedical Research Centre, the NIHR Surgical Reconstruction and Microbiology Research Centre, NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics and NIHR Applied Research Collaboration West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, UCB Pharma and GSK. MC has received personal fees from Astellas, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute (PCORI) outside the submitted work.

DK reports grants from Macmillan Cancer Support, Kidney Research UK, Innovate UK, the NIHR, NIHR Birmingham Biomedical Research Centre, and NIHR SRMRC at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, and personal fees from Merck and GSK outside the submitted work.

OLA receives funding from the NIHR Birmingham Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), West Midlands, NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics at the University of Birmingham and University Hospitals Birmingham NHS Foundation, Innovate UK (part of UK Research and Innovation), Gilead Sciences Ltd, Janssen pharmaceuticals, Inc, and Sarcoma UK. OLA declares personal fees from Gilead Sciences Ltd, GlaxoSmithKline (GSK) and Merck outside the submitted work.

The remaining authors declare no competing interests.

The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Care. Funders had no role in the design and conduct of the study, including the collection, management, analysis, and interpretation of the data, and preparation and review of the manuscript.

References

1. Nair D, Wilson FP. Patient-Reported Outcome Measures for Adults With Kidney Disease: Current Measures, Ongoing Initiatives, and Future Opportunities for Incorporation Into Patient-Centered Kidney Care. Am J Kidney Dis. 2019;74(6):791-802.
2. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Gheorghe A, Keeley T, et al. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. PLoS One. 2017;12(6):e0179733.
3. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954.
4. Anderson NE, McMullan C, Calvert M, Dutton M, Cockwell P, Aiyegbusi OL, et al. Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. BMJ Open. 2021;11(8):e052629.
5. Coulter A. Measuring what matters to patients. BMJ. 2017;356:j816.
6. Standardised Outcomes in Nephrology Haemodiaysis SONG HD. The SONG Handbook Sydney, Australia2017 [updated 18th Dec 2021. Available from: https://songinitiative.org/reports-and-publications/.
7. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney International Supplements. 2022;12(1):7-11.
8. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Nephrol Dial Transplant. 2019;34(11):1803-5.
9. Bello AK, Okpechi IG, Osman MA, Cho Y, Htay H, Jha V, et al. Epidemiology of haemodialysis outcomes. Nat Rev Nephrol. 2022;18:378–95.
10. Flythe JE, Dorough A, Narendra JH, Forfang D, Hartwell L, Abdel-Rahman E. Perspectives on symptom experiences and symptom reporting among individuals on hemodialysis. Nephrol Dial Transplant. 2018;33(10):1842-52.
11. Almutary H, Bonner, A, Douglas, C. Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced CKD stage and dialysis modality. Journal of Renal Care. 2016;42(Issue 2):73-82.
12. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. Nature Reviews Nephrology. 2020;16(10):573-85.
13. Urquhart-Secord R, Craig JC, Hemmelgarn B, Tam-Tham H, Manns B, Howell M, et al. Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study. Am J Kidney Dis. 2016;68(3):444-54.
14. United States of America Department of Health and Human Services Food and Drug Administration. Guidance for industry. Patient reported outcomes measaures: Use in medical product development to support labeling claims.; 2009 Dec 2009. Report No.: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

15. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. BMJ. 2019;364:k5267.
16. Schick-Makaroff K, Levay A, Thompson S, Flynn R, Sawatzky R, Thummapol O, et al. An Evidence-Based Theory About PRO Use in Kidney Care: A Realist Synthesis. The Patient. 2021;15(1):21-38.
17. International Consortium for Health Outcomes Measurement. ICHOM Chronic Kidney Disease: Data Collection Reference Guide 2021 [updated Revised Oct 28th 2021. Available from: https://connect.ichom.org/patient-centered-outcome-measures/chronic-kidney-disease/.
18. Gargon E WP, Altman DG, Blazeby J M, Clarke M. The COMET Initiative database: progress and activities from 2011 to 2013. Trials. 2014(15):279.
19. Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(Suppl 3):280.
20. Kirkham JJ, Davis K, Altman DG, Blazeby JM, Clarke M, Tunis S, et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. PLoS Med. 2017;14(11):e1002447.
21. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology. 2005;8(1):19-32.
22. Peters MDJ, Marnie C, Colquhoun H, Garritty CM, Hempel S, Horsley T, et al. Scoping reviews: reinforcing and advancing the methodology and application. Syst Rev. 2021;10(1):263.
23. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.
24. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic Reviews. 2016;5(1):210.
25. Rao S, Carter W B, Mapes D L, Kallich J D, Kamberg C J, Spritzer K L , Hays R D. Development of Subscales from the Symptoms/Problems and Effects of Kidney Disease Scales of the Kidney Disease Quality of Life Instrument. Clinical Therapeutics. 2000;22:1099-111.
26. Elamin S, A.H EE, S.E EA, Abu-Aisha H. Arabic translation, adaptation, and validation of the kidney disease quality of life short-form 36. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia.30(6):1322-32.
27. Bautovich A, Katz I, Loo CK, Harvey SB. Beck Depression Inventory as a screening tool for depression in chronic haemodialysis patients. Australasian Psychiatry. 2018;26(3):281-4.
28. Nochaiwong S, Ruengorn C, Koyratkoson K, Chaisai C, Awiphan R, Thavorn K, et al. Clinical interpretation of the Uremic Pruritus in Dialysis Patients (UP-Dial) scale: a novel instrument for the assessment of uremic pruritus. Journal of the European Academy of Dermatology & Venereology. 2018;32(7):1188-94.
29. Goh KKK, Lai PSM, Lim SK. Cross cultural adaptation and validation of the Malay Kidney Disease Quality of Life (KDQOL-36TM). BMC Nephrology. 2019;20(226).

30. Flythe JE, Dorough A, Narendra JH, Wingard RL, Dalrymple LS, DeWalt DA. Development and content validity of a hemodialysis symptom patient-reported outcome measure. Qual Life Res. 2019;28(1):253-65.
31. Schouten RW, Harmse VJ, Dekker FW, Van Ballegooijen W, Siegert CEH, Honig A. Dimensions of Depressive Symptoms and Their Association with Mortality, Hospitalization, and Quality of Life in Dialysis Patients: A Cohort Study. Psychosomatic Medicine. 2019;81(7):649-58.
32. Finkelstein FO, van Nooten F, Wiklund I, Trundell D, Cella D. Measurement properties of the Short Form-36 (SF-36) and the Functional Assessment of Cancer Therapy - Anemia (FACT-An) in patients with anemia associated with chronic kidney disease. Health and Quality of Life Outcomes. 2018;16(1):111.
33. Picariello F, Moss-Morris R, Macdougall IC, Chilcot J. Measuring fatigue in haemodialysis patients: The factor structure of the Chalder Fatigue Questionnaire (CFQ). Journal of Psychosomatic Research. 2016;84:81-3.
34. Peipert JD, Bentler P, Klicko K, Hays RD. Negligible impact of differential item functioning between Black and White dialysis patients on the Kidney Disease Quality of Life 36-item short form survey (KDQOL^{TM}-36). Qual Life Res. 2018;27(10):2699-707.
35. Rodakowska E, Wilczynska-Borawska M, Fryc J, Baginska J, Naumnik B. Oral health-related quality of life in patients undergoing chronic hemodialysis. Patient Preference and Adherence. 2018;12:955-61.
36. Van Der Willik E, Leegte M, Van Ittersum F, Prantl K, Bart H, Dekker F, et al. First dutch registry of patient-reported outcome measures (proms) has a low response in dialysis patients. Nephrology Dialysis Transplantation. 2018;33(suppl 1):i262.
37. Dang TL, Lai F-C, Lin Y-K, Chou K-R, Miao N-F, Liao Y-M. Psychometric Evaluation of the Vietnamese Hemodialysis Stressor Scale. Clinical Nursing Research. 2018;27(3):364-85.
38. Sharif Nia H, Pahlevan Sharif S, Koocher GP, Yaghoobzadeh A, Haghdoost AA, Mar Win MT, et al. Psychometric Properties of the Death Anxiety Scale-Extended among Patients with End-Stage Renal Disease. Omega: Journal of Death & Dying. 2020;80(3):380-96.
39. Chao S, Yen M, Lin T-C, Sung J-M, Wang M-C, Hung S-Y. Psychometric Properties of the Kidney Disease Quality of Life–36 Questionnaire (KDQOL-36™). Western Journal of Nursing Research. 2016;38(8):1067-82.
40. Chilcot J, Hudson JL, Moss-Morris R, Carroll A, Game D, Simpson A, et al. Screening for psychological distress using the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS): Initial validation of structural validity in dialysis patients. General Hospital Psychiatry. 2018;50:15-9.
41. Collister D, Rodrigues JC, Mazzetti A, Salisbury K, Morosin L, Rabbat C, et al. Screening questions for the diagnosis of restless legs syndrome in hemodialysis. Clinical Kidney Journal.12(4):559-63.
42. Chilcot J, Almond MK, Guirguis A, Friedli K, Day C, Davenport A, et al. Self-reported depression symptoms in haemodialysis patients: Bi-factor structures of two common measures and their association with clinical factors. General Hospital Psychiatry. 2018;54:31-6.

43. Collister D, Rodrigues JC, Mazzetti A, Salisbury K, Morosin L, Rabbat C, et al. Single Questions for the Screening of Anxiety and Depression in Hemodialysis. Canadian Journal of Kidney Health & Disease. 2019;6:2054358118825441.
44. Gutierrez-Sanchez D, Leiva-Santos JP, Sanchez-Hern, ez R, Hern, ez-Marrero D, et al. Spanish modified version of the palliative care outcome scale-symptoms renal: cross-cultural adaptation and validation. BMC Nephrology. 2016;17(1):180.
45. Biniaz V, Moonaghi HK, Froutan R, Ebadi A. Subjective hemodialysis adequacy can also be measured: Development and psychometric properties evaluation of subjective adequacy questionnaire. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia. 2019;30(6):1333-41.
46. Hadjiioannou I, Wong K, Lindup H, Mayes J, Castle E, Greenwood S. Test-Retest Reliability for Physical Function Measures in Patients with Chronic Kidney Disease. Journal of Renal Care. 2020;46(1):25-34.
47. Dehesa-Lopez E, Correa-Rotter R, Olvera-Castillo D, Gonzalez-Parra C, Baizabal-Olarte R, Orozco-Vega R. Transcultural adaptation and validation of the Mexican version of the kidney disease questionnaire KDQOL-SF36 version 1.3. Quality of Life Research. 2017;26(1):193-8.
48. Jia-Wen L, Hung-Chih C, Che-Yi C, Hung-Rong Y, Tsai-Chung L, Mao-Feng S, et al. Transformation of 5-D itch scale and numerical rating scale in chronic hemodialysis patients. BMC Nephrology. 2017;18:1-5.
49. Prado de Souza D, de Souza Orlandi, F. Translation and cultural adaptation of Patient Perceptions of Hemodialysis Scale in Brazil. Revista Brasileira de Enfermagem. 2019;72(2):314-20.
50. Cohen DE, Lee A, Sibbel S, Benner D, Brunelli SM, Tentori F. Use of the KDQOL-36™ for assessment of health-related quality of life among dialysis patients in the United States. BMC Nephrology. 2019;20(1):112.
51. Kittiskulnam P, Sheshadri A, Johansen KL. Validation of a New Physical Activity Instrument Against Pedometers Among Dialysis Patients. Journal of Renal Nutrition. 2019;29(6):498-503.
52. Raj R, Ahuja K, Fr, sen M, Murtagh FE, Jose M. Validation of the IPOS-renal symptom survey in advanced kidney disease: A cross-sectional study. Journal of Pain and Symptom Management. 2018;56(2):281-7.
53. Cho MK, Kim SY, Shim HY. Validity and Reliability of the Korean Version of the Dialysis Symptom Index for Hemodialysis Patients. Journal of Nursing Research. 2018;26(6):399-410.
54. Rehman IU, Khan TM. Validity and reliability of the Urdu version of the 5D itching scale to assess pruritus among patients with chronic kidney disease in Pakistan. BMC Nephrology. 2017;18:1-6.
55. Nordyke RJ, Nicholson G, Gage SM, Lithgow T, Himmelfarb J, Rivara MB, et al. Vascular access-specific health-related quality of life impacts among hemodialysis patients: qualitative development of the hemodialysis access-related quality of life (HARQ) instrument. BMC Nephrology. 2020;21(1).
56. Schouten RW, Nadort E, Harmse V, Honig A, van Ballegooijen W, Broekman BFP, et al. Symptom dimensions of anxiety and their association with mortality,

hospitalization and quality of life in dialysis patients. Journal of Psychosomatic Research. 2020;133(109995).
57. Prest MA, Parrott JS, Byham-Gray L. Test-Retest Reliability and Validity of the Nutrition-Specific Quality of Life Questionnaire. Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation. 2020;30(2):145-53.
58. Manju L, Joseph J, Beevi N. Validation of kidney disease quality of life short form 36 (KDQOL-SF™) in malayalam among patients undergoing haemodialysis in South Kerala. Indian Journal of Nephrology. 2020;30(5):316-20.
59. Tang E, Dano S, Edwards N, Macanovic S, Ford H, Bartlett S, et al. Screening for symptoms of anxiety and depression in patients treated with renal replacement therapy: utility of the Edmonton Symptom Assessment System-Revised. Qual Life Res. 2021;31(2):597-605.
60. Richarz S, Greenwood S, Kingsmore DB, Thomson PC, Dunlop M, Bouamrane MM, et al. Validation of a vascular access specific quality of life measure (VASQoL). J Vasc Access. 2021:11297298211046746.
61. Ajeebi A, Saeed A, Aljamaan A, Alshehri M, Nasradeen M, Alharbi N, et al. A study of quality of life among hemodialysis patients and its associated factors using kidney disease quality of life instrument-SF36 in Riyadh, Saudi Arabia. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia. 2020;31(6):1225-33.
62. Chen MC, Ho YF, Lin CC, Wu CC. Development and testing of the hemodialysis symptom distress scale (HSD-22) to identify the symptom cluster by using exploratory factor analysis. BMC Nephrology. 2021;22:128.
63. Joshwa B. Multiple Dimensions and Correlates of Fatigue in Individuals on Hemodialysis. Nephrology Nursing Journal. 2020;47(3):215-51.
64. Rui H, Haifen Z, Yan Y, Nina F, Qian L, Jun M, et al. Validation of the Chinese version of the low physical activity questionnaire (LoPAQ) with ActiGraph accelerometer in hemodialysis patients. BMC Nephrology. 2021;22(1):1-8.
65. Salazar-robles E, Lerma A, Calderon-juarez M, Ibarra A, Perez-grovas H, Bermudez-aceves LA, et al. Assessment of factors related to diminished appetite in hemodialysis patients with a new adapted and validated questionnaire. Nutrients. 2021;13(14):1371.
66. Yoosefinejad AK, Karjalian F, Momennasab M, Jahromi SE. Reliability and validity of the Persian version of 5-D itching scale among patients with chronic kidney disease. BMC Nephrology. 2021;22(1):16.
67. Ju A, Teixeira-Pinto A, Tong A, Smith AC, Unruh M, Davison SN, et al. Validation of a Core Patient-Reported Outcome Measure for Fatigue in Patients Receiving Hemodialysis. The SONG-HD Fatigue Instrument. 2020;15(11):1614-21.
68. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. Journal of Consulting and Clinical Psychology. 1988;56:893-7.
69. Suet-Ching WL. The psychometric properties of the Chinese Dialysis Quality of Life Scale for Hong Kong dialysis patients. Journal of Advanced Nursing. 2001;36(3):441-9.

70. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. J Psychosom Res. 1993;37(2):147-53.
71. Aiyasanon N PN, Nimmannit A, Jetanavanich P, Sritippayawan S. Validity and Reliability of CHOICE Health Experience Questionnaire: Thai Version. J Med Assoc Thai. 2009;92:1159-66.
72. Wu A, Fink N, Cagney K, Bass E, Rubin H, Meyer K, et al. Developing a Health-Related Quality-of-Life Measure for End-Stage Renal Disease: The CHOICE Health Experience Questionnaire1, 2. American Journal of Kidney Diseases. 2001;37(1):11-21.
73. Wilson MM TD, Rubenstein LZ, Chibnall JT, Anderson S, Baxi A, Diebold MR, Morley JE. Appetite assessment: simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. American Journal of Clinical Nutrition. 2005;82(5):1074-81.
74. Almutary H, Bonner A, Douglas C. Arabic translation, adaptation and modification of the Dialysis Symptom Index for chronic kidney disease stages four and five. BMC Nephrol. 2015;16:36.
75. van der Willik EM, Meuleman Y, Prantl K, van Rijn G, Bos WJW, van Ittersum FJ, et al. Patient-reported outcome measures: selection of a valid questionnaire for routine symptom assessment in patients with advanced chronic kidney disease - a four-phase mixed methods study. BMC Nephrol. 2019;20(1):344.
76. Weisbord SD, Fried LF, Arnold RM, Rotondi AJ, Fine MJ, Levenson DJ, et al. Development of a symptom assessment instrument for chronic hemodialysis patients: the Dialysis Symptom Index. Journal of Pain & Symptom Management. 2004;27(3):226-40.
77. Davison SN, Jhangri GS, Johnson JA. Cross-sectional validity of a modified Edmonton symptom assessment system in dialysis patients: a simple assessment of symptom burden. Kidney International. 2006;69(9):1621-5.
78. Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, et al. A brief self-administered questionnaire to determine functional capacity (The Duke Activity Status Index). The American Journal of Cardiology. 1989;64(10):651-4.
79. Cella D. The Functional Assessment of Cancer Therapy-Anemia (FACT-An) Scale: a new tool for the assessment of outcomes in cancer anemia and fatigue. Semin Hematol. 1997;34(3 Suppl 2):13-9.
80. Atchison KA, Dolan TA. Development of the Geriatric Oral Health Assessment Index. J Dent Educ. 1990;54(11):680-7.
81. Denis F, Hamad M, Trojak B, Tubert-Jeannin S, Rat C, Pelletier JF, et al. Psychometric characteristics of the General Oral Health Assessment Index (GOHAI) in a French representative sample of patients with schizophrenia. BMC Oral Health. 2017;17(1):75.
82. Elman S, Hynan LS, Gabriel V, Mayo MJ. The 5-D itch scale: a new measure of pruritus. The British journal of dermatology. 2010;162(3):587-93.
83. Laupacis A, Muirhead N, Keown P, Wong C. A disease-specific questionnaire for assessing quality of life in patients on hemodialysis.[Erratum appears in Nephron 1992;61(2):248]. Nephron. 1992;60(3):302-6.
84. Hays R D KJD, Mapes D L, Coons S J, Amin N, Carter W B, Kamberg C. Kidney Disease Quality of Life Short Form (KDQOL-SF): A Manual for use and scoring 1997

[Available from: https://www.rand.org/content/dam/rand/pubs/papers/2006/P7994.pdf.
85. Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB. Development of the kidney disease quality of life (KDQOL) instrument. Quality of Life Research. 1994;3(5):329-38.
86. Peipert JD, Bentler PM, Klicko K, Hays RD. Psychometric Properties of the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) in the United States. Am J Kidney Dis. 2018;71(4):461-8.
87. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. Cancer. 2000;88(9):2164-71.
88. Bihl MA, Ferrans CE, Powers MJ. Comparison stressors and quality of life of dialysis patients. Anna Journal. 1988;15(1):27-37.
89. Murphy SP PM, Jalowiec A. Psychometric evaluation of the Hemodialysis Stressor Scale. Nur Res. 1985;34:368-71.
90. Zengin N, Oren, B, Gul, A, Ustundag, H. Assessment of quality of life in haemodialysis patients: a comparison of the Nottingham Health Profile and the Short Form 36. International Journal of Nursing Practice. 2014;20(2):115-25.
91. Kind P, Carr-Hill, R. The Nottingham Health Profile - A useful tool for epidemiologists. Soc Sci Med. 1987;26(8):905-10.
92. Han H, Burrowes JD, Houser R, Chung MC, Dwyer JT. What is the impact of nutritional status on health-related quality of life in hemodialysis patients? Journal of Renal Nutrition. 2012;22(2):237-43.
93. Slade GD. Derivation and validation of a short-form oral health impact profile. Community Dent Oral Epidemiol. 1997;25(4):284-90.
94. Reeve BB, Stover AM, Alfano CM, Smith AW, Ballard-Barbash R, Bernstein L, et al. The Piper Fatigue Scale-12 (PFS-12): psychometric findings and item reduction in a cohort of breast cancer survivors. Breast Cancer Res Treat. 2012;136(1):9-20.
95. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-13.
96. Kroenke K, Baye F, Lourens SG. Comparative validity and responsiveness of PHQ-ADS and other composite anxiety-depression measures. J Affect Disord. 2019;246:437-43.
97. Twomey JC, Way CY, Parfrey PS, Churchill DN, Barrett BJ. Instrument Refinement: The Patient's Perception of Life on Hemodialysis Scale. SAGE Open. 2017;7(4).
98. Cella D, Riley W, Stone A. The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J Clin Epidemiol. 2010;63(11):1179-94.
99. Health Measures. A brief guide to the PROMIS® Fatigue instruments 2019 [Available from: http://www.healthmeasures.net/images/promis/manuals/PROMIS_Fatigue_Scoring_Manual.pdf.
100. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. Qual Life Res. 2009;18(7):873-80.

101. Ferrans CE, Powers MJ. Quality of life index: development and psychometric properties. ANS Adv Nurs Sci. 1985;8(1):15-24.
102. RAND Corporation. 36-item short form survey SF-36 2022 [Available from: https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html.
103. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33.
104. Nochaiwong S, Ruengorn C, Awiphan R, Panyathong S, Noppakun K, Chongruksut W, et al. Development of a multidimensional assessment tool for uraemic pruritus: Uraemic Pruritus in Dialysis Patients (UP-Dial). Br J Dermatol. 2017;176(6):1516-24.
105. Yang s KP, Wang J, Lin M, Su S. Development and Psychometric Properties of the Dialysis Module of the WHOQOL-BREF Taiwan Version. Journal of the Formosan Medical Association. 2006;105:299-309.
106. Evangelidis N, Tong A, Manns B, Hemmelgarn B, Wheeler DC, Tugwell P, et al. Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi Survey. Am J Kidney Dis. 2017;70(4):464-75.
107. Tong A, Craig JC, Nagler EV, Van Biesen W, Committee SE, the European Renal Best Practice Advisory B, et al. Composing a new song for trials: the Standardized Outcomes in Nephrology (SONG) initiative. Nephrol Dial Transplant. 2017;32(12):1963-6.
108. Tong A, Manns B, Wang AYM, Hemmelgarn B, Wheeler DC, Gill J, et al. Implementing core outcomes in kidney disease: report of the Standardized Outcomes in Nephrology (SONG) implementation workshop. Kidney International. 2018;94(6):1053-68.
109. Verberne WR, Das-Gupta Z, Allegretti AS, Bart HAJ, van Biesen W, Garcia-Garcia G, et al. Development of an International Standard Set of Value-Based Outcome Measures for Patients With Chronic Kidney Disease: A Report of the International Consortium for Health Outcomes Measurement (ICHOM) CKD Working Group. Am J Kidney Dis. 2019;73(3):372-84.
110. Ju A, Unruh M, Davison S, Dapueto J, Dew MA, Fluck R, et al. Establishing a Core Outcome Measure for Fatigue in Patients on Hemodialysis: A Standardized Outcomes in Nephrology–Hemodialysis (SONG-HD) Consensus Workshop Report. American Journal of Kidney Diseases. 2018;72(1):104-12.
111. Ju A, Unruh ML, Davison SN, Dapueto J, Dew MA, Fluck R, et al. Patient-Reported Outcome Measures for Fatigue in Patients on Hemodialysis: A Systematic Review. Am J Kidney Dis. 2018;71(3):327-43.
112. Ju A, Craig J, Tong A. Standardised outcome measures for fatigue in patients on haemodialysis. Nephrology. 2016;21:175.
113. Ju A, Unruh M, Davison SN, Dapueto J, Dew MA, Fluck R, et al. Identifying dimensions of fatigue in haemodialysis important to patients, caregivers and health professionals: An international survey. Nephrology (Carlton). 2020;25(3):239-47.
114. Duncanson E, Bennett PN, Viecelli A, Dansie K, Handke W, Tong A, et al. Feasibility and acceptability of e-PROMs data capture and feedback among patients

receiving haemodialysis in the Symptom monitoring WIth Feedback Trial (SWIFT) pilot: protocol for a qualitative study in Australia. BMJ Open. 2020;10(11):e039014.
115. Viecelli AK, Tong A, O'Lone E, Ju A, Hanson CS, Sautenet B, et al. Report of the Standardized Outcomes in Nephrology-Hemodialysis (SONG-HD) Consensus Workshop on Establishing a Core Outcome Measure for Hemodialysis Vascular Access. Am J Kidney Dis. 2018;71(5):690-700.
116. Ricardo AC, Hacker, E., Lora, C. M., Ackerson, L., DeSalvo, K. B., Go, A., Kusek, J. W., Nessel, L., Ojo, A., Townsend, R. R., Xie, D., Ferrans, C. E., Lash, J. P., & CRIC Investigators. Validation of the kidney disease quality of life short form 36 (KDQOL-36) US Spanish and English versions in a cohort of Hispanics with chronic kidney disease. Ethn Dis. 2013;23(2):202-9.
117. Aiyegbusi OL, Roydhouse J, Rivera SC, Kamudoni P, Schache P, Wilson R, et al. Key considerations to reduce or address respondent burden in patient-reported outcome (PRO) data collection. Nat Commun. 2022;13(1):6026.
118. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ. 2002;21(2):271-92.
119. Brazier JE, Roberts J. The estimation of a preference-based measure of health from the SF-12. Med Care. 2004;42(9):851-9.
120. University of Michigan Kidney Epidemiology and Cost Center (UM KECC). End-Stage Renal Disease Patient-Reported Outcomes Technical Expert Panel Summary Report 2017 [Available from: https://www.dialysisdata.org/sites/default/files/content/ESRD_Measures/ESRD_Patient_Reported_Outcomes_TEP_Summary_Report.pdf.
121. Finkelstein FO, Finkelstein SH. Time to rethink our approach to patient-reported outcome measures for ESRD. Clinical Journal of the American Society of Nephrology. 2017;12(11):1885-8.
122. Gelfand SL, Fitchett G, Moss AH. Recognizing the Potential Importance of Religion and Spirituality in the Care of Black Americans with Kidney Failure. Journal of the American Society of Nephrology JASN. 2022;33(7):1255-7.
123. Ware JE, Richardson MM, Meyer KB, Gandek B. Improving CKD-Specific Patient-Reported Measures of Health-Related Quality of Life. Journal of the American Society of Nephrology JASN. 2019;30(4):664-77.
124. Peters MDJ, Marnie, C., Tricco, A. C., Pollock, D., Munn, Z., Alexander, L., McInerney, P., Godfrey, C. M., Khalil, H. Updated methodological guidance for the conduct of scoping reviews. JBI Evidence Synthesis. 2020;18(10):2119-26.
125. Colquhoun HL, Levac D, O'Brien KK, Straus S, Tricco AC, Perrier L, et al. Scoping reviews: time for clarity in definition, methods, and reporting. J Clin Epidemiol. 2014;67(12):1291-4.
126. Levac D, Colquhoun H, O'Brien K. Scoping studies: Advancing the methodology. Implementation Science. 2010;5:69.
127. Davis K, Drey N, Gould D. What are scoping studies? A review of the nursing literature. Int J Nurs Stud. 2009;46(10):1386-400.
128. PROQOLID Database. 2022 [Available from: https://eprovide.mapi-trust.org/about/about-proqolid.

Appendices for Chapter 4

Appendix 4.1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews (PRISMA-ScR) Checklist

Appendix 4.2 Scoping review sample search strategy

Chapter 5: Global Use of Electronic Patient-Reported Outcome Systems in Nephrology: A Mixed Methods Study

5.1. Introduction

As was evident from the findings presented in Chapter 4, patients with CKD often experience multiple symptoms, with symptom burden being one of the most important predictors of reduced HRQOL (1) and it has been argued that recognition and subsequent treatment of these symptoms may have the greatest impact on HRQOL for patients receiving dialysis other than kidney transplantation (2). While findings from Chapter 4 demonstrate that ePROs may effectively capture the patient voice and help deliver a personalized approach to care, their use and implementation is not straightforward.

To inform the adoption and effective use of a complex intervention, such as ePROs, it is necessary to consider implementation strategies to optimise uptake and maximize adherence. Chapter 3 used qualitative methods to explore and identify the experiences and perceptions of patients and clinicians of the key factors at individual and organisational levels which could assist future prospective implementation efforts. The following chapter takes this a step further, and using a mixed methods study design, comprehensively identifies existing and developing ePROs systems around the world which were designed specifically for use in kidney care, ascertaining their key characteristics and the factors for successful implementation.

This chapter presents the findings from this study, in a paper format ahead of submission to a peer-reviewed journal; written in BMJ Open format. The protocol, outlining the full study rationale and methods can be found in Appendix 2.1.

The study paper refers to the RePROM (Renal electronic Patient-Reported Outcome Measure) pilot trial (ISRCTN12669006) and two publications outlining this research study which were co-authored by the author of this thesis, which can be found in Appendices 5.1 and 5.2. They are cited below:

(Appendix 5.1) Kyte D, Anderson N et al. (2020) **Development of an electronic patient reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease** Journal of Patient-Reported Outcomes https://doi.org/10.1186/s41687-020-00223-8

(Appendix 5.2) Kyte D, Anderson N, Bishop J, et al. (2022) **Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient reported outcome measure in the management of UK patients with advanced chronic kidney disease**. BMJ Open 2022;12:e050610.

References

1. Davison SN, Jhangri GS, Johnson JA. Longitudinal validation of a modified Edmonton symptom assessment system (ESAS) in haemodialysis patients. Nephrology Dialysis Transplantation. 2006;21(11):3189-95.
2. Almutary H, Bonner, A, Douglas, C. Symptom burden in Chronic Kidney Disease: a review of recent literature. Journal of Renal Care. 2013;39(3):140-50.

Global Use of Electronic Patient-Reported Outcome Systems in Nephrology: A Mixed Methods Study

This study was presented at the following conferences as outlined below.

Year	Conference	Location	Presentation type
2022	UK Kidney Week	Birmingham, UK	Oral
2022	ISOQOL (International Society for Quality-of-Life Research) 29th Annual Conference	Prague, Czech Republic	Oral

Global Use of Electronic Patient-Reported Outcome Systems in Nephrology: A Mixed Methods Study

Nicola Anderson MSc, RN Dip HE[1,2], Derek Kyte PhD[3] Christel McMullan PhD[1,4.5], Paul Cockwell PhD[7], Olalekan L Aiyegbusi PhD [1,5,6,8,9] Ravinder Verdi [10,] Melanie J Calvert PhD[1,4,5,6,8,9]

[1] Institute of Applied Health Research, Centre for Patient Reported Outcomes Research, University of Birmingham, Birmingham, United Kingdom

[2]Research and Development, University Hospitals Birmingham NHS Foundation Trust

[3] School of Allied Health and Community, University of Worcester, Worcester, UK

[4] NIHR SRMRC, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, UK

[5]NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics

[6]NIHR Birmingham Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust and University of Birmingham, UK

[7]Department of Nephrology, University Hospitals Birmingham NHS Foundation Trust

[8]Birmingham Health Partners Centre for Regulatory Science and Innovation

[9]NIHR Applied Research Collaboration West Midlands, University of Birmingham

[10] Patient Partner, University of Birmingham, UK

Corresponding author: Nicola Anderson [redacted]

5.2 ABSTRACT

5.2.1 Objectives

The use of electronic patient-reported outcome (ePRO) systems to support the management of patients with chronic kidney disease is increasing. This mixed methods study aimed to comprehensively identify existing and developing ePRO systems, used in nephrology settings globally, ascertaining key characteristics and factors for successful implementation.

5.2.2 Study design

ePRO systems and developers were identified through a rapid scoping review of the literature and contact with field experts. Developers were invited to participate in a structured survey, to summarise key system characteristics including: (i) system objectives; (ii) population; (iii) PRO measures used; (iv) level of automation; (v) reporting; (vi) integration into workflow; and (vii) links to electronic health records/national registries. Subsequent semi-structured interviews were conducted to explore responses.

5.2.3 Setting and participants

Eligible systems included those being developed or used in nephrology settings to assess ePROs and summarise results to care providers. System developers included those with a key responsibility for aspects of the design, development, or implementation of an eligible system.

5.2.4 Analytical Approach

Structured survey data was summarised using descriptive statistics. Interview transcripts were analysed using Codebook Thematic Analysis using domains from the Consolidated Framework for Implementation Research.

5.2.5 Results

Fifteen unique ePRO systems were identified across seven countries, ten system developers completed the structured survey and seven participated in semi-structured interviews. Despite system heterogeneity, reported features required for effective implementation included early and sustained patient involvement, clinician champions, and expanding existing electronic platforms to integrate ePROs. Systems demonstrated several common features, with the majority being implemented within research settings thereby affecting system implementation readiness for real-world application.

5.2.6 Conclusions

There has been considerable research investment in ePRO systems. Study findings may accelerate the implementation gap between research and practice by outlining key system features and factors to support the successful implementation of ePROs in routine kidney care.

5.2.7 Key Words:

Nephrology, Chronic Kidney Disease, Haemodialysis, Patients Reported Outcomes, Electronic Patient Reported Outcomes, Health Related Quality of Life

5.2.8 Article Summary

Strengths and limitations of this study

- This study summarises for the first-time characteristics of ePRO systems used globally to support the management of chronic kidney disease (CKD).
- The mixed methods approach offered a greater understanding of the barriers and facilitators of ePROs implementation, supplementing survey findings on key system characteristics.
- The review was restricted to English language publications of ePRO systems. Therefore, it is possible that potentially relevant publications published in other languages were excluded.
- It is possible that other ePRO systems that could be used in nephrology settings were not identified by this study.

5.3 INTRODUCTION

Patients at all stages of chronic kidney disease (CKD), and particularly those undertaking kidney replacement therapy, experience a high symptom burden and often report diminished health-related quality of life (HRQOL) (1-3). However, some symptoms remain under-recognized and unalleviated, leading to increased patient burden (4). HRQOL, is not only an important outcome in itself, it is associated with clinical outcomes such as healthcare utilisation and mortality (5). Symptom burden and impact on HRQOL can be assessed through the use of patient-reported outcomes (PROs), defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone" (6). PROs assessing the impact of CKD and associated treatments can be collected electronically (ePROs).

With the increase in telemedicine, accelerated by the COVID-19 pandemic (7, 8), the collection of ePROs has increasing significance. Web-based systems and 'bring your own device' schemes offer patients new ways to report symptoms, function, and HRQOL; they can report PROs in 'real-time' from home or in clinic prior to their consultation. Such use could assist in the management of symptoms, whilst ensuring that healthcare resources are used effectively to maximize impact (9).

There is increasing evidence, particularly from oncology, that ePROs are cost-effective (10), can facilitate shared-decision making, promote self-management, improve symptoms and HRQOL, reduce unplanned hospitalisation and enhance long-term outcomes including survival (11-14). In contrast to paper-based collection, ePRO

systems offer enhanced ease of use and reduced burden, increased user satisfaction and lower rates of missing data for both patients and clinicians (15-18).

The evidence around implementation of ePROs in nephrology is growing. Studies from North America demonstrate the feasibility of ePRO collection in haemodialysis (HD) settings (16, 19, 20) and the Australian SWIFT (Symptom monitoring With Feedback Trial) study (21) and Canadian EMPATHY study (22) are cluster randomised controlled trials exploring the usefulness of integrating PRO assessments in the clinical management of patients receiving HD. In advanced CKD populations, the RePROM study in the UK piloted the use, and established feasibility, of an ePRO for remote symptom monitoring in real-time (9, 23) (see Appendix 5.1 and 5.2), whilst the AmbuFlex telepro system is used in practice to manage renal follow up in Denmark (24, 25).

With this growth of ePRO system research and implementation in CKD globally, there is an opportunity to explore the key characteristics associated with successful implementation to support widespread adoption. Therefore, the objectives of this study were to (1) comprehensively identify ePRO systems for CKD, including those under development, (2) to explore system characteristics including methods of administration, levels of integration into existing workflow and electronic health records (EHR) and the reporting of ePROs to manage patient safety.

The overall aim being to provide a comprehensive classification of core factors which contribute to successful implementation of ePROs in nephrology, including common facilitators and barriers.

5.4 Study Design

5.4.1 Methods

This was a three phased study which used mixed methods:

Phase 1 comprised a rapid scoping review identifying ePRO Systems and corresponding developers (26). Eligible systems were those used in nephrology practice (excluding acute kidney injury) including related treatment areas (e.g., dialysis units), that assessed PROs electronically and provided a summary of the patients' responses to their care provider. Eligible systems from any country were included, in routine use or under development/study. A system developer could have a clinical or non-clinical role but must have carried key responsibility for aspects of design, development, or implementation of an eligible ePRO system. Systems were identified through publications in English, including conference abstracts and grey literature, using 'pearl' and 'snowballing' methodology, i.e., searching from known key references and checking reference lists. (27-29). Field experts were consulted. Data from these publications were used to create a structured survey exploring key system characteristics.

Phase 2 involved survey administration via an online survey platform Smart Survey ™ (www.smartsurvey.co.uk) piloted prior to use. System developers were invited to participate via email. The survey focused on system design and software features, integration of e-PRO collection and reporting in clinical care (see Appendix 5.3).

Phase 3: Optional follow up semi-structured interviews were undertaken online via videoconferencing software with survey participants, or a suitable team member

nominated by the original survey respondent. The purpose of these interviews was to expand on survey responses and allow more detailed system/organisational enquiry. All follow up interviews used a piloted study-specific topic guide (see Appendix 5.4)

5.4.2 Analysis

Data derived from the Phase 1 review was abstracted and charted, and descriptive statistics from the Phase 2 structured survey were tabulated. Analysis of Phase 3 interview data was undertaken using Codebook Thematic Analysis (30, 31) and the domains from the Consolidated Framework for Implementation Research (CFIR) (Figure 1). The CFIR is a determinant framework that can be used to identify and delineate contextual factors (i.e., barriers or facilitators) that influence the outcome of implementation efforts. (32, 33). Computer Assisted Qualitative Data Analysis Software CASDAQ (QSR NVIVO 12 (34)) was used to facilitate qualitative data analysis. Thematic analysis using a framework approach was chosen to systematically identify and analyse patterns of meaning within data, with the aim of highlighting the most salient features (30). The CFIR was used to gain insight into the overall effectiveness of the ePRO systems and associated implementation strategies. It is possible to rate constructs using the CFIR to undertake organisational comparison via Qualitative Comparative Analysis (QCA) (35). Due to the heterogeneity of systems, their context and stage of development, there was a danger of oversimplifying complex, dynamic descriptions of implementation processes and contexts so an aggregated data approach was not taken.

5.4.3 Patient and Public Involvement (PPI)

Patient partners were involved in the design of this study, and co-authored the final manuscript; where they specifically highlighted the importance of ensuring ePROs do not exacerbate existing health inequalities due to digital poverty (lack of digital access or skills) and health data poverty: which has been defined as the inability for individuals, groups, or populations to benefit from a discovery or innovation due to insufficient data that are adequately representative (36).

5.5 RESULTS

The review identified 15 ePRO systems across seven countries: Canada n=4, United States of America n=3, United Kingdom n=4, Denmark n=1, France n=1, The Netherlands n=1, Australia n=1 (Table 1). Ten system developers responded to the survey request (66% response rate). System developers held varying academic and clinical academic research posts, all demonstrating outcomes methodology expertise. Key responsibilities ranged from funding acquisition and stakeholder engagement, to overseeing system development, piloting, and evaluation. Seven developers agreed to a follow up semi-structured interview: one expert delegated this task to a member of their study team.

5.5.1 Key system characteristics

Table 2 outlines characteristics of surveyed systems and figure 1 illustrates system objectives. The most common primary objective was symptom management associated with CKD and/or renal replacement therapy by HD. However, systems were implemented across kidney disease stages and treatment modalities (see Table 1). A key secondary goal was the identification of psychosocial problems. Aggregate uses of

ePROs for benchmarking or commissioning of services were not common; one system collected satisfaction with care data (37), and two others assessed quality of care (21, 38). There was variation in funding source; academic (40%), government (30%) and charitable funding (30%), with 70% of systems being developed in the last five years. Half of the systems were developed in-house by local informatics teams, with the rest reporting collaborations across sectors with registries and technology companies. Systems allowed ePROs to be completed in different settings; the most common setting for completion was hospital clinic (80%). Only one system could be accessed by primary care (38).

One surveyed system had been implemented into routine practice, Ambuflex (25); all other systems were at varying stages of development with most having conducted pilot/feasibility testing. Two identified systems were being evaluated within a cluster randomised controlled trial (21, 22), while another was being evaluated in a co-designed demonstration trial (38) (see Table 1). Tablet was the most popular mode of administration. Two systems offered a clinic-based kiosk facility (25, 39). Training was available or planned for clinical staff in all systems but focused largely on system access and functionality. Seven systems had developed training materials for patients and four for administrative staff. Four systems had patient education material administered within the system, only one of these linked self-management guidelines to scores (9). Systems were evaluated by various means including formative research (57.1%), progress-focused evaluation concurrent to implementation (57.1%) and retrospective evaluation (14.3%). Patients were involved in evaluation strategies, influencing changes to content/order of measures, timing and frequency of

administration, improved data visualisation to show trends and the addition of symptom guidance. Only 60% of systems were currently linked with the EHR.

5.5.2 Data collection and assessment

Table 3 summarises key data collection functions. Half the developers reported using a newly developed PRO measure, either completely new or a mix of existing tools. Only three systems had ePRO availability in languages other than English (20, 21, 39, 40), although several developers reported plans for future translations, dependent on funding. There were a mixture of mechanisms to remind patients to complete their ePROs, with email (50%) and verbal reminders (50%) being most popular. Reminders were seen as the best way to avoid missing data (55.6%), but some systems offered a save and return function.

5.5.3 System reporting

Table 4 outlines system reporting features. Frequency of reporting was varied, with most common timing of assessment being prior to a clinical assessment (40%). However, some systems did have set time points ranging from one to six monthly. Two systems allowed patients to complete as required (9, 39).

All systems allowed patients and clinicians direct access to ePRO results or summary reports. Doctors (44.4%) and nurses (55.6%) were responsible for initial review and action of results. Follow-up (face to face, virtual, telephone) was largely dependent on scores. Electronic PRO reports contained current scores (summary and individual scores) in 70% of systems, 80% presented longitudinal changes and 40% offered cut scores (low, medium, high). One system was part of an overall dashboard with the option for patients to combine ePRO scores with lab values in a graph (38). In terms of

data visualisation, graphical presentation was most popular (80%) with 50% of ePROs using colour coding to highlight significance of scores. Less frequently used approaches of score presentation were tables (30%), numerical scores (30%) and emoticons (10%). Assistance with interpretation within the report was uncommon, but 30% of ePROs had developed a safety alert system dependent on respondent scores (9, 20, 25). Two of these systems could produce real-time alerts directly to clinicians (9, 20), while the AmbuFlex system keeps track by giving patients a red and yellow status and non-responders, who are presented to clinicians on an alert list (25).

5.5.4 Follow up interviews

Semi-structured interviews were carried out with seven ePROs developers, which allowed clarification of survey responses and explored the development process, to identify contextual factors working for and against implementation. Analysis of the interviews generated rich data which are presented in line with the CFIR key domains (32). Figure 2 outlines the conceptual framework; Illustrative quotations to support the key findings are provided in Box 1. Although presented in a linear fashion, the five domains and their respective constructs together provide context for implementation.

A. Intervention Characteristics: Factors associated with design and quality of the intervention, including how intervention is perceived.

Analysis highlighted the heterogeneity of the systems. However, developers agreed that systems need to be flexible, responsive, and follow an iterative development strategy that involves a process of refinement and evaluation using stakeholder feedback. All interview participants felt that their systems would need future

refinement, whether simple adaption to increase language availability or more complex programming to allow real-time symptom alerting or provision of self-management tools. Knowledge of context (population and setting) and purpose of ePRO data collection should be clearly defined and communicated to all stakeholders including patients. Developers acknowledged that the evidence base of the benefit of ePROs is less mature in nephrology than other clinical specialities. However, participants indicated ePROs could deliver a relative advantage over current care delivery: improving communication, supporting symptom management, enhancing self-care and shared decision making, with potential to reduce healthcare utilisation. However, all participants recognised the challenges, particularly of clinician engagement. They cited clinician anxieties around potential increases in workload and attendance to symptoms and problems unrelated to kidney disease. Consequently, several developers chose not to include real-time safety alerts associated with severe symptom reports.

Several systems used currently available infrastructure, utilising existing platforms, registries, and validated measures. Whilst this offered the advantage of existing expertise and reduced cost, this was offset by restrictions on local adaption and global comparability due to lack of harmonisation.

B. Outer Setting: the wider societal, economic, and organisational context

Developers all reported that their ePROs system programs had been impacted and delayed by the COVID-19 pandemic. Several developers reported that key staff including informatics teams reprioritised activity and had less availability to support

ePRO implementation. However, they stated that the rapid shift to virtual consultations and the recognition of the potential impact of ePROs in managing care and particularly outpatient planning invigorated interest in ePROs.

Developers highlighted the importance of partnership and collaboration – across clinical, academic, and commercial organisations. Registries were seen as an ideal collection platform. However, developers indicated multi-organisational approaches could lead to competing interests and governance issues that can cause delays.

Developers acknowledged the value of integration of ePROs directly into the EHR, but not all systems had this functionality. Some still required manual entry, which was reported as time consuming, costly and would not support real-time care. Many systems were standalone in nephrology secondary care, meaning data would not 'follow' patients across care settings and therefore could not be used to manage transition of care needs.

C. Inner Setting: the structural and cultural contexts around where the implementation will take place

Developers suggested the potential unintended consequences of ePRO implementation included further widening of health inequities, due to inadequate accessibility to digital devices, variable digital competence, and lack of inclusivity caused by poor availability of systems in multiple languages or failure to assess cultural compatibility. Some developers were investigating such outcomes in particularly vulnerable groups, e.g., elderly, ethnic minorities.

Some developers cited the continued prevalence of biomedical models of care, despite general acceptance of the need to move to person-centred care, as a barrier to ePRO implementation. They indicated approaches for shifting 'power' to patients by focusing on patient understanding of ePROs and involvement at all stages of design and implementation, along with patient peer support to counteract cultural barriers.

Doctors were the professional group most often involved in review and action of ePRO responses, but several systems directed ePRO scores to nursing staff or physician assistants as the initial handler. Resources needed to be available to allow the engagement of the wider multi-disciplinary team including supportive and rehabilitation services.

While clinicians were largely receptive to ePROs, workflow compatibility was seen as crucial to uptake, and this was reflected in the preference for a focus on symptom management as primary objective of capture. Several systems included free text options to report symptoms or problems and clinicians needed reassurance that this would not significantly impact workload. Participants reported that pilot study data suggested free text responses did not adversely increase workload but provided another mechanism for patient/provider communication, likewise with initial data on use of symptom report alerts.

D. Characteristics of Individuals: Factors associated with individuals involved in implementation

Participants discussed the importance of measuring outcomes which matter most to patients but emphasized the hypothetical danger of over digitising the patient experience, meaning that clinicians risk responding to scores alone rather than listening and connecting with the patient to further interpret ePRO data. Several participants looked forward to a future when ePROs might be given similar status to other forms of medical data. They noted clinicians frequently discuss burden associated with the collection and use of ePROs but did not consider similar factors associated with non-essential blood or invasive tests.

Developers reflected on the varied ability to deal effectively with responses, both at an organisational and individual level. They recognised the heavy and complex workload within the speciality, and while some systems offered management guides or further resources, participants were not all in favour of prescriptive treatment decision algorithms, some preferring to allow the exercise of clinical judgement.

E. The Process of Implementation

Systems were in different stages of planning, development, and feasibility to assess implementation and some were part of wider programs of research. A pragmatic approach to implementation was often described: for example, measures were chosen according to what was already being used and what patients would be prepared to complete. Existing platforms that had been previously assessed for governance and regulatory compliance were exploited. Implementation readiness for use in routine care was affected by most systems being investigated outside a real-world context.

Sustainability was an issue: future planning would need to include activities undertaken by research personnel including administration tasks, completion support and training. Long term IT and informatics support needs to be factored into costing for maintenance and adaption.

All developers stated the importance of patient involvement at all stages and outlined different ways patients had offered input and insight from co-design/production to research participation in usability testing. Staff dedicated to engagement were useful, ensuring extended community groups were involved.

Training associated with the education and knowledge needed to support ePROs appeared to be under-developed when compared to other aspects of system design. Several developers stated that training resources were in development and current iterations focused predominantly on how you use the system and did not extend to interpreting or actioning responses. It was recognised that training was time consuming and needed to be ongoing.

5.5.5 Overarching themes: Barriers and Facilitators to effective implementation

Across all CFIR constructs, analysis identified potential barriers and facilitators. Key barriers included the culture associated with biomedical models, variable clinical engagement particularly from doctors, and governance issues. Participants suggested facilitators included the development of patient driven systems, utilisation of clinical

champions who need both time and belief to promote the system, and developing existing resources where adaption was possible.

5.6 DISCUSSION

This review summarises available data on the features and implementation facilitators and barriers of 15 nephrology specific ePRO systems used across seven countries.

The majority of systems prioritised symptom management associated with underlying CKD (70%) or treatment (50%), over other potential uses of ePROs such as benchmarking and commissioning (see figure 1). While some systems were designed to collect ePROs across stages of kidney disease and treatment modalities, patients undergoing HD were the most common population for ePROs use. According to recent reviews, patients with CKD report between 56-68 common and/or severe signs and symptoms, with the exact symptom burden often determined by stage of disease and treatment (3, 41). Participants in this study reflected that management of symptoms was a good primary objective on which to concentrate early implementation efforts, with capability to add additional functionality and use in the future.

5.6.1 Stakeholder involvement

Our study has highlighted the increased development of nephrology ePROs in the last five years, with all developers reporting positive and negative effects of the COVID-19 pandemic. While there were delays to implementation due to reprioritisation of activity, the increased drive to deliver patient centred care via telemedicine has enhanced attention on ePROs.

To deliver person-centred care it is necessary to focus on what matters to patients, and correspondingly patients must be involved in determining which health outcomes to measure (42). All the surveyed systems had involved patients in aspects of development, including evaluation. Patient and public involvement (PPI) is a prerequisite to inclusive and equitable PROs research (43) and the meaningful involvement of patients in ePROs implementation programs is crucial to effective uptake (44). Well-established PPI groups, reflective of the total population, can offer advice on measure choice, language requirements and support resources. Patient input in design of software features including reporting and data visualization can ensure data is interpreted correctly (45) using various devices such as graphs, emoticons and heat maps (46, 47). Patient 'navigators' can offer health literacy and communication peer support for successful digital completion (48).

While important contributors to ePROs implementation are quality assurance, governance, informatics, and information technology departments, any successful ePROs system will need effective clinician 'buy in'. This study identified this as a key challenge, particularly from those clinicians not involved in ePROs research. Clinical staff state they are anxious about disruptions to already tight workflows and while ePROs are seen as a useful conversation starter, clinicians fear ePROs lack clinical utility for decision making, citing the current lack of empirical evidence on the benefits of using this data in nephrology (49, 50). There is a need for research to improve the evidence-base of ePRO use at individual and aggregated levels of kidney care (51), including studies which employ cluster designs and utilise techniques to maintain

allocation concealment (52). Studies included in this review are going some way to provide this evidence.

Developers described utilising the assistance of 'clinician champions'; individuals with both the time and influence to drive ePRO implementation. These champions would encourage clinicians to view ePRO scores as key health data, in the same way as a biomarker or a lab test, to manage care.

Studies have highlighted tension from clinicians in their ability to respond to ePROs, whether due to workload or belief that their scope of practice should be confined to matters related to nephrology (50, 53, 54). Some clinicians indicate they are more comfortable assessing, rather than actively managing, psychosocial symptoms (39). While holistic care is advocated within kidney care, it is not necessarily supported within the system and multidisciplinary approaches and further training in managing mental health problems is needed (55). Although research from other specialities suggests patient encounters using ePROs do not take longer (56), studies on workflow changes and impact are required.

5.6.2 Real-world implementation

A shift to implementation science for guidance on how to promote adoption, enhance readiness and optimise use of ePROs in real-world settings will also identify any unintended consequences of use. These include exacerbation of health inequalities and potential over digitisation of the patient experience in an already highly technical speciality (57, 58).

Many groups who are already subject to disadvantage and worse health outcomes are also subject to digital exclusion (59). Flexible systems enhance accessibility, offering patients' choice on time, frequency, mode of administration and place of completion. Electronic PROs are commonly completed in a healthcare facility via tablet, where completion support is available. However, onsite completion may impact workflow and support assistance from research staff will need to be factored into sustainability plans. Home completion may need to be incentivised and alternative means of completion should be offered as required i.e., voice response systems, hardcopy by post, following assessment of local population needs. Combinations of digital inclusion approaches are likely needed, to support patients with the digital and health literacy skills required to negotiate both their electronic health records (EHR) and any corresponding ePRO data (60) and offer access to hardware (43, 59). Evaluation of current ePROs systems should investigate whether ePROs are excluding already disadvantaged groups or if these groups might benefit through access to remote follow up; perhaps saving money from reduced transport and time off work costs.

While most systems offered or were developing self-management guidance for patients, a minority offered guidelines for health professionals in the form of treatment algorithms or decision tools based on patient scores. Effective training needs analysis at the planning stage is crucial to assess the support needed by the multidisciplinary team to respond to ePROs. Generally, systems were being developed iteratively, with training and support materials being developed or expanded after launch and this may be counterproductive to early and sustained engagement from clinical teams.

A pragmatic approach was adopted by developers, recognising the need for flexible, iterative systems capable of capturing and giving responses in real time, to meet needs of local population. Three systems had chosen to collect data via an existing national renal registry (21, 61, 62) and while this existing infrastructure supports secure collection, transfer and display of ePRO data with advantages for scaling up, this has to be offset against overall registry priorities and functionality; i.e., it may not be possible to offer real-time responses without local adaptions.

5.6.3 Areas for future research

Data linkage is central to multiple usages and harmonisation of collection platforms and associated measures will support this. Integration of ePROs within the EHR can offer 'one stop' access for clinicians and patients, if given access. Extended accessibility across healthcare providers would allow long-term monitoring across the kidney care continuum; none of the systems currently have this level of functionality.

New technologies, such as computerized adaptive tests (CATs) offer sophisticated measure delivery using algorithms based on item response theory to personalize ePROs for patients. CAT based measures are shorter, more accurate, and efficient (63). None of the reviewed systems were currently using CAT administration, however, several developers reported this was where they saw the future of ePROs and were actively researching this area; a renal specific item bank and associated CAT is currently being developed for use in the UK (64).

There has been considerable research investment in the development of ePROs to measure CKD symptoms and HRQOL. The next step is to accelerate the

implementation gap between research and practice; this study supports this objective by outlining key system features and exploring factors to optimise the delivery ePROs in routine care settings within nephrology.

Author's Contributions:

NA,MC, CM, PC, OLA, DK: Substantial contribution to the conception and design of the study
NA: Data collection NA, CM Analysis and interpretation of data for the work
NA, CM, DK, PC, OLA, MC, RV: Drafting and revising the work critically for important intellectual content and final approval of version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgments:

Mary Dutton

Data Availability Statement:

De identified data may be available upon reasonable request via the corresponding author (ORCID 0000-0002-0614-3198).

Ethical Approval:

Ethics approval was issued on 06/07/2021 by University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee: ERN_21-0495

Funding Statement

This manuscript refers to independent research funded by the National Institute for Health and Care Research (NIHR) under its Clinical Doctoral Research Fellowship Programme (Grant Reference ICA-CDRF-2018-04-ST2-027)

Competing interests

NEA receives funding from the National Institute of Health and Care Research (NIHR) under its Clinical Doctoral Research Fellowship Programme (Grant Reference ICA-CDRF-2018-04-ST2-027) and declares personal fees from GlaxoSmithKline (GSK) outside the submitted work.

MC is Director of the Birmingham Health Partners Centre for Regulatory Science and Innovation, Director of the Centre for the Centre for Patient Reported Outcomes Research and is a National Institute for Health and Care Research (NIHR) Senior Investigator. MC receives funding from the NIHR Birmingham Biomedical Research Centre, NIHR Surgical Reconstruction and Microbiology Research Centre, NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, and NIHR ARC West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, SPINE UK,UKRI, UCB Pharma, Janssen, GSK and Gilead. MC has received personal fees from Astellas, Aparito Ltd, CIS Oncology, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute (PCORI) outside the submitted work.

DK reports grants from Macmillan Cancer Support, Innovate UK, the NIHR, NIHR Birmingham Biomedical Research Centre, and NIHR SRMRC at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, and personal fees from Merck and GSK outside the submitted work. DK has received funding from

the NIHR and Kidney Research UK and is Chief Investigator for the RePROM and RCAT studies. CM receives funding from the National Institute for Health Research (NIHR) Surgical Reconstruction and Microbiology Research Centre, the NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, Innovate UK, and has received personal fees from Aparito Ltd outside the submitted work. OLA receives funding from the NIHR Birmingham Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), West Midlands, NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics at the University of Birmingham and University Hospitals Birmingham NHS Foundation, Innovate UK (part of UK Research and Innovation), Gilead Sciences Ltd, Janssen pharmaceuticals, Inc, and Sarcoma UK. OLA declares personal fees from Gilead Sciences Ltd, GlaxoSmithKline (GSK) and Merck outside the submitted work.

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. The study sponsor and funders have no role in study design, including collection, management, analysis, and interpretation of data; writing of the report and the decision to submit the report for publication.

References

1. Almutary H, Bonner, A, Douglas, C. Symptom burden in Chronic Kidney Disease: a review of recent literature. Journal of Renal Care. 2013;39(3):140-50.
2. Lowney AC, Myles HT, Bristowe K, Lowney EL, Shepherd K, Murphy M, et al. Understanding What Influences the Health-Related Quality of Life of Hemodialysis Patients: A Collaborative Study in England and Ireland. J Pain Symptom Manage. 2015;50(6):778-85.
3. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954.
4. Anderson NE, Calvert M, Cockwell P, Dutton M, Kyte D. The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective. Am J Kidney Dis. 2019;74(3):399-406.
5. Tang E, Bansal A, Novak M, Mucsi I. Patient-Reported Outcomes in Patients with Chronic Kidney Disease and Kidney Transplant-Part 1. Front Med (Lausanne). 2017;4:254.
6. United States of America Department of Health and Human Services Food and Drug Administration. Guidance for industry. Patient reported outcomes measaures: Use in medical product development to support labeling claims.; 2009 Dec 2009. Report No.: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.
7. Hull SA, Rajabzadeh V, Thomas N, Hoong S, Dreyer G, Rainey H, et al. Do virtual renal clinics improve access to kidney care? A preliminary impact evaluation of a virtual clinic in East London. BMC Nephrol. 2020;21(1):10.
8. Young A, Orchanian-Cheff A, Chan CT, Wald R, Ong SW. Video-Based Telemedicine for Kidney Disease Care. Clinical Journal of the American Society of Nephrology. 2021;16(12):1813-23.
9. Kyte D, Anderson N, Auti R, Aiyegbusi OL, Bishop J, Bissell A, et al. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. J Patient Rep Outcomes. 2020;4(1):55.
10. Lizée TB, Ethan ; Trémolières, Pierre ; Voog, Eric ; Domont, Julien ; Peyraga, Guillaume ; Urban, Thierry ; Bennouna, Jaafar ; Septans, Anne-Lise ; Balavoine, Magali ; Detournay, Bruno ; Denis, Fabrice. Cost-Effectiveness of Web-Based Patient-Reported Outcome Surveillance in Patients With Lung Cancer. Journal of Thoracic Oncology. 2019;14(6):1012-21.
11. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol. 2004;22(4):714-24.
12. McCann L, Maguire R, Miller M, Kearney N. Patients' perceptions and experiences of using a mobile phone-based advanced symptom management system (ASyMS) to monitor and manage chemotherapy related toxicity. Eur J Cancer Care (Engl). 2009;18(2):156-64.
13. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA. 2017;318(2):197-8.
14. Basch E, Stover , A, M, Schrag, D, Chung, M, Jansen, J, et al. Clinical Utility and User Perceptions of a Digital System for Electronic Patient-Reported Symptom Monitoring During Routine Cancer Care: Findings From the PRO-TECT Trial. JCO Clinical Cancer Informatics. 2020;4:947-57.

15. Meirte J, Hellemans N, Anthonissen M, Denteneer L, Maertens K, Moortgat P, et al. Benefits and Disadvantages of Electronic Patient-reported Outcome Measures: Systematic Review. JMIR Perioper Med. 2020;3(1):e15588.
16. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).
17. Schick-Makaroff K, Molzahn AE. Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. BMC Health Serv Res. 2017;17(1):439.
18. Aiyegbusi OL, Nair D, Peipert JD, Schick-Makaroff K, Mucsi I. A narrative review of current evidence supporting the implementation of electronic patient-reported outcome measures in the management of chronic diseases. Therapeutic Advances in Chronic Disease. 2021;12.
19. Gabbard J, McLouth CJ, Brenes G, Claudel S, Ongchuan S, Burkart J, et al. Rapid Electronic Capturing of Patient-Reported Outcome Measures in Older Adults With End-Stage Renal Disease: A Feasibility Study. The American journal of hospice & palliative medicine. 2020;38:432-40.
20. Flythe JE, Tugman MJ, Narendra JH, Dorough A, Hilbert J, Assimon MM, et al. Feasibility of Tablet-Based Patient-Reported Symptom Data Collection Among Hemodialysis Patients. Kidney Int Rep. 2020;5(7):1026-39.
21. Greenham L, Bennett PN, Dansie K, Viecelli AK, Jesudason S, Mister R, et al. The Symptom Monitoring with Feedback Trial (SWIFT): protocol for a registry-based cluster randomised controlled trial in haemodialysis. Trials. 2022;23(1):419.
22. Johnson JA, Al Sayah F, Buzinski R, Corradetti B, Davison SN, Elliott MJ, et al. A cluster randomized controlled trial for the Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care (EMPATHY): a study protocol. BMC Health Services Research. 2020;20(1):1-14.
23. Kyte D, Anderson N, Bishop J, Bissell A, Brettell E, Calvert M, et al. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease. BMJ Open. 2022;12(3):e050610.
24. Grove BE, Ivarsen P, de Thurah A, Schougaard LM, Kyte D, Hjollund NH. Remote follow-up using patient-reported outcome measures in patients with chronic kidney disease: the PROKID study - study protocol for a non-inferiority pragmatic randomised controlled trial. BMC Health Serv Res. 2019;19(1):631.
25. Schougaard LMV, Larsen LP, Jessen AMK, Sidenius P, Dørflinger L, de Thurah A, et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow-up in chronic and malignant diseases. Quality of Life Research. 2015;25:525 - 34.
26. Tricco AC, Antony J, Zarin W, Strifler L, Ghassemi M, Ivory J, et al. A scoping review of rapid review methods. BMC Med. 2015;13:224.
27. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. BMJ. 2005;331(7524):1064-5.
28. Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. Cochrane Database Syst Rev. 2011(8):MR000026.
29. Lefebvre C, Glanville J, Wieland LS, Coles B, Weightman AL. Methodological developments in searching for studies for systematic reviews: past, present and future? Syst Rev. 2013;2:78.
30. Braun V, Clarke V. Can I use TA? Should I use TA? Should I not use TA? Comparing reflexive thematic analysis and other pattern-based qualitative analytic approaches. Counselling & Psychotherapy Research. 2021;21(2):37-47.

31. Braun V, Clarke,V. One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qualitative Research in Psychology. 2020:1-25.
32. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
33. Damschroder LJ, Reardon CM, Opra Widerquist MA, Lowery J. Conceptualizing outcomes for use with the Consolidated Framework for Implementation Research (CFIR): the CFIR Outcomes Addendum. Implement Sci. 2022;17(1):7.
34. QSR International Pty Ltd. NVivo (Version 12) 2018 [Available from: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home.
35. Damschroder LJ, Lowery, J. C,. Evaluation of a large-scale weight management program using the consolidated framework for implementation research (CFIR). Implement Sci. 2013;10(8).
36. Ibrahim H, Liu X, Zariffa N, Morris AD, Denniston AK. Health data poverty: an assailable barrier to equitable digital health care. The Lancet Digital Health. 2021;3(4):e260-e5.
37. Schick-Makaroff K, Tate K, Molzahn A. Use of Electronic Patient Reported Outcomes in Clinical Nephrology Practice: A Qualitative Pilot Study. Canadian Journal of Kidney Health & Disease. 2019;6:2054358119879451.
38. Perry LM, Morken V, Peipert JD, Yanez B, Garcia SF, Barnard C, et al. Patient-Reported Outcome Dashboards Within the Electronic Health Record to Support Shared Decision-making: Protocol for Co-design and Clinical Evaluation With Patients With Advanced Cancer and Chronic Kidney Disease. JMIR Res Protoc. 2022;11(9):e38461.
39. Evans JM, Glazer A, Lum R, Heale E, Mackinnon M, Blake PG, et al. Implementing a patient-reported outcome measure for hemodialysis patients in routine clinical care perspectives of patients and providers on esas-r:Renal. Clinical Journal of the American Society of Nephrology. 2020;15(9):1299-309.
40. Flythe JE, Dorough A, Narendra JH, Wingard RL, Dalrymple LS, DeWalt DA. Development and content validity of a hemodialysis symptom patient-reported outcome measure. Qual Life Res. 2019;28(1):253-65.
41. Flythe JE, Karlsson N, Sundgren A, Cordero P, Grandinetti A, Cremisi H, et al. Development of a preliminary conceptual model of the patient experience of chronic kidney disease: a targeted literature review and analysis. BMC Nephrology. 2021;22(1):233.
42. Coulter A. Measuring what matters to patients. BMJ. 2017;356:j816.
43. Calvert MJ, Cruz Rivera S, Retzer A, Hughes SE, Campbell L, Molony-Oates B, et al. Patient reported outcome assessment must be inclusive and equitable. Nature Medicine. 2022;28:1120-4.
44. Absolom K, Holch P, Woroncow B, Wright EP, Velikova G. Beyond lip service and box ticking: how effective patient engagement is integral to the development and delivery of patient-reported outcomes. Qual Life Res. 2015;24(5):1077-85.
45. Albers EAC, Fraterman I, Walraven I, Wilthagen E, Schagen SB, van der Ploeg IM, et al. Visualization formats of patient-reported outcome measures in clinical practice: a systematic review about preferences and interpretation accuracy. J Patient Rep Outcomes. 2022;6(1):18.
46. Snyder C, Smith K, Holzner B, Rivera YM, Bantug E, Brundage M, et al. Making a picture worth a thousand numbers: recommendations for graphically displaying patient-reported outcomes data. Qual Life Res. 2019;28(2):345-56.
47. Grossman LV, Feiner SK, Mitchell EG, Masterson Creber RM. Leveraging Patient-Reported Outcomes Using Data Visualization. Appl Clin Inform. 2018;9(3):565-75.
48. Guha C, Lopez-Vargas P, Ju A, Gutman T, Scholes-Robertson NJ, Baumgart A, et al. Patient needs and priorities for patient navigator programmes in chronic kidney disease: a workshop report. BMJ Open. 2020;10(11):e040617.

49. Zhang R, Burgess ER, Reddy MC, Rothrock NE, Bhatt S, Rasmussen LV, et al. Provider perspectives on the integration of patient-reported outcomes in an electronic health record. JAMIA Open. 2019;2(1):73-80.
50. Anderson NE, McMullan C, Calvert M, Dutton M, Cockwell P, Aiyegbusi OL, et al. Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. BMJ Open. 2021;11(8):e052629.
51. Schick-Makaroff K, Levay A, Thompson S, Flynn R, Sawatzky R, Thummapol O, et al. An Evidence-Based Theory About PRO Use in Kidney Care: A Realist Synthesis. The Patient. 2021;15(1):21-38.
52. Gibbons C, Porter I, Goncalves-Bradley DC, Stoilov S, Ricci-Cabello I, Tsangaris E, et al. Routine provision of feedback from patient-reported outcome measurements to healthcare providers and patients in clinical practice. Cochrane Database Syst Rev. 2021;10:CD011589.
53. Tong A, Winkelmayer WC, Wheeler DC, Biesen WV, Tugwell P, Manns B, et al. Nephrologists' perspectives on defining and applying patient-centered outcomes in hemodialysis. Clinical Journal of the American Society of Nephrology. 2017;12(3):454-66.
54. Viecelli AK, Duncanson E, Bennett PN, D'Antoine M, Dansie K, Handke W, et al. Perspectives of Patients, Nurses, and Nephrologists About Electronic Symptom Monitoring With Feedback in Hemodialysis Care. Am J Kidney Dis. 2022;80(2):215-26.
55. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. Burden of mental health symptoms and perceptions of their management in in-centre hemodialysis care: a mixed methods study. J Patient Rep Outcomes. 2021;5(1):111.
56. Basch E BL, Kerrigan C L, Velikova G. Implementation of Patient Reported Outcomes in routine medical care. American Society of Clinical Oncology Educational Book. 2018;38:122-34.
57. Rabin BA, Brownson RC, Haire-Joshu D, Kreuter MW, Weaver NL. A glossary for dissemination and implementation research in health. Journal of public health management and practice : JPHMP. 2008;14 2:117-23.
58. Stover AM, Haverman L, van Oers HA, Greenhalgh J, Potter CM, Group IPPiCPISW. Using an implementation science approach to implement and evaluate patient-reported outcome measures (PROM) initiatives in routine care settings. Qual Life Res. 2020;30(11):3015-33.
59. Honeyman M MD, Evans H, Davies A. Digital technology and health inequalities: a scoping review (2020) Cardiff: Public Health Wales NHS Trust; 2020 [Available from: https://phw.nhs.wales/publications/publications1/digital-technology-and-health-inequalities-a-scoping-review/?dm_i=21A8,75FES,2H1914,SZM5X,1.
60. Chapman R, Haroon S, Simms-Williams N, Bhala N, Miah F, Nirantharakumar K, et al. Socioeconomic deprivation, age and language are barriers to accessing personal health records: a cross-sectional study of a large hospital-based personal health record system. BMJ Open. 2022;12(1): e054655.
61. van der Veer SN, Couchoud C, Morton RL. The role of kidney registries in expediting large-scale collection of patient-reported outcome measures for people with chronic kidney disease. Clin Kidney J. 2021;14(6):1495-503.
62. van der Willik EM, Hemmelder MH, Bart HAJ, van Ittersum FJ, Hoogendijk-van den Akker JM, Bos WJW, et al. Routinely measuring symptom burden and health-related quality of life in dialysis patients: first results from the Dutch registry of patient-reported outcome measures. Clin Kidney J. 2021;14(6):1535-44.
63. Bass M, Morris, S., Neapolitan, R. Utilizing Multidimensional Computer Adaptive Testing to Mitigate Burden With Patient Reported Outcomes. AMIA Annual Symposium proceedings AMIA Symposium,. 2015:320-8.

64. Institute of Applied Health Research UoB. RCAT-Renal Computerised Adaptive Test Birmingham: University of Birmingham; 2022 [Available from: https://tinyurl.com/13vdwh0m.

Tables, Figures and Boxes

Table 1: Overview of ePRO systems

Name of System	Country	Renal Population	In current use Yes/No Research or routine care	System ePROs
ANZDATA SWIFT PROMs Module (1-4)	Australia	In-centre HD	Yes – pilot study reported, Cluster RCT in progress	SONG-HD fatigue measure IPOS-Renal EQ-5D-5L
cPRO-Collaborate Kidney Care (5)	United States of America	CKD Stages 1-3 CKD Stages 4-5 pre dialysis	Yes – clinical demonstration model	PROMIS and FACIT measures to assess symptoms, social isolation, practical/psychosocial needs, nutritional needs, global health
Cambian (ePRO-KIDNEY) (6-10)	Canada	Home HD, PD	No – platform used within reported research projects	Patient Assessment of Care for Chronic Conditions-20 questionnaire (PACIC-20) Kidney Disease Quality of Life-36 (KDQOL-36) Edmonton Symptom Assessment System renal (ESAS-r) EQ-5D-5L
OPT-ePRO (11-13)	United Kingdom	CKD Stages 1-3, CKD Stages 4-5 pre dialysis In-centre HD, Home HD, PD Transplant, Conservative Care	No – pilot study reported	POS-S-RENAL, EQ-5D-5L
Penguin (Cievert Ltd) (no published data)	United Kingdom	Transplant	Yes- Research pilot in progress	Penguin - New System specific measure (items unspecified)

RePROM (14-16)	United Kingdom	CKD Stages 4-5 pre dialysis	No – pilot study reported.	New study specific measure – items on fatigue; shortness of breath; loss of appetite; nausea or vomiting; itchiness or dry skin; pain; problems with fistula; faintness or dizziness; difficulty sleeping; restless legs; diarrhoea and ankle swelling. The questionnaire also includes an open text item
Unnamed System (17)	Canada	In-centre HD, Transplant	No – in development. Pilot study reported	PROMIS CATs (unspecified)
'Your symptoms matter' (18, 19)	Canada	In-centre HD	Yes – pilot study reported	ESAS-r: Renal
Survey data only – developers declined participation in optional FU interview				
Ambuflex (20-22)	Denmark	CKD Stages 4-5 pre dialysis, Conservative Care	Yes – in routine care	Single items from KDQOL, EORTC and SF-36
SMaRRT-HD (23, 24)	United States of America	In-centre HD	Unknown – feasibility study reported	SMaRRT-HD

System identified only – no survey or interview data included in evidence synthesis				
"Derby Evaluation of Illness" (25)	United Kingdom	CKD stages 4/5 pre-dialysis, in-centre HD, PD	Unknown – feasibility study reported	Six separate domains assessed by VAS: general wellbeing, pain, sleep, breathing, energy, fistula function and appetite.
EMPATHY study (26-29)	Canada	In-centre HD	Yes – Cluster RCT in progress	ESAS-r: Renal/IPOS-Renal and/or the EQ-5D-5L PROMs are administered by pen and paper or through an electronic platform on a tablet in accordance with HD unit resources.
K-Pal (30)	United States of America	Patient's ≥60 years of age with ESRD on HD	Unknown – feasibility study reported	Short-Form McGill Pain Questionnaire 2 (SF-MPQ-2), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder 7 Item Survey (GAD-7), Dialysis Symptom Index (DSI), Kidney Disease Quality of Life (KDQOL-36)
Unnamed system (31)	France	HD patients in a dialysis unit	Unknown – ePRO system used to describe symptom prevalence – unclear if responses feedback to care provider.	New study specific measures (items on stress/fatigue/sleep disturbance and overall health status)

Dutch Renal Registry (32-34)	The Netherlands	Advanced CKD and ESKD with and without renal replacement therapy	Yes – part of development of national registry of PROMs included in Dutch Renal Registry	Dialysis Symptom Index (DSI), SF-12

References for Table 1

1. Duncanson E, Bennett PN, Viecelli A, Dansie K, Handke W, Tong A, et al. Feasibility and acceptability of e-PROMs data capture and feedback among patients receiving haemodialysis in the Symptom monitoring WIth Feedback Trial (SWIFT) pilot: protocol for a qualitative study in Australia. BMJ Open.10(11):e039014.
2. Morton RL, Lioufas N, Dansie K, Palmer SC, Jose MD, Raj R, et al. Use of patient-reported outcome measures and patient-reported experience measures in renal units in Australia and New Zealand: A cross-sectional survey study. Nephrology. 2020;25(1):14-21.
3. Viecelli AK, Duncanson E, Bennett PN, D'Antoine M, Dansie K, Handke W, et al. Perspectives of Patients, Nurses, and Nephrologists About Electronic Symptom Monitoring With Feedback in Hemodialysis Care. Am J Kidney Dis. 2022;80(2):215-26.
4. Greenham L, Bennett PN, Dansie K, Viecelli AK, Jesudason S, Mister R, et al. The Symptom Monitoring with Feedback Trial (SWIFT): protocol for a registry-based cluster randomised controlled trial in haemodialysis. Trials. 2022;23(1).
5. Perry LM, Morken V, Peipert JD, Yanez B, Garcia SF, Barnard C, et al. Patient-Reported Outcome Dashboards Within the Electronic Health Record to Support Shared Decision-making: Protocol for Co-design and Clinical Evaluation With Patients With Advanced Cancer and Chronic Kidney Disease. JMIR Res Protoc. 2022;11(9):e38461.
6. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).
7. Schick-Makaroff K, Mharapara P. Use of Electronic Patient-Reported Outcomes in the Care of Patients with Kidney Failure. Nephrology Nursing Journal: Journal of the American Nephrology Nurses' Association. 2020;47(5):465-72.
8. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. Health & Quality of Life Outcomes. 2015;13:2.

9. Schick-Makaroff K, Thummapol O, Thompson S, Flynn R, Karimi-Dehkordi M, Klarenbach S, et al. Strategies for incorporating patient-reported outcomes in the care of people with chronic kidney disease (PRO kidney): a protocol for a realist synthesis. Syst Rev. 2019;8(1):20.
10. Schick-Makaroff K, Tate K, Molzahn A. Use of Electronic Patient Reported Outcomes in Clinical Nephrology Practice: A Qualitative Pilot Study. Can J Kidney Health Dis. 2019;6:2054358119879451.
11. Van Der Veer SN, Ercia A, Caskey FJ, Farrington K, Jury F, Rees M, et al. Developing an Intervention to Implement Electronic Patient-Reported Outcomes in Renal Services in the UK. Studies in Health Technology & Informatics. 2020;270:936-40.
12. Knowles SE, Ercia A, Caskey F, Rees M, Farrington K, Van der Veer SN. Participatory co-design and normalisation process theory with staff and patients to implement digital ways of working into routine care: the example of electronic patient-reported outcomes in UK renal services. BMC Health Serv Res. 2021;21(1):706.
13. Breckenridge K, Bekker HL, Gibbons E, van der Veer SN, Abbott D, Briancon S, et al. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. Nephrol Dial Transplant. 2015;30(10):1605-14.
14. Kyte D, Anderson N, Auti R, Aiyegbusi OL, Bishop J, Bissell A, et al. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. J Patient Rep Outcomes. 2020;4(1):55.
15. Kyte D, Anderson N, Bishop J, Bissell A, Brettell E, Calvert M, et al. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease. BMJ Open. 2022;12(3):e050610.
16. Kyte D, Bishop J, Brettell E, Calvert M, Cockwell P, Dutton M, et al. Use of an electronic patient-reported outcome measure in the management of patients with advanced chronic kidney disease: the RePROM pilot trial protocol. BMJ Open. 2018;8(10):e026080.
17. Wong D, Cao S, Ford H, Richardson C, ice, Belenko D, et al. Exploring the use of tablet computer-based electronic data capture system to assess patient reported measures among patients with chronic kidney disease: a pilot study. BMC Nephrology. 2017;18:1-10.
18. Evans JM, Glazer A, Lum R, Heale E, Mackinnon M, Blake PG, et al. Implementing a patient-reported outcome measure for hemodialysis patients in routine clinical care perspectives of patients and providers on esas-r:Renal. Clinical Journal of the American Society of Nephrology. 2020;15(9):1299-309.
19. Schell JO, Lupu DE. A step in the right direction the promise of proms in routine hemodialysis care. Clinical Journal of the American Society of Nephrology. 2020;15(9):1228-30.
20. Grove BE, Ivarsen P, de Thurah A, Schougaard LM, Kyte D, Hjollund NH. Remote follow-up using patient-reported outcome measures in patients with chronic kidney disease: the PROKID study - study protocol for a non-inferiority pragmatic randomised controlled trial. BMC Health Serv Res. 2019;19(1):631.
21. Grove BE, Schougaard LMV, Ivarsen PR, Kyte D, Hjollund NH, de Thurah A. Patient-reported outcome measures for clinical decision-making in outpatient follow-up: validity and reliability of a renal disease questionnaire. Journal of Patient-Reported Outcomes. 2021;5(1):1-11.

22. Schougaard L M LLP, Jessen A et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow up in chronic and malignant diseases. Qual Life Res. 2016;25(3):525-34.
23. Flythe JE, Dorough A, Narendra JH, Wingard RL, Dalrymple LS, DeWalt DA. Development and content validity of a hemodialysis symptom patient-reported outcome measure. Qual Life Res. 2019;28(1):253-65.
24. Flythe JE, Tugman MJ, Narendra JH, Dorough A, Hilbert J, Assimon MM, et al. Feasibility of Tablet-Based Patient-Reported Symptom Data Collection Among Hemodialysis Patients. Kidney Int Rep. 2020;5(7):1026-39.
25. Pittman ZC, John SG, McIntyre CW. Collection of daily patient reported outcomes is feasible and demonstrates differential patient experience in chronic kidney disease. Hemodial Int. 2017;21(2):265-73.
26. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. Burden of mental health symptoms and perceptions of their management in in-centre hemodialysis care: a mixed methods study. J Patient Rep Outcomes. 2021;5(1):111.
27. Johnson JA, Al Sayah F, Buzinski R, Corradetti B, Davison SN, Elliott MJ, et al. A cluster randomized controlled trial for the Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care (EMPATHY): a study protocol. BMC Health Services Research. 2020;20(1):1-14.
28. Davison SN, Klarenbach S, Manns B, Schnick-Makaroff K, Buzinski R, Corradetti B, et al. Patient-reported outcome measures in the care of in-centre hemodialysis patients. Journal of Patient-Reported Outcomes. 2021;5(1):1-8.
29. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. How the Routine Use of Patient-Reported Outcome Measures for Hemodialysis Care Influences Patient-Clinician Communication: A Mixed-Methods Study. Clin J Am Soc Nephrol. 2022;17(11):1631-45.
30. Gabbard J, McLouth CJ, Brenes G, Claudel S, Ongchuan S, Burkart J, et al. Rapid Electronic Capturing of Patient-Reported Outcome Measures in Older Adults With End-Stage Renal Disease: A Feasibility Study. Am J Hosp Palliat Care. 2021;38(5):432-40.
31. Guerraoui A, Prezelin-Reydit M, Kolko A, Lino-Daniel M, de Roque CD, Urena P, et al. Patient-reported outcome measures in hemodialysis patients: results of the first multicenter cross-sectional ePROMs study in France. BMC Nephrol. 2021;22(1):357.
32. van der Willik EM, Hemmelder MH, Bart HAJ, van Ittersum FJ, Hoogendijk-van den Akker JM, Bos WJW, et al. Routinely measuring symptom burden and health-related quality of life in dialysis patients: first results from the Dutch registry of patient-reported outcome measures. Clin Kidney J. 2021;14(6):1535-44.
33. van der Willik EM, Meuleman Y, Prantl K, van Rijn G, Bos WJW, van Ittersum FJ, et al. Patient-reported outcome measures: selection of a valid questionnaire for routine symptom assessment in patients with advanced chronic kidney disease - a four-phase mixed methods study. BMC Nephrol. 2019;20(1):344.
34. van der Willik EM, Milders J, Bart JAJ, Bos WJW, van Ittersum FJ, Ten Dam M, et al. Discussing results of patient-reported outcome measures (PROMs) between patients and healthcare professionals in routine dialysis care: a qualitative study. BMJ Open. 2022;12(11):e067044.

Table 2: System Characteristics

System Characteristic/Feature *multiple response options total ≠ 100%	Number n=10 (Skipped response)	Response %
System launched	(0)	
In development	1	10%
<1 year	1	10%
1-5 years	5	50%
>5 years	3	30%
How developed?	(0)	
In house informatics team	5	50%
Collaboration across sectors	4	40%
Commercial product	1	10%
Funding Source*	(0)	
Commercial	1	10.0%
Academic	4	40.0%
Charitable	3	30.0%
Government	3	30.0%
No of patient users	(1)	
In development	1	11.1%
<100	3	33.3%
100-500	3	33.3%
>500	2	22.2%
Primary location of use*	(0)	
Primary Care (Community/General Practice clinic)	10.0%	1
Secondary Care (Hospital clinic)	80.0%	8
Dialysis Centre	60.0%	6
Home	20.0%	2
System platform*	(0)	
Non-responsive website	2	20.0%
Responsive/mobile website	8	80.0%
Mobile application	2	20.0%
System Access*	(0)	
Computer	7	70.0%
Tablet	10	100.0%
Interactive Voice Response System	0	0.0%
Clinic Based kiosk	2	20.0%
Smartphone	7	70.0%

PRO selection*	(2)	
Automatic (by system) i.e., Provider	8	100%
By Patient	0	0.0%
System security features*	(1)	
Secure Log in	9	100.0
Encryption	7	77.8%
two factor log in	1	11.1%
Unsure	1	11.1%
Page features*	(1)	
Progress Bar	6	66.7%
Visual graphics i.e., graph, diagram, chart	4	44.4%
Automatic save function, Option to save and return later	1	11.1%
Training available	(0)	
Yes	9	90%
No	1	10%
Who receives training? *	(1)	
Clinical staff	9	100.0%
Administrative staff	4	44.4%
Patients	7	77.8%
Carers	0	0.0%
Form of e PRO system training*	(1)	
Face to face	7	77.8%
Online	7	77.8%
Integrated into ePRO system	2	22.2%
Facility for patient education*	(2)	
Administered in system	4	50.0%
Education linked to ePRO scores	1	12.5%
Automatic documentation of action	0	0.0%
No patient education offered	4	50.0%
In development	1	12.5%
Has the system been evaluated?	(0)	
Yes	7	70%
No	3	30%

Table 3: Data collection and assessment

Data Collection/Assessment *multiple response options total ≠ 100%	Number n=10 (Skipped responses)	Response %
Measure development*	(0)	
System uses new PROM	5	50%
System uses existing PROM	7	70%
Timing of Assessment*	(0)	
Prior to clinical assessment	4	40.0%
Set time point weekly	0	0.0%
Set time point monthly	1	10.0%
Set time point 3 monthly	3	30.0%
Set time point 6 monthly	1	10.0%
Set time point annually	0	0.0%
As required (by patient)	2	20.0%
Other	4	40.0%
Question format	(1)	
One question per page	3	33.3%
Multiple questions per page	0	0.0%
Mixed format of single and multiple questions	6	66.7%
Question Advancement	(1)	
Mouse click	6	66.7%
Automatic on completion	3	33.3%
Analysis Metric*	(0)	
Change from baseline	7	70.0%
Final value	6	60.0%
Time to event	0	0.0%
Other (system defined)	2	20.0%
Avoidance of Missing data*	(1)	
Allows multiple logins per assessment with automatic save function	0	0.0%
Allows multiple logins per assessment with save and return later function	3	33.3%
Allows not applicable (N/A) response	2	22.2%
Default response pre-selected (pre-populated neutral response)	0	0.0%
Reminders	5	55.6%
Other: i.e., Mandatory fields	4	44.4%
Notification of completed assessments*	(0)	
Automated submission notification to patient	1	10.0%
Automated submission notification to clinicians	4	40.0%
Email notification to patient from clinical team following review of responses	2	20.0%
App based notification	0	0.0%
Other: None/unsure	3	30.0%

Patient Reminder format*	(0)	
Email	5	50.0%
Telephone call	2	20.0%
Text message: SMS	2	20.0%
Verbally	5	50.0%
By letter	3	30.0%
No reminder	0	0.0%
App based push notification	1	10.0%
Flexible system features*	(1)	
Web based home and clinic login access	7	77.8%
Multiple assessment scheduling options	3	33.3%
Two or more sources for PRO selection (patient/provider)	1	11.1%
Self-identification of important issues by patient (CAT functionality)	3	33.3%
Free text availability	8	88.9%
Multiple language availability	3	33.3%
In app or push notifications	0	0.0%
Other: facility for multiple Lang/CAT currently not used	1	11.1%

Table 4: System reporting

System reporting/Integration *multiple response options total ≠ 100%	Number n=10 (Skipped responses)	% Response
ePRO report access*	(0)	
Via clinical portal/EPR	7	70.0%
Via immediate access i.e., summary print out on completion	4	40.0%
Results restricted to clinical encounter	0	0.0%
Other: Registry, emailed PDF to patient	2	20.0%
ePRO report content*	(0)	
Current scores including summary and individual scores	7	70.0%
Longitudinal change	8	80.0%
Interpretation included in report	3	30.0%
Cut scores (e.g., low, medium, high)	4	40.0%
Population norms or reference values	2	20.0%
Identification of meaningful change	1	10.0%
Modifiable reports	1	10.0%
General guidelines	4	40.0%
Other i.e., colour coding	3	30.0%
Who has access to report/summary*	(0)	
Patient	10	100.0%
Clinicians	10	100.0%
Care Provider	3	30.0%
Multiple care provider access	3	30.0%
Researcher	1	10.0%
Who is responsible for initial review & action	(1)	
Medical staff	4	44.4%
Nursing staff	5	55.6%
Administrative staff	0	0.0%
Other member of multidisciplinary team	0	0.0%
Form of clinical response*	(0)	
Prescribed electronic response dependent on score	2	20.0%
Clinician/staff follow up; follow up type (face to face, virtual) dependent on score/decision aids	9	90.0%
Automatic referral to member of multidisciplinary tea	1	10.0%
Automated patient education/message regardless of score	1	10.0%
Self-management support resource dependent on score	1	10.0%

Visual presentation of PROs scores*	(0)	
Graphical	8	80.0%
Tabular	3	30.0%
Numerical	3	30.0%
Emoticon	1	10.0%
Colour coded	5	50.0%
Other: No score/being developed for longitudinal data	2	20.0%
Safety Alert System (eAlert) – dependent on PRO score	(0)	
Yes	3	30.0%
No	7	70.0%
Intended recipient for eAlert	(7)	
Clinician/Staff	3	100%
Patients	0	0.0%
Care provider	0	0.0%
Caregiver	0	0.0%
Multiple recipients i.e., clinicians and patients	0	0.0%
Form of eAlert*	(7)	
Email	2	66.7%
Text message/SMS	0	0.0%
Telephone call	0	0.0%
Verbal	0	0.0%
Real time alert	2	66.7%
In App notification	0	0.0%
None	0	0.0%

Figure 1: ePRO systems objectives

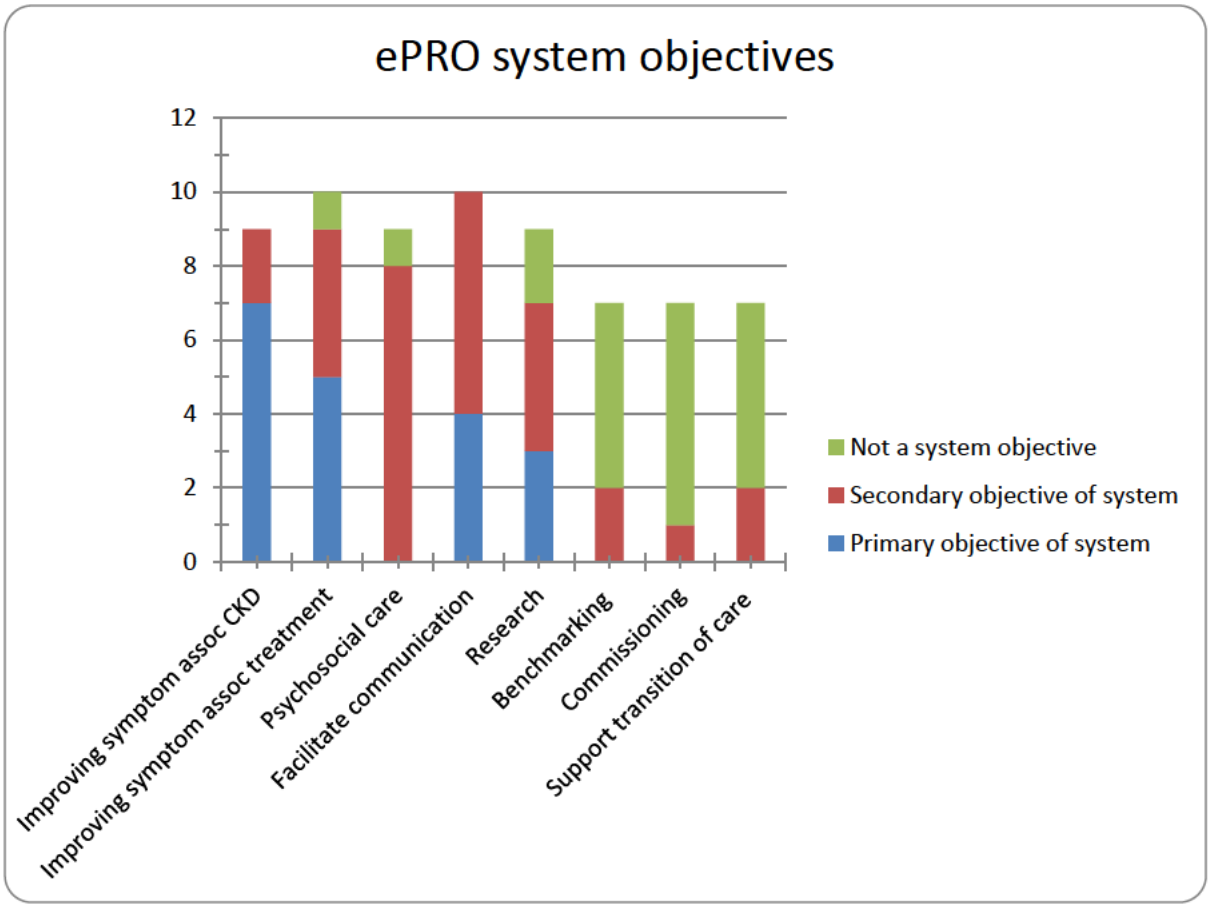
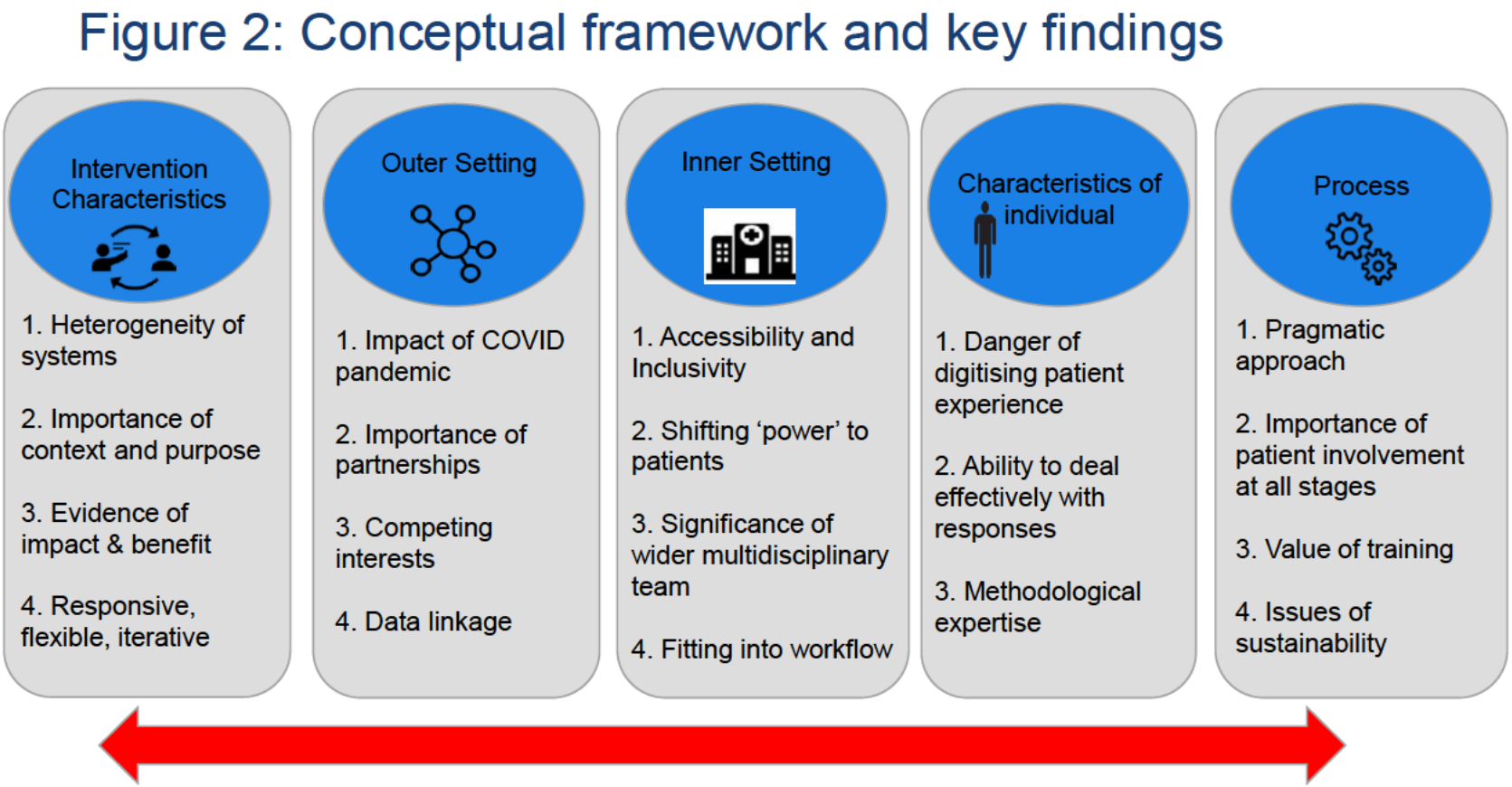


Figure 2: Conceptual framework and key findings



Box 1: Example illustrative quotations

Intervention characteristics 	*'huge variety of different PROMs available but no single PROM measured even 50% of the symptoms that were reported by the population. So I think that kind of sends a clear message that maybe there's a gap here for a PROM that's maybe a bit more comprehensive that meets patient's needs. But of course, the challenge of that is you don't want to make it too long or burdensome.' (01)* – **Heterogeneity of measures** *'the main learning is that if we want to make ePRO collection a success in renal or in any other specialty, we need to find concrete decisions or concrete situations where ePRO information really adds value. My learning is that just coming ePROs as a concept and saying, 'Now we're going to collect this data for anything,' I think that's not the way to go '(09).* **Importance of context and purpose** *'It's a huge investment to make ePROS part of a registry and create that extra platform, and so we need to really provide the evidence that it's going to work before we just outlay everything, don't we?' (010)* **– Evidence of impact & benefit**
Outer setting 	*'The way we designed the study was that we had intentionally iterations planned. We start with a certain package, then look at what works and what doesn't work and then add stuff. So related to what I said at the beginning, I think we started off with focusing on the patient side of things but acknowledging that we would need to do something to improve clinician engagement later on. So, I think I've always envisaged that being part of the later iterations, but we never got there because the study got paused halfway through the second wave' (09*) **– Impact of COVID** *'It's really like hospital IT department, we kind of conceived of them as like a vendor who we were purchasing their services to launch something, which I guess is good, really wanted to be full partners, but that means they brought in their whole ideas about what informatics kind of launches should be like and this stuff. Which they were included in the co-production from the very beginning, which was good, but that relationship still isn't totally as good as it could be and so that's a challenge too……. there's always sort of push and pull on the priorities (02)* – **Partnerships and competing interests** '*we were really planning to use this existing framework because this platform is integrated and linked to the local EPR and so once patients complete the questionnaires, their scores are displayed for the team' (04)* – **Data linkage**

Inner setting 	*'And that was one thing that we had thought of going into it, was that any time you have a new sort of feature that's going to be in the clinic, it can actually exacerbate disparities because the patients who are most ready to benefit from that, who are already doing the best probably will, right? And so now they've got this new thing that they can use and the patients that are already doing worse or have the most challenges or barriers, that's just another thing that they're not going to be able to take advantage of…' (02)* – **Accessibility and inclusivity** *'I think giving the people in these units the opportunity to fill out a survey in their own language also then increases the inclusivity of the trial' (010)* - **Accessibility and inclusivity** *But they [patients] did use words like feeling empowered to be a partner in the discussion. And obviously bringing up things, they had permission to bring things up and so it would be easier to start a conversation on mental health for example '(012)* – **shifting power to patients** *And if I was going to do it over again, I would have taken all the emphasis off the clinicians, and I would have put it on the patients. I would have educated the patients. I would have told them how they could use it. Initiating discussion with the clinician. Giving it to them to share with their clinician or, like I would have turned the tables (03***) – shifting power to patients** *'They [clinicians] felt that when you have the ePRO data in advance of a consultation it allowed them to focus in on the really important aspects around patient symptoms from the outset so maybe more efficient use of time' (01)* – **fitting into workflow**
Characteristics of individuals 	*'we also want to link the whole assessment to response pathways, both self-management support for patients and decision support for the professional teams' (04)* – **Ability to deal with responses** *'But I think what I'm resisting is the, to quote Foucault, which is about the technology of self which is going to put it in a box. And say, this is not so bad, this is okay. This is a screaming alert and so the screaming alert gets all of our attention and all of sudden we've 'technologicalised' a life. And we don't want to do that so, I'm worried about moving to the technological simplification of something that isn't simple…….Yes, particularly in our context right, particularly where we see high technological dependence primarily in the nursing role…' (03)* – **Danger of digitising the patient experience**

Process 	*'so the registry is a really important tool. We have this huge platform where we collect this information and it's already put in there in real time for the most part' (010)* – **Pragmatic approach** *'The patient advisory group was really important especially during development. There are a number of times where we sort of went in with a plan and for the intervention, for the ePRO and we changed our plans based on what they were telling us in terms of how this would actually work in practice' (01)* – **Importance of patient involvement** *'They got face-to-face training because they needed to understand the system really well and they needed to be able to explain what certain things meant. We did train nurses but that was more in groups. We maybe joined a multidisciplinary team meeting or a team meeting for the nurses in the morning, explaining where they could find the results' (09)* – **Value of training** *'I guess the sustainability is the question because you can envision training and so-called patient [involvement] at the launch of this initiative and hoping that it will be cascaded down further and sustained but probably some kind of ongoing training or at least continuing education in services for nurses is going to be necessary. That's also part of a sustainability plan. It needs to become part of the quality systems (04)* **– Sustainability**

Box 2: Key priorities for successful implementation

Macro level priorities (National) – formation of national collaborative groups to promote equitable and sustainable uptake of ePROs systems that have multiple application	Harmonisation of collection platforms e.g., National Registry – allowing data linkage to other healthcare settings i.e. primary care Harmonisation of measures (including item banks) Harmonisation of methods of interpretation and analysis metrics High quality research to demonstrate empirical evidence of benefit including real world evaluation Continued research on psychometric properties and interpretation of measures Investigation of new technologies i.e. CAT Endorsement of key guidelines such as the PCORI Users' Guide to Integrating Patient-Reported Outcomes in Electronic Health Records (1), ISOQOL Implementing PROs in clinical practice (2) and the ISPOR Validation of Electronic Systems to Collect Patient-Reported Outcome (PRO) Data Recommendations (3).
Meso level priorities (organisational) - key contributors to include clinicians, patients, carers, IT, informatics, QA, governance departments - Local systems specificity to maximise implementation and minimise effects on workflow	Involve all stakeholders – define and communicate key system objectives Use flexible system design to facilitate local, regional and national compatability EHR compatability Allow varying modes of administration, including paper Reminders – varying forms (email, app alert etc.) Alert systems – develop pathways and algorithms for action that compliment workflow High levels of automation to reduce workload Data collection features – need efficient, easy user experience Easy to access, save, submit and review Optimise data interpretation and visualisation Infrastructure support to deliver 'holistic care' – treatment and care algorithms Appointment and support for clinical 'champions' Patient peer support via 'Patient Navigators' Training packages to support implementations for all users Sustained IT support Ongoing evaluation programmes
Micro level priorities (Individual) Involve all key stakeholders and undertake meaningful PPI activity to ensure ePROs are accessible and inclusive for population	Identify local needs i.e., language availability requirements Provide support for those with poor health or digital literacy (need an assessment of needs) Optimise accessibility – allow onsite completion via kiosk or tablet, enable 'bring your own device' Evalution by patients to ensure systems are not over-digitising the patient experience by not discussing responses with individuals.

References for Box 2

1. Snyder C W, A.W., eds. Users' Guide to Integrating Patient-Reported Outcomes in Electronic Health Records Baltimore, MD: John Hopkins University; 2017 [Available from: https://www.pcori.org/document/users-guide-integrating-patient-reported-outcomes-electronic-health-records.
2. Aaronsen N ET, Greenhalgh J, Halyard M, Hess R, Miller D, Reeve B, Santana M, Snyder C. User's Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice: International Society of Quality of Life Research; 2015 [Jan 2015]. Available from: https://www.isoqol.org/wp-content/uploads/2019/09/2015UsersGuide-Version2.pdf.
3. Zbrozek A, Hebert J, Gogates G, Thorell R, Dell C, Molsen E, et al. Validation of electronic systems to collect patient-reported outcome (PRO) data-recommendations for clinical trial teams: report of the ISPOR ePRO systems validation good research practices task force. Value Health. 2013;16(4):480-9.

Appendices for Chapter 5

Appendix 5.1 Link to publication: Kyte D, Anderson N et al. **Development of an electronic patient reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease** Journal of Patient-Reported Outcomes https://doi.org/10.1186/s41687-020-00223-8

Appendix 5.2 Link to publication: Kyte D, Anderson N, Bishop J, et al. **Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient reported outcome measure in the management of UK patients with advanced chronic kidney disease**. BMJ Open 2022;12:e050610. doi:10.1136/ bmjopen-2021-050610

Appendix 5.3. Structured Survey *(www.smartsurvey.co.uk)* includes combined consent sheet v10.06.2021

Appendix 5.4. Topic Guide for semi-structured interviews v4 11.06.2021

Appendix 5.5 REC approved invitation email v1 10.06.2021

Appendix 5.6 REC approved Participant Information Sheet v3 06.06.2021

Chapter 6:
Discussion

6.1 Introduction

This final chapter summarises the principal findings of this PhD thesis. It offers an examination of the implications of these findings, the strengths and limitations of inquiry and recommendations for future research. It draws together a range of original research to discuss both how ePROs are, and could be, used in the management of patients with ESKD requiring HD. It summarises findings on how ePROs might be effectively implemented in HD settings to support safe, high-quality care; by offering views on potential measures, existing and emerging ePRO systems and priority areas for future investigation. It concludes with a comment article published in Nature Reviews Nephrology by the thesis author that offers a perspective on the fact that while considerable research and investment have focused on the use of ePROs in nephrology, systematic collection of ePROs to inform the care of patients with CKD remains sporadic, suggesting a change in culture is needed to encourage their wider adoption in clinical practice (1) . Together, the findings from this thesis can offer guidance on optimising the use and implementation of ePROs in the management of patients with ESKD requiring treatment with HD, to promote quality of care and safety.

6.2 Summary of principal findings

The narrative review was published as a perspectives article reproduced in Chapter 1. This paper provided a summary of the use of PROs data in HD settings including research, highlighting recent developments, gaps in the field and areas for future research (2). In terms of use in research settings, Chapter 1 highlighted that PROs use

in HD trials is uncommon, with a focus on surrogate rather than patient-reported outcomes such as phosphate concentration (3) and that trial design can be deficient (4). A recent review by Tong et al (2022) on patient-centred trial design in nephrology has indicated that this remains the case (5). This review emphasised the need for meaningful and impactful patient involvement in trials; from agenda setting and prioritisation to study design, implementation and evaluation, to ensure that trials generate evidence capable of addressing kidney patient needs and priorities (5). The imperative for high quality, non-tokenistic patient, and public involvement (PPI) and stakeholder engagement to inform ePRO use and implementation is further elaborated later in this chapter.

The narrative review also explored the use of PROs in routine clinical practice and highlighted the importance of defining the goals and purpose of PRO collection. Qualitative research studies were identified as a valuable next step to explore the perspectives of clinicians and patients to inform decisions around the operational delivery of PROs in HD settings i.e., timing, setting and frequency. Results of this work are summarised in chapter 3: Using PROMs during the management of patients with ESKD requiring treatment with haemodialysis (PROM-HD): a qualitative study.

The narrative review stressed the careful selection of PROMs to measure outcomes or domains of importance to key stakeholders, particularly patients. This review noted that the validated measures that were currently being advocated for use in HD settings (6) may not cover all recommended outcomes which had been included in HD-specific core outcome sets (COS) (2), and suggested further research was warranted to

investigate available validated PROMs and their item coverage, to determine whether new tools were required. This potential gap in measurement coverage was explored in chapter 4: A scoping review of patient-reported outcome measures used in haemodialysis: Are we measuring what matters?

The narrative review generated findings which indicated there could be considerable implementation challenges to using ePROs in routine care; such as dealing with interpretation of scores and feedback of responses, while maintaining patient safety and patient-clinician relationships, particularly if patient responses were difficult to action or address in the HD environment (2). The studies reported in chapters 3 (qualitative study exploring the perspectives of kidney patients and clinicians on PROs use and implementation) and Chapter 5 (mixed methods study investigating ePROs systems currently being used or developed in nephrology settings) will add to the body of evidence exploring these aspects of ePROs use in kidney care.

6.2.1 Experience and perspectives of clinicians and patients on ePROs use in HD settings

Chapter 3 reports a qualitative study which explored the experiences, views and perceptions of patients and healthcare professionals (HCPs) on the collection and use of PROs in HD settings. Semi-structured interviews with patients undergoing HD and HCPs involved in their care management highlighted the importance of the availability of empirical evidence to gain 'buy-in' from clinicians, particularly from doctors. Participants indicated that ePRO systems needed to be operationally flexible for routine functioning if such systems were going to be used to assess individual patient

data and aggregate use. Findings from this study resonated with key findings generated by the mixed methods study reported in chapter 5: where qualitative data derived from interviews with nephrology ePROs system developers appeared to concur with patients and HCPs views that any implementation must sit within a wider framework of education and support. In chapter 3, patients and HCPs felt that careful consideration needed to be given to barriers and facilitators of ePROs implementation: including effective leadership, consideration of the role of 'champions', effective launch plans and ongoing evaluation. Box 1 outlines the common barriers and facilitators to ePROs implementation generated following analysis of the qualitative data derived from the studies reported in chapters 3 and 5, using the Consolidated Framework for Interventional Research (CFIR) as a determinant framework to identify contextual factors pertinent to successful ePROs implementation (7).

Box 1: Common Barriers and Facilitators to ePROs implementation

Key Barriers	Key Facilitators
Culture associated with biomedical models	Patient driven systems
Poor clinical and patient engagement	Clinician champions and Peer navigator programs Key stakeholder engagement to understand context of implementation
Systems that do not meet needs of population	Patient and public involvement that is meaningful and non-tokenistic – to ensure systems are inclusive and meet needs of diverse populations Responsive, Flexible, simple to use E-Systems
Data linkage and governance	Use of existing platforms, development of governance frameworks for ePROs implementation and data linkage, reference to best practice guidelines
Conscious and unconscious gatekeeping	Increase the evidence base, improve health literacy, education and training on use and purpose of ePROs
Lack of knowledge about ePROs	Integration of ePROs education into systems Effective pre-launch engagement
Perceived complexity of ePROs implementation	Use of existing resources on ePROs use and implementation, education and training on use and purpose of ePROs
Poor digital and health literacy	Completion support and Integration with patient education systems, development of multi-media PROMs.
Lack of resources	'Buy in' at organisational and national level including professional bodies, networking to disseminate best practice, use of case-studies
Ability to deal with responses	Adequate resourcing, multi-disciplinary team approach, education for both clinicians and patients (response algorithms, ePROs interpretation guidance, self-management tools)

6.2.2 A scoping review of PROMs used in HD: Are we measuring what matters?

The objective of chapter 4 was to explore whether currently available PROMs used in HD adequately cover outcomes/domains recommended in HD-specific COS (8, 9), alongside collated data on key measure characteristics such as number of

items/domains, scoring, available translations, modes of administration, time to complete, recall period and accessibility and permissions. Findings from this scoping review offer an increased understanding of COS and instrument alignment and key questionnaire delivery characteristics in order to support clinicians and other key stakeholders in measure selection. The key findings from this review demonstrate that we do not currently have a single PROM which can measure all COS-endorsed outcomes, and many assess less than half of the endorsed outcomes.

It is acknowledged that measure choice will be heavily influenced by the purpose of use, preferences of the target population and ease of accessibility and interpretation. But using the approach described in chapter 4, measurement choice currently involves a trade-off between coverage, measurement length and evidence of adequate measurement properties. Based on coverage of COS-endorsed outcomes, the four best candidate measures were the CHEQ - CHOICE Health Experience Questionnaire (Choices for Healthy Outcomes in Caring for End-Stage Renal Disease) (83 items) (10), the legacy long form of the Kidney Disease Quality of Life questionnaire KDQOL™ (134 items) (11), the KDQOL-SF v1.3 (80 items) (12) and the KDQOL-36 (36 items) (13). Clinicians could opt to use the CHEQ-CHOICE, or KDQOL-SF which offer good coverage of outcomes but are lengthy and time-consuming to complete, or a shorter measure such as the KDQOL-36 which although shorter, offers less coverage. A combination of shorter measures might offer good coverage of outcomes but will likely add complexity in terms of varied recall times, repetition of items and may ultimately lead to increased respondent burden and reduced compliance (14). There is support within the literature for the use of the KDQOL-SF and particularly the KDQOL-36 in HD

populations based upon their psychometric properties (6, 15, 16), but further validation work is required, particularly in English-speaking populations. According to a systematic review by Aiyegbusi et al (2017) (6) the KDQOL-SF had strong evidence for internal consistency and structural validity and moderate evidence for test-retest reliability and construct validity while the KDQOL-36 had moderate evidence of internal consistency, test-retest reliability and construct validity. Ware et al (2019) state that the KDQOL and its iterations were developed decades ago and have not kept pace with conceptual and methodological advances in PROs measurement, and they discuss a new approach to assessing and summarising CKD-specific QOL using computer adaptive testing (CAT) (17). New technologies such as CAT offer one solution to potentially ease those tensions of coverage and precision with respondent burden and are discussed in more detail later in this chapter.

6.2.3 Electronic PRO systems being used and being developed in nephrology

To inform the adoption and effective use of a complex intervention, such as ePROs, it is necessary to consider implementation strategies to optimise uptake and maximize adherence. Chapter 3 used qualitative methods to explore and identify the experiences and perceptions of patients and HCPs of the key factors, at individual and organisational levels, which could assist future prospective implementation efforts. Chapter 5 takes this exploration further, using a mixed methods study design to comprehensively identify existing and developing ePROs systems which were designed specifically for use in kidney care around the world, ascertaining their key characteristics and the factors for successful implementation.

This review summarised available data on the features, implementation facilitators and barriers of 15 nephrology specific ePRO systems in use across seven countries. It identified the heterogeneity of ePRO systems but also areas of commonality in terms of population focus, chosen measures and key aspects of functionality. The study highlighted the importance of stakeholder engagement at all stages of the implementation and evaluation process and how a shift to implementation science might accelerate moves to use ePROs in nephrology routine care. As well as informing key priorities for implementation (see Chapter 5, Box 2 page 214) analysis of the semi-structured interviews with ePRO systems developers using the CFIR (7), generated findings on key barriers and facilitators relevant to nephrology settings (see Box 1, page 226).

6.3 Interpretation and implication of findings

This thesis has identified several key factors that need to be addressed for effective implementation of ePROs into the management of care for patients with ESKD requiring treatment with HD.

6.3.1 Expanding and disseminating the evidence base

Since 2015 there have been several trials external to the UK, largely from oncology settings, which have demonstrated that use of ePROs as an intervention in routine care settings can lead to improvements in patient-provider communication, care satisfaction, survival (18-20), quality of life and symptom control (21), and cost-effectiveness (22). In the UK, a research programme to develop and evaluate an

electronic system, called eRAPID, for cancer patients to remotely self-report adverse events had less clear signals (23). The primary hypothesis that eRAPID would have a significant positive impact on symptom control during chemotherapy (measured by FACT-G PWB subscale at 18 weeks) was not confirmed, although improvements in symptoms/side effects were seen earlier at 6 and 12 weeks (23). However, the study does appear to show a benefit in increased self-efficacy and perception of better overall QoL (23). Online reporting did not appear to increase the NHS workload in terms of calls or admissions and the cost-effectiveness analysis indicates that the eRAPID IT system may be preferred as the more cost-effective option over usual care (23).

More importantly for this thesis, the RePROM study (pilot feasibility randomised controlled trial exploring the use of an ePROs in the management of patients with advanced CKD – see Appendix 5.2) showed early indicators of the positive effects of ePRO symptom monitoring on healthcare utilisation; exploratory data demonstrated patients in the intervention arm reported fewer episodes of healthcare utilisation than those receiving usual care (24). A recent review summarising evidence of the impact of ePROs on clinical outcomes relevant to the management of chronic diseases, including CKD, argues that since most of the evidence they found was derived from oncology, that there is an urgent need for similar work in other specialties that care for medically complex patients (25).

In Canada, the Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care (EMPATHY) cluster randomised controlled trial is implementing and

evaluating the use of disease-specific and generic PROMs which are linked to treatment aids for clinicians and patients. In this study the primary outcome was patient-provider communication measured using a communication assessment tool, with secondary outcomes including patient management and symptoms, healthcare utilisation, and estimation of implementation costs (26). A mixed methods study using data from the EMPATHY study found the tool showed no significant improvement in communication between dialysis units which routinely collected PROs and those which did not, indicating that PROM use did not substantially improve patient-clinician communication (27). However, semi-structured interviews to explore patients' and nurses' perceptions of communication in relation to routine PROs suggested reasons why this might have been the case; the purpose of PRO use was not always clearly understood by patients and clinicians, PROs were not always used as intended despite clinician training and there was a perception of limited value (27). The overall study findings run counter to the narrative that PROs could improve patient-clinician communication (28, 29) but highlight the importance of further research into validation processes to express what core mechanisms are necessary for PROs use to enhance HD communication pathways. These include filling knowledge gaps, on the purpose and how to use responses, which eroded perceived value of PROs use (27). However, another qualitative study offers insight and practical guidance into how to discuss PROM results with patients undergoing HD. Highlighting the importance of preparation, time and setting to set up an active, trusting engagement where the clinician acted as a guide (30). They acknowledged the importance of feedback and a

multidisciplinary approach to responses, while recognising that clinicians might need to take more of a leading role when discussing sensitive topics (30).

Thus, the evidence base for the use of ePROs in nephrology is expanding, including methodological studies (i.e., new PROM development and assessment pf psychometric properties for new and legacy measures) as demonstrated in chapter 4, and with regard to feasibility and acceptability of ePROs seen in chapter 5 (24, 31-36). Yet, there is a pressing need for empirical research to improve the evidence base on the impact and benefits of using ePROs in nephrology, where currently the evidence is primarily theoretical (28). This evaluation void or empirical research gap (37), is currently being filled by another cluster randomised controlled trial taking place in Australia; the Symptom monitoring WIth Feedback Trial (SWIFT) is monitoring ePROs 3-monthly through the ANZDATA national registry, and feedback is given to participants and clinicians. The primary outcome of this registry based study is change in HRQoL, as measured by EuroQol 5-Dimension, 5-Level (EQ-5D-5L) instrument and secondary outcomes include overall survival, symptom severity (including haemodialysis-associated fatigue), healthcare utilisation and cost-effectiveness (38). In Denmark, although the population focus is advanced CKD pre-dialysis, a pragmatic, non-inferiority, randomised controlled trial is exploring PRO-based follow up in outpatients with CKD in order to evaluate the effectiveness of the quality of care, use of resources and clinical outcomes including initiation of acute dialysis, hospitalisation and mortality (39).

There is continued evidence building in other areas; such as the development of conceptual models of the patient experience of CKD (40), review and synthesis of common CKD symptoms (41) and exploration of CKD symptom clusters and ePROs (42-44). Such studies will assist selection of symptoms for inclusion in remote monitoring and consequently help prioritise those in need of intervention (41). The main reason for the necessity of such evidence is to secure the 'buy in' of key stakeholders, including decision makers in health authorities and government who require this evidence to inform and support future policy decisions, but particularly clinicians (45). The qualitative research study reported in chapter 3 found that HCPs were unwilling to invest their time or change their practice for an intervention that they felt could potentially be a 'tick-box' exercise (45) and some doctors were sceptical about benefits reported in other specialities, outlined above (45). Such findings were reflected in the semi-structured interviews undertaken with ePROs developers in chapter 5, who saw the 'buy in' of clinicians not actively involved in ePROs research as critical for effective implementation. Other studies have also identified that evidence of significant impact of ePROs on patient outcomes are required to influence change to current practices (46). Evidence from the SWIFT pilot study shows that the active engagement of nurses in encouraging and supporting patients during survey completion, and clinicians' prompt action following symptom feedback, were thought to improve the uptake and acceptability of ePROs symptom monitoring and management (47). However, this is countered by findings from the EMPATHY study where nurses sometimes offered a negative presentation of PROs, and researchers felt nurses had misunderstood the purpose of PROs collection as standardisation of care

rather than individualisation, meaning they and patients did not perceive the value of PROs (27).

One of the key challenges reported by clinicians in Chapter 3 was the perceived inability to effectively mediate responses; this could be due to lack of resources, expertise (not kidney-related) or lack of available interventions. These concerns are reflected in other studies, with HCPs concerned that repeated ePROs without the ability to intervene could antagonise therapeutic relationships (47) use of ePROs might lead to unrealistic expectations (46) and meaningful follow-up hindered by the lack of continuity of care in HD (27). In contrast patients have reported that being given the opportunity to discuss their symptoms and HRQOL, even if their condition could not be substantially improved, is enough to maintain the patient-clinician relationship, provided feedback was given and ePROs completion did not appear to be a 'tick-box exercise' (45, 47). Secondary analysis as part of EMPATHY trial, demonstrated PROM use had the potential to identify and prompt surface management of mental health concerns (depression/anxiety), but there were varying opinions on whether this fell under the purview of dialysis HCPs, particularly since there were limited available mental health resources, limiting management (48). A key finding of that study was that although holistic care was promoted, it was not supported by the system (48). Findings from this thesis demonstrate that implementation needs to occur alongside an educational framework about PROs which also includes further training on chronic disease management and multi-disciplinary approaches, termed the 'information loop' in chapter 3 (45). However, wider conversations about routine PROM use that includes mental health assessment and the required infrastructure needed to support such an

approach in HD settings are required. Particularly as psychosocial distress is common in patients undergoing HD and is associated with poor outcomes including shorter time to hospitalisation (49). This is set against a background of current lack of renal psychosocial service provision in the UK (50), which is reflected worldwide. Pre-pandemic there was already a global shortage of allied healthcare professionals, such as social workers and psychologists (51-53) and it is likely that the workforce capacity crisis has only worsened since the pandemic.

Appropriate training of HCPs to handle and respond to ePROs needs to be provided in order to facilitate integration with existing clinical workflows (54). Silbernagel et al (2018) found clinicians and patients in CKD settings had received no previous training on PROs use, nor did they instinctively know how to use PRO scores. They identified four areas for focus: 1) PROs use and interpretation in clinical practice, 2) Patients valuing of, and relationship to, the use of PROs in their own care, 3) Strategies for PROs to support multidisciplinary team working, and 4) Routine integration of PROs is a fundamental change to practice (55). Such training could be integrated within E-Systems or standalone; studies suggest modular e-learning with interactive case-based examples were effective (56).

6.3.2 The value of stakeholder engagement

The qualitative components of this thesis have clearly demonstrated the importance of effective stakeholder engagement to increase the likelihood of successful ePROs implementation. The mixed methods study (chapter 5) highlighted that interested

parties included not only clinicians and patients, but also informatics, IT, quality assurance and external parties such as commercial application developers.

Well-resourced PPI in clinical trials, across the all stages of the process from priority setting, to study design and dissemination and implementation can potentially increase the uptake of interventions and the potential impact on overall outcomes (5). For reasons that remain poorly understood, rapid progression of kidney disease is higher in patients from minority ethnic groups (57, 58). It is recognised that variables between ethnic groups exist at both individual and system levels throughout the kidney care system, leading to observable inequalities, indicating a need for culturally intelligent policy informed by research to prevent disadvantage (59). For patients from ethnic minority backgrounds, religious beliefs, cultural differences, language and mistrust may be barriers to discussions surrounding their CKD, care and treatment (60). A recent comment in Nature Medicine, co-authored by the writer of this thesis, highlights current challenges related to PRO data collection in underserved groups including but not exclusive to ethnic minorities, and identifies approaches for greater inclusion (61) – see Appendix 6.1. This paper advises consideration of the diversity, clinical characteristics and likely co-morbidities, cultural needs and languages, and literacy (overall, health and digital) of your population (61). Early engagement, in the context of trials, with the regulator to discuss enablers for increased enrolment of underserved populations is also advised (61). There are now significant resources to support and maximise effective engagement and involvement with patient and public stakeholders, including underserved groups, both at individual and community levels (62); highlighting the importance of funding to ensure adequate resources and cultural

competency of researchers (63, 64). Feedback to PPI contributors, informing them of how and why their input was useful to researchers and the overall research project, is seen as key to a reciprocal relationship but is often neglected (65). With regard to PROs, there are emerging frameworks identifying ways in which PPI can have a meaningful role and contribution to the co-development of PROMs (66), Patient partners and other key stakeholders can take a key role in choosing appropriate PROM functionalities shown to increase compliance, such as patient engagement features which could include an estimation of ePROM completion time, progress bar and/or navigation buttons, graphical presentation of PRO data to show longitudinal progress data and positive messaging (67).

6.3.3 Minimising potential undesirable consequences of ePROs implementation

The use of a determinant framework (CFIR) to assess those contextual factors which can act as powerful forces against implementation in the real world (7, 68), has highlighted several potential undesirable consequences of ePROs implementation which should be addressed:

Increasing existing inequalities: Underserved groups may reflect demographic, socioeconomic and health status factors relevant to the context and population being served (61). In the UK, people from lower socio-economic backgrounds and/or from Black, Asian or minority ethnic backgrounds are more likely to experience poorer outcomes including faster disease progression (69). The use of measures that were not developed, or culturally validated with these populations (70), as well as barriers to ePRO data completion (poor health/digital literacy, access to devices) could further

exacerbate inequalities through health data poverty (71) and the preferential use of ePROs by the health literate (61). However, further studies are needed to ascertain if ePROs use does intensify health inequalities and which populations are most vulnerable. A study from the USA reported that 'computer-inexperienced' participants, who were significantly older, more often men, more often black, and less educated than computer-experienced participants, derived more benefit from ePROs (19) while a study from Denmark has indicated that socioeconomically advantaged patients were referred more often to PRO-based follow-up than socioeconomically disadvantaged patients (72). In the UK, preliminary findings suggest that CKD patients who are older or from ethnic minorities are less likely to engage with ePROs (73). Similarly, findings from both the USA and UK show that socioeconomic deprivation, older age and non-English language and ethnicity were significant barriers to accessing hospital-based electronic health records (74, 75); of relevance if this is used as the platform for ePRO collection and feedback.

In the UK limited health literacy affects 25% of people with CKD which again disproportionately affects patients with low socio-economic status and non-white ethnicity (76). The ability to access, understand and use health-related information is further affected by cognitive decline (77) which is increasingly seen in patients undergoing HD, with prevalence rates between 51-76% (78-80). Such factors may reduce self-management skills resulting in poorer clinical outcomes (76). Whilst there is evidence that health literacy improves outcomes, and consequently improvements in population health literacy or increasing access to health services for patients with low health literacy may be a means reduce health disparities (81), what is

less clear is whether use of ePROs could improve overall health literacy, if implemented within a framework of patient education and self-management materials. The eRAPID intervention which included detailed severity-dependent advice to patients on how to self-manage mild/moderate symptoms associated with chemotherapy and when to contact their medical team, demonstrated observable improvements in self-efficacy (23). However, the eRAPID intervention was closely integrated in the site's care pathway (23), highlighting the importance of minimising disruptions to existing workflow.

In CKD, the EMPATHY study offered the use of actionable treatment and assessment aids developed by expert clinicians and patient partners for the management of key symptoms, alongside guidance on local resources and care pathways i.e., referrals. Patient facing materials on symptoms and aspects of self-care were also utilised (82). The RePROM study offered guidance and advice within the system associated with reported symptoms (83). Thereby reducing the burden on patients to find or remember advice around lifestyle, medications, and symptoms. It is important that patient needs are evaluated, and effective training and support given so that patients can understand the purpose of ePRO collection and maximise their usage, highlighted as so important by qualitative studies (45, 46). Engaging low literacy patients might need further exploration around use of multi-media PROMs (mPROMs) using features such as audio, animated gifs, avatars, icons, illustrated response scales and progress indicators (84). Supporting patients through the first steps of establishing access to their online records is associated with much higher rates of long-term use (85) and the likelihood is that such an approach to ePROs would find similar results. Further

intervention development and evaluation will determine whether health literacy is a modifiable determinant of ePROs use in CKD.

The importance of resourced, meaningful, and non-tokenistic PPI has already been discussed, but consideration of local context and population is imperative to offset potential inequalities and the findings from chapter 3 and 5 emphasised the importance of flexibility in mode, language availability and setting of completion. There should be consideration of alternatives to home completion for those unable to access their own device or those who wish to compartmentalise their healthcare i.e., using tablet/kiosks at the hospital or dialysis unit. Interactive voice recognition systems (IVRS) or personal digital assistants using artificial intelligence (AI) algorithms may be required. For those who don't want or can't use a computer or smart phone, a paper version may be necessary as a last resort to avoid digital exclusion (45). A systematic review has found paper and electronic modes of administration can be used interchangeably across settings without introducing bias and was useful to avoid missing data (86). However, delays with paper questionnaire return and data entry may hinder real-time monitoring, and with increased human resources costs associated with data handling; paper options can be an expensive alternative to web-based tools (87). Stakeholder engagement through all stages of ePRO systems design, delivery and evaluation can draw attention to issues of actual or potential inequality with a view to minimising its effects.

Over-digitising the patient experience: It has been said that time and workflow factors mean that HCPs often have insufficient time to listen to patients' health perceptions

leading to a focus on recording biomedical metrics rather than on individual patient needs, and that use of ePROs to assess symptoms and HRQOL might be a better way to develop appropriate goals of care (88)**.** However, participants in the mixed methods study emphasised the danger that clinicians using ePROs might respond to pure scores rather than using responses to engage in patient-centred communication. This finding is reflected in two recent qualitative studies where patients and clinicians stated ePROs might 'be a substitute for a clinical conversation rather than a conversation starter' (47) and the difficulty in assigning a number to an experience (27). Patients expressed anxiety about what that number could mean for their care i.e., would it remove them from a transplant list (27). Such risk could be mitigated through education and training: The PROmunication tool has been developed for cancer settings and uses a one-page work instruction to give clinicians a clear overview of how to prepare for, undergo and document a PRO-based consultation, with example Illustrations and verbal phrases. Associated training sessions covered evidence-based knowledge about the rationale, benefits and challenges of using PROs and experiential training (89).

Another facilitator identified during qualitative data analysis, is careful definition and communication of the purpose of ePROs implementation (45). HCPs have indicated the importance of understanding why and how ePROs are being used (45, 47). For patients, barriers have been the failure to appreciate the value of completing PROMs (90) lack of perceived utility (91), and an understanding how ePROs are being used to manage their care (28). Furthermore, deciding a clear purpose i.e., symptom monitoring or benchmarking, will affect other operational decisions including choice of

measure, frequency, recall, and feedback mechanisms (92, 93) and understanding and clarity of purpose will have an effect on perception of burden and could improve compliance (46).

Findings in chapter 5 emphasised the potential for clinical champion and patient navigator roles to support implementation and associated education programs for clinicians and patients alike. Patient navigators are trained non- medical personnel, who might be patients themselves, who help patients negotiate and transition across the care pathway (94). Within ePROs implementation, such roles should be held by individuals that are credible (94) and who have both time and knowledge to convey to colleagues and patients the potential importance and purpose of ePROs. Who these champions should be is context specific and studies have demonstrated that administrative staff and healthcare assistants might be best placed to provide ePROs support (73). There is a danger that within the high-pressure clinical environment, HCPs are acting as conscious and unconscious gatekeepers. In palliative care settings, clinicians have reported declining to use PROs for various reasons i.e., if they decide a patient is too unwell, patient lacks ability, there is not enough time, they are unable to deal with responses or general reluctance (95). Likewise, a study in Denmark recognised that some clinicians were more reluctant to introduce PRO-based follow-up and did not refer all relevant patients (72). Findings from the EMPATHY study indicated nurses sometimes offered a negative presentation of PROMs, which affected patient reception (27). The qualitative component of the mixed methods study (chapter 5) indicated the necessity for a cultural shift from the continued pervasiveness of the biomedical model to person-centred care as defined in chapter 2. Evidence that ePROs

can enhance workflow efficiency and improve patient care needs to be demonstrated and promotion of ePROs from international and national professional societies along with integration of ePROs into clinical service specifications is needed to enable their widespread implementation (1). The sharing of case studies which demonstrate best practices for successful and sustained patient and HCP engagement is needed (25). Patient-reported outcomes need to have parity alongside other clinical outcome measures. The SONG-HD initiative and findings from chapter 4 highlight that many outcomes of importance are self-reportable (96) and there needs to be a cultural shift in the perception of the hierarchy of data available for clinical decision making.

The final undesirable potential consequence of ePROs to be discussed is the creation of additional work; unexpected outcomes from innovations which lead to increased workload (97). While studies suggest adding ePROs symptom monitoring to usual care does not generate more hospital-based NHS work in terms of emergency calls, acute admissions and calls to clinical nurse specialists (23, 24), a qualitative study found that clinicians experienced more complexity in the patients seen in-clinic after implementation of PRO-based follow-up and there were heavy increases in administrative activity and support needed for HCPs inexperienced in complex decision making (98). Increase in workload needs to be balanced against the positive impacts of ePROs and in the above study clinicians were convinced that overall PRO based follow up was of superior quality to traditional outpatient care (98). As part of ePROs implementation evaluation, there needs to be a workforce impact assessment in addition to wide stakeholder engagement, including workflow observation and

participatory co-design, to explore ways to recognise and minimise additional work thereby optimising ePROs integration into workflow.

6.3.4 The implications of digital delivery

Previous chapters helped identify contextual factors specific to the kidney care setting that will affect the use of PRO data. These are compounded by issues such as the complexity of kidney disease, stigma associated with some symptoms such as depression and sexual dysfunction, comorbidities, and treatment-related constraints in dialysis units. It has been argued that electronic data capture may facilitate PRO use given these contexts (28). The 2019 NHS Long Term Plan endorsed the development of digitally-enabled services to replace the 'unsustainable' growth of the traditional out-patient model of care (99), further reinforced by the NHS 2022/23 Priorities and Operational Planning Guidance which prioritises using digital technologies to transform the delivery of care and patient outcomes and making the most effective use of resources (100). Technology means a conventional outpatient appointment might no longer be the optimum way of providing specialist advice on diagnosis or chronic disease management (101). Virtual CKD clinics are becoming normalised to improve primary care management of CKD. They provide timely access to specialist advice and offer time savings: one clinic finding the average virtual consultation took 20 min, when compared to a first attendance outpatient template time slot of 30 min per new patient for a general nephrology clinic (102, 103). Such systems largely rely on laboratory tests for clinical decision making but appear to offer robust follow up with a low level of unplanned dialysis (103). The inclusion of ePROs in the data reviewed in such clinics would ensure the patient voice continued to be present.

The COVID-19 pandemic has accelerated changes to care delivery including the growth of telemedicine: electronic information and communications technology to provide and support healthcare remotely (104). Many patients requiring HD are elderly, have significant co-morbidities and are immune-compromised, leading to increased risk of COVID-19 infection and complications (105). Managing ICHD patients who were unable to isolate was particularly challenging because of their close proximity to each other during treatment, in waiting areas, and on shared transport to and from dialysis centres (106). Consequently, mechanisms to minimise clinical contacts as much as possible were developed with increasing moves towards models of remote and virtual care for patients where possible (107). Establishing a diagnostic pathway, with biochemical tests and investigations close to home in the community, for patients attending virtual clinics was identified as essential in enabling patients to progress on a virtual pathway and review of ePROs was seen as a potential substitute for a telephone consultation in stable patients on long-term follow-up (107). A recent scoping review of patient perspectives and experiences of remote consultations in people receiving kidney care found that while such care delivery is more convenient, there was a perceived loss of interpersonal interaction: with challenges in building rapport and discussing sensitive topics (108). Telemedicine as an alternative health care delivery model for patients with CKD is now well established (109), however, it is argued that inclusion of ePROs could help support telemedicine to achieve patient-centred, collaborative care.

A potential enabler of digital delivery is the use of existing platforms and associated support in data linkage, making the potential for multiple application of ePROs a reality

(110, 111). Chapter 5 highlighted the role of national registries in ePROs collection. The UK Renal Registry (UKRR) infrastructure supported a pilot ePRO system to collect and feedback data (112), similarly the Dutch (113) and Swedish renal registries (114). Previously described, the Australia and New Zealand Dialysis and Transplant (ANZDATA) registry is being used to facilitate the SWIFT study – a cluster RCT investigating symptom monitoring and feedback in patients undergoing HD (34, 38). Since registries are already set up to track and feedback to providers longitudinal clinical outcomes, it is intuitive that they collect, process and report ePROs to support routine patient care (111). However, while registries might be well-placed to facilitate large scale ePROs collection, early findings suggest low response rates and sub-optimal patient and HCP engagement (113, 114) , suggesting further work is required to expedite registry based ePROs (111).

Integration of ePROs into the electronic health record (EHR) is not a new concept to support both management of routine care and comparative effectiveness research (115). EHR portals, which allow patients to both enter and retrieve data, present as resilient, well-supported systems that can be accessed by patients and clinicians (116). However, the collection of ePROs for multiple usages via EHRs has largely not been realised. Standardisation and harmonisation efforts need to ensure that comparable ePROs are available across organizations, and the results are interpreted similarly (115). There is no agreement across health care organisations for governance standards of ePROs integration into the EHR, or how data is transferred from standalone ePRO repositories or via application programming interfaces. This

significant barrier to effective integration was highlighted during the mixed methods study (Chapter 5).

A harmonised approach to ePROs implementation is one way to overcome such challenges and in the UK, work is currently being undertaken to establish national collection of ePROs for people with CKD (117). Key stakeholders, including patients, HCPs, commissioners and facilitating organisations (e.g., national audit) took part in focus groups during an online summit event and individual semi-structured interviews to create recommendations to guide national collection (117). The recommendations concur with several key findings from this thesis: strengthening the evidence base on the potential impacts of ePROs, the importance of local champions, sharing best practice as well as harnessing professional groups such as regional service improvement networks (117).

6.3.5 Best practice guidelines

Regarding best practice, there is now significant guidance available on the use of ePROs in both research and clinical settings. The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)-PRO and Consolidated Standards of Reporting Trials (CONSORT)-PRO extensions support the use and reporting of PROs within clinical trials (118-120). These guidelines have been further supplemented by work on the ethical considerations for the inclusion of PROs in clinical research: the PROs ethics guidelines provide recommendations for ethical issues that should be addressed in PRO clinical research to ensure high-quality PRO data while minimizing participant risk, burden, and harm thus protecting participant and researcher welfare

(121) (see Appendix 6.2). The PROTEUS Consortium (www.proteusconsortium.org) [1]provides curated resources, original tools, and other support to help optimise the use of PROs in clinical trials and routine practice and is currently collating a mega-tool from key ePROs resources (122-125) to assist implementation and integration of ePROs into EHRs. PROQOLID™ (About PROQOLID - ePROVIDE™ (mapi-trust.org) is a comprehensive online database curated by the Mapi Trust designed to assist in the search and evaluation of Clinical Outcome Assessments (COAs) including PROs. With varying levels of access, this database offers details on availability of translations, copyrights, and access as well as domains, scoring and measurement properties to inform and assist measure selection. These resources along with context-specific details can be used to inform ePROs training materials by creating knowledge translation resources tailored for different audiences i.e., patients/carers, HCPs, commissioners and decision-makers (126); such co-designed resources can be integrated into ePRO systems or exist as separate web-pages, manuals or infographics.

Importantly, as PROs are collected for research and increasingly for routine care, several ethical issues arise. There is a need to ensure that patients understand why PROs are being collected, who will be able to access their data and how it will be used. The PRO ethics guidelines identified 14 key questions that capture core ethical issues that should be addressed in PRO clinical research; acting as an implementation tool for research ethic committees and PROs researchers to ensure high-quality PRO data while minimizing participant risk, burden, and harm and protecting participant and

[1] The author of this thesis is part of the stakeholder group for PROTEUS-Practice: currently creating a mega-tool resource to support implementing PROs in clinical practice and integration into the electronic health record.

researcher welfare (121). While these consensus-based guidelines were developed specifically for PROs use in clinical trials, the issues raised will be of direct relevance to ethical PROs use in routine care settings. The author of this thesis participated in the Delphi process, consensus meeting and final wording of the guideline. A copy of the Journal of the American Medical Association (JAMA) paper reporting the development and final guidelines is included in Appendix 6.2 (121).

6.4 Recommendations for future research

Figure 1 Areas for future research



6.4.1. Computer Adaptive Testing and item banks

The scoping review reported in chapter 4 demonstrated the complexity of measure choice and highlighted that long or multiple measures may be required to capture all relevant outcomes, dependent on purpose of collection. The use of multiple, lengthy and/or repetitive measures can lead to significant burden both for patients to reflect and complete, and for clinicians to review and respond (45). Respondent burden has

been defined as 'the degree to which a survey respondent perceives their participation in the project as difficult, time-consuming, or emotionally stressful' (14). There is a concern that a possible consequence of this burden is poor compliance (14, 46). Furthermore, low self-reported cognitive function has been found to be a significant predictor of higher response burden (127), of relevance given the high prevalence of cognitive impairment in patients undertaking HD (78-80). While length is a factor, it should be balanced against the need to collect outcomes that matter to patients (14). It has been proposed that development of ePROMs which have been reported as easier and faster for patients to complete, could reduce respondent burden and improve compliance (14, 25).

Consequently, a potential solution for reducing questionnaire burden, whilst maintaining relevance and reliability is the use of computer adaptive testing (CAT) and associated item banks to administer ePROs (14). CAT offers a computer algorithm that has been designed using item response theory, whereby it adapts the difficulty or delivery of items to the respondent's previous answers. After an item has been administered, the ability/trait level is estimated. Based on this estimate, the item which provides most information at the patient's estimated ability/trait level is selected to be presented next, thereby offering a tailored questionnaire. Thus, it reduces burden to the patient by only presenting 'relevant' items and the overall length of the questionnaire will usually be much shorter (128, 129). Overall adaptive tests are more accurate for most test takers (130), but they offer other advantages including more accurate risk screening, less respondent burden, management of

ceiling and floor effects and allow data quality and precision monitoring in real time (131) .

Examples of CATs in real-world use are the PROMIS item banks which can be administered by CAT PROMIS® (Patient-Reported Outcomes Measurement Information System) or as fixed length short forms: The item response theory–based calibration of PROMIS item banks ensures that scores obtained with CAT or static versions of these generic person-centred measures can evaluate and monitor physical, mental, and social health in adults and children that are near identical (132). They can be used with the general population and with individuals living with chronic conditions including CKD and a recent study has compared the psychometric properties of seven PROMIS CATs (assessing physical function, pain interference, fatigue, sleep disturbance, anxiety, depression, and the ability to participate in social roles and activities) against the SF-12, a well validated generic PROM currently used in Dutch routine nephrology care, with patients who have advanced CKD but are not receiving dialysis treatment (133). The results gave evidence for sufficient construct validity and test-retest reliability of all PROMIS CATs, but noted that while they showed better reliability than the SF-12 (12 items), the CATs required more items overall (median 45 items, with a 10 min completion time) (133). There is further evidence on the validity and reliability specifically for the PROMIS-Sleep Disturbance CATs, suggesting they can be used for research and as potential screening tool among patients on RRT including HD (134). Additionally, a preference-based health utilities score (PROPr) can be calculated using PROMIS domain scores to estimate quality-adjusted life years and has been validated with patients undergoing HD (132).

In practical terms, studies are demonstrating that administering ePROMs with CAT are feasible in outpatient clinics to assess pre-dialysis CKD and patients undergoing peritoneal dialysis to assess their perception of their symptom burden and HRQOL (88). However, it was found that while CAT might reduce questionnaire length, they do not necessarily improve user experience (129). It could be argued that it is better to develop short form (SF) measures where items are completed by all, using statistical methods such as factor analysis and Rasch measurement theory to assist with item reduction during the validation of PROMs (14). However, when comparing accuracy and number of administered items, CAT performs better than SFs (135), so it may be that CATs are better for individual point of care use, while SFs may have a role when PROs are used to asses group level changes in research and all items are completed. Further studies to explore the relationship between mode of administration, assessment length, satisfaction with feedback and response burden are need in HD populations.

In the UK, work is currently ongoing on the development of a renal specific item bank focusing on symptom burden in CKD, including for patients receiving HD. After psychometric evaluation and calibration of this item bank, it can be adapted for CAT administration using CAT simulations (computer modelling), tailoring the questions for individual patients (136). Since this item bank is being developed with patients who are pre-dialysis and who are undertaking different modalities of RRT (41, 136), it has the potential to be used across the CKD trajectory and future research is required to demonstrate whether such an approach can be used to support shared decision-making around modality choice and inform risk stratification/prognostics using ePRO

data. Overall further research is needed to investigate the optimal use of CATs in routine CKD and HD care.

6.4.2 Clinical decision making and interpretability

Chapter 4 highlighted the complexity of measure choice and interpreting scores. Findings highlighting the fact that no single current validated instrument offers complete coverage of HD-specific COS outcomes, and that while four candidate measures (CHEQ-CHOICE, KDQOL, KDQOL-SF, KDQOL-36) offered good coverage (i.e., >75%) there were still issues regarding length, ease of access to legacy measures and assessment of psychometric properties. Although exploring CKD more broadly, a study has confirmed this limitation of current measures in capturing the complete experience of living with CKD (40). Flythe et al (2021) undertook a literature review to develop a preliminary conceptual model of the patient experience of CKD: which included 13 domains covering signs/symptoms and life impacts (40). They further identified 11 PRO instruments, including the KDQOL and KDQOL-36, as promising for use in patients with CKD based on content validity, available psychometric properties, overall item cover and use in trials, including labelling claims (40). They assessed these measures against their preliminary model and found evidence gaps in terms of limited content validity and psychometric validation in CKD (40). This preliminary conceptual model requires direct patient input but might be valuable in adaption of existing instruments as discussed in chapter 4.

Further research is needed on the measurement properties of existing measures so that they might be used for clinical decision-making with confidence, such as threshold

setting for safety alerts by distinguishing real changes from random variation by exploring both minimally detectable changes and minimally important changes (the smallest change in score in the construct to be measured which patients perceive as important) (137). Such measurement properties will vary with instrument purpose; instruments used in routine care need to be responsive, while instruments used for discrimination at group level in research might not (138). Standardisation and harmonisation of ePROs would allow aggregate group-level data to be used to create insight into score variability in CKD to allow comparison to norm or reference scores for patients undergoing HD (139). Further research is needed on recall periods for patients undergoing HD who may be experiencing cognitive impairment; commonly used symptom measures, such as the KDQOL-SF and KDQOL-36 have a recall of 4-weeks and it has been argued such a period precludes the linkage of symptoms to specific dialysis treatments and is ineffective at capturing the washed out feeling post HD (140).

Given the number of available measures for use in HD settings (40), clear justification needs to be made for the development of new measures and an argument for optimising and adapting current measures can be made. For example Peipert et al 2017 (141) have suggested the KDQOL-36 could be improved by replacing the core generic SF-12 items with the Patient-Reported Outcomes Measurement Information System (PROMIS®) measures and fine-tuning the kidney disease-targeted scales.

This includes investigation of the best way to present ePRO data to optimise interpretability for clinicians and patients (124); whether this is by use of radar plots,

bar charts, graphs, emoticons, heat maps, free text, grid or reference lines or a mixture of methods. There is increasing interest in adding ePROs to patient EHR dashboards, so that they can be considered alongside other clinical data to support shared decision-making (142).

The use of aggregated PRO data, both at point of care and by organizations, is largely unexplored in nephrology, the limited reported empirical studies have focused on the use of individual-level PRO data at point of care (28). Van der Willik et al 2020 suggest funnel plots comparing observed against expected ePROs scores could be used to provide insight into organisational level performance, once challenges of high and consistent response rates, adequate case mix correction and the availability of high-quality PRO measures have been met (143). Exploration of using ePROs as prognostic/risk stratification tools using longitudinal data that can assess treatment or changes over time to support replacement treatment modalities is required, alongside institutional use of ePROs to improve quality of care by flagging service gaps and to inform workforce planning.

The focus of the review was PROs coverage for patients undergoing HD. However, it is recognised that tools capable of being used across the CKD journey would be useful. Patients and clinicians would become familiar with use and interpretation and PROMs could support transitions between disease status and treatment modalities. For example, the KDQOL-SF and KDQOL-36 can be used in pre-dialysis populations by excluding questions specific to dialysis. However, although multiple users have omitted these items, according to the www.Rand.org KDQOL frequently asked questions

webpage (144), for scoring purposes these should be considered as missing items and caution should be exercised when comparing symptom/problems scale scores from the pre-dialysis sample to results for persons on dialysis.

6.4.3 Exploration of relationship between PROs and PREMs

While this thesis has focused on ePROs, it can be hard to separate these outcomes from the experience of receiving HD care. Patients have reported how their mood is influenced by both the act of dialysis and what they observed at the dialysis unit (145) and an Italian cross-sectional study has suggested a significant association between patients' satisfaction with quality of care and HRQOL; highlighting the central role of doctor-patient communication (146). Patient Reported Experience Measures (PREMs) are questionnaires which capture the experience of care delivery, and it is noted that some PROMs have elements of experience within. For example, the CDQOL Chinese Dialysis Quality of Life Scale (147) and WHOQOL BREF Dialysis module (148) both have items on access to/satisfaction with transport and the KDQOL includes items on care satisfaction(11).

While there was confusion regarding the related concepts of PROMs and PREMs demonstrated by some patient participants in the qualitative study reported in chapter 3 (45), it is arguable that PREMs might be more actionable than some PROs from an organisational perspective. The validated UK Renal PREM which is administered annually has been adopted by the UK Kidney Association (UKKA) as part of the national audit scheme for renal services and is a driver for change and quality improvement (149), and the UKKA are currently collating case studies of examples of changes that

kidney teams have introduced as a result of the Kidney PREM (150). Correspondingly there is increasing interest in the development of new PREMs, such as a home-therapies specific PREM developed in the United States: the HomeDialysis Care Experience instrument is a 26-item PREM for use in patients undertaking peritoneal dialysis or home HD (151). Further research on the interplay between PROs and PREMs is required.

6.4.4 Real world studies and implementation science

As so wonderfully put by Flythe et al (2022) (152), 'it is becoming increasingly apparent that the devil of PROM effectiveness may be in the details of PROM implementation'. There is a huge economic investment in health research worldwide, with efforts largely concentrated on discovery, with less focus on implementation and dissemination (153), leading to the argument that health research is 'all break-through and no follow-through' (154). Knowledge translation and implementation science may address this; by developing an understanding of implementation factors that support change, and approaches to evaluate and demonstrate such change (155).

All but two of the ePRO systems (156) identified in the mixed methods study reported in chapter 5 were being implemented and evaluated under a research protocol or as part of a pragmatic demonstration trial (142), and while valuable empirical evidence is being produced to support or refute the systematic and routine use of ePROs in nephrology, research studies show considerably higher completion rates of weekly ePROs monitoring than real-world implementation data of ePROs (157). Research infrastructures in terms of human and monetary resources are likely to affect

adherence and completion rates. The real-world changes required at individual and organisational levels to effectively integrate ePROs into HD care need to be considered; this requires a shift to implementation science for guidance on how to promote widespread adoption and use of ePROs in real-world clinical settings with the goal of improving quality of care and outcomes. Implementation science studies factors and strategies that lead to successful integration of evidence-based interventions within specific settings (158). Another, often-overlooked but essential component of implementation research involves the enhancement of readiness through the creation of an effective climate and culture in an organization or community (158). This thesis has provided a first step in this process by exploring contextual factors that influence implementation at the policy, community, organizational, provider, and individual levels using the Consolidated Framework for Implementation Research (CFIR) (7).

To increase the potential for successful scaling up, ePROs should align with existing workflows, use existing staff resources, minimize staff and patient burden, and maximize uptake (159). Girgis et al (2022) used the RE-AIM planning and evaluation framework to guide implementation of a clinically effective ePRO system into lung cancer routine care; using its five domains: Reach (R), effectiveness (E), and maintenance and adoption (A), implementation (I), and maintenance (M) (159, 160) . The value of the RE-AIM framework was seen in the planning phase and in defining outcomes to measure implementation success in a real-world setting, with strategies specially tailored to local contexts (159). Rocque et al (2022) described a process of adapting a remote symptom monitoring intervention developed in a research setting

to real-world clinical oncology settings (161). They conducted a mixed methods formal evaluation using the updated Framework for Modifications and Adaptations (FRAME) by Wiltsey Stirman et al (162) as a means for real-time reporting on adaptations to the intervention that occurred during the implementation process. Whilst maintaining the integrity of the intervention itself, context-specific adaptations were specific, planned, and purposeful changes that increase the likelihood of acceptance and fit to existing workflow. This study identified adaptations, categorized using FRAME, that addressed barriers related to workflow challenges, alert fatigue, and data visibility. Such a mixed methods formative evaluation approach exploring adaptions to nephrology ePROs developed and tested in research settings might offer an effective mechanism for scaling up and sustainability of ePROs for use in real-world CKD settings.

6.4.5 Regulatory focused clinical trials

There is a need for more nephrology trials to focus on the development of drugs and innovations that improve those patient-reported outcomes that are important to patients undergoing HD (5). It was recommended in 2017 at the Improving Global Outcomes (KDIGO) Controversies Conference that PROMs be incorporated into clinical trials and kidney disease care registries (163), however they have largely only been used as secondary outcome measures (164). A core outcome from the SONG-HD initiative that was regarded as critically important by patients receiving HD and their caregivers is fatigue; an outcome reported in <1% of trials in this patient population (3). The consideration of PROs in regulatory-focused clinical trials has been recognised by the US Food and Drug Administration (FDA) who are working with the ASN

(American Society of nephrology) to develop a conceptual framework for a HRQOL PROM for transformative kidney replacement therapy (KRT) devices (165). The proposed framework includes three common domains and unlimited, device-specific symptom domains: The underlying theory being that HRQOL could be affected directly or indirectly through changes in physiologic effects (e.g., improvement in fluid balance, reduction in intradialytic hypotension), and/or changes in the experience of treatment (e.g., more dialysis-free time, fewer dietary restrictions) (165). This framework will support the integration of patient perspectives into the KRT product life cycle, from conception to post marketing surveillance (165).

6.4.6 Green nephrology

Finally, the environmental impact of HD is high, compared to other specialities, using large volumes of water and energy and considerable waste generation (166) with associated strategies to reduce the carbon footprint associated with the physical delivery of HD (recycling reverse osmosis reject water, reducing dialysate flow rates, using renewable energy sources and improved waste management) (166). Studies exploring the implementation of ePROs should assess the potential carbon savings associated with telemedicine, particularly transport-associated emissions (167); for reduced face to face hospital or dialysis unit visits not associated with HD delivery.

6.5 Strengths and limitations of the thesis

The research reported in this thesis contributes important findings to the existing and emerging body of evidence to support and optimise the use and implementation of

ePROs in the care of patients undergoing HD. A multiple/mixed methods approach with involvement of patient partners from prioritisation of the study of ePROs usage in HD settings to co-production of final study manuscripts has enriched the overall findings.

In terms of novelty, this is the first time that currently validated PROMs have been affinity mapped against complete HD-Specific COS to inform measure choice, and the first time ePRO systems developed specifically for use in kidney care have been summarised in terms of functional characteristics and context of implementation. Abstracts based on research from this thesis have been accepted for five oral and seven poster presentations at national and international conferences; highlighting the interest in ePROs use from the wider nephrology and outcomes methodology communities.

The qualitative study reported in chapter 3 was conducted according to the published peer-reviewed protocol (168) and reported according to the Consolidated criteria for reporting qualitative research (COREQ) guidelines for transparent reporting (169). Purposive sampling methods ensured patient participants reflected the diversity of ESKD patients requiring HD in the United Kingdom, in terms of age, gender and ethnicity. However, all interviewees had to be able to speak English. Another potential limitation of the qualitative method was researcher influence on the data and efforts were taken to mitigate this through the process of reflexivity, reported in chapter 2. It is noted that the data for this study was collected before the outbreak of the COVID-19 pandemic and it is accepted that experiences and perceptions of digital collection of

data, including ePROs, might have changed with the rapid acceleration of telemedicine from March 2020.

The protocol for the scoping review presented in chapter 4 was prospectively registered on the Research registry database (Review Registry 1269 https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/registryofsystematicreviewsmeta-analysesdetails/61b5c2584c1323001f3b011f/) to demonstrate transparency and reduce the risk of reporting bias and a successfully used and tested search strategy was employed for the search strategy (6). However, as this review was conducted as a scoping review a formal assessment of methodological quality of the included studies was not performed (170) but reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (see Appendix 4.1) (171).

The mixed methods study of nephrology ePROs systems presented in chapter 5 was confined to systems reported in English language publications, and despite global interest in ePROs this means much of the evidence collated within this thesis might have limited transferability to kidney care systems in low- and middle-income countries. When using the CFIR, a common evaluation objective is to identify and rate constructs that appear to distinguish between organisations with effective and ineffective implementation; providing insights into the key constructs that influence implementation (172). This information can be used to design implementation plans or to influence scaling up (172). It was originally hoped to be able to aggregate and

summarise organisational ePRO system data and rate constructs. However, given the heterogeneity of ePROs systems and their different stages of implementation, such an approach was not possible.

Publication 4

Comment Article Nature Reviews Nephrology

Based on the key findings of this thesis and pertinent to the overall thesis discussion, the following comment was published in the peer-reviewed journal Nature Reviews Nephrology *(Impact factor 42.22)*, which is reproduced within this thesis with permission. It offers the perspective that while considerable research and investment have focused on the use of ePROs in nephrology, systematic collection of ePROs to inform the care of patients with CKD, including those requiring KRT by HD remains sporadic, and suggests a change in culture is needed to encourage their wider adoption in clinical practice.

This publication was cited as:

Anderson, N., Kyte, D., McMullan, C. et al. Electronic patient-reported outcomes in chronic kidney disease. Nat Rev Nephrol (2022). https://doi.org/10.1038/s41581-022-00619-3

6.6.2 Dissemination

Data from discussion and thesis was presented at the following conference as outlined below:

Year	Conference	Location	Presentation type
2022	International Society of Nephrology World Congress	Kuala Lumpur, Malaysia	Oral (GSK supported symposium)

Publication 4: Electronic patient-reported outcomes in chronic kidney disease

Check for updates

Electronic patient-reported outcomes in chronic kidney disease

Nicola Anderson[1] ✉, *Derek Kyte*[2], *Christel McMullan*[1], *Paul Cockwell*[3], *Olalekan L. Aiyegbusi*[1], *Ravinder Verdi*[4] *and Melanie J. Calvert*[1]

Considerable research and investment have focused on the use of electronic patient-reported outcomes (ePROs) in nephrology. However, systematic collection of ePROs to inform the care of patients with chronic kidney disease remains sporadic. A change in culture is needed to encourage their wider adoption in clinical practice.

Patients with chronic kidney disease (CKD) often report a high symptom burden that has a considerable negative impact on their health-related quality of life (HRQoL)[1]. Information on symptoms and HRQoL can be obtained from patients using validated, psychometrically robust questionnaires. Responses have traditionally been collected on paper, but there is increasing interest in the digital collection and real-time use of electronic patient-reported outcomes (ePROs). Data on ePROs offer unique insights: in clinical trials they can provide valuable evidence on the efficacy and tolerability of treatments and in routine clinical care they can be used to deliver personalized care and to assist auditing and benchmarking to improve services[2]. Increasing evidence from specialities such as oncology indicates that use of ePROs in routine care is a cost-effective method of improving clinician–patient communication, enhancing symptom management, reducing hospitalizations and improving HRQoL and overall survival[3,4]. Yet, despite some prioritization at a national policy level, routine collection of ePROs to inform kidney care is limited.

Current use and evidence of benefit

The majority of healthcare systems do not report routine collection of ePROs for patients with CKD. However, in Denmark, a generic web-administered ePRO system known as AmbuFlex is used to manage kidney outpatient follow-up[5]. Key areas of ePRO research in nephrology include outcome selection, which should be aligned with recommended core outcome sets; the development of outcome measures, including assessment of their reliability, validity and ability to detect change; and the feasibility and acceptability of ePRO use for patients[1]. However, clinicians have highlighted a lack of empirical evidence on the efficacy of use of ePROs in kidney care as a reason for slow adoption into routine practice[6].

Several studies are exploring the effectiveness of ePROs in kidney care. For example, the Australian SWIFT study is a registry-based, cluster randomized controlled trial (RCT) that is investigating the effect of 3 monthly ePRO symptom monitoring with clinician feedback over 12 months on HRQoL; secondary outcomes are overall survival, symptom severity, healthcare utilization and cost effectiveness[7]. In Canada, the EMPATHY pragmatic multi-centre cluster RCT will implement and evaluate the use of disease-specific and generic ePRO monitoring with linked treatment aids for clinicians and patient information handouts[8]. The primary outcome of this study is patient–provider communication assessed using a communication assessment tool. Both SWIFT and EMPATHY are focusing on in-centre haemodialysis populations.

In the UK, the OPT-ePRO study developed an intervention that utilizes existing infrastructure to securely collect, transfer and display ePRO data across all stages of CKD and treatment modalities[9]. An evaluation of this intervention in routine practice is planned. The RePROM pilot trial demonstrated the feasibility of a RCT of ePRO symptom monitoring in patients with advanced CKD[10]. The intervention comprised real-time integration of ePRO symptom data into the electronic health record with automated alerting of the clinical team when participants reported severe symptoms. The preliminary findings suggest that healthcare utilization was lower in the ePRO group than in the control group. These data will inform a future RCT aimed at exploring the efficacy and cost-effectiveness of the ePROs intervention.

Real-world implementation

Successful implementation of ePROs in real-world settings requires a clear understanding of the patient population, the purpose of ePRO collection and pathways for clinical responses. Although RCTs provide valuable evidence, contextual factors that can subvert implementation efforts in real-world settings must be considered.

Barriers to collection and use of ePROs include poor clinician 'buy-in', which is associated with difficulty in integrating ePROs into existing digital systems, impact on workflow, anxiety about interpretation and inability to effectively deal with responses[6]. Commonly reported facilitators of ePRO use include 'champions' who have

[1]*Centre for Patient Reported Outcomes Research, NIHR Birmingham Biomedical Research Centre and NIHR Applied Research Collaboration West Midlands, University of Birmingham, Birmingham, UK.*

[2]*School of Allied Health and Community, University of Worcester, Worcester, UK.*

[3]*Department of Nephrology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK.*

[4]*Patient Partner, University of Birmingham, Birmingham, UK.*

✉*e-mail: NEA451@bham.ac.uk*

https://doi.org/10.1038/s41581-022-00619-3

the time and knowledge to explain the potential importance of ePROs to colleagues and patients[6]. The complexity of decisions involved in treating kidney disease highlights the importance of shared decision making in nephrology, and ePROs can support this model of care. Within a high-pressure clinical environment, clinicians could potentially act as gatekeepers to ePRO use by controlling access to systems and review of data; a change in culture is required to address this issue. A systematic case needs to be made that ePROs can enhance workflow efficiency and improve patient care. Support from international and national professional societies and integration of ePROs into clinical service specifications is required to facilitate their widespread adoption.

Potential unintended consequences of ePRO use include worsening of healthcare inequalities due to a lack of access to digital devices, single-language systems and the poor health literacy of some patients. Care must also be taken to communicate directly with patients about what their results mean for them rather than over-digitizing the patient experience by acting on raw scores alone. Effective patient and public involvement at all stages of ePROs implementation from measure selection to system evaluation can mitigate some of these issues. Non-context-specific facilitators of ePRO use include access to resources to guide their use, such as those collated by the PROTEUS consortium, which was formed to optimize the use of patient-reported outcomes in research studies and clinical practice.

Future directions

Use of new technologies, such as computer adaptive testing, which generates specific questionnaires for each individual based on their previous responses, could reduce the burden of ePRO collection for patients[6]. In addition, application programming interfaces that enable secure exchange of data can be used to facilitate linkage and aggregation of ePROs data across platforms, potentially including electronic health records and registries.

CKD is heterogeneous, and subtype-specific outcome measures may be required. However, in our opinion, ePROs methodology should concentrate on standardization of domains and items in questionnaires to enable effective comparison and multiple usage of the collected data, with further investigation of the psychometric properties of existing measures to improve their interpretation, rather than the development of new questionnaires. Better understanding of individual ePRO scores and changes over time, including minimal clinically important differences, will assist clinical decision making. Trust in the ability of ePROs to enhance risk stratification when used alongside other data will increase uptake and improve shared decision making, particularly when used to inform choice of treatment.

In addition to general guidance on score interpretation, understanding of the true meaning of ePROs can only be undertaken through discussion with patients. To facilitate such conversations, data must be presented in a clear and informative way. The use of clinical dashboards and the addition of ePROs to other forms of data in these dashboards can augment patient–provider communication.

The COVID-19 pandemic has led to a huge increase in the use of telemedicine. It is important to design ePRO systems that can support sustainable healthcare programmes, making best use of resources including time and infrastructure. Studies are needed to investigate the cost effectiveness of use of ePROs in kidney care and to calculate their other impacts, including the potential carbon savings associated with reduced clinic visits, transport and healthcare utilization as a result of use of ePROs to manage and triage outpatient activity.

Optimized use of ePROs can strengthen the patient voice in routine kidney care, but effective implementation requires more than research efforts and interest from the nephrology community. A willingness to change culture and to consider ePRO data to be equal in value and complementary to other forms of health data, including clinical outcomes, is required to deliver truly patient-centred care.

1. Fletcher, B. R. et al. Symptom burden and health-related quality of life in chronic kidney disease: a global systematic review and meta-analysis. *PLoS Med.* **19**, e1003954 (2022).
2. Schick-Makaroff, K. et al. An evidence-based theory about PRO use in kidney care: a realist synthesis. *Patient* **15**, 21–38 (2021).
3. Basch, E. et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *J. Am. Med. Assoc.* **318**, 197–198 (2017).
4. Lizée, T. et al. Cost-effectiveness of web-based patient-reported outcome surveillance in patients with lung cancer. *J. Thorac. Oncol.* **14**, 1012–1020 (2019).
5. Schougaard, L. M. V. et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow-up in chronic and malignant diseases. *Qual. Life Res.* **25**, 525–534 (2016).
6. Anderson, N. E. et al. Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. *BMJ Open* **11**, e052629 (2021).
7. Greenham, L. et al. The Symptom Monitoring with Feedback Trial (SWIFT): protocol for a registry-based cluster randomised controlled trial in haemodialysis. *Trials* **23**, 419 (2022).
8. Johnson, J. A. et al. A cluster randomized controlled trial for the Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care (EMPATHY): a study protocol. *BMC Health Serv. Res.* **20**, 731 (2020).
9. Van Der Veer, S. N. et al. Developing an intervention to implement electronic patient-reported outcomes in renal services in the UK. *Stud. Health Technol. Inform.* **270**, 936–940 (2020).
10. Kyte, D. et al. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease. *BMJ Open* **12**, e050610 (2022).

Competing interests

N.A. receives funding from the National Institute for Health and Care Research (NIHR) and personal fees from GlaxoSmithKline (GSK) outside the submitted work. M.J.C. is director of the Birmingham Health Partners Centre for Regulatory Science and Innovation, director of the Centre for Patient Reported Outcomes Research and a NIHR senior investigator. M.J.C. receives funding from the NIHR Birmingham Biomedical Research Centre (BRC), NIHR Surgical Reconstruction and Microbiology Research Centre (SRMRC), NIHR Birmingham-Oxford Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, and NIHR Applied Research Collaboration (ARC) West Midlands, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, SPINE UK, UKRI, UCB Pharma, Janssen, GSK and Gilead. M.J.C. has received personal fees from Astellas, Aparito Ltd, CIS Oncology, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute (PCORI) outside the submitted work. D.K. reports grants from Macmillan Cancer Support, Innovate UK, the NIHR, NIHR Birmingham BRC, and NIHR SRMRC, and personal fees from Merck and GSK outside the submitted work. C.M. receives funding from the NIHR SRMRC, the NIHR Birmingham-Oxford BTRU in Precision Transplant and Cellular Therapeutics, and Innovate UK, and has received personal fees from Aparito Ltd outside the submitted work. O.L.A. receives funding from the NIHR BRC, NIHR ARC, West Midlands, NIHR Birmingham-Oxford BTRU in Precision Transplant and Cellular Therapeutics, Innovate UK, Gilead Sciences Ltd, Janssen Pharmaceuticals, Inc. and Sarcoma UK. O.L.A. declares personal fees from Gilead Sciences Ltd, GSK and Merck outside the submitted work. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

RELATED LINKS

Proteus Consortium: https://theproteusconsortium.org/

6.6 Overall Conclusions

The COVID-19 pandemic has accelerated an irreversible shift towards digital healthcare and telemedicine, of which the implementation and use of ePROs is a part. This thesis demonstrates the interest and support from patients and clinicians in the implementation and use of ePROs in HD settings but highlights the importance of empirical evidence on the benefits of PROs use to justify any changes to current practices alongside packages of education and training in addition to resources required support successful ePROs implementation. It aims to give an increased understanding of the potential opportunities for use of ePRO systems in the management of patients with ESKD requiring treatment with HD, including the range of features and functionality of ePROs systems. Identification of gaps in the evidence base, including potential barriers and facilitators to integration in existing workflows, along with knowledge of new technologies and methodologies will help ensure ePROs are optimised to improve care and maximise outcomes for patients with CKD. Findings from this thesis will increase our understanding of how to embed ePROs in routine renal care and can inform the development of ePRO strategy at local and national levels.

References

1. Anderson N, Kyte D, McMullan C, Cockwell P, Aiyegbusi OL, Verdi R, et al. Electronic patient-reported outcomes in chronic kidney disease. Nature Reviews Nephrology. 2022;18(12):739-40.
2. Anderson NE, Calvert M, Cockwell P, Dutton M, Kyte D. The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective. Am J Kidney Dis. 2019;74(3):399-406.
3. Sautenet B, Tong A, Williams G, Hemmelgarn BR, Manns B, Wheeler DC, et al. Scope and Consistency of Outcomes Reported in Randomized Trials Conducted in Adults Receiving Hemodialysis: A Systematic Review. Am J Kidney Dis. 2018;72(1):62-74.
4. Kyte D, Duffy H, Fletcher B, Gheorghe A, Mercieca-Bebber R, King M, et al. Systematic evaluation of the patient-reported outcome (PRO) content of clinical trial protocols. PLoS One. 2014;9(10):e110229.
5. Tong A, Scholes-Robertson N, Hawley C, Viecelli AK, Carter SA, Levin A, et al. Patient-centred clinical trial design. Nature Reviews Nephrology. 2022;18(8):514-23.
6. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Gheorghe A, Keeley T, et al. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. PLoS One. 2017;12(6):e0179733.
7. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
8. Standardised Outcomes in Nephrology Haemodiaysis SONG HD. The SONG Handbook Sydney, Australia2017 [updated 18th Dec 2021. Available from: https://songinitiative.org/reports-and-publications/.
9. International Consortium for Health Outcomes Measurement. ICHOM Chronic Kidney Disease: Data Collection Reference Guide 2021 [updated Revised Oct 28th 2021. Available from: https://connect.ichom.org/patient-centered-outcome-measures/chronic-kidney-disease/.
10. Wu A, Fink N, Cagney K, Bass E, Rubin H, Meyer K, et al. Developing a Health-Related Quality-of-Life Measure for End-Stage Renal Disease: The CHOICE Health Experience Questionnaire1, 2. American Journal of Kidney Diseases. 2001;37(1):11-21.
11. Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB. Development of the kidney disease quality of life (KDQOL) instrument. Quality of Life Research. 1994;3(5):329-38.
12. Hays R D KJD, Mapes D L, Coons S J, Amin N, Carter W B, Kamberg C. Kidney Disease Quality of Life Short Form (KDQOL-SF): A Manual for use and scoring 1997 [Available from: https://www.rand.org/content/dam/rand/pubs/papers/2006/P7994.pdf.
13. Ricardo AC, Hacker, E., Lora, C. M., Ackerson, L., DeSalvo, K. B., Go, A., Kusek, J. W., Nessel, L., Ojo, A., Townsend, R. R., Xie, D., Ferrans, C. E., Lash, J. P., & CRIC Investigators. Validation of the kidney disease quality of life short form 36 (KDQOL-36) US Spanish and English versions in a cohort of Hispanics with chronic kidney disease. Ethn Dis. 2013;23(2):202-9.
14. Aiyegbusi OL, Roydhouse J, Rivera SC, Kamudoni P, Schache P, Wilson R, et al. Key considerations to reduce or address respondent burden in patient-reported outcome (PRO) data collection. Nat Commun. 2022;13(1):6026.
15. Peipert JD, Bentler PM, Klicko K, Hays RD. Psychometric Properties of the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) in the United States. Am J Kidney Dis. 2018;71(4):461-8.

16. Peipert JD, Bentler P, Klicko K, Hays RD. Negligible impact of differential item functioning between Black and White dialysis patients on the Kidney Disease Quality of Life 36-item short form survey (KDQOL™-36). Qual Life Res. 2018;27(10):2699-707.
17. Ware JE, Richardson MM, Meyer KB, Gandek B. Improving CKD-Specific Patient-Reported Measures of Health-Related Quality of Life. Journal of the American Society of Nephrology JASN. 2019;30(4):664-77.
18. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA. 2017;318(2):197-8.
19. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. J Clin Oncol. 2016;34(6):557-65.
20. Denis F, Basch EM, Lethrosne C, Pourel N, Molinier O, Pointreau Y, et al. Randomized trial comparing a web-mediated follow-up via patient-reported outcomes (PRO) vs. routine surveillance in lung cancer patients: Final results. Journal of Clinical Oncology. 2018;36(15_suppl):6500.
21. Basch E, Schrag D, Henson S, Jansen J, Ginos B, Stover AM, et al. Effect of Electronic Symptom Monitoring on Patient-Reported Outcomes Among Patients With Metastatic Cancer. Jama. 2022;327(74):2413-22.
22. Lizée TB, Ethan ; Trémolières, Pierre ; Voog, Eric ; Domont, Julien ; Peyraga, Guillaume ; Urban, Thierry ; Bennouna, Jaafar ; Septans, Anne-Lise ; Balavoine, Magali ; Detournay, Bruno ; Denis, Fabrice. Cost-Effectiveness of Web-Based Patient-Reported Outcome Surveillance in Patients With Lung Cancer. Journal of Thoracic Oncology. 2019;14(6):1012-21.
23. Velikova G, Absolom K, Hewison J, Holch P, Warrington L, Avery K, et al. Electronic self-reporting of adverse events for patients undergoing cancer treatment: the eRAPID research programme including two RCTs. Southampton (UK)2022 [Available from: https://www.ncbi.nlm.nih.gov/pubmed/35138783.
24. Kyte D, Anderson N, Bishop J, Bissell A, Brettell E, Calvert M, et al. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease. BMJ Open. 2022;12(3):e050610.
25. Aiyegbusi OL, Nair D, Peipert JD, Schick-Makaroff K, Mucsi I. A narrative review of current evidence supporting the implementation of electronic patient-reported outcome measures in the management of chronic diseases. Therapeutic Advances in Chronic Disease. 2021;12.
26. Johnson JA, Al Sayah F, Buzinski R, Corradetti B, Davison SN, Elliott MJ, et al. A cluster randomized controlled trial for the Evaluation of routinely Measured PATient reported outcomes in HemodialYsis care (EMPATHY): a study protocol. BMC Health Serv Res. 2020;20(1):731.
27. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. How the Routine Use of Patient-Reported Outcome Measures for Hemodialysis Care Influences Patient-Clinician Communication: A Mixed-Methods Study. Clin J Am Soc Nephrol. 2022;17(11):1631-45.
28. Schick-Makaroff K, Levay A, Thompson S, Flynn R, Sawatzky R, Thummapol O, et al. An Evidence-Based Theory About PRO Use in Kidney Care: A Realist Synthesis. Patient. 2022;15(1):21-38.
29. Ong SW, Jassal SV, Miller JA, Porter EC, Cafazzo JA, Seto E, et al. Integrating a Smartphone-Based Self-Management System into Usual Care of Advanced CKD. Clin J Am Soc Nephrol. 2016;11(6):1054-62.

30. van der Willik EM, Milders J, Bart JAJ, Bos WJW, van Ittersum FJ, Ten Dam M, et al. Discussing results of patient-reported outcome measures (PROMs) between patients and healthcare professionals in routine dialysis care: a qualitative study. BMJ Open. 2022;12(11):e067044.
31. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).
32. Schick-Makaroff K, Molzahn AE. Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. BMC Health Serv Res. 2017;17(1):439.
33. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Walmsley-Allen N, et al. Development and usability testing of an electronic patient-reported outcome measure (ePROM) system for patients with advanced chronic kidney disease. Computers in Biology & Medicine. 2018;101:120-7.
34. Duncanson E, Bennett PN, Viecelli A, Dansie K, Handke W, Tong A, et al. Feasibility and acceptability of e-PROMs data capture and feedback among patients receiving haemodialysis in the Symptom monitoring WIth Feedback Trial (SWIFT) pilot: protocol for a qualitative study in Australia. BMJ Open. 2020;10(11):e039014.
35. Evans JM, Glazer A, Lum R, Heale E, Mackinnon M, Blake PG, et al. Implementing a patient-reported outcome measure for hemodialysis patients in routine clinical care perspectives of patients and providers on esas-r:Renal. Clinical Journal of the American Society of Nephrology. 2020;15(9):1299-309.
36. Wong D, Cao S, Ford H, Richardson C, Belenko D, Tang E, et al. Exploring the use of tablet computer-based electronic data capture system to assess patient reported measures among patients with chronic kidney disease: a pilot study. BMC Nephrol. 2017;18(1):356.
37. Miles A, D. A Taxonomy of Research Gaps: Identifying and Defining the Seven Research Gaps. Journal of Research Methods and Strategies. 2017;1:1-15.
38. Greenham L, Bennett PN, Dansie K, Viecelli AK, Jesudason S, Mister R, et al. The Symptom Monitoring with Feedback Trial (SWIFT): protocol for a registry-based cluster randomised controlled trial in haemodialysis. Trials. 2022;23(1).
39. Grove BE, Ivarsen P, de Thurah A, Schougaard LM, Kyte D, Hjollund NH. Remote follow-up using patient-reported outcome measures in patients with chronic kidney disease: the PROKID study - study protocol for a non-inferiority pragmatic randomised controlled trial. BMC Health Serv Res. 2019;19(1):631.
40. Flythe JE, Karlsson N, Sundgren A, Cordero P, Grandinetti A, Cremisi H, et al. Development of a preliminary conceptual model of the patient experience of chronic kidney disease: a targeted literature review and analysis. BMC Nephrology. 2021;22(1):233.
41. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med. 2022;19(4):e1003954.
42. Chen MC, Ho YF, Lin CC, Wu CC. Development and testing of the hemodialysis symptom distress scale (HSD-22) to identify the symptom cluster by using exploratory factor analysis. BMC Nephrology. 2021;22:128.
43. Almutary H, Douglas C, Bonner A. Multidimensional symptom clusters: an exploratory factor analysis in advanced chronic kidney disease. Journal of Advanced Nursing. 2016;72(10):2389-400.
44. Lockwood MB, Lash JP, Pauls H, Chung SY, Samra M, Ryan C, et al. Physical Symptom Cluster Subgroups in Chronic Kidney Disease. Nursing Research. 2020;69(2):100-8.
45. Anderson NE, McMullan C, Calvert M, Dutton M, Cockwell P, Aiyegbusi OL, et al. Using patient-reported outcome measures during the management of patients with end-stage

kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. BMJ Open. 2021;11(8):e052629.
46. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Walmsley-Allen N, et al. Patient and Clinician Perspectives on Electronic Patient-Reported Outcome Measures in the Management of Advanced CKD: A Qualitative Study. Am J Kidney Dis. 2019;74(2):167-78.
47. Viecelli AK, Duncanson E, Bennett PN, D'Antoine M, Dansie K, Handke W, et al. Perspectives of Patients, Nurses, and Nephrologists About Electronic Symptom Monitoring With Feedback in Hemodialysis Care. Am J Kidney Dis. 2022;80(2):215-26.
48. Schick-Makaroff K, Wozniak LA, Short H, Davison SN, Klarenbach S, Buzinski R, et al. Burden of mental health symptoms and perceptions of their management in in-centre hemodialysis care: a mixed methods study. J Patient Rep Outcomes. 2021;5(1):111.
49. El-Majzoub S, Mucsi I, Li M, Moussaoui G, Lipman ML, Looper KJ, et al. Psychosocial Distress and Health Service Utilization in Patients Undergoing Hemodialysis: A Prospective Study. Psychosomatics. 2019;60(4):385-92.
50. Seekles ML, Ormandy P, Coyne E. Mapping the UK renal psychosocial workforce: the first comprehensive workforce survey. BMC Nephrology. 2019;20(1):100.
51. Sharif MU, Elsayed ME, Stack AG. The global nephrology workforce: emerging threats and potential solutions! Clin Kidney J. 2016;9(1):11-22.
52. Campbell KL, Murray EM. Allied Health Services to Nephrology: An audit of current workforce and meeting future challenges. Journal of Renal Care. 2013;39(1):52-61.
53. Wolfe WA. Adequacy of Dialysis Clinic Staffing and Quality of Care: A Review of Evidence and Areas of Needed Research. American Journal of Kidney Diseases. 2011;58(2):166-76.
54. Santana MJ, Haverman L, Absolom K, Takeuchi E, Feeny D, Grootenhuis M, et al. Training clinicians in how to use patient-reported outcome measures in routine clinical practice. Qual Life Res. 2015;24(7):1707-18.
55. Silbernagel P, Sawatzky R, Klarenbach S, Czupryn J, Iradukunda R, Palfreyman S, et al. Patient-Reported Outcomes in Clinical Kidney Practice: Development of Education Sessions for Clinicians. Journal of Pain and Symptom Management. 2018;56(6).
56. Sztankay M, Wintner LM, Roggendorf S, Nordhausen T, Dirven L, Taphoorn MJB, et al. Developing an e-learning course on the use of PRO measures in oncological practice: health care professionals' preferences for learning content and methods. Supportive Care Cancer. 2021;30(3):2555-67.
57. Mathur R, Dreyer G, Yaqoob MM, Hull SA. Ethnic differences in the progression of chronic kidney disease and risk of death in a UK diabetic population: an observational cohort study. BMJ Open. 2018;8(3):e020145.
58. Gama RM, Kalyesubula R, Fabian J, Mahalingasivam V. NICE takes ethnicity out of estimating kidney function. BMJ. 2021;374:n2159.
59. Wilkinson E, Brettle A, Waqar M, Randhawa G. Inequalities and outcomes: end stage kidney disease in ethnic minorities. BMC Nephrol. 2019;20(1):234.
60. Kidney Research UK. Kidney disease in people from minority ethnic groups: KRUK; 2022 [Available from: https://www.kidneyresearchuk.org/kidney-health-information/about-kidney-disease/am-i-at-risk/kidney-disease-in-minority-ethnic-groups/.
61. Calvert MJ, Cruz Rivera S, Retzer A, Hughes SE, Campbell L, Molony-Oates B, et al. Patient reported outcome assessment must be inclusive and equitable. Nature Medicine. 2022;28:1120-4.
62. Banerjee D, Lowe-Jones R, Damster S, Thomas N, Scholes-Robertson N, Tong A, et al. International perspectives on patient involvement in clinical trials in nephrology. Kidney Int. 2020;98(3):566-71.

63. Farooqi A, Jutlla K, Raghavan R, Wilson A, Uddin MS, Akroyd C, et al. Developing a toolkit for increasing the participation of black, Asian and minority ethnic communities in health and social care research. BMC Med Res Methodol. 2022;22(1):17.
64. Tembo D, Hickey G, Montenegro C, Chandler D, Nelson E, Porter K, et al. Effective engagement and involvement with community stakeholders in the co-production of global health research. BMJ. 2021;372:n178.
65. Mathie E, Wythe H, Munday D, Millac P, Rhodes G, Roberts N, et al. Reciprocal relationships and the importance of feedback in patient and public involvement: A mixed methods study. Health Expect. 2018;21(5):899-908.
66. Carlton J, Peasgood T, Khan S, Barber R, Bostock J, Keetharuth AD. An emerging framework for fully incorporating public involvement (PI) into patient-reported outcome measures (PROMs). J Patient Rep Outcomes. 2020;4(1):4.
67. Dumais KM, Dias N, Khurana L, Gary ST, Witherspoon B, Evans CJ, et al. Preferences for Use and Design of Electronic Patient-Reported Outcomes in Patients with Chronic Obstructive Pulmonary Disease. Patient. 2019;12(6):621-9.
68. Damschroder LJ, Reardon CM, Widerquist MAO, Lowery J. The updated Consolidated Framework for Implementation Research based on user feedback. Implement Sci. 2022;17(1):75.
69. Kidney Research UK. Kidney Health Inequalities in the United Kingdom: Reflecting on the past, reducing in the future. Peterborough; 2018. Contract No.: ISBN 978-1-9993081-0-0.
70. Slade AL, Retzer A, Ahmed K, Kyte D, Keeley T, Armes J, et al. Systematic review of the use of translated patient-reported outcome measures in cancer trials. Trials. 2021;22(1):306.
71. Ibrahim H, Liu X, Zariffa N, Morris AD, Denniston AK. Health data poverty: an assailable barrier to equitable digital health care. The Lancet Digital Health. 2021;3(4):e260-e5.
72. Schougaard LMV, de Thurah A, Christensen J, Lomborg K, Maindal HT, Mejdahl CT, et al. Sociodemographic, personal, and disease-related determinants of referral to patient-reported outcome-based follow-up of remote outpatients: a prospective cohort study. Qual Life Res. 2020;29(5):1335-47.
73. Knowles SE, Ercia A, Caskey F, Rees M, Farrington K, Van der Veer SN. Participatory co-design and normalisation process theory with staff and patients to implement digital ways of working into routine care: the example of electronic patient-reported outcomes in UK renal services. BMC Health Serv Res. 2021;21(1):706.
74. Tome J, Ahmed S, Fagerlin A, Powell C, Mourao M, Chen E, et al. Patient Electronic Health Record Portal Use and Patient-Centered Outcomes in CKD. Kidney Med. 2021;3(2):231-40 e1.
75. Chapman R, Haroon S, Simms-Williams N, Bhala N, Miah F, Nirantharakumar K, et al. Socioeconomic deprivation, age and language are barriers to accessing personal health records: a cross-sectional study of a large hospital-based personal health record system. BMJ Open. 2022;12(1): e054655.
76. Taylor DM, Fraser S, Dudley C, Oniscu GC, Tomson C, Ravanan R, et al. Health literacy and patient outcomes in chronic kidney disease: a systematic review. Nephrol Dial Transplant. 2018;33(9):1545-58.
77. Nutbeam D. The evolving concept of health literacy. Social Science & Medicine. 2008;67(12):2072-8.
78. San A, Hiremagalur B, Muircroft W, Grealish L. Screening of Cognitive Impairment in the Dialysis Population: A Scoping Review. Dement Geriatr Cogn Disord. 2017;44(3-4):182-95.
79. Dasgupta I, Patel M, Mohammed N, Baharani J, Subramanian T, Thomas GN, et al. Cognitive Function Declines Significantly during Haemodialysis in a Majority of Patients: A Call for Further Research. Blood Purification. 2018;45(4):347-55.

80. Karakizlis H, Thiele S, Greene B, Hoyer J. Cognitive performance in dialysis patients - "when is the right time to test?". BMC Nephrol. 2021;22(1):205.
81. Stormacq C, Van den Broucke S, Wosinski J. Does health literacy mediate the relationship between socioeconomic status and health disparities? Integrative review. Health Promotion International. 2019;34(5):e1-e17.
82. Davison SN, Klarenbach S, Manns B, Schnick-Makaroff K, Buzinski R, Corradetti B, et al. Patient-reported outcome measures in the care of in-centre hemodialysis patients. Journal of Patient-Reported Outcomes. 2021;5(1):1-8.
83. Kyte D, Anderson N, Auti R, Aiyegbusi OL, Bishop J, Bissell A, et al. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. J Patient Rep Outcomes. 2020;4(1):55.
84. Long C, Beres LK, Wu AW, Giladi AM. Developing a protocol for adapting multimedia patient-reported outcomes measures for low literacy patients. PLoS One. 2021;16(6):e0252684.
85. Phelps RG, Taylor J, Simpson K, Samuel J, Turner AN. Patients' Continuing Use of an Online Health Record: A Quantitative Evaluation of 14,000 Patient Years of Access Data. J Med Internet Res. 2014;16(10):e241.
86. Rutherford C, Costa D, Mercieca-Bebber R, Rice H, Gabb L, King M. Mode of administration does not cause bias in patient-reported outcome results: a meta-analysis. Qual Life Res. 2016;25(3):559-74.
87. Meirte J, Hellemans N, Anthonissen M, Denteneer L, Maertens K, Moortgat P, et al. Benefits and Disadvantages of Electronic Patient-reported Outcome Measures: Systematic Review. JMIR Perioper Med. 2020;3(1):e15588.
88. Finkelstein FO, Cimini M, Finkelstein SH, Kliger AS. Computerized adaptive technology for the assessment of HRQOL of PD and CKD patients. Perit Dial Int. 2021;41(5):509-12.
89. Skovlund PC, Ravn S, Seibaek L, Thaysen HV, Lomborg K, Nielsen BK. The development of PROmunication: a training-tool for clinicians using patient-reported outcomes to promote patient-centred communication in clinical cancer settings. J Patient Rep Outcomes. 2020;4(1):10.
90. Stehlik J, Rodriguez-Correa C, Spertus JA, Biber J, Nativi-Nicolau J, Zickmund S, et al. Implementation of Real-Time Assessment of Patient-Reported Outcomes in a Heart Failure Clinic: A Feasibility Study. Journal of Cardiac Failure. 2017;23(11):813-6.
91. Cronin RM, Conway D, Condon D, Jerome RN, Byrne DW, Harris PA. Patient and healthcare provider views on a patient-reported outcomes portal. J Am Med Inform Assoc. 2018;25(11):1470-80.
92. Turner RR, Quittner AL, Parasuraman BM, Kallich JD, Cleeland CS, Mayo FDAP-ROCMG. Patient-reported outcomes: instrument development and selection issues. Value Health. 2007;10 Suppl 2:S86-93.
93. Norquist JM, Girman C, Fehnel S, DeMuro-Mercon C, Santanello N. Choice of recall period for patient-reported outcome (PRO) measures: criteria for consideration. Qual Life Res. 2012;21(6):1013-20.
94. Guha C, Lopez-Vargas P, Ju A, Gutman T, Scholes-Robertson NJ, Baumgart A, et al. Patient needs and priorities for patient navigator programmes in chronic kidney disease: a workshop report. BMJ Open. 2020;10(11):e040617.
95. Bausewein C, Simon ST, Benalia H, Downing J, Mwangi-Powell FN, Daveson BA, et al. Implementing patient reported outcome measures (PROMs) in palliative care - users' cry for help. Health and Quality of Life Outcomes. 2011;9(1):27.
96. Tong A, Manns B, Hemmelgarn B, Wheeler DC, Evangelidis N, Tugwell P, et al. Establishing Core Outcome Domains in Hemodialysis: Report of the Standardized Outcomes in

Nephrology-Hemodialysis (SONG-HD) Consensus Workshop. Am J Kidney Dis. 2017;69(1):97-107.
97. Leary A. Saved bed days: the ultimate currency. BMJ. 2022;378:o1686.
98. Mejdahl CT, Schougaard LMV, Hjollund NH, Riiskjaer E, Lomborg K. Exploring organisational mechanisms in PRO-based follow-up in routine outpatient care - an interpretive description of the clinician perspective. BMC Health Serv Res. 2018;18(1):546.
99. Department of Health. The NHS Long term plan London2019 [Available from: https://www.longtermplan.nhs.uk/.
100. NHS England. 2022/23 priorities and operational planning guidance 2022 [Available from: https://www.england.nhs.uk/wp-content/uploads/2022/02/20211223-B1160-2022-23-priorities-and-operational-planning-guidance-v3.2.pdf.
101. Royal College of Physicians. Outpatients: the future – adding value through sustainability London: RCP; 2018 [Available from: https://www.rcplondon.ac.uk/projects/outputs/outpatients-future-adding-value-through-sustainability.
102. Hull SA, Rajabzadeh V, Thomas N, Hoong S, Dreyer G, Rainey H, et al. Do virtual renal clinics improve access to kidney care? A preliminary impact evaluation of a virtual clinic in East London. BMC Nephrol. 2020;21(1):10.
103. Harnett P, Jones M, Almond M, Ballasubramaniam G, Kunnath V. A virtual clinic to improve long-term outcomes in chronic kidney disease. Clin Med (Lond). 2018;18(5):356-63.
104. Omboni S, Padwal RS, Alessa T, Benczúr B, Green BB, Hubbard I, et al. The worldwide impact of telemedicine during COVID-19: current evidence and recommendations for the future. Connect Health. 2022;1:7-35.
105. Babel N, Hugo C, Westhoff TH. Vaccination in patients with kidney failure: lessons from COVID-19. Nat Rev Nephrol. 2022;18(11):708-23.
106. Roper T, Kumar N, Lewis-Morris T, Moxham V, Kassimatis T, Game D, et al. Delivering Dialysis During the COVID-19 Outbreak: Strategies and Outcomes. Kidney Int Rep. 2020;5(7):1090-4.
107. Vas V, North S, Rua T, Chilton D, Cashman M, Malhotra B, et al. Delivering outpatient virtual clinics during the COVID-19 pandemic: early evaluation of clinicians' experiences. BMJ Open Qual. 2022;11(1).
108. Ewart C, Baharani J, Wilkie M, Thomas N. Patient perspectives and experiences of remote consultations in people receiving kidney care: A scoping review. J Ren Care. 2022;48(3):143-53.
109. Young A, Orchanian-Cheff A, Chan CT, Wald R, Ong SW. Video-Based Telemedicine for Kidney Disease Care. Clinical Journal of the American Society of Nephrology. 2021;16(12):1813-23.
110. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. BMJ. 2019;364:k5267.
111. van der Veer SN, Couchoud C, Morton RL. The role of kidney registries in expediting large-scale collection of patient-reported outcome measures for people with chronic kidney disease. Clin Kidney J. 2021;14(6):1495-503.
112. Van Der Veer SN, Ercia A, Caskey FJ, Farrington K, Jury F, Rees M, et al. Developing an Intervention to Implement Electronic Patient-Reported Outcomes in Renal Services in the UK. Studies in Health Technology & Informatics. 2020;270:936-40.
113. van der Willik EM, Hemmelder MH, Bart HAJ, van Ittersum FJ, Hoogendijk-van den Akker JM, Bos WJW, et al. Routinely measuring symptom burden and health-related quality of life in dialysis patients: first results from the Dutch registry of patient-reported outcome measures. Clin Kidney J. 2021;14(6):1535-44.

114. Pagels AA, Stendahl M, Evans M. Patient-reported outcome measures as a new application in the Swedish Renal Registry: health-related quality of life through RAND-36. Clin Kidney J. 2020;13(3):442-9.
115. Wu AW, Kharrazi H, Boulware LE, Snyder CF. Measure once, cut twice--adding patient-reported outcome measures to the electronic health record for comparative effectiveness research. J Clin Epidemiol. 2013;66(8 Suppl):S12-20.
116. Tang PC, Ash JS, Bates DW, Overhage JM, Sands DZ. Personal health records: definitions, benefits, and strategies for overcoming barriers to adoption. J Am Med Inform Assoc. 2006;13(2):121-6.
117. Chadwick H EA, Finnigan R, Sharma S, Gair R, Kyte D, Fraser S, Cockwell P, Knowles S, van der Veer S. Stakeholder-informed recommendations for national collection of electronic patient-reported outcomes for peple with chronic kidney disease in the UK. International Society for Quality of Life (ISOQOL); 21 Oct 2022; Prague: ISOQOL; 2022.
118. Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan AW, King MT, et al. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension. JAMA. 2018;319(5):483-94.
119. Mercieca-Bebber R, Rouette J, Calvert M, King MT, McLeod L, Holch P, et al. Preliminary evidence on the uptake, use and benefits of the CONSORT-PRO extension. Qual Life Res. 2017;26(6):1427-37.
120. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: The consort pro extension. JAMA. 2013;309(8):814-22.
121. Cruz Rivera S, Aiyegbusi OL, Ives J, Draper H, Mercieca-Bebber R, Ells C, et al. Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines. JAMA. 2022;327(19):1910-9.
122. Aaronsen N ET, Greenhalgh J, Halyard M, Hess R, Miller D, Reeve B, Santana M, Snyder C. User's Guide to Implementing Patient-Reported Outcomes Assessment in Clinical Practice: International Society of Quality of Life Research; 2015 [Jan 2015]. Available from: https://www.isoqol.org/wp-content/uploads/2019/09/2015UsersGuide-Version2.pdf.
123. Snyder C W, A.W., eds. Users' Guide to Integrating Patient-Reported Outcomes in Electronic Health Records Baltimore, MD: John Hopkins University; 2017 [Available from: https://www.pcori.org/document/users-guide-integrating-patient-reported-outcomes-electronic-health-records.
124. Snyder C, Smith K, Holzner B, Rivera YM, Bantug E, Brundage M, et al. Making a picture worth a thousand numbers: recommendations for graphically displaying patient-reported outcomes data. Qual Life Res. 2019;28(2):345-56.
125. Snyder C, Brundage M, Rivera YM, Wu AW. A PRO-cision Medicine Methods Toolkit to Address the Challenges of Personalizing Cancer Care Using Patient-Reported Outcomes: Introduction to the Supplement. Med Care. 2019;57 Suppl 5 Suppl 1:S1-S7.
126. Schick-Makaroff K, Sawatzky R, Cuthbertson L, Ohlen J, Beemer A, Duquette D, et al. Knowledge translation resources to support the use of quality of life assessment tools for the care of older adults living at home and their family caregivers. Qual Life Res. 2021;31:1727-47.
127. Atkinson TM, Schwartz CE, Goldstein L, Garcia I, Storfer DF, Li Y, et al. How much is too much? predictors of patient response burden in the completion of patient-reported outcome assessments. Quality of Life Research. 2017;26 (1 Supplement 1):47-8.
128. Michel P, Baumstarck K, Lancon C, Ghattas B, Loundou A, Auquier P, et al. Modernizing quality of life assessment: development of a multidimensional computerized adaptive questionnaire for patients with schizophrenia. Qual Life Res. 2018;27(4):1041-54.
129. Geerards D, Pusic A, Hoogbergen M, van der Hulst R, Sidey-Gibbons C. Computerized Quality of Life Assessment: A Randomized Experiment to Determine the Impact of Individualized Feedback on Assessment Experience. J Med Internet Res. 2019;21(7):e12212.

130. Bass M, Morris, S., Neapolitan, R. Utilizing Multidimensional Computer Adaptive Testing to Mitigate Burden With Patient Reported Outcomes. AMIA Annual Symposium proceedings AMIA Symposium,. 2015:320-8.
131. Gausden EB, Levack A, Nwachukwu BU, Sin D, Wellman DS, Lorich DG. Computerized Adaptive Testing for Patient Reported Outcomes in Ankle Fracture Surgery. Foot & Ankle International. 2018;39(10):1192-8.
132. Zhang J, Dewitt B, Tang E, Breitner D, Saqib M, Li D, et al. Evaluation of PROMIS Preference Scoring System (PROPr) in Patients Undergoing Hemodialysis or Kidney Transplant. Clin J Am Soc Nephrol. 2021;16(9):1328-36.
133. van der Willik EM, van Breda F, van Jaarsveld BC, van de Putte M, Jetten IW, Dekker FW, et al. Validity and reliability of Patient-Reported Outcomes Measurement Information System (PROMIS(R)) using Computerized Adaptive Testing (CAT) in patients with advanced chronic kidney disease. Nephrol Dial Transplant. 2022;gfac231.
134. Hussain J, Chawla G, Rafiqzad H, Huang S, Bartlett SJ, Li M, et al. Validation of the PROMIS sleep disturbance item bank computer adaptive test (CAT) in patients on renal replacement therapy. Sleep Med. 2022;90:36-43.
135. Segawa E, Schalet B, Cella D. A comparison of computer adaptive tests (CATs) and short forms in terms of accuracy and number of items administrated using PROMIS profile. Quality of Life Research. 2019;29(1):213-21.
136. Institute of Applied Health Research UoB. RCAT-Renal Computerised Adaptive Test Birmingham: University of Birmingham; 2022 [Available from: https://tinyurl.com/13vdwh0m.
137. Terwee CB, Peipert JD, Chapman R, Lai JS, Terluin B, Cella D, et al. Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures. Qual Life Res. 2021;30(10):2729-54.
138. Mokkink L B TCB, Patrick D L, Alonson J, Stratford P W, Knol D L, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Qual Life Res. 2010;19(4):539-49.
139. van der Willik EM, Terwee CB, Bos WJW, Hemmelder MH, Jager KJ, Zoccali C, et al. Patient-reported outcome measures (PROMs): making sense of individual PROM scores and changes in PROM scores over time. Nephrology (Carlton). 2021;26(5):391-9.
140. Flythe JE, Dorough A, Narendra JH, Wingard RL, Dalrymple LS, DeWalt DA. Development and content validity of a hemodialysis symptom patient-reported outcome measure. Qual Life Res. 2019;28(1):253-65.
141. Peipert JD, Hays RD. Methodological considerations in using patient reported measures in dialysis clinics. Journal of Patient-Reported Outcomes. 2017;1(11).
142. Perry LM, Morken V, Peipert JD, Yanez B, Garcia SF, Barnard C, et al. Patient-Reported Outcome Dashboards Within the Electronic Health Record to Support Shared Decision-making: Protocol for Co-design and Clinical Evaluation With Patients With Advanced Cancer and Chronic Kidney Disease. JMIR Res Protoc. 2022;11(9):e38461.
143. Esmee M. Van der Willik EVZ, Frans J. Van Ittersum, Marc, H. Hemmelder, Friedo W. Dekker, Yvette Meuleman. Funnel plots of patient-reported outcomes (PROs) to evaluate nephrological care:basic principles and considerations. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2020;35(3).
144. RAND Corporation. KDQOL Frequently Asked Questions: RAND; 2022 [Available from: https://www.rand.org/health-care/surveys_tools/kdqol/faq.html.
145. Hartwell L. Developing patient-reported outcome measures that can improve kidney care. Clinical Journal of the American Society of Nephrology CJASN. 2021;16(9):1301-2.

146. Cirillo L, Toccafondi A, Cutruzzula R, Miraglia Raineri A, Pernazza M, Fiasella S, et al. Association between Satisfaction with Dialysis Treatment and Quality of Life: A Cross-Sectional Study. Blood Purification. 2021;50(2):188-95.
147. Suet-Ching WL. The psychometric properties of the Chinese Dialysis Quality of Life Scale for Hong Kong dialysis patients. Journal of Advanced Nursing. 2001;36(3):441-9.
148. Yang SC, Kuo PW, Wang JD, Lin MI, Su S. Development and psychometric properties of the dialysis module of the WHOQOL-BREF Taiwan version. Journal of the Formosan Medical Association. 2006;105(4):299-309.
149. Hawkins J, Wellsted D, Corps C, Fluck R, Gair R, Hall N, et al. Measuring patients' experience with renal services in the UK: development and validation of the Kidney PREM. Nephrol Dial Transplant. 2022;37(8):1507-19.
150. UK Kidney Association. Kidney Patient Reported Experience Measure 2022 [Available from: https://ukkidney.org/kidney-patient-reported-experience-measure.
151. Rivara MB, Edwards T, Patrick D, Anderson L, Himmelfarb J, Mehrotra R. Development and Content Validity of a Patient-Reported Experience Measure for Home Dialysis. Clin J Am Soc Nephrol. 2021;16(4):588-98.
152. Flythe JE. Integrating PROMs in Routine Dialysis Care: The Devil Is in the (Implementation) Details. Clin J Am Soc Nephrol. 2022;17(11):1580-2.
153. Presseau J, Kasperavicius D, Rodrigues IB, Braimoh J, Chambers A, Etherington C, et al. Selecting implementation models, theories, and frameworks in which to integrate intersectional approaches. BMC Med Res Methodol. 2022;22(1):212.
154. Woolf S, H. Unheatlhy medicine: all breakthrough, no follow-through 2006 [updated Jan 8. Available from: https://www.washingtonpost.com/archive/opinions/2006/01/08/unhealthy-medicine-span-classbankheadall-breakthrough-no-follow-throughspan/d3b838a9-db0b-4b23-a410-c5de185f51d0/.
155. Nilsen P. Making sense of implementation theories, models and frameworks. Implement Sci. 2015;10:53.
156. Schougaard L M LLP, Jessen A et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow up in chronic and malignant diseases. Qual Life Res. 2016;25(3):525-34.
157. Velazquez AI, Florez N. Electronic Monitoring of Patient-Reported Outcomes-Ready for Prime Time? JAMA Oncol. 2022;8(8):1099-100.
158. Rabin BA, Brownson RC, Haire-Joshu D, Kreuter MW, Weaver NL. A glossary for dissemination and implementation research in health. Journal of public health management and practice : JPHMP. 2008;14 2:117-23.
159. Girgis A, Bamgboje-Ayodele A, Rincones O, Vinod SK, Avery S, Descallar J, et al. Stepping into the real world: a mixed-methods evaluation of the implementation of electronic patient reported outcomes in routine lung cancer care. Journal of Patient-Reported Outcomes. 2022;6(1).
160. Glasgow RE, Harden SM, Gaglio B, Rabin B, Smith ML, Porter GC, et al. RE-AIM Planning and Evaluation Framework: Adapting to New Science and Practice With a 20-Year Review. Front Public Health. 2019;7:64.
161. Rocque GB, Dent DAN, Ingram SA, Caston NE, Thigpen HB, Lalor FR, et al. Adaptation of Remote Symptom Monitoring Using Electronic Patient-Reported Outcomes for Implementation in Real-World Settings. JCO Oncology Practice. 2022;0(0):OP.22.00360.
162. Wiltsey Stirman S, Baumann AA, Miller CJ. The FRAME: an expanded framework for reporting adaptations and modifications to evidence-based interventions. Implement Sci. 2019;14(1):58.

163. Ayme S, Bockenhauer D, Day S, Devuyst O, Guay-Woodford LM, Ingelfinger JR, et al. Common Elements in Rare Kidney Diseases: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2017;92(4):796-808.
164. Nair D, Wilson FP. Patient-Reported Outcome Measures for Adults With Kidney Disease: Current Measures, Ongoing Initiatives, and Future Opportunities for Incorporation Into Patient-Centered Kidney Care. Am J Kidney Dis. 2019;74(6):791-802.
165. Flythe JE, Hilliard TS, Ikeler K, Keller S, Gipson DS, Grandinetti AC, et al. Toward patient-centered innovation a conceptual framework for patient-reported outcome measures for transformative kidney replacement devices. Clinical Journal of the American Society of Nephrology. 2020;15(10):1522-30.
166. Barraclough KA, Agar JWM. Green nephrology. Nat Rev Nephrol. 2020;16(5):257-68.
167. Purohit A, Smith J, Hibble A. Does telemedicine reduce the carbon footprint of healthcare? A systematic review. Future Healthc J. 2021;8(1):e85-e91.
168. Anderson NE, Calvert M, Cockwell P, Dutton M, Aiyegbusi OL, Kyte D. Using patient-reported outcome measures (PROMs) to promote quality of care in the management of patients with established kidney disease requiring treatment with haemodialysis in the UK (PROM-HD): a qualitative study protocol. BMJ Open. 2018;8(10):e021532.
169. Tong A SP, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32 item checklist for interviews and focus groups. International Journal for Quality in Health Care. 2007;19(6):349-57.
170. Peters MDJ, Marnie C, Colquhoun H, Garritty CM, Hempel S, Horsley T, et al. Scoping reviews: reinforcing and advancing the methodology and application. Syst Rev. 2021;10(1):263.
171. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.
172. Consolidated Framework for Implmentation Research (CFIR). Qualitative data - data analysis Ann Arbor, MI 481092022 [Available from: https://cfirguide.org/evaluation-desin/qualitative-data/.

Appendices for Chapter 6

Appendix 6.1: Link to publication: Calvert, M.J., Cruz Rivera, S., Retzer, A., Hughes S.E., Campbell, L., Molony-Oates, B., Aiyegbusi, O L., Stover, A, M., Wilson, R., McMullan, C., Anderson, N E., Turner, G M., Haf Davies, E., Verdi, R., Velikova G., Kamudoni P., Muslim, S., Gheorge, A., O'Connor, D., Xiaoxuan, L., Wu, A,W., & Denniston, A,K. ***Patient reported outcome assessment must be inclusive and equitable*.** Nat Med 28, 1120–1124 (2022). https://doi.org/10.1038/s41591-022-01781-8

Appendix 6.2 Link to publication: Samantha Cruz Rivera, PhD; Olalekan Lee Aiyegbusi, PhD; Jonathan Ives, PhD; Heather Draper, PhD; Rebecca Mercieca-Bebber, PhD; Carolyn Ells, PhD; Amanda Hunn, MA; Jane A. Scott, PhD; Conrad V. Fernandez, MD; Andrew P. Dickens, PhD; Nicola Anderson, MSc; Vishal Bhatnagar, MD; Andrew Bottomley, PhD; Lisa Campbell, MD; Clive Collett, MA; Philip Collis; Kathrine Craig, PhD; Hugh Davies, MD;Robert Golub, MD; Lesley Gosden; Ari Gnanasakthy, MSc; Elin Haf Davies, PhD; Maria von Hildebrand; Janet M. Lord, PhD;Nirosha Mahendraratnam, PhD; Tempei Miyaji, MSc; Thomas Morel, PhD; Joao Monteiro, PhD; Ann-Dorthe Olsen Zwisler, PhD; John Devin Peipert, PhD; Jessica Roydhouse, PhD; Angela M. Stover, PhD; Roger Wilson, CBE; Christina Yap, PhD; Melanie J. Calvert, PhD. ***Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines***. JAMA. 2022;327(19):1910–1919. doi:10.1001/jama.2022.6421

Appendix 1

Appendix 1.1: Publication

Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. (2022) Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. PLoS Med 19(4): e1003954. https://doi.org/10.1371/journal.pmed.1003954

Link to open access publication:

Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis | PLOS Medicine

(https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003954)

Appendix 1.2: Publication

Anderson, Nicola Elizabeth et al. (2019) In Reply to 'A Psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis'. American Journal of Kidney Diseases, Volume 74, Issue 5, 711 – 712 https://doi.org/10.1053/j.ajkd.2019.07.009

Link to open access publication:

In Reply to 'A Psychiatrist's View on Patient-Reported Outcomes in Patients Undergoing Hemodialysis' - American Journal of Kidney Diseases (ajkd.org)

(https://www.ajkd.org/article/S0272-6386(19)30916-3/fulltext#back-bib1)

Appendix 1.3: Search Strategy for narrative review

A search of Ovid Medline, Embase and the Cochrane databases (https://www.cochrane.org) was conducted from inception to 18th January 2018. Eligibility was assessed by two independent reviews (NEA, DK). A total of 34 papers were identified for full text screening. Additional papers of relevance were obtained from forwards and backwards citation searching and via contact with experts. Duplicates and papers which did not focus on HD and the implementation of PROs were excluded, resulting in 19 papers for inclusion in the review

Eligibility Criteria:

Inclusion: Papers must involve i) focus on haemodialysis ii) can include any study type i.e., review, RCT, feasibility study iii) main focus of paper is the implementation of PROMs in a routine or research setting to inform the management of patient care

Exclusion: Studies that i) do not focus on haemodialysis i.e., focus on Peritoneal Dialysis ii) conference abstracts iii) focus of paper is validation of identified PROM, focus is implementation in a paediatric setting

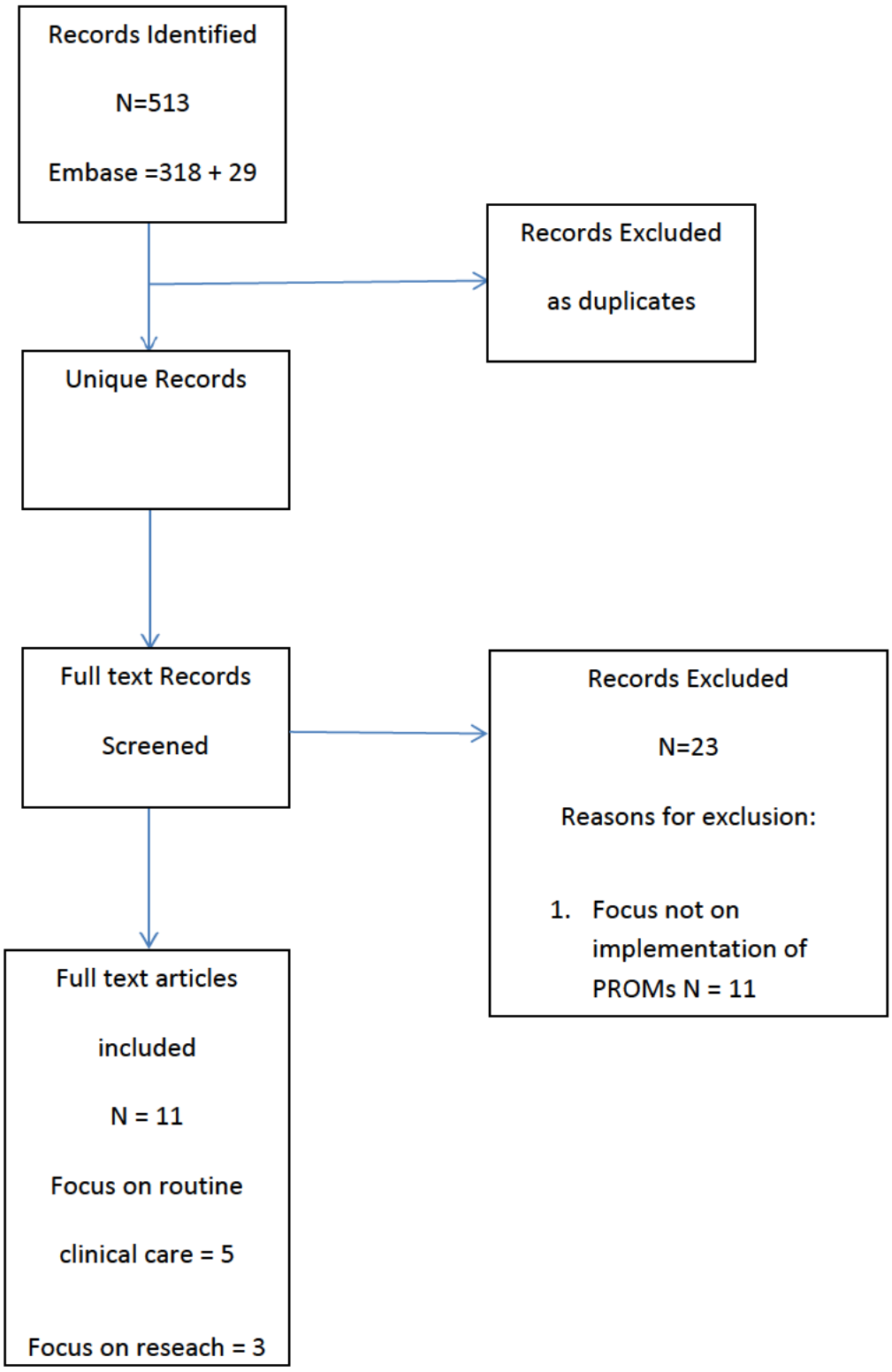
Medline
Search Terms
1. patient reported outcome.mp. or exp Patient Reported Outcome Measures/
2. renal dialysis.mp. or exp Renal Dialysis/
3. exp Kidney Failure, Chronic/ or exp Renal Dialysis/ or haemodialysis*.mp
4. 1 and 2 and 3
5. “clinical practice” or clinical care” or “secondary care” or primary care”.m_titl.
6. Routine adj2 practice.mp
7. Routine adj2 care.mp
8. 5 and 6 and 7

9. 1 and 8

Embase
Search Terms
1. "patient reported outcome*".m_titl.
2. haemodialysis.mp. or exp hemodialysis/
3. exp kidney failure/ or exp end stage renal disease/ or exp chronic kidney failure/ or exp hemodialysis patient/ or exp renal replacement therapy/ or exp hemodialysis/ or renal dialysis*.mp. or exp dialysis/
4. 1 and 2 and 3

Cochrane Library
Search Terms
1. "patient reported outcome" ti,abs,kw
2. "patient reported outcome measure" ti,abs,kw
3. "self-reported health" ti,abs,kw
4. "haemodialysis" ti,abs,kw
5. "hemodialysis" ti,abs,kw
6. 1 and 2 and 3 and 4 and 5

Appendix 1.4: PRISMA diagram for Narrative Review



Appendix 1.5: Table 1 Papers discussing implementation of PROMs in HD settings

Paper	Journal	Brief Overview/Aim of paper	Goal of collection	Mode of collection	Suggested Future Research Areas
A patient-centred approach to measuring quality in kidney care: Patient-reported outcome measures and patient-reported experience measures. Aiyegbusi et al. 2017 [α] (1)	Current Opinion in Nephrology and Hypertension	Review focuses on evidence from recent studies exploring the role of PROMs and PREMs in the measurement of quality in CKD care, including HD settings	Examines Individual/aggregate uses in both routine clinical care and research HD settings.	Electronic including registry collection	Recognition that ePROM collection is advancing in terms of available platforms, administration and uses i.e., remote symptom monitoring, use of computer adaptive testing (CAT) and electronic item banks and integration of PROM data into electronic health record.
Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. Aiyegbusi et al. 2017 [α] (2)	Plos One	Review of the measurement properties of 25 PROMs using the COSMIN checklist, used in patients in CKD including those receiving HD. Strong evidence to support the use of the KDQOL-SF and KDQOL-36 with the dialysis population. Results could be used to support PROM selection in both routine clinical and research settings.	Acceptance of multiplicity of uses.	Not the focus of paper	Further validation of currently available measures required: Content validity needs to be established according to FDA guidelines to ensure PROMs measure the concept of interest and some PROMs require further validation studies with English-speaking populations.

Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: a systematic review protocol Aiyegbusi et al. 2016 [α] (3)	BMJ Open	Paper outlining methodology for systematic review outlined in Paper 2. Results could be used to support PROM selection in both routine clinical and research settings	Acceptance of multiplicity of uses.	Not the focus of the paper	See Paper 2.
How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: An expert consensus meeting. Breckenridge et al. 2015 [α] (4)	Nephrology, Dialysis, Transplantation.	Report of a consensus meeting on how to routinely collect PROM and PREM data for European registry use. Includes survey of current and planned efforts to collect PROM/PREM data, systematic review of literature on barriers and facilitators of PROM/PREM data collection, harmonisation of future collection by agreement on preferred instruments (SF-12, KDQOL-36, EQ-5D-5L).	Registry use	Focus on registry collection No clear preference for paper/web based	Paper identified the scarcity of robust data om the measurement and reporting of PROMs and PREMs in renal patients. Instruments were developed for use at an individual patient level, rather than centre or national use. More research was needed before a specific PREM for broader use within registries can be recommended.
Time to rethink our approach to patient-reported outcome measures for ESRD. Finkelstein & Finkelstein 2017 [α] (5)	Clinical Journal of the American Society of Nephrology	Commentary questions whether standardised tools meet unique needs of patients and can truly deliver patient centred care.	Individual patient use.	Recognition of the utility of electronic collection including CAT.	Encourages innovative approaches for integration of PROMs into routine care, including incorporation of ePROM data into the electronic patient record

		Makes recommendations for implementing PROMS within routine clinical care settings			
Patient-reported outcome instruments for physical symptoms among patients receiving maintenance dialysis: A systematic review Flythe et al. 2015 [α] (6)	American Journal of Kidney Diseases	Physical symptoms are highly prevalent and play an important role in the HRQOL for dialysis dependent patients. This systematic review assesses current symptom measures for use in HD settings in terms of content, validity and reliability.	Collection of symptom data for use in research and routine clinical HD settings.	Not the focus of the paper	Review of symptom specific instruments, this review excluded instruments with single or mood related symptoms. Overall, the study identified a lack of valid symptom focused instruments with short recall and assessment of multiple symptom attributes.
Design and rationale of health-related quality of life and patient-reported outcomes assessment in the frequent hemodialysis network trials Jhamb et al. 2011 [α] (7)	Blood Purification	This study demonstrates a set of HRQOL measures (SF36, BDI, HUI, Sleep Problems Index) can be collected centrally by telephone within a research trial setting. Focus on collection of PROMs in HD Trials	Trial use – to assess effectiveness of HD interventions in terms of HRQOL	Computer assisted Telephone interview with blinded interviewers	Suggests future trials may wish to consider using computer assisted telephone interviews to collect PROs in patients undergoing HD.
Considerations and challenges in selecting patient-reported outcome measures for clinical trials in nephrology. Ju & Tong 2017 [α] (8)	Clinical Journal of the American Society of Nephrology	Overview of use of PROMs in research trials: key challenge is PROM selection.	Trial use	Not focus	Commentary identifies that PROMs remain infrequently used in nephrology trials due to in part to the challenges and uncertainties of PROM selection, which requires further trial-based evidence.

Patient-Reported Outcome Measures for Fatigue in Patients on Hemodialysis: A Systematic Review. Ju et al. 2017 [α] (9)	American Journal of Kidney Diseases	Systematic review of the characteristics and psychometric properties of outcome measures for assessment of fatigue in patients receiving HD, to inform the selection of a robust and feasible measure for use in HD RCT's.	Trial use	Not focus	A standardised and psychometrically robust measure that captures the dimensions of fatigue that are important to patients is needed.
Collection of daily patient reported outcomes is feasible and demonstrates differential patient experience in chronic kidney disease. Pittman, John & McIntyre 2017 [α] (10)	Haemodialysis International	Study demonstrates the feasibility of an online, patient acceptable, iterative PROM, capable of detecting clinically relevant change in PROs in both the short and longer term.	Feasibility/pilot of PROMs implementation in routine clinical care	Customised website to capture PRO data utilising visual analogue scales.	Further work identified to examine the predictive power of changes in PRO data and the use of PROMs for symptom or alert flagging.
Strategies to use tablet computers for collection of electronic patient-reported outcomes. Schick-Makaroff & Molzahn 2015 [α] (11)	Health Qual Life Outcomes	Feasibility of using tablet computers to collect electronic PROs (KDQOL-36, Edmonton Disease Assessment Scale, satisfaction measure). Four core issues emerged: logistics of IT, security, institutional and IT support, electronic design. Consider these factors in advance of implementation	Feasibility/pilot of PROMs implementation in routine clinical care.	Electronic PRO collection via mobile device i.e., tablet computer	Whilst the study offers useful strategies for employing ePROs it recommends real-world testing i.e., in linkage of PRO date with electronic health records, feedback of PRO data, further work on the challenges posed by the use of technology.

Nephrologists' Perspectives on Defining and Applying Patient-Centred Outcomes in Hemodialysis. Tong et al. 2017 ∞ (12)	Clinical Journal of the American Society of Nephrology	Nephrologists' perspectives on implementation of PROs in HD: Challenges of prioritising, measuring and managing comorbidities and broader QoL outcomes in a technically demanding care setting	Results of this multi-national qualitative research could be applied in both routine clinical and research HD settings.	Not the focus of the paper	Use and development of core outcome sets to identify outcomes identified as directly relevant to patients and integration into practice to deliver patient centred care
Methodological considerations in using patient reported measures in dialysis clinics. Peipert & Hays 2017 ∞ (13)	Journal of Patient-Reported Outcomes	Examination of the key methodological concerns on the use of PRO data in US Dialysis centers in relation to PROM selection, mode of administration and support for use, with recommendations for key stakeholders on how to enhance PRO data use in dialysis settings.	Aggregate use for quality improvement and performance monitoring	Considers various modes of administration including paper, electronic methods and telephone.	Further areas of study include evaluation of the equivalence of paper and electronic versions of PROMs, exploration of the cost of reimbursement and continued development of provider training in administration and interpretation of PROMs, prior to widespread implementation.
Brief Communication: patient satisfaction with the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Schick-Makaroff & Molzahn 2014 ∞ (14)	Canadian Journal of Kidney Health and Disease	Pilot study to evaluate patient satisfaction with and time required in administering PROMs using tablet computers in home dialysis clinics.	Feasibility/pilot of PROMs implementation in routine clinical care.	Electronic PRO collection via mobile device i.e., tablet computer	Whilst the pilot demonstrated overall satisfaction in time required and mode of administration, further research required due to small sample size, and lack of generalisability.

Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. Schick- Makaroff & Molzahn 2017 ∞ (15)	BMC Health Serv Res	Study to assess nurses' perspectives on the usefulness and impact of ePRO administration in home dialysis clinics. Nurses reported that sharing ePROs in real time informed their practice, it did not lead to a significant change in patient satisfaction scores.	Routine clinical care of individual patients.	Electronic PRO collection via mobile device i.e., tablet computer	Identified that further research is needed to provide guidance about how ePRO data could enhance person-centred care i.e., an RCT may be helpful in assessing whether ePROs provide a better means of patient assessment as compared to traditional means in order to improve outcomes and care quality.
Health-Related Quality of Life in End-Stage Renal Disease Patients: How often should we ask and what do we do with the answer. Chen, Mewed & Unruh 2016 ∞ (16)	Blood Purification	Article reviews the symptoms associated with poor HRQOL and how frequently QOL should be evaluated to improve outcome. It is noted measurement of PROs may provide opportunity to improve outcomes in ESRD, frequent measurement of symptoms and QoL may be burdensome – data for optimal frequency of assessment are lacking.	Routine clinical care of individual patients to manage symptoms.	Recognition that ePRO capture integrated to EHR could be beneficial	Evaluation of frequency of HRQOL assessment for symptom management is required as data on optimal frequency of assessment is currently lacking.
Incorporating patient-reported symptom assessment into routine care for people with CKD. van de Veer, Aresi & Gair 2017 ∞ (17)	Clinical Kidney Journal	Editorial to review how systematic patient-reported symptom assessments can be incorporated into CKD care.	Collection of PROMs for symptom assessment in routine clinical care	How to move from paper-based questionnaires to digital PRO capture	Research into novel methods for collecting PRO data to support and improve symptom assessment while minimising burden of data collection i.e., use of wearable and smart phone sensors.

Collection and determinants of patient reported outcome measures in haemodialysis patients in Scotland. Nimmo 2018 ∞ (18)	QJM: An international journal of medicine	Paper describes the Scottish Renal Registries (SRR) experience of collecting annual PROMs (KDQOL-36) with patients undergoing HD, with linkage of PROMs to demographic and clinical parameters	Routine collection of PROMs for Registry use	Focus on registry collection	Authors hope that other registries will collect similar data sets allowing wider comparisons to be drawn thereby ultimately leading to improvements in care for patients with ESRD.
When All You Have Is a Hammer: The Need for Tools to Define and Apply Patient- centred Outcomes in Hemodialysis. Barrett Bowling & Plantinga 2017 ∞ (19)	Clinical Journal of American Society of Nephrologists	Editorial commenting on Paper 12 (Tong et al. 2017 (12)). The paper identified that the provision of patient centred care included the ability to interpret and apply evidence to individual patients and the communication skills to discuss trade-offs.	Focus on patient-centred care, collection for individual use in routine clinical practice.	Not the focus of the paper	Key strategy in the implementation of PROMs is the need to develop, practice and role-model effective patient-centred communication via communication skills training and to determine how best to provide interdisciplinary care.

α Studies identified in database search outlined in Appendix 1.3

∞ Studies identified by citation searching

References

1. Aiyegbusi OL, Kyte D, Cockwell P, Anderson N, Calvert M. A patient-centred approach to measuring quality in kidney care: patient-reported outcome measures and patient-reported experience measures. Curr Opin Nephrol Hypertens. 2017;26(6):442-9.
2. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Gheorghe A, Keeley T, et al. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review. PLoS One. 2017;12(6):e0179733.
3. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Keeley T, Gheorghe A, et al. Measurement properties of patient-reported outcome measures (PROMs) used in adult patients with chronic kidney disease: A systematic review protocol. BMJ Open. 2016;6 (10) (no pagination)(e012014).
4. Breckenridge K, Bekker HL, Gibbons E, van der Veer SN, Abbott D, Briancon S, et al. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. Nephrol Dial Transplant. 2015;30(10):1605-14.
5. Finkelstein FO, Finkelstein SH. Time to Rethink Our Approach to Patient-Reported Outcome Measures for ESRD. Clin J Am Soc Nephrol. 2017.
6. Flythe JE, Powell JD, Poulton CJ, Westreich KD, Handler L, Reeve BB, et al. Patient-Reported Outcome Instruments for Physical Symptoms Among Patients Receiving Maintenance Dialysis: A Systematic Review. Am J Kidney Dis. 2015;66(6):1033-46.
7. Jhamb M, Tamura MK, Gassman J, Garg AX, Lindsay RM, Suri RS, et al. Design and rationale of health-related quality of life and patient-reported outcomes assessment in the Frequent Hemodialysis Network trials. Blood Purif. 2011;31(1-3):151-8.
8. Ju A, Tong A. Considerations and Challenges in Selecting Patient-Reported Outcome Measures for Clinical Trials in Nephrology. Clin J Am Soc Nephrol. 2017.
9. Ju A, Unruh ML, Davison SN, Dapueto J, Dew MA, Fluck R, et al. Patient-Reported Outcome Measures for Fatigue in Patients on Hemodialysis: A Systematic Review. American Journal of Kidney Diseases. 2017.
10. Pittman ZC, John SG, McIntyre CW. Collection of daily patient reported outcomes is feasible and demonstrates differential patient experience in chronic kidney disease. Hemodial Int. 2017;21(2):265-73.
11. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. Health & Quality of Life Outcomes. 2015;13:2.
12. Tong A, Winkelmayer WC, Wheeler DC, van Biesen W, Tugwell P, Manns B, et al. Nephrologists' Perspectives on Defining and Applying Patient-Centered Outcomes in Hemodialysis. Clin J Am Soc Nephrol. 2017;12(3):454-66.
13. Peipert JD, Hays RD. Methodological considerations in using patient reported measures in dialysis clinics. Journal of Patient-Reported Outcomes. 2017;1(1).
14. Schick-Makaroff K, Molzahn A. Brief Communication: patient satisfaction wit the use of tablet computers: a pilot study in two outpatient home dialysis clinics. Canadian Journal of Kidney Health and Disease. 2014;1(22).
15. Schick-Makaroff K, Molzahn AE. Evaluation of real-time use of electronic patient-reported outcome data by nurses with patients in home dialysis clinics. BMC Health Serv Res. 2017;17(1):439.
16. Chen SS, Al Mawed S, Unruh M. Health-Related Quality of Life in End-Stage Renal Disease Patients: How Often Should We Ask and What Do We Do with the Answer? Blood Purif. 2016;41(1-3):218-24.

17. van der Veer SN, Aresi G, Gair R. Incorporating patient-reported symptom assessments into routine care for people with chronic kidney disease. Clinical Kidney Journal. 2017.
18. Nimmo A, Bell S, Brunton C, Campbell J, Doyle A, MacKinnon B, et al. Collection and determinants of patient reported outcome measures in haemodialysis patients in Scotland. QJM. 2018;111(1):15-21.
19. Bowling CB, Plantinga LC. When All You Have Is a Hammer: The Need for Tools to Define and Apply Patient-Centered Outcomes in Hemodialysis. Clin J Am Soc Nephrol. 2017;12(3):382-4.

Appendix 2

Appendix 2.1: Mixed Methods study protocol



Full title of the study: Using electronic Patient-Reported Outcome Measures (ePROs) to promote quality of care and safety in the management of patients with End Stage Kidney Disease: Review of Electronic Patient-Reported Outcomes Systems used in Nephrology settings – a mixed methods study protocol

Short Title: Nephrology ePRO systems review

PROTOCOL VERSION 3.0 9th June 2020

SPONSOR: University of Birmingham

FULL TITLE OF STUDY:

Using electronic Patient-Reported Outcome Measures (ePROs) to promote quality of care and safety in the management of patients with End Stage Kidney Disease: Review of Electronic Patient-Reported Outcomes Systems used in Nephrology settings – a mixed methods study protocol

SHORT STUDY TITLE/ACRONYM:

Nephrology ePROs Systems Review

PROTOCOL VERSION NUMBER 3.0 9th June 2021

RESEARCH REFERENCE NUMBERS

University of Birmingham Research Support Group Ref Number: ERN_21-0495

FUNDERS Number: NIHR ICA-CDRF-2018-04-ST2-027

KEY STUDY CONTACTS

Principal Investigator

Professor Melanie Calvert

Institute of Applied Health Research
Centre for Patient Reported Outcome Research (CPROR)

Institute of Applied Health Research
University of Birmingham
The Learning Centre,

University of Birmingham

Edgbaston

Birmingham

B15 2TT

Email [redacted]

Tel: [redacted]

Doctoral Research Student

Nicola Anderson

Institute of Applied Health Research
Centre for Patient Reported Outcome Research (CPROR)
Institute of Applied Health Research
University of Birmingham
The Learning Centre,
Edgbaston
Birmingham
B15 2TT

Email [redacted]

Sponsor	University of Birmingham
Funder	HEE/NIHR ICA Clinical Academic Doctoral Fellowship program (ICA-CDRF-2018-04-ST2-027)
Key Protocol Contributors	Dr Derek Kyte School of Applied Health and Community University of Worcester E-mail [redacted]
	Dr Olalekan Lee Aiyegbusi Centre for Patient Reported Outcomes Research, Institute of Applied Health Research, University of Birmingham Edgbaston, Birmingham B15 2TT E-mail [redacted]
	Dr Christel McMullan Centre for Patient Reported Outcomes Research, Institute of Applied Health Research, University of Birmingham Edgbaston, Birmingham B15 2TT E-mail [redacted]
	Dr Grace Turner Centre for Patient Reported Outcomes Research, Institute of Applied Health Research, University of Birmingham Edgbaston, Birmingham B15 2TT E-mai [redacted]
	Professor Paul Cockwell Department of Renal Medicine, University Hospitals Birmingham NHS Foundation Trust Mindelsohn Way Edgbaston, Birmingham B15 2GW E-mail [redacted]

Senior Research Nurse Mary Dutton
Renal Research Team, R & D, University Hospitals Birmingham NHS Foundation Trust, Room 25 Clinical Research Offices, 1st Floor Heritage Building Old QEH, Mindelsohn Way, Edgbaston Birmingham B15 2TH

E-mail [redacted]

Mr Ravinder Verdi (Member of the Renal Research Patient Advisory Group):

STUDY SUMMARY

Study Title	Using electronic Patient-Reported Outcome Measures (ePROs) to promote quality of care and safety in the management of patients with End Stage Kidney Disease: Review of Electronic Patient-Reported Outcomes Systems used in Nephrology settings – a mixed methods study protocol
Short title	Nephrology ePROs Systems Review ERN_21-0495
Study Design	Mixed Methods Study Part One – Semi-structured Review to identify ePRO Systems and associated System Leads. Part Two – ePRO System Leads Survey via structured review form Part Three – Optional follow up semi-structured interviews, where required
Study Participants for Part Two and Part Three	Eligibility criteria: Adults (Aged 18 years over), able to speak and read English (survey will only be available in English) • System Lead of an eligible ePRO system. A System Lead may have a clinical or non-clinical role but must have carried key responsibility for aspects of design, development or implementation of an eligible ePRO system. • Eligible systems are defined as those used in nephrology practice settings including related treatment areas (e.g., dialysis units), that assess PROs electronically and summarize kidney patients' responses to their care provider. Eligible systems from any country will be included. • Willing to provide valid informed consent for study participation
Planned Size of Sample	A preliminary scoping exercise of nephrology ePRO systems in use and currently being developed suggests approximately 7-15 System

	Leads may meet the eligibility criteria, be sent the survey, and asked to attend follow up interviews. The sample size will be confirmed following Part One of this mixed methods study.
Follow up duration	Optional follow up interviews will be undertaken with survey participants or a designated team member, if required, following preliminary analysis of survey responses
Planned Study Period	1 year
Research Question/Aim(s)	The aim of this research is to comprehensively identify existing ePRO systems being used in nephrology settings and to explore and summarise the purpose of ePRO collection and how such systems work i.e., key system characteristics. Thereby allowing classification of the core factors which contribute to successful implementation of an ePRO in nephrology settings, including facilitators and barriers.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Management Group

The Study Management Group comprises the Principal Investigator, Doctoral Research Fellow and members of the academic and clinical supervisory team listed above.

The group will meet every 1-2 months, to oversee and supervise study progress towards its interim and overall objectives. They will assess study adherence to the protocol.

The Study Management Group will oversee data collection and analysis and report any problems to the Sponsor.

Patient partners will be involved in all aspects of the study, where possible.

Protocol contributors

The protocol contributors are outlined above.

The sponsor and funder of this study will not be involved in the study design, data analysis and interpretation and manuscript writing of results.

Decisions regarding study design, conduct, data analysis, interpretation of results, write up and dissemination will be undertaken by the Study Management Group in collaboration with the Sponsor.

KEY WORDS:

Patient Reported Outcomes (PROs)
Electronic Patient Reported Outcome Measures (ePROs)
ePRO Systems
Quality of life
Symptom Management
PRO assessment
Routine monitoring in clinical care
Digital health
Telehealth/ Telemedicine

STUDY PROTOCOL

1. RATIONALE

There is an increased interest in the use of digital data capture systems, including electronic patient-reported outcome (ePRO) systems; exacerbated by the shift from face to face to virtual care delivery in the intra and post pandemic landscape.

The aim of this research is to comprehensively explore the design, implementation and use of ePRO systems being used in nephrology settings, to support future implementation and use with patients who have end stage kidney disease requiring treatment with haemodialysis.

The study objectives are:

- To identify existing ePRO systems being used in nephrology settings and those under development.

- To explore and summarise the key components of system characteristics including i) administration ii) levels of automation iii) reporting and use of ePROs to manage patient safety iv) integration into existing workflow and electronic health records,

- To classify the core factors which contribute to successful implementation of an ePRO in nephrology settings, including facilitators and barriers

2. BACKGROUND

Patient Reported Outcomes (PROs) are defined as 'any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else'(1) . Any measure, generic or disease specific, capable of assessing and capturing the health, illness or result of health care from the patient's perspective e.g., Health-related Quality of Life (HRQOL) or symptom questionnaire is defined as a Patient Reported Outcome Measure (PROM).

Data collected by these tools can highlight relevant symptoms, and perhaps most importantly, any changes in symptoms and/or HRQOL, thus promoting patient engagement in their treatment and ultimately improving overall patient outcomes (2). There is increasing interest in collecting such data electronically (ePROs).

Patients at all stages of chronic kidney disease (CKD), including those undertaking renal replacement therapy experience a high symptom burden and often report diminished HRQOL (3-5). It is argued the true extent of the symptom burden carried by patients with established kidney disease is unrecognized and the multidimensional nature of the burden is not fully understood. While clinicians focus on highly prevalent symptoms, other noteworthy symptoms, and attributes such as frequency, effect, and severity of symptoms, might go unreported and hence unrecognized and unalleviated, leading to an increased overall burden (12). ePROs can be used to provide a multidimensional assessment, capturing the full impact of living with established renal failure and the consequences of its treatments.

There is increasing evidence, particularly from oncology settings, on the potential impacts of the collection and use of ePRO data. Studies have shown symptom monitoring during chemotherapy treatments using ePROs can aid patient self-management, but may also improve service delivery, facilitate shared-decision making, promote patient autonomy and correspondingly improve QoL, reduce unplanned hospitalisation, and enhance long-term outcomes including survival (6-10), whilst maintaining cost-effectiveness (11).

However, there is a general lack of consensus in the renal community over how and which PROs should be routinely collected (12). With the increase in the use of digital care delivery, particularly following the SARs-COV19 pandemic (13), the collection of ePRO data has taken new and increasing significance. Such use could assist in the management of symptoms, whilst ensuring that limited healthcare resources are used effectively to maximize impact (14). In order to capture and act on this data, ePROs are assuming an increasing role in augmenting clinician understanding of the patient's health status leading to overall improvements in patient care (6).

Correspondingly the corpus of evidence around implementation of ePROs in nephrology is growing. Studies from North America demonstrate the feasibility of ePRO collection in Haemodialysis settings (15, 16) and an Australian pilot study further explored both feasibility and acceptability of ePROs among patients receiving haemodialysis in the Symptom monitoring With Feedback Trial (SWIFT) (17, 18). In advanced CKD populations, the RePROM study piloted the use of an ePRO for remote symptom monitoring in the UK (19), whilst the AmbuFlex telepro system is used to manage renal follow up in Denmark (20).

A review and synthesis of evidence is currently being undertaken to investigate how PROs might work to enhance patient-centred care in renal settings, to offer strategy and guidance at individual and aggregate levels of decision-making (21). For effective multiple uses of data, implementation needs to be viewed within the context of complex data linkage and accessibility issues. Studies in the UK and Australia are currently exploring and testing such linkage of symptoms and HRQOL data to the Australia and New Zealand Dialysis and Transplant Registry and UK Renal Registry respectively (17, 22, 23).

Aiyegbusi et al. (2019) explored key stakeholder perspectives on the use of PROs in pre-dialysis patients (19) and found that such systems could play a supportive role in the management of patients with advanced CKD, with the rider that future research would need to address the concerns of patients and clinicians. These concerns included questionnaire burden to patients, the creation of unrealistic expectations around delivery of care and consequent increases to clinician workload. To have desired impacts, ePRO systems need to be 'efficient, effective and satisfactory' for stakeholders (19, 20).

In November 2020, Key stakeholders including patients, carers, professional bodies (Renal Association, British Renal Society, Association of Nephrology Nurses UK), charitable organisations (Kidney Research UK, Kidney Care UK) and industry partners

were invited to attend an online UK Summit on 'ePROs for the Kidney Patient Community' – the aim of this summit being to create a comprehensive, UK-wide roadmap to facilitate and optimize the collection and use of ePROs for the benefit of people with CKD. This study will support and inform this initiative.

In 2014 Jensen et al undertook a review of ePRO systems used in cancer clinical care. They concluded that there are various features that can optimize integration of ePROs monitoring into routine clinical care, including barriers to widespread adoption (24). Given the number of emerging ePROs systems for use in nephrology settings, it is essential that a similar review is conducted for the field for the UK wide initiative to succeed.

To minimize the key limitations of the Jensen review (reliance on reported information not direct observation, incomplete survey data due to incomplete answers or reluctance to release proprietary information, failure to identify key systems) (25) we have designed a mixed methods review in three parts.

This mixed methods review will provide key information to further the vision of a national roadmap by comprehensively identifying existing ePRO systems being used in nephrology settings and those under development, to explore and summarise the key components of system characteristics, in order to classify the core factors which contribute to successful implementation of an ePRO in nephrology settings. Thereby addressing concerns of patients and clinicians which arose in previous studies.

3 THEORETICAL FRAMEWORK

Since it was important to gain a comprehensive understanding of the use and implementation of ePROs in nephrology settings, a study design allowing researchers to relate complimentary findings to each other, resulting from the use of methods from different methodological traditions of quantitative (structured review and survey) and qualitative research (semi-structured follow up interviews) was sought.

According to Johnson et al (2007) 'Mixed methods research is an intellectual and practical synthesis based on qualitative and quantitative research; it is the third methodological or research paradigm (along with qualitative and quantitative research)…….Based within the philosophy of pragmatism, this method relies on qualitative and quantitative viewpoints, data collection, analysis, and inference techniques combined according to the logic of mixed methods research to address one's research question(s); and (d) is cognizant, appreciative, and inclusive of local and broader socio-political realities, resources, and needs.'

4 RESEARCH QUESTION

4.1 Objectives

The aim of this research is to comprehensively explore the design, implementation and use of ePRO systems being used in nephrology settings.

The study objectives are:

- To identify existing ePRO systems being used in nephrology settings and those under development.

- To explore and summarise the key components of system characteristics including i) administration ii) levels of automation iii) reporting and use of ePROs to manage patient safety iv) integration into existing workflow and electronic health records,

- To classify the core factors which contribute to successful implementation of an ePRO in nephrology settings, including facilitators and barriers

5 STUDY DESIGN

Methods

This is a three phased study using mixed methods.

Part One – Semi-structured review to identify ePRO System Leads: This will comprise review of literature on the use and implementation of ePRO systems in nephrology settings. Systems will be identified through publications including conference abstracts and grey literature using 'pearl' and 'snowballing' methodology (26-28). Field experts will also be consulted.

The results of this review will be used to further identify key system characteristics and clinical implementation fields, (e.g., administration of PRO assessments/level of automation, integration into existing systems and reporting of responses) using a structured review form created by the authors.

Part Two - A survey form, prepopulated from available information gathered in Part One (structured review form) will be administered electronically (using SmartSurvey) and distributed through email to System Leads for verification and to obtain missing system characteristics. This survey will focus on system design and software features, integration of e-PRO collection and reporting into nephrology clinical care. Additionally, data on other critical elements, such as PRO instruments used, and analytic approaches will be collected via a mix of multiple-choice questions and free text responses (see Appendices). Data on role and responsibilities in system development from the System Lead will also be collected. The survey will be constructed to allow respondents to skip questions or include 'rather not say' in a free text option, to avoid disclosing proprietary information and breaching copyright or non-disclosure agreements.

Part Three – Optional follow up semi-structured interviews will be undertaken with survey participants or a designated team member, if required, following preliminary analysis of survey responses. The purpose of these interviews will be to further explore survey responses and allow more detailed organisational comparison, where the survey details require expansion. First contact will be made with Primary System Lead who completed survey. Development team members may attend the semi-structured interview instead, at request of the System Lead, if specific roles in development and implementation were delegated. Interviews will be conducted by University of

Birmingham approved video conferencing platform (Zoom or MS Teams) or telephone. Video conferencing has been demonstrated to work well as a viable alternative qualitative data collection tool to face to face interviews (29); Telephone interviews can also be used productively in qualitative research (30, 31).

OUTCOME

This mixed methods review will identify the key features and functionality of ePRO systems currently being used or developed in clinical nephrology settings. An increased understanding of the range of features and utilities of these systems, including potential barriers and facilitators to use and implementation, will help ensure such systems are applied to improve care and maximise patient outcomes.

6 STUDY SETTING

As participant recruitment and data collection are taking place during the ongoing Covid-19 pandemic, all contacts will be web-based, using email, telephone and video conferencing facilities.

Identified ePRO System Leads outside the United Kingdom will also be invited to participate in the survey and follow up interview, if required.

Part Two Survey: will be administered via email and associated web link.

Part Three Optional follow up interview: will be conducted via telephone or University of Birmingham approved video communications link – Zoom/MS Teams.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

- Adults (Aged 18 years over), able to speak and read English (survey will only be available in English.
- System Lead of an eligible ePRO system. A System Lead may have a clinical or non-clinical role but must have carried key responsibility for aspects of design, development or implementation of an eligible ePRO system.
- Eligible systems are defined as those used in nephrology practice settings including related treatment areas (e.g., dialysis units), that assess PROs electronically and summarize kidney patients' responses to their care provider. Eligible systems from any country will be included.
- Willing to provide valid informed consent for study participation.

7.1.2 Exclusion criteria

- System Lead of a non-eligible system.
- Non-eligible systems are defined as an ePRO system hardware adapted and implemented in a non-nephrology setting.

7.2 Sampling

7.2.1 Size of sample

A preliminary scoping exercise of nephrology ePRO systems in use and currently being developed suggests approximately 7-15 Primary System Leads will be sent the survey and may be asked to attend follow up interviews. The expected sample size will be confirmed following Part One of this mixed methods study.

Optional follow up interviews will be undertaken following preliminary analysis of survey responses and will be indicated if there is partial or missing data without which it is hard to undertake a comparison or evaluation of ePRO systems.

7.2.2 Sampling technique

Purposive sampling will be undertaken following identification of eligible systems and associated System Leads.

7.3 Recruitment and Consent Process

7.3.1 Sample identification

Participants will be approached directly by email from the Doctoral Research Fellow, in collaboration with the Principal Investigator, following their identification as a System Lead. The survey will be accessed through a web link sent out via email. System Leads will be asked if they are happy to be contacted for a follow up interview as part of the survey completion. System Leads who completed the survey may also refer team members for participation in the survey and/or a follow up interview if key system activities were delegated. If preferable to participants, more than one team member could take part in an interview.

Following initial contact, up to 2 reminder emails may be sent before contact is abandoned as non-participation. This will include an email co-signed by the Primary Investigator/Supervisor.

7.4 Consent

Informed consent must be obtained prior to the participant undergoing any activities that are specifically for the purposes of the study i.e., survey completion or follow up semi-structured interviews.

Participant consent for survey participation.

An electronic link will take participants to the online Participant Information Sheet (PIS) which will include details about the purpose of the study, what the study involves, data protection and contact details for further information. Participants will be required to click a button to acknowledge that they have read the PIS. After reading the PIS, participants will be directed to an electronic consent form comprising

statements which participants are asked to agree to (indicated by ticking a box next to each consent item). Participants will not be able to access the survey unless they agree to all non-optional consent items. The Consent Form will include an optional question on follow up interview – participants will need to indicate if they are happy to take part in a follow up interview on this consent form. The survey will be constructed to allow respondents to skip questions or include 'rather not say' in a free text option, to avoid disclosing proprietary information and breaching copyright or non-disclosure agreements.

Participant consent for follow up interview

Consent will be reaffirmed prior to any follow up interview: An electronic link will take participants back to the online Participant Information Sheet (PIS) which will include details about the purpose of the study, what the study involves and data protection issues. The PIS will state research team contact details, should participants have any questions or wish to discuss the study before deciding whether or not to take part. Before the interview commences, the interviewer will go through the PIS and original consent form to ensure that the participant fully understands the study and their participation. Consent will be reaffirmed verbally and recorded. Participants will already have an electronic copy of their consent form.
Participants will be assessed on an individual basis as to how long they require to consider study participation and whether they have capacity to consent to participation. For consent to be ethical and valid in law, participants must be capable of giving consent for themselves. A capable person will:

- understand the purpose and nature of the research
- understand what the research involves, its benefits (or lack of benefits), risks and burdens
- understand the alternatives to taking part

- be able to retain the information long enough to make an effective decision.
- be able to make a free choice
- be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity)

7.5 Data Collection

See Appendix 1 for Part Two survey and Part Three follow up interview topic guides indicating content of survey and semi-structured interviews. Content of the survey will be refined following completion of Part One semi-structured review and interview topic guide will be refined iteratively as analysis is conducted concurrently with data collection phase in Part Three.

7.5.1 Survey

Data collection will be via a web-based survey application (SMART Survey). The survey will include a mix of drop-down boxes with minimal free text to ensure the survey is as non-burdensome as possible. There will be the option to give multiple responses to some questions. The survey will be piloted so that participants can be informed of a realistic completion time. The survey will also ask if they are happy to be contacted for a follow up interview, if required.

7.5.2 Individual follow up semi-structured interviews with ePRO System Leads

Using qualitative methodology, follow up semi structured interviews will be held with ePRO System Leads or nominated members of their team. The purpose of these interviews will be to examine the content of their systems survey, complete any missing fields and discuss the various issues that relate to the use and administration of PROMs using the CFIR-based topic guide. These interviews will last approximately 60 mins.

The Doctoral Research Fellow will arrange a date and time for the individual follow up interview that will be most convenient for the participant. The Doctoral Research Fellow will confirm with the participant if they would like to receive a reminder in the form of a text message, email or a telephone call a few days before the follow up interview.

Electronic Informed consent will be reaffirmed prior to any interview, using a study specific consent form. Follow up interviews will be led by the use of a piloted study specific topic guide, based around the CFIR domains (see Appendix 1). This topic guide may be refined following the semi-structured review (Part One) and ePRO System survey (Part Two) of this mixed methods study. The topic guide will provide a general direction for each interview and ensure that important issues are covered whilst allowing enough flexibility to capture other relevant themes that may be arise during any session.

Interviews will be conducted via approved videoconferencing platform (Zoom/MS Teams) or telephone, depending on participant's preference.

7.6 Study withdrawal.

Study participants will be informed that they have the right to withdraw from the study, for any reason before survey completion or follow up interview. It will be made clear to participants that they will not be required to supply a reason for their withdrawal. Participants can withdraw at any point during the survey by exiting their browser. Partially completed forms may be saved for completion at a later time and this data is available to researchers. In addition, participants can request withdrawal of their full or partially submitted data up to 5 days after completing the survey by contacting the study team. After this point, analysis will commence, and withdrawal of data will not be possible. Contact details will be provided in the PIS and at the end of the survey. Survey data that is not downloaded from SMART Survey is automatically deleted after 30 days.

Participants will also be able to withdraw following participation in follow up interview. A copy of the interview transcript will be sent to participants for review following their interview, allowing them to redact any proprietary information they no longer wish to disclose. It is requested within the PIS that participants return any reviewed transcripts within 10 working days from receipt; non-return indicates the participant is happy with the content. After this point, analysis will commence, and withdrawal of data will not be possible. Contact details will be provided in the PIS and at the end of the survey. Again, participants will not be expected to give a reason for study withdrawal

7.8 Data Analysis

7.8.1 Part One Semi-structured review:

Data will be analysed by content analysis using structured review form to be used in survey stage (Part Two) (see appendices). The focus of the structured review form will be (I) system design and software features, (II) integration of collection into clinical care (III) ePRO Reporting.

7.8.2 Part Two Survey:

The data derived from the survey will be presented in tabular form using descriptive content analysis. Mixed methods studies explore how qualitative data can be quantified for statistical analysis i.e., the generation of descriptive measures such as frequencies and percentages (30). Thematic analysis techniques (32) will be used to summarise the qualitative data components.

7.8.3 Part Three Semi-structured follow up interviews:

Analysis will be undertaken using Codebook Thematic Analysis (CFIR) (32) and the Consolidated Framework for Interventional Research (see Figure One) (33, 34). For all qualitative data we will use Computer Assisted Qualitative Data Analysis Software CASDAQ i.e., QSR NVIVO 12 to manage and organise data. Thematic analysis using a framework approach is well suited to meet the aims of the study as it is able to systematically identify and analyse patterns of meaning within data, with the aim of

highlighting those that are most salient. Using NVivo software, the researchers will code the interviews using a mixed deductive and inductive approach. The CFIR will be used to assess the overall effectiveness of the ePRO Systems and associated implementation strategies and thereby highlight best practice across organisations 'Examining research (and real-world implementation efforts) through the lens of the CFIR gives us some indication of how comprehensively strategies address important aspects of implementation." (35)

Aggregating Data from CFIR it will be possible to conduct organisational comparison (https://cfirguide.org/evaluation-design/qualitative-data/)

After data have been coded, data aggregation queries can be used to create case memos. The Microsoft Word memo template provided via the CFIR website facilitates aggregating, summarizing, and rating data. One memo is typically created for each unit of analysis (e.g., organization) at each time point (e.g., pre-implementation, post-implementation). The memo is organized by CFIR construct.

Using the CFIR it is possible to rate the data with an analyst (a minimum of two is recommended) to apply ratings based on the qualitative data from individual transcripts and the organization as a whole. A Rating Rules PDF for guidance on assigning ratings is available via the CFIR website.

This allows production of a summary all of the data for each construct, e.g., how it manifests in the organization.

Once summary statements and supporting data have been documented, the constructs can be rated. Ratings have great utility for identifying constructs that appear to influence implementation. In addition, rating the data adds significant value to the project because the results can be added to a repository, which allows researchers to synthesize findings more reliably across studies, building an urgently needed knowledgebase.

There is a danger of oversimplifying complex, dynamic descriptions of implementation processes and contexts when applying ratings. The CFIR developers strongly encourage reliance on the underlying qualitative data in addition to the aggregate ratings.

Data Interpretation:

A common evaluation objective is to identify constructs that appear to distinguish between organizations with high and low implementation success, which provides insights into the key constructs that influence implementation. This information can be used to design implementation strategies for individual or larger-scale implementation efforts.

Using these methods analysts can identify patterns by sorting sites by implementation outcome.

Qualitative Comparative Analysis (QCA)

Analysts can use QCA to provide in-depth information about clusters of constructs that contribute to success or failure of implementation. QCA considers “equi-finality,” meaning that more than one combination of positively (or negatively) rated constructs may lead to success (36-38) and can be a powerful approach for building knowledge.

8 ETHICAL AND REGULATORY CONSIDERATIONS

8.1 Assessment and management of risk

In the highly unlikely event that any participant becomes distressed during completion of the survey, they can close their browser and study participation will be discontinued. In the event of distress during a follow up interview, they will be given the option to either stop or temporarily discontinue the interview, allowing resumption at a later time.
It is highly unlikely that the researcher becomes upset during an interview. The supervisory team members who are experienced in qualitative research will provide support, if required.

8.2 Research Ethics Committee (REC) review & reports

Before the start of the study, approval will be sought from University of Birmingham REC for the study protocol, informed consent forms and other relevant documents.

Substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the study.

All correspondence with the REC will be retained.

8.3 Peer review

The study protocol and associated documents has been reviewed by the experienced supervisory and study management team including clinical and academic members.

8.4 Patient & Public Involvement

This mixed methods study has been funded by the NIHR. This protocol was presented for review and
comment to members of the Renal Research Patient Advisory Group: patients within this group have extensive previous experience of PRO related research within nephrology settings.

8.5 Data protection and patient confidentiality

The study will adhere to the following: Data Protection Act 2018, General Data Protection Regulation 2018 (GDPR), University of Birmingham Research Data Management Policy, last updated Jan 2018.https://intranet.birmingham.ac.uk/as/libraryservices/library/research/rdm/policies/research-data-management-policy.aspx

All individual personal participant data will be pseudonymised. Identifiable details including name, place of work, role and responsibilities will be stored on the participant log along with a corresponding unique study identifier for each participant. The participant log will be stored in an electronic format in a password protected study folder on the University of Birmingham server. This file will be accessed only by a

member of the research team. However, system and institution identifiers will remain within the transcript and will be used within publications and presentations; this will be made explicit within the consent process Participants will be given the opportunity to read transcripts and to redact any proprietary information before analysis.

The CI, research team and members of the study management group, including University of Birmingham supervisory team, will be the only people with access to pseudonymised research data pertaining to the study. The exception will be permissions given to authorised personnel to conduct audits and inspections on behalf of the regulatory authorities and Sponsor.

Survey data will be captured using SmartSurvey which is compliant with the UK Data Protection act. Data will be collected and stored on UK based servers in accordance with the SmartSurvey security policies as described at: http://www.smartsurvey.co.uk/security.aspx. The data will be owned by the University of Birmingham. Data from SmartSurvey will be exported into a database which will be stored on the secure university server which is backed up daily. Once data collection is completed, the data will be downloaded into an Excel sheet. Online data will be deleted and SmartSurvey will remove this from their servers within 30 days.

All data will be stored on a secure server which is backed up daily at the University of Birmingham. The computer used for this study is password protected.

Semi- structured interview data

Video recording audio will be downloaded immediately after interview from the approved platform (Zoom/MS Teams) onto a password protected laptop, then transferred and stored on the University of Birmingham server in a password protected file. Audio recordings will not be stored on the cloud/ app platform server. Audio recordings from any telephone interviews will be deleted from the encrypted audio recorder as soon as possible after each interview i.e., once transferred to password protected laptop. Where possible, audio recordings of interviews will be

professionally transcribed by designated transcription company; employees of which will be asked to sign a confidentiality agreement. The recordings on the digital audio recorder or password protected laptop will be deleted as soon as successful transfers of the electronic files to the University of Birmingham server have been confirmed. Personal identifiers will be pseudo anonymised when transcribed prior to analysis. However, system/institution identifiers will remain within the transcript. Electronic copies of interview transcripts may be stored for up to ten years, on a secure server at University of Birmingham, for the purpose of publication after which they will also be destroyed.

The Trial Master file will be stored in a locked cabinet within a secure office at University of Birmingham.

Anonymised direct quotes only will be used in any publication following this study. Any identifiable direct quotes would only be used with permission.

Following study end, all essential documentation will be stored in a suitable repository at the University of Birmingham for a period of 10 years from study conclusion. An archive log will be maintained to track and retrieve documentation. Any decision to dispose of Research Data is the responsibility of the Principal Investigator, consulting with their College Director of Research and appropriate Professional Services staff, where appropriate. If Research Data are to be disposed of, then the reasons for doing so should be properly documented and stored as part of an updated Data Management Plan for the project.

Electronic study data will be stored within the University of Birmingham server.

The Principal Investigator at University of Birmingham will act as custodian for the data.

8.6 Payment and financial incentives

In recognition for time spent completing the survey, participants will be offered a £50 gift voucher.

8.7 Indemnity

Due to the low risk profile associated with this study, following risk assessment, there are no formal arrangements in place for payment of compensation in the event of harm to research participants where no legal liability arises.

8.8 Amendments

Any decision to amend the protocol and/or supporting documentation will be made by the Study Management Group.

All substantive changes will be communicated to the relevant stakeholders for approval.

Amendment history will be logged in Appendix 2 of the protocol and within the version control log held within the Trial Master File.

8.9 Access to the final study dataset

Members of the Study Management Team will have access to the full pseudonymised dataset. It is envisaged that the dataset may be used for secondary analysis. This will only be undertaken with the consent of the participants; the consent form includes a request for the future use of these data in associated research projects, investigating the use of PROs with nephrology patients.

9 DISSEMINATION POLICY

9.1 Dissemination policy

The data arising from the study will be owned by the Sponsor. However, members of the study management group will have access to the pseudonymised data set and will have rights to publish research findings from this data. On completion of the study, the data will be analysed, tabulated and a Final Study Report prepared. A copy of the full study report will be accessible following application to the Study Management Group via the Principal Investigator.

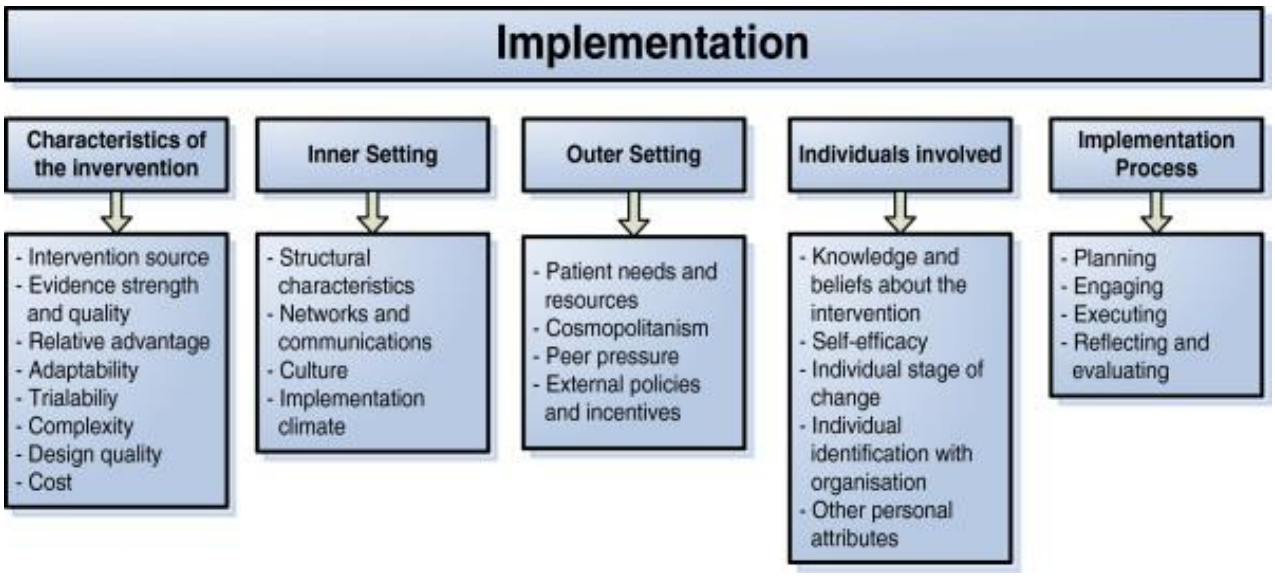
The NIHR, as funder to the study, will be acknowledged in any publications but will not have publication rights to the data.

It is planned to publish results in an open access publication and disseminate relevant findings at conferences.

At the end of the study, participants will be provided with details of where they can access a summary of the study findings.

Figure One

Consolidated Framework for Implementation Research (33)



REFERENCES

1. Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Rockville, MD: U.S. Department of Health and Human Services,;2009.
2. Breckenridge K, Bekker HL, Gibbons E. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: An expert consensus meeting. Nephrol Dial Transplant. 2015;30.
3. Almutary H, Bonner, A, Douglas, C. Symptom burden in Chronic Kidney Disease: a review of recent literature. Journal of Renal Care. 2013;39(3):140-50.
4. Jager KJ, Fraser SDS. The ascending rank of chronic kidney disease in the global burden of disease study. Nephrol Dial Transplant. 2017;32(suppl_2):ii121-ii8.
5. Lowney AC, Myles HT, Bristowe K, Lowney EL, Shepherd K, Murphy M, et al. Understanding What Influences the Health-Related Quality of Life of Hemodialysis Patients: A Collaborative Study in England and Ireland. J Pain Symptom Manage. 2015;50(6):778-85.
6. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial. J Clin Oncol. 2004;22(4):714-24.
7. McCann L, Maguire R, Miller M, Kearney N. Patients' perceptions and experiences of using a mobile phone-based advanced symptom management system (ASyMS) to monitor and manage chemotherapy related toxicity. Eur J Cancer Care (Engl). 2009;18(2):156-64.
8. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA. 2017;318(2):197-8.
9. Denis F, Basch EM, Lethrosne C, Pourel N, Molinier O, Pointreau Y, et al. Randomized trial comparing a web-mediated follow-up via patient-reported outcomes (PRO) vs. routine surveillance in lung cancer patients: Final results. Journal of Clinical Oncology. 2018;36(15_suppl):6500-.
10. Basch E, Stover AM, Schrag D, Chung A, Jansen J, Henson S, et al. Clinical Utility and User Perceptions of a Digital System for Electronic Patient-Reported Symptom Monitoring During Routine Cancer Care: Findings From the PRO-TECT Trial. JCO Clinical Cancer Informatics. 2020(4):947-57.
11. Lizée TB, Ethan ; Trémolières, Pierre ; Voog, Eric ; Domont, Julien ; Peyraga, Guillaume ; Urban, Thierry ; Bennouna, Jaafar ; Septans, Anne-Lise ; Balavoine, Magali ; Detournay, Bruno ; Denis, Fabrice. Cost-Effectiveness of Web-Based Patient-Reported Outcome Surveillance in Patients With Lung Cancer. Journal of Thoracic Oncology. 2019;14(6):1012-21.
12. Anderson NE, Calvert M, Cockwell P, Dutton M, Kyte D. The Use of Patient-Reported Outcomes in Patients Treated With Maintenance Hemodialysis: A Perspective. Am J Kidney Dis. 2019.
13. Hull SA, Rajabzadeh V, Thomas N, Hoong S, Dreyer G, Rainey H, et al. Do virtual renal clinics improve access to kidney care? A preliminary impact evaluation of a virtual clinic in East London. BMC Nephrol. 2020;21(1):10.

14. Kyte D, Anderson N, Auti R, Aiyegbusi OL, Bishop J, Bissell A, et al. Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease. J Patient Rep Outcomes. 2020;4(1):55.
15. Schick-Makaroff K, Molzahn A. Strategies to use tablet computers for collection of electronic patient-reported outcomes. Health & Quality of Life Outcomes. 2015;13:2.
16. Gabbard J, McLouth CJ, Brenes G, Claudel S, Ongchuan S, Burkart J, et al. Rapid Electronic Capturing of Patient-Reported Outcome Measures in Older Adults With End-Stage Renal Disease: A Feasibility Study. The American journal of hospice & palliative care. 2020:1049909120954805.
17. Viecelli A, Dansie K, McDonald S, Jesudason S, Duncanson E, Bennett P, et al. Symptom monitoring with feedback trial (SWIFT) pilot to explore the feasibility and acceptability of electronic patient reported outcome measures (e-proms) data capture and feedback. Nephrology Dialysis Transplantation. 2020;35 (SUPPL 3):iii137.
18. Duncanson E, Bennett PN, Viecelli A, Dansie K, Handke W, Tong A, et al. Feasibility and acceptability of e-PROMs data capture and feedback among patients receiving haemodialysis in the Symptom monitoring WIth Feedback Trial (SWIFT) pilot: protocol for a qualitative study in Australia. BMJ Open. 2020;10(11):e039014.
19. Kyte D, Bishop J, Brettell E, Calvert M, Cockwell P, Dutton M, et al. Use of an electronic patient-reported outcome measure in the management of patients with advanced chronic kidney disease: the RePROM pilot trial protocol. BMJ Open. 2018;8(10):e026080.
20. Schougaard L M LLP, Jessen A et al. AmbuFlex: tele-patient-reported outcomes (telePRO) as the basis for follow up in chronic and malignant diseases. Qual Life Res. 2016;25(3):525-34.
21. Schick-Makaroff K, Thummapol O, Thompson S, Flynn R, Karimi-Dehkordi M, Klarenbach S, et al. Strategies for incorporating patient-reported outcomes in the care of people with chronic kidney disease (PRO kidney): a protocol for a realist synthesis. Syst Rev. 2019;8(1):20.
22. Morton RL, Lioufas N, Dansie K, Palmer S, Jose M, Raj R, et al. Patient reported outcome measures in australian and new zealand renal units: An anzdata survey of current practice. Nephrology.23:32.
23. Van Der Veer SN, Ercia A, Caskey FJ, Farrington K, Jury F, Rees M, et al. Developing an Intervention to Implement Electronic Patient-Reported Outcomes in Renal Services in the UK. Studies in Health Technology & Informatics. 2020;270:936-40.
24. Jensen RE, Snyder CF, Abernethy AP, Basch E, Potosky AL, Roberts AC, et al. Review of electronic patient-reported outcomes systems used in cancer clinical care. Journal of oncology practice/American Society of Clinical Oncology. 2014;10(4):e215-22.
25. Jensen RE, Snyder, C. F, Abernethy, M.D, Basch, E, Potosky, A.L, Roberts, A.C, Loeffler, M.A, Reeve, B.B. Review of Electronic Patient-Reported Outcomes Systems Used in Cancer Clinical Care. American Society of Clinical Oncology. 2013;10(4).
26. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. BMJ. 2005;331(7524):1064-5.

27. Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. Cochrane Database Syst Rev. 2011(8):MR000026.
28. Lefebvre C, Glanville J, Wieland LS, Coles B, Weightman AL. Methodological developments in searching for studies for systematic reviews: past, present and future? Syst Rev. 2013;2:78.
29. Lacono V, L, Symonds,P, Brown, D,H,K. Skype as a Tool for Qualitative Research Interviews. Sociological Research Online. 2016.
30. Sturges JE, Hanrahan, K.J. Comparing telephone and face-to-face qualitative interviewing:a research note. Qualitative Research. 2004;4(1):107-18.
31. Oltmann S. Qualitative interviews: A methodological discussion of the interviewer and responsent contexts Forum Qualitative Sizialforschung. 2016;17(2).
32. Braun V, Clarke V. One size fits all? What counts as quality practice in (reflexive) thematic analysis? Qualitative Research in Psychology. 2020:1-25.
33. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.
34. Damschroder LJ, Lowery, J. C,. Evaluation of a large-scale weight management program using the consolidated framework for implementation research (CFIR). Implement Sci. 2013;10(8).
35. Powell BJ, Proctor EK, Glass JE. A Systematic Review of Strategies for Implementing Empirically Supported Mental Health Interventions. Res Soc Work Pract. 2014;24(2):192-212.
36. Kahwati LC, Lewis MA, Kane H, Williams PA, Nerz P, Jones KR, et al. Best practices in the Veterans Health Administration's MOVE! Weight management program. Am J Prev Med. 2011;41(5):457-64.
37. Kane H, Lewis MA, Williams PA, Kahwati LC. Using qualitative comparative analysis to understand and quantify translation and implementation. Transl Behav Med. 2014;4(2):201-8.
38. Cragun D, Pal T, Vadaparampil ST, Baldwin J, Hampel H, DeBate RD. Qualitative Comparative Analysis: A Hybrid Method for Identifying Factors Associated with Program Effectiveness. J Mix Methods Res. 2016;10(3):251-72.

Appendix 2.2: Consolidated Framework for Interventional Research (CFIR) Codebook Template.

Taken from: Consolidated Framework for Implementation Research (CFIR) Website. CFIR Constructs table Available from https://cfirguide.org/constructs/ [last accessed 13 Nov 2022]

CFIR Codebook

Note: This template provides inclusion and exclusion criteria for most constructs. Please post additional inclusion and exclusion criteria, guidance, or questions to the CFIR Wiki discussion tab in order to help improve the CFIR.

This template only includes CFIR definitions and coding criteria; codebooks may include other information, such as examples of coded text, rating guidelines, and related interview questions.

Innovation Characteristics	
A. Innovation Source	Definition: Perception of key stakeholders about whether the innovation is externally or internally developed. Inclusion Criteria: Include statements about the source of the innovation and the extent to which interviewees view the change as internal to the organization, e.g., an internally developed program, or external to the organization, e.g., a program coming from the outside. Note: May code and rate as "I" for internal or "E" for external. Exclusion Criteria: Exclude or double code statements related to who participated in the decision process to implement the innovation to Engaging, as an indication of early (or late) engagement. Participation in decision-making is an effective engagement strategy to help people feel ownership of the innovation.
B. Evidence Strength & Quality	Definition: Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the innovation will have desired outcomes. Inclusion Criteria: Include statements regarding awareness of evidence and the strength and quality of evidence, as well as the absence of evidence or a desire for different types of evidence, such as pilot results instead of evidence from literature. Exclusion Criteria: Exclude or double code statements regarding the receipt of evidence as an engagement strategy to Engaging: Key Stakeholders. Exclude or double code descriptions of use of results from local or regional pilots to Trialability.

C. Relative Advantage	Definition: Stakeholders' perception of the advantage of implementing the innovation versus an alternative solution. Inclusion Criteria: Include statements that demonstrate the innovation is better (or worse) than existing programs. Exclusion Criteria: Exclude statements that demonstrate a strong need for the innovation and/or that the current situation is untenable and code to Tension for Change.
D. Adaptability	Definition: The degree to which an innovation can be adapted, tailored, refined, or reinvented to meet local needs. Inclusion Criteria: Include statements regarding the (in)ability to adapt the innovation to their context, e.g., complaints about the rigidity of the protocol. Suggestions for improvement can be captured in this code but should not be included in the rating process, unless it is clear that the participant feels the change is needed but that the program cannot be adapted. However, it may be possible to infer that a large number of suggestions for improvement demonstrates lack of compatibility, see exclusion criteria below. Exclusion Criteria: Exclude or double code statements that the innovation did or did not need to be adapted to Compatibility.
E. Trialability	Definition: The ability to test the innovation on a small scale in the organization, and to be able to reverse course (undo implementation) if warranted. Inclusion Criteria: Include statements related to whether the site piloted the innovation in the past or has plans to in the future, and comments about whether they believe it is (im)possible to conduct a pilot. Exclusion Criteria: Exclude or double code descriptions of use of results from local or regional pilots to Evidence Strength & Quality.
F. Complexity	Definition: Perceived difficulty of the innovation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement. Inclusion Criteria: Code statements regarding the complexity of the innovation itself. Exclusion Criteria: Exclude statements regarding the complexity of implementation and code to the appropriate CFIR code, e.g., difficulties related to space are coded to Available Resources and difficulties related to engaging participants in a new program are coded to Engaging: Innovation Participants.
G. Design Quality & Packaging	Definition: Perceived excellence in how the innovation is bundled, presented, and assembled.

	Inclusion Criteria: Include statements regarding the quality of the materials and packaging. Exclusion Criteria: Exclude statements regarding the presence or absence of materials and code to Available Resources. Exclude statements regarding the receipt of materials as an engagement strategy and code to Engaging.
H. Cost	Definition: Costs of the innovation and costs associated with implementing the innovation including investment, supply, and opportunity costs. Inclusion Criteria: Include statements related to the cost of the innovation and its implementation. Exclusion Criteria: Exclude statements related to physical space and time, and code to Available Resources. In a research study, exclude statements related to costs of conducting the research components (e.g., funding for research staff, participant incentives).
II. Outer Setting	
A. Needs & Resources of Those Served by the Organization	Definition: The extent to which the needs of those served by the organization (e.g., patients), as well as barriers and facilitators to meet those needs, are accurately known and prioritized by the organization. Inclusion Criteria: Include statements demonstrating (lack of) awareness of the needs and resources of those served by the organization. Analysts may be able to infer the level of awareness based on statements about: 1. Perceived need for the innovation based on the needs of those served by the organization and if the innovation will meet those needs; 2. Barriers and facilitators of those served by the organization to participating in the innovation; 3. Participant feedback on the innovation, i.e., satisfaction and success in a program. In addition, include statements that capture whether or not awareness of the needs and resources of those served by the organization influenced the implementation or adaptation of the innovation. Exclusion Criteria: Exclude statements that demonstrate a strong need for the innovation and/or that the current situation is untenable and code to Tension for Change. Exclude statements related to engagement strategies and outcomes, e.g., how innovation participants became engaged with the innovation, and code to Engaging: Innovation Participants.
B. Cosmopolitanism	Definition: The degree to which an organization is networked with other external organizations.

	Inclusion Criteria: Include descriptions of outside group memberships and networking done outside the organization. Exclusion Criteria: Exclude statements about general networking, communication, and relationships in the organization, such as descriptions of meetings, email groups, or other methods of keeping people connected and informed, and statements related to team formation, quality, and functioning, and code to Networks & Communications.
C. Peer Pressure	Definition: Mimetic or competitive pressure to implement an innovation, typically because most or other key peer or competing organizations have already implemented or are in a bid for a competitive edge. Inclusion Criteria: Include statements about perceived pressure or motivation from other entities or organizations in the local geographic area or system to implement the innovation. Exclusion Criteria:
D. External Policy & Incentives	Definition: A broad construct that includes external strategies to spread innovations including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting. Inclusion Criteria: Include descriptions of external performance measures from the system. Exclusion Criteria:
III. Inner Setting	
A. Structural Characteristics	Definition: The social architecture, age, maturity, and size of an organization. Inclusion Criteria: Exclusion Criteria:
B. Networks & Communications	Definition: The nature and quality of webs of social networks, and the nature and quality of formal and informal communications within an organization. Inclusion Criteria: Include statements about general networking, communication, and relationships in the organization, such as descriptions of meetings, email groups, or other methods of keeping people connected and informed, and statements related to team formation, quality, and functioning. Exclusion Criteria: Exclude statements related to implementation

	leaders' and users' access to knowledge and information regarding using the program, i.e., training on the mechanics of the program and code to Access to Knowledge & Information. Exclude statements related to engagement strategies and outcomes, e.g., how key stakeholders became engaged with the innovation and what their role is in implementation, and code to Engaging: Key Stakeholders. Exclude descriptions of outside group memberships and networking done outside the organization and code to Cosmopolitanism.
C. Culture	Definition: Norms, values, and basic assumptions of a given organization. Inclusion Criteria: Inclusion criteria, and potential sub-codes, will depend on the framework or definition used for "culture." For example, if using the Competing Values Framework (CVF), you may include four sub-codes related to the four dimensions of the CVF and code statements regarding one or more of the four dimension in an organization. Exclusion Criteria:
D. Implementation Climate	Definition: The absorptive capacity for change, shared receptivity of involved individuals to an innovation, and the extent to which use of that innovation will be rewarded, supported, and expected within their organization. Inclusion Criteria: Include statements regarding the general level of receptivity to implementing the innovation. Exclusion Criteria: Exclude statements regarding the general level of receptivity that are captured in the sub-codes.
1. Tension for Change	Definition: The degree to which stakeholders perceive the current situation as intolerable or needing change. Inclusion Criteria: Include statements that (do not) demonstrate a strong need for the innovation and/or that the current situation is untenable, e.g., statements that the innovation is absolutely necessary or that the innovation is redundant with other programs. Note: If a participant states that the innovation is redundant with a preferred existing program, (double) code lack of Relative Advantage, see exclusion criteria below. Exclusion Criteria: Exclude statements regarding specific needs of individuals that demonstrate a need for the innovation, but do not necessarily represent a strong need or an untenable status quo, and code to Needs and Resources of Those Served by the Organization.

		Exclude statements that demonstrate the innovation is better (or worse) than existing programs and code to Relative Advantage.
2.	Compatibility	Definition: The degree of tangible fit between meaning and values attached to the innovation by involved individuals, how those align with individuals' own norms, values, and perceived risks and needs, and how the innovation fits with existing workflows and systems. Inclusion Criteria: Include statements that demonstrate the level of compatibility the innovation has with organizational values and work processes. Include statements that the innovation did or did not need to be adapted as evidence of compatibility or lack of compatibility. Exclusion Criteria: Exclude or double code statements regarding the priority of the innovation based on compatibility with organizational values to Relative Priority, e.g., if an innovation is not prioritized because it is not compatible with organizational values.
3.	Relative Priority	Definition: Individuals' shared perception of the importance of the implementation within the organization. Inclusion Criteria: Include statements that reflect the relative priority of the innovation, e.g., statements related to change fatigue in the organization due to implementation of many other programs. Exclusion Criteria: Exclude or double code statements regarding the priority of the innovation based on compatibility with organizational values to Compatibility, e.g., if an innovation is not prioritized because it is not compatible with organizational values.
4.	Organizational Incentives & Rewards	Definition: Extrinsic incentives such as goal-sharing, awards, performance reviews, promotions, and raises in salary, and less tangible incentives such as increased stature or respect. Inclusion Criteria: Include statements related to whether organizational incentive systems are in place to foster (or hinder) implementation, e.g., rewards or disincentives for staff engaging in the innovation. Exclusion Criteria:
5.	Goals & Feedback	Definition: The degree to which goals are clearly communicated, acted upon, and fed back to staff, and alignment of that feedback with goals. Inclusion Criteria: Include statements related to the (lack of) alignment of implementation and innovation goals with larger organizational goals, as well as feedback to staff regarding those goals, e.g., regular audit and feedback showing any gaps between the current organizational status and the goal. Goals and Feedback include organizational processes and supporting structures

	independent of the implementation process. Evidence of the integration of evaluation components used as part of "Reflecting and Evaluating" into **on-going or sustained** organizational structures and processes may be (double) coded to Goals and Feedback. Exclusion Criteria: Exclude statements that refer to the implementation team's (lack of) assessment of the progress toward and impact of implementation, as well as the interpretation of outcomes related to implementation, and code to Reflecting & Evaluating. Reflecting and Evaluating is part of the implementation process; it likely ends when implementation activities end. It does not require goals be explicitly articulated; it can focus on descriptions of the current state with real-time judgment, though there may be an implied goal (e.g., we need to implement the innovation) when the implementation team discusses feedback in terms of adjustments needed to complete implementation.
6. Learning Climate	Definition: A climate in which: 1. Leaders express their own fallibility and need for team members' assistance and input; 2. Team members feel that they are essential, valued, and knowledgeable partners in the change process; 3. Individuals feel psychologically safe to try new methods; and 4. There is sufficient time and space for reflective thinking and evaluation. Inclusion Criteria: Include statements that support (or refute) the degree to which key components of an organization exhibit a "learning climate." Exclusion Criteria:
E. Readiness for Implementation	Definition: Tangible and immediate indicators of organizational commitment to its decision to implement an innovation. Inclusion Criteria: Include statements regarding the general level of readiness for implementation. Exclusion Criteria: Exclude statements regarding the general level of readiness for implementation that are captured in the sub-codes.
1. Leadership Engagement	Definition: Commitment, involvement, and accountability of leaders and managers with the implementation of the innovation. Inclusion Criteria: Include statements regarding the level of engagement of organizational leadership. Exclusion Criteria: Exclude or double code statements regarding leadership engagement to Engaging: Formally Appointed Internal Implementation Leaders or Champions *if* an organizational leader is also an implementation leader, e.g., if a director of primary care takes the lead in implementing a new treatment guideline. Note that a key characteristic of this

	Implementation Leader/Champion is that s/he is also an Organizational Leader.
2. Available Resources	Definition: The level of resources organizational dedicated for implementation and on-going operations including physical space and time. Inclusion Criteria: Include statements related to the presence or absence of resources specific to the innovation that is being implemented. Exclusion Criteria: Exclude statements related to training and education and code to Access to Knowledge & Information. Exclude statements related to the quality of materials and code to Design Quality & Packaging. In a research study, exclude statements related to resources needed for conducting the research components (e.g., time to complete research tasks, such as IRB applications, consenting patients).
3. Access to Knowledge & Information	Definition: Ease of access to digestible information and knowledge about the innovation and how to incorporate it into work tasks. Inclusion Criteria: Include statements related to implementation leaders' and users' access to knowledge and information regarding use of the program, i.e., training on the mechanics of the program. Exclusion Criteria: Exclude statements related to engagement strategies and outcomes, e.g., how key stakeholders became engaged with the innovation and what their role is in implementation, and code to Engaging: Key Stakeholders. Exclude statements about general networking, communication, and relationships in the organization, such as descriptions of meetings, email groups, or other methods of keeping people connected and informed, and statements related to team formation, quality, and functioning, and code to Networks & Communications.
IV. Characteristics of Individuals	
1. Knowledge & Beliefs about the Innovation	Definition: Individuals' attitudes toward and value placed on the innovation, as well as familiarity with facts, truths, and principles related to the innovation. Inclusion Criteria: Exclusion Criteria: Exclude statements related to familiarity with evidence about the innovation and code to Evidence Strength & Quality.
2. Self-efficacy	Definition: Individual belief in their own capabilities to execute

	courses of action to achieve implementation goals. Inclusion Criteria: Exclusion Criteria:
3. Individual Stage of Change	Definition: Characterization of the phase an individual is in, as s/he progresses toward skilled, enthusiastic, and sustained use of the innovation. Inclusion Criteria: Exclusion Criteria:
4. Individual Identification with Organization	Definition: A broad construct related to how individuals perceive the organization, and their relationship and degree of commitment with that organization. Inclusion Criteria: Exclusion Criteria:
5. Other Personal Attributes	Definition: A broad construct to include other personal traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style. Inclusion Criteria: Exclusion Criteria:
V. Process	
A. Planning	Definition: The degree to which a scheme or method of behavior and tasks for implementing an innovation are developed in advance, and the quality of those schemes or methods. Inclusion Criteria: Include evidence of pre-implementation diagnostic assessments and planning, as well as refinements to the plan. Exclusion Criteria:
B. Engaging	Definition: Attracting and involving appropriate individuals in the implementation and use of the innovation through a combined strategy of social marketing, education, role modeling, training, and other similar activities. Inclusion Criteria: Include statements related to engagement strategies and outcomes, i.e., if and how staff and innovation participants became engaged with the innovation and what their role is in implementation. Note: Although both strategies and outcomes are coded here, the outcome of engagement efforts determines the rating, i.e., if there are repeated attempts to engage staff that are unsuccessful, or if a role is vacant, the construct receives a negative

	rating. In addition, you may also want to code the "quality" of staff - their capabilities, motivation, and skills, i.e., how good they are at their job, and this data affects the rating as well. Exclusion Criteria: Exclude statements related to specific sub constructs, e.g., Champions or Opinion Leaders. Exclude or double code statements related to who participated in the decision process to implement the innovation to Innovation Source, as an indicator of internal or external innovation source.
1. Opinion Leaders	Definition: Individuals in an organization that have formal or informal influence on the attitudes and beliefs of their colleagues with respect to implementing the innovation. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how the opinion leader became engaged with the innovation and what their role is in implementation. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage staff determines the rating, i.e., if there are repeated attempts to engage an opinion leader that are unsuccessful, or if the opinion leader leaves the organization and this role is vacant, the construct receives a negative rating. In addition, you may also want to code the "quality" of the opinion leader here - their capabilities, motivation, and skills, i.e., how good they are at their job, and this data affects the rating as well. Exclusion Criteria:
2. Formally Appointed Internal Implementation Leaders	Definition: Individuals from within the organization who have been formally appointed with responsibility for implementing an innovation as coordinator, project manager, team leader, or other similar role. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how the formally appointed internal implementation leader became engaged with the innovation and what their role is in implementation. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage staff determines the rating, i.e., if there are repeated attempts to engage an implementation leader that are unsuccessful, or if the implementation leader leaves the organization and this role is vacant, the construct receives a negative rating. In addition, you may also want to code the "quality" of the implementation leader here - their capabilities, motivation, and skills, i.e., how good they are at their job, and this data affects the rating as well. Exclusion Criteria: Exclude or double code statements regarding leadership engagement to Leadership Engagement *if* an implementation leader is also an organizational leader, e.g., if a

		director of primary care takes the lead in implementing a new treatment guideline.
3.	Champions	Definition: "Individuals who dedicate themselves to supporting, marketing, and 'driving through' an [implementation]", overcoming indifference or resistance that the innovation may provoke in an organization. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how the champion became engaged with the innovation and what their role is in implementation. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage staff determines the rating, i.e., if there are repeated attempts to engage a champion that are unsuccessful, or if the champion leaves the organization and this role is vacant, the construct receives a negative rating. In addition, you may also want to code the "quality" of the champion here - their capabilities, motivation, and skills, i.e., how good they are at their job, and this data affects the rating as well. Exclusion Criteria: Exclude or double code statements regarding leadership engagement to Leadership Engagement *if* a champion is also an organizational leader, e.g., if a director of primary care takes the lead in implementing a new treatment guideline.
4.	External Change Agents	Definition: Individuals who are affiliated with an outside entity who formally influence or facilitate innovation decisions in a desirable direction. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how the external change agent (entities outside the organization that facilitate change) became engaged with the innovation and what their role is in implementation, e.g., how they supported implementation efforts. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage staff determines the rating, i.e., if there are repeated attempts to engage an external change agent that are unsuccessful, or if the external change agent leaves their organization and this role is vacant, the construct receives a negative rating. In addition, you may also want to code the "quality" of the external change agent here - their capabilities, motivation, and skills, i.e., how good they are at their job, and this data affects the rating as well. Exclusion Criteria: Note: It is important to clearly define what roles are external and internal to the organization. Exclude statements regarding facilitating activities, such as training in the mechanics of the program, and code to Access to Knowledge & Information *if* the change agent is considered internal to the study, e.g., a staff member at the national office. If the study considers this staff member

	internal to the organization, it should be coded to Access to Knowledge & Information, even though their support may overlap with what would be expected from an External Change Agent.
5. Key Stakeholders	Definition: Individuals from within the organization that are directly impacted by the innovation, e.g., staff responsible for making referrals to a new program or using a new work process. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how key stakeholders became engaged with the innovation and what their role is in implementation. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage staff determines the rating, i.e., if there are repeated attempts to engage key stakeholders that are unsuccessful, the construct receives a negative rating. Exclusion Criteria: Exclude statements related to implementation leaders' and users' access to knowledge and information regarding using the program, i.e., training on the mechanics of the program, and code to Access to Knowledge & Information. Exclude statements about general networking, communication, and relationships in the organization, such as descriptions of meetings, email groups, or other methods of keeping people connected and informed, and statements related to team formation, quality, and functioning, and code to Networks & Communications.
6. Innovation Participants	Definition: Individuals served by the organization that participate in the innovation, e.g., patients in a prevention program in a hospital. Inclusion Criteria: Include statements related to engagement strategies and outcomes, e.g., how innovation participants became engaged with the innovation. Note: Although both strategies and outcomes are coded here, the outcome of efforts to engage participants determines the rating, i.e., if there are repeated attempts to engage participants that are unsuccessful, the construct receives a negative rating. Exclusion Criteria: Exclude statements demonstrating (lack of) awareness of the needs and resources of those served by the organization and whether or not that awareness influenced the implementation or adaptation of the innovation and code to Needs & Resources of Those Served by the Organization.
C. Executing	Definition: Carrying out or accomplishing the implementation according to plan. Inclusion Criteria: Include statements that demonstrate how implementation occurred with respect to the implementation plan. Note: Executing is coded very infrequently due to a lack of planning. However, some studies have used fidelity measures to

	assess executing, as an indication of the degree to which implementation was accomplished according to plan. Exclusion Criteria:
D. Reflecting & Evaluating	Definition: Quantitative and qualitative feedback about the progress and quality of implementation accompanied with regular personal and team debriefing about progress and experience. Inclusion Criteria: Include statements that refer to the implementation team's (lack of) assessment of the progress toward and impact of implementation, as well as the interpretation of outcomes related to implementation. Reflecting and Evaluating is part of the implementation process; it likely ends when implementation activities end. It does not require goals be explicitly articulated; it can focus on descriptions of the current state with real-time judgment, though there may be an implied goal (e.g., we need to implement the innovation) when the implementation team discusses feedback in terms of adjustments needed to complete implementation. Exclusion Criteria: Exclude statements related to the (lack of) alignment of implementation and innovation goals with larger organizational goals, as well as feedback to staff regarding those goals, e.g., regular audit and feedback showing any gaps between the current organizational status and the goal, and code to Goals & Feedback. Goals and Feedback include organizational processes and supporting structures independent of the implementation process. Evidence of the integration of evaluation components used as part of "Reflecting and Evaluating" into **on-going or sustained** organizational structures and processes may be (double) coded to Goals and Feedback. Exclude statements that capture reflecting and evaluating that participants may do during the interview, for example, related to the success of the implementation, and code to Knowledge & Beliefs about the Innovation.
VI. Additional Codes	
A. Code Name	Definition: Inclusion Criteria: Exclusion Criteria:
B. Code Name	Definition: Inclusion Criteria: Exclusion Criteria:

General Coding Rules:
When two codes are in question for a passage, consider the primary meaning of the passage to assign code; consider what the participant is truly saying. Analysts may wish to err on the side of inclusion or double coding.

General Rating Rules:

Ratings						
M	-2	-1	0	X	+1	+2

In general, ratings are determined based on two factors: 1) valence and 2) strength.

Valence: positive or negative influence on implementation
Rating component: X, 0, +, -
The valence component of a rating is determined by the influence the coded data has on the implementation process, i.e., contextual factors that facilitate or hinder implementation. Due to limited data, analysts may have to infer the influence on implementation based on simple presence or absence of a construct. For example, if a participant states that the intervention has advantages over existing programs, but does not state how this has influenced implementation, the analyst can infer that the presence of relative advantage facilitated implementation. However, whenever the data allows, the analysts should apply ratings based on the influence the construct has on implementation, not the presence or absence of a construct; presence or absence of a positive construct (e.g., relative advantage) does not always constitute a matching positive or negative influence on implementation.

In the event that comments are mixed, i.e., some comments are negative, and some comments are positive, try to tip the rating to a weak positive or weak negative, based on the aggregate of the comments. However, if you feel the comments are equally positive and negative, apply a mixed (X) rating. Some users of the CFIR have denoted level of agreement among participants in their rating by adding a * to the rating if comments were mixed. For example, if the aggregate of mixed comments was positive, the rating was +1*. Some users feel it's important to record discord among participants because it indicates a negative influence on implementation.

In the event that the comments are neutral, i.e., comments are related to a construct but have no bearing on the implementation, apply the neutral (0) rating.

Strength: weak or strong influence on implementation
Rating component: 1, 2
The strength component of a rating is determined by a number of factors, including level of agreement among participants, strength of language, and use of concrete examples. However, sometimes analysts may choose to apply relative ratings, versus absolute ratings, in order to differentiate between organization in the study.

Appendix 3

Appendix 3.1: PROM-HD Participant Information Sheet – Patient

University Hospitals Birmingham NHS
NHS Foundation Trust

PROM-HD Study

Using Patient Reported Outcome measures (PROMs) to promote quality of care and safety in the management of patients with end stage renal disease requiring treatment with haemodialysis

Participant Information Sheet

Interviews

PART 1

We would like to invite you to take part in our research study. Joining the study is entirely up to you. To help you decide whether you take part we would like you to understand why the research is being done and what it would involve for you.

Therefore one of our team will go through this information sheet with you, to help you decide if you would like to take part and answer any questions you may have. Please feel free to talk to others about the study if you wish.

The first part of this Participant Information Sheet tells you the purpose of the study and what will happen to you if you take part. Then we give you more detailed information about the conduct of the study. Do ask if anything is unclear.

- Traditionally we have measured the success of a patient's treatment on dialysis by looking at those things we can measure, for example how well the blood is cleaned, how well the blood pressure is controlled. Although the nurses and doctors often ask about how you are feeling, we don't have very good ways of measuring those other important aspects of your health. We also don't always know what is important to you in your life as these can vary from person to person.
- This information on health and wellbeing can be collected by using questionnaires known as 'Patient-Reported Outcome Measures' or PROMs.

- In other health care settings, these PROMS have been used by patients to guide doctors in knowing what is important to them and also to indicate and highlight changes in their health that might need attention before they are next due to be seen in a clinic.
- The purpose of our study is to find out the opinions and perspectives of patients receiving haemodialysis on the use and collection of this quality of life and symptom information using the PROM questionnaires. During a one to one interview with a researcher, you will be asked to talk about a range of issues, including who, why, when and how we collect PROMs with patients receiving haemodialysis.

Why have I been invited?

You have been invited because as a patient receiving haemodialysis, you are in the best position to provide the information we are seeking. We would like to know your thoughts on the collection and use of patient reported outcome measures (PROMs)

What is the purpose of the study?

The purpose of this study is to find out the opinions and perspectives of patients undergoing haemodialysis on the use of PROMs. PROMs are an important way to promote patient and doctor communication. These questionnaires can be used to self-report symptoms and quality of life. It is hoped that the routine collection and use of PROMs will assist doctors managing the care of patients receiving haemodialysis.

What are the possible benefits of taking part?

Although there will be no direct benefit to you for in this study, your input will help the development and use of an effective PROM system which may enhance the care you and other patients receive in the future. In addition, by taking part you will get the chance to provide your opinions/experiences which you may find rewarding and worthwhile.

Do I have to take part?

No, you do not have to take part. It is up to you to decide. Taking part in this research will be based around your commitments. The time and place for the interview will be arranged at your convenience.

If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw within 5 working days following your interview, without giving a reason. A decision not to take part or to withdraw at any time, will not affect the standard of care you receive from the NHS.

What will happen to me if I decide to take part?

You will be asked to take part in one face-to-face interview. You will be given three sample questionnaires to look at before the interview but not to fill in. The interview will take place at either your dialysis unit, the Queen Elizabeth Hospital or at another location convenient for you. We will ensure that your routine dialysis session will not be delayed. The interview will be tape recorded and will last for about one hour. Your views and perspectives on a range of issues, including comments on the content of the sample questionnaires and the practicalities of collecting this information, will be asked for. We will also collect some information on your age, gender, how long you have been on dialysis, your dialysis access and any other relevant medical conditions you may have, from your medical records.

In some cases, following a review of the first interview, you will be invited to return for a second, shorter follow up interview, to explore your views and perspectives further. This may take place by telephone.

In the unlikely event that you become distressed during your interview, you will be given the option to either delay or discontinue the interview. Contact details of the senior clinician (a consultant nephrologist) on the research team will be given to you if you wish to seek support and a referral can be made to your usual clinical team. Whilst we do not anticipate these interviews will raise significant issues regarding your care, if you do have or bring up any concerns, you will be given the relevant contact details.

Expenses

If you decide to take part, we will reimburse you with up to £20 to cover any reasonable travel costs associated with taking part in the study.

What if there is a problem?

Any complaint about the way you have been dealt with during the study, or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision

Part 2

What if there is a problem?

If you have concerns about any aspect of this study, you should ask to speak to the researcher:

Nicola Anderson,
Renal Research Team, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham
Centre for Patient Reported Outcomes Research, University of Birmingham, Edgbaston, Birmingham B15 2TT
Tel: *0121 371 8777*
Email: nicola.anderson@uhb.nhs.uk
Or the supervisor, Professor Paul Cockwell, Department of Nephrology
Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Edgbaston Birmingham, B15 2GW
Tel: +44 (0) 121 371 5839

Email: Paul.Cockwell@uhb.nhs.uk

If you remain unhappy you are advised to contact the UHB Patient Advisory Liaison service (PALs) on 0121 371 3280.

Will my taking part in the study be kept confidential?

Yes, we will follow ethical procedures and all information about you will be handled in confidence. All information provided throughout this research is protected under the *UK Data Protection Act (1998)* and will only be used by those on the research team. The study team will do its utmost to preserve your anonymity and keep comments unidentifiable. Your name will not be mentioned in any report of this research.

What will happen to any data I give?

The audio-recording of the interview will be used to produce a typed record of the discussion, known as a transcript, which will be anonymised. A professional transcription company or a member of the renal admin team will carry out the transcription. Any external company will sign a confidentiality agreement before receiving such recordings, which will be anonymised before we send to the company. The transcript will be analysed as part of our research. The audio recording will be stored securely at the University Hospitals Birmingham NHS Foundation Trust (UHBFT) until the end of the study when it will be destroyed. The data you provide will only be accessed by the research team at the Hospital and the University of Birmingham, or by authorised people to check that the study is being carried out correctly.

All data will be saved and stored securely at UHBFT. Study data will be held in the UHBFT archive for 10 years before being destroyed.

What will happen to the results of the research study?

The results of the study will be used by the research team to inform further research on the introduction and use of PROMs into the routine care of patients receiving haemodialysis. We plan to publish the results in a scientific journal and present at conferences. You will not be identifiable in any published report or presentation. You will be sent a summary of the final results (unless you tell us that you do not want one).

Who is organising and funding this research?

This project is funded by the Queen Elizabeth Hospital Kidney Patients Association and UHBFT and is being undertaken as part of a postgraduate programme (MRes by Research) at the University of Birmingham. The project is sponsored by University Hospitals Birmingham NHS Foundation Trust.

This project is being undertaken as part of a PhD educational qualification.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has received approval from *Wales REC 7 Ref: 17/WA/0281*.

Contact details for further information

For further information please contact Nicola Anderson. Tel: *0121 371 8777*.

3.2 PROM-HD Participant Information Sheet – HCP

University Hospitals Birmingham NHS
NHS Foundation Trust

PROM-HD Study

Using Patient Reported Outcome measures (PROMs) to promote quality of care and safety in the management of patients with end stage renal disease requiring treatment with haemodialysis

Participant Information Sheet

MDT Focus Groups/interviews

PART 1

We would like to invite you to take part in our research study. Joining the study is entirely up to you. To help you decide whether you take part we would like you to understand why the research is being done and what it would involve for you.

Therefore, one of our team will go through this information sheet with you, to help you decide if you would like to take part and answer any questions you may have. Please feel free to talk to others about the study if you wish.

The first part of this Participant Information Sheet tells you the purpose of the study and what will happen to you if you take part.

Then we give you more detailed information about the conduct of the study.
Do ask if anything is unclear.

- Traditionally we have measured the success of a patient's treatment with dialysis by looking at biochemical outcomes, for example phosphate levels and blood pressure control. Although nurses, doctors and other clinicians often ask about how patients are feeling, we don't routinely collect and measure how patients feel and/or collect good information on quality of life.

- This information on health and wellbeing can be collected by using questionnaires known as 'Patient Reported Outcome Measures' or PROMs.
- In other health care settings, PROMS have been used by patients to guide clinicians in knowing what is important to them and to indicate and highlight changes in their health that might need attention before they are next due to be seen in a clinic.
- The purpose of our study is to find out the opinions and perspectives of members of the clinical multidisciplinary team (MDT) caring for patients receiving haemodialysis on the use and collection of this quality of life and symptom information using PROM questionnaires. During a focus group discussion with a moderator or an individual semi-structured interview, the participants will be asked to talk about a range of issues, including who, why, when and how we collect PROMs on patients receiving haemodialysis.

Why have I been invited?

You have been invited because as a clinician/member of the MDT caring for patients receiving haemodialysis, you are in the best position to provide the information we are seeking. We would like to know your thoughts on the collection, use and feedback of patient reported outcome measures (PROMs)

What is the purpose of the study?

The purpose of this study is to find out the opinions and perspectives of members of the MDT caring for patients undergoing haemodialysis on the use of PROMs. PROMs have the potential to promote clinician and doctor communication. These questionnaires can be used to self-report symptoms and quality of life. It is hoped that the routine collection and use of PROMs will assist clinicians managing the care of patients receiving haemodialysis.

What are the possible benefits of taking part?

Although there will be no direct benefit to you for participating in this study, your input will inform further study into the development and use of an effective PROM systems which may enhance the care delivered to patients in the future. In addition, by taking part you will get the chance to provide your opinions/experiences which you may find rewarding and worthwhile.

Do I have to take part?

No, you do not have to take part. It is up to you to decide. Taking part in this research will be based around your commitments. The time and place for the focus group session or individual interview will be arranged at a mutually convenient time and place for participants.

If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You are free to withdraw at any point before the focus group meeting, without giving a reason. However, it will not be possible to remove your data once the session has commenced due to nature of evolving group discussion.

Study participants who are participate in an individual semi-structured interview will have the right to freely withdraw from the study, for any reason, at any time prior to their data being integrated into the data set (i.e. within 5 working days following their interview).

What will happen to me if I decide to take part?

You will be asked to take part in a focus group meeting with up to 6 other members of the MDT caring for patients who receive haemodialysis. The focus group will take place at either your dialysis unit or the Queen Elizabeth Hospital. Whilst every effort will be made to arrange a focus group time that is convenient, focus groups meetings may take place both within and without work hours. The focus group will be led by a suitable moderator who will ensure ground rules agreed by all participants are followed. The focus group will be tape recorded. We expect each focus group to last for approximately 1-1.5 hours. In some cases, following a review of the focus group transcript, you will be invited to participate in a short follow up interview, to explore your views and perspectives further. This interview may take place face to face or by telephone. We will send you a selection of PROM questionnaires to look at before the focus group session.

If you are unable to attend a focus group, you will be offered the opportunity to participate in a one-to-one semi-structured interview. The interview will be arranged

at a time and place which is convenient for you. With you permission, the interview will be tape recorded and may last up to an hour. This interview may take place face to face or by telephone. We will send you a selection of PROM questionnaires to look at before the interview.

In the unlikely event that you become distressed during the focus group meeting, you will be able to leave the group, if you wish. In the event that you become distressed during an interview, the interview will be stopped.

Expenses

Whilst every effort will be made to schedule focus groups in existing time set aside for renal department meetings, where this is not possible and focus group or interview attendance is being made in someone's own time, we will reimburse you with up to £20 to cover any reasonable travel costs associated with taking part in the study.

What if there is a problem?

Any complaint about the way you have been dealt with during the study, or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision

Part 2

What if there is a problem?

If you have concerns about any aspect of this study, you should ask to speak to the researcher:

Nicola Anderson,
Renal Research Team, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham
Centre for Patient Reported Outcomes Research, University of Birmingham, Edgbaston, Birmingham B15 2TT
Tel: *0121 371 8779*
Email: nicola.anderson@uhb.nhs.uk
Or the supervisor, Professor Paul Cockwell, Department of Nephrology
Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Edgbaston Birmingham, B15 2GW
Tel: +44 (0) 121 371 5839
Email: Paul.Cockwell@uhb.nhs.uk

If you remain unhappy you are advised to contact the UHB Patient Advisory Liaison service (PALs) on 0121 371 3280.

Will my taking part in the study be kept confidential?

Yes.

We will follow ethical procedures and all information will be handled in confidence. All information provided throughout this research is protected under the *UK Data Protection Act (1998)* and will only be used by those on the research team. The study team will do its utmost to preserve your anonymity and keep comments unidentifiable. Your name will not be mentioned in any report of this research.

What will happen to any data I give?

The audio-recording of the interview will be used to produce a typed record of the discussion, known as a transcript, which will be anonymised. A professional

transcription company or a member of the renal admin team will carry out the transcription. Any external company will sign a confidentiality agreement before receiving such recordings, which will be anonymised before we send to the company. The transcript will be analysed as part of our research. The audio recording will be stored securely at the University Hospitals Birmingham NHS Foundation Trust (UHBFT) until the end of the study when it will be destroyed.
The data you provide will only be accessed by the research team at the Hospital and the University of Birmingham, or by authorised people to check that the study is being carried out correctly.
All data will be saved and stored securely at UHBFT. Study data will be held in the UHBFT archive for 10 years before being destroyed.

What will happen to the results of the research study?

The results of the study will be used by the research team to inform further research on the introduction and use of PROMs into the routine care of patients receiving haemodialysis. We plan to publish the results in a scientific journal and present at conferences. You will not be identifiable in any published report or presentation. You will be sent a summary of the final results (unless you tell us that you do not want one).

Who is organising and funding this research?

This project is funded by the Queen Elizabeth Hospital Kidney Patients Association and UHBFT and is being undertaken as part of a postgraduate programme (MRes by Research) at the University of Birmingham. The project is being sponsored by University Hospitals Birmingham NHS Foundation Trust.
This project is being undertaken as part of a PhD educational qualification.

.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has received approval from *Wales REC 7 Ref: 17/WA/0281*.

Contact details for further information

For further information please contact Nicola Anderson. Tel: *0121 371 8779*

3.3 PROM-HD Exemplar PROMs – KDQOL-SF, KDQOL-36, IPOS-

Your Health

– and –

Well-Being

Kidney Disease and Quality of Life (KDQOL-SF™ 1.3)

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.



Thank you for completing these questions!

Kidney Disease and Quality of Life™ Short Form (KDQOL-SF™)
English Version 1.3
Copyright © 1993, 1994, 1995 by RAND and the University of Arizona

Study of Quality of Life For Patients on Dialysis

What is the purpose of the study?

This study is being carried out in cooperation with physicians and their patients. The purpose is to assess the quality of life of patients with kidney disease.

What will I be asked to do?

For this study, we want you to complete a survey today about your health, how you feel and your background.

Confidentiality of information?

We do not ask for your name. Your answers will be combined with those of other participants in reporting the findings of the study. Any information that would permit identification of you will be regarded as strictly confidential. In addition, all information collected will be used only for purposes of the study, and will not be disclosed or released for any other purpose without your prior consent.

How will participation benefit me?

The information you provide will tell us how you feel about your care and further understanding about the effects of medical care on the health of patients. This information will help to evaluate the care delivered.

Do I have to take part?

You do not have to fill out the survey and you can refuse to answer any question. Your decision to participate will not affect your opportunity to receive care.

Your Kidney Disease

12. How true or false is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My kidney disease interferes too much with my life	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Too much of my time is spent dealing with my kidney disease	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I feel frustrated dealing with my kidney disease	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. I feel like a burden on my family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

13. These questions are about how you feel and how things have been going during the <u>past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the <u>past 4 weeks</u>…

	None of the time ▼	A little of the time ▼	Some of the time ▼	A good bit of the time ▼	Most of the time ▼	All of the time ▼
a. Did you isolate yourself from people around you?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
b. Did you react slowly to things that were said or done?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
c. Did you act irritable toward those around you?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
d. Did you have difficulty concentrating or thinking?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
e. Did you get along well with other people?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
f. Did you become confused?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

14. During the <u>past 4 weeks</u>, to what extent were you bothered by each of the following?

		Not at all bothered	Somewhat bothered	Moderately bothered	Very much bothered	Extremely bothered
		▼	▼	▼	▼	▼
a	Soreness in your muscles?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Chest pain?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Cramps?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Itchy skin?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	Dry skin?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f	Shortness of breath?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g	Faintness or dizziness?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h	Lack of appetite?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i	Washed out or drained?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
j	Numbness in hands or feet?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
k	Nausea or upset stomach?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
l	(Hemodialysis patient only) Problems with your access site?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
m	(Peritoneal dialysis patient only) Problems with your catheter site?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Effects of Kidney Disease on Your Daily Life

15. Some people are bothered by the effects of kidney disease on their daily life, while others are not. How much does kidney disease <u>bother</u> you in each of the following areas?

		Not at all bothered	Somewhat bothered	Moderately bothered	Very much bothered	Extremely bothered
a	Fluid restriction?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Dietary restriction?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Your ability to work around the house?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d	Your ability to travel?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e	Being dependent on doctors and other medical staff?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f	Stress or worries caused by kidney disease?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g	Your sex life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h	Your personal appearance?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

The next three questions are personal and relate to your sexual activity, but your answers are important in understanding how kidney disease impacts on people's lives.

16. Have you had any sexual activity in the <u>past 4 weeks</u>?

(Circle One Number)

No .....1 → If no, please skip to Question 17

Yes 2

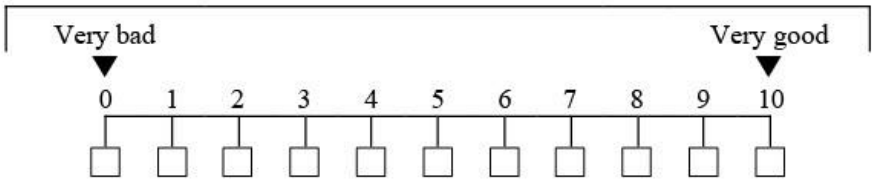
How much of a problem was each of the following in the <u>past 4 weeks</u>?

	Not a problem	A little problem	Somewhat of a problem	Very much a problem	Severe problem
a Enjoying sex?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Becoming sexually aroused?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

17. For the following question, please rate your sleep using a scale ranging from 0 representing "very bad" to 10 representing "very good."

If you think your sleep is half-way between "very bad" and "very good," please mark the box under the number 5. If you think you sleep is one level better than 5, mark the box under 6. If you think your sleep is one level worse than 5, mark the box under 4 (and so on).

On a scale from 0 to 10, how would you rate your sleep overall? [Mark an ☒ in one box.]



18. How often during the past 4 weeks did you...

	None of the time	A little of the time	Some of the time	A good bit of the time	Most of the time	All of the time
	▼	▼	▼	▼	▼	▼
a. Awaken during the night and have trouble falling asleep again?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
b. Get the amount of sleep you need?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
c. Have trouble staying awake during the day?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

19. Concerning your family and friends, how satisfied are you with...

	Very dissatisfied	Somewhat dissatisfied	Somewhat satisfied	Very satisfied
	▼	▼	▼	▼
a. The amount of time you are able to spend with your family and friends?	☐ 1	☐ 2	☐ 3	☐ 4
b. The support you receive from your family and friends?	☐ 1	☐ 2	☐ 3	☐ 4

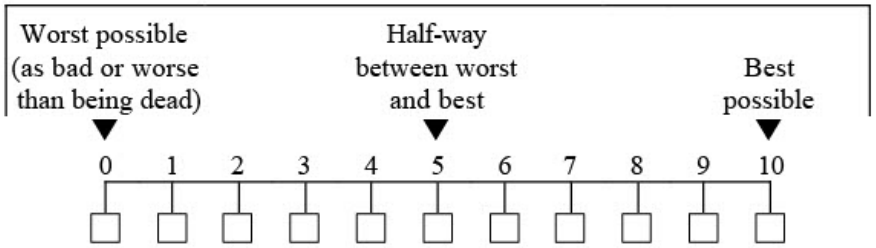
20. During the <u>past 4 weeks</u>, did you work at a paying job?

Yes ☐ 1 No ☐ 2

21. Does your health keep you from working at a paying job?

Yes ☐ 1 No ☐ 2

22. Overall, how would you rate your health?



Page 14

Satisfaction With Care

23. Think about the care you receive for kidney dialysis. In terms of your satisfaction, how would you rate the friendliness and interest shown in you as a person?

Very poor	Poor	Fair	Good	Very good	Excellent	The Best
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7

24. How <u>true</u> or <u>false</u> is each of the following statements?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. Dialysis staff encourage me to be as independent as possible	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Dialysis staff support me in coping with my kidney disease.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Your Health
– *and* –
Well-Being

Kidney Disease and Quality of Life (KDQOL™-36)

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.



Thank you for completing these questions!

Kidney Disease and Quality of Life™ (KDQOL™-36)
English Version 1.
Copyright © 2000 by RAND and the University of Arizona

Study of Quality of Life For Patients on Dialysis

What is the purpose of the study?

This study is being carried out in cooperation with physicians and their patients. The purpose is to assess the quality of life of patients with kidney disease.

What will I be asked to do?

For this study, we want you to complete a survey today about your health, how you feel and your background.

Confidentiality of information?

We do not ask for your name. Your answers will be combined with those of other participants in reporting the findings of the study. Any information that would permit identification of you will be regarded as strictly confidential. In addition, all information collected will be used only for purposes of the study, and will not be disclosed or released for any other purpose without your prior consent.

How will participation benefit me?

The information you provide will tell us how you feel about your care and further understanding about the effects of medical care on the health of patients. This information will help to evaluate the care delivered.

Do I have to take part?

You do not have to fill out the survey and you can refuse to answer any question. Your decision to participate will not affect your opportunity to receive care.

Your Health

This survey includes a wide variety of questions about your health and your life. We are interested in how you feel about each of these issues.

1. In general, would you say your health is: [Mark an ☒ in the one box that best describes your answer.]

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

The following items are about activities you might do during a typical day. <u>Does your health now limit</u> you in these activities? If so, how much? [Mark an ☒ in a box on each line.]

	Yes, limited a lot	Yes, limited a little	No, not limited at all
2. <u>Moderate activities</u>, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
3. Climbing <u>several</u> flights of stairs	☐ 1	☐ 2	☐ 3

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	Yes	No
4. Accomplished less than you would like.....	☐ 1	☐ 2
5. Were limited in the kind of work or other activities.....	☐ 1	☐ 2

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	Yes	No
6. Accomplished less than you would like.....	☐ 1	☐ 2
7. Didn't do work or other activities as carefully as usual.....	☐ 1	☐ 2

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
9. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
10. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
11. Have you felt downhearted and blue?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Your Kidney Disease

How true or false is each of the following statements for you?

		Definitely true	Mostly true	Don't know	Mostly false	Definitely false
		▼	▼	▼	▼	▼
13.	My kidney disease interferes too much with my life	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
14.	Too much of my time is spent dealing with my kidney disease.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
15.	I feel frustrated dealing with my kidney disease.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
16.	I feel like a burden on my family	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

During the <u>past 4 weeks</u>, to what extent were you bothered by each of the following?

		Not at all bothered	Somewhat bothered	Moderately bothered	Very much bothered	Extremely bothered
		▼	▼	▼	▼	▼
17.	Soreness in your muscles?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
18.	Chest pain?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
19.	Cramps?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
20.	Itchy skin?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
21.	Dry skin?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
22.	Shortness of breath?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
23.	Faintness or dizziness?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
24.	Lack of appetite?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
25.	Washed out or drained?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
26.	Numbness in hands or feet?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
27.	Nausea or upset stomach?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
28[a].	(Hemodialysis patient only) Problems with your access site?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
28[b].	(Peritoneal dialysis patient only) Problems with your catheter site?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Page 5

Effects of Kidney Disease on Your Daily Life

Some people are bothered by the effects of kidney disease on their daily life, while others are not. How much does kidney disease <u>bother</u> you in each of the following areas?

		Not at all bothered	Somewhat bothered	Moderately bothered	Very much bothered	Extremely bothered
		▼	▼	▼	▼	▼
29.	Fluid restriction?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
30.	Dietary restriction?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
31.	Your ability to work around the house?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
32.	Your ability to travel?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
33.	Being dependent on doctors and other medical staff?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
34.	Stress or worries caused by kidney disease?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
35.	Your sex life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
36.	Your personal appearance?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

Page 6

IPOS-Renal Patient Version



www.pos-pal.org

Patient name : .....

Date (dd/mm/yyyy) : .....

Patient number : ..... *(for staff use)*

Q1. What have been your main problems or concerns over the past week??

1. .....

2. .....

3. .....

Q2. Below is a list of symptoms, which you may or may not have experienced. For each symptom, please tick the box that best describes how it has affected you over the past week?

	Not at all	Slightly	Moderately	Severely	Overwhelmingly
Pain	0☐	1☐	2☐	3☐	4☐
Shortness of breath	0☐	1☐	2☐	3☐	4☐
Weakness or lack of energy	0☐	1☐	2☐	3☐	4☐
Nausea (feeling like you are going to be sick)	0☐	1☐	2☐	3☐	4☐
Vomiting (being sick)	0☐	1☐	2☐	3☐	4☐
Poor appetite	0☐	1☐	2☐	3☐	4☐
Constipation	0☐	1☐	2☐	3☐	4☐
Sore or dry mouth	0☐	1☐	2☐	3☐	4☐
Drowsiness	0☐	1☐	2☐	3☐	4☐
Poor mobility	0☐	1☐	2☐	3☐	4☐
Itching	0☐	1☐	2☐	3☐	4☐
Difficulty Sleeping	0☐	1☐	2☐	3☐	4☐
Restless legs or difficulty keeping legs still	0☐	1☐	2☐	3☐	4☐
Changes in skin	0☐	1☐	2☐	3☐	4☐
Diarrhoea	0☐	1☐	2☐	3☐	4☐

Please list any other symptoms not mentioned above, and tick the box to show how they have affected you over the past week?

1._____	0☐	1☐	2☐	3☐	4☐
2._____	0☐	1☐	2☐	3☐	4☐
3._____	0☐	1☐	2☐	3☐	4☐

Over the past week:

	Not at all	Occasionally	Sometimes	Most of the time	Always
Q3. Have you been feeling anxious or worried about your illness or treatment?	0☐	1☐	2☐	3☐	4☐
Q4. Have any of your family or friends been anxious or worried about you?	0☐	1☐	2☐	3☐	4☐
Q5. Have you been feeling depressed?	0☐	1☐	2☐	3☐	4☐

	Always	Most of the time	Sometimes	Occasionally	Not at all
Q6. Have you felt at peace?	0☐	1☐	2☐	3☐	4☐
Q7. Have you been able to share how you are feeling with your family or friends as much as you wanted?	0☐	1☐	2☐	3☐	4☐
Q8. Have you had as much information as you wanted?	0☐	1☐	2☐	3☐	4☐

	Problems addressed/ No problems	Problems mostly addressed	Problems partly addressed	Problems hardly addressed	Problems not addressed
Q9. Have any practical problems resulting from your illness been addressed? (such as financial or personal)	0☐	1☐	2☐	3☐	4☐

	None at all	Up to half a day wasted	More than half a day wasted
Q10. How much time do you feel has been wasted on appointments relating to your healthcare, e.g. waiting around for transport or repeating tests	0☐	1☐	2☐

	On my own	With help from a friend or relative	With help from a member of staff
Q11. How did you complete this questionnaire?	☐	☐	☐

If you are worried about any of the issues raised on this questionnaire then please speak to your doctor or nurse

3.4 PROM-HD Topic Guide for use with patient participants

RRK6261 IRAS ID: 224576

PROM-HD Study

Using patient reported outcome measures (PROMs) to promote quality of care and safety in the management of patients with established kidney disease requiring treatment with haemodialysis

Topic Guide – Patient Participant Interviews

Research Objectives

To explore the feasibility of using routine PROM assessment to aid the management of patients with established renal failure undergoing HD

Respondent Profile

18 years or over, patients who are receiving renal replacement therapy in the form of HD, who meet the study inclusion/exclusion criteria

Logistics

Face-to face interviews: place, date, and time (start and end) of the interviews to be recorded.

Telephone interviews: write the name, title, telephone number of the respondent and record data and time (start and end time) of interview.

Introduction

Introduce self as a Nurse Researcher but explain that whilst I have a nursing background I am not part of their direct healthcare team, so please feel to talk openly and honestly. Participants should be reassured about the confidential nature of the interview and that all comments will be anonymised before use.

Topics and areas of questioning

A: Awareness of PROMs

1. Have you ever completed questionnaires about your QoL or experiences of receiving dialysis before?
2. Having looked at the sample questionnaires – do they capture the things you think are most important about living with kidney disease and being on dialysis
3. Do you think the collection of PROM questionnaires would be beneficial? Do you think the capture of these outcomes is important?

B. Practical Aspects around PROM collection

1. Would you be able to complete a PROM questionnaire successfully on your own, and if not, how much assistance do you think you would require?
2. How often should they be completed and how long should completion take?

Version 2.0 31.10.17

3. Where and when would you want to complete the PROMs i.e. at home? At the Unit? Before or during dialysis?

4. How should PROM data be collected i.e. in paper or electronic formats such as mobile app or telephone recognition systems?

C. Feedback of PROM data

1. How would you like to receive feedback from the clinical team on your PROM data? i.e. email, letter, graphs in person etc.

D. Barriers or facilitators

1. What do you think are the likely factors (barriers and facilitators) that may improve or discourage the completion of PROMs?

2. What do you think are the issues about PROM collection in different patient groups (e.g. older patients, patients of non-white ethnicity)?

E. Use of PROMs in Research

1. Have you have been involved in PROM collection for research purposes?

2. Should PROMs that collect data for routine clinical and research purposes be different?

3. Do you think any of the practical considerations change when you are collecting PROMs for research rather than as part of routine practice? i.e. would you be prepared to complete them more often for research

4. Are there any special considerations to be given to feedback when using PROMs in a research setting?

3.5 PROM-HD Topic guide for use with HCP's

RRK6261 IRAS ID: 224576

PROM-HD Study

Using patient reported outcome measures (PROMs) to promote quality of care and safety in the management of patients with established kidney disease requiring treatment with haemodialysis

Topic Guide – HCP Interviews

Research Objectives

To explore the feasibility of using routine PROM assessment to aid the management of patients with established renal failure undergoing HD

Respondent Profile

Healthcare Professionals (HCPs) who meet the study inclusion/exclusion criteria.

Logistics

Interview: place, date, and time (start and end) of the interviews to be recorded.

Introduction

Introduce self as a Nurse Researcher but explain that whilst I have a nursing background I am not part of the direct healthcare team, so please feel to talk openly and honestly. Participants should be reassured about the confidential nature of the interview and that all comments will be anonymised before use.

Topics and areas of questioning

A: Awareness of PROMs

1. Have you ever been involved in the collection of PROMs or data regarding QoL and patient experience before?

   Do you think the collection of PROM questionnaires would be beneficial?

   Do you think the capture of these outcomes is important? What do you think about the current measures available and the use of core outcome sets.

   Do you think they could help focus a consultation? Should a 'good' clinician already be able to elicit those outcomes that are important to a patient? Would PROMs alter the way a clinician talks or engages with a patient?

   If yes, how, do you think they could help improve care for a group of patients?

   Do you think they could assist in the multidisciplinary team (MDT) care/follow up of the patient?

   How much time do you spend talking to patients in a typical consultation? Would you like to spend more/less?

2. Having looked at the sample questionnaires – do they capture the things you think are most important about living with kidney disease and being on dialysis from your

Version 5.0 10.10.2019

perspective as a MDT member?

a. Are there specific aspects of dialysis care that you think would be effected by the use of PROMs

b. How do you think PROMs differ from PREMs? Do you think collection of one is more important than the other?

B. Practical Aspects around PROM collection

1. Do you think most patients would be able to complete a PROM questionnaire successfully on their own, and if not, how much assistance do you think they would require and from whom? Could assistance affect the responses?
2. How often should they be completed and how long should review of the results take?
3. Where and when would you want the PROMs completed i.e. at home? Before or during dialysis?
4. How should PROM data be collected i.e. in paper or electronic formats such as mobile app or telephone recognition systems?

C. Feedback of PROM data

1. Who would be the best member of the MDT to review the data initially? What about alerts? How should they be managed? Some staff said they don't have time, is that true?
2. What might be the best way the feedback the PROM data to the (a) clinical team, (b) patient? i.e. email, letter, graphs in person etc.
3. How to do you deliver your QA results?
4. How do you feel dealing with problems that you can't solve – do you feel there are areas outside your area of expertise you would not want to discuss? Is listening enough?
5. Specifically, what PROM data do you think would be important within (a) a clinic environment, (b) an MDT meeting, and how might it be presented? E.g. line graphs, bar charts, raw tabulated data etc.
6. Could they be used to show longitudinal trends? Do you think they would be able to pick up ceiling effects or sensitive changes?

D. Barriers or facilitators

1. What do you think are the likely factors (barriers and facilitators) that may improve or discourage the completion of PROMs? IT issues/time? Importance of leadership during any implementation phase
2. Is there a risk we are going to overburden patients with multiple questionnaires? Have you heard of CAT/item banking?

Version 5.0 10.10.2019

3. What is the best way to implement into your workflow – could they affect your work flow patterns?

4. Would you want educating about PROMs – what form would that learning take? What specifically would you want more information on? Theory behind collection of PROS, Core outcome sets? Measures available, how they may be used in routine care?
   Are there opportunities to undertake advanced communications training?

5. What do you think about are the key issues about PROM collection in different patient groups (e.g. older patients, patients of non-white ethnicity)?

E. Use of PROMs with patients undergoing Home HD

1. In your opinion, how do patients dialysing at home differ from those dialysing in satellite units? Are they better at 'coping', dealing with change or is it their support structures? Do you think there is utility measuring PROs with this group of patients in particular? Role of carers in this group, how much should they be involved in the process?

2. Would any of your answers differ for patients undergoing Home HD in terms of when, where, how often, who should review and provide feedback?

3. Do you think Home HD patients are more likely to engage with digital technology?

F. Use of PROMs in Research

1. Have you have been involved in PROM use for research purposes? do you know how the measurement tool was chosen? Do you think it captured outcomes that were relevant for the research project?

2. Do you think it would be a good idea to use core outcome sets for renal trials? Should outcomes and the associated PROM that collects them differ between use for routine clinical and research purposes?

3. Do you think any of the practical considerations change when you are collecting PROMs for research rather than as part of routine practice? i.e. how often and where they are completed

4. Are there any special considerations to be given to feedback when using PROMs in a research setting?

3.6 Patient Data Saturation tables and interview characteristics

Supp Table 1 Patient saturation table and interview characteristics

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
	Setting	x		x	x	x		x	x		x	x	x	x		x	x	x		x	x	x	x
	Timing	x	x		x	x	x		x	x	x			x	x	x		x	x	x		x	x
	Outcomes that matter	x	x		x	x	x			x			x	x	x	x			x	x		x	
	Current Measures				x	x	x	x	x		x	x	x	x	x		x	x	x		x	x	x
	Safety Alerts	x																	x			x	
	Self-help information		x						x				x	x			x					x	
	ComputerAdaptiveTechnology										x	x		x		x	x		x	x			
	Review and Feedback	x	x		x		x	x	x	x	/	x	x	/	x	x	/	x	x	x		x	x
	Sensitivity to change	/	/	/	/	/	/	/	/	/		/	/		/	/		/	/	/	/	/	/
IH Cost																			x				
2 Outer Setting																							
2A Needs and resources	Identification		x	x	x		x	x	x			x	x	x	x			x	x	x	x	x	x
	Barriers	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Facilitators	x	x	x	x		x			x	x	x	x	x				x	x	x		x	
2B Cosmopolitanism				x				x			x				x					x			
2C Peer Pressure		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
2D External policies and incentives		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
3 Inner Setting																							
3A Structural Characteristics																x							
3B Networks and Communications	Nature and Quality		x	x	x	x	x	x	x	x	x	x	x		x	x		x	x	x	x	x	x
	Shared Decision Making	x	x	x							x	x	x	x	x	x		x		x	x		x
3C Culture											x			x	x	x					x		
3D Implementation Climate	Tension for change		x	x					x			x	x	x	x			x	x	x	x		x
	Compatibility							x				x	x									x	x
	Relative Priority	x			x						x										x	x	
	Organisational Incentives	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Anderson NE, *et al. BMJ Open* 2021; 11:e052629. doi: 10.1136/bmjopen-2021-052629

Supp Table 1 Patient saturation table and interview characteristics

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
	Goals and Feedback	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
	Learning Climate												x										
3E Readiness	Leadership Engagement	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
for	Available Resources		x		x											x		x				x	
Implementation	Access to knowledge and info		x			x	x						x		x	x	x				x	x	x
4 Characteristics of Individuals																							
Knowledge and beliefs		x	x	x	x			x	x	x		x		x	x	x	x	x	x	x	x	x	
Self-efficacy	Ability to self-complete	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x		x		x	
	Patient as an Expert			x				x				x	x	x	x					x			
	PROMs v PREMs		x		x	x		x											x		x		
Individual	Previous experience of PROMs	x			x	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
stage of change	usage																						
Individual identification with organisation		x	x		x	x	x	x	x	x	x	x	x	x	x		x			x	x	x	x
Other personal	Multidimensionality of ESKD:																						
attributes	Symptomology	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Life on Dialysis	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
5 Process																							
5A Planning		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
5B Engaging																							
	Opinion Leaders	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
	Formally appointed leaders					x		x															
	Champions					x							x	x									
	External Change Agents	/	/	/	/	/		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
	Key Stakeholders	/	/	/	/	/		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
	Innovation Participants				x								x										
	Role of Carers	x		x	x		x	x		x			x				x						
5C Executing		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
5D Reflecting and Evaluating		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Supp Table 1 Patient saturation table and interview characteristics

First time data coded to node in NVIVO	x
Nothing coded to node in NVIVO	/
Nothing coded to node in NVIVO	/

3.7 HCP Data Saturation tables and interview characteristics

Suppl Table 2 Healthcare Professional Participants: Saturation table and interview characteristics

	Value
HCP Interviews	
Number invited/Number participating	19/17
Reasons for non-participation	Competing clinical commitments
Duration of patient interviews (min)	Range 29-63 Mean 48 mins
Patient Saturation Data	
No of codes generated	134
Point of data saturation	16th Interview
Note n=17	

Participants n=17		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1 Innovation Characteristics																		
1A Innovation Source						x										x		
1B Evidence strength and quality		x				x				x		x		x	x	x	x	x
1C Relative Advantage		x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	x
												x	x		x		x	x
	How PROMs might work to deliver advantage		x		x	x	x	x	x	x								
1D Adaptability		x				x												x
	Use within research				x	x							x		x	x	x	
1E Trialability																	x	
IF Complexity		x				x	x		x		x						x	
IG Design and Packaging		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Frequency	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x
	Length			x	x	x	x		x		x	x	x	x	x		x	
	Mode	x	x		x	x			x	x	x	x	x	x		x	x	

Suppl Table 2 Healthcare Professional Participants: Saturation table and interview characteristics

Participants n=17		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
	Setting		x	x	x	x		x	x	x	x			x			x	x
	Timing		x	x	x		x		x	x	x	x	x	x	x		x	
	Self-completion		x	x	x	x	x	x				x	x	x	x	x		x
	Outcomes that matter	x	x	x	x		x		x	x	x		x			x		x
	Safety Alerts			x			x				x			x	x	x	x	
	Sensitivity						x		x		x	x						
	Computer Adaptive Technology					x		x	x	x	x	x	x	x		x	x	
	Review and Feedback	x	x	x	x	x	x	x				x	x	x	x	x	x	x
IH Cost														x		x		
2 Outer Setting																		
2A Needs and resources						x	x	x		x	x	x	x	x		x		
	Barriers		x		x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Facilitators			x	x	x			x		x	x	x				x	
2B Cosmopolitanism				x	x		x	x					x					
2C Peer Pressure																		
2D External policies and incentives				x		x	x	x	x					x	x		x	x
3 Inner Setting																		
3A Structural Characteristics		x	x	x	x		x	x				x	x	x	x			
3B Networks and Communications		x		x	x	x		x	x	x	x	x	x		x	x		x
3C Culture		x	x	x		x	x	x			x	x	x			x	x	x
3D Implementation Climate																		
	Tension for change	x	x	x		x			x	x	x			x				
	Task focused approach to care							x	x			x	x		x	x	x	x
	Compatibility	x				x	x		x		x	x					x	
	Relative Priority	x					x								x			
	Organisational Incentives																	
	Goals and Feedback		x			x				x								
	Learning Climate		x	x								x						x
3E Readiness for Implementation	Leadership Engagement		x									x						

Suppl Table 2 Healthcare Professional Participants: Saturation table and interview characteristics

Participants n=17		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
	Available Resources	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Access to knowledge and info		x	x	x	x		x	x	x	x		x				x	x
4 Characteristics of Individuals																		
Knowledge and beliefs		x	x	x		x		x	x	x			x		x		x	x
Self-efficacy		x	x	x		x	x		x	x	x		x		x	x		
	Ability of patients to self-complete	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Individual stage of change	Previous experience of PROMs usage	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x	
Individual identification with organisation			x	x						x	x		x					
Other personal attributes		x	x	x	x		x	x				x	x	x	x	x	x	
5 Process																		
5A Planning						x		x										
5B Engaging						x	x		x									x
	Opinion Leaders	x				x	x				x							x
	Formally appointed leaders	x		x	x	x		x	x	x	x		x		x			x
	Champions		x	x				x			x		x					x
	External Change Agents												x			x		x
	Key Stakeholders					x												
	Innovation Participants					x												
5C Executing																		
5D Reflecting and Evaluating																x		

First time data coded to this node in NVIVO	x
Nothing coded to this node in NVIVO	

3.8 Pre-publication Consolidated Criteria for Reporting Qualitative Studies (COREQ) checklist

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	7
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	1
Occupation	3	What was their occupation at the time of the study?	8
Gender	4	Was the researcher male or female?	8
Experience and training	5	What experience or training did the researcher have?	8
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	8
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	8, PIS
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	8
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	6
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	7
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	7
Sample size	12	How many participants were in the study?	7
Non-participation	13	How many people refused to participate or dropped out? Reasons?	Suppl table 1&
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	7
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	7
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	In text table 1 &
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	7
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	7
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	7
Field notes	20	Were field notes made during and/or after the inter view or focus group?	8
Duration	21	What was the duration of the inter views or focus group?	Supp Table 1 &
Data saturation	22	Was data saturation discussed?	9 Suppl Table 1
Transcripts returned	23	Were transcripts returned to participants for comment and/or	8

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	8
Description of the coding tree	25	Did authors provide a description of the coding tree?	Figure 1, Supp
Derivation of themes	26	Were themes identified in advance or derived from the data?	8
Software	27	What software, if applicable, was used to manage the data?	8
Participant checking	28	Did participants provide feedback on the findings?	9
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	In text Box 1 &
Data and findings consistent	30	Was there consistency between the data presented and the findings?	Figure 1
Clarity of major themes	31	Were major themes clearly presented in the findings?	9-16
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	16-20

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

Appendix 4

Appendix 4.1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	90
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	91-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	93-5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	95
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web	95

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
		address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	97
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	96
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	See Appendix 4.2
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	97
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	99
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	See tables 1-4

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	99
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	See PRISMA-Scr figure 1 pg 138
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	See tables 1-3, refs page 136
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Tables 2-3 pages 101-131
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	Table 4 pages 132-135

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	139-144
Limitations	20	Discuss the limitations of the scoping review process.	149-150
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	150-151
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	90

Appendix 4.2: Scoping review sample search strategy

Scoping Review Search strategy:

Example Search Strategy (MEDLINE):

1. (HR-PRO or HRPRO or HRQL or HRQoL or QL or QoL).ti,ab.
2. quality of life.mp.
3. (health index* or health indices or health profile*).ti,ab.
4. health status.mp.
5. ((patient or self or child or parent or carer or proxy) adj (appraisal* or appraised or report or reported or reporting or rated or rating or based or assessed or assessment*)).ti,ab.
6. ((disability or function or functional or functions or subjective or utility or utilities or wellbeing or well being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire* or profile or profiles or scale or scales or score or scores or status or survey or surveys)).ti,ab.
7. ((((patient adj reported adj outcome adj measure*) or patient) adj reported adj outcome*) or capability or capabilities).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. (Renal replacement therapy or APD or Automated Peritoneal Dialysis or CAPD, Continuous Ambulatory Peritoneal Dialysis or CCPD or Continuous cyclic peritoneal dialysis or dialysis or h*emofiltration or h*emodiafiltration or h*emodialysis or kidney transplant* or predialysis or renal replacement or renal transplant*).mp.
10. (CRF or chronic renal failure or CKF or chronic kidney failure or kidney disease* or renal disease or kidney failure or renal failure or CKD or chronic kidney disease or ESKD or end stage kidney disease or ESKF or end stage kidney failure or ESRF or end stage renal failure or ESRD or end stage renal disease or kidney insufficiency).mp.
11. Renal Insufficiency, Chronic/
12. 9 or 10 or 11
13. ((((((((((((((((((((((((((((Instrumentation or method* or Validation Studies or Comparative Study).mp. or psychometrics/ or psychometr*.mp. or clinimetr*.mp. or clinometr*.mp. or outcome assessment health care/ or outcome assessment*.ti,ab. or outcome measure*.mp. or observer variation/ or observer variation*.ti,ab. or Health Status Indicators/ or reproducibility of results/ or reproducib*.ti,ab. or discriminant analysis/ or reliab*.ti,ab. or unreliab*.ti,ab. or valid*.ti,ab. or coefficient of variation.ti,ab. or coefficient*.ti,ab. or homogeneity.ti,ab. or homogeneous.ti,ab. or internal consistency.ti,ab. or cronbach*.ti,ab.) and alpha*.ti,ab.) or item*.ti,ab.) and correlation*.ti,ab.) or selection*.ti,ab. or reduction*.ti,ab. or agreement.mp. or precision.mp. or imprecision.mp. or precise value*.mp. or test-retest.ti,ab. or test.ti,ab.) and retest.ti,ab.) or reliab*.ti,ab.) and test.ti,ab.) or retest.ti,ab. or stability.ti,ab. or interrater.ti,ab. or inter-rater.ti,ab. or intrarater.ti,ab. or intra- rater.ti,ab. or intertester.ti,ab. or inter-tester.ti,ab. or intratester.ti,ab. or intra- tester.ti,ab. or interobserver.ti,ab. or inter-observer.ti,ab. or intraobserver.ti,ab. or intra-observer.ti,ab. or intertechnician.ti,ab. or inter-technician.ti,ab. or intratechnician.ti,ab. or intra-technician.ti,ab. or interexaminer.ti,ab. or inter-examiner.ti,ab. or intraexaminer.ti,ab. or intra-examiner.ti,ab. or interassay.ti,ab. or inter-assay.ti,ab. or intraassay.ti,ab. or intra-assay.ti,ab. or interindividual.ti,ab. or inter-individual.ti,ab. or intraindividual.ti,ab. or intra-individual.ti,ab. or interparticipant.ti,ab. or inter-participant.ti,ab. or intraparticipant.ti,ab. or intra- participant.ti,ab. or kappa*.ti,ab. or kappa's.ti,ab. or repeatab*.mp. or replicab*.mp. or repeated.mp.) and measure*.mp.) or finding*.mp. or result*.mp. or test*.mp. or generaliza*.ti,ab. or generalisa*.ti,ab. or concordance.ti,ab. or intraclass.ti,ab.) and correlation*.ti,ab.) or discriminative.ti,ab. or known group.ti,ab. or factor analysis.ti,ab. or factor analyses.ti,ab. or factor structure.ti,ab. or factor structure.ti,ab. or dimension*.ti,ab. or subscale*.ti,ab. or multitrait.ti,ab.) and scaling.ti,ab. and analysis.ti,ab.) or analyses.ti,ab. or item discriminant.ti,ab. or interscale

correlation*.ti,ab. or error.ti,ab. or errors.ti,ab. or individual variability.ti,ab. or interval variability.ti,ab. or rate variability.ti,ab. or variability.ti,ab.) and analysis.ti,ab.) or value*.ti,ab. or uncertainty.ti,ab.) and measurement.ti,ab.) or measuring.ti,ab. or standard error of measurement.ti,ab. or sensitiv*.ti,ab. or responsive*.ti,ab. or limit*.ti,ab.) and detection.ti,ab.) or minimal detectable concentration.ti,ab. or interpretab*.ti,ab. or minimal.ti,ab. or minimally.ti,ab. or clinical.ti,ab. or clinically.ti,ab.) and important.ti,ab.) or significant.ti,ab. or detectable.ti,ab.) and change.ti,ab.) or difference.ti,ab. or small*.ti,ab.) and real.ti,ab.) or detectable.ti,ab.) and change.ti,ab.) or difference.ti,ab. or meaningful change.ti,ab. or ceiling effect.ti,ab. or floor effect.ti,ab. or Item response model.ti,ab. or IRT.ti,ab. or Rasch.ti,ab. or Differential item functioning.ti,ab. or DIF.ti,ab. or computer adaptive testing.ti,ab. or item bank.ti,ab. or cross-cultural equivalence.ti,ab.

14. (PRO integration or Clinical PRO application* or telePRO or automated PRO algorithm* or screening purpose* or PRO questionnaire* or Patient-reported outcome questionnaire* or Patient-reported symptom* or Patient-centred care or Patient self- report* or Self-report health or Self-rated health or Self-reported measure* of health or Health outcome* or Health communication* or Hospital performance evaluation* or Automated telephone survey system* or paper-based survey* or web-based survey* or web-based PRO platform* or web-based system* or PRO collection* or PRO measure* or PRO intervention* or PRO assessment intervention* or PRO data or PRO assessment* or Routine PRO assessment* or Routine PRO collection or Symptom assessment* or Symptom monitoring or Symptom data or Functional status or Electronic PRO assessment* or Electronic PRO system* or ePRO or ePRO* or ePRO system* or PRO system* or Generic PRO system* or PRO-based clinical alert system* or PROM or ePROM or electronic PROM).mp.
15. 13 or 14
16. 8 and 12 and 15
17. limit 16 to dt=

Appendix 5

5.1 Publication: Kyte D, Anderson N et al. (2020) ***Development of an electronic patient reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease*** **Journal of Patient-Reported Outcomes https://doi.org/10.1186/s41687-020-00223-8**

Link to open access publication:

Development of an electronic patient-reported outcome measure (ePROM) system to aid the management of patients with advanced chronic kidney disease | Journal of Patient-Reported Outcomes | Full Text (springeropen.com)

(https://jpro.springeropen.com/articles/10.1186/s41687-020-00223-8)

5.2 Publication: Kyte D, Anderson N, Bishop J, Bissell A, Brettell E, Calvert M, Chadburn M, Cockwell P, Dutton M, Eddington H, Forster E, Hadley G, Ives NJ, Jackson LJ, O'Brien S, Price G, Sharpe K, Stringer S, Verdi R, Waters J, Wilcockson A. Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease**. BMJ Open. 2022 Mar 18;12(3):e050610. doi: 10.1136/bmjopen-2021-050610. PMID: 35304391; PMCID: PMC8935185.**

Link to open access publication:

Results of a pilot feasibility randomised controlled trial exploring the use of an electronic patient-reported outcome measure in the management of UK patients with advanced chronic kidney disease | BMJ Open

(https://bmjopen.bmj.com/content/12/3/e050610.long)

5.3. Structured Survey (www.smartsurvey.co.uk) includes combined consent sheet v10.06.2021

Electronic Patient-Reported Outcomes (ePRO) systems used in nephrology settings

1. Electronic Patient-Reported Outcomes (ePRO) Systems used in Nephrology settings

Consent Form.

Please note you may choose to save and continue your survey response at a later time. If you choose this option at the end of each page, you will be directed to enter your email address and we will email you a link for you to access the survey in the future.

1. I confirm that I have read and understood the information in the Participant information sheet version 3.0 dated 06.06.2021 and understand what is expected of me. *

2. I confirm that I have been given the opportunity to ask questions regarding the study, and if asked, the questions were answered to my full satisfaction. *

3. I understand that my participation is voluntary and that I am free to withdraw at any time, but within 5 working days following survey completion (before my data is integrated into the dataset), without giving any reason. *

4. I understand that any personal information will be anonymized but institutional or system identifiers will be used in research outputs i.e. publications/presentations. *

5. I understand that the information collected may be used to support other research in the future and may be shared anonymously with other researchers. *

6. I understand that my personal data will be processed for the purposes detailed above, in accordance with the General Data Protection Regulation and Data Protection Act 2018 *

7. I agree to take part in the survey (please note, if you answer no to this question you will be taken to the end of this survey) *

8. OPTIONAL I am willing to take part in a follow up interview following survey completion, where required.
I understand:

The interview will be audio-recorded and that the transcript of the recording will be shared with researchers working on the above study at the University of Birmingham.

My participation in this interview is voluntary and that I am free to withdraw at any time, up to 10 working days following interview (before my data is integrated into the dataset), without giving any reason.

I will have the opportunity to review any interview transcript and redact any proprietary information before analysis.

I must return reviewed transcripts within 10 working days, otherwise it will be assumed I am happy with the contents.

*

9. Thank you very much for offering to take part in the the optional interview. Please enter your preferred contact details below and a member of the team will be in contact to arrange a convenient date and time. *

First name *

Last name *

Email *

3. ePRO System Characteristics

Survey

10. Please enter your name (this information is for administrative purposes only and your data will be pseudonymised) *

11. What was your job title during system development?

12. What is your system called?

Name

Version number

13. Please describe your key responsibilities in the ePRO system development/implementation, please include clinical and non-clinical responsibilities as appropriate.

14. Please state the purpose of your ePRO system (please tick those that apply, there may be more than one primary purpose)

	Primary objective of system	Secondary objective of system	Not a system objective
Improving symptom management (associated with underlying chronic kidney disease)	☐	☐	☐
Improving symptom management (associated with treatment monitoring e.g. Haemodialysis)	☐	☐	☐
Identification of psychosocial problems	☐	☐	☐
To facilitate patient-provider communication	☐	☐	☐
Research	☐	☐	☐
Benchmarking of services	☐	☐	☐
Clinical service commissioning	☐	☐	☐
Support transition of care e.g. to renal replacement therapy or conservative care	☐	☐	☐

If your ePRO system has another purpose, please state

15. What is the population focus of the system (please tick all that apply)

- ☐ Chronic Kidney Disease Stages 1-3
- ☐ Chronic Kidney Disease Stages 4-5 pre dialysis
- ☐ In-centre Haemodialysis
- ☐ Home Haemodialysis
- ☐ Peritoneal Dialysis
- ☐ Transplant
- ☐ Conservative Care

16. When was ePRO system launched?

DD/MM/YYYY

17. How was the system developed?

- ☐ Informatics team within the host organisation (single organisation)
- ☐ Collaboration across two or more organisations
- ☐ Already available Commercial product

Comments:

18. Approximate number of patient users

19. Approximate number of clinician users

20. Primary location of use (please tick all that apply)

- ☐ Primary Care (Community/General Practice clinic)
- ☐ Secondary Care (Hospital clinic)
- ☐ Dialysis Centre
- ☐ Home

21. What PRO Measure (s) are you using?

	PRO Measure
Are you using a new measure?	
Are you using an existing measure(s)?	
Do you need to use a licence for use?	

Comments: Please state name of PRO measure(s)

22. Has the PRO Measure been validated with your patient population? *

- ☐ Yes
- ☐ No

23. How was your ePRO system validated?

- ☐ Formal paper-electronic equivalence testing
- ☐ None
- ☐ Other (please specify):

24. What analysis metric is being used to make or inform clinical decisions?

- ☐ Change from baseline
- ☐ Final value
- ☐ Time to event
- ☐ Other (please specify):

25. How was your ePRO system funded? (you may tick more than one option if mixed model funding used)

- ☐ Commercial
- ☐ Academic
- ☐ Charitable
- ☐ Governmental

Other: Please state

26. What security features does your ePRO system employ? (please tick all that apply)

- ☐ Secure log in (password)
- ☐ Encryption
- ☐ Other (please specify):

6. Administration of PRO assessments/level of automation

27. Is your ePRO system web-based and/or App based (please tick all that apply)

- ☐ Non-responsive website i.e. for display on desk top computer
- ☐ Responsive/mobile website i.e. content displays and function across all devices
- ☐ Mobile App

28. How is the ePRO system accessed? (please tick all that apply)

- ☐ Computer
- ☐ Tablet
- ☐ Interactive Voice Response System
- ☐ Clinic based kiosk
- ☐ Smartphone
- ☐ Other (please specify):

29. Timing of ePRO assessment

- ☐ Prior to clinical assessment
- ☐ Set timepoint weekly
- ☐ Set timepoint monthly
- ☐ Set timepoint 3 monthly
- ☐ Set timepoint 6 monthly
- ☐ Set timepoint annually
- ☐ As required (by patient)
- ☐ Other (please specify):

30. PRO assessment selection: How does your ePRO system select which PRO to use?

- [ ] Automatic (by system) i.e. Provider
- [ ] Patient

Comments:

31. Question Format: How does the ePRO system present questions?

- [ ] One question per page
- [ ] Multiple questions per page
- [ ] Mixed format of single and multiple questions

32. Question advancement: how does the ePRO system move from one question to the next?

- [ ] Mouse click
- [ ] Automatic on completion

33. What page features are available? (please tick all that apply)

- [ ] Progress Bar
- [ ] Visual graphics i.e. graph, diagram, chart
- [ ] Other (please specify):

34. How does your ePRO system avoid missing data during completion? (Please tick all that apply)

- [ ] Allows multiple logins per assessment with automatic save function
- [ ] Allows multiple logins per assessment with save and return later function
- [ ] Allows not applicable (N/A) response
- [ ] Default response pre-selected (pre-populated neutral response)
- [ ] Reminders
- [ ] Other (please specify):

35. Is the ePRO available in more than one language? *

	Yes	No
Is the ePRO available in more than one language?	☐	☐

Comments: Please state available languages

7. Cross cultural validation

36. Has the ePRO measure been validated for use in multiple languages?

- ☐ Yes
- ☐ No

Comments: if yes, please specify languages

37. How does the ePRO system notify that assessments have been completed? (Please tick all that apply)

- ☐ Automated submission notification to patient
- ☐ Automated submission notification to clinicians
- ☐ Email notification to patient from clinical team following review of responses
- ☐ App based notification
- ☐ Other (please specify):

38. How are patients reminded to complete their ePRO assessment? (Please tick all that apply)

- ☐ Email
- ☐ Telephone call
- ☐ Text message: SMS
- ☐ Verbally
- ☐ By letter
- ☐ No reminder
- ☐ App based push notification

39. Does the ePRO system offer flexible system features (please tick all that apply)

- ☐ Web based home and clinic login access
- ☐ Multiple assessment scheduling options
- ☐ Two or more sources for PRO selection (patient/provider)

- [ ] Self identification of important issues by patient (computer adaptive testing functionality)
- [ ] Free text availability
- [ ] Multiple language availability
- [ ] In app or push notifications
- [ ] Other (please specify):

9. ePRO System integration and reporting

40. Please outline the ePRO report content (Please tick all that apply)

- [ ] Current scores including summary and individual scores
- [ ] Longitudinal change
- [ ] Interpretation included in report
- [ ] Cut scores (e.g. low, medium, high)
- [ ] Population norms or reference values
- [ ] Identification of meaningful change
- [ ] Modifiable reports
- [ ] General guidelines
- [ ] Other (please specify):

41. How are ePRO reports accessed? (Please tick all that apply)

- [ ] Via clinical portal/electronic patient health record
- [ ] Via immediate access i.e. summary print out on completion
- [ ] Results restricted to clinical encounter
- [ ] Other (please specify):

42. Who has access to ePRO results/summary reports (please tick all that apply)

- [ ] Patient
- [ ] Clinicians
- [ ] Care Provider
- [ ] Multiple care provider access
- [ ] Other (please specify):

43. Who is responsible for initial review and action of ePRO results?

- [ ] Medical staff
- [ ] Nursing staff
- [ ] Administrative staff
- [ ] Other member of multidisciplinary team

Comments:

44. What form does the clinical response to ePRO report take? (please tick all that apply)

- ☐ Prescribed electronic response dependent on score
- ☐ Clinician/staff follow up; follow up type (face to face, virtual) dependent on score/decision aids
- ☐ Automatic referral to member of multidisciplinary team
- ☐ Automated patient education/message regardless of score
- ☐ Other (please specify):

45. Is there visual presentation of the ePRO scores? (please tick all that apply)

- ☐ Graphical
- ☐ Tabular
- ☐ Numerical
- ☐ Emoticon
- ☐ Colour coded
- ☐ Other (please specify):

46. Does your ePRO system have a safety alert system, dependent on respondent scores? *

- ☐ Yes
- ☐ No

10. Management of safety

47. Management of safety: Who is the intended primary recipient and audience of the ePRO score alert and associated response?

- ☐ Clinician/Staff
- ☐ Patients
- ☐ Care provider
- ☐ Caregiver
- ☐ Multiple recipients i.e. clinicians and patients

Comments:

48. Management of safety: what form do ePRO score alerts take? (please tick all that apply)

- [ ] Email
- [ ] Text message/SMS
- [ ] Telephone call
- [ ] Verbal
- [ ] Real time alert
- [ ] In App notification
- [ ] None

11. Training

49. Do you offer training on the ePRO system? *

- [ ] Yes
- [ ] No

12. Training

50. Who receives training on the ePRO system? (Please tick all that apply)

- [ ] Clinical staff
- [ ] Administrative staff
- [ ] Patients
- [ ] Carers
- [ ] Training available but not specified
- [ ] No formal training available

51. What form does ePRO system training take? (Please tick all that apply)

- [ ] Face to face
- [ ] Online
- [ ] Integrated into ePRO system
- [ ] No formal training

52. Is there a facility for patient education through the ePRO system? (please tick all that may apply)

- ☐ Patient education administered within system
- ☐ Education linked to ePRO scores
- ☐ Automatic documentation of actions
- ☐ No patient education offered

Comments:

13. Evaluation

53. Has your ePRO system been evaluated? *

14. Evaluation

54. What form of evaluation did you undertake?

- ☐ Formative research
- ☐ Pre implementation feasibility testing
- ☐ Progress focused evaluation concurrent to implementation
- ☐ Retrospective evaluation

Comments:

55. Did you include patients in your evaluation?

56. What, if any, changes did you make following the evaluation process

15. Additional features

57. Is there linkage between the ePRO system and other electronic data systems? (Please tick all that apply)

- ☐ Patient Electronic Health Record
- ☐ Appointment/scheduling systems
- ☐ Patient Billing systems
- ☐ No linkage
- ☐ Other (please specify):

58. Accessibility: is the data available to areas outside nephrology settings?

- ☐ Yes
- ☐ No

Comments: If yes, please state

59. Does your ePRO system offer any additional features (please tick all that apply)

- ☐ Quality of care evaluation
- ☐ Patient satisfaction data collected
- ☐ Accreditation reporting
- ☐ None
- ☐ Other (please specify):

60. Is IT support available for your ePRO system?

- ☐ Full
- ☐ Limited
- ☐ User Manual available
- ☐ None

Comments: if Limited, please state what support is offered

16. Contact details

61. Would you like a summary of the findings of this survey?

- ☐ Yes
- ☐ No

If yes, please enter your preferred contact details below

Thank you very much for taking part in this survey.
Would you like to get in touch with the research team?
If you would like any more information, please contact Nicola Anderson at NEA451@student.bham.ac.uk

5.4. Topic Guide for semi-structured interviews v4 11.06.2021

Nephrology ePRO systems review - Topic Guide

Introduction/Ice breaker

The introduction will set the tone and start building rapport:
Introduce self as a Nurse Researcher with a clinical background specialising in nephrology research and that this interview is being undertaken as part of a clinician doctoral research fellowship funded by the National Institute for Health Research.

Tell respondents the general purpose of the interview

Before the interview, check that the respondents are still happy to take part and have signed the study specific electronic consent form.

Participants will be reminded that all individual self-identifiers will be removed before transcripts are analysed but that the System/institution itself will be named.

1. Icebreaker question: Please outline your role and key responsibilities as a System Lead for the ePRO outlined in your survey responses

2. Can you describe how the ePRO is being implemented in your institution?
Prompts: What was/is your implementation plan? What stage are you at?

3. What is the purpose of assessment?
Prompt: To inform clinical care, identify symptoms/tailor care, audit, benchmark, real-world evidence, trials Mixture?

4. Did you use internal/external change agents to help implementation?
Did you use peer support/champions to help implementation?
Prompt: Did you get endorsement or support from leaders? If yes, what form did it take, if no, why do you think not?

5. Did you use an existing PROM? Or develop a new measure?
Prompt: Did you measure the psychometric properties of any existing measure? If a new measure was created – what methodological approach was taken? Use of core outcome sets? COSMIN assessment? Level of patient input? FDA guidance?

6. Who are the key influential stakeholders for the ePRO? What was your engagement strategy to get these people on board?
Prompts: Stakeholders could be Health care professionals, patients, carers, senior managers, administration staff. Were these individuals involved in c0-designing the system – in particular were patients involved?

7. What is the general level of receptivity in your organization?
Prompt: Are users (patients/Healthcare Professionals) happy to use the ePRO, are they confident? If not, do you know why not?

8. Were any supports developed to help you implement and use the ePRO?
Prompts: Training resources? Marketing material?> toolkit? Were these resources

available digitally, was face to face training made available.

9. What is the priority for getting the ePRO implemented relative to other initiatives that are happening now?
   Prompt: for example was it affected by the COVID 19 pandemic?

10. Was the ePRO piloted prior to full-scale implementation?
    Prompt: Can you describe the context of the pilot? What worked well? What did not work well?

11. Was the ePRO available in more than one language? Were there mechanisms to allow use by as many patients as possible?
    Prompt: were any translations culturally validated?

12. What mechanisms do you have in place to allow maximum accessibility?
    Prompt was the ePRO available for use with patients who have impairments, or can't access IT

13. What direct and indirect costs were incurred to implement the ePRO?
    Prompts: Did you need to make changes to infrastructure i.e., IT systems, staffing to support ePRO, adaptions to existing workflow and care delivery systems

14. Did you have sufficient resources to implement the ePRO?
    Prompt: if not, what should be prioritised? Links to EPR? Safety features?

15. Do you think the ePRO has improved the way care is being delivered? If yes, how do you think this takes effect?
    Prompt: Improved access to services? Help with self-management? Reduced travel time and expense? To support individual care/tailor care to individual needs, audit, benchmarking, real-world evidence generation – all of these? Other

16. Are you collecting any information to assess impact of the ePRO? If so what type of data?
    Prompt: health economic data to assess cost effectiveness, average length of consultation , hospitalisations, death rate, health service interactions, patient and clinician satisfaction

17. What kind of performance measures, policies, regulations, or guidelines influenced the decision to implement the ePRO? Does it provide your organisation with an advantage?
    Prompt: Local, state, national measures? Were there incentives to support the ePRO

18. Overall has the ePRO been implemented according to the implementation plan?
    Prompt: What worked well (Facilitators), what did not (Barriers), what would you change?

19. Are you aware of other ePROs systems in regular/systematic use in nephrology settings?
    Prompt: If yes, which systems and what are the associated institution? Do you know who the System Lead is?

20. How does your ePRO compare to other similar/existing ePROs in your setting?
    Prompt: Are you aware of any specific advantages/disadvantages of your digital PRO?

21. Do you have anything else to add?

We have now reached the end of the interview. Please be reminded that any personal identifiers will be removed but institutional and system identifiers will be used in any subsequent outputs. You will be given a copy of the transcript after the interview and will have 10 working days to inform the lead researchers of any redactions you wish to make or study withdrawal. Many thanks for your participation.

Appendix 5.5: REC approved invitation email v1 10.06.2021

Email

Dear …,

We are inviting people who have had involvement in the development, design and implementation of ePRO Systems, specifically for use in nephrology settings, to complete a survey and optional follow up interview, if required, about system characteristics including assessment, automation, integration and reporting. The aim of this research is to summarise the latest developments worldwide and help inform development of ePRO systems for use in haemodialysis settings in the United Kingdom.

You have been contacted, as you have been identified as a key ePRO System Lead within nephrology and we would be very keen for your participation.

This research is being undertaken as part of a National Institute of Health Research Clinical Doctoral Research Fellowship at the Centre for Patient Reported Outcomes Research (CPROR) University of Birmingham in the UK.

A participant information sheet with further information is attached to this email.

For more information, please contact Doctoral Research Fellow Nicola Anderson: [redacted] or Principal Investigator/Supervisor Professor Melanie Calvert [redacted]

If you wish to take part – your unique study identifier is *[enter identifier].* Please make a note of this number and use it in any communications with the research team.

The survey can be found at:

<insert link>

Please feel free to pass on details of this research and the research team contacts to anyone who you think would be interested.

Kind regards and many thanks,

Nicola Anderson and Professor Melanie Calvert.

Appendix 5.6: REC approved Participant Information Sheet v3 06.06.2021

Using electronic Patient-Reported Outcome Measures (ePROs) to promote quality of care and safety in the management of patients with End Stage Kidney Disease: Review of Electronic Patient-Reported Outcomes Systems used in Nephrology settings

Why are you doing the survey?

The aim of this research is to comprehensively explore the design, implementation and use of ePRO systems being used or developed for use in nephrology settings to help inform the development of an ePRO system to support individuals with end stage kidney disease. Therefore, we are inviting people who have been identified as System Leads in the application of ePRO Systems, specifically for use with kidney patients to take part.

Taking part is voluntary and it is up to you to decide whether or not to take part.

Who can take part in the survey?

A System Lead of an eligible ePRO system. Eligible systems are defined as those used in nephrology practice settings including related treatment areas (e.g., dialysis units) that assess PROs electronically and summarize kidney patients' responses to their care provider. Eligible systems from any country can be included. System leads may have clinical or non-clinical roles but will have taken central responsibility for key aspects of ePRO design, development and implementation.

What would taking part involve?

The survey will take around one hour to complete. The survey will ask questions about system characteristics including methods of assessment, levels of automation, integration into the electronic health record, safety alerts and reporting of responses. We will also ask you to complete questions about your role and responsibilities. The survey is constructed to allow you to skip questions or include 'rather not say' in a free text option, to avoid disclosing proprietary information and breaching copyright or non-disclosure agreements.

Before you complete the survey, you will be asked to complete an online form to give your consent to take part in the study. You will be given a unique study ID number. Please keep a record of this number for any communication with the researchers.

Participants can withdraw at any point during the survey by exiting your browser without submitting the completed survey form. Partially completed forms will be saved for completion at a later time and this data is available to researchers. In addition, you can withdraw your data up to 5 days after completing or partially completing the survey by contacting the study team. After this point, analysis will commence, and withdrawal of data will not be possible. Participants will not be expected to give a reason for survey withdrawal.

You will also be asked if you are happy to be contacted for an optional follow up interview, if required, to explore your survey responses and implementation factors in further detail.

Do I have to take part in a follow up interview?

No, you do not have to take part in a follow up interview. It is up to you to decide. Taking part in this part of the research will be based around your commitments. The date and time of the interview will be arranged at your convenience. Development team members may attend semi-structured interview, at request of the System Lead, if specific roles in development and implementation were delegated.

What will happen to me if I decide to take part in a follow up interview?

The optional follow up interview will take place via telephone or approved video conferencing platform. The interview will be recorded and will last for about one hour. Any recording of a follow up interview will be used to produce a typed record of the discussion, known as a transcript, which will be anonymised. A professional transcription company will carry out the transcription. Any external company will sign a confidentiality agreement before receiving such recordings. The transcript will be analysed as part of our research.

What are the possible benefits of taking part?

Participants will be offered a £50 gift voucher in recognition for your involvement in survey completion.

What are the possible disadvantages and risks of taking part?

We do not anticipate any risks in taking part in either the survey or the follow up interview.

What happens if I change my mind?

You can end the survey at any point whilst you are completing it, by exiting your browser and not submitting the survey.

Once you have submitted the survey you will be able to withdraw up to 5 days after you have taken part. If you take part in an optional follow up interview you will be able to withdraw up to 10 working days following receipt of a completed interview transcript for review. You do not have to provide a reason for this. We advise you to keep a note of the researchers' contact details below and your unique study ID number if you wish to contact the study team regarding withdrawal.

How will my information be used?

We will produce a summary of the findings from the survey and any follow up interviews. Any personal identifiable information will be anonymised, but we will use institution and system identifiers when we report this study in academic journals or presentations at academic conferences. Whilst you will not be directly identifiable in any way through these outputs, it may be possible to identify you via your system or institution. To mitigate for this, you will be given opportunity to review any interview transcript and to redact any information you wish. Reviewed transcripts will need to be returned within 10 working days, otherwise it is assumed you are happy with the content.

How will my information be kept confidential?

Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. Once we have finished the study, we will keep some of the data so we can check the results.

Minimal Identifiable personal information will be collected (Role, experience in field) but any such individual personal information will be anonymised and there will be no reference to individual names or direct named quotes. However, institution and system identifiers will be kept and will be used in research outputs, including publications and presentations.

All identifiable electronic data including contact details and interview recordings will be held within encrypted files and stored on a secure server which is backed up daily at the University of Birmingham.

The data you provide will only be accessed by the research team at the University of Birmingham, or by authorised people to check that the study is being carried out correctly.

All data will be saved and stored securely at the University of Birmingham. Study data will be held for 10 years before being destroyed.

The information collected may be used to support other research in the future and may be shared anonymously with other researchers.

You can find out more about how we use your information:

- At www.birmingham.ac.uk/privacy/index.aspx
- By sending an email to Nicola Anderson: [redacted]

What will happen to the results of this study?

A summary of the results will be made available at the end of the study. The results may be published in academic journals or presented at academic conferences.

Who is conducting the research?

This independent research is funded by the National Institute of Health Research (NIHR) under its Clinical Doctoral Research Fellowship Programme (Grant Reference ICA-CDRF-2018-04-ST2-027) and forms part of a PhD educational qualification through the Centre for Patient Reported Outcomes Research (CPROR). The project is sponsored by University of Birmingham.

Who has reviewed the study?

This research has been reviewed by the University of Birmingham Research Ethics Committee.

Further information and contact details

If you would like any more information, please contact Doctoral Research Fellow Nicola Anderson: [redacted] or Principal Investigator Professor Melanie Calvert [redacted]

If you have any complaints about this project, you may contact Susan Cottam, Research Ethics Manager, University of Birmingham, B15 2TT ([redacted]

If you have a complaint about the way, you have been approached or treated during this study or a concern about any aspect of it you should ask to speak to the researcher, who will do their best to answer your questions.

Appendix 6

Appendix 6.1: Publication: Calvert, M.J., Cruz Rivera, S., Ritzer, A., Hughes S.E., Campbell, L., Molony-Oates, B., Aiyegbusi, O L., Stover, A, M., Wilson, R., McMullan, C., **Anderson, N E**., Turner, G M., Have Davies, E., Verdi, R., Volkova G., Kamoni P., Muslim, S., George, A., O'Connor, D., Xiaoxia, L., Wu, A,W., & Denniston, A,K. ***Patient reported outcome assessment must be inclusive and equitable***. Nat Med 28, 1120–1124 (2022). **https://doi.org/10.1038/s41591-022-01781-8**

Link to open access publication:

Patient reported outcome assessment must be inclusive and equitable | Nature Medicine

(https://www.nature.com/articles/s41591-022-01781-8)

Appendix 6.2 Publication: Samantha Cruz Rivera, PhD; Olalekan Lee Aiyegbusi, PhD; Jonathan Ives, PhD; Heather Draper, PhD; Rebecca Mercieca-Bebber, PhD; Carolyn Ells, PhD; Amanda Hunn, MA; Jane A. Scott, PhD; Conrad V. Fernandez, MD; Andrew P. Dickens, PhD; **Nicola Anderson, MSc**; Vishal Bhatnagar, MD; Andrew Bottomley, PhD; Lisa Campbell, MD; Clive Collett, MA; Philip Collis; Kathrine Craig, PhD; Hugh Davies, MD;Robert Golub, MD; Lesley Gosden; Ari Gnanasakthy, MSc; Elin Haf Davies, PhD; Maria von Hildebrand; Janet M. Lord, PhD;Nirosha Mahendraratnam, PhD; Tempei Miyaji, MSc; Thomas Morel, PhD; Joao Monteiro, PhD; Ann-Dorthe Olsen Zwisler, PhD; John Devin Peipert, PhD; Jessica Roydhouse, PhD; Angela M. Stover, PhD; Roger Wilson, CBE; Christina Yap, PhD; Melanie J. Calvert,PhD. ***Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines.*** JAMA. 2022;327(19):1910–1919. doi:10.1001/jama.2022.6421

Link to open access publication:

Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines | Guidelines | JAMA | JAMA Network

(https://jamanetwork.com/journals/jama/fullarticle/2792247)