DEVELOPMENT OF A STRATIFIED CARE PATHWAY FOR PRIMARY BILIARY CHOLANGITIS: PATIENT AND CLINICIAN PERSPECTIVES ON MANAGEMENT IN PRIMARY CARE

by

MARGARET CORRIGAN

A thesis submitted to the University of Birmingham for the degree of

DOCTOR OF MEDICINE

Institute of Applied Health Research

College of Medical and Dental Sciences

University of Birmingham

April 2020

ABSTRACT

With the introduction of new guidelines for the management of Primary Biliary Cholangitis based on a stratified approach to care, the purpose of this research was to establish current practice in the UK and to ascertain the stakeholder perspective around the management of patients with low-risk disease in primary care.

Using a mixed-methods approach, this research combined the results of patient and clinician surveys, a scoping review, and semi-structured qualitative interviews with patients, representatives from the patient support groups, and clinicians from primary, secondary and tertiary care, in order to identify whether there were barriers to implantation of this pathway and, if so, what the factors were underlying these barriers.

Results from this research identified that a stratified approach is not currently widespread in clinical practice in the UK and that a number of barriers to implementing this approach to care exist from both the patient and clinician perspective. In addition to the general barriers to discharge of patients with chronic disease to primary care (including financial, strategic and workload related issues), as a rare disease PBC carries a number of specific challenges to the involvement of primary care in its management.

ACKNOWLEDGEMENTS

I would like to thank the following people for their roles in the process of creating this thesis

My supervisors Professor Sheila Greenfield, Professor Jayne Parry and Professor Gideon Hirschfield for their advice throughout this process both in terms of the academic work undertaken and the pastoral support provided.

My colleagues within the Institute of Applied Health Research and Immunology and Immunotherapy especially my fellow doctoral students Sarah, Katie, Gwil and Debs.

The Queen Elizabeth Hospital Charity who provided financial support.

My friends and family who have listened to me and supported me and never doubted that I would reach this point.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

LIST OF ABBREVIATIONS

AASLD	American Association for the Study of Liver disease
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AMA	Antimitochondrial antibody
ANA	Antinuclear antibody
AST	Aspartate aminotransferase
BASL	British Association for the Study of the Liver
BSG	British Society of Gastroenterology
CCG	Clinical Commissioning Group
DOH	Department of Health
DZ	Dizygotic
EASL	European Association for the Study of the Liver
GP	General Practitioner
GWAS	Genome wide association studies
HCC	Hepatocellular carcinoma
HLA	Human leukocyte antigen
LFT	Liver function test
MELD	Model of End-stage Liver Disease
MZ	Monozygotic
NHS	National Health Service
OCA	Obeticholic acid
PBC	Primary biliary cholangitis
QEHB	Queen Elizabeth Hospital Birmingham
QOF	Quality and Outcomes Framework

UDCA	Ursodeoxycholic acid
UKELD	UK model for End-stage Liver disease
ULN	Upper limit of normal

CHAPTER 1: BACKGROUND TO RESEARCH

1.1 Overview

The most recent guidelines for the management of Primary Biliary Cholangitis (PBC) published by the British Society of Gastroenterology have, for the first time, recommended that, as part of standard care, patients are stratified into low and high-risk groups using risk stratification tools (1). Furthermore, a tailored approach to care is suggested whereby those with high-risk disease and/or high symptom burden access enhanced specialist care earlier in the course of their disease (where previously this resource has mostly been focussed on those who already have more advanced disease requiring referral for liver transplantation (2, 3). At the same time, the guidelines also suggest that patients who have been deemed to be low-risk for disease progression could be discharged from hospital follow-up to the care of their general practitioner (GP). These recommendations represent an approach to management that has not been previously incorporated into guidelines, and the impact of these recommendations has not been formally studied. The goal of the research described within this thesis is to develop a better understanding of the extent to which the recommendation for the discharge of low-risk patients to primary care differ to current real world clinical practice, and whether there are barriers to implementation of this recommendation.

This chapter provides an introduction to Primary Biliary Cholangitis (PBC) starting with a brief overview of the epidemiology, pathogenesis, presentation, diagnostic criteria, and symptom profile of the condition. It then goes on to discuss the treatments available with a focus on ursodeoxycholic acid (UDCA), the concept of treatment response, and the role of response

criteria in the stratification of patients into low-risk and high-risk categories. Next, it discusses the processes behind clinical pathway implementation, the rationale for identifying barriers to change, and why research such as that described in this thesis is necessary. Finally, the specific aims of this research and the rationale for the chosen research design (which includes quantitative data analysis, a literature review and qualitative interviews) are discussed.

1.2 What is Primary Biliary Cholangitis (PBC)?

Primary biliary cholangitis, formerly known as primary biliary cirrhosis, is a form of chronic autoimmune liver disease "characterised by circulating antimitochondrial antibodies (AMAs) and selective destruction of the intrahepatic cholangiocytes, the cells that form the biliary tract" (4). It was first described by Addison and Gull in 1851 (5) and gained the name "Primary Biliary Cirrhosis" in 1950 (6); the naming of the disease reflecting the underlying autoimmune dysfunction resulting in the destruction of the small and medium-sized bile ducts (7). This name remained in use for over 60 years. However, in 2015, the new name "Primary Biliary Cholangitis" was adopted into use by clinicians, researchers, and patients, retaining the acronym PBC. This change in nomenclature highlighted both the changing natural history of the disease, whereby a minority of patients with PBC will go on to develop cirrhosis, as well as aiming to reduce the stigma that patients with this condition reported and attributed to the public perception of the association between cirrhosis and alcohol (8).

Whilst there is no cure for PBC, it is known that outcomes (in terms of risk of mortality or liver transplantation) vary between patients and depend on several factors including patient characteristics (including gender and age at the time of diagnosis) (9) and the biochemical response to treatment (1). Therefore, the new UK guidelines have been developed to incorporate

risk stratification tools and recommend their use in clinical practice both to predict long-term outcomes and to tailor management strategies to a patient's individual risk (1).

1.2.1 Epidemiology

Over 90% of patients with PBC are female (10) and it is most common in the 5th and 6th decade of life (11). Worldwide, previously published prevalence rates range between 1.91 and 40.2 per 100,000 population (10) with two studies from England which have looked specifically at the North East population reporting a prevalence around 30/100,000 (12). More recent studies (the two UK epidemiological studies date back to the late 1990s and early 2000s with a lack of more up to date studies in the UK) including a population-based study of patients in the Netherlands published in 2014 indicate a significant increase in both prevalence and incidence (15). Whilst, based on overall prevalence, PBC is categorised as a rare disease (a rare disease is a life-threatening or chronically debilitating disease that affects five people or fewer in 10,000) (13), combining the age, gender and prevalence data indicates that 1 in 1000 women over the age of 40 years have this condition (14). The cause for this increase is unclear although the authors of the Dutch study suggested that this was likely to represent increased disease awareness, improved diagnostic tools, better therapies, and the development of digital registries as possible causes.

1.2.2 Pathogenesis

PBC is a disease of both genetic and environmental origin which, in combination, are thought to trigger an immune-mediated destruction of the biliary epithelial cells and loss of the small and medium bile ducts. As a result of the biliary damage, there is subsequent cholestasis (decrease in the flow of bile) resulting in inflammation. If left untreated, this can progress to liver fibrosis and cirrhosis (16).

1.2.2.1 Genetics

Early evidence suggesting a genetic component to the development of PBC came from cohort studies which identified both an increased prevalence of PBC and non-PBC autoimmune disorders in relatives of patients with PBC, as well as an increased rate of other autoimmune conditions in patients with PBC. A geographically based cohort of 160 patients living in the North East of England (17) found that 53% of patients with PBC had one other autoimmune condition themselves whilst 32% had two or more autoimmune conditions. Six percent of patients had a family history of PBC with 61% having a family history of another autoimmune disease. In addition, there is an increased prevalence of AMA positivity in first degree relatives of patients with PBC (13.1%) vs. 1% of age, sex, race, and location matched controls (18).

Further evidence for the role of genetics in PBC has come from twin studies. A study of sixteen sets of twins (eight monozygotic (MZ) and eight dizygotic (DZ) pairs) identified disease concordance in 5/8 MZ pairs whilst no DZ pairs were concordant. In addition, there was also a similarity in the age of onset and disease characteristics in concordant pairs (19). More recently, the evolution of the genome-wide association studies (GWAS) (20) and the identification of strong human leukocyte antigen (HLA) associations (21) have strengthened the evidence for an underlying genetic component to the development of PBC. The former have identified loci containing genes involved in IL-12 signalling, activation of nuclear factor κB and TNFα signalling pathways (22).

1.2.2.2 Environment

Cohort studies have sought to identify the environmental trigger that leads to the onset of disease in the genetically predisposed. In a UK-based cohort, multivariate analysis identified that use of hair dye, smoking, and history of urinary tract infections were significant associations with PBC (23). The latter two were also found to be risk factors in a French cohort study (24). In this population, hormonal risk factors including age at menarche, number of previous pregnancies, younger age at first pregnancy, and use of the oral contraceptive pill were also identified. A similar range of factors (smoking, hormone replacement therapy, and age at the time of first pregnancy) were identified as risk factors in a North American study (25).

1.2.2.3 The role of autoantibodies

As is common to other autoimmune conditions, the presence of autoantibodies is an important component of diagnosis, and the specific autoantibody profile seen can help to predict the clinical phenotype (the observable characteristics or traits of the disease). There is a strong correlation between antimitochondrial antibody (AMA) positivity and PBC (26) which was first described in the mid-1960s and remains true to date; in current clinical practice, AMA is positive in over 90% of cases (27). Approximately 50% of patients with PBC are also antinuclear antibody (ANA) positive (28). Whilst this is a non-specific antibody seen in several conditions, certain immunofluorescence patterns are specific to PBC including nuclear rim (gp210), multinuclear dot (sp100) and anti-centromere antibodies. Presence of these particular autoantibodies can be helpful in cases where AMA is negative. In addition to their diagnostic significance, they are also of prognostic importance; a patient who is identified to be gp210 or sp100 positive has a poorer prognosis compared to the PBC population generally (29). This association between gp210 positivity and disease progression was also identified by Nakamura

et al. who additionally found that those who are anti-centromere positive commonly have a phenotype dominated by portal hypertension (an increase in the blood pressure in the portal vein, which carries blood from the bowel and spleen towards the liver) (30).

1.2.3 Presentation

There is a paucity of specific studies describing how patients with PBC initially present and the time from presentation to diagnosis. In 2002, Prince et al. reported that in their cohort of 770 patients in the North East of England, 469 (61%) were asymptomatic at diagnosis (14). Asymptomatic patients may be identified when they undergo testing of liver function for reasons such as a routine medical review, for life insurance, or where the patient has another autoimmune condition and screening is undertaken (31). Most of the remaining patients will present with a symptom related to PBC, most often pruritus (itch), fatigue, abdominal or joint pain whilst late presentations with advanced disease and complications of cirrhosis are now rare (32).

1.2.4 Diagnosis

Once the possibility of PBC has been considered, establishing the diagnosis requires two out of three of the following criteria to be present (32):

1. Cholestatic liver biochemistry (raised alkaline phosphatase (ALP) on blood tests) on two occasions at least six months apart
2. Positive antimitochondrial antibody (AMA) at a titre ≥ 1:40
3. Characteristic liver biopsy changes

In clinical practice, few patients undergo liver biopsy routinely and most are diagnosed in the presence of the first two criteria. In patients who are AMA negative (<10% of all patients with PBC) but the diagnosis is still suspected, and to avoid a liver biopsy, the next step is to check for the presence of the specific antinuclear antibodies discussed previously (gp210, sp100). If these are positive in the presence of cholestatic liver biochemistry, then the diagnosis has been made, and biopsy can be avoided. Histological examination of liver tissue (through biopsy sampling) is reserved for those where there is diagnostic uncertainty (for example, where the extended autoantibody screen is negative or not offered by the local hospital laboratory, or in the presence of a possible second concurrent diagnosis).

1.2.5 Natural history of the disease

The progression of chronic liver disease from injury (whether that be immunological (for example PBC), viral (for example Hepatitis C), or metabolic (for example non-alcoholic fatty liver disease) to fibrosis then cirrhosis and, ultimately, liver failure has been well described (33). In the case of PBC specifically, natural history studies of patients before or around the time of early clinical trials suggested that life expectancy from time of diagnosis was less than ten years (14). However, in current practice, the widespread use of ursodeoxycholic acid (UDCA) means that PBC is no longer the "uniformly fatal" disease described by Hamlyn and Sherlock in the early 1970s (34). The ability to diagnose patients earlier in their disease course (before the development of significant fibrosis or cirrhosis) and early initiation of disease-modifying therapy means that for many patients, PBC is a chronic but not life-threatening condition. However, in the absence of curative treatment, there is still an associated mortality and, in 2015/2016, PBC accounted for 9% of all elective liver transplants in the UK (35).

1.2.6 Management of PBC

Guidelines for the management of PBC focus primarily on the use of medications for disease modification and symptom control. These are discussed in detail below. Whilst patients who develop cirrhosis are entered into surveillance programmes for hepatocellular carcinoma (36) and varices (37) there is an absence of consensus on where, how often and by whom, patients should be followed up. These factors have not previously been incorporated formally into management guidelines.

1.2.6.1 Ursodeoxycholic acid (UDCA)

UDCA is hydrophilic, naturally occurring, bile acid which, for many years, was the only licensed treatment for PBC. Its mechanism of action is not fully understood but includes an increase in the hydrophilic bile acid pool and relative reduction in hydrophobic toxic bile acids, cytoprotection (through cell membrane stabilisation) as well as an immunomodulatory component (38). It is given at a weight-based dose of between 13-15mg/kg and is well tolerated by most patients. Side effects include bowel disturbance, skin reactions, nausea, and vomiting (39).

1.2.6.2 Obeticholic acid

Obeticholic acid (OCA) is a semi-structured bile acid analogue which has been found to activate the Farsenoid X receptor and in 2017, following clinical trials, was approved by the National Institute for Health and Care Excellence (NICE) for the treatment of PBC in patients who have had an inadequate response to treatment with UDCA or are unable to tolerate UDCA (40). Its availability is currently limited to a specific patient access scheme.

1.2.6.3 Symptomatology

Whilst most patients are asymptomatic at the time of diagnosis, many will develop symptoms at some point over the course of their life. The most common being fatigue and pruritus (itch).

Fatigue: low energy levels are a common symptom in PBC reported in up to 80% of patients (11). It has been referred to as “an overwhelming sustained state of exhaustion that occurs without relation to antecedent events and is unrelieved by rest or sleep” (41) and has been noted to have a significant or life-altering impact in up to 20% of cases (42). Despite its prevalence, the pathogenesis of fatigue in PBC is not fully understood, and it does not correlate with biochemical or radiological disease severity. Currently, there is no recommended pharmacological therapy for the management of fatigue and management focuses on strategies to help patients cope with the symptoms; for example graded exercise programmes and "energy management" (43). Guidelines from the European Association for the Study of the Liver (EASL) highlight the importance of looking for and treating concomitant illness such as depression, anaemia, and hypothyroidism (2).

Pruritus (itch) is reported in up to 70% of patients with PBC in the UK (44). European guidelines set out a step-wise strategy for the management of pruritus in patients with cholestasis (2) which is also employed in UK practice. Cholestyramine (a bile acid sequestrant) is the first-line treatment for pruritus associated with PBC. If this fails, or is not tolerated, then rifampicin (an antibiotic which is also a pregnane X receptor agonist) may be used, followed by naltrexone (an oral opiate antagonist) as the third line. Sertraline, (an antidepressant of the selective serotonin reuptake inhibitor (SSRI) class) is also used. Where pharmacological

therapy is ineffective, and pruritus is intractable, strategies such as nasobiliary drainage and plasmapheresis may be employed (43).

An online survey of patients with PBC living in Canada identified that having a diagnosis of PBC was associated with a significant impact on a patient's day to day life as a consequence of the symptoms of the condition; 62% reported that they required assistance to undertake activities of daily living including cleaning, shopping, cooking and driving, while 30% reported that the symptom burden affected their relationships with friends and family. 60% of patients had adjusted their life to accommodate symptoms (45).

1.2.7 Complications

Osteoporosis: The underlying mechanism for the development of osteoporosis in PBC is unclear, with several theories being posited including the decreased absorption of the fat-soluble vitamins including vitamin D in the presence of cholestasis. In addition the demographics of PBC patients often overlap with known risk factors for osteoporosis; predominantly being female, postmenopausal, and with a history of or current smoking status. Rates of osteoporosis vary but a mild reduction in bone density occurs in 30% of patients with osteoporosis reported in 10% (4). This thinning of the bone comes with an associated morbidity. A study within a Spanish population of women with PBC reported a fracture prevalence of 20.8% (46). In the absence of large trials, there is no consensus on how best to manage fracture risk in these patients. European and American guidelines suggest that bone mineral density is assessed at presentation and at intervals after (32, 47).

Screening for complications of cirrhosis: For patients who have developed cirrhosis as a consequence of their underlying condition, there is a risk of developing complications including gastric and/or oesophageal varices (dilated blood vessels which are at risk of bleeding) and hepatocellular carcinoma. The British Society of Gastroenterology recommends that all patients should have an endoscopy (camera test into the upper gastrointestinal tract) to look for varices at the time of diagnosis with cirrhosis with the frequency of follow-up determined by the findings (37). In terms of screening for hepatocellular carcinoma, the European Association for the Study of the Liver (EASL) recommends six-monthly ultrasound imaging (48).

1.3 Response criteria and risk stratification

The first study of UDCA for the treatment of PBC was carried out in France in the early 1980s (49). In this prospective, uncontrolled study, fifteen patients received treatment with UDCA. The treatment was well tolerated, was associated with a significant reduction in pruritus, and also an improvement in the biochemical markers of disease activity. Those patients who underwent a repeat liver biopsy during the study showed no worsening of the histological stage (severity of liver damage and fibrosis). Subsequent studies of UDCA were not universally positive, however. A systematic review published in 1999 looked at the outcome of eleven randomised control trials (comparing UDCA and placebo) and six switch-over studies; in total data from >1200 patients was analysed (50). Whilst the use of UDCA was associated with significant improvement in liver biochemistry, there was no effect on the degree of hepatic fibrosis, and only one study showed evidence that UDCA prevented the progression of the histological stage. Importantly, there was no difference between UDCA and placebo in terms of incidence of death or liver-related death, transplantation, or the development of liver-related complications.

These early studies attributed the poor clinical outcomes to several factors including the dose of UDCA used and the disease stage of patients at the time they were enrolled in the study. However, it is now recognised that, when looking at clinical outcomes, patients with PBC can be broadly categorised into two categories – UDCA responders and non-responders – based on their biochemical response following 12 months of treatment. It is this "response" that determines the long-term outcome of patients; those who fail to respond will progress, and most will eventually require a liver transplant. Several studies have sought to determine the optimum "response criteria" to be used within a given population. The currently available criteria are discussed below and summarised below in Table 1.

Table 1: UDCA response criteria currently in use

Barcelona (51)	ALP decrease by >40% from baseline or returns to normal
Paris 1 (29)	ALP < 3 x ULN, AST < 2 x ULN, bilirubin < ULN
Paris 2 (52)	ALP and AST < 1.5 x ULN and normal
Rotterdam (53)	Normal bilirubin and albumin
Toronto (54)	ALP < 1.67 x ULN

AST: aspartate aminotransferase, ULN: upper limit of normal

The Barcelona criteria (51) published in 2006 defined response as a reduction in ALP of >40% and/or normalisation of ALP following one year of treatment. This study looked at a total of 192 patients treated with UDCA at a dose of 15mg/kg. In those who responded to UDCA, the rate of treatment failure (defined as death or need for liver transplantation) was 3.4% vs 17.4 in the non-responder group (p=0.001). In 2008, Corpechot et al. set out to determine what the best

biochemical response criteria were in their French population and to evaluate the Barcelona criteria within their cohort of patients (29). In this study of 292 patients of which 57% had early stage disease (histological stage I-II) and 17% of whom had established cirrhosis, they found that after twelve months of treatment a level of bilirubin ≤ 1 x ULN, AST ≤2 x ULN and ALP ≤ 3 x ULN was the most reliable in predicting a favourable outcome. For the cohort of patients that met all three of these biochemical criteria, there was a 90% ten-year transplant-free survival dropping to 51% amongst those who did not meet these criteria. In 2009, a study in a Dutch cohort consisting of 375 patients found that a normal bilirubin and albumin after one year of treatment (when one or both were abnormal before treatment) predicted an overall transplant-free survival of 100% at one year and 78% at ten years (53). An update to the Paris 1 criteria was published in 2011 and termed the Paris 2 criteria (52). This study found that ALP and AST ≤ 1.5 x ULN and normal bilirubin predicted the risk of adverse outcomes in those with early disease and out-performed the Paris 1 criteria in these patients. The Toronto criteria published in 2010 were unique in that they looked at histological progression rather than transplant and death as their outcome. This group found that ALP <1.67 x ULN at two years of treatment with UDCA predicted the risk of histological progression (54).

Factors predicting response have also been studied; baseline bilirubin, histological stage, and severity of interface hepatitis were identified in the Paris 1 cohort, while in a UK study it was found that a patient was more likely to achieve the Paris criteria for response if they were over 70 years of age at the time of diagnosis (90% response rate) compared to a 50% response rate for those who were under the age of 30 at the time of diagnosis. Men were significantly less likely to respond to treatment (72% response vs 80% females, $p<0.05$) (9).

In addition to specific UDCA response criteria, several prognostic scores exist to predict clinical outcome in patients with all forms of chronic liver disease regardless of aetiology including the Child-Pugh Score (55), Model of End-Stage Liver Disease (MELD) (56) and United Kingdom Model for End-Stage Liver Disease (UKELD) (57). Other specific scores for PBC include the Mayo PBC score (58) which uses bilirubin, albumin, presence of oedema, prothrombin time and use of diuretics, and more recently the UK-PBC risk score (59) and the Globe score (60). The UK-PBC score identifies the risk of a PBC related event (liver disease related death, transplant, bilirubin >100) at three future time points (five years, ten years, fifteen years) while the Globe score combines age, bilirubin, albumin, platelets, and ALP; those with a score > 0.3 have a significantly lower survival compared to the matched general population, while those with a Globe score ≤ 0.3 have a life expectancy comparable with a matched general population.

1.4 Proposed model for stratified care

Applying a model of stratified care to the management of PBC means that patients will be divided into "low-risk" or "high-risk" depending on factors such as treatment response, age, gender and presence of cirrhosis. This approach to care has not previously been utilised in clinical guidelines; however, a schematic for this has been incorporated into the most recent BSG guidelines (1) and is shown in Figure 1.

Figure 1: Proposed algorithm for management of PBC

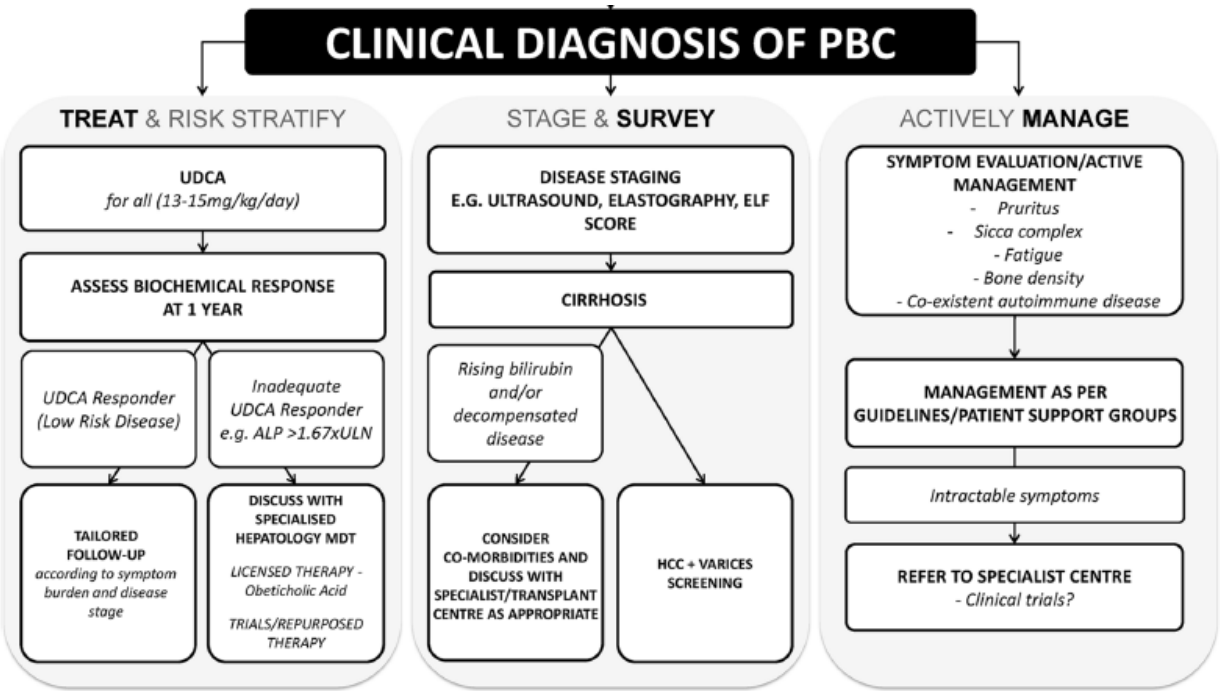


Figure is taken from the recently published British Society of Gastroenterology Guidelines for the management of PBC (1).

The flow diagram on the left of the figure sets out the stratification of patients according to response to UDCA. For those with low-risk disease, a tailored follow-up strategy is suggested. The guideline goes on to state as one of its recommendations that "patients with non-cirrhotic, UDCA responsive disease without high symptom burden may have disease that, in the context of appropriate service configuration and agreed care pathways, can be led from primary care" (1). The exact impact of this in terms of the number of patients impacted and the infrastructure required to facilitate this has yet to be determined. In addition, the patient and clinician perspectives on this strategy have yet to be sought.

1.5 Why implement a stratified care approach?

Creating better models of care for the management of chronic liver disease is essential and timely. In contrast to other countries in Western Europe, rates of liver disease are increasing in the UK; over 600,000 people are known to have liver disease with 10% of these having cirrhosis, and liver disease mortality has increased by 400% over the last 40 years (61). Given this burden of disease, The Lancet Commission on liver disease highlighted the numerous challenges currently faced by the NHS and by patients including the need to tackle inequalities in service provision, to look at how services can be reconfigured to provide high-quality care and also to best use the resources available (61). The role for primary care, as envisaged by the Lancet Commission was in the primary prevention of liver disease, screening of high-risk populations for viral hepatitis and the use of liver function tests in the early detection of liver disease. However, it also acknowledged that not all patients with liver disease need to be referred to secondary care and that some patients could continue to be managed in the community.

1.6 Guideline implementation

The use of guidelines in clinical practice is "intended to improve the quality of care and to promote patient safety by presenting the current evidence base and translating it into clinical practice" (62). However, it is known that adherence to clinical guidelines after publication is poor (63). The literature surrounding the reasons why guidelines are not always taken up into clinical practice is vast and highlights various factors that can impact adherence as well as posing strategies to improve guideline uptake. A model for implementing change was set out by Grol in 1997 and described the following stages: 1) development of a proposal, 2)

identification of obstacles, 3) linking of interventions to obstacles, 4) development of a plan, 5) carry out and evaluation of the plan (64).

A review published in The Lancet in 2003 identified several attributes that can affect compliance including the type of health care problem (acute conditions proving easier than more chronic conditions), quality of evidence presented in the guideline, compatibility with existing practice, level of complexity of decision making, clarity of the recommendations, need for new skills, and extent of organisational change involved (65). This review acknowledged that within each of these factors there existed potential "barriers to change" and that, in order to implement a change in practice successfully, it was "important to understand these and tailor strategies to them". This model divided obstacles to change into three categories acknowledging not just the clinician within this paradigm but also the role of the social context for change which included the impact of the patients' perception of change.

Two literature reviews on the subject of barriers to guidelines implementation have been published; the first (a systematic review) was published in 1999 (66) and the second (a scoping review) in 2016 (62). The results from the systematic review concluded that barriers fall into a number of themes: those related to the physician, external factors including aspects of the guideline, and the impact of the patient perspective. The later review revealed similar results dividing barriers into the following groups: physician knowledge, physician attitude, guidelines related and external factors.

1.7 Research question

The use of a stratified approach to care to guide where a patient with PBC is followed up and increasing the role for primary care in the management of low-risk patients represents a change to previously published guidelines. However, it is not currently known how the service within the UK is configured, to what extent stratification is already happening in practice, and if this is not the case, whether barriers to this proposed change exist and if so what they are.

1.8 Rationale for the research strategy

As a clinician with experience of the management of PBC and having worked as a clinical research fellow alongside the UK-PBC research group, it was evident to me that implementing a new guideline which incorporated risk stratification tools and saw patients with low-risk disease being discharged to primary care could well be met with resistance from clinicians and patients alike. However, to my knowledge, there was an absence of empirical data to support this assumption and, as such, it was apparent that specific research into this was required.

In order to establish what data needed to be captured to answer the research question, the potential pathway for a patient with low-risk disease was broken down into its component parts. Firstly, the patient would need to be correctly diagnosed in a timely manner before the onset of advanced disease and commenced on treatment. Once on the correct treatment, the patient would then need to be risk-stratified. Finally, once the patient had been identified as low-risk, they would need to be discharged to primary care. These pathway components were then broken down into the relevant stages and factors to be considered for them to be successfully achieved. These factors are shown below in Table 2.

Table 2: Components of a stratified care pathway

Diagnosis	Patient presents to the clinician Clinician recognises the possibility of PBC Clinician undertakes testing for PBC Test is interpreted and the diagnosis made
Treatment	The patient is seen by a clinician who is able to start treatment The patient is started on disease-modifying treatment at an appropriate dose
Risk stratification	The clinician is aware of risk stratification tools and when to undertake The clinician is competent to use the tool and interpret the result
Discharge to primary care	Understanding of low-risk disease Stakeholder agreement to discharge to primary care Identification of barriers to follow-up in primary care

1.8.1. Use of mixed methods

The research undertaken and presented in this thesis uses a mixed methods approach to obtain data of relevance to these four areas and combines both the analysis of a number of quantitative datasets, a literature review, and a qualitative research study. Mixed methods research has been defined as “a research approach whereby researchers collect and analyse both quantitative and qualitative data within the same study” (67). However, a true mixed methods approach requires not just the inclusion of more than one type of data but actually integrates the two, and then draws interpretations based in the combined strengths of both data sets to understand the research problem" (68). A mixed methods approach draws on the strengths of quantitative and

qualitative data whilst also recognising their weaknesses. For example, quantitative research has the ability to incorporate large amounts of data but does not always allow for an understanding of the context of the participants or to understand the "why" for a given answer. The questions asked and the availability of response are researcher driven. In contrast, qualitative research is based mostly on the view of the participants and allows for a fuller understanding of the context and experience behind the responses. However, it involves much smaller numbers of participants and its generalisability may be limited (68). For the research question posed here, the quantitative approach is ideal for looking at large datasets looking at current practice, while the qualitative approach will be used to look in more depth at the stakeholder perspective.

1.8.2 Stages of research

The research described here was divided into three stages:

1) Chapters 2-4: An overview of current UK practice and identification of areas where the process of diagnosis, treatment and risk stratification may need to be improved and how this could be done. In the absence of a single quantitative database that captures all the relevant data around current practices in the management of PBC in the UK, data from a variety of data sources were analysed. These included an electronic survey of UK clinicians, a patient questionnaire, and an audit of referrals of patients with a diagnosis of PBC to the out-patient clinic at a large teaching hospital.
2) Chapter 5: A literature review of the available PBC literature to identify what is currently known about patient and clinician perspectives on place of care.

3) Chapters 6-9: A qualitative study using semi-structured interviews with patients, patient group representatives, general practitioners and hospital-based clinicians, the design of which will be partially informed by the quantitative data analysis and literature review.
4) Chapter 10: A discussion integrating all of the data identifying the potential barriers to the discharge of low-risk patients to primary care as well as the underlying reasons for these barriers and how these could be addressed.

CHAPTER 2: UK-PBC PATIENT QUESTIONNAIRE DATA

2.1 Chapter overview

The previous introductory chapter discusses the most recent guidelines for the management of PBC and set out the rationale for implementing new guidelines based on risk stratification and the factors that would need to be considered when introducing a new pathway into routine care. It also provides an overview of the currently published PBC literature and details what is currently known about the pathogenesis, the role of genetics and environment, the criteria for diagnosis, the role of UDCA and the evidence for its use, and the available response criteria and prognostic scores available. However, within the current literature, there is an absence of real world data looking at the patient journey and clinical practice. This data is essential to understand the impact of a stratified care pathway and how the patient journey may impact on the perspectives of patients and clinicians when considering their preferences for place for care.

As a Clinical Research Fellow within the field of autoimmune liver disease, I was aware that there was data available that could be of relevance to the research question and could be accessed and analysed to try to address these knowledge gaps. Firstly, the UK-PBC research platform (discussed in this chapter) had undertaken a series of patient questionnaires around a variety of aspects of PBC, as well as a survey of clinicians in the UK around the use of risk stratification tools (Chapter 3). Finally, I also had access to a specialist clinic at a large teaching hospital with a specialist PBC clinic which accepted referrals from primary care and hospitals across a wide geographical area (Chapter 4). This chapter and the two subsequent chapters discuss the data that was obtained from these sources (including why they were chosen, how the data was obtained and analysed, and the results of the analysis) starting with the UK-PBC patient questionnaires.

2.2 What is UK-PBC?

UK-PBC is an MRC funded research platform which began in 2007 with the primary goal of establishing why a significant proportion of patients with PBC do not respond to UDCA and to utilise this information to develop treatment strategies for these patients (http://www.uk-pbc.com/). The work of UK-PBC is divided into three work strands each with their own specific research goals. Workstrand 1 involved the recruitment of patients through both the NHS and the national patient group (The PBC Foundation) to obtain demographic and clinical data as well as blood samples in order to phenotype and stratify the UK patient cohort. Workstrand 2 looked specifically at the mechanisms of UDCA non-response by comparing data from responders and non-responders. Finally, Workstrand 3 of UK-PBC termed "the user interface" was designed to bring together pharmaceutical companies, academics researchers, clinicians and patients with the goal of pursuing clinical trials for patients who were UDCA non-responders and to develop standard of care guidelines for this condition. UK-PBC allows external researchers to access their data to answer specific research questions through a process of submitting a written application for data access.

In 2015, as part of the UK-PBC project, printed questionnaires were sent via post to patients registered in the UK-PBC research cohort. The questionnaires were undertaken in two parts: a "Health and Social care" questionnaire and a "Symptoms, Complications and Treatment of PBC" questionnaire. For this thesis, the author was able to access the blank questionnaires and following a review of the questions posed, identified six questions which had the potential to contain data relevant to the research question. The questions that were included are shown in

Appendix 1 in their original questionnaire format. Table 3 details why these questions were deemed to be relevant to the research question.

Table 3: Questions from the UK-PBC patient questionnaires of relevance to the research topic

Question	Relevance to the thesis
Do you attend a hospital for treatment of your PBC?	What proportion of patients with PBC are currently managed solely in primary care? Will the new pathway see a significant shift in where patients are managed?
What is the name of the hospital where you currently receive most of your care?	What hospitals in the UK are managing patients with PBC? - Geographical spread - Are patients managed in district general hospitals or specialist centres
How were you first discovered to have PBC?	What percentage of patients have early asymptomatic disease at the time of diagnosis, what percentage are symptomatic, and what percentage have late presentations with advanced disease?
Thinking back, how long did you have symptoms of PBC or abnormal blood tests before you were told by the doctor that you had PBC?	In real world practice, are there delays in reaching the diagnosis?
Have you ever taken UDCA for treatment of your PBC?	Are patients with PBC being treated with disease-modifying therapy?
Do you still take UDCA nowadays? And if so what is your current dose of UDCA? What is your current weight?	Are patients being treated with the correct dose of UDCA, thus permitting effective use of risk stratification tools?

2.3 Data analysis

After establishing that the questionnaire results could yield data relevant to this thesis, a written request to access the data relevant to these specific questions was made to UK-PBC and approval was received. The data was received in the form of anonymised password protected

excel spreadsheets wherein each respondent had been given an alphanumeric code. The spreadsheets were uploaded to a secure server at the Queen Elizabeth Hospital Birmingham as per the agreement of UK-PBC. The password was then forwarded in a separate email. Once the data had been downloaded onto the server, the next step was to manually review all of the data in the spreadsheet and prepare it for analysis.

2.3.1 Cleaning the dataset

The questionnaires had been all completed by hand and then submitted to UK-PBC where they were transcribed into excel spreadsheets. Where the answer was not legible, these had only been partly transcribed with asterisks placed by the UK-PBC data transcriber to identify unclear responses. Once received by the author, all of these data points were re-reviewed. Where it was felt that the information was unclear or open to interpretation, this was removed and coded as missing. In addition, all the data that had been transcribed in full was reviewed and, where incomplete or obviously erroneous answers were identified, these were removed and coded as missing. Finally, spelling errors were corrected, and standardisation of responses was undertaken; for example, when different versions of a hospital name were given i.e. Aintree Hospital and University Hospital Aintree. Once all the data had been cleaned, it was then coded for analysis.

2.3.2 Data coding

Prior to analysis all data was coded. The structure for the data coding is shown in Table 4.

Table 4: Overview of spreadsheet coding strategy

Data point	Coding
Does the respondent attend hospital for PBC?	Yes = 1 No = 2
Name of the hospital where the respondent is managed?	Free text (standardised)
What type of health care setting is patient managed in?	Primary care = 1 Secondary care = 2 Tertiary care = 3
Mode of presentation	Incidental finding = 1 Symptom of PBC = 2 Investigation of non PBC-related symptom = 3 Risk factor for PBC = 4 Advanced liver disease = 5
Thinking back, how long did you have symptoms of PBC or abnormal blood tests before you were told by the doctor that you had PBC?	<6 months = 1 6-12 months = 2 1-2 years = 3 >2 years = 4 + free text
Have you ever taken UDCA for treatment of your PBC?	Yes = 1 No = 2
Do you still take UDCA nowadays?	Yes = 1 No =2
Current dose of UDCA?	Free text (mg/day)
What is your current weight?	Free text (kg)
Weight-based UDCA dose	Free text (mg/kg/day)

For some data points this was straightforward (i.e. do you attend hospital – Yes or No) but, for others, more complex coding was undertaken. For the question of the mode of presentation, there was a choice of responses available including tick boxes and a free text box related to

symptomatology. In the cases, where the patient described a symptom prompting their presentation, the nature of the symptom was reviewed by the author using their knowledge of the symptoms of PBC. Where the symptom is well reported in the PBC literature e.g. joint pain this was categorised into symptoms of PBC. However, where the symptom is not recognised within the PBC literature e.g. dizziness, this was categorised as a non PBC-related symptom. In total, sixteen distinct responses were identified from the data set. These were then grouped into five major categories (using the structure set out in Table 5): 1) incidental finding, 2) symptoms of PBC, 3) investigation of a non-PBC symptom, 3) presence of a risk factor for PBC or 4) investigation of advanced liver disease.

Table 5: Categories of mode of presentations

Incidental funding	Symptom of PBC	Investigation of a non PBC-related symptom	Presence of a risk factor for PBC	Investigation of advanced liver disease
• Routine medical • Routine review for other medical condition • Well person check-up	• Abdominal pain • Pruritus • Fatigue • Joint pains • Poor memory • Xanthoma	• All other symptoms	• Family history • Known other autoimmune diseases	• Ascites • Variceal bleed • Jaundice • Spider naevi

2.3.3 Statistical analysis

Descriptive statistics were used to summarise the data and all charts were generated in Excel.

2.4 Results

A total of 2263 respondents answered one or more of the questions as part of their questionnaire response. The results are summarised below.

2.4.1 Place of care

In total, 2084 responses were analysed (176 of questionnaire respondents did not answer this question while in three cases, the name of the hospital was unclear, and five named a hospital outside of the UK). Of the 2084 valid responses, 330 patients (15.8%) reported that they were managed solely in primary care, while 442 (21.2%) were managed in a hospital with access to specialist liver services including a liver transplant unit. The vast majority (1312/2084, 63.1%) were managed in a hospital that does not have a transplant centre. A total of 255 hospitals were named. The geographical spread of these hospitals is shown in Appendix 2.

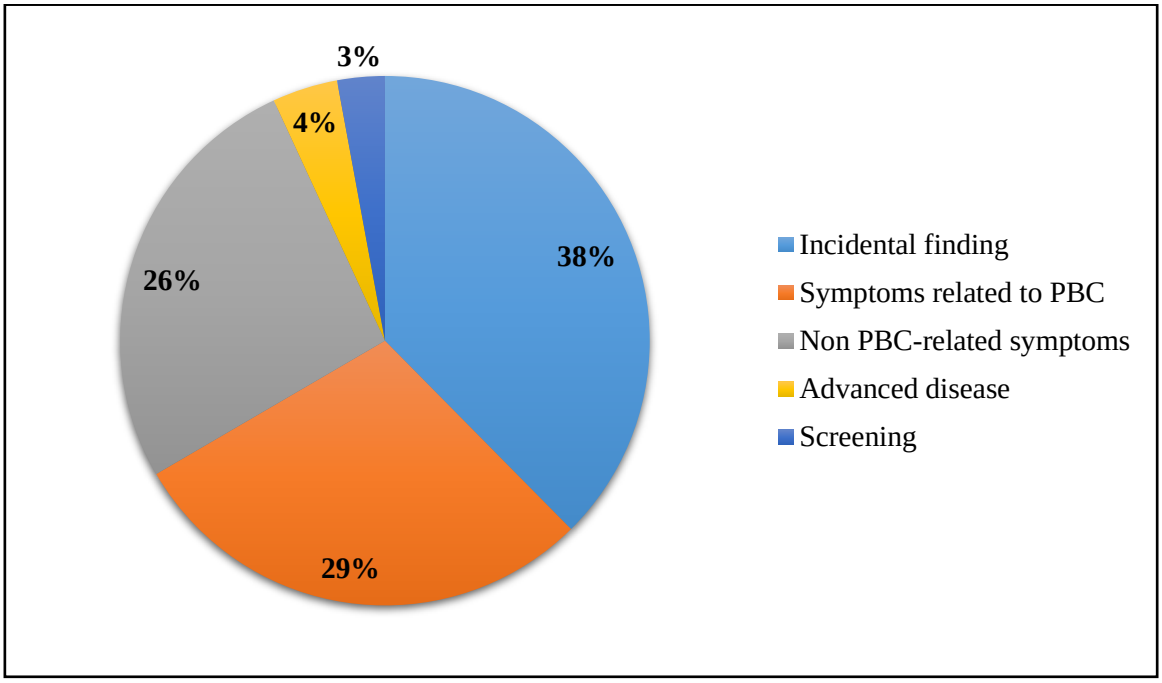
2.4.2 Modes of presentation

A total of 1844 respondents answered this question. However, four answers were removed before analysis (two answers were unclear and two answered that they could not remember) leaving a total of 1840 responses. The results are summarised in Table 6 (which shows a complete breakdown of the responses). Graph 1 shows the trend in the modes of presentation with the majority of patients diagnosed as the result of seeking medical care as the result of a symptom, although in many cases the symptom was not specific to PBC. Over a third were asymptomatic at the time of diagnosis. Only a very small number (4%) had advanced disease at the time of presentation.

Table 6: Modes of presentation of patients subsequently diagnosed with PBC

Response	Number of respondents (% of total)
Incidental finding	
- Routine review for other medical condition	460 (25.0)
- Routine medical	178 (9.7)
- Well-man/woman check	53 (2.9)
Non PBC-related symptoms	488 (26.5)
PBC symptom	
- Low energy levels	274 (14.9)
- Pruritus	200 (10.9)
- Joint problems	39 (2.1)
- Abdominal pain	18 (1.0)
- Poor memory	2 (<1.0)
Advanced liver disease	
- Jaundice	46 (2.5)
- Gastrointestinal bleeding	21 (1.1)
- Ascites	6 (<1.0)
- Xanthoma	1 (<1.0)
- Spider naevi	1 (<1.0)
Risk factor for PBC	
- Presence of other autoimmune condition	34 (1.8)
- Family history of PBC	19 (1.0)

Graph 1: Trends in the mode of presentation



2.4.3 Time from initial presentation to diagnosis

A total of 1752 respondents answered the question of the length of time (in years) from first presentation to subsequent diagnosis of PBC. 304 respondents (17.3%) reported a time from presentation to a diagnosis of greater than two years (range 2.25 – 35 years with a mean of 7.7 years). Of note, the reason for the gap in time from presentation to diagnosis was not captured by the questionnaire.

2.4.4 Use of UDCA

All respondents were asked whether they had ever taken UDCA and, if they answered yes, were then asked if they still took this medication and if so, what their current dose of UDCA was. Additionally, they were asked for their current weight. Respondents were given the option of

reporting their weight in either stones or kg; where they reported this figure in stones this was converted to kg prior to further analysis (as dosing guidelines for PBC are 13-15mg/kg). For those who gave a weight range rather than a single number, the middle value was chosen (e.g. where they said between 10 and 11 stone, 10 and a half was chosen). This data was then used to work out what their current weight-based dose was in mg/kg by diving their dose by their weight (rounded to the nearest 0.1mg/kg).

Of the 2183 respondents who answered this question, 1961 (89.8%) reported having ever been prescribed UDCA with 1775 (81.3%) taking this medication at the time of completing the questionnaire indicating that the use of UDCA is common although not universal in practice. However, only 356 of the 1552 respondents (22.9%) were on the correct dose of UDCA for their weight. The range of doses was from 1.3-47mg/kg with a mean dose of 12.6mg/kg.

2.5 Relevance of results to the research topic

The results presented above highlight a number of areas within current clinical practice that need to be considered when looking at guideline implementation and would be appropriate for further exploration in the patient and clinician interviews.

2.5.1 Current patterns of place of care

Whilst it is estimated that between 60-70% of patients are responders to UDCA and therefore could be managed within primary care, only 15.8% of those questioned report that they are currently managed in primary care. This finding would suggest that implementation of stratified care pathways would result in a significant shift in the pattern of care in the UK.

2.5.2 The path to diagnosis

As has been reported in the literature previously, presentations with advanced liver disease were uncommon within this population with the majority being diagnosed when undergoing investigation for unrelated symptoms or at the time of routine health checks. This may explain why the time from presentation to diagnosis was so variable (ranging from <6 months to over 35 years with a mean of 7.7 years). This is in keeping with previously published data on the diagnosis of rare disease. In 2004, a survey encompassing eight rare diseases carried out by EURODIS (a non-governmental alliance of patient organisations representing 905 rare disease patient organisations in 72 countries) found that 25% of patients had to wait between 5 and 30 years from early symptoms to confirmatory diagnosis of their disease (69). From the UK-PBC data, it is not possible to conclude as to the reason for the delays and this again requires further study as does whether the impact of the time to reach a diagnosis may be relevant to how patients view primary care as the place for long-term follow-up and disease management. These will be explored in more detail in the interviews with patients and clinicians.

2.5.3 The use of UDCA and adherence to dosing guidelines

Lastly, UDCA response underpins the concept of risk stratification in PBC and it is interesting to note that while 89.8% of respondents reported ever having been on this medication only 23% appeared to be on the correct weight-based dosing. This data however, having not been captured from the patients' medical records should be viewed with caution, especially given the extremes of dosing reported.

2.6 Limitations to the data

Whilst the data presented above highlights a number of areas that are relevant to the implementation of stratified care in practice and captures data from a large group of patients across the UK there are limitations to this data. The questionnaires were designed by UK-PBC independently from the research described in this thesis, and as such, the questions were not devised by the researcher and the data was analysed post hoc. Due to the nature of how the patients within the UK-PBC research cohort were recruited, those within hospital-based follow-up as opposed to primary care are likely to be over-represented. In addition, the findings of long lag times from the time of presentation to diagnosis are entirely self-reported by patients and without the ability by the author to access the patients' medical records, and may overestimate time to diagnosis. Finally, in the case of UDCA dosing, the patients' responder status was not captured, and neither was the reason (if any) for being on lower than recommended doses.

2.7 Chapter summary

This chapter describes data looking at features of PBC within a UK population including place of care, modes of presentation, time to diagnosis and use of disease-modifying treatment. The data shows that the majority of patients in the UK are managed in secondary care and highlights that the early phase of the disease pathway is not straightforward with potential challenges to making the diagnosis. The impact and underlying reasons for these findings will be explored in more detail in later chapters presenting and discussing the qualitative portion of this research.

The next chapter will look at aspects of management of PBC from the perspective of the secondary care clinician.

CHAPTER 3: SURVEY OF UK CLINICIANS

Disclaimer:

Results from the UK clinician survey have been presented in poster format at AASLD in 2015 (70) and the BSG Annual meeting in 2016. Dr Corrigan was a co-author on a paper based on the findings of the US survey developed by Projects in Knowledge (71).

3.1. Chapter overview

The previous chapter describes data from a series of patient questionnaires looking at a range of aspects of PBC care in the UK. This data analysis identified that the majority of patients with PBC are currently managed either in a secondary care or tertiary care based setting, that modes of presentation and time from presentation to diagnosis are variable, and that while the majority of patients are currently or have previously been treated with UDCA, the majority are not on the recommended doses. This chapter presents results from a survey of UK clinicians undertaken in 2015. The rationale for undertaking this survey analysis as part of this thesis, as well as the development of the survey tool, data analysis methods and the results, are described below.

3.2 Background to undertaking the UK clinician survey

As set out in Chapter 1, in order for a stratified care approach to the management of PBC to be implemented and for patients with low-risk disease to be successfully discharged to primary care, there are a core group of factors to be considered (Table 2). These include the diagnosis of the condition when patients have early disease, use of UDCA at the correct weight-based dose, and the use of risk stratification tools to determine which patients are low-risk. As a

Clinical research fellow working in the field of PBC, I was aware of a US survey of clinicians that addressed some of these factors and that could be relevant to the research question posed by this thesis. This survey was presented initially in 2014 in the form of a poster at the EASL annual conference (http://www.projectsinknowledge.com/Activity/pdfs/posters/2224-EASL_poster.pdf) and was later published in full in 2018 (71). It was undertaken by a company called "Projects in Knowledge" which is a company based in the United States (US) providing online medication education across a variety of health care specialities. The survey took the form of an online questionnaire emailed to Gastroenterologists and Hepatologists working in the US who were involved in the care of patients with PBC. Respondents were asked to self-rate their competence in a number of areas related to the management of PBC and to state how often they would perform specific interventions in clinical practice. The results demonstrated that over 85% of both hepatologists and gastroenterologists rated themselves as highly competent in diagnosis, and 80% reported that they always or often used UDCA in patients with PBC. When it came to new emerging therapies at the time, such as Obeticholic acid, Nor-UDCA, Rituximab and Fibrates, competence levels were lower. Finally, and of most relevance to the research question posed within this thesis, only 76% of Hepatologists and 42% of Gastroenterologists reported that they always or often used criteria to assess UDCA response while only 36% of Hepatologists and 30% of Gastroenterologists felt highly competent in the use of these tools.

Given these findings, and with permission from Projects in Knowledge, a survey of UK based clinicians was undertaken by UK-PBC using similar questions. As a clinical research fellow within the NIHR Birmingham Liver BRU Centre for Liver Research, I was part of the team that carried out the survey. I was responsible for developing the initial draft of the UK survey with

input from representatives from UK-PBC who provided feedback on the initial draft of questions before the final survey was generated. I was also responsible for creating the electronic survey tool, arranging distribution of the survey and analysing the data. This data has been analysed in further detail for inclusion in this thesis and the results are discussed below.

3.3 Survey development

Once the questions to be included had been finalised, they were converted into an electronic survey using the SurveyMonkey tool. SurveyMonkey is a commonly used platform for healthcare surveys and was likely to be well known to the recipients of the survey. Secondly, the online survey tool had several features that were desirable including a running "tracker" which gave the respondent a clear indicator of how many questions were left to complete in the survey and the likely time remaining. This form of within-survey feedback has been shown to reduce the likelihood of responder drop-out and non-completion (72). Another advantage to an internet-based format in comparison to paper-based questionnaires is that, once completed, the results are easily downloaded meaning that there is no need for data to be manually inputted by the researcher which is both time-efficient and eliminates the risk of transcription errors (73). The SurveyMonkey tool also employs survey logic meaning that the respondent is directed through the questions based on their response to previous questions. For example, in the case of the survey described within this chapter, where a respondent answered that they always used UDCA response criteria, they were then directed to a question asking which criteria they most commonly used. However, where a respondent indicated an option other than "Always" they were then directed to a question which asked them to give the reason for not using response criteria before then moving on to the next question. Once the survey tool had been created, a

number of trials were undertaken to ensure that, where survey logic had been used, the tool correctly guided the respondent through the correct series of questions.

The question styles used took two distinct forms:

1) Tick box structure was used where a statement of fact was required (for example How many patients with PBC have you seen in the last 12 months?)

2) Five-point Likert scale which was used when respondents were asked to rate their confidence in a particular aspect of management.

The use of scales within a questionnaire which allows respondents to self-rate their "attitude" to a given statement was first described by Rensis Likert in 1932 (74). Likert type scales are commonly used in questionnaires and surveys where respondents are asked to state the likelihood of them undertaking a particular action, to rate the strength of an opinion, or to self-rate confidence levels. Most commonly these types of scale are based on a 5 or 7 point (although higher or lower numbers can be used) ordinal scale where the choices comprise a series of options in a clear ascending or descending order for example "Always, Often, Sometimes, Rarely, Never". However, unlike a purely numerical scale, the difference between each point or choice is not necessarily equal (75). Likert type scales were used in this questionnaire for both the self-rating of confidence and where respondents were asked about the likelihood of undertaking an action. The decision to use a Likert scale was made as it was felt that firstly it would allow respondents more scope to report their confidence level compared to a "yes/no" question style. Secondly, as these scales had been used within the US survey it allowed the potential for comparisons to be made between the two sets of results. In contrast to the US survey however, the term confidence was used instead of competence as it was felt to be a

preferable term without the negative connotations that could be interpreted from being "not competent".

3.4 Survey distribution

Once the survey was deemed to be working correctly, it was distributed to all clinicians registered on the mailing lists of two UK health care professional groups: The British Society of Gastroenterology (BSG) and the British Association for the Study of Liver disease (BASL). Clinicians within the UK may be a member of one or both of the groups. Inclusion of both groups was chosen to ensure access to a broad range of clinicians across the UK. Both groups distribute similar surveys to their respondents through both mailing lists, websites and newsletters regularly. In addition, as membership of these organisations is through a formal application process and confirmation of professional status is required, this ensured that while respondent identity was anonymous, there was confirmation that respondents were registered medical practitioners within the disciplines targeted by the survey.

The BSG is an organisation comprising gastroenterologists, surgeons, pathologists, radiologists, academics, nurses and other allied health professionals. It has approximately 3000 trainee and full members with 1897 subscribed to the mailing list at the time this survey was undertaken. A link to the survey was sent to all of those on the mailing list through the weekly e-newsletter followed by an email reminder. BASL is a multi-disciplinary society made up of over 1000 clinicians, academic scientists and allied health professionals. A link to the survey was sent to all subscribing members through the e-newsletter (n=850) and was highlighted as a news item on the website.

The survey link was active for a total of 6 weeks in April – May 2015. No limit on respondents was set and, by the end of the survey period, a total of 206 responders had taken part in the survey (defined as opening the survey and responding to at least one question).

3.5 Methods

The following section details the questions that were posed to survey respondents, the rationale for question inclusion and data analysis techniques. The full list of questions is shown in Appendix 3.

3.5.1 Respondent demographics

Respondents were first asked to choose their professional role from a series of options. Unlike the US survey which captured only Hepatologists or Gastroenterologists, the UK survey also sought responses from trainees within Gastroenterology and Specialist nurses. For those describing themselves as Hepatologists, this term was further sub-divided into those working within transplant centres, those working in tertiary centres, and those in secondary care. For Gastroenterologists, the option was given for those with a specialist interest in hepatology, general gastroenterology, or gastroenterology with another specialist interest. In addition, respondents were asked to report how many patients with PBC they had seen in the previous 12 months. The decision to capture data on specific professional roles and number of patients seen was deemed to be important in determining the range of respondents and to see the impact of specialist knowledge of the clinicians who are managing patients with PBC.

3.5.2 Diagnosis

In order to diagnose PBC, a patient must have chronic cholestatic liver biochemistry in addition to a positive AMA titre and/or liver histology in keeping with PBC. When AMA testing is undertaken, the results are often in the form of an antibody titre and it is the role of the clinician to review the results and correlate with the clinical scenario in order to make the diagnosis. However, the clinical scenarios in which PBC may be considered and tested for are variable, and include not just the presence of cholestatic liver biochemistry, but also symptoms such as itch or fatigue, identification of the presence of cirrhosis, or in the screening of a patient who has another autoimmune disease. Respondents were asked to choose from a list of clinical scenarios to indicate those in which they would check AMA and then how confident they felt in the interpretation of the results.

3.5.3 Use of UDCA and response criteria

Once PBC has been diagnosed, the first-line treatment as set out in existing guidelines is UDCA prescribed at a dose of 13-15mg/kg. Respondents were asked how often they would initiate UDCA in a patient with confirmed PBC. Those who responded with an answer other than "Always" were then asked a follow-up question as to the reason they would not initiate UDCA and were given the opportunity to complete a free text answer. In addition to the use of UDCA, the appropriate use of response criteria is essential for the use of stratified models of care. As such, respondents were asked to state whether they used formal response criteria in practice, and if so, which criteria they used. Where a respondent indicated that they did not always use UDCA response criteria, they were then given a free text to explain why they would not use response criteria. Finally, all respondents were asked to rate their confidence in using UDCA response criteria.

3.5.4 Symptom management

The symptoms of PBC, specifically itch and fatigue, are common concerns for patients with PBC and can be challenging in practice. Therefore, respondents were asked to rate their confidence in the management of itch as well as to give a free text response to their first-line treatment. They were then asked to self-rate their confidence in the management of fatigue. In the absence of any guidelines for the management of fatigue which remains a challenging area in PBC care, respondents were not asked any further questions about its management.

3.5.5 Complications of cirrhosis

Whilst not all patients with PBC will develop cirrhosis, the management of the complications of cirrhosis, including varices and hepatocellular carcinoma are relevant to PBC. In addition, given that these conditions are common to all forms of chronic liver disease it was felt that the comparison between self-rated confidence levels in these areas versus confidence in areas specific to PBC would be of interest.

3.5.6 Discharge to primary care

As a final question, all respondents were asked to rate how likely they were to discharge a patient who was not cirrhotic and deemed to have "low-risk" PBC to primary care. This question had not been included in the Projects in Knowledge survey but was added to the UK survey due to its relevance to the implementation of stratified care.

3.6 Data analysis

At the end of the survey period, the results were downloaded from the SurveyMonkey site to an excel spreadsheet which was stored on a University of Birmingham server under password protection. Prior to analysis, the data was "cleaned" removing any answers that were obviously incorrect and, where free-text answers were given, these were grouped into categories to aid analysis. This process is described in more detail in the relevant section below. Descriptive statistics are used to present the results. Charts were produced using Excel.

3.7 Results

3.7.1 Respondent characteristics

Of the 206 respondents who started the survey, all completed the question related to their professional role (Table 7) and 204 reported the number of patients seen over the previous 12-month period (Table 8). The majority of survey respondents were Gastroenterologists, many of whom did not have a specialist interest in PBC and over half of the respondents stated that they saw ten patients or fewer with PBC per year. This is in keeping with the results from the patient questionnaires showing that the majority of patients are seen within secondary care settings (rather than tertiary specialist units), and that patient care is spread across multiple hospitals.

Table 7: Professional role of respondents

	Number of respondents (% of total)
Consultant hepatologist in a transplant centre	6 (2.9)
Consultant hepatologist in a non-transplant centre	9 (4.8)
Consultant gastroenterologist with a specialist interest in hepatology	31 (15)
Consultant gastroenterologist with other specialist interest	33 (16)
Consultant gastroenterologist (general)	42 (20.3)
Registrar/trainee	83 (40.3)
Clinical nurse specialist	2 (1)

Table 8: Number of patients with PBC seen by respondents over the previous 12 months

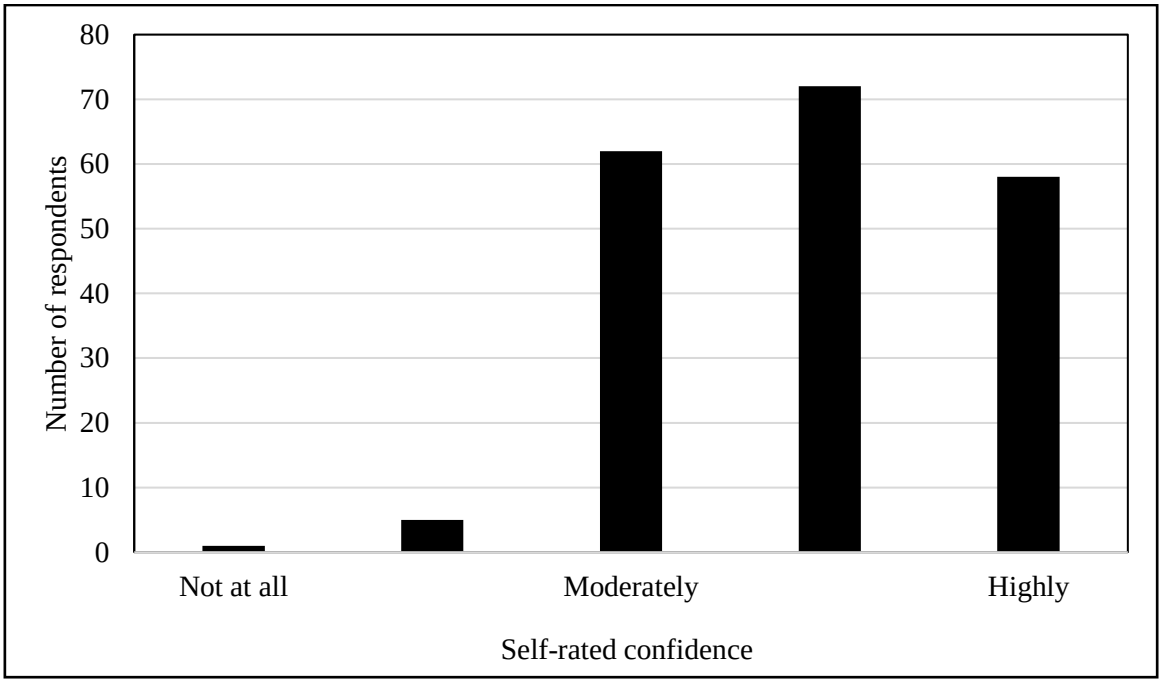
	Number of respondents (%)
0	6 (3%)
1-10	103 (52%)
11-20	49 (25%)
21-50	36 (18%)
51-100	4 (2%)
100+	6 (3%)

3.8.2 Use and interpretation of AMA

One hundred and ninety-nine respondents completed the self-assessment of confidence in the interpretation of AMA in patients with suspected PBC where confidence was rated on a Likert

scale of 1-5 (where 1 was not confident and 5 was highly confident) with the majority rating themselves towards the higher confidence end of the spectrum.

Graph 2: Interpretation of AMA results in a patient with suspected PBC



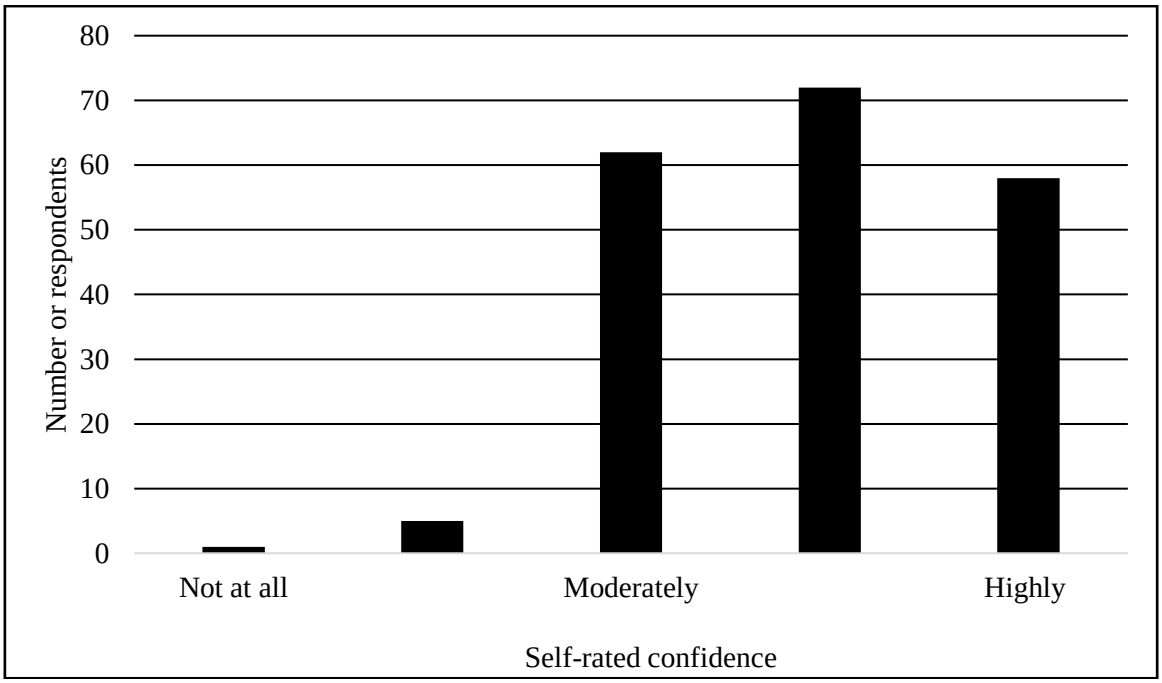
	Not at all		Moderately		Highly
n (%)	1 (0.5)	5 (2.5)	62 (31.3)	72 (36.4)	58 (29.3)

3.8.3 Use of UDCA and assessment of response

Two hundred respondents answered the question regarding UDCA initiation. In keeping with the results from the patient questionnaires, use of UDCA was common although not universal. However, unlike the patient questionnaire which did not capture why a patient was not on UDCA, within this survey there was the opportunity to ask clinicians for their reasons for not using UDCA and all those responded with an answer other than "Always" were then asked a follow-up question. In order to allow respondents' scope to state their reasons, this question was

asked as a free text. When all the free-text responses were reviewed, they were then grouped into categories according to the reason given; these categories are shown in Table 9.

Graph 3: Initiation of UDCA in a patient with a confirmed diagnosis of PBC



	Not at all		Moderately		Highly
n (%)	1 (0.5)	5 (2.5)	62 (31.3)	72 (36.4)	58 (29.3)

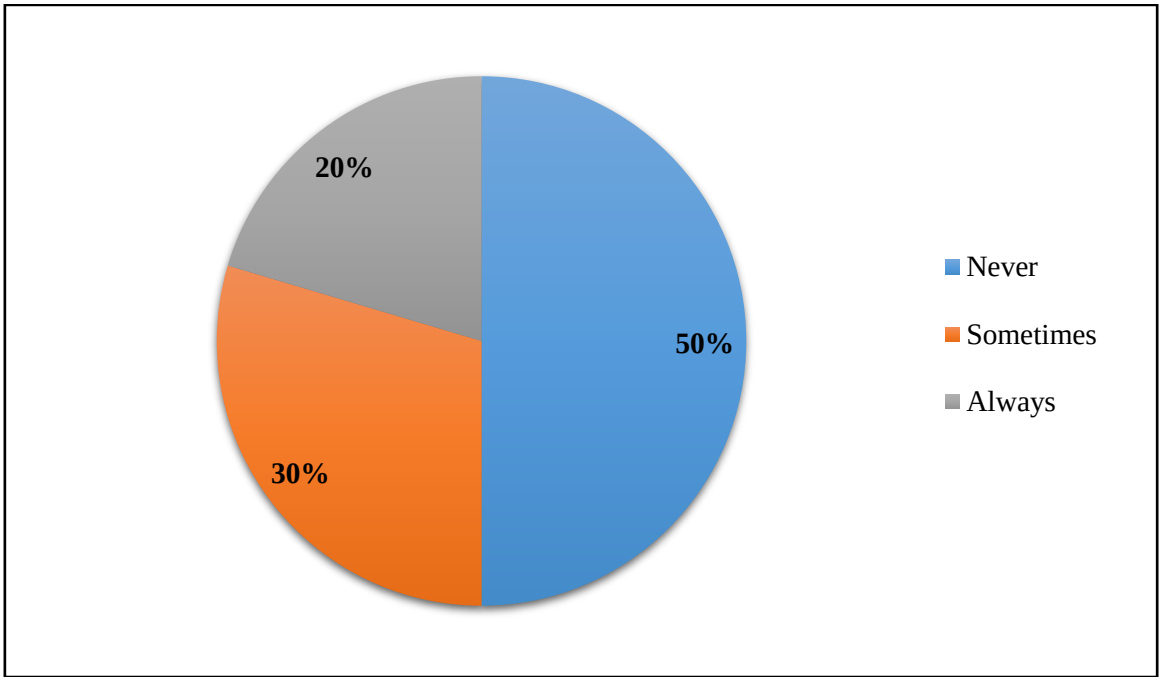
Table 9: Reasons for not initiating UDCA at the time of diagnosis

	Number of respondents (%)
Advanced disease at the time of diagnosis	5
Age/frailty	18
Allergy	8
Asymptomatic	21
Drug interaction	2
Itch	3
Normal or near normal liver biochemistry	61
Patient choice	28
Referral on to specialist	4
Referral to participate in a clinical trial	2

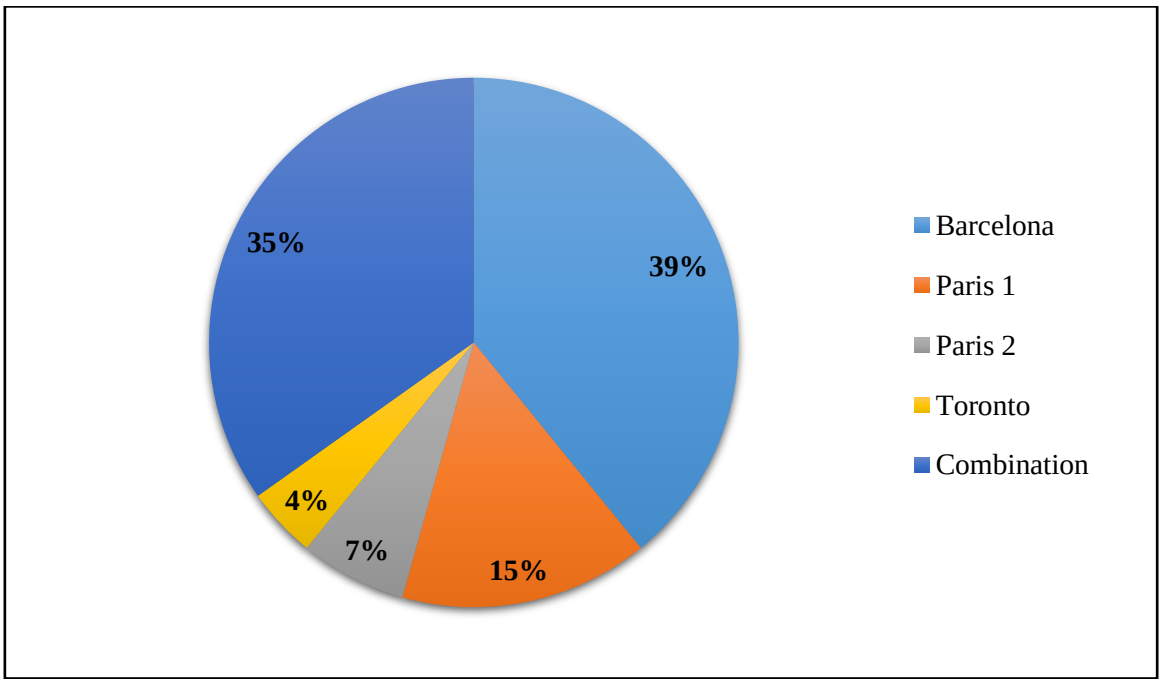
NB: some respondents gave more than one answer in the free text box

In addition, respondents were also asked to state whether they used specific criteria to determine a patient's response to UDCA (Graph 4) and, if so, what criteria they used (Graph 5) along with their self-rating of confidence in using these scoring systems (Graph 6). Those who did not use response criteria were asked to provide the reason why not (Graph 7). In total 98 respondents (50%) reported that they never used UDCA response criteria in clinical practice, while 58 (29.6%) used it in some cases and 40 respondents (20.4%) always performed formal UDCA response assessment.

Graph 4: Use of UDCA response criteria in clinical practice

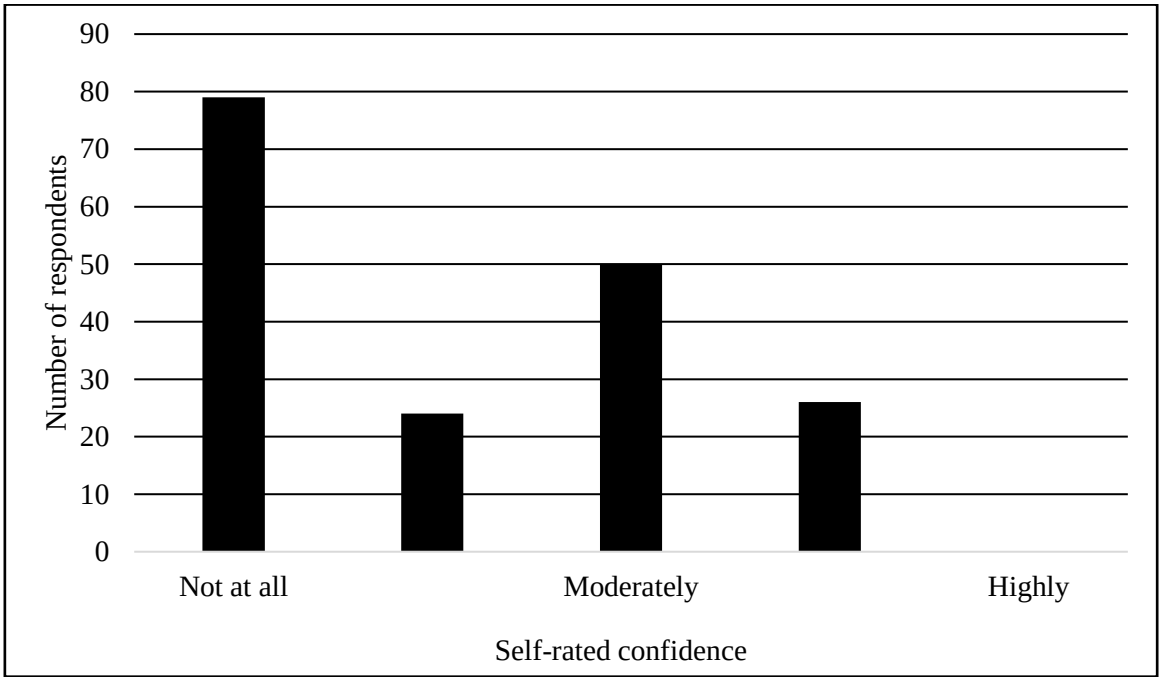


Graph 5: Response criteria used in current practice



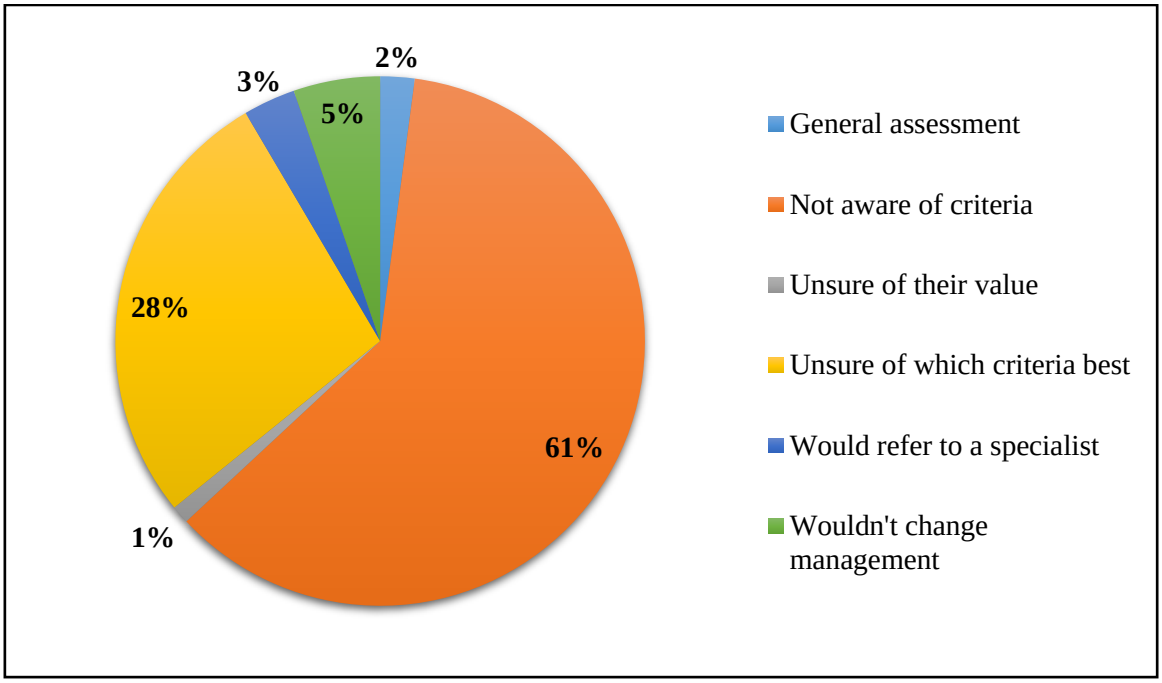
In terms of reasons for not using formal response criteria, nearly two-thirds of respondents (58/95, 61%) stated they were not aware of criteria, and a quarter (26/95, 27%) were unsure which criteria were best. This lack of knowledge around UDCA response criteria is highly relevant to the implementation of stratified care.

Graph 6: Use of UDCA response criteria



	Not at all		Moderately		Highly
n (%)	79 (41.8)	24 (12.7)	50 (26.5)	26 (13.8)	10 (5.3)

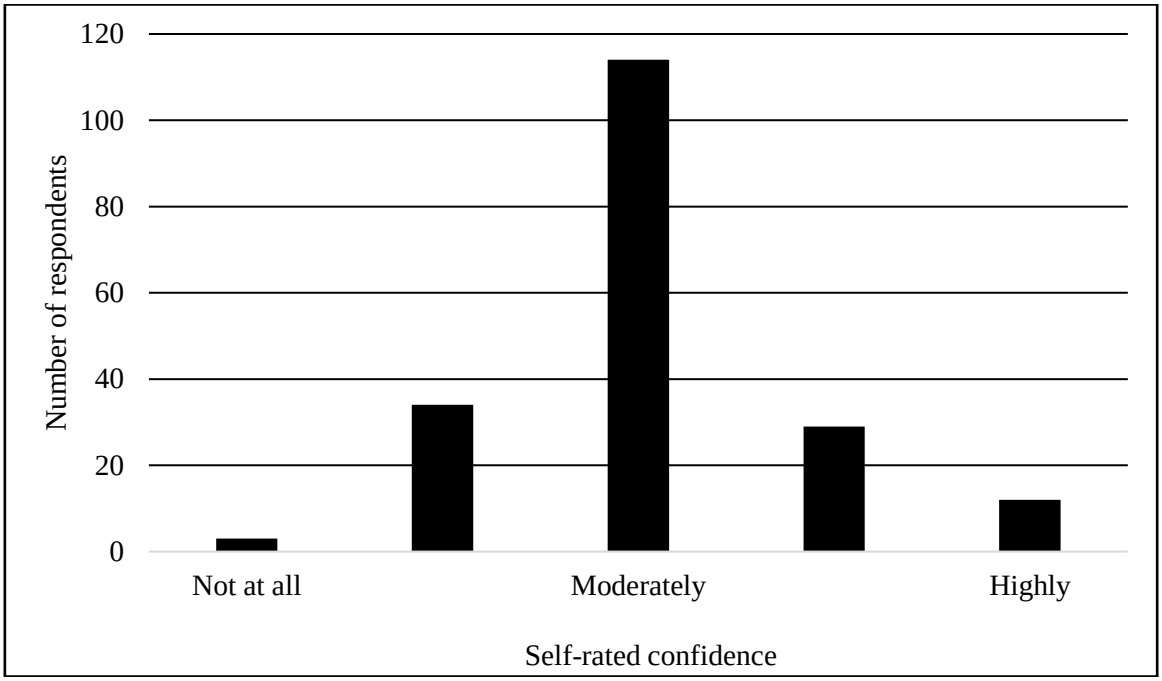
Graph 7: Reason for not using UDCA response criteria



3.8.4 Assessment and management of pruritus

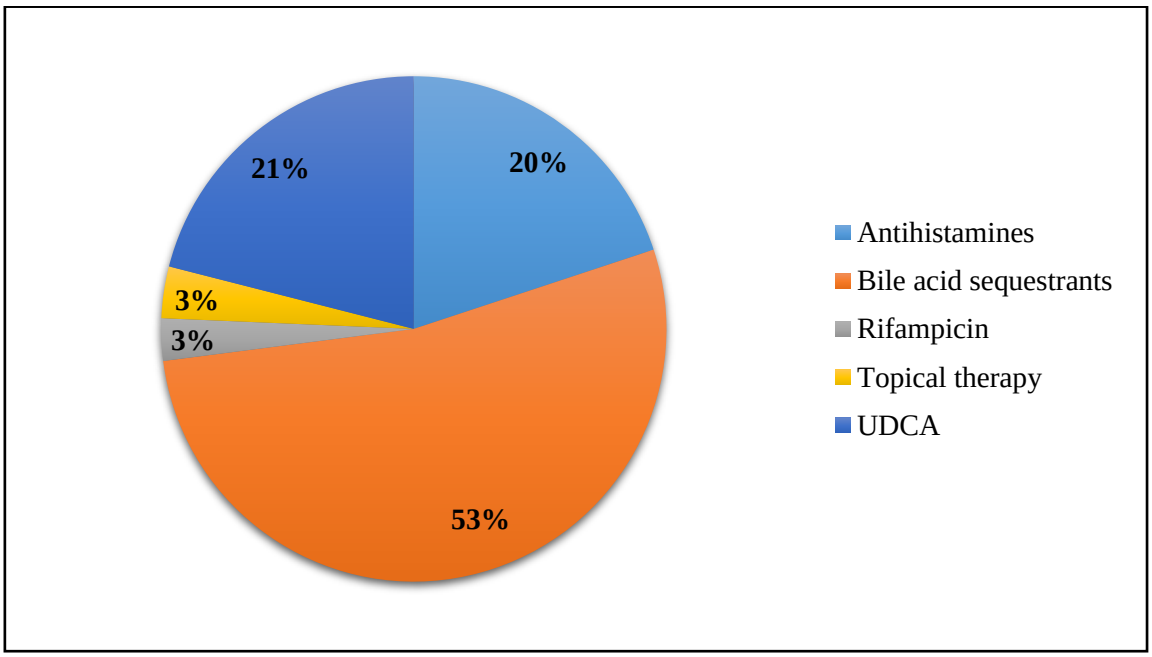
One hundred and ninety respondents rated their confidence in the management of itch in patients with PBC (Graph 8). Scores here were higher than those for UDCA response criteria. However, while most rated themselves towards the top end of the scale when given a free text option to state their first-line treatment of choice for itch, a variety of responses were given (Graph 9).

Graph 8: Management of pruritus



	Not at all		Moderately		Highly
n (%)	3 (1.6)	34 (17.7)	114 (59.4)	29 (15.1)	12 (6.3)

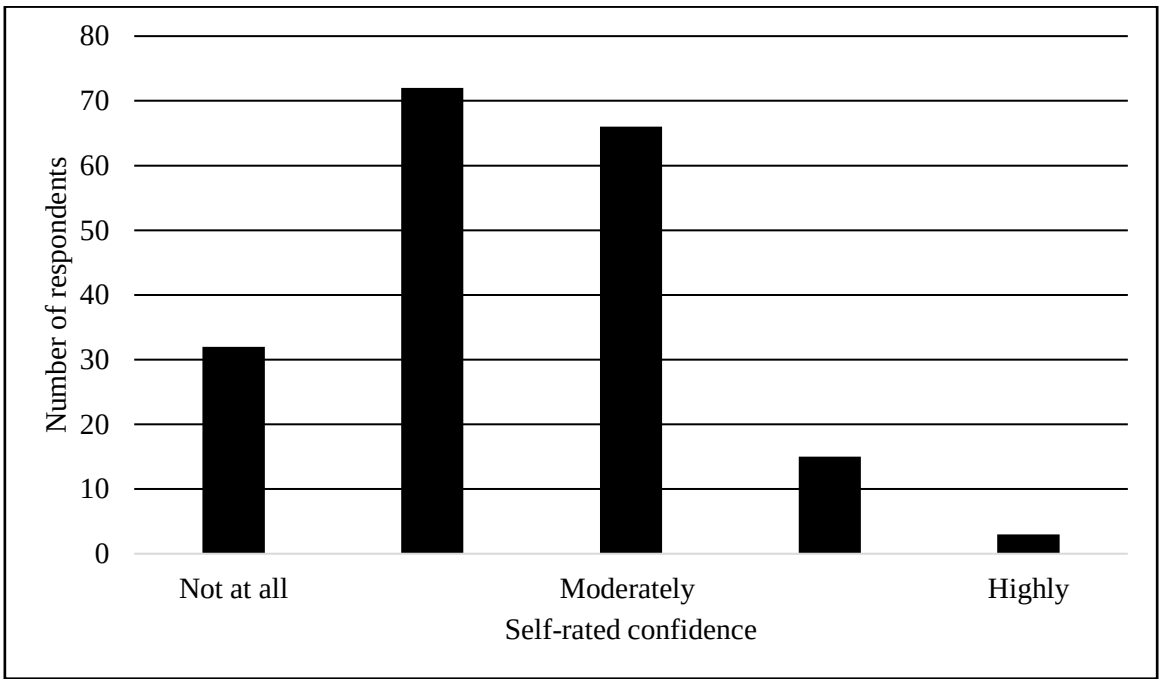
Graph 9: First-line treatment for itch in patients with PBC



3.8.5 Assessment and management of fatigue

Unlike itch, for which there is a clear treatment algorithm, fatigue management in PBC is more challenging. This was evidenced by the results from the 188 respondents who rated their confidence in the management of fatigue in patients with PBC (Graph 10) with more rating themselves towards the lower end of the scale.

Graph 10: Management of fatigue

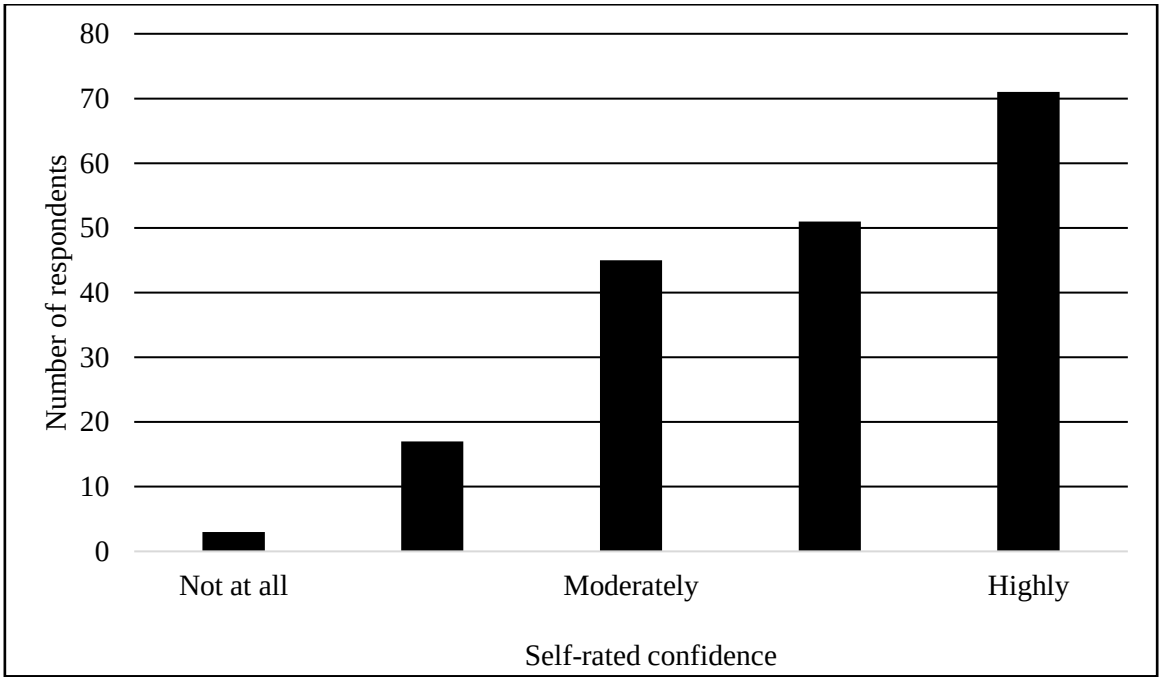


	Not at all		Moderately		Highly
n (%)	32 (17)	72 (38.3)	66 (35.1)	15 (8)	3 (1.6)

3.8.6 Management of the complications of cirrhosis

As might have been expected, when asked to self-rate their confidence in the management of cirrhotic complications in the context of PBC, many respondents rated themselves towards the higher end of the scale (Graph 11).

Graph 11: Surveillance and screening for complications



	Not at all		Moderately		Highly
n (%)	3 (1.6)	17 (9.1)	45 (24.1)	51 (27.3)	71 (38)

3.8.7 Comparison of confidence scores

It is clear from the data that there are some areas on PBC management that are less well understood by clinicians that are looking after patients. Of particularly relevance to the research question posed by this thesis are the low knowledge levels and confidence levels around the use of UDCA response criteria that are necessary to implement a stratified care approach. This

lack of knowledge cannot purely be explained by PBC being a rare disease where clinicians manage only a small number of patients but rather seems to be specific to this aspect of care. When confidence scores for different aspects of PBC management were compared, there was evidence of variability in confidence levels. In the case of AMA interpretation and cirrhotic complications, the results were skewed towards the higher ratings. However, when it came to using UDCA response criteria, the results trended towards the lower rating and were more similar to the responses for the management of fatigue in PBC. Whilst difficulties in managing fatigue can be readily explained (the pathophysiology is poorly understood and there are no treatments that have been shown to be effective) this explanation cannot be as easily given to use of UDCA response criteria.

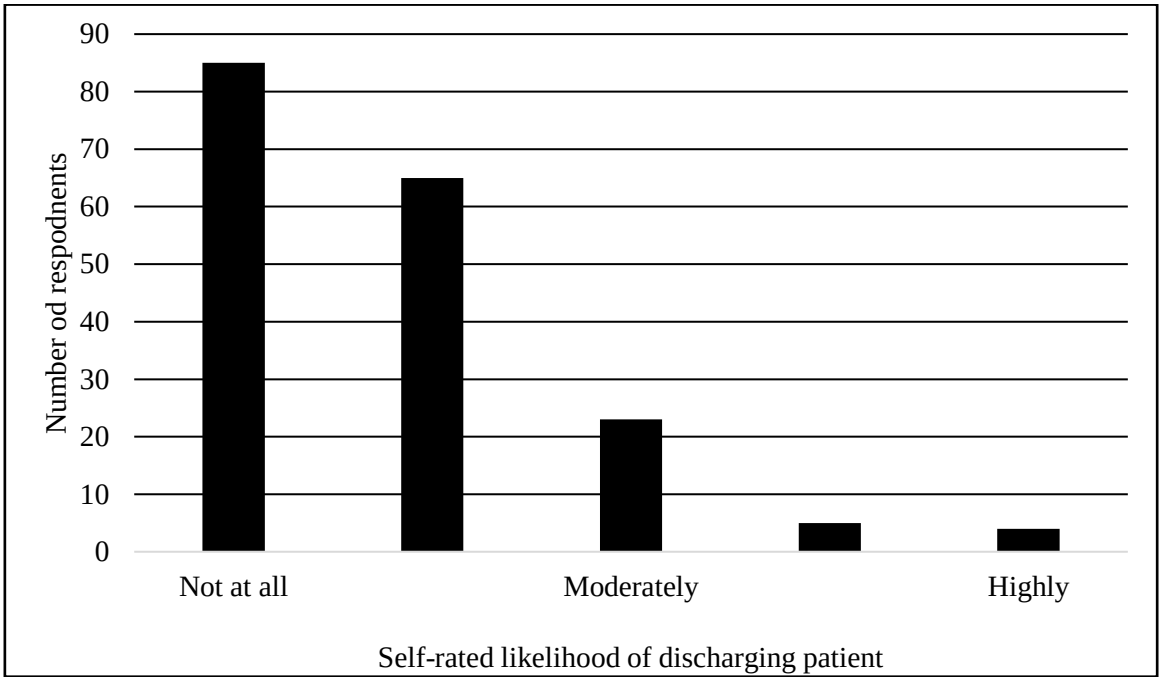
Table 10: Comparison of confidence scores

	Not at all		Moderately		Highly
AMA interpretation	1 (0.5)	5 (2.5)	62 (31.3)	72 (36.4)	58 (29.3)
Use of response criteria	79 (41.8)	24 (12.7)	50 (26.5)	26 (13.8)	10 (5.3)
Management of itch	3 (1.6)	34 (17.7)	114 (59.4)	29 (15.1)	12 (6.3)
Management of fatigue	32 (17)	72 (38.3)	66 (35.1)	15 (8)	3 (1.6)
Screening for complications	3 (1.6)	17 (9.1)	45 (24.1)	51 (27.3)	71 (38)

3.8.8 Discharge of UDCA responders to primary care

It is currently unknown whether it is common in UK clinical practice to discharge patients deemed to have low-risk disease back to the care of their GP or whether clinicians would consider this approach. As such, all respondents were asked this question in order to capture a snapshot of opinion from clinicians. Of the 182 respondents who answered this question, the majority stated that they would be unlikely to do this (Graph 12).

Graph 12: Discharge of a low-risk patient to primary care



	Not at all		Moderately		Highly
n (%)	85 (46.7)	65 (35.7)	23 (12.6)	5 (2.7)	4 (2.2)

3.9 Discussion

Results from this survey of UK clinicians identified a number of themes that are of potential relevance to the implementation of stratified care. Whilst not capturing data from all UK clinicians, data from this survey would suggest that care of these patients is currently spread across a large number of clinicians with various levels of expertise, many of whom manage small numbers of patients. In a number of cases by those who report a specialist interest that is not related to chronic liver disease.

Whilst reported levels of confidence levels are high for several aspects of management including AMA interpretation, management of itch and surveillance for cirrhotic complications, when it comes to UDCA, use is not universal, and neither is the routine use of UDCA response criteria. This latter result has implications for the introduction of stratified care pathways and reflects the patterns seen in the US. In the US survey, only 76% of Hepatologists and 42% of Gastroenterologists reported that they always or often used criteria to assess UDCA response. In the UK survey, this number was 50%. In terms of confidence, while in the US data 36% of Hepatologists and 30% of Gastroenterologists felt highly competent in the use of these tools, these scores were lower in the UK clinician survey with less than 20% of respondents scoring themselves as more than moderately confident. Reasons stated in this survey for not using response criteria were variable but included lack of knowledge of the existence of the tools and confusion over which tool was best to use. Those regularly using the tools using a variety of criteria. Finally, only a small number of clinicians would consider discharging a low-risk patient to primary care. The reasons for this were not ascertained and are a topic for future study.

3.10 Chapter summary

The results of this survey highlight a number of potential barriers to the implementation of a stratified care pathway in PBC. Most importantly, even though UDCA response criteria have been available for many years, most clinicians are not using them, due to factors including a lack of knowledge about their existence and a lack of confidence in their use. In addition, most clinicians would currently not consider discharging a low-risk patient to primary care. The

reasons why most clinicians do not favour the discharge of these patients to primary care need to be identified and will be evaluated further during the qualitative interviews with clinicians.

CHAPTER 4: REFERRAL PATHWAY FOR PATIENTS WITH KNOWN OR SUSPECTED PRIMARY BILIARY CHOLANGITIS

4.1 Chapter overview

Previous chapters have identified that the majority of patients with PBC are managed within secondary care settings. In addition, while hospital-based clinicians report high levels of confidence in making the diagnosis of PBC, patients report that the time from initial presentation to diagnosis can be lengthy. In order to get a better understanding of how patients with suspected PBC come to be diagnosed and the patient pathway once they have entered secondary care, an audit was undertaken. This chapter describes the audit of referrals for patients with suspected or established PBC from primary and secondary care to the Queen Elizabeth Hospital Birmingham.

4.2 Background

There are no existing standards for the referral from primary to secondary care or from secondary to tertiary care, with both the previous British and European society guidelines only setting recommendations for when to refer for transplant assessment. As evidenced in the data from UK-PBC described in Chapter 2 and the clinician survey in Chapter 3, there is a wide variation in how patients present before being diagnosed with PBC and, once the diagnosis has been established, patients are managed in a variety of health care settings by clinicians with varying levels of expertise and knowledge. The majority appear to remain within secondary care being managed by non-specialists.

The QEHB has a specialist clinic dedicated to the management of patients with PBC accepting referrals from secondary care hospitals from an area extending to parts of Northwest England, Wales, the South of England, and Leicestershire. However, in addition to being a tertiary transplant centre, the QEHB is also the local hospital for patients living within the Birmingham region and referrals from primary care will also be seen directly within the out-patients clinic. As such, a review of referrals to this service was undertaken to provide insight into the spectrum of referrals made to hospital care and the reasons for referral between services.

4.3 Aims of this audit

1) To establish in which setting patients with a suspected or confirmed new diagnosis of PBC receive the diagnosis
2) To look at the pathway from primary care to out-patient clinic follow up for patients with a known or suspected diagnosis of PBC
3) To establish why patients with an established diagnosis of PBC who were previously managed by a Gastroenterologist or Hepatologist within a secondary care setting are referred to a tertiary centre
4) To look at the outcome of referrals to a specialist service

4.4 Methods

A database of all patients referred to the liver out-patient clinic at QEHB is kept on secure servers by staff employed by the hospital trust and the University of Birmingham. Information is made available to medical and academic staff at written request for specific research projects following formal registration through the hospital audit department. The hospital numbers of all patients referred to the QEHB over an 18 month period between 1st February 2013 and 30th

September 2014 with a diagnosis of definite or possible PBC was obtained from this database following request to the QEHB audit department. The data was downloaded in the form of an excel spreadsheet onto a secure hospital-based server. A total of 100 records were obtained initially; however, nine were removed due to an incorrect coded diagnosis (the patient did not have PBC). The electronic health records of the remaining 91 patients were then reviewed and the following data was collected using the data capture tool shown in Appendix 4 and added to the excel spreadsheet database.

Data collected from electronic records

- Patient demographics
- Source of initial referral – primary care, secondary care, internal referral from another speciality within QEHB
- Reason for referral from secondary care
- First clinic seen in – general hepatology, specialist PBC clinic, other specialist liver clinic
- The clinic followed up in if different from above

Data on patient demographics (age at the time of referral and gender) and source of referral was captured directly from the initial referral letter. Where patients were referred from secondary care, the hospital postcode was noted. The first clinic seen in (general hepatology, specialist PBC clinic, transplant assessment clinic, other) was identified by looking at the clinic code assigned to the patients' first attendance and corroborated following review of the first clinical correspondence (in all cases the written out-patient letter). Details of which clinic the patient was followed up in following initial review was identified using the same method. The reason for the referral was identified from a review of the referral letter. Based on the researchers existing clinical knowledge of PBC and the out-patient service at QEHB, a list of possible

reasons for referral was generated and added to the data capture tool (see Appendix 4). These were then refined following review of the first twenty records. Where a reason for referral was identified that had not been considered by the researcher, these were given a new code.

4.5 Results

Data from 100 patients were reviewed, and nine were excluded following a preliminary review of the referral letter as they had been coded as having PBC but did not have the condition. Therefore, 91 patients were included in the final analysis.

4.5.1 Source of referral

Fifty-seven patients (63%) were referred from another secondary care hospital for a specialist opinion, 23 (25%) were referred from primary care, and 11 patients (12%) were internal referrals from other specialities within the QEHB. Figure 2 shows the pathway of patients from initial referral source to QEHB. Figure 3 shows the geographical spread of hospitals referring to QEHB.

Figure 2 : Schematic of the pathway into the QEHB PBC or hepatology service and outcome following first clinic review

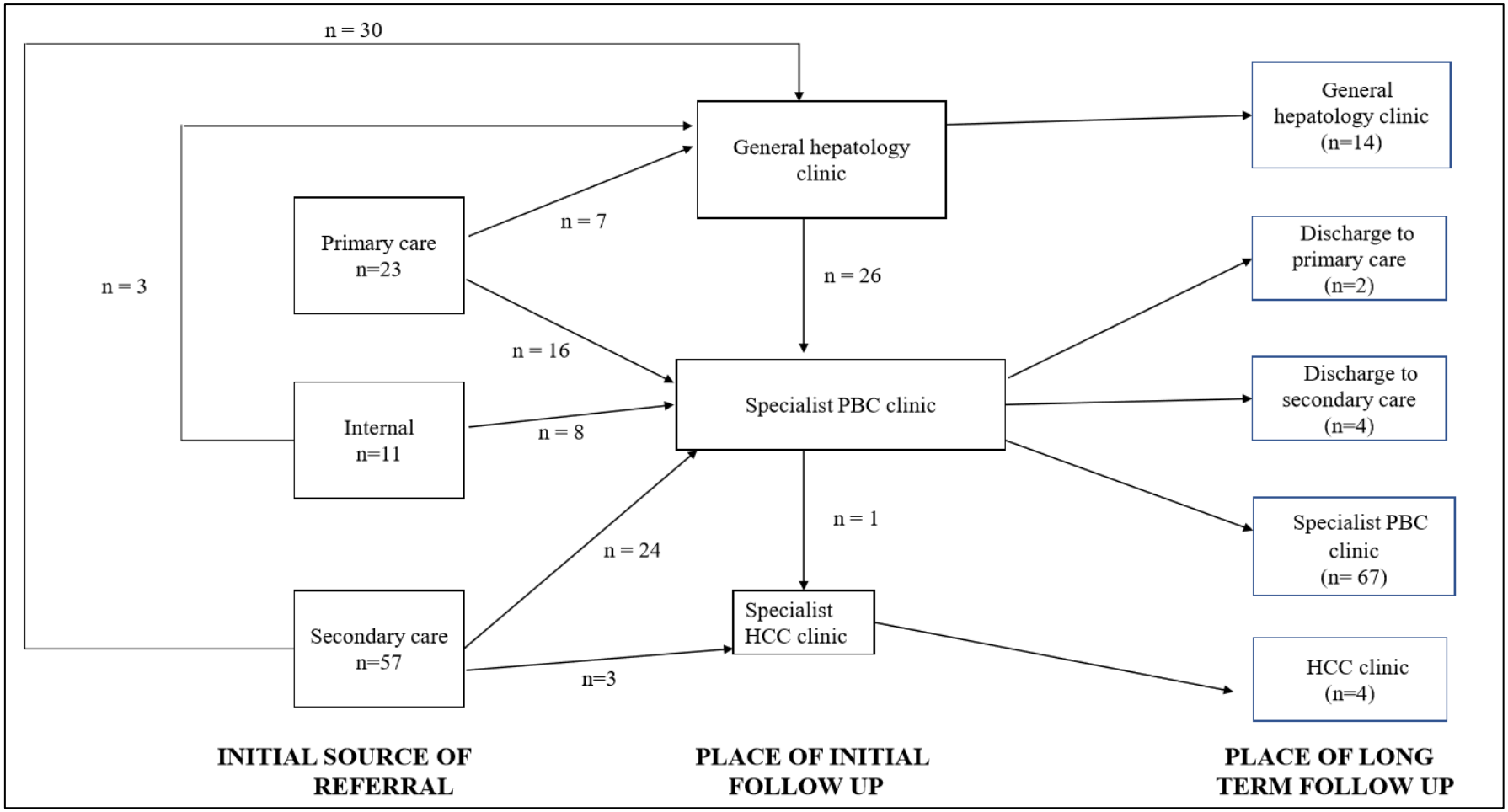


Figure 3 : Geographical spread of hospitals referring patients with PBC to the QEHB

Each numbered dot on this figure indicates the location of a hospital or hospitals that referred a patient with PBC to the QEHB during the timescale of the audit. The number in the dot indicates the number of patients referred.

4.5.2 Patient demographics

The gender and age of the patients are detailed in Table 11. Of the patients referred, 76 were female (83.5%) and 15 were male (16.5%). This is a higher percentage of males than would be suspected for a cohort of PBC patients but this was likely compounded by the high number of males within the referrals from secondary care. Within this specific cohort, males compromised 23% of all referrals, whereas only 4% of patients referred from primary care were male. The median age at the time of referral for those patients referred from secondary care was slightly younger than those referred from primary care.

Table 11: Demographics of patients referred to the QEHB

	Females total (%)	Males total (%)	Median age in years (range)
Primary care	22 (96)	1 (4)	64 (33-85)
Secondary care	44 (77)	13 (23)	53 (24-78)
Internal referrals	10 (91)	1 (9)	62 (27-78)

4.5.3 Reason for referral

Patients were referred for a variety of reasons and with varying degrees of certainty about the diagnosis of PBC, especially in the case of those referred from primary care. The stated reasons for referral are shown below.

Table 12: Summary of reasons for referral (divided by referral source)

Reason for referral	Primary care	Secondary care	Internal referral from another speciality	Total
Confirmed PBC: cholestatic liver biochemistry and positive AMA	14	0	8	22
Possible PBC – cholestatic liver biochemistry, AMA not yet checked	5	0	0	5
AMA positive, normal LFTs	4	0	3	7
Diagnosis of PBC suspected but AMA negative, referred for consideration of biopsy	0	2	0	2
Uncontrolled symptoms of pruritus	0	4	0	4
Presence of hepatocellular carcinoma on a background of HCC	0	3	0	3
Patient requested to be seen at QEHB	0	3	0	3
Transplant assessment	0	25	0	25
Suspected overlap with autoimmune hepatitis	0	9	0	9
UDCA non-responder or intolerant	0	6	0	6
Pregnant patient with known PBC	0	1	0	1
Request for a specific procedure	0	1	0	1
Reason for referral unclear	0	3	0	3

4.5.3.1 Primary care referrals

As would be expected for the referrals coming from primary care, patients were in the early stages of being diagnosed with PBC. The majority (60.9%) had confirmed PBC with both cholestatic liver biochemistry and a positive AMA; however, a small number of referrals (21.7%) had only had cholestatic liver biochemistry identified with no further investigations performed in the primary care setting (all of these five patients were seen initially in a general

hepatology clinic where AMA testing was performed to confirm the diagnosis. In four cases, AMA testing had been carried out (for reasons unclear) and was positive, however, liver biochemistry was normal.

4.5.3.2 Secondary care referrals

The reasons that patients were referred from secondary care to the QEHB were more varied. The most common reason for referral was advanced liver disease and consideration of transplant assessment (43.9%). These patients were mostly seen in general hepatology clinics rather than the specialist PBC clinic. Diagnostic uncertainty and/or complexity was the next most common reason: in two cases the secondary care physician was suspicious of the diagnosis of PBC but was unable to access liver biopsy at their hospital, in nine cases (15.8%) the secondary care physician suspected a diagnosis of overlap syndrome and requested specialist input in making the diagnosis. Of note, in three cases, the referrer stated that the patient had asked to be seen at the QEHB clinic, although in all cases, their disease was straightforward.

4.5.4 Patterns of follow up

In most cases, once the patient had been referred to the QEHB they remained under follow up long term with only six patients of the total referred (10.5%) discharged back to the referrer; of these, four were discharged back to their referring secondary care hospital and two were discharged back to primary care. In these latter two cases, the reason for this decision was that the patients were frail with significant comorbidity and it was identified that they had very mild derangement of their liver biochemistry and the clinician felt that, following discussion with the patient, that addition of UDCA and long-term follow-up would not be of benefit.

4.6 Discussion

In total, 91 patients with confirmed or suspected PBC were referred to the QEHB over the audit period of 18 months comprising referrals from secondary and primary care. Analysis of the data from this audit identified the following potential barriers to implementation of stratified care in PBC. Primary care awareness of PBC is a factor with variability in the degree of investigation of abnormal LFTs undertaken prior to referral to hospital. A third of patients referred had not had further workup beyond the finding of an abnormal ALP. It was not clear however why this had not been undertaken and whether this was due to lack of knowledge on the part of primary care clinicians or that this was felt to be the role of the specialist within secondary care to investigate for the cause of abnormal liver tests. There was evidence of patient preference for specialist input with three patients referred from secondary care being referred as they wished to be seen within a specialist unit although they did not appear to have high-risk disease. In addition, patients being referred to specialist care seemed to have advanced disease with the need for transplant assessment being the most common reason. There was however some evidence of awareness of UDCA response criteria with non-response accounting for approximately 10% of the total referrals.

4.7 Chapter summary

This audit of referrals to the QEHB clinic has confirmed the variability in the patient journey from the point of diagnosis to referral, and adds to the data from the UK-PBC patient questionnaire and the UK clinician survey regarding the variability of practice across patient care. The results in this chapter complement the data from the previous two chapters which highlight the diversity in patient care and identify that practice amongst clinicians and between hospitals is variable. Whilst there is some awareness of UDCA response, its use is not

widespread and this is an area that needs to be addressed. The data presented here also supports the suspicion that once patients enter a hospital-based follow-up, few are discharged back to primary care. In this chapter which looked at the follow-up practice of specialist clinicians who should be well aware of the criteria, the majority of patients remain in long-term follow-up in keeping with the findings in Chapter 3 where when clinicians were posed the question of whether they would consider discharging a low-risk non-cirrhotic patient to primary care follow up, the vast majority of respondents stated that they were unlikely to do this. The reasons for this will be investigated further in the qualitative interviews with clinicians.

CHAPTER 5: SCOPING REVIEW

5.1 Chapter overview

The previous quantitative data chapters have presented results from a patient questionnaire and clinician survey as well as an audit of referrals to a specialist PBC clinic. The work undertaken in these chapters and the data presented thus has set the scene in terms of current practice in PBC care in the UK from initial symptoms and first presentation, to diagnosis, management and specialist referral. However, apart from one question in the UK clinician survey around discharge to primary care, this data has not provided specific information on the patient or clinician perspective on PBC management and whether any preferences exist for management in a particular health care setting. Neither has it established whether there are barriers to management of PBC in primary care, a factor that is critical to pathway implementation. As such, the next stage of the research was to establish what is currently known about the patient and clinician perspectives on management generally and specifically around primary care and whether there is published data already available that answers the research question posed by this thesis

5.2 Scoping review manuscript

The remainder of this chapter is presented in the form of a manuscript that was developed as a result of a scoping review undertaken as part of this research thesis and which was published in BMJ Open Gastroenterology in 2018 (76).

BMJ Open Gastroenterology

Barriers to implementation of stratified care in primary biliary cholangitis: a scoping exercise

Margaret Corrigan,[1,2] Gideon Hirschfield,[1,2] Sheila Greenfield,[3] Jayne Parry[3]

To cite: Corrigan M, Hirschfield G, Greenfield S, *et al*. Barriers to implementation of stratified care in primary biliary cholangitis: a scoping exercise. *BMJ Open Gastro* 2019;6:e000226. doi:10.1136/bmjgast-2018-000226

Received 17 July 2018
Revised 31 August 2018
Accepted 7 September 2018

ABSTRACT

Patients with primary biliary cholangitis (PBC) can be stratified into low-risk and high-risk groups based on their response to treatment. Newly published guidelines from the British Society of Gastroenterology suggest low-risk patients can be managed substantially in primary care. This represents a shift from existing practice and makes assumptions about service capacity and the willingness of both patients and health care practitioners (HCPs) to make this change. The aim of this paper is to identify possible barriers to the implementation of these new care pathways through review of the PBC-specific literature and by identifying the experiences of patients and HCPs managing a different condition with comparable patients and disease characteristics. Searches of MEDLINE, CINAHL and EMBASE were undertaken. Within the existing PBC literature there is little data surrounding stakeholder perspectives on place of care. Review of the breast cancer literature highlights a number of barriers to change including primary care practitioner knowledge and work load, communication between healthcare settings, and the significance of the established doctor–patient relationship. Further research is needed to establish the extent to which these barriers may surface when changing PBC care pathways, and the actions required to overcome them.

[1]University of Birmingham, NIHR Birmingham Biomedical Research Centre, Centre for Liver Research, Birmingham, UK
[2]Department of Liver medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[3]University of Birmingham, Institute of Applied Health Research, Birmingham, UK

Correspondence to
Dr Margaret Corrigan;
m.corrigan@bham.ac.uk

INTRODUCTION

Primary biliary cholangitis (PBC), formerly known as primary biliary cirrhosis, is a chronic autoimmune liver disease. The incidence of PBC in the UK is 32.2 per 100 000,[1] with approximately 20 000 people presently affected. Incidence is higher in females compared with males (10:1) and in the fifth and sixth decade of life such that a woman over 40 years of age has a 1/1000 chance of having this condition.[2] While early natural history studies suggested that life expectancy from time of diagnosis was less than 10 years,[3] this is no longer true. Increasing understanding of the pathophysiology of the disease, along with the ability to diagnose PBC earlier in its course, and the widespread use of ursodeoxycholic acid (UDCA) has led to the recognition that, for many patients, PBC is a chronic disease but not life limiting. The name changes from 'primary biliary cirrhosis' to 'primary biliary cholangitis' was adopted into use by clinicians, researchers and patients in 2015 to reflect the emerging evidence that only a minority of patients go on to develop cirrhosis and end-stage liver failure.

Patients with PBC can be categorised or 'stratified' into two groups (responders or non-responders) based on whether or not there is an improvement in biochemical parameters following 12 months of treatment with UDCA. Those who respond to treatment with UDCA (between 60% and 70% of all patients) do not go on to develop progressive disease and have a transplant free survival similar to the general population.[4–7] Up until a few years ago, in the absence of second line treatment, those who failed to respond to UDCA were at risk of progression to end stage liver disease and liver transplantation, with younger patients and males with PBC over-represented in this group.[8] However, following recent positive outcomes in trials, obeticholic acid (OCA), a Farsenoid X receptor agonist has been approved by the National Institute for Health and Care Excellence (NICE) for the treatment of patients who have had an inadequate response to treatment with UDCA or were unable to tolerate UDCA.[9] However, despite the availability of effective treatment, there is no cure for the disease and even for those who respond, life-long treatment with UDCA is still required and patients will requirement regular follow-up.

Reflecting both the increased understanding of the natural history of PBC and the availability of second line therapy, recently published guidelines from the British Society of Gastroenterology[10] highlight the importance of formal risk stratification for all patients at 1-year postdiagnosis with management of treatment non-response or high-risk

patients necessitating discussion with specialist services for consideration of OCA or clinical trials. For those with low-risk disease, while long-term treatment and follow-up are required, it has been suggested that this does not necessarily need to take place in a hospital-based setting and there is the opportunity for an increased role for primary care services in the long-term care of these patients. These recommendations are echoed in the recent guidelines from the European Association for the Study of Liver Disease.[11]

New models of care for management of chronic liver disease as a whole are essential and timely. In contrast to other countries in Western Europe, rates of liver disease are increasing in the UK; over 600 000 people are known to have liver disease with 10% of these having cirrhosis and liver disease mortality has increased by 400% over the last 40 years.[12] The Lancet Commission on Liver Disease has highlighted the numerous challenges currently faced by the National Health Service (NHS) and by patients including inequalities in service provision (the so-called 'postcode lottery'). The Commission's recommendations included the need to improve access to specialist care and services for those most in need as well as increasing involvement from primary care and community services.[12]

However, changing patterns of established care requires 'buy in' from all users of the pathways: patients, stakeholders, and health care practitioners (HCPs) in primary, secondary and tertiary settings. This requires an appreciation of the various user's perspectives of current care, of the possible impacts any changes will have on them as new pathways are introduced, and in turn the identification of potential barriers to change and the facilitators required for these to be overcome. This paper seeks to identify what is already known about these factors in the currently available PBC literature. In addition, we also review the existing literature around patient and HCP perspectives on follow-up in a comparable condition where recent changes in management parallel the proposed evolution of PBC in order to gain insights that may be relevant to reforms in PBC care.

METHODS

Review of the PBC literature

A scoping review was chosen with the goal of establishing the type and breadth of literature available.[13] The potential remained to perform a systematic review if the scoping study revealed a large body of relevant literature. Using the framework set out by Arksey and O'Malley,[14] the following stages were undertaken: (1) identification of the research question, (2) identification of relevant studies, (3) selection of studies, (4) charting of the data (5) collation, summarising and reporting of results.

The research question was divided into two parts. (1) What is the breadth and type of literature available looking at the perspectives of patients and clinicians on all aspects of PBC and its management? (2) Is there existing data looking specifically at how patients and clinicians view the role of primary care in the management of PBC?

A search of three electronic databases: MEDLINE, CINAHL and EMBASE was carried out. A schematic of the study selection process is shown in figure 1. The following search terms were used: Primary biliary cirrhosis OR primary biliary cholangitis AND quality OR experience OR perception* OR perspective* OR attitude* OR expectation* OR understand* OR view*. Eleven hundred and fifty-one distinct citations were identified by the initial database searches with 24 included in the final analysis. In order to establish whether there were any additional resources available but not captured by the initial electronic database searches, a review of all

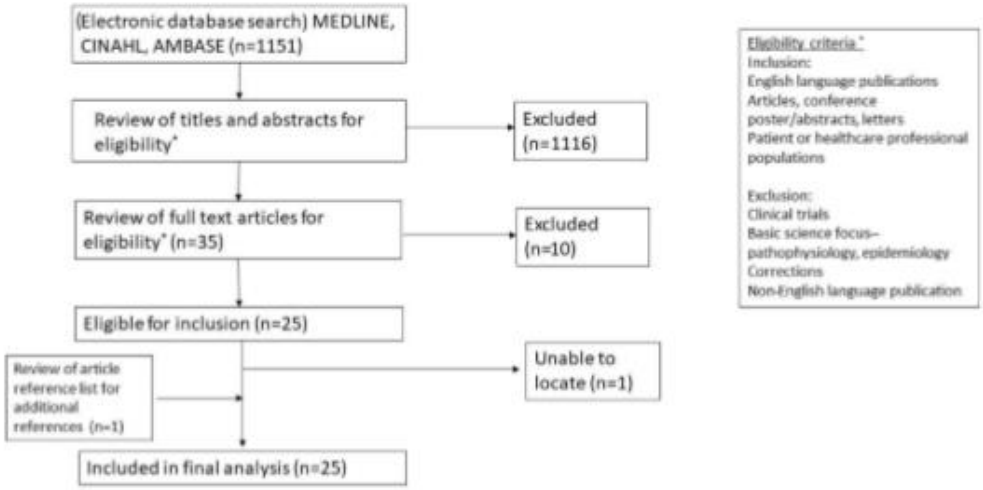


Figure 1 Study selection process for primary biliary cholangitis.

the reference lists from the 24 texts was undertaken; this yielded one further article. A search of the grey literature using Open Grey (http://www.opengrey.eu) using the search terms 'primary biliary cirrhosis' and 'primary biliary cholangitis' returned 18 and five citations, respectively. None were relevant to the research question. The key characteristics and emerging research themes of the 25 studies are summarised in table 1.

Choosing a comparable condition

A number of factors were deemed to be of relevance when selecting a comparable condition including the demographics of the patient population, availability of clear stratification parameters and the need for ongoing but minimal input long-term follow-up for low-risk groups. Possible conditions considered included other forms of liver disease, other chronic diseases (including autoimmune and non-autoimmune) and malignancies. Breast cancer satisfied the criteria (see table 2); it is mainly a disease of older females, patients are stratified after primary treatment into those who have achieved remission and those who have not responded, and even where remission has been achieved, there continues to be a need for a form of life-long input for responders that does not necessarily require specialist input.[15] A number of other parallels are also evident, including the ongoing psychological morbidity, and symptoms that may persist despite remission being achieved. In addition, issues around how best to follow-up patients who have undergone curative treatment remain a source of debate.[16] NICE guidelines on breast cancer from 2002 stated that all patients should be followed up for a minimum of 3 years (although they did not state how frequently patients should be seen) before care could be transferred back to primary care.[17] A systematic review of the breast cancer literature in 2007[18] identified seven randomised controlled trials which compared different forms of follow-up care both in terms of frequency of review and appropriate healthcare professional. Overall, they found no difference in recurrence rates, survival or quality of life. The updated NICE guidelines in 2009[19] reflect the existing research and recommend patients decide how they would like to be followed up after primary treatment is completed with options including primary care, secondary care or shared care.

Review of the breast cancer literature

The second scoping exercise again followed the Arksey and O'Malley structure.[14] As the topic of long-term follow-up in breast cancer survivorship has been widely studied, the goal of this review was to (1) gain an overview of the commonly occurring themes in this literature and (2) identify barriers to follow-up in primary care which may have potential relevance in PBC. An electronic database search was undertaken using the same three databases. A schematic of the sample selection process is shown in figure 2. The following search terms were used: breast cancer OR breast carcinoma OR breast neoplasm AND perspective* OR opinion* OR view* OR attitude* OR experience* or perception* AND discharge OR 'follow-up' OR 'primary care' OR 'secondary care' OR hospital* OR special* OR general practice*. A date limit was set to cover 1996–2016 in order to capture data relevant to recent changes in breast cancer follow-up strategies between the 2002 and 2009 NICE guidelines and studies undertaken following this change in practice. Review of the reference lists from relevant articles did not identify any further relevant citations within the specified date range. For each study the following data were extracted: authorship, publication date, location, population type, sample size and barriers to primary care follow-up.

RESULTS

PBC literature

Twenty-five studies identified from the PBC literature were included in the final analysis (table 1). Seventeen quantitative studies were identified,[20–36] four qualitative,[37–40] two mixed methods study,[41 42] one literature review[43] and one patient narrative.[44] Of these studies, 24 focused on the patient perspective only, with one looking at both patient and physician perspectives.[31] The majority of the studies focused on symptoms and quality of life. Of those that took a qualitative or mixed approach, one study looked specifically at the impact of fatigue,[37] one at the experience of receiving a diagnosis[40] and the other at stigma associated with PBC.[42] Two studies explored the experience of living with PBC.[39 41]

While no studies directly addressed issues surrounding follow-up care and the role of primary, secondary and tertiary care, there were a number of emerging themes that are likely to be of relevance when looking at the impact of changes in the structure of care. Montali *et al*[39] identified the theme of 'delegitimisation' and how, when patients look well (as is often the case in PBC), the impact of their disease is minimised by familial and social contacts. Discharge from specialist care to the primary care setting may further impact these perceptions both for the patient and their social contacts. The significance of the disease may be perceived as lesser when care is transferred to practitioners who may be seen as being less 'specialist' or 'expert'.[40 44] In addition, the stigma experienced by patients may also be influenced by new changes in care structure. A study looking at posts on an internet forum for patients with PBC revealed that a number of posts were related to stigma[38] and when directly asked many patients reported that they felt a degree of stigma associated with their disease.[42] This stigma seemed to stem not specifically from the diagnosis of PBC itself but with the associations between liver disease and cirrhosis with drugs and alcohol. Of note, this stigma was not just related to the perception of lay people but also to non-specialist HCPs.

Breast cancer literature

From the breast cancer literature, 14 papers were included in the final analysis (table 3). Quantitative

Table 1 Summary of research themes in PBC addressing patient and physician perspectives on disease

Authorship	Publication date	Location	Methodology	Population (size of sample with PBC)	Research question
Blackburn *et al* [20]	2007	UK	Quantitative	Patients (n=24)	Are patients with fatigue more psychologically impaired than those without fatigue and is there a role for CBT?
Dyson *et al* [21]	2016	UK	Quantitative	Patients (n=2055)	Impact of age at presentation on quality of life and the role of symptomatology
Fahey [43]	1999	UK	Literature review	Patients	Experience of women living with PBC and how understanding this may improve nursing care
Gross *et al* [22]	1999	USA	Quantitative	Patients post liver transplant (n=157, 42% PBC)	Quality of life post-transplant Comparison between PBC and PSC patients Relationship between quality of life and clinical factors
Hale *et al* [44]	2012	UK	Patient narrative	Patients (n=1)	Experience of living with fatigue
Huet *et al* [23]	2000	Canada	Quantitative	Patients (n=116) Healthy controls	Validation of the fatigue impact score in a large patient cohort Link between fatigue and mental health status Relationship between psychosocial and physical factors
Ismond *et al* *conference abstract only[41]	2018	Canada	Mixed methods (quantitative with post hoc qualitative analysis	Patients (n=119)	Experience of living with PBC Impact on daily life and relationships
Jorgensen [37]	2006	USA	Qualitative	Patients (n=8)	Experience of living with fatigue
Lasker *et al* [38]	2005	USA	Qualitative	Patients (n=275)	Why do patients use internet resources? Does disease stage affect disease experience? What are the similarities between issues experiences by patients with PBC and those with other chronic disease?
Lasker *et al* [24]	2010	USA	Quantitative	Patients on waiting list or post-transplant (n=100)	Uncertainty and how it relates to quality of life scores
Mells *et al* [25]	2013	UK	Quantitative	Patients (n=2402)	Quality of life scores and the role of fatigue, depression, sleep, social and cognitive function
Miura *et al* *conference abstract only[26]	2016	Japan	Quantitative	Patients (n=217)	Symptom profile and impact on quality of life
Montali *et al* [39]	2011	Italy	Qualitative	Patients (n=23)	Illness experience of women with PBC, sick role and relationship with others
Navasa *et al* [27]	1996	Spain	Quantitative	Patients post liver transplant (n=29)	Quality of life scores, complications and use of medical services post-transplant
Pearce *et al* [40]	2011	UK	Qualitative	Patients (n=28+)	Experience of receiving a diagnosis of PBC Use of this information to develop resources for patients at diagnosis
Poupon *et al* [28]	2004	France	Quantitative	Patients (n=276)	Comparison of quality of life scores among patients compared with healthy controls Relationship between clinical parameters and quality of life Impact of UDCA use on quality of life
Raszeja-Wyszomirska *et al* [29]	2015	Poland	Quantitative	Patients (n=205) Healthy controls	Comparison of quality of life domains between patients and controls Impact of patient and disease related factors on quality of life
Rishe *et al* [30]	2008	USA	Quantitative	Patients (n=238)	Experience of living with itch
Saich *et al* *conference abstract only[31]	2015	USA	Quantitative	Patients (n=214) and physicians (n=322)	Comparison of patient perceptions of care versus physician perspectives

Continued

Table 1 Continued

Authorship	Publication date	Location	Methodology	Population (size of sample with PBC)	Research question
Selmi *et al* [32]	2007	USA	Quantitative	Patients (n=1032)	Comparison of activity scores, symptoms and social life scores between patients and healthy controls
Sogolow *et al* [42]	2010	USA	Mixed methods	Patients (n=100)	Experience of stigma associated with diagnosis Why do some women experience more stigma than others? What impact does stigma have on quality of life?
Stanca *et al* [33]	2005	USA	Quantitative	Patients (n=70)	Impact of fatigue on quality of life
Untas *et al* [34]	2015	France	Quantitative	Patients (n=130)	Quality of life perception among women with PBC compared with a group of women with diabetes
Yagi *et al* *conference abstract only[35]	2016	Japan	Quantitative	Patients (n=180)	Comparison between patient and physician reported symptoms
Wong *et al* [36]	2008	China	Quantitative	Patients (n=44)	Comparison of symptoms scores, quality of life scores and depression scores between patients with PBC and two control groups (hypertension and chronic hepatitis B)

CBT, cognitive behavioural therapy; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis; UDCA, ursodeoxycholic acid.

methods were used in eight of the studies,[45–52] five used qualitative methods[53–58] and one mixed methods study[58] was identified. Nine studies looked at the views of the patient population,[40–48 50 53–57] six included primary care clinicians[46 48 49 55 57 58] and five included specialists (comprising surgeons, oncologists and nurses).[45 51 52 55 56]

Barriers to primary care follow-up identified included lack of knowledge among primary care physicians which was a recurrent theme among patients,[50 53 54 57] specialists[45 51 56] and primary care physicians themselves.[49 57 58] Allied to this concern was a fear that recurrence could be missed which was expressed by both primary care and specialist care[55] with some primary care clinicians expressly mentioning medicolegal concerns.[40 55] There was an association between cases where patients had experienced delays at the time of initial diagnosis and reduced confidence in their primary care practitioners ability to provide adequate follow-up.[57] When asked to rate their survival outcomes in different healthcare settings, patients felt that their chance of survival long term was higher if they were followed up by a specialist.[47]

In terms of practical aspects of care, both patients and doctors felt that primary care clinicians are already overworked,[40 49 53] that communication between primary care and specialists was poor[54 55] and this may impact on care. Specialists highlighted that they would lose long-term outcome data if they did not follow-up patients themselves.[45] They also described the relationship that forms with patients over time which was echoed by patients who described forming a bond with their specialists and feelings of abandonment when discharged.[54 55] The specialists reported the positive reinforcement they received from following up patients in remission rather than just seeing patients with complications and more advanced/untreatable disease.[55]

DISCUSSION

This scoping exercise identified the paucity of available literature exploring patient and HCP perspectives on the follow-up and management of PBC and a lack of any data around the role of primary care in the long-term management of patients with low-risk PBC. However, studies reporting stakeholder perspectives on changes to the delivery of breast cancer follow-up care have shown that not all patients or practitioners are comfortable with management being located substantially in the primary care setting. A series of themes emerged which have relevance to proposed care pathway changes including the knowledge base and workload of primary care,

Table 2 Comparison of primary biliary cholangitis and breast cancer

	PBC	Breast cancer
Gender	F:M 9:1 (2)	F:M 99:1 (40)
Age	Most common in fifth and sixth decade[2]	50% over 65[15]
Prognosis	70% response rate[6]	>70% 5-year survival[15]
Long-term treatment required	Yes, UDCA	Some cases—hormonal treatment
Long-term symptoms	Itch and fatigue	Lymphoedema

PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid.

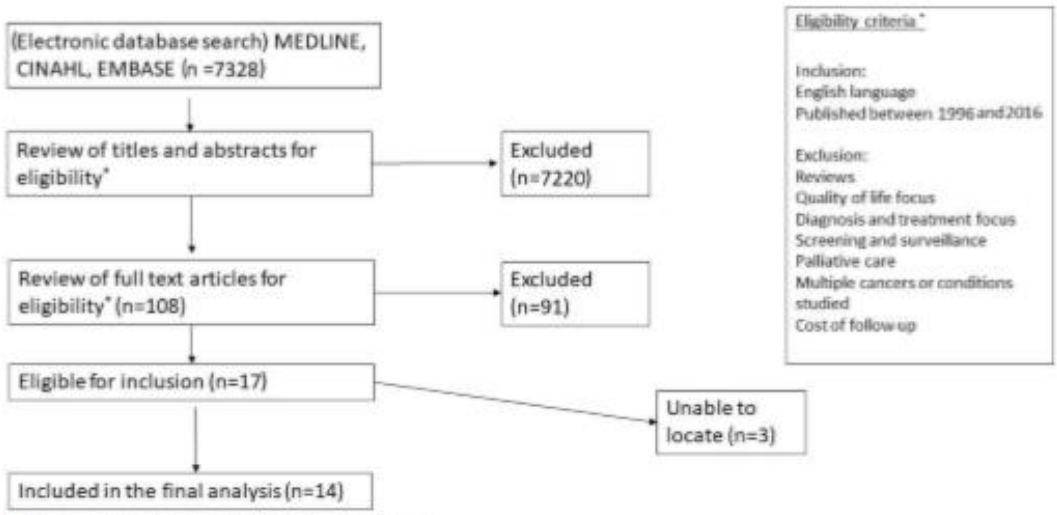


Figure 2 Study selection process for breast cancer.

communication between care settings and the importance of the doctor–patient relationship. Within the data available specifically for PBC, the impact of delegitimisation and stigmatisation felt by PBC patients is likely to be of relevance when developing new strategies for follow-up care.

This scoping review has identified a gap in the literature around patient and HCP perspectives on management in primary care and the need for further study in this area to look specifically at the potential concerns of users of this pathway and whether or not the themes identified in this scoping review are relevant, if there are additional barriers or facilitators not identified here and, if so, how they can be overcome.

As is common with the use of a scoping review rather than a systematic review, there was a focus on identifying the breadth of literature available rather than looking at the available studies in depth and the quality of the studies identified was not assessed. However, the identification that there is little relevant literature in this field meant that this was less important. We aimed to conduct a comprehensive search of the literature, using a multiple database strategy. However, it is possible that some relevant articles were missed. The lack of identification of additional relevant studies from reference lists of the chosen papers would support the belief that the search identified the relevant data in the field. Finally, it is not possible to know whether, and to what extent, any of the conditions considered by the authors for the second stage of the scoping study (including other forms of autoimmune disease, other forms of chronic liver disease and breast cancer) truly act as comparators to PBC. While breast cancer was chosen as a comparator condition due to its similarities to PBC in terms of demographics of the patient population, this decision makes the assumption about the overall importance of patient demographics in determining its healthcare related behaviours. In addition, there are likely to be fundamental differences in comparing a malignant and non-malignant condition that will impact on how patients and clinicians view their future care needs. Finally, PBC as a rare disease is likely to pose different challenges to breast cancer which is now relatively common.

CONCLUSION

The recent guidelines from both the UK and European Societies propose a shift towards individualised care for patients with PBC. While individualised care is not explicitly defined, one potential consequence that is discussed in the British Guidelines is the discharge of patients deemed 'low risk' from hospital care to follow-up in primary care. The feasibility of this strategy is unclear and as such, the purpose of this scoping review was to identify the breadth and depth of the data already available about patient and clinician perspectives on management in primary care in order to identify facilitators and barriers to implementing this in practice. This review however highlighted that there is in fact a lack of data and that in order to be able to definitively answer the question of feasibility within PBC, further study may be required.

In developing a stratified approach to the care of the patient with PBC it will be essential to frame changes in care around high quality research. Underpinning this are opportunities to change practice by first of all an emphasis on education. This should address specific education for patients with PBC, and for primary care physicians, a broader education effort on the management of chronic liver diseases. With such an approach there would then be a greater opportunity to perhaps implement further change though targeted education, and use of smart technology/Apps to aid individualise risk assessment and changes to care pathways. Any approaches to change would require sensitive implementation adapted to local

Table 3 Summary of themes identified in breast cancer literature

Authorship	Publication date	Location	Methodology	Population (size of sample)	Findings/themes identified
Adewuyi-Dalton *et al* [53]	1998	UK	Qualitative—face to face one on one interviews	Patients (n=109)	GPs—overworked; lack specialist knowledge; specialist care less important over time as concern about recurrence lessens
Brennan *et al* [51]	2010	Australia	Quantitative—questionnaire	Secondary care (n=217)	GPs need more training to follow-up patients
Brennan *et al* [54]	2011	Australia	Qualitative—telephone interviews	Patients (n=20)	Advantages GP care: convenience, reduced travel involved, take pressure off specialists Disadvantages of GP care: poor communication between specialist and GP, GPs lack of knowledge, established relationship with specialist during treatment
Dawes *et al* [58]	2015	USA	Mixed methods—questionnaire and focus group	Primary care (Survey n=59 Focus group n=36+)	Favoured specialists to provide follow-up care Lack of knowledge especially endocrine treatment
Donelly *et al* [45]	2007	UK	Quantitative—questionnaire	Secondary care (n=256)	Advantages of GP care: reduced clinic workload Disadvantages: lack of training, loss of outcome data
Kantsiper *et al* [55]	2009	USA	Qualitative—focus group	Patients (n=21) Primary care (n=15) Secondary care (n=160	Specialists are experts and GPs role is in referral not management. Feelings of abandonment on discharge Fear of missing recurrence and medicolegal implications, not able to keep up to date with information, poor communication from specialists Better at detecting recurrence and managing side effects than GPs, like following up survivors (positive experience), establish bond with patient
Kerrigan *et al* [46]	2014	Ireland	Quantitative	Patients (n=87) Primary care (n=53)	Supportive of GP care: able to explain breast cancer, able to perform examination, easy links to specialist if needed Increased workload and costs, concern regarding medicolegal aspects of care
Kwast *et al* [56]	2013	Netherlands	Qualitative—face to face interviews	Patients (n=23) Clinicians (n=18)	GP—role in psychosocial aspects of care; lacks specialist knowledge; too busy GP care cheaper; lack specialist knowledge
Luker *et al* [57]	2000	UK	Qualitative—face to face/telephone interviews	Patients (n=67) Primary care (n=31)	GP—lacks knowledge; delay in diagnosis associated with decreased confidence in follow-up Difficult to keep up to date with new information, prognostication challenging
Mao *et al* [50]	2009	USA	Quantitative	Patients (n=300)	Holistic care through GP; psychosocial aspects of management; variable breast cancer specific knowledge
Mayer *et al* [47]	2012	Canada	Quantitative	Patients (n=218)	Specialist visit reduces anxiety and improves survival compared with primary care
Roorda *et al* [49]	2013	Netherlands	Quantitative—questionnaires	Primary care (n=502)	40% of GPs happy to provide exclusive care after 5 years; barriers—patient preference, lack of knowledge, workload improving GP care improving GP care—active discharge from specialist care, written information, education, easy access back to specialist care if required
Smith *et al* [48]	2015	Canada	Quantitative	Patients (n=1065) Primary care (n=587)	Confident in GPs ability to screen for recurrence, less confident in GPs managing osteoporosis, hormonal treatment Confident in screening for recurrence, lower confidence in lymphoedema, family counselling, psychosocial aspects
Van Hezewijk *et al*[52]	2011	Netherlands	Quantitative—questionnaire	Secondary care (n=130)	GPs should play a minor role in follow-up. Reasons not specified

GP, general practitioner.

resources: for example, where large group practices and primary networks exist in primary care, opportunities to use a few embedded primary care liver champions may be effective, whereas in rural areas, IT/nurse supported change to care for GPs may be better.

Across the various models of healthcare delivery, it will be essential to evaluate feasibility of stratified care for patients with PBC in many different settings and healthcare models. Solutions for urban areas may, for example, be distinct to those for rural environments, and obstacles to implementation may include economic and personnel issues. Nevertheless, there exists the opportunity to be innovative in-service design and then to evaluate the impact of any service change.

We believe the similarities between the patient, disease and management characteristics of postsurgery breast cancer and low-risk PBC patients to be such that it is reasonable to anticipate comparable barriers will emerge to the implementation of the new management guidelines for PBC. Dedicated research involving patients and clinicians is still required to confirm that barriers to change exist, to identify what these barriers are and to plan strategies for intervention in this group of patients and clinicians. This information will be relevant not only to the possible future implementation of stratified care models in the PBC population but will also be applicable to other rare chronic diseases including, but not exclusive to, liver disease.

Acknowledgements This paper presents independent research supported by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Contributors MC contributed to the conception and design of this scoping review, the acquisition and analysis of the data, and drafted and revised the paper for final submission. GH, SG and JP contributed to conception and design and revised the draft paper for final submission. MC acts as the guarantor for this submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests MC and GH are collaborating investigators for UK-PBC, a MC stratified medicine platform. SG and JP declare no competing interests.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No additional data are available.

REFERENCES

1. James OF, Bhopal R, Howel D, *et al*. Primary biliary cirrhosis once rare, now common in the United Kingdom? *Hepatology* 1999;30:390–4.
2. Mells GF, Hirschfield GM. *Genetics of primary biliary cirrhosis*. eLS, 2013.
3. Prince M, Chetwynd A, Newman W, *et al*. Survival and symptom progression in a geographically based cohort of patients with primary biliary cirrhosis: follow-up for up to 28 years. *Gastroenterology* 2002;123:1044–51.
4. Parés A, Caballería L, Rodés J. Excellent long-term survival in patients with primary biliary cirrhosis and biochemical response to ursodeoxycholic acid. *Gastroenterology* 2006;130:715–20.
5. Corpechot C, Abenavoli L, Rabahi N, *et al*. Biochemical response to ursodeoxycholic acid and long-term prognosis in primary biliary cirrhosis. *Hepatology* 2008;48:871–7.
6. Corpechot C, Chazouillères O, Poupon R. Early primary biliary cirrhosis: biochemical response to treatment and prediction of long-term outcome. *J Hepatol* 2011;55:1361–7.
7. Kuiper EMM, Hansen BE, de Vries RA, *et al*. Improved prognosis of patients with primary biliary cirrhosis that have a biochemical response to ursodeoxycholic acid. *Gastroenterology* 2009;136:1281–7.
8. Carbone M, Mells GF, Pells G, *et al*. Sex and age are determinants of the clinical phenotype of primary biliary cirrhosis and response to ursodeoxycholic acid. *Gastroenterology* 2013;144:560–9.
9. Nationalinstitute for Health and Care Excellence. *Obeticholic acid for treating primary biliary cholangitis. nice.org.uk/guidance/ta443: NICE; 2017. Report no.: TA443 contract No.: TA443*, 2017.
10. Hirschfield GM, Dyson JK, Alexander GJM, *et al*. The british society of Gastroenterology/UK-PBC primary biliary cholangitis treatment and management guidelines. *Gut* 2018;67:1568–94.
11. European association for the study of the liver. Electronic address eee, European association for the study of the L. EASL clinical practice guidelines: the diagnosis and management of patients with primary biliary cholangitis. *J Hepatol* 2017;67:145–72.
12. Williams R, Aspinall R, Bellis M, *et al*. Addressing liver disease in the UK: A blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. *The Lancet* 2014;384:1953–97.
13. Armstrong R, Hall BJ, Doyle J, *et al*. 'Scoping the scope' of a cochrane review. *Journal of Public Health* 2011;33:147–50.
14. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology* 2005;8:19–32.
15. Cancer Research UK. Breast Cancer statistics. Available: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer
16. Taggart F, Donnelly P, Dunn J. Options for early breast cancer follow-up in primary and secondary care - a systematic review. *BMC Cancer* 2012;12.
17. National Institute for Clinical Excellence. *Improving outcomes in breast cancer*, 2002.
18. Montgomery DA, Krupa K, Cooke TG. Alternative methods of follow up in breast cancer: a systematic review of the literature. *Br J Cancer* 2007;96:1625–32.
19. National Institute of Clinical Excellence. *Early and locally advanced breast cancer: diagnosis and treatment*, 2009.
20. Blackburn P, Freeston M, Baker CR, *et al*. The role of psychological factors in the fatigue of primary biliary cirrhosis. *Liver International* 2007;27:654–61.
21. Dyson JK, Wilkinson N, Jopson L, *et al*. The inter-relationship of symptom severity and quality of life in 2055 patients with primary biliary cholangitis. *Aliment Pharmacol Ther* 2016;44:1039–50.
22. Gross CR, Malinchoc M, Kim WR, *et al*. Quality of life before and after liver transplantation for cholestatic liver disease. *Hepatology* 1999;29:356–64.
23. Huet P-M, Deslauriers J, Tran A, *et al*. Impact of fatigue on the quality of life of patients with primary biliary cirrhosis. *Am J Gastroenterology* 2000;95:760–7.
24. Lasker JN, Sogolow ED, Olenik JM, *et al*. Uncertainty and liver transplantation: women with primary biliary cirrhosis before and after transplant. *Women & Health* 2010;50:359–75.
25. Mells GF, Pells G, Newton JL, *et al*. Impact of primary biliary cirrhosis on perceived quality of life: the UK-PBC national study. *Hepatology* 2013;58:273–83.
26. Miura K, Tanaka A, Takikawa H. Assessment of quality of life of Japanese patients with primary biliary cirrhosis using PBC-40. *Hepatology International* 2016;10:S37–S8.
27. Navasa M, Forns X, Sánchez V, *et al*. Quality of life, major medical complications and hospital service utilization in patients with primary biliary cirrhosis after liver transplantation. *Journal of Hepatology* 1996;25:129–34.
28. Poupon RE, Chretien Y, Chazouilleres O, *et al*. French pBC Study Group. Quality of life in patients with primary biliary cirrhosis. *Hepatology* 2004;40:489–94.
29. Raszeja-Wyszomirska J, Wunsch E, Krawczyk M, *et al*. Assessment of health related quality of life in Polish patients with primary biliary

cirrhosis. *Clinics and Research in Hepatology and Gastroenterology* 2016;40:471–9.
30. Rishe E, Azarm A, Bergasa NV. Itch in Primary Biliary Cirrhosis: A Patients' Perspective. *Acta Derm Venereol* 2008;88:34–7.
31. Saich A, Swanson H, Mayer TJ, intercept Pharmaceuticals. Physician versus patient perceptions of medical care quality in primary biliary cirrhosis. In: *American Association for the study of liver disease*. San Francisco, CA: Hepatology, 2015.
32. Selmi C, Gershwin ME, Lindor KD, *et al*. Quality of life and everyday activities in patients with primary biliary cirrhosis. *Hepatology* 2007;46:1836–43.
33. Stanca CM, Bach N, Krause C, *et al*. Evaluation of fatigue in U.S. Patients with primary biliary cirrhosis. *Am J Gastroenterol* 2005;100:1104–9.
34. Untas A, Boujut E, Corpechot C, *et al*. Quality of life and illness perception in primary biliary cirrhosis: a controlled cross-sectional study. *Clinics and Research in Hepatology and Gastroenterology* 2015;39:52–8.
35. Yagi M, Tanaka A, Miura K, *et al*. The assessment of subjective symptoms and patient-rported outcomes in patients with primary biliary cholangitis using PBC-40. *Journal of Gastroenterology and Hepatology* 2016;31.
36. Wong GL-H, Law FM-Y, Wong VW-S, *et al*. Health-related quality of life in Chinese patients with primary biliary cirrhosis. *Journal of Gastroenterology and Hepatology* 2008;23:592–8.
37. Jorgensen R. A phenomenological study of fatigue in patients with primary biliary cirrhosis. *Journal of Advanced Nursing* 2006;55:689–97.
38. Lasker JN, Sogolow ED, Sharim RR. The role of an online community for people with a rare disease: content analysis of messages posted on a primary biliary cirrhosis Mailinglist. *J Med Internet Res* 2005;7:e10.
39. Montali L, Frigerio A, Riva P, *et al*. 'It's as if PBC didn't exist': The illness experience of women affected by primary biliary cirrhosis. *Psychology & Health* 2011;26:1429–45.
40. Pearce RM, Jones DE, Newton JL. Development of an evidence-based patient information medium: empowering newly diagnosed patients with primary biliary cirrhosis. *J Vis Commun Med* 2011;34:4–13.
41. Ismond K, Azziz B, Wright G, *et al*. Self reported experiences of patients living with primary biliary cholangitis (pBC) and ursodiol. *Hepatol Int* 2018;12(supplement 2).
42. Sogolow ED, Lasker JN, Sharim RR, *et al*. Stigma and liver disease. *Illness, Crisis & Loss* 2010;18:229–55.
43. Fahey S. The experience of women with primary biliary cirrhosis: a literature review. *J Adv Nurs* 1999;30:506–12.
44. Hale M, Newton JL, Jones DEJ. Fatigue in primary biliary cirrhosis. *BMJ* 2012;345:e7004.
45. Donnelly P, Hiller L, Bathers S, *et al*. Questioning specialists' attitudes to breast cancer follow-up in primary care. *Ann Oncol* 2007;18:1467–76.
46. Kerrigan D, Waters P, Ryan M, *et al*. Follow up arrangements for breast cancer patients: is it appropriate to trabsfer surveillance to general practitioners. *Irish Medical Journal* 2014;107:273–5.
47. Mayer EL, Gropper AB, Neville BA, *et al*. Breast cancer survivors' perceptions of survivorship care options. *JCO* 2012;30:158–63.
48. Smith SL, Murchison S, Singh-Carlson S, *et al*. Survivorship care in breast cancer: perceptions of patients and primary care physicians. *Canadian family physician* 2015;61:277–83.
49. Roorda C, Berendsen AJ, Haverkamp M, *et al*. Discharge of breast cancer patients to primary care at the end of hospital follow-up: a cross-sectional survey. *European Journal of Cancer* 2013;49:1836–44.
50. Mao JJ, Bowman MA, Stricker CT, *et al*. Delivery of survivorship care by primary care physicians: the perspective of breast cancer patients. *JCO* 2009;27:933–8.
51. Brennan ME, Butow P, Spillane AJ, *et al*. Survivorship care after breast cancer: follow-up practices of Australian health professionals and attitudes to a survivorship care plan. *Asia Pac J Clin Oncol* 2010;6:116–25.
52. van Hezewijk M, Hille ETM, Scholten AN, *et al*. Professionals' opinion on follow-up in breast cancer patients; perceived purpose and influence of patients' risk factors. *European Journal of Surgical Oncology* 2011;37:217–24.
53. Adewuyi-Dalton R, Ziebland S, Grunfeld E, *et al*. Patients' views of routine hospital follow-up: a qualitative study of women with breast cancer in remission. *Psycho-Oncology* 1998;7:436–9.
54. Brennan ME, Butow P, Marven M, *et al*. Survivorship care after breast cancer treatment – Experiences and preferences of Australian women. *The Breast* 2011;20:271–7.
55. Kantsiper M, McDonald EL, Geller G, *et al*. Transitioning to breast cancer survivorship: perspectives of patients, cancer specialists, and primary care providers. *J Gen Intern Med* 2009;24:459–66.
56. Kwast ABG, Drossaert CHC, Siesling S, *et al*. Breast cancer follow-up: from the perspective of health professionals and patients. *Eur J Cancer Care* 2013;22:754–64.
57. Luker K, Beaver K, Austin L, *et al*. An evaluation of information cards as a means of improving communication between hospital and primary care for women with breast cancer. *J Adv Nurs* 2000;31:1174–82.
58. Dawes AJ, Hemmelgarn M, Nguyen DK, *et al*. Are primary care providers prepared to care for survivors of breast cancer in the safety net? *Cancer* 2015;121:1249–56.

5.3 How does this scoping review impact on the research question

The goal of this scoping review was two-fold. Firstly, to gain an overview of the breadth and type of literature available looking at the perspectives of patients and clinicians on all aspects of PBC and its management and, secondly, to see whether the question of perspectives on management in primary care and discharge of low-risk patients had previously been addressed. The work undertaken identified that the majority of the literature was based on quantitative methodology and focussed on symptoms and severity scores. There was a small amount of qualitative literature specific to PBC that suggested that there could be challenges to discharge and that further dedicated was work was needed. For example, an Italian study of patients with PBC (77) identified that patients with this condition report that the condition is not well understood by others (both in terms of personal relationships and health care professionals) and that the impact of their illness and its symptoms are often overlooked or trivialised. The authors referred to this as "delegitimation". In addition, the scoping review of the breast cancer literature identified that in a condition with a number of parallels to PBC, discharge of low-risk patients was met with a number of challenges.

5.4 Chapter summary

This chapter is presented in the form of a manuscript which was generated from a scoping review undertaken in the early stages of this research. The work undertaken confirmed that the question of perspectives on management of PBC in primary has not previously been studied but that there was evidence from some of the general qualitative work in PBC and a review of the breast cancer literature that there could be barriers to pathway implementation and that there was a need for specific research in this area.

The next chapters of this thesis describe the qualitative components of this research thesis starting with the qualitative methodology (Chapter 6) followed by the results of interviews with patients (Chapter 7), patient group representatives (Chapter 8) and clinicians (Chapter 9).

CHAPTER 6: METHODOLOGICAL PROCESS FOR QUALITATIVE INTERVIEWS

6.1 Chapter overview

The previous chapters have set out what is currently known about the management of PBC in the UK. In the absence of a single source of data, Chapters 2-4 detailed the analysis of quantitative data from patient questionnaires carried out by UK-PBC, a survey of hospital based clinicians in the UK, and a review of a referral pathway to a specialist PBC clinic. Chapter 5 presented a scoping review of the PBC literature undertaken in order to establish whether the patient and clinician perspective on place of care had been previously studied. The goal of these analyses was, firstly, to establish whether the assumption that implementation of a stratified approach to care would represent a shift in current practice was correct and, secondly, to begin to identify what the barriers to change implantation would be. The findings discussed within these chapters confirmed the researcher's supposition that stratified care is not currently being used in routine practice and that the majority of patients are currently being managed in secondary care. In addition, this work also identified that there is a lack of knowledge amongst clinicians regarding the use of UDCA response criteria, and a reluctance to discharge low-risk patients to primary care. Whilst the scoping review of the PBC literature identified that, within this population, patient and clinician preferences for place of care has not been previously studied, when looking at a condition with a number of similarities to PBC where the issues of barriers to discharge have been studied, a number of barriers were identified.

With this information available, and in order to explore the findings of the previous chapters in more detail, a series of qualitative interviews were conducted with patients, clinicians from a variety of healthcare settings and representatives from the national patient support groups. This chapter sets out the rationale for conducting qualitative interviews, the ethical approval process,

the recruitment strategy, interview process and the data analysis methods. The results from the qualitative interviews will be presented in Chapter 7 (patients), Chapter 8 (the representatives of the patient groups) and Chapter 9 (health care professionals).

6.2 Rationale for using a qualitative approach

Morse and Field set out the following criteria for when a qualitative approach may be most appropriate: 1) there is little currently known about the topic, 2) the topic under study is from the perspective of a patient, relative or caregiver, 3) the research answers questions pertaining to what the experience is like and 4) may provide insights that revise or alter clinical practice (78). The research topic being posed in this thesis is a fitting question for the qualitative approach; previous results presented in this thesis have shown that there is little currently known about the patient and clinician perspective around stratified care in PBC, and as such this research aims to understand the perspectives of the stakeholders in a new pathway for managing low-risk PBC in primary care. By identifying what the barriers are, the goal is to provide insights into what would need to be done in order to facilitate the implementation of a new pathway into practice.

6.3 Ethical approval process

The initial application for ethical review was submitted to the University of Birmingham on the 31st of March 2016. The study protocol and documents were reviewed by the Science, Technology, Engineering and Mathematics Ethical Review Committee. After some clarifications including support to participants if distressed, action to be taken if poor/malpractice disclosed, and updates to the participant documentation (to include a clear timeline for withdrawal, use of quotations in publications and the option for interviews to be

undertaken on the university campus with reimbursement of travel expenses), approval was received on the 8th of July 2016 (ERN_16-0130). An additional application for ethical approval was also submitted to the Health Research Authority (HRA) in order to cover the recruitment of National Health Service (NHS) staff and to allow research activity to be conducted on NHS property. This application was submitted on the 22nd of September 2016 and approval was received on the 19th of January 2017 (IRAS 204690). The sponsor of this study was the University of Birmingham. During the course of the study, an amendment was submitted to add an additional participant group – Group 4: representatives from the patient groups. This amendment was approved on the 10th of April 2017. Lastly, a further amendment to add another hospital site within the West Midlands area to the HRA (as the site had been overlooked in the original application) was submitted and approved on the 21st of July 2017.

The study was conducted in accordance with the principles of the Declaration of Helsinki (79). Ethical considerations for this study included data management and confidentiality, the potential for emotional distress, and the right of study participants to withdraw. The full identity of each participant was known to the researcher only and each participant was assigned an alphanumeric code. The following data was stored as part of the study: completed consent forms, participant details including contact information, interview recordings, electronic and hard copies of typed transcripts, and field notes. All electronic data was stored on a University of Birmingham computer and was password protected. All physical data was stored in a locked cabinet within an area of the University of Birmingham open only to those with swipe card access. As per the University Of Birmingham Code Of Practice, all data is due to be stored for up to 10 years and then destroyed. Data access was restricted to members of the research team. However, if requested, direct access would be granted to authorised representatives from the

Sponsor or Host institution for the purposes of monitoring and audit to ensure compliance with regulations. Taped interviews were transcribed by professional transcribers external to the research team. However, transcribers were bound by a confidentiality agreement and data was anonymised prior to transcription with each recording given an alphanumeric code.

As participants, particularly within the patient group, may find it difficult to talk about their experiences, this was highlighted in the participant information sheet and participants were advised that they had the right not to talk about any subject that they found distressing. If a specific issue or concern was identified during the interview process, then the participant would be provided with information on how to seek input from a patient support group, their GP or consultant, or the local complaints process relevant to their concern. Each participant was informed verbally and through the participant information sheet of their right to withdraw from the study. Participants were given the option to withdraw at any point up to two weeks after the date of the interview. If a participant chose to withdraw then all collected data (both paper and electronic) would be destroyed. As some of the research was undertaken away from the university campus, this was identified as a potential risk to the researcher. All work undertaken adhered to the guidelines set out in the University of Birmingham's Code of Practice.

6.4 Interview format and design

A semi-structured interview approach was used, wherein open questioning was used alongside a topic guide as an “aide memoire” to the researcher to ensure potential areas of interest were covered. The terms "structured", "semi-structured", and "unstructured" refer to the degree to which all participants are asked the same questions as well as the order in which these questions are asked (80). The semi-structured interview technique allows flexibility in the questions asked

and the order in which they are asked and is used when the researcher knows most of the questions to ask but cannot predict the answers they will receive (78). The previous analysis of the patient questionnaires, clinician survey and an audit of referrals to a specialist clinic as well as scoping reviews of the PBC and breast cancer literature had revealed a number of potential barriers to pathway implementation and these informed the development of the interview topic guides.

6.5 Sampling strategy and sample sizes

A purposive approach to sampling was chosen in order to ensure that those recruited to take part in qualitative interviews would be able to provide data relevant to the research question. Purposive sampling has been defined as a deliberate, non-random method of sampling which aims to sample a group of people, or settings, with a particular characteristic (81). Using this approach, four separate groups of participants were identified for recruitment into the qualitative study. These four groups were chosen in order to capture the main stakeholders in the implementation of a stratified care pathway for PBC. In addition, within each group, specific characteristics of the respondents were identified in order to ensure variation within each group.

Table 13: Sampling characteristics

Group number	Group characteristic	Variables considered relevant to sampling
1	Patients with PBC	Duration of diagnosis Age at time of interview Age at time of diagnosis Severity of disease Current place of care
2	General practitioners	Size of GP practice patient list Location – rural vs urban Clinical commissioning group

3	Hospital-based doctors	Specialist interest area Type of hospital
4	Patient group representatives	PBC specific or general liver

Unlike quantitative analysis, where the number of participants required to ensure that a studied is "powered" to be able to provide a statistically significant outcome, in qualitative research design, data collection is continued until data saturation is reached. Data saturation refers to the point when ongoing analysis reveals that no additional data is being found and was first described by Glaser and Strauss (82). Whilst it is not possible to predict, for an individual study, at which point data saturation will be reached and provide an exact figure as to how many participants will be recruited to each group, the literature would suggest that for this type of study between ten and thirty participants would be required in each group (68, 83). The following inclusion and exclusion criteria were set for the purposes of participant recruitment.

Inclusion criteria:

- The participant is willing and able to give informed consent for participation in the study
- Male or female
- Aged 18 years or above
- Meet criteria for entry into one of the groups (1-4) above

Exclusion criteria:

- Those for whom English was not the first language and who were unable to undertake the interview without the use of an interpreter.

The decision to exclude those for whom an interpreter would be required was made due to the challenges that this would pose to the interview process, particularly for a new researcher, as involvement of an interpreter in the qualitative interview process has been shown in some cases to threaten the validity of the results, with a risk of error both when the question is translated to the participant and also when the answer is translated back to the interviewer (84, 85).

6.6 Recruitment strategy

For groups 1, 2 and 3, the decision was made that participants would be recruited from the West Midlands area only. As a researcher based at the University of Birmingham and with the likelihood of conducting interviews in participants' homes and places of work, it was decided to limit recruitment to a single geographical area. This geographical limitation was not felt to have an impact on the diversity of the population from which research participants could be recruited as the West Midlands provides a diverse environment both in terms of population and NHS structure. The West Midlands region has a population of over 5.4 million within an area of 13,000 square km, making it the third-largest English region by area, after London and the North East (86). It includes the densely populated city of Birmingham, which is the largest urban area in England outside London, as well as areas of remote countryside within the counties of Herefordshire and Shropshire. It contains areas of high deprivation, particularly in Birmingham, Coventry and Stoke-on-Trent, but also contains very prosperous areas like Solihull, south Warwickshire and Evesham (86). In terms of hospital and primary care structure, the West Midlands contains a large tertiary liver transplant centre (the Queen Elizabeth Hospital Birmingham) which has PBC amongst one if its specialist interests, as well as small and medium-sized District General Hospitals alongside primary care settings varying from large urban teaching practices based close to specialist hospitals and the universities to

more rural practices. Initial recruitment of patients, GPs and hospital clinicians took the approach of widespread advertisements in order to target as many potential subjects as possible within the defined geographical area. Different approaches were used for each specific group as shown below:

Group 1: Patients

Patients with PBC were made aware of the research study through advertisements distributed via the main patient charity (The PBC Foundation). This group has a website where research studies are regularly advertised as well as a quarterly newsletter (see Appendix 5 for the advert).

Group 2: Primary care clinicians

Introductory letters were posted to a random sample of practices in the West Midlands area using the following strategy. A list of all UK primary care facilities published by the Health and Social Care Information Centre was obtained (https://data.gov.uk/dataset/england-nhs-connecting-for-health-organisation-data-service-data-files-of-general-medical-practices).

This list was then edited firstly to exclude walk-in centres, care homes, and prisons and then to include only those practices with a West Midlands postcode (B, CV, DY, HR, NN, ST, TF, WR, WS, and WV). In order to try to ensure variation in those recruited, practices were then divided into groups based on their Clinical Commissioning Group (CCGs) and practice size. From each CCG, six practices were chosen using the NHS choices website based on the number of patients registered at the practice: two practices with less than 5,000 patients registered, two with between 5,000 and 10,000 patients registered, and two with more than 10,000 patients registered (the average patient list for a GP practice in the UK is approximately 7000 (87). An introductory letter was sent to the lead GP/practice manager. The letter included an expression of interest slip with return envelope as well as email contact details for the study team. This

letter was then followed up by contacting practice managers to ensure that the information had been received. Due to poor initial uptake from this method, a further approach was made to GPs via the Department of Community Based Medicine and the Institute of Applied Health Research at the University of Birmingham, and the Primary Care Clinical Research Network: West Midlands in the form of an email with information about the study attached.

Group 3: Hospital-based clinicians

The study was advertised to Gastroenterologists and Hepatologists through the mailing lists, newsletters, and websites of the two main professional groups: the British Society of Gastroenterology (BSG) and the British Association for the Study of the Liver (BASL). The study was also advertised through the Hepatology Clinical Research Network (CRN): West Midlands.

Group 4: Representatives of the patient support groups

UK patient support groups with a specific interest in PBC were approached directly via publically available email addresses to take part in the study.

6.7 The interview process

All those who expressed an interest in the study and met the inclusion/exclusion criteria were provided with a copy of the participant information sheet. They were then asked to contact the researcher if they were happy to go ahead or if they had any further questions. If they had not made contact with the researcher after 10-14 days, then the researcher contacted them to ensure the information had been received. Once the participant had verbally agreed to take part in the study, an appointment was made to conduct the interview. In order to ensure both participant

comfort as well as to separate the researcher from her role as a medical doctor, all interviews were undertaken either in the participant's home or workplace, or within a meeting room at the university (88).

At the time of interview, the researcher explained to the participant again the research goals and explained their background as both a medically qualified doctor with an interest in PBC and as a researcher at the University. The participant was given the opportunity to ask any further questions they may have. Following this, formal written consent was obtained by the researcher who was trained in Good Clinical Practice (GCP) and aspects of obtaining informed consent.

Each interview followed a semi-structured approach using the topic guides in Appendix 14, 15, and 16. Each interview started with an open question that allowed the participant to talk about themselves and about their experience with PBC. For example:

- For patients "*Could you start by telling me about how you came to be diagnosed with PBC*?"
- For clinicians "*Can I just start just by asking you about your experience to date of managing PBC*"?

The participant was then allowed to speak for as long as they wanted without interruption and subsequent questions were based on the response to the opening questions. However, the topic guide which had been generated for each participant group was used to guide the interview and to ensure broad topics of potential interest were covered.

At the end of the interview, participants had the opportunity to talk about any aspect of PBC that they felt was relevant to the research that had not already been mentioned. Once the interview was completed, the researcher thanked the participant and explained again that if they were to change their mind about the data being included in the study then they had two weeks to get in contact. They were also reminded that it may be some time before the results were available and that they would be made available as a summary to them if desired.

6.8 Data analysis

All recordings were sent by secure transfer to the transcription company and were transcribed verbatim. The transcript was returned within 48 hours. Once the transcript was received, the researcher read the transcript while listening to the recording to ensure accuracy of transcription and any errors or omissions were corrected. The transcript was then saved onto the computer under the alphanumeric code assigned to the participant. In order to support the next stage (data analysis), all transcripts (once cleaned) were imported into computer assisted data analysis software (CAQDAS), specifically NVivo (initially version 11 then 12).

Each set of interviews was analysed independently: firstly the patient interviews, followed by the clinician interviews and finally, the interviews with the patient group representatives. Data analysis followed the same standard format for all. Analysis of the data was carried out using an approach based on the process of Framework Analysis described by Ritchie and Lewis (89). Each transcript was printed out and read through from start to finish without any coding being undertaken (commonly referred to as familiarisation). Next, the transcript was read through but this time assigning codes to sections of the transcript by annotating in the transcript margin. Coding was carried out using the constant comparison method. As each transcript was analysed a list of codes was generated. At the end of each transcript analysis, codes were reviewed and

any that were felt to overlap too much were amalgamated – for example in one transcript there was a code for both low energy and fatigue, and fatigue was chosen. The next transcript was then coded and new codes added to the master list. A note was made of any new codes as they were generated and the previously coded transcripts were reviewed in order to see whether that code was relevant to the transcript. Once the transcripts had been coded, the next step was to upload the transcripts themselves to NVivo and link relevant sections of the text to the codes. The use of NVivo allowed the codes that had been generated by manual review to be organised systematically and to link and store relevant sections of transcript text to the relevant code. Once all the transcripts had been coded, the codes were arranged into categories (or themes).

6.9 Research philosophy

As a first-time qualitative researcher prior to undertaking these interviews, I had not considered my philosophical approach to research (or indeed that I even had a specific philosophical approach) or how my approach could impact the design and conduct of the research. However, through reading the literature it became clear that I was employing a pragmatic paradigm (or way of looking at the world). The pragmatic paradigm has been defined as being based on the following beliefs (90):

- Gaining knowledge in pursuit of desired ends as influenced by the researcher's values and politics
- There is a single reality and all individuals have their own unique interpretation of reality
- Relationships in research are determined by what the researcher deems as appropriate to that particular study

- Methods are matched to the specific questions and purposes of the research and mixed methods can be used

These beliefs are reflected in the work that is being undertaken within this thesis. As a methodological approach to problem solving, pragmatism requires detection of a socially situate problem and adequate action to address the problem (91). As well as the practical aspects of research conduct, the pragmatist philosophy also states that current actions are inherently linked to past experiences and from the beliefs that have originated from these experiences (91). The qualitative component of this thesis looks to understand all aspects of the patient and clinician experience in order to understand how previous experience impacts how they view the implementation of a stratified approach to PBC management and where barriers to the discharge of low-risk patients to primary care are identified, to understand why these exist.

6.10 Ensuring quality in research

Whilst two of the research supervisors were skilled in Qualitative Research methodology, the researcher had never undertaken this type of research before. In preparation to carry out the qualitative component of the research, the researcher undertook a series of courses run by the Health Experiences Research Group at the University of Oxford looking at both the process of conducting and analysing of qualitative interviews, along with a course in the use of NVIVO software. Prior to undertaking interviews with recruited subjects, mock interviews were undertaken with experienced Qualitative Researchers within the Institute of Applied Health Research at the University of Birmingham and the recordings reviewed in conjunction with experienced supervisors. In addition, the first two interview recordings with recruited subjects were listened to in the presence of a supervisor.

6.10 Chapter summary

This chapter describes the processes involved in developing the research protocols for carrying out the qualitative research component of this thesis including the ethical considerations, recruitment strategies, data analysis and preparations for undertaking interviews. The next three chapters present the results from the interviews starting with the patient interviews.

CHAPTER 7: RESULTS FROM INTERVIEWS WITH PATIENTS

7.1 Chapter overview

This chapter presents the results from qualitative interviews with patients who have a known diagnosis of PBC. Whilst the goal of this research is to look specifically at perspectives on management in primary care, in order to more fully understand these perspectives, the interviews undertaken focussed not solely on the subject of discharge but also looked to understand the patients' broader perspective on all aspects of having a diagnosis of PBC from initial symptoms, through receiving the diagnosis, and living with the diagnosis, as well as their experience of medical care in a variety of settings. The process of patient recruitment, development of the topic guide and the interview format have already been discussed in the previous chapter. The results from the interviews are presented and then discussed in the context of the published literature.

7.2. Participant characteristics

Following placement of an advertisement in the PBC Foundation quarterly magazine "The Bear Facts" asking for people with PBC living within the West Midlands area to take part in face to face interviews (see Appendix 5), email responses were received from a total of fifty one people with PBC. Twenty-eight were excluded: the reasons for exclusion were:

- Respondent was located outside of the West Midlands (n=24)
- Respondents reported that the diagnosis of PBC had not been confirmed (n=2)
- Respondent had another liver disease diagnosis in addition to PBC (n=2)

Following the initial expression of interest, copies of the patient information sheet were sent to eligible respondents as they came forward. Three of the eligible respondents did not reply to follow-up emails. In two cases, despite multiple communications, it was not possible to arrange a mutually convenient date and time for interviews. In total, sixteen patients were interviewed: fourteen of these occurred at the participant's home and two at the University of Birmingham. Each participant was assigned an alphanumeric code beginning with the letter P (to represent patient) and a number in order of interview. The characteristics of the participants are summarised in Table 14 below.

Table 14: Characteristics of the patients recruited

	Gender	Current age	Age at diagnosis	Year of diagnosis	UDCA response status	Place of care
P-01	Female	66	44	1994	Responder	Secondary
P-02	Female	67	66	2016	Responder	Secondary
P-03	Female	45	42	2013	Responder	Secondary
P-04	Female	42	41	2016	Unknown	Tertiary
P-05	Female	52	48	2012	Unknown	Tertiary
P-06	Female	48	41	2009	Responder	Secondary
P-07	Female	66	57	2007	Responder	Primary
P-08	Female	66	50	2000	Non-responder	Secondary
P-09	Female	76	55	1995	Responder	Secondary
P-10	Female	64	38	1992	Transplanted	Tertiary
P-11	Female	74	55	1996	Responder	Tertiary
P-12	Female	64	47	1999	Unknown	Tertiary
P-13	Female	68	46	1995	Responder	Tertiary
P-14	Female	50	40	2007	Transplanted	Tertiary
P-15	Female	41	39	2015	Responder	Secondary
P-16	Female	47	41	2011	Responder	Secondary

7.3 Interview process

Interviews were carried out using a semi-structured format and with the use of a topic guide (seen Appendix 14). All interview participants were aware that the question being posed by this research was around the management of patients with PBC within primary care, and all participants were given the opportunity to discuss their perspective on both the hypothetical concept of discharging patients from hospital care to follow up by their general practitioner, and also to talk about their personal experience of management within various healthcare settings and their preferences. Not all participants were asked the question directly, for example, where the interviewee had clearly expressed concerns about primary care management. However when, over the course of the interview, it was unclear or ambiguous to the interviewer as to how the interviewee viewed the idea of long-term follow-up of patients with PBC in a primary care setting, the interviewee was asked the question directly. Data saturation appeared to have been reached by interview 14, however, a further two interviews were conducted to confirm that saturation had been reached.

7.4 Results

Prior to formal coding, it was clear to the interviewer that a number of overall trends were emerging and that, from the patient perspective, there were concerns about the management of PBC in primary care. These initial observations were noted as follows:

1) The path to diagnosis from presentation was variable and often prolonged and difficult for patients
2) Symptom burden was high
3) The moment of receiving the diagnosis was recalled in detail often with negative emotions and this initial reaction permeated into how they thought about the condition

4) PBC is regarded as a condition with a poor and unpredictable prognosis
5) Patients recalled negative interactions with their GP around their PBC care to a greater extent than they reported negative aspects of hospital-based care.

With this in mind, the next step in the analysis was to code the interview transcripts formally and then to categorise the codes into themes that would begin to explain these initial findings, and look to understand in more detail the underlying reasons for this preference for specialist care follow-up and what could be done to address these. Despite multiple attempts at creating distinct categories, it was impossible to separate the initial codes into distinct entities as the concepts were continually found to overlap. As such, a schematic of the codes and categories was created showing how these overlap and the link between the various categories (Figure 4).

In terms of understanding why patients were unwilling to be managed in primary care, the following five factors were identified and are discussed in detail below:

1) The characteristics of the disease
2) Perceptions of primary care
3) The benefits of specialist care
4) The characteristics of the patients
5) Fears for the future

Figure 4: Links between codes and categories from patient interviews

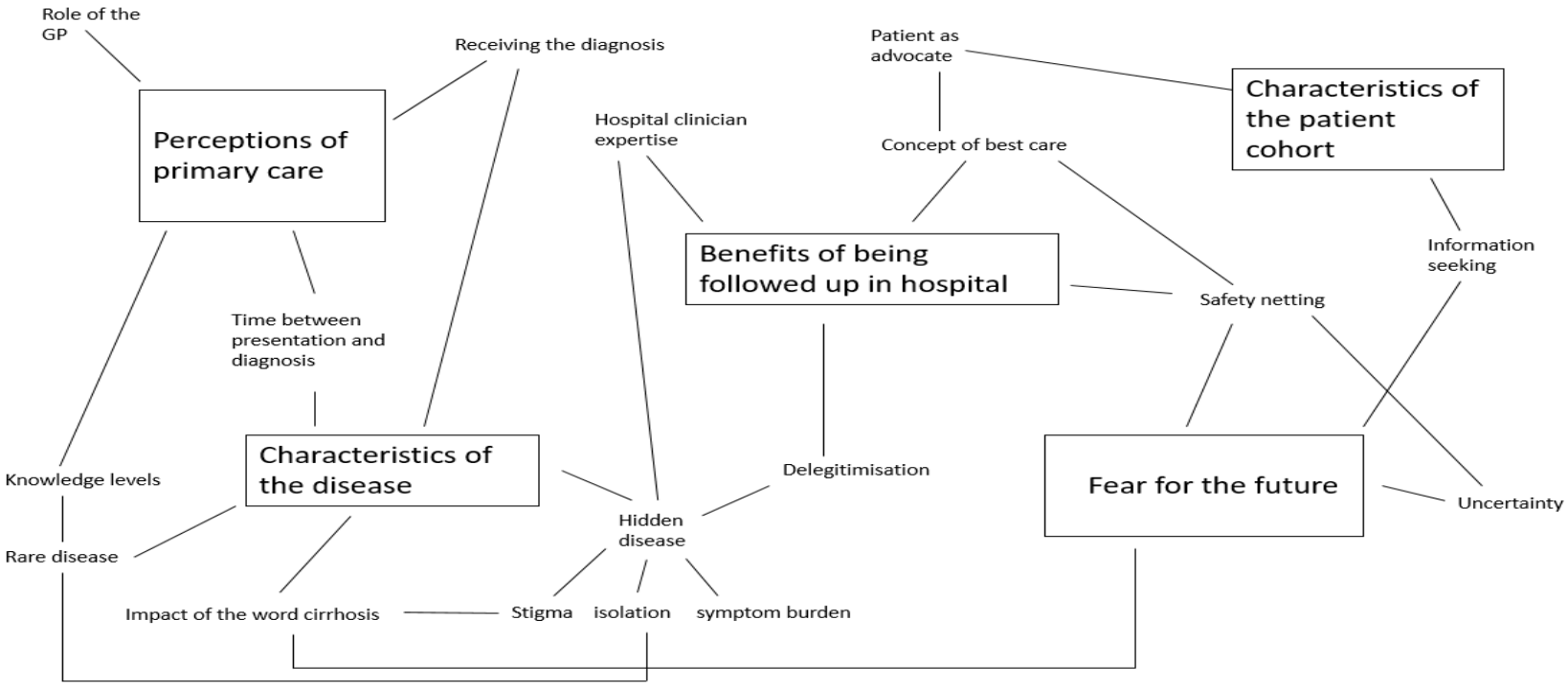


Figure showing how the codes identified from analysis of the patient interviews were grouped into categories. Some codes were found to fit into more than one category

7.4.1 Characteristics of the disease

PBC is a rare disease which is autoimmune in nature and associated with a high symptom burden. As has been identified from previous research cohorts including the UK-PBC research cohort questionnaire data discussed in Chapter 2, the presentation of PBC is variable with the majority of patients either found to have abnormal liver biochemistry at routine follow-up for another condition, or following a presentation to primary care with symptoms often unrelated to PBC. Due to the non-specific nature of the symptoms and the rarity of the condition, there can often be a protracted path to diagnosis and many patients expressed frustration, often with primary care, related to the time taken to reach the diagnosis. In addition, it was found that patients felt that their GP did not understand the impact that the delay in diagnosis was having.

> *"It wouldn't have been weeks because I badgered him (the GP), I rang him and he said something about "well there's no immediate rush". And I remembered thinking there would be if it was happening to you"* **P-01**

In other cases, symptoms were dismissed, and more than one clinician was consulted before the diagnosis was considered.

> *"I had two occasions I felt really, really faint and I didn't know what it was, so one was in bed, one was at work, so totally unrelated. So I went to the GP who said I was an alcoholic, stop drinking. She sent me for some blood tests. When I went back for the results the other GP tested me for PBC and it came back positive"* **P-16**

The impact of receiving the diagnosis of a rare disease containing the term cirrhosis with all the associated connotations (both in terms of stigma and fear for their long-term prognosis) weighed heavily and many patients could recall, in detail, the moment they received the diagnosis (even when this was many years ago) as well as the impact it had.

> *"Somebody's chucked a grenade into your life and blown it up into a million pieces and somehow, you've got to put all those pieces back together. It was like having this lovely vase that was absolutely perfect and somebody dropped it on the floor and said, 'Right, make a new one'. Well, I didn't know which piece to pick up first. I didn't know how to start rebuilding my life. I didn't know what it was going to look like when I did rebuild it"* **P-06**

> **"***very shocked cause obviously, I'd, I'd never heard of it before and also my dad Had that's what my dad died of cirrhosis of the liver, although he did, he drank but I'm thinking, 'Oh my god, is that going to be me?' and, and like I I did go through a woe is me stage and I got quite depressed and, and all that and yeah, it wasn't a good time"* **P-03**

> **"***they said it was something in my liver the only time I was really upset when I was sitting in the sun at the top of the garden thinking of the letters I'd write to the boys"* **P-07**

As well as the emotional impact of the diagnosis, there were practical considerations for their future in terms of their ability to work.

"I was diagnosed just before I qualified as a physio. Um, which was very upsetting and I thought I'd struggled to get this far, because it was hard work for me, doing the studying, my children at home as well, my husband had only just got over bone cancer, so he was at home. And I did, I did the physio because I thought I'd have to be the, the main bread winner or the sole bread winner, if I'm honest. So um, it was hard work. Um, and then I was disappointed that I thought I can't do the job I've trained hard to do" **P-01**

The symptoms associated with PBC were described along with a sense of frustration at the impact that these had, and how they were not always understood by those around them.

On the subject of fatigue:

"I get so that if I'm standing I want to sit, if I'm sitting I want to lie on a bad day and it frustrates me so much, I hate it. I absolutely hate this disease, I despise it, because of the tiredness. I want more energy. I want to do things. I want to be how I used to be" **P-01**

"Sometimes, I don't know how I, I carry on. I don't sleep well. I'm up most nights, every night and then, through the day, I could just zonk out but it's, it's literally having to try and keep going as much as I can" **P-04**

"On the Monday morning, I couldn't get out of bed and, I phoned where I was working and my colleague came on the phone and I said… She said,

'You're late, you're late,' and I said, 'Yes, I know,' I said, 'But I can't get out of bed,' which she thought was hugely funny, because she said, 'I've heard some excuses, but…" **P-08**

Others talked about itch and the associated social embarrassment that could ensue.

"I'd had sort of odd itches but this really was, I was just spending nights itching and it only starts about 9 o'clock at night and it's my arms and I was sat up in bed scratching away and, as I say it actually got to the stage of it bleeding" **P-09**

I'd scratch my head and say,"im not lousy" try and make fun of you, 'not lousy' you know, ha-ha, then scratching my arms. I then ended up like scratching and scratching and scratching everywhere, until like my hands are raw, that I lose all the tips of my fingers because I – I scratch like that" **P-10**

In addition to the impact of the symptoms themselves, patients described a disparity between the symptoms they had and the visible signs of the disease:

"People would say, 'Oh, you look so well,' you know, 'Have you been on holiday?'. I'm actually yellow. but you don't say that. People know, but not too many people. You just smile and say, 'Yeah, I've been away,' or whatever" **P-08**

There was frustration that this dichotomy meant that others (friend, family, and work colleagues) did not understand the impact of symptom burden.

> *"the horrible thing is, like everybody will say, and have said, that nobody understands. They, you say "oh I'm so tired today" and they say "yes and me, it's the weather and uh, I did this last night or something". They have no idea of the tiredness"* **P-01**

As a rare disease, many lay people will not know much about the condition if they have even heard of it at all. For those living with this condition, this can pose an additional burden; they can often feel isolated by the fact that friends, family and work colleagues do not have an awareness of the condition. Isolation was a common theme related both to the rare nature of the condition and the disparity between symptom burden and outward signs.

> *"It's not a very common disease is it, it's not that many people in the UK got it compared to breast cancer, or diabetes, heart problems. Um, so I do find it a bit isolated. I think that's the second issue I've had is not knowing anybody"* **P-02**

Due to the lack of outward signs of the condition, patients felt that others may not believe them as to the impact and the need to make life adjustments.

> *"it's not easy in that respect because your work colleagues are also then questioning 'how come you've – how come – you don't look that ill, but you're having all this time off,' because you can look quite well"* **P-10**

In addition to the forced isolation, there are also instances when patients describe actively choosing not to tell others. Participants reported keeping their diagnosis of PBC hidden from others; sharing the information only with close friends and family. The reasons for not discussing the diagnosis were varied. In some cases, the patient did not want to be treated differently by others once the diagnosis was known.

> *"I've just kept it to myself because I don't want people to treat me any different. I still want them to think of me as me and not think, 'Oh, we'd better not do that in case she gets too tired'. If I get too tired, I will make an excuse and I will drop out but I try and live my life as full and as much as I've ever done"* **P-06**

Another trigger for patients not telling others about the diagnosis is the association that is made between cirrhosis and alcohol.

> *"I have stopped telling people because they automatically think, what they say is well you've got to stop drinking then haven't you? And I said, drinking's never been an issue with me. But I find I'm defending myself and why should I have to defend myself? It's nothing to do with, with the drink"* **P-02**

Prior to 2015, PBC was officially known as Primary Biliary Cirrhosis. However, the new name Primary Biliary Cholangitis has subsequently been adopted. This change in nomenclature was undertaken not only to highlight the changing natural history of the disease, whereby a minority of patients with PBC will go on to develop cirrhosis, but also with the aim of reducing the stigma that patients with this condition reported and attributed to the public perception of the

association between cirrhosis and alcohol (8). The stigma associated with the word cirrhosis was brought up by several patients.

> *"And it's improved a lot since you can say primary biliary cholangitis, before that was cirrhosis; they thought you were hiding the gin bottles in the pantry"* **P-09**

The stigma around alcohol was not just related to the perception of lay people but also by primary care clinicians whereas patients described that hospital clinicians had both an understanding of the erroneous nature of the perceived link and the impact that the link could have. More than one patient mentioned that their GP had mentioned alcohol as the first likely cause of their symptoms and abnormal blood tests.

> *"I had two occasions I felt really, really faint and I didn't know what it was, so One was in bed, one was at work, so totally unrelated. So I went to the GP who said I was an alcoholic, stop drinking……..she just put it down to alcohol. So bearing in mind I'm not a heavy drinker, I only drink two days a week so I don't know if she just wasn't interested, I'm not too sure but so she just sent me for blood tests"* **P-16**

> *"I explained the symptoms and I wondered if she thought I'd been on a blinder or something, thing but I don't drink and anyway so she did the appropriate things and she gave me a prescription and as I got up to leave with my back to her she said, 'Be careful with the drinking.' And that was awful, absolutely*

awful. So I, I, I was shocked, I was so shocked" **P-07 discussing a visit to see a locum GP**

In contrast to this comment from their primary care clinician, the patient used an interaction they had previously had with their specialist clinician regarding the issue of alcohol and the often false attribution to cirrhosis and impact that this could have on PBC patients.

"Dr X 'is an absolute expert on PBC…….He said if he wants to annoy his patients he always say how well they look and how much do they drink" **P-07**

In keeping with the data from the UK-PBC questionnaires, the majority of patients who took part in these interviews were seen in hospital for follow-up. Only one patient within the interview cohort had been discharged to primary care, although in other cases this was being considered. When they described the rationale that had been given for this decision to discharge this wasn't universally met with positive feelings and one patient expressed a concern that this was not standard practice and was different from the care received by others.

" It's just as an underlying, I suppose, concern the fact that a lot of people are still seen by consultant, aren't they? And what, what percentage of people are normally seen by a consultant?" **P-07**

7.4.2 Perceptions of primary care

Although the majority of patients were managed in either secondary or tertiary care at the time of interview, all were able to describe interactions with primary care at various points during the time from the first presentation to the present day. These descriptions, as a whole, identified that there was a sense of dissatisfaction with their interactions with primary care based on experiences from the early stages of presentation and diagnosis, through to more recent interactions. In addition to the associations with alcohol discussed above, this dissatisfaction was related to a number of other factors including knowledge levels, experience of lack of empathy, and a sense of disinterest on the part of primary care.

Patients described that clinicians in primary care had a lack of knowledge about the condition.

> *"the GP didn't know very much about it at all because he was having to read up – in fact, he got his book out, to just check that what I was saying was what actually the book was saying about PBC"* **P-10**

> *"I don't feel that my GP knows enough about the situation to really be able to – he'll just be looking online himself"* **P-15**

In addition to lack of knowledge, there was a perception of unwillingness on the part of GPs to take an interest in the condition.

> "*They don't know anything about it and but then they don't really seem that interested to find out about it and I would just feel like I wasn't being looked after properly."* **P-03**

"I phoned up and asked if I could have an earlier appointment, because I if I go to my GP they're only gonna say, 'Well, really, you should be seen by who you're under,'" **P-12**

This lack of knowledge had a direct impact on how patients viewed discharge to primary care.

"If you tried to tell me that I was going to be treated by a GP then I would not be happy because they don't know enough about it." **P-09**

The experience of receiving a diagnosis of PBC was recalled as a negative experience with patients recollecting that the information was often delivered bluntly with a lack of empathy.

"I went back to my GP who had a very unfortunate manner by saying, 'Ooh well, you've got PBC', briefly explained as much as he knew about it and said, 'Well don't worry about it if you get 10 years. That's given you three score years and 10'. And, that's it" **P-09**

Not all interactions with primary care were negative, however, the positive interactions described were separate from the actual management of the condition and related to a view of the more holistic role of the GP in contrast to the role of the specialist.

"he has always been extremely nice and he's never made me feel I was making a fuss because I didn't go unless I've really got to but he's always been incredibly kind and he didn't know, he didn't know what PBC was. None of them did. But he has been extremely kind, you know" **P-07**

In other cases, the GP was seen as the coordinator for care and their role was to help the patient navigate the world of specialist care within a hospital-based setting rather than to manage the condition themselves.

> *"He's kind of – the whole thing, he's kind of almost project managed dealing with what it is I've got."* **P-15**

When considering the potential for primary care to manage PBC, the factors taken into consideration also included the patient's past experience with primary care related to the management of other conditions. Where these interactions were viewed negatively this impacted on how they viewed being seen by the GP in the future.

> *"When I was first….. after I had my gall bladder removed, and I was getting my pain, I just felt like he was telling me it was all in my head and it wasn't real. So I felt a bit let down, so I do try and stay away from my GP"* **P-04**

The impact of past experiences did not only have to relate specifically to the patient's own care and could involve interactions between a patient's family member and primary care. One patient who expressed satisfaction with their GP and viewed possible discharge in a positive light discussed how the GP had been involved in their husband's care and how witnessing this had impacted on their confidence levels.

> *"he had a problem which they thought might be cancer and she rang him the next morning, she wanted him back at the surgery and he was at the hospital within two weeks. She uh, was like a dog with a bone and wouldn't let that one go. I was really impressed with her and uh, so I just felt that I could perhaps have a chat with her about how I was feeling"* **P-02**

7.4.3 Benefits of being followed up in hospital

Compared to descriptions of primary care, hospital clinicians were viewed as more knowledgeable, and interactions with clinicians in a hospital setting were presented in a more positive light with fewer negative experiences discussed overall. Hierarchies within hospital-based care were also identified and patients reported that if their disease progressed then they would wish to be seen at a specialist centre rather than their local hospital. Hospital-based care was perceived as the "gold standard" of care and where patients would receive the best treatment in comparison to being managed by less experienced clinicians with a correlation drawn between this expertise and better outcomes.

> *"Life's precious and you don't want to miss out the optimum treatment. So I think, for purely selfish reasons, I would want to, want to go somewhere where I, you know... I'd – I felt confident that they knew the best treatment and what to do with me, rather than leave it right till the last minute and then I haven't got any other options"* **P-06**

When asked about discharge to primary care, patients recalled previous difficulties accessing secondary care from primary care which meant that remaining under hospital follow up even on an infrequent basis was preferential.

> *"by the time you'd been referred, you're talking about six months, you know, half the time, and that, by the time the appointment's been cancelled twice and such like"* **P-11**

Participants reported being under regular hospital follow up even in infrequent as a "safety net"; both psychologically and from a practical perspective.

> *"at the moment, I feel confident because I've had regular liver scans and things that – all showing that everything's absolutely normal; then that's – that makes me feel confident and that backs up the way I'm feeling, you know"* **P-06**

> *"it is reassuring and it also feels, well, I can forget about it and I'm not obsessive about it. Just once a year I go and it's great"* **P-05**

> *"I think it's worthwhile just, you know, I think just to put my own mind at rest that everything is fine and the blood tests are okay, everything is normal"* **P-16**

Having a specialist involved helped patients realise that many of the non-specific symptoms they were having and had been going on for some time without any apparent cause being assigned were, in fact, connected to PBC.

> *" I didn't connect it to that and I don't like going to the doctor as well. So I've just put up with it and then when he said, 'Do you get this? Do you get that?' and it's like, 'Yeah, I do actually' and then they said, 'It's all connected'. So then it all starts – the jigsaw starts putting, putting together"* **P-04**

However, not all interactions within the hospital were positive. In the case of a patient who had been diagnosed almost five years prior to the interview taking place, they recalled receiving the diagnosis and whether the condition was explained to them.

> *"a little bit but I'd looked it up, you know, once I was diagnosed. I thought, 'Well I'll have a look into it, see what it is', but, I don't think he clarified exactly what it was so yeah still a bit in the dark kind of thing"* **P-16**

Where negative interactions were described that related to hospital-based care, patients looked to provide an explanation for these.

> *"I think my longest wait is two hours but then if the person ahead of me needed that to, you know, extra time. I might need it one day"* **P-05**

When asked when they were next due to be seen, one patient realised that they were overdue their appointment. A field note made by the researcher related to this comment described that the respondent was quick to dismiss this realisation which contrasted with their previous demeanour when talking about negative experiences with primary care.

> *"I don't know, I think I've slipped through the nets……I certainly haven't been this year so I must have, I need to give them a ring"* **P-01**

Negative practical aspects of hospital care such as time off work and delays in appointment times were justified by the benefit gained from the appointment.

"It's good to just get a catch up and just, you know, despite the fact you're usually waiting for 40 minutes to go and see him for two minutes but, I think it's worthwhile just, you know" **P-16**

7.4.4. Characteristics of the patient cohort

Patients were confident to advocate for themselves in pushing for this access to expert care. One patient reported that she had actively asked her GP to refer her to a specialist centre and when told this might not be possible had used the patient support group to find the name of a specialist and push for this referral.

"he said that he would have to go in front of the panel because it was out of area. but if I wanted to search around for my own, and I think – I'm – I can't remember now cause it was coming up to 18 years ago, I think it was I went through the PBC Foundation to see if they could give me a list of consultants" **P-12**

Other patients reported that although that hadn't needed to do this yet that they would actively push for a specialist referral if they felt their health was deteriorating.

"while I'm stable and not really doing anything, I'm happy to stay where I am but the minute I felt that it was progressing, I'd want to go somewhere where would know exactly, you know, what treatment and what to do next because I do feel, locally, that there's not the knowledge

that there is in (the specialist centre)" **P-06**

Overall, hospital-based care was most beneficial if the patient was able to see the same doctor at each visit and were happy to wait longer to be seen if this meant this would happen.

"I think you get to know them you know and they know how you're feeling. When I used to go and see him he could tell if I was having a good day or not so he got to know me the same as I got to know him. And – and you know I just think it's easier than having to go in and see someone completely different and have to explain it all over again" **P-14**

Even in the case of those with mild disease who recognised that the condition would not have long-term negative prognostic implications for them, living with a chronic disease, especially one where the symptom burden is high continued to have a negative psychosocial impact.

"probably it won't be this that kills me, you know? I'm, I'm fairly relaxed about it. Um, yeah, I just um, I just don't like the way it makes me feel and I would really like it to lift and fly away. Because I find it's very, it's it's very heavy on me, you know, it's, yeah" **P-01**

7.4.5 Fears for the future

Before the advent of the use of UDCA, natural history studies and early clinical trials suggested that life expectancy from time of diagnosis was less than ten years (14) and was described as universally fatal (34). However, this is no longer the case and in many cases PBC is a chronic

condition with no significant impact on mortality. However, there remains a level of misinformation about the nature of the condition. The name change from cirrhosis to cholangitis occurred just prior to the time of these interviewees being undertaken and therefore the majority of patients had received a diagnosis of "Primary biliary cirrhosis".

> *"All I remember was that you die from it and the word cirrhosis. I remember going around my mums and saying I've got cirrhosis of the liver and we both cried"* **P-01**

A number of participants mentioned the likely prognosis for PBC being 10-15 years from the point of diagnosis. This was reported not just by patients diagnosed in a pre-UDCA era but also for those who had been diagnosed within the last few years. In some instances, this misinformation came both from patients own information-seeking through books and internet sources, and from consultation with healthcare professionals.

> *"the data that I was reading, it was from years and years ago. It wasn't really looking at women like me that were first diagnosed; this was looking at like end stage PBC"* **P-06**

> *"I saw the main consultant there and he said um, I think his opening words were you've got a protein in your blood that's attacking the bile ducts in your liver… And he said about the ten to fifteen years um, and we don't know how long you've had it because you haven't had a blood test for four years*" **P-02**

Despite being a group of patients that exhibits a number of features of self-advocacy and a wish to be informed about the disease in general terms, when it came to their specific case, some patients appeared reluctant to ask about their own prognosis, and many were in a state of not knowing what the future holds for them. When asked why they had not asked their doctor about their specific prognosis, a range of responses were given. One patient reported that they did not want to trouble the doctor whilst another tried to avoid thinking about prognosis.

> *"I'm going back to the doctor, next month, so I might ask more questions; instead of, you know, just listening to him when I don't understand what he's saying but they are busy as well. Do you know what I mean? I mean that place is so crowded"* **P-13**

> *"I do try not to think about that too much because I'm on my own and I'm thinking, you know, I don't want to be really ill and being on my own and I don't want my son to have to look after me and, and that sort of thing"* **P-03**

Amongst patients there was a lack of understanding about UDCA response and how this translated into risk of disease progression with a sense of inevitability of deterioration in health.

> *"And nobody can predict the future can they, so I know they're just going to keep, keep their eye on me"* **P-02**

> *"Doesn't make it any different. It's going to happen. It's just a matter of when, isn't it?"* **P-03**

However, where there had been discussion about the concept of response and what this meant for the future, and when this discussion had been used to discuss the possibility of discharge to

primary care, this was met with positivity and a greater understanding of the rationale for this decision.

> *"I'm due to go back in six months. And he said they'll decide then whether just blood tests and stopping on the Urso with my GP or whether to carry on at the hospital. But I can understand if they do put me back to the GP because what, what are they going to do at the hospital?* **P-02**

Where this wasn't explained, patients were less likely to view discharge to primary care in a positive light instead they attributed alternative reasons to the decision such as pressures on the NHS.

> *"I guess it's NHS funding, isn't it, but, as I say, having been told I'd be seen at (Hospital) for life. I was then discharged and, and given back to the care of my GP, who I make an appointment to see once a year"* **P-07**

7.5 Discussion

The interviews undertaken with patients were intended to establish the patient perspective on management in primary care and to understand why patients have particular perspectives and what the factors are that underpin these. It was apparent from early in the interview process that, overall, patients have a preference for management by a specialist in a hospital setting. The reasons for this were complex and were related to both the psychosocial aspects of living with chronic illness, specific patient and disease factors, and past healthcare experiences.

The results of the patient interviews draw a number of parallels with the work of Bury in patients with rheumatoid arthritis and the concept of chronic illness as a disruptive event (92). When diagnosed with PBC, patients are forced to face a possible mortality risk or at least an uncertainty about the future. Associated with this is a sense of fear but also, for some, a relief especially where symptoms have been ongoing for some clear diagnosis having been reached. There is also a sense of disruption to life plans; the diagnosis itself as well as the high symptom burden impacts on family life, relationships with friends, and their work life. This is compounded by the sometimes hidden nature of the condition (both in terms of it being rare and with few outward signs except in the advanced stages) and this results in isolation from others. It is these factors which, for patients, play an important role in how they make judgements about their preferred place of care for the long-term management of their condition, which is often independent of the purely medical perspective of stratified care and risk. Because of this, along with their previous, often negative, interactions with primary care, patients report a clear preference for hospital-based care.

PBC as a rare disease comes with specific challenges which impact on the patient perspective and present barriers to primary care discharge. The patient questionnaires discussed in Chapter 2 identified that modes of presentation are variable and that time to diagnosis can be lengthy. This finding is supported by the results from these interviews which provide a series of detailed accounts of the process of reaching diagnosis. More importantly they also describe how these difficulties in reaching the diagnosis impact how patients view primary care as a location for their ongoing care.

The concept of delegitimation is defined as "the experience of having one's perceptions and definitions of illness systematically disconfirmed by significant others" (93) and this is apparent in the patient interviews discussed in this chapter. This is not the first time the phenomenon has been identified in the PBC literature. Montali et al (77) in their study of patients with PBC in Italy referred to delegitimation appearing in three forms, Firstly the denial of the patients' sick role with a tendency by others to minimise the impact that the illness was having on their lives especially when the patient does not look unwell. Secondly, the trivialisation of fatigue with non-PBC sufferers reporting that they also experience this symptom and, thirdly, the lack of consideration of patients' needs especially in interactions between family members or colleagues when the patient struggles to continue to achieve their expected role. The impact of delegitimation on the doctor-patient relationship has also been discussed in the context of other illnesses. In the chronic fatigue syndrome literature, for example, health care professionals often made particular attributions to the cause of the symptoms (often as being psychological in nature or dismissed as another condition such as depression or even the menopause). The authors of this study noted that as a consequence of this "the mutual trust, respect and communication associated with good doctor–patient relationships eroded" and, in addition, there was a "shift in the power dynamics between the participants and the GPs". This could lead to a shift in the doctor-patient dynamic with the patient as expert and the importance and "expert status" of the GP removed (94).

The issue of time to reach a diagnosis is key. In a systematic review by Kostopoulou published in 2008, the authors set out to establish what features of a condition make it difficult diagnose, with a specific focus on missed diagnoses in primary care (95). They identified the following five features: 1) an atypical presentation (meaning that the signs or symptoms are not classic of

the presentation), 2) perceptual features (where there are visual or auditory signs or symptoms), 3) comorbidity (where another or pre-existing diagnosis can mask the condition, 4) conditions of low prevalence and 5) non-specific presentations. The latter two factors are of particular relevance to PBC as a rare disease and also one where the symptoms (if there are any) can be those of many different conditions, many of which are more common than PBC and also where the biochemical changes that can be seen (rises in bilirubin, and ALP, and sometimes to a lesser extent ALT and AST) can be caused by other more common conditions. The biochemical changes of PBC and the differentials that exist for abnormal liver function tests are notable here not just for the fact that they pose potential diagnostic delays but also for the recurring theme in a number of interviews of the association between liver disease and alcohol use.

It is not just the time in reaching the diagnosis that is important however. The way in which the diagnosis is given is important and can also have a long-term impact on the relationship between the patient and their GP. Survey data from the EURODIS project in 2004, which included more than 6000 patients with eight rare diseases found that in 33% of cases, the diagnosis was announced in unsatisfactory terms or conditions (69). This is also reported in the PBC patient interviews with the added and recurrent issue around the misconceptions around alcohol and how this factors into the discussions patients have with clinicians around their presentations. Within the interviews undertaken for this thesis the subject of alcohol was brought up spontaneously by 11 out of the 16 participants and many described an associated stigma that comes from having a disease which includes the word cirrhosis. This theme has been identified previously in the PBC literature in work by Sogolow et al (96) who found that, while stigma can arise from a range of interpersonal interactions, it is most common in

interactions with health care professionals with the experiences of patients in their cohort in the United States mirroring the experiences of patients in the interviews described above.

The doctor-patient relationship is key to the implementation of a stratified care pathway and these experiences of delegitimation from a disease with hidden symptoms, alongside the issue stigma of having a condition falsely attributed to alcohol are negatively impacting on this relationship especially in primary care. Putting these factors together it is clear that the patient experience in the early stages of their disease in terms of time to and experience of being given the diagnosis is key to what happens later on and this will need to be addressed in order to allow successful risk stratification and potential discharge later on. In its paper setting out its strategy for rare disease in the UK, the Department of Health (DOH) noted that fact that these diseases are rare means that health and social care professionals especially those in primary care are unlikely to have previous experience of the patient's condition (13). The paper goes on to state that it is unrealistic to expect GPs to recognise all rare diseases as, for some, a GP is unlikely to see a single case in their whole career. It did, however, point out that education and information of provision to health care professionals was vital. How this could be best undertaken for a condition such as PBC is an area to be addressed in the later interviews with GPs (Chapter 9).

7.6 Chapter summary

The results from the interviews undertaken with patients with PBC have identified that overall there is a lack of willingness by patients to be discharged to primary care. The barriers identified correlate with many of the barriers identified from the breast cancer scoping review (Chapter 5) but have also identified concepts specific to PBC as a rare and hidden disease. How these

barriers can be addressed will be discussed later. The next chapter discusses the results of the interviews undertaken with representatives from the patient groups and will look to compare the findings from the small group of patients discussed here with the broader perspective of a larger group of patients.

CHAPTER 8: RESULTS FROM INTERVIEWS WITH REPRESENTATIVES FROM THE PATIENT GROUPS

8.1 Chapter overview

The previous chapter details the findings from qualitative interviews with patients with PBC. The results identified that the patient perspective on management in primary care is impacted by five interlinked factors: 1) characteristics of the disease, 2) previous experience with primary care, 3) characteristics of the patient cohort, 4) benefits of being followed-up in hospital, 5) fears for the future. This chapter presents the results from interviews with representatives from two of the national patient support groups and discusses both the data generated from these interviews as well as looking at the correlation between these findings and those in the previous chapter.

8.2 Rationale for involving patient group representatives

When comparing qualitative data to quantitative data, a commonly stated disadvantage to the former is that it involves only a small number of participants, that the data is "soft" (as opposed to the hard numerical data) and that the results may not be generalisable (68). In order to improve the validity of qualitative research, a number of techniques can be employed to address these potential disadvantages. For example, comparing the results from either two different methods of data collection or two data sources to look for evidence of convergence also known as triangulation (97). In order to strengthen the validity of the data obtained around the patient perspective, representatives from the patient support groups were also recruited to take part in qualitative interviews to look at both their specific perspective and also to determine whether

the themes identified from the patient interviews thus far are reflective of the experiences of patients more generally.

8.3 Participant characteristics

Representatives from two of the national patient groups were interviewed. One participant was from a patient group specific to PBC and the other was from a patient group for patients with chronic liver disease in general. These participants were given the alphanumeric code R-01 and R-02. The interviews were both carried out after all the interviews with patients were completed.

8.4 Data analysis

In the case of these two transcripts, open coding was undertaken with the awareness of the codes that had been generated from the patient interviews. This did not mean that new codes could not be added. As there were only two participants in this group, it was not possible to state whether saturation had been reached. As with the results from the patient interviews, once the list of codes had been finalised, the codes were then reviewed and then grouped them into distinct categories.

8.5 Results

Based on the initial analysis of the interviews and notes taken at the time of interview, the overall impression from the interviews was that the patient support group representatives were more positive than the patients interviewed regarding the concept of discharge of low-risk patients to primary care although there were some caveats to this and the participants recognised

why some patients would be concerned about this approach. The final codes and categories identified are shown in Table 15.

Table 15: Codes and categories generated from patient group representative interviews

Code	Category
Seeking information Self-advocacy	Characteristics of patients
Access to specialist care Shared decision making Acknowledgement of anxieties	Patient-centred care
Knowledge levels Accessing information	Expectations of primary care
Fears for the future Financial worries Isolation Hidden disease Stigma Symptoms Telling others	Impact of living with PBC
Sources of information available to patients Role of the patient support groups	Importance of access to information

8.5.1 Characteristics of the patients

As was the case in the patient interviews, the patient group representatives reported that patients with PBC are keen to know as much about their condition as possible and take an active role in their care.

"PBC people – there's definitely…….I don't know what it is but they, they, they really are hungry for information" **R-02**

Whilst this finding could be influenced by the fact that the interviewees are from patient support groups and therefore this may not be the case for all patients with PBC, it was noted by the representative from the general group that patients with PBC were more active within the group compared to members with other liver conditions. When talking about patients who join the group it was noted that:

"they come on and they're enthusiastic and they want to help and then we never hear from them again. That doesn't happen with PBC people. Once they're on the mailing list, they're there and they're interested and they'll respond" **R-02**

Patients are willing to make an effort in order to access high-quality care whether this is through attending educational meetings or travelling to a hospital that may not be their local hospital.

"I think they just want the best treatment. I think once they understand that, perhaps, they're not seeing the hepatologist, because some of them don't even realise that they're not seeing a Liver Specialist then I think they're happy, if they can travel do that" **R-02**

Patients undertake other proactive measures to ensure they received the best treatment. One of the patient representatives talked about the feedback they had received from clinicians who manage patients with PBC.

"it's a very consumer society and he now gets patients phoning him up, 20 years ago I'm pretty sure we wouldn't have dreamt of doing that. You would write a letter and hope to get a reply and if they didn't so what? So, I guess it is changing, isn't it? **R-01**

8.5.2 Patient-centred care

The concept of quality of care is a theme throughout the interviews with the patient group representatives and is underpinned by the concept of equality and that all patients should be able to access the treatment they need regardless of factors such as age or where they live. This sense that there may be an existing inequality in access to services is allied to the feeling that the doctor is deciding what is best for the patient and the underlying rationale for decisions is not always fully discussed with the patient. In contrast, where a decision is made and the rationale for this in clinical terms is explained with the patient is involved in the process, the decision is more likely to be accepted.

"You do that, you view it with them say, 'Well things are looking good, I wouldn't expect any changes or you can use the you know the score', PBC score that they have now and, 'How do you feel about monitoring? Being monitored by your GP?', etc I think that's what should be happening" **R-01**

Contrasts were drawn between this approach and situations where the rationale for the decision making is not explained and, as a consequence, it is felt to be based on prejudice. It is in this scenario when place of care decisions are deemed to be less acceptable.

> *But when somebody is told, 'No you can't access a hospital, there's nothing can be done for you, I'll look after you and I'll see you once or twice a year, we'll do your bloods', that's not good, that doesn't sit well at all"* **R-01**

> *" I think so somebody to be told, you know your over 60 you'll stay with the GP, that's, I don't think that's fair. It's not quality, is it?"* **R-01**

Whilst the rationale behind a stratified approach is that those patients at low-risk can be discharged to allow specialist input and resources to be directed to high-risk patients, there is the recognition that being seen in a hospital by a specialist has an impact on the patient beyond the management of long-term risk and consideration of second line treatment and that there is an additional unseen benefit.

> *"is it wasting a resource? Not if it makes people feel better, there's never a waste of resource"* **R-01**

> *"I just think they want to understand what the condition is; what – you know, what they can expect and, and I think as well they get great comfort from knowing that they're not alone; that there are lots of people out there"* **R-02**

Specialists may be better able to acknowledge a patient's symptoms and the fact that while there is no treatment for them, the fact that this is an expected part of having the condition can itself impact on the patient.

> *"Whereas if a doctor were to say, 'Yes that is part of PBC however it's worth reading up and you know listening to others what can help'. And encourage them and just take it on board that that is one of the symptoms that's troubling them"* **R-01**

In this respect, the patient support groups are a source of help not just to patients who will receive better information but also to clinicians who can focus on the more medical aspects of the condition.

> *"instead of spending half an hour with a patient and explain things over and over when the information was there they could maybe get two patients into that time or at least see the patient a little more settled and not so hand ringing, worrying, frightened"* **R-01**

There is an acknowledgement that while not every patient will live close to a specialist centre, although patients are willing to travel to see a specialist, in reality, it is also the case that not every patient may need to access to specialist input. However, from the patient perspective, it is important that there is a system in place so that if this is the case then this is accessible and the route into this service is clear and that all patients have equal access to resources.

"I think people are more comfortable that a liver centre has an outreach, you know has an arm if needed……..I think as long as they know it's there in case things change, I think that's what's important" **R-01**

8.5.3 Expectations of primary care

Regarding the role of primary care, there is an acknowledgement and also an acceptance that knowledge levels about PBC are lower amongst GPs than hospital-based clinicians and that the role of the GP is a challenging one.

"But it is something you know people coming in, you don't know what they're coming in for and what they want and you get a rare condition and so you've obviously got a big obligation, professionally, you've got the legal things that go on these days if you really want to sue the bloody doctors. And you know it's a huge thing" **R-01**

"you can't expect every doctor to be experts on these orphan conditions so those that are, I think, not only have a responsibility to the patient I think they have a responsibility to help" **R-01**

Whilst there is an understanding that GPs cannot be expected to have the same level of knowledge about a rare disease as an expert would, this does not mean that this lack of knowledge should be allowed to impact on a patients care. The impetus is placed on the GP to ensure that this lack of knowledge does not detrimentally impact a patient's care.

"They are allowed not to know but they are not allowed to see you walk out

the door distressed, without the information you need, they have, I think they are duty bound to find out what it is the patient needs" **R-01**

"I know a doctor can't give you a pill for lethargy, but acknowledging that You do have it your half way there. Other than saying well you, you know there's nothing you can do about it" **R-01**

The interviewees reported that some GPs are more willing to be involved in care than others and that in the case where a patient is discharged to the care of a GP who was less understanding of the overall symptoms of PBC this could potentially be detrimental to patient care.

"I mean if you've got somebody from the "old school" who would look at some – a middle-aged woman saying that's she tired and just dismissing it, then no, I don't think the GP's the, the, the place to be managed" **R-02**

8.5.4 Impact of living with PBC

The subject of PBC as a hidden disease which isolated sufferers from others, which was identified in the patient interviews, was echoed by the patient group representatives.

"when people come on, on the phone or emails, they, they think they're the only person who's, who's got it and they've never heard of it" **R-02**

"I think the fact that they can talk to people who are going through the same thing but I guess that's the same with whatever disease you have. If you're not alone, then it's, it's a good thing. It's not nice being on an island" **R-02**

" we can get alone with an illness and maybe they haven't it connected with your GP or maybe you haven't been asked to go to a hospital or you know you're feeling isolated" **R-01**

There was a recognition of the burden of the diagnosis in terms of symptoms with a focus on itch and fatigue.

"as far as PBC is concerned there's two things that concern people; are the lack of information – the three things – the itch, and the fatigue, by far, you know, they're, they're the biggest issues people have" **R-02**

"they're not sleeping with their husband because of the itch, the tiredness" **R-01**

"this fatigue the tiredness, the lethargy, there just isn't a word that really covers it. You know this feeling of walking in tar and all of these things" **R-01**

The subject of fear identified in the patient interviews was also acknowledged as being a widespread problem, and that many patients are uncertain of what may happen in the future and how this may impact themselves and those around them.

"lying in bed at night worrying what's gonna happen, you know whether

people have got elderly parents, have got young children…disabled children living at home you know and it's not just about themselves, it's about the various systems" **R-01**

As was found in the patient interviews, not all patients ask their clinician about prognosis and the patient group representatives felt that this reluctance to ask about prognosis occurred especially if the patient believed that the outcome of the conversation was likely to be bad.

"They're frightened of what they're going to be told. They want to ask the question but they don't want the answer or they don't – you know, there's an answer they don't want and an answer they do want and... the whole situation can be just overwhelming really." **R-02**

The patient group representatives did however note that the nature of the questions being asked to the patient support groups has changed over time. When the groups were originally set up UDCA was only starting to become available and the natural history of disease was still very much that of a disease with a life limiting prognosis. In the current day the practicalities of living with a chronic disease rather than outcomes were of increasing concern.

"in the early days the first question was, 'When am I going to die?' and that has changed. People……. you know it's more about well what's the numbers of the transplant etc". **R-01**

"they ask about employment you know what are the rules and regulations, what are they duty bound to say to their employers. People ask us about benefits" **R-01**

As a result of this sense of fear was the sense of the emotional and psychological impact of having a rare disease that is hidden both inadvertently as there are few external signs and also actively due to many patient's embarrassment around the perceived stigma from having the condition.

"nobody believing them because they look so well and feeling worthless, feeling useless, not wanting to tell their children, their family" **R-01**

"the families don't understand and I think... certainly with the, with the GPs the GPs don't understand. They don't understand the condition, and women, in particular, are told, you know, 'Oh, it's, it's your age" **R-02**

Echoing the patient interviews, the association between alcohol and liver disease was mentioned by both of the representatives of the patient groups as a recurrent topic that they heard from their members.

"*because of the word cirrhosis tagged onto the end of the name and a lot of my members, our members didn't tell people they had it. A couple of ladies, 'I'm not having them think I'm a drinker"* **R-01**

" when somebody gets told they've got liver disease, their, their response is, 'I don't drink' and they think they're being judged" **R-02**

8.5.5 Importance of access to support and information

For patients early in their PBC journey, there is a lack of information available through primary care or poor quality information and where there is a lack of knowledge, patients are therefore accessing other sources of information. Whilst this may be done through joining a patient support group, other sources of information are used and not all of which are reliable and accurate.

> *"They just haven't got that knowledge and, so people will get on to the internet and – which can be very dangerous and, and get the wrong end of the stick and all sorts of things*" **R-02**

The need for psychological support is one of the other reasons that patients join a patient group.

> *" people seem to want to access us, we run a telephone helpline so it's a 24/7 helpline. Years and years ago people needed us at all times at day and night, sometimes just to talk"* **R-01**

Due to the rare nature of the condition and lack of knowledge amongst primary care, the onus for the provision of information and support is separated from primary care and falls on specialists and the patient support groups to provide this resource. Describing the early days of setting up the patient support groups (both were first set up in the mid-1990s) there was an absence of resources available for patients and of the information that did exist much of it was outdated or focussed on the more advanced disease. The groups were created in order to fill this gap in information.

" there was many people out there who knew nothing, who were frightened or there was a couple of mothers contacted me 'my daughter died with an oesophageal bleed, we didn't know what was wrong with her" or somebody had problems itching, it wasn't diagnosed but it was there was just problems across the board" **R-01**

Being part of a support group also allows patients to connect with peers and can, for some, be the first time that they have spoken to someone else who either has the condition or has knowledge of it.

"people wanted to talk to one another, they wanted to know, you know first hand what happened to you? What happened to somebody else? All the variances as well and what hints, tips people had to live with this thing" **R-01**

Joining a patient support group can offer this access and patients are keen to take up the opportunities associated with being a member of these groups. Many will access the newsletters and online resources of these groups or attend educational meetings. Once they join patient support groups they are not passive in their membership and look for opportunities to engage actively with the group.

"We sometimes get as many as 200 people because not everybody can see a hepatologist or an experience" **R-01**

8.7 Discussion

The results from the two interviews with the patient group representatives draw several direct comparisons with the patient interviews. As was shown in the interviews with patients, there are specific characteristics of the PBC patient cohort and factors related to the impact of living with PBC that influence how patients view the role of different healthcare settings and healthcare professionals in the management of their disease. These include the stigma associated with the diagnosis, the desire for information, and fear about the future. Overall, there is a lack of confidence in primary care management. The negative past experiences described by the patients interviewed in Chapter 7 appear to be reflective of the wider PBC cohort. Whilst the patient group representatives identified that there is a lack of knowledge within primary care around PBC, they also recognise that this should not be a permanent barrier to management or patient care within this setting but rather puts the onus on healthcare professionals to acknowledge where deficiencies may lie and to have strategies in place to ensure that the lack of knowledge does not impact patient care. This statement mirrors the recommendations from the Department of Health in their UK Strategy for Rare Diseases (13)

However, whilst patients most commonly talked about their specific experience and wishes, the representatives from the patient groups took a broader and more holistic perspective when thinking about stratified care. They acknowledged that tailoring care is appropriate with variation in clinical need between patients and also over the course of a patient's disease trajectory, and as such the best place of care will be different for different people. However, they pointed out that it is not solely the decision that is made (follow-up vs discharge) but, for many patients, the negative experience of discharge may come from the level of the patient involvement in the process and the desire for more shared decision making rather than the

doctor as the sole decision-maker. Shared decision making has been defined as the involvement of both patients and healthcare providers in which both partied provide information, express preferences and participate in decision making (98) and the following steps have been set out: 1) establishing a context in which patients' views about treatment options are valued and deemed necessary, 2) transferring technical information, 3) making sure patients understand this information, 4) helping patients base their preference on the best evidence, 5) eliciting patients' preferences, 6) sharing treatment recommendations, and 7) making explicit the component of uncertainty in the clinical decision-making process (99). The ability to truly undertake shared decision making while also adhering to evidence-based clinical guidelines and pathways has been called into question and, indeed, there may be challenges to undertaking both of these simultaneously (100). However, the results from the qualitative interviews thus far suggest that the most important aspect, at least in the PBC population, is that patients have an accurate understanding of their disease, its likely trajectory, the rationale for why they have been chosen to be discharged to primary care, and the process for re-referral if needed. Not only do healthcare professionals have a role in this aspect of care but, in addition, the support groups are key. Patient support groups can take many forms, but they have broadly been defined as "a group of people with common experiences and concerns who provide emotional and moral support for one another" but they can fulfill many other functions including education for patients and families and sharing the illness experience (101). It is clear from the patient interviews that there is still widespread misinformation around PBC and as a result, high levels of anxiety and psychological impact of the diagnosis. It has been noted that primary care clinicians who may rarely see a patient with PBC can struggle to address these aspects of care and that this is a crucial area to address when looking at pathway implementation.

8.8 Chapter summary

This chapter details the results with representatives from two patient support groups and has supported the results from the patient interviews presented in Chapter 7. It has also provided some potential strategies to address these barriers to change including highlighting the role of the patient group. The next, and final, results chapter will present the results of the interviews with primary care and hospital-based clinicians.

CHAPTER 9: RESULTS OF INTERVIEWS WITH CLINICIANS

9.1 Chapter overview

This chapter will discuss the results of interviews with clinicians from primary, secondary and tertiary care looking at their perspectives on PBC management and addressing the potential barriers to discharge to primary care. The process of recruitment, development of the topic guide and the interview format have already been discussed in previous chapters. The results from the interviews are presented and then discussed in the context of the published literature.

9.2 Participant characteristics

A total of five clinicians were interviewed: two GPs, a Gastroenterologist with an interest in Hepatology, and two Hepatologists. All interviews with clinicians were carried out after the completion of the patient interviews.

9.3 Data analysis

Analysis of these interviews followed the same process as the previous interviews discussed in Chapters 7 and 8. Due to the low numbers of clinicians recruitment, it was not possible to determine when data saturation. The issues of challenges to clinician recruitment are discussed in Chapter 10.

9.4 Results

As with the previous interviews, all transcripts and field notes were reviewed before coding. In comparison to the patient interviews in Chapter 7, the initial impression from the clinician

interviews was that they were broadly in favour of the concept of discharge of low-risk patients to primary care although a number of potential challenges were highlighted. Where concerns were raised, their focus was on the practical aspects of this change in management.

Table 16: Codes and categories generated from clinician interviews

Codes	Categories
Clinician expertise Holistic approach to care Patient convenience Role of research	Defining quality of care
Rare disease management Recognition of serious disease	The role of primary care vs secondary care
Access to specialist advice Resource allocation Communication between health care professionals Funding Pressures on primary care	NHS structure

9.4.1 Defining quality of care

When clinicians discussed the differences between the management of a patient who is seen within primary care versus specialist care in a hospital-based out-patients clinic, the issues raised were similar to those raised by the patients. The disparity in knowledge levels between primary care and specialists was acknowledged by the clinicians who took part in the interviews and how this could impact on patient care. When thinking about the symptom burden of PBC, there was a concern that when a low-risk patient with few symptoms is discharged the primary care team may not be well placed to assess these and this aspect of PBC care may suffer.

"Unless it's at the forefront of their mind, PBC equals sicca syndrome etc,

they are not going to ask about the sticky eyes and the, things like that, so

they may not have the time to put two and two together or the patient doesn't feel they need to bother the GP about something as mundane as a bit of an itch or tiredness" **H-01**

In addition to the aspects of disease management that would be viewed as purely clinical, there are were additional important aspects of care. One factor mentioned was the time that was given to a hospital appointment versus a GP appointment.

"They get more time with a doctor, they see somebody who, hopefully, has more knowledge about the condition than the GP, that's not to say GP's aren't bright, they are incredibly bright, but they can never be expected to be specialists, that's why they pay me to do my job I suppose" **H-01**

There was also a worry about the more serious implications of missed diagnoses where the knowledge and skillset in primary care may mean that sinister diagnoses could be missed. The consequences of this lack of insight into what is important could have a detrimental effect on patient care and clinical outcomes.

" what happens if a GP misses a scan? Do they realise that it's actually really important that the scan is rebooked and if they say, 'Well, they looked fine'? It's that kind of familiarity that GPs really don't have with liver" **H-03**

Concerns about knowledge were not just limited to the role of primary care in the management of patients with PBC. The UK clinician survey results presented in Chapter 3 highlighted that many patients with PBC are seen by a generalist rather than a sub-specialist within the hospital setting, that many clinicians see small numbers of patients with this condition, and that there are the issues around the assessment of treatment response and risk stratification. This was a concern for those with a more specialist interest in PBC.

> *"I'm beginning to get a vibe that that is an understanding that's more general but I think for your – shall I call a general gastroenterologist – the classically trained gastroenterologist who gets sent to a hospital, is expected to do everything. No, I don't think they have any, any clue of that"* **H-03**

In order to fill knowledge gaps, primary care doctors access a range of sources with the internet being a major source of information but there was a recognition that not all information is correct. It was also felt that it was important for primary care clinicians to acknowledge to their patients that they may not have the knowledge but will look to find the information.

> *"it's obviously appraising what you find on the Internet and being able to interpret it. So if you've got a good clinical experience and you know a bit about the condition I think you can interpret the evidence a bit more that you read on the Internet otherwise sometimes I find it a bit difficult interpreting"* **G-01**

> *"it's a hard thing to say, I think, but once you've been doing it for a while, I've Been seeing these patients for years and, you know, I think it's an easier thing to*

say that, 'I'm not sure but I can find out.'. I think you need to be honest and keep a good relationship with the patient" **G-02**

When asked about their perspective on what a patient wanted from their care and the patient definition of quality of care, a number of different aspects of the patient experience were mentioned. These mirrored findings from the previous patient and patient group interviews.

"my impression is that the quality of the appointment…is what patients are looking for, if they know they're going to be seen by somebody who will listen to them and give them an authoritative response and give them the best treatment that's on option, I think that's what they're looking for" **H-02**

Whilst it would be possible for the quality of care in terms of specific aspects of clinical practice to be the same in both primary care and hospital, it was felt that when the clinician looking after a patient had a specialist interest in liver disease and felt competent and comfortable in its management, this would translate to be more reassuring to the patient.

"You have that perceptible ease about the fact that – 'Yeah, yeah. This is quite relaxing. I'm enjoying this clinic. We're going to do this. We're going to do that. I'll see you in six months'; whereas, if they go to the GP, there's possibly a little bit more fumbling around in the drawer for, for notes or for – and it doesn't quite have that…but that doesn't necessarily mean the actual outcome of quality is different; it's just they don't feel that it is the same" **H-03**

This extended beyond the clinician as an specific entity and more broadly into the physical attributes of a specialist centre that could add to the perception of patients attending them that the quality of care may be higher than that in a local hospital.

> *"us they come from what is a small hospital and they think all hospitals are like this and they come to this ivory monstrosity and everything is slick and then they don't ever want to go back to Wales"* **H-03**

The relationship between research and good quality care was seen as a feature of hospital-based care that could be lost if patients were discharged to primary care.

> *"research is critical to improving outcomes and that's why you need specialist units where you have access to enough patients across the spectrum, with enough security of follow up, where you can start to maintain clinical databases, serum databases, DNA databases and so on, or act as a hub to collaborate…"* **H-02**

Unlike patients who did not seem to be concerned about travel and waiting times if it meant being seen by a specialist, clinicians felt that this was relevant factor to patients. When it came to hospital vs primary care issue of inconvenience was mentioned.

> "*It's mainly the parking. It's nearly all centred around the parking. And, You know, saying about would we look at them going out of area, patients like to go to (the local hospital) because that's got good parking. They're really happy if they can be seen there"* **G-02**

9.4.2 The role of primary vs secondary care

Supporting the findings from the patient interviews, primary care clinicians acknowledged that as a rare disease with a presentation that comes with a varied differential diagnosis, that PBC management can pose specific challenges. From their perspective, the focus in primary care is felt to be on common disease or picking up serious and imminently life-threatening conditions promptly. As such this can mean that reaching a rare diagnosis can take longer.

> *"it's very hard in general practice because obviously we see a lot of things that are common. We do see some rarer things and it's weaning out the rarer things and also it's seeing people who - a lot of people come with non-specific symptoms and a lot of people have nothing wrong with them but there might be some people who have underlying something serious or something rare that we have this opportunity to diagnose"* **G-01**

> *"they sometimes come with, you know, tiredness and things, which there can be, you know, a hundred and one causes of tiredness, and things like that"* **G-01**

When discussing the topic of deferring decisions and management to the hospital specialist both the primary care and hospital clinicians recognised this approach and hospital clinicians were aware of instances in their own practice when dealing with an issue not related to their speciality when this was the case.

"there's probably not enough in the average GP practice to have a specialist GP who can focus on that…" **H-03**

"it's like asking me to deal with Huntingdon's Disease, I've a vague idea what it's about but the actual treatment I'm going to defer to a neurologist or geneticist" **H-01**

9.4.3 NHS structure

When thinking about the management of chronic disease, in contrast to hospital-based out-patient clinics, accessing an appointment with a health care professional in primary care is often done at a point close in time to the point of planned contact meaning that chronic condition routine follow-up could be challenging in practice (87). Currently, where primary care is responsible for the regular review of patients with a chronic condition then the Quality Outcome Framework (QOF) which was first set up in 2004 supports practices to fulfil this role (102).

"if you have a condition that has QOF attached to it then you're on to a good thing because there are quite robust recall processes and that because that's part of our payment. Then you get into this grey area where you want to do recall for things that are not QOF related and particularly gastro has no QOF attachment at all as a, as a subheading" **G-02**

Specialists did not feel that the structure of primary care was set up with the management of long term conditions with few patients having a dedicated GP in practice.

"Walk-In Centres are where it's all going and that actually, would be quite hard to do because you might have six different GPs over six years picking up a case file for the annual review, going, 'Well, what the heck am I supposed to do with this?' and that letter and the Advice Sheet was lost long ago in, in the, the hard drive and so they kind of go, 'Well, I don't know. Well, send some bloods then'" **H-03**

Due to the nature of primary care structure, it was felt that patients would have to take on more of a role in their disease management.

"there is some responsibility on the patient to come and see us at six months or come and say, 'We need a blood test,' and things like that, you know. But we - I mean we can put a note or a flag on their record saying, you know, that but it's hard for us to go and chase, you know, we can't chase everybody up so there is a bit of responsibility on the patients for that" **G-01**

In order to overcome this specific challenge, both primary care and hospital clinicians had ideas about what would be needed. The concept of written plans and advice was mentioned by both GPs and hospital clinicians.

"I don't know for rare conditions whether it's worth, you know, making one or doing one but, yeah, for all these conditions we have like a template that has to be filled in, like blood pressure, you know, weight, you know, all the things, medication review, you know, all the things that we think are important for that condition that they've written templates for" **G-01**

"they just need a, a letter or an Advice Sheet clipped to the letter to say,'Could you please measure X, Y and Z each year. Please send them for bone scans for densitometry. Make sure that they're on Vitamin D. Blah, blah, blah and let me know if there's any change" **H-03**

In order for high quality care to be provided in primary care, it was felt that there needs to be awareness on the part of GPs of what they do not know and for them to have the ability to make contact with specialists and for there to be ease of access back into hospital if needed. From the specialist perspective, this was seen as straightforward. However, GPs described their experience of dealing with patients who have specialists in different hospitals and who work in different ways and it was noted that the variability in the processes made this challenging.

"you could just write a quick letter saying 'look do you mind seeing back in clinic' and I could pop them in in the next month or two" **H-01**

"I might write to the gastroenterologist for advice and the ones locally are quite good so I could write to them and say, you know, 'This is what I've got. Is this something you'd want to see or have you got any advice?" **G-01**

"The cardiologists have got an email advice line. That's absolutely fantastic. That's been a brilliant thing. So you can email the cardiologist at (the hospital), they reply within 48 hours, just for advice" **G-02**

Making contact could be challenging and while GPs reported a willingness to take on aspects of management within the primary care setting provided that had support from specialists, failures of the ability to access this support in a timely fashion led to delays.

> *"It's frustrating. We're trying - where we're working at the moment we're trying to get more contact, I don't know whether you're doing it here, but where you can have a contact with a consultant which is advice"* **G-02**

When patients are seen within a hospital setting, there is then a return of information from the specialist to primary care regarding the consultation. For those in primary care, the main concern was the time taken for letters to come back to primary care.

> *"We get letters but, at the moment, it's taking a long time to get letters so it's quite difficult because you can wait weeks/months to get a letter"* **G-01**

This issue is also apparent in the communication between the secondary and tertiary care settings.

> *"it's just sometimes you don't get the letters back so you kind of, the issue then is that they might have been not included in a clinic here for a year or so and actually they've been at the (specialist centre) fairly regularly, and then they rock up on your doorstep in A&E and we don't know what's been happening for the last year, I suppose that's the only failing with the tertiary system"* **H-01**

The increase in pressures on primary care in terms of workload was a factor as chronic condition management moves away from the acute hospital. Primary care clinicians were unhappy with this change in service configuration and this was expressed both by GPs themselves and also by hospital clinicians.

> *"lots more things, unfortunately, are coming out into primary care and we don't mind most of them but, you know, there's a lot of work coming from the hospital and there's a lot more things we can do in primary care now and a lot more people don't have to go to the hospital"* **G-01**

> *"It's just I think you'll come across a general sense in primary care versus secondary care that a lot of things are being pushed outwards and, you know, there is a slight pushback the other way"* **G-02**

> *"I think Primary Care has so many challenges at the moment and this is too far down the list for it to be realistic"* **H-03**

With the pressures on primary care and the need for patients to take on ownership for making appointments, there was concern that this could disadvantage some patients who were less well informed about their condition or who felt less able to manage their health for whatever reason.

> *"Your smart patient who has no fear of the professional hierarchies that doctors usually hide behind; they – of course they will succeed – yeah, because they'll be telling the GP what they want but there are also the patients that go to the PBC interest groups and will be completely plugged in with the latest*

developments and they are probably a small proportion and one – when you're designing a service, you, you have to design the service for the majority of people; not the few……..And you've got to have a service that allows the person….. who themselves is a bit confused about what's wrong with their liver, and, you've got to allow a service to look after them and not lose them and I think that involves having to set something up that's simple to use, very easy to interact with" **H-03**

9.6 Discussion

The interviews with clinicians identified that there could be a future role for primary care in the management of patients with low-risk PBC but also that there are a number of challenges that this strategy would face. Many of the themes mirrored those arising from the patient interviews including the difficulties arising at the time to presentation in reaching a diagnosis, and both primary care and specialist clinicians raised concerns about knowledge levels within primary care. Whilst the primary care clinicians who took part in these interviews identified as being willing to take on a more significant role in patient care, the need for a clear structure and access to timely advice were highlighted. It is noteworthy that there were challenges to recruiting primary care clinicians to take part in the research (see Chapter 10 for further discussion) and those who did take part came from larger practices with a focus on teaching and research and may not be representative of primary care clinicians overall.

Quality of care has been defined as care that is "safe, effective, patient-centered, timely, efficient, equitable" (103). The concept of the difference between the quality of the care that a patient may receive in primary care vs hospital-based care and how to ensure that the quality

remains for those who are discharged was a recurrent issue raised. The topics arising from these interviews correspond with those from the patient interviews and include being seen by someone with appropriate knowledge levels and where there is a lack of knowledge having the means to seek out this knowledge, and for primary care clinicians to be supported in their care of PBC patients by specialists with clear guidance on what they need to be doing and ease of access to specialist advice as needed.

9.7 Chapter summary

This chapter details the results from qualitative interviews with clinicians. Its findings have supported many of the key findings from the patient interviews as well as providing an understanding from a clinician point of view about the practical aspects of managing a long-term condition such as PBC in primary care. It has also provided some potential strategies to address barriers to change including the need for templates and clear documentation as to what is required from primary care. The next and final chapter in this thesis will amalgamate the results from both the qualitative interviews and the earlier quantitative analysis to present the patient and clinician perspectives on management in primary care, identify the barriers to change, present the strengths and limitations of the work undertaken, and propose ideas for future research.

CHAPTER 10: DISCUSSION

10.1 Chapter overview

The final chapter of this thesis summarises the rationale for undertaking the research presented and how the quantitative and qualitative data presented in the previous chapters comes together to answer the research question posed. It presents the key findings from the research undertaken and discusses the implications of these findings for future practice and the development of new models of care in PBC. It also provides an examination of the strengths and weaknesses of the work undertaken and discusses potential future research strategies.

10.2 Research aims

The 2018 guidelines for the management of PBC published by the British Society of Gastroenterology recommended that, as part of standard care, patients should be stratified into low and high-risk groups using risk stratification tools and proposed that patients deemed to be low-risk for disease progression could be discharged from hospital follow-up to the care of their GP (1). The goal of the research described within this thesis was to develop a better understanding of the extent to which this recommendation differs to current real world clinical practice, to establish the patient and clinician perspectives on management in primary care versus hospital based care, and to determine whether there are barriers to implementation of this recommendation.

10.3 Data synthesis

The work described within this thesis has followed a mixed methods approach (68) in order to gain a broad understanding of the current management of PBC in clinical practice in the UK

and to establish the stakeholder perspective on the management of low-risk PBC in primary care. Chapter 1 presents a background to the research being undertaken, discussing PBC as a disease generally and with a specific focus on the concept of risk stratification, and how this concept can be used to identify a group of patients that could potentially be discharged from hospital-based specialist care to primary care. It also sets out the stages of the patient journey from presentation to discharge and describes why an understanding of the stages within this journey is required. Finally it sets out the rationale for the research strategy used to answer the research question.

In order to understand how risk stratification and different health care settings are currently utilised in UK practice, Chapters 2, 3 and 4 present quantitative data from three sources (a patient questionnaire, a survey of hospital based clinicians, and an audit of referrals to a specialist centre). These data sources provide an overview of the various stages of the patient journey (as set out in Chapter 1); from presentation to diagnosis, use of disease modifying therapy, use of risk-stratification tools, and establish the proportion of patients currently managed in primary care. From this data it was identified that there is variability in the patient journey, that risk-stratification is not currently widespread in clinical practice, and that once a patient is referred to a hospital based specialist, the majority stay within the hospital based setting. As these data sources were developed independently of the research question posed by this thesis, the reasons behind these findings were not identified but with this knowledge a qualitative research study was developed to investigate this further. Simultaneously to this data analysis, and presented in Chapter 5, a scoping review of the available literature from PBC was conducted and identified that neither the concept of using risk stratification to determine place of care nor the stakeholder perspective on preferences regarding health care setting have

previously been studied. This suggested that this was an area of worthwhile and along with the results of the scoping review of the literature related to a comparator condition (breast cancer) suggested that there could be stakeholder preference for management in specialist care and identified specific challenges to discharge to primary care that may be relevant to the implementation of a new model of care in PBC.

With the results from these chapters in mind, a qualitative research study protocol was developed and undertaken. Chapter 6 describes the methodology for a qualitative research study undertaken, the rationale for the choice of research participants and how a semi-structured approach including the use of topic guides which were developed with the findings from the previous chapters in mind. Data from the qualitative interviews is presented in Chapters 7-9, firstly from the patient perspective, then the patient group representatives, and finally the clinician perspective. This data was analysed with the goal of identifying the potential barriers to management of patients with low-risk PBC in primary care, to understand the reasons underlying these barriers, and to determine whether it is possible to develop interventions to modify these barriers and implement a stratified model of care.

10.4 Summary of research findings

A model of care based on the discharge of low-risk UDCA responders to primary care represents a significant shift from current practice and implementation of a new model of care based on the BSG guideline recommendation would have an impact on a significant number of patients. The results of this research have identified that there a number of potential barriers to discharge of patients with PBC to primary care from both the patient and clinician perspective

that would need to be addressed in order for this to happen. These are summarised below in Table 17 and discussed below.

Table 17: Barriers to discharge to primary care

Poor understanding of risk stratification	Patient understanding of their disease and future risk Clinician knowledge of risk stratification tools
The discharge process	Importance of shared decision making and patient understanding of the rationale for discharge Lack of pathways for primary care follow up
Patient preference for specialist care	Poor experiences at the time of diagnosis Primary care knowledge levels Living with a rare disease Hidden illness
Clinician preference for specialist care	Lack of willingness to discharge low-risk patients Concerns about the quality of PBC care
NHS structure	Managing chronic disease in primary care Workload

10.4.1 Poor understanding of risk stratification

In order to incorporate stratification into decision making around follow-up and discharge, it is first essential that, once diagnosed, patients are receiving the correct treatment (with a weight based dose of UDCA) and that evidence based criteria are used to assess response. As such the results from the UK-PBC questionnaires and clinician survey are highly relevant. Firstly, they suggest that less than a quarter of patients are being treated with the correct dose of UDCA and that only 50% of clinicians managing patients with PBC use response criteria in their clinical practice. Those who do not use response criteria report a lack of awareness of their existence and/or uncertainty regarding which criteria is best. Where criteria are used, there is limited

standardisation regarding which criteria is used and in fact, the criteria which are set out in the BSG guidelines (ALP <1.67 x ULN) is the least commonly used in practice.

10.4.2 The discharge process

Following on from assessment of risk, when it is deemed that a patient may be appropriate for discharge, results from the qualitative study indicate that there is a need to improve the discussions that are taking place between clinicians and patients. Firstly to ensure that when discussions are taking place around risk and the rationale for discharge, that patients understand what UDCA response means long-term and that the decision is being made in the context of evidence based practice. This may mean that conversations about potential discharge happen early on in the patient journey and that patients understand that they may not always remain under hospital follow-up. The issue of how patient expectation impacts on the experience of discharge is not unique to PBC with the findings from the qualitative study presented here echoing similar studies in other disease groups. For example in a study of patients with type 2 diabetes, Dutton et al. (104) identified that where patients reported a negative reaction to being discharge, the underlying reasons for this stemmed from the fact that most patients thought they would always be under specialist care and several stated that they would have liked to have known at the time of initial referral that hospital-based follow-up might not be long term. In addition, they were unclear on the rationale for discharge, they did not feel that they had any input in the decision, and were not sure what would happen following discharge. This mirrors the fears expressed by patients with PBC in chapter 7.

As a long-term condition with no cure management does not end with discharge and this poses an additional challenge. The guidelines from the BSG state that for those who are discharged to primary care suggest yearly tests of liver biochemistry and repeat risk assessment every three

years. Given that the data presented in Chapter 3 which suggests that hospital based clinicians struggle with the use of UDCA response criteria and risk assessment, this is likely to be challenging for primary care. In addition, it is known that symptomatology will vary over the course of the disease and even those with low-risk disease may experience symptoms. The negative experiences of patients regarding input from primary care around symptom control is highly relevant. These factors will need to be considered at the point of discharge. Given the variation in NHS structures in different regions and health care settings, processes are likely to vary but from the clinician interviews and especially the GPs involved, it would seem that a documented post discharge plan will be needed with written advice to patients and GPS regarding risk assessment, monitoring and management of common symptoms. The development of such templates are an area for further research

10.4.3 Patient preference for specialist care

One of the most striking findings from the qualitative interviews that took place with the patients is the emotional and psychological impact that comes with having a diagnosis of PBC and how this impacts their view of care. The perception of delays in diagnosis alongside the negative experiences in primary care when it comes to understanding of PBC symptoms, the "delegitimation" of having a hidden disease, and the recurrent topic of alcohol as the perceived cause of cirrhosis and associated stigma mean that by the point the discussion is being had with patients around discharge to primary care, the relationship with their GP may be damaged.

The patient interviews highlighted the struggles that patients had when trying to reach a diagnosis, and this was supported by the results from the UK-PBC patient questionnaires wherein over 17% of cases it took over two years to reach the diagnosis. As is clear from the

data in the patient questionnaire, there is variability in how patients present (over a third are asymptomatic and found to have abnormal LFTs on routine testing). It is not unexpected that, with PBC being a rare disease, when presented with a patient with abnormal LFTs that primary care clinicians may consider diagnoses such as alcohol-related liver disease first it is clear that the nature of the discussion that takes place can have a long-standing impact on the patient doctor relationship. Improving primary care awareness of PBC and the consideration of the diagnosis earlier in the patient journey may have a positive impact on this relationship and make later discussions around primary care follow-up easier.

10.4.4 Clinician preference for specialist care

Resistance to discharge is not limited to the patient perspective. The UK clinician survey presented in Chapter 3 found that just under half of all those surveyed (46.7%) rated themselves as not at all likely to discharge a patient who had responded to PBC to primary care. This survey did not capture the reasoning behind this decision however the clinician interviews provide some insight into this. Both primary care and specialist clinicians were concerned about knowledge levels amongst non-specialists and whether primary care can provide the same quality of care as a specialist service.

10.4.5 NHS structure

When looking to implement a new model of care, the practicalities of management of long-term conditions in primary care need to be considered. As highlighted by the clinician interviews, the process for how patients are reviewed within primary care and how primary care receives payment for the work undertaken is different from secondary care. Up to a third of the payment received in primary care is from their work towards meeting targets set out in the QOF

(105). As of 2019/2020, it remains the case that PBC specifically, and chronic liver disease more generally are not recognised within this payment structure (106). As it is unlikely that this process of payment will change or that a rare disease such as PBC would be considered for this tariff, in order to ensure that patients who are discharged will have appropriate follow up, the focus may need to be on empowering patients to seek out these appointments (again using a specific discharge template that sets out the expectations for follow-up). Data from the patient and patient group interviews suggests that the PBC patient population are pro-active in their care, and there is the possibility of using this characteristic to the advantage of patient care.

10.5 Strengths and limitations of the research

10.5.1 Relevance of the research question

The most recently published guidelines by the BSG have recommended that patients with low-risk PBC could be discharged to primary care. However, this approach to management had not been formally studied and, prior to the work undertaken here, little was known about the pathway stakeholder perspective. Results from the scoping review in Chapter 5 identified that there was a lack of data available in the PBC literature to help answer the research question but that there was evidence to suggest that barriers may exist and dedicated research was needed. The work presented within this thesis uses a mixed methodology to combine both quantitative and qualitative data to look at all aspects of the pathway of care for PBC patients from the point of first presentation to potential discharge, to establish how a new guideline would differ to current practice, and to obtain the stakeholder perspective in order to identify the barriers to management in primary care. Using a pragmatic paradigm, it seeks to understand the experiences and perspectives of these pathway stakeholders, and how these experiences impact on their willingness to accept a new care pathway.

10.5.2 Research strategy

The overall strength of the research was the use of a mixed methodology to combine both quantitative and qualitative data. This approach allowed the researcher to draw on the advantages of the different strategies used combining large volume quantitative data, with a literature review and in-depth qualitative interviews with pathway stakeholders.

10.5.3 Quantitative data analysis

The goal of the quantitative data analysis discussed within this thesis was to establish a background to current care for PBC in the UK and provisionally identify barriers to implementation of stratified care. As no one source was available to allow this to be done in a fully comprehensive manner, data from a range of sources was analysed in order to develop an overview of practice. In order to be as robust as possible, data from a patient completed questionnaire, a clinician completed survey, and an audit of referrals to a specialist clinic were combined. Using data from a variety of sources ensured that the broadest possible data was captured. However, there are limitations to the quantitative data analysis. Firstly, the patient questionnaire and clinician survey were not designed with this specific research question in mind, although the data chosen for analysis aimed to address the question. The clinic chosen for referral pathway analysis was from a single hospital in one geographical location in the UK and it is not possible to state that the experience identified within this hospital would be generalisable to other settings around the UK. However, as both a secondary and tertiary care hospital, the data obtained allowed both perspectives to be captured within one analysis and the data identified is looked at in combination with the other quantitative data.

10.5.4 Scoping review

The original intention of the scoping review of the PBC literature was to determine whether the theory that barriers to implementation of stratified care in PBC existed was supported by the available literature and if this was an area worthy of more in-depth research. However, rather than identifying that there were barriers to implementation it was instead identified that there was a lack of evidence to either support or refute this hypothesis and that this area had not been explored previously in the PBC population. However, conducting a second scoping review in a comparator condition revealed that barriers were likely to exist and the lack of data in the literature reflected a gap in current research and that further work was needed. As such the data set out within this thesis is unique within its field and answers a question not posed before.

10.5.5 Issues around poor clinician recruitment to qualitative research

When designing the qualitative component of the research it was anticipated that a sample size of between ten and thirty participants would be required in each group in order to reach data saturation (68, 83). Whilst data saturation was achieved in the patient group, with a total of sixteen patients interviewed, due to poor recruitment in the clinician group, it was not possible to determine whether data saturation was reached and this must be borne in mind when looking at the results obtained as should the characteristics of those who took part. The challenges of recruiting clinicians to take part in research is not unique to this study. Factors influencing the decision of clinicians to take part in research include time pressures (with respondents more likely to take part in questionnaire based research than an interview), the perceived relevance of the research, and whether they will received remuneration either education or monetary (107-109).

10.5.6 Sources of potential bias

For the patient questionnaires described in Chapter 2, the invitations to take part were sent out through UK-PBC which recruits patients primarily through hospital based settings with those managed in primary care being less likely to be involved. As respondents completed their own questionnaires and the results were not cross-checked with medical records, the findings of time lags from presentation to diagnosis and UDCA dosing do need to be interpreted with caution. The clinician survey in Chapter 3 was advertised through the professional groups which whilst capturing a large proportion of clinicians based in the UK would receive or see an invite. This may have impacted on the generalisability of the results obtained. However, it is unlikely that any strategy will capture all potential respondents.

From the qualitative interviews with patients, it was clear that there was a preference towards secondary care over primary care with various negative experiences with primary care described. When thinking about generalisability of these experiences to the patient cohort overall it is important to consider whether those with poor experiences were more likely to come forward to take part and whether this could have biased the data. However, using the patient group representatives as a source of access to the wider patient experience, it would appear that negative experiences are not limited to those patients interviewed here and the experiences described by the patients who did take part were not universally negative. When looking at the published literature on bias in recruitment to studies around the patient healthcare experience there is limited published data on the topic of bias. One study which looked at why patients took part in qualitative research around their diabetes care found that the following factors were relevant including altruism, being encouraged by their health care professional, seeing the research as being non-harmful and also the process of the interview as therapeutic

(110). There was no evidence that those with negative experiences were more likely to take part.

Whilst the primary care clinicians taking part were, in contrast, broadly supportive of the concept of discharge to primary care, it is important to note both the small number of participants and the potential for bias due to the background of the participants. The published literature around recruitment of primary care clinicians to research indicates that those involved in medical education and teaching, and those who are members of professional royal colleges are more likely to take part in research (107,109). In the qualitative portion of study presented in this thesis, clinicians from primary care were from large teaching practices with an academic interest and history of taking part in research. Whilst it is not possible to say definitively what the impact this characteristic had on the results, it is worthwhile exercising caution when looking to generalise the findings to the wider primary care population especially with the results from the scoping review of the breast cancer literature identifying that workload pressures are a factor in clinicians being reluctant to accept patients back to primary care.

10.6 Self reflection

As a clinician, the researcher had established knowledge of the condition that was being studied, as well as experience of quantitative data collection and analysis methods. They also had vast experience of undertaking face to face medical consultations one on one but had not previously undertaken any qualitative research nor had they much previous knowledge of this methodology. As such, two of the supervisors chosen including the lead supervisor for this research were experienced qualitative researchers. In addition, in order to prepare to undertake the research, the researcher undertook a series of courses in qualitative interviewing and

analysis. These included "Introduction to Qualitative Interviewing" and "Analysing Qualitative Interviews" conducted by the Health Experiences Research Group at the University of Oxford and an Nvivo training workshop at the University of Surrey. Following on from this, the researcher then went on to undertake a series of practice interviews with qualitative researchers based in the Institute of Applied Health Research at the University of Birmingham. These were conducted using the topic guides which had been created for the research and taped using a digital tape recorder. These were then listened back to in the presence of one of the research supervisors and feedback was given.

Understanding the impact of the researcher's identity on the interview process is an essential part of undertaking qualitative research. Health researchers who use interviews need to understand the impact of various characteristics for example status, gender, race and culture, on the interview process and outcomes. (80). How a participant perceives an interviewer can affect the interaction and the information obtained (111) as can the location of the interview (112). The researcher for this study was a medically qualified doctor with an interest in liver disease working as a Clinical Research Fellow in the field of autoimmune liver disease specifically PBC, and had an interest and knowledge both of the clinical aspects of the disease and the work of UK-PBC and the stratified medicine approach to care. Whilst none of those recruited to take part in the patient interviews had met the researcher before, they were aware of her background and she introduced herself at the time of meeting as a medical doctor taking time away from her clinical job to work as a researcher at the University of Birmingham. As clinicians were recruited from the West Midlands region, those working in hospital were known to some extent to the researcher. Those in primary care however were not. In addition, the researcher had previous interactions with the patient support group representatives before

although not in person. Location of interviews is also important. For the work undertaken for this thesis, interviews were undertaken at a location of the participants choosing (in the case of the patients either at their home or at the University or, for clinicians their place of work or at the University). The decision not to interview patients within the hospital was made deliberately in order to reinforce the interviewer's role (at the time of interview) as a researcher and not a clinician. However, despite the researcher's attempts to distance themselves from their clinical role, there were instances when it is clear that the interviewee is aware during conversation of the interviewers' other role (in both the patient and clinician interviews) and it is brought up in conversation. For example, one interviewee describes a poor opinion of the NHS then apologises to the researcher.

> *"But I think I've always felt, you know, that if there's anything wrong you've got to sort it yourself. You've got to, which I still strongly believe, you can't wait for others to, I've seen too many mistakes, sorry because you're a doctor. I don't mean that to sound horrible"* **P-01**

In other instances, the interviewee asks clinical questions about PBC to the researcher.

> *"But you can only find out if you've actually got the PBC by biopsy, is it?"* **P-12**

This mirrored what was found by Richards and Emslie in their comparison of interviews undertaken by a researcher identifying themselves as a GP and the other a researcher (113)

10.7 Application of research findings

The work undertaken in this thesis has identified that there are a number of barriers to implementation of a stratified care pathway in PBC (from both the patient and clinician perspective) and to the discharge of patients with low-risk disease to primary care. Whilst some of these barriers may be easy to address (e.g. improving clinician knowledge levels around UDCA response criteria), others are likely to be much more challenging (e.g. the concept of isolation in rare disease). As such, a model of care whereby all low-risk patients are discharged to primary care is unlikely to be practical. However, other models of care may be able to be successfully implemented, for example the discharge of selected patients with the creation of individualised care plans between patients, primary care and hospital specialists or models of joint care with involvement of both primary care and hospital based clinicians with the level and frequency of involvement of the hospital clinician tailored to the specific patient. In addition, there may be a role for the increased utilisation of specialist nurses to manage low-risk patients with secondary health care settings. Telemedicine and the use of virtual clinical reviews have been shown to have a number of advantages within health care models with the main advantage being the ability to provide specialist care without the need for patient or specialists to travel long distances with the associated potential benefit of time and cost savings (114). However, there have also been many barriers to the widespread use of this form of healthcare provision including challenges to the use of technology, set-up costs, data security, computer literacy and equality (114). However, the worldwide COVID-19 pandemic has normalised the use of remote consultations and driven through the implementation of the technology required circumventing a number of the barriers and use of non-face to face clinical review is now common within healthcare services (115). The use of virtual care for the

management of long-term chronic disease generally and PBC specifically is an area fort further study.

10.8 Future directions for research

Further research is required to develop and test these alternatives models, and the development of the research methodology will need to draw on the strengths and limitations of the research presented here. In the absence of an existing literature in this area prior to the research presented in this thesis the goal was to gain a broad perspective on the topic with the quantitative and qualitative data targeting participants from across the spectrum of PBC. However with the knowledge obtained thus far having provided a broad overview of the themes related to place of care and discharge, future research would target specific groups (low-risk PBC patients, clinicians responsible for discharge and primary care clinicians known to have patients with PBC on their practice list). The methodology used would need to be chosen both to ensure that the data achieved is high quality but also aiming to ensure that sufficient numbers of participants take part and strategies to ensure sufficient recruitment would need to be considered. Whilst the qualitative methodology used here worked well within the patient population, the main limitation of the qualitative work within the clinician population was poor recruitment despite various recruitment attempts. This would need to be taken into consideration when designing any future research. One potential option could be to move away from a qualitative methodology towards quantitative data collection for clinicians (with the data from the qualitative study presented within this thesis used as a basis to develop a questionnaire) with targeted recruitment, provision of incentives or involvement of commercial agents with a track record of engaging clinicians in this form of research. However, this approach and the possible (but not guaranteed) higher volume of responses would need to balanced against the quality of

the data that would be obtained using this methodology versus a further qualitative approach. Alternatively, focus groups rather than individual interviews may be a preferable alternative with the advantage of being able to undertake data collection from a larger group of participants within the same time frame.

10.9 Conclusion

The underlying rationale for undertaking the work described in this thesis was the supposition that there were likely to be a number of barriers to the discharge of patients with low-risk PBC to primary care. The initial qualitative analysis identified that this approach is currently not being undertaken in routine practice and this work, combined with a series of scoping reviews, identified that this was a topic in need of formal study.

The findings presented within this thesis have shown that there are significant barriers to implementation of a stratified care pathway for the management of patients with PBC in the UK that would see low-risk patients managed solely within primary care. Whilst there are benefits to creating pathways based on risk stratification tools (in terms of resource allocation), this approach underestimates the benefits to management within a specialist care setting that PBC patients experience. However, using the knowledge obtained from this research, there is an opportunity to develop a more sophisticated model of care for PBC which incorporates not just risk stratification but also patient and clinician preferences, with alternative strategies including joint care models, and the use of virtual care. Once developed, these models of care would need to undergo further dedicated research with the recruitment of targeted pathway stake holders (low-risk PBC patients, primary care clinicians and specialists), and involvement

of the patient support groups and clinical commissioners prior being implemented in routine practice.

REFERENCES

1. Hirschfield GM, Dyson JK, Alexander GJM, Chapman MH, Collier J, Hubscher S, et al. The British Society of Gastroenterology/UK-PBC primary biliary cholangitis treatment and management guidelines. Gut. 2018.

2. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol. 2009;51(2):237-67.

3. Devlin J, O'Grady J. Indications for referral and assessment in adult liver transplantation: a clinical guideline. Gut. 1999;45.

4. Lleo A, Marzorati S, Anaya JM, Gershwin ME. Primary biliary cholangitis: a comprehensive overview. Hepatol Int. 2017;11(6):485-99.

5. Addison T, Gull W. On a certain affection of the skin, Vitiligoidea - α plana, β tuberosa. Guy's Hospital Reports. 1851:265-76.

6. Ahrens EH, Payne MA, Kunkel HG, Eisenmenger WJ, Blondheim SH. Primary biliary cirrhosis. Medicine (Baltimore). 1950;29:299-364.

7. Rubin E, Schaffner F, Popper H. Primary biliary cirrhosis. Chronic non-suppuratuve destructive cholangitis. American Journal of Pathology. 1965;46:387-407.

8. Beuers U, Gershwin ME, Gish RG, Invernizzi P, Jones DE, Lindor KD, et al. Changing Nomenclature for PBC: From 'Cirrhosis' to 'Cholangitis'. Am J Gastroenterol. 2015;110(11):1536-8.

9. Carbone M, Mells GF, Pells G, Dawwas MF, Newton JL, Heneghan MA, et al. Sex and age are determinants of the clinical phenotype of primary biliary cirrhosis and response to ursodeoxycholic acid. Gastroenterology. 2013;144(3):560-9 e7.

10. Boonstra K, Beuers U, Ponsioen CY. Epidemiology of primary sclerosing cholangitis and primary biliary cirrhosis: a systematic review. J Hepatol. 2012;56(5):1181-8.

11. Carey EJ, Ali AH, Lindor KD. Primary Biliary Cirrhosis. The Lancet. 2015; 386 10003):11.

12. James OFW, Bhopal R, Howel D, Gray J, Burt AD, Metcalf JV. Primary biliary cirrhosis once rare, now common in the United Kingdom. Hepatology. 1999;30:390-4.

13. Department of Health. The UK strategy for rare diseases. 2013.

14. Prince M, Chetwynd A, Newman W, Metcalf JV, James OFW. Survival and symptom progression in a geographically based cohort of patients with primary biliary cirrhosis: Follow-up for up to 28 years. Gastroenterology. 2002;123(4):1044-51.

15. Boonstra K, Kunst AE, Stadhouders PH, Tuynman HA, Poen AC, van Nieuwkerk KM, et al. Rising incidence and prevalence of primary biliary cirrhosis: a large population-based study. Liver Int. 2014;34(6):e31-8.

16. Corrigan M, Hirschfield GM. Aspects of the Pathophysiology of Primary Biliary Cirrhosis. Dig Dis. 2015;33 Suppl 2:102-8.

17. Watt FE, James OFW, Jones DEJ. Patterns of autoimmunity in primary biliary cirrhosis patients and their families: a population-based cohort study. Qjm. 2004;97(7):397-406.

18. Lazaridis KN, Juran BD, Boe GM, Slusser JP, de Andrade M, Homburger HA, et al. Increased prevalence of antimitochondrial antibodies in first-degree relatives of patients with primary biliary cirrhosis. Hepatology. 2007;46(3):785-92.

19. Selmi C, Mayo MJ, Bach N, Ishibashi H, Invernizzi P, Gish RG, et al. Primary biliary cirrhosis in monozygotic and dizygotic twins: Genetics, epigenetics, and environment. Gastroenterology. 2004;127(2):485-92.

20. Mells GF, Floyd JA, Morley KI, Cordell HJ, Franklin CS, Shin SY, et al. Genome-wide association study identifies 12 new susceptibility loci for primary biliary cirrhosis. Nat Genet. 2011;43(4):329-32.

21. Karlsen TH, Chung BK. Genetic Risk and the Development of Autoimmune Liver Disease. Dig Dis. 2015;33 Suppl 2:13-24.

22. Carbone M, Lleo A, Sandford RN, Invernizzi P. Implications of genome-wide association studies in novel therapeutics in primary biliary cirrhosis. Eur J Immunol. 2014;44(4):945-54.

23. Prince MI, Ducker SJ, James OF. Case-control studies of risk factors for primary biliary cirrhosis in two United Kingdom populations. Gut. 2010;59(4):508-12.

24. Corpechot C, Chretien Y, Chazouilleres O, Poupon R. Demographic, lifestyle, medical and familial factors associated with primary biliary cirrhosis. Journal of Hepatology. 2010;53:162-9.

25. Gershwin ME, Selmi C, Worman HJ, Gold EB, Watnik M, Utts J, et al. Risk factors and comorbidities in primary biliary cirrhosis: a controlled interview-based study of 1032 patients. Hepatology. 2005;42(5):1194-202.

26. Walker JG, Doniach D, Roitt IM, Sherlock S. Serological tests in diagnosis of primary biliary cirrhosis. The Lancet. 1965;285(7390):827-31.

27. Bogdanos DP, Invernizzi P, Mackay IR, Vergani D. Autoimmune liver serology: Current diagnostic and clinical challenges. World Journal of Gastroenterology. 2008;14(21):3374.

28. Yamagiwa S, Kamimura H, Takamura M, Aoyagi Y. Autoantibodies in primary biliary cirrhosis: recent progress in research on the pathogenetic and clinical significance. World J Gastroenterol. 2014;20(10):2606-12.

29. Corpechot C, Abenavoli L, Rabahi N, Chretien Y, Andreani T, Johanet C, et al. Biochemical response to ursodeoxycholic acid and long-term prognosis in primary biliary cirrhosis. Hepatology. 2008;48(3):871-7.

30. Nakamura M, Kondo H, Mori T, Komori A, Matsuyama M, Ito M, et al. Anti-gp210 and anti-centromere antibodies are different risk factors for the progression of primary biliary cirrhosis. Hepatology. 2007;45(1):118-27.

31. Hirschfield GM. Diagnosis of primary biliary cirrhosis. Best Pract Res Clin Gastroenterol. 2011;25:701-12.

32. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol. 2009;51(2):237-67.

33. Pellicoro A, Ramachandran P, Iredale JP, Fallowfield JA. Liver fibrosis and repair: immune regulation of wound healing in a solid organ. Nat Rev Immunol. 2014;14(3):181-94.

34. Hamlyn AN, Sherlock S. The epidemiology of primary biliary cirrhosis: a survey of mortality in England and Wales. Gut. 1974;15:473-9.

35. NHS Blood and Transplant. Annual Report on Liver Transplantation. Report for 2015/2016 (2016).

36. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol. 2018;69(1):182-236.

37. Tripathi D, Stanley AJ, Hayes PC, Patch D, Millson C, Mehrzad H, et al. U.K. guidelines on the management of variceal haemorrhage in cirrhotic patients. Gut. 2015;64(11):1680-704.

38. Saksena S, Tandon RK. Ursodeoxycholic acid in the treatment of liver diseases. Postgraduate Medical Journal. 1997;73:75-80.

39. Committee JF. British National Formulary: London: BMJ Group and Pharmaceutical press; 2018.

40. National institute for Health and Care Excellence. Obeticholic acid for treating primary biliary cholangitis. nice.org.uk/guidance/ta443: NICE; 2017. Report No.: TA443.

41. Jorgenson R. A phenomenological study of fatigue in patients with primary biliary cirrhosis. Journal of advanced nursing. 2006;55(6):689-97.

42. Jopson L, Jones DE. Fatigue in primary biliary cirrhosis: prevalence, pathogenesis and management. Dig Dis. 2015;33 (supp2):109-14.

43. Khanna A, Leighton J, Lee Wong L, Jones DE. Symptoms of PBC - Pathophysiology and management. Best Pract Res Clin Gastroenterol. 2018;34-35:41-7.

44. Hegade VS, Mells GF, Beuers U, Kremer AE, Invernizzi P. Patient experience and characteristics of cholestatic pruritus in the UK-PBC research cohort. Hepatology. 2014;60(supplement):339A-69A.

45. Ismond K, Azziz B, Wright G, Mason A. Self reported experiences of patients living with primary biliary cholangitis (PBC) and ursodiol. Hepatol Int. 2018;12(supplement 2):206.

46. Guanabens N, Cerda D, Monegal A, Pons F, Caballeria L, Peris P, et al. Low bone mass and severity of cholestasis affect fracture risk in patients with primary biliary cirrhosis. Gastroenterology. 2010;138(7):2348-56.

47. Lindor KD, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote EJ, et al. Primary biliary cirrhosis. Hepatology. 2009;50(1):291-308.

48. EASL. Clinical practice guidelines: Management of hepatocellular carcinoma. Journal of Hepatology. 2018;69:182-236.

49. Poupon R, Chretien Y, Poupon R, Ballet F, Calmus Y, Darnis F. Is ursodeoxycholic acid an effective treatment for primary biliary cirrhosis? The Lancet. 1987;1:834-6.

50. Goulis J, Leandro G, Burroughs AK. Randomised controlled trials of ursodeoxycholic-acid therapy for primary biliary cirrhosis: a meta-analysis. The Lancet. 1999;354(9184):1053-60.

51. Pares A, Caballeria L, Rodes J. Excellent long-term survival in patients with primary biliary cirrhosis and biochemical response to ursodeoxycholic Acid. Gastroenterology. 2006;130(3):715-20.

52. Corpechot C, Chazouilleres O, Poupon R. Early primary biliary cirrhosis: biochemical response to treatment and prediction of long-term outcome. J Hepatol. 2011;55(6):1361-7.

53. Kuiper EM, Hansen BE, de Vries RA, den Ouden-Muller JW, van Ditzhuijsen TJ, Haagsma EB, et al. Improved prognosis of patients with primary biliary cirrhosis that have a biochemical response to ursodeoxycholic acid. Gastroenterology. 2009;136(4):1281-7.

54. Kumagi T, Guindi M, Fischer SE, Arenovich T, Abdalian R, Coltescu C, et al. Baseline ductopenia and treatment response predict long-term histological progression in primary biliary cirrhosis. Am J Gastroenterol. 2010;105(10):2186-94.

55. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. British Journal of Surgery.1973;60(8):646-9.

56. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31(4):864-71.

57. Neuberger J, Gimson A, Davies M, Akyol M, O'Grady J, Burroughs A, et al. Selection of patients for liver transplantation and allocation of donated livers in the UK. Gut. 2008;57(2):252-7.

58. Dickson ER, Grambsch PM, Fleming TR, Fisher LD, Langworthy A. Prognosis in Primary Biliary Cirrhosis: Model for decision making. Hepatology. 1989;10(1):1-7.

59. Carbone M, Sharp SJ, Flack S, Paximadas D, Spiess K, Adgey C, et al. The UK-PBC risk scores: Derivation and validation of a scoring system for long-term prediction of end-stage liver disease in primary biliary cholangitis. Hepatology. 2016;63(3):930-50.

60. Lammers WJ, Hirschfield GM, Corpechot C, Nevens F, Lindor KD, Janssen HL, et al. Development and Validation of a Scoring System to Predict Outcomes of Patients With Primary Biliary Cirrhosis Receiving Ursodeoxycholic Acid Therapy. Gastroenterology. 2015;149(7):1804-12 e4.

61. Williams R, Aspinall R, Bellis M, Camps-Walsh G, Cramp M, Dhawan A, et al. Addressing liver disease in the UK: a blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. The Lancet. 2014;384(9958):1953-97.

62. Fischer F, Lange K, Klose K, Greiner W, Kraemer A. Barriers and strategies in guideline implementation - a scoping review. Healthcare. 2016;4(3):36.

63. Grol R. Successes and failures in the implemetation of evidence-based guidelines for clinical practice. Medical care. 2001;39(8 supp 2):II46-52.

64. Grol R. Beliefs and evidence in changine clinical practice. BMJ. 1997;315:418-21.

65. Grol R, Grimshaw J. From best evidence to practice: effective implementation of change in patient's care. Lancet. 2003;362:1225-30.

66. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PC, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA. 1999;282(15):1458-65.

67. Shorten A, Smith J. Mixed methods research: expanding the evidence. BMJ. 2017;20(3):74-5.

68. Cresswell JW. A concise introduction to mixed methods research. First ed: SAGE Publications; 2015.

69. EURODIS. Survey of the delay in diagnosis for 8 rare diseases in Europe 2004 [Available from: https://www.eurordis.org/publication/survey-delay-diagnosis-8-rare-diseases-europe-%E2%80%98eurordiscare2%E2%80%99.

70. Corrigan M, Vale L, Coughlan D, Jones DE, Hirschfield GM, editors. Clinician confidence in stratifying risk in primary biliary cirrhosis - a UK-PBC survey. American Association for the study of Liver Disease; 2015; San Francisco, USA. Hepatology2015.

71. Jopson L, Khanna A, Peterson P, Rudell E, Corrigan M, Jones DE. Are clinicians ready for safe use of stratified therapy in primary biliary cholangitis (PBC)? A study of educational awareness. Digestive diseases and sciences. 2018;63(10):2547-54.

72. Hoonaker P, Carayon P. Questionnaire survey non response: a comparison of postal mail and internet surveys. International Journal of Human-Computer Interaction. 2009;25(5):348-73.

73. Braithwaite D, Emery J, dE Lusignan S, Sutton S. Using the internet to conduct surveys of health professionals: a valid alternative. Family Practice. 2003;20(5):545-51.

74. Likert R. A technique for the measurement of attitudes. Archives of Psychology. 1932;140:1-55.

75. Sullivan GM, Artino AR, Jr. Analyzing and interpreting data from Likert-type scales. J Grad Med Educ. 2013;5(4):541-2.

76. Corrigan M, Hirschfield GM, Greenfield S, Parry J. Barriers to implementation of stratified care in primary biliary cholangitis: a scoping exercise. BMJ Open Gastroenterology. 2018;6(1):e000226.

77. Montali L, Frigerio A, Riva P, Invernizzi P. 'It's as if PBC didn't exist': the illness experience of women affected by primary biliary cirrhosis. Psychol Health. 2011;26(11):1429-45.

78. Morse JM, Field PA. Nursing research: the application of qualitative approaches. 2nd ed: Chapman and Hall; 1996. p208 .

79. Declaration of Helsinki ethical principles for medical research involving human subjects. Journal of the American Medical Association. 2013;310(20):2191-4.

80. Nunkoosing K. The problem with interviews. Qualitative Health Research. 2005;15(5):698-706.

81. Bowling A. Research Methods in Health : Investigating Health and Health Services. Maidenhead, United Kingdom: McGraw-Hill Education; 2009.

82. Glaser BG, Strauss AL. The Discovery of Grounded Theory Strategies for Qualitative Research. 1 ed: Aldine Transaction; 1967. 283 p.

83. Morse JM. Determining sample size. Qualitative Health Research. 2000;10(1):305.

84. Kapborga I, Bertero C. Using an interpreter in qualitative interviews: Does it threaten validity? Nursing inquiry. 2002;9(1):52-6.

85. Plumridge G, Redwood S, Greenfield S, Akhtar N, Chowdury R, Khalade A, et al. Involving interpreters in research studies. Journal of health service and research policy. 2012;17(3):190-2.

86. Medland A. Portrait of the West Midlands. Office for National Statistics; 2011.

87. Baird B, Charles A, Honeyman M, Maguire D, Das P. Understanding pressures in general practice. In: Fund TKs, editor. 2016.

88. Elwood S, Martin D. Placing interviews: location and sacles of power in qualitative research. Professional Geographer. 2000;52:649-57.

89. Ritchie J, Lewis J. Qualitative research pratice: a guide for social science students and researchers. London: Sage; 2003.

90. Mertens DM. Research and Evaluation in Education and Psychology. 3rd ed: SAGE Publications Inc; 2010 2010.

91. Kaushik V, Walsh CA. Pragmatism as a research paradigm and its implications for social work research. Social Sciences. 2019;8(9):255-71.

92. Bury M. Chronic illness as a biographical disruption. Sociology of Health and Illness. 1982;4(2167-182).

93. Kleinman A. Pain and resistance: The delegitimation and relegitimation of local worlds. In: Del Vecchio Good MJ, Brodwin PE, Good BJ, Kleinman A, editors. Pain as human experience : an anthropological perspective. Berkeley :: University of California Press; 1992.

94. Dickson A, Knussen C, Flowers P. Stigma and the delegitimation experience: an interpretative phenomonological analyis of people living with chronic fatigue syndrome. Psychology and Health. 2007;22(7):851-67.

95. Kostopoulou O, Delaney BC, Munro CW. Diagnostic difficulty and error in primary care - a systematic review. Family Practice. 2008;25(6):400-13.

96. Sogolow ED, Lasker JN, Sharim RR, Weinrieb RM, Sass DA. Stigma and liver disease. Illness, Crisis and Loss. 2010;18(3).

97. Mays N, Pope C. Assessing quality in qualitative research. British Medical Journal. 2000;320:50-2.

98. Briss P, Rimer B, Reilley B, Coates RC, Lee NC, Mullen P, et al. Promoting informed decisions about cancer screening in communities and healthcare systems. American Journal of Preventive Medicine. 2004;26(1):67-80.

99. Gravel K, Legare F, Graham ID. Barriers and facilitators to implementing shared decision making in clinical practice: a systematic review of health care professional' perceptions. Implementation Science. 2006;1:16.

100. Barrett A. Evidence based medicine and shared decision making: the challenge of getting both evidence and preferences into health care. Patient education and counselling. 2008;73(3):407-12.

101. Hu A. Reflections: the value of patient support groups. Otolaryngology - Head and Neck Surgery. 2017;156(4):587-8.

102. Forbes LJL, Marchand C, Doran T, Peckham S. The role of the Quality and Outcomes Framework in the care of long-term conditions: a systematic review. British Journal of General Practice. 2017;67(667):e775-84.

103. Medicine Io. Crossing the quality chasm: a new health system for the 21st century. In: America CoQoHCi, editor. Washington DC: National Academies Press 2001.

104. Dutton H, Rowan MS, Liddy C, Maranger J, Ooi TC, Malcolm J, et al. Patient perspectives on discharge from specialist type 2 diabetes care back to primary care: a qualitative study. Canadian Journal of Diabetes. 2013;38(3):191-7.

105. Swinglehurst D, Emmerich N, Maybin J, Park S, Quiligan S. Rethinking 'quality' in healthcare. Journal of health service and research policy. 2014;19(2):65-6.

106. 2019/20 General medical services (GMS) contract Quality and Outcomes Framework (QOF). 2019.

107. Hummers-Pradier E, Scheidt-Nave C, Martin H, Heinemann S, Kochen MM, Himmel W. Simply no time? Barriers to GPs' participation in primary care health research. Family Practice. 2008;25(2):105-12.

108. Brodaty H, Gibson LHR, Waine ML, Shell AM, Lilian R, Dimity Pond C. Research in general practice: a survey of incentives and disincentives for research participation. Mental Health in Family Medicine. 2013;10(3):163-7.

109. Stocks N, Braunack-Mayer A, Somerset M, Gunnell D. Binners, fillers and filers: A qualitative study of GPs who don't return postal questionnaires. European Journal of General Practice. 2004;10(4):146-51.

110. Peel EA, Parry O, Douglas M, Lawton J. "It's no skin off my nose": Why people take part in qualitative research. Qualitative Health Research. 2006;16(10):1335-49.

111. Robson C. Real world research: a resource for social scientists and practitioner-researchers. 2nd ed2002 2002.

112. Manderson L, Bennett E, Andajani-Sutjahjo S. The social dynamics od the interview: age, class and gender. Qualitative Health Research. 2006;16(10):1317-34.

113. Richards H, Emslie C. The 'doctor' or the 'girl from the University? Considering the influence of professional roles on qualitative interviewing Family Practice. 2000;17(1):71-5.

114. Scott Kruse C, Karem P, Shifflett K, Vegi L, Ravi K, Brooks M. Evaluating barriers to adopting telemedicine worldwide: a systematic review. J Telemed Telecare. 2018; 24(1): 4-12

115. Strokel-Walker. Why telemedicine is here to stay. British Medical Journal. 2020; 371: m3603

APPENDIX 1 – UK-PBC QUESTIONNAIRES

Shown below are the relevant extracts from the two patient questionnaires conducted by UK-PBC in 2015 showing the questions that were analysed as part of the quantitative analysis in Chapter 2 of this thesis.

Questionnaire 1: 'Health and social care needs in PBC'

Management of your PBC
PBC is looked after by many different health professionals (e.g. GPs and hospital consultants). We would like to know where you currently receive most of your care for PBC, and who provides this care.

Do you attend a hospital for treatment of your PBC, nowadays?

- ☐ **NO**, only the GP looks after my ➔ Go directly to **Question 7** on page 4
- ☐ **YES**, I attend the hospital for my ➔ Complete **Section A**, below

Section A: Hospital treatment for your PBC

1. **What is the name of the hospital where you currently receive <u>most</u> of your care for PBC?**

2. **Do you currently receive <u>any</u> treatment for your PBC at another hospital?**
   - ➲ For example, some people with PBC receive *shared care* from their local district hospital as well as their regional specialist centre.

☐ Yes, I receive treatment for my PBC at more than one hospital

☐ No, I receive all of my treatment for PBC at a single hospital

3. **If yes, what is the name of the second hospital which currently provides <u>some</u> of the treatment for your PBC?**

☐ Not applicable (I receive all of my treatment at one hospital)

<u>Questionnaire 2: 'Symptoms, complications and treatment of PBC'</u>

How were you first discovered to have PBC?

- ➲ Please read the list of options below and choose one option that <u>best</u> describes how you were first discovered to have PBC.

☐ I attended a **well-man clinic** or a **well-woman clinic** and my liver tests were found to be abnormal

☐ I had a **medical** and my blood tests were found to be abnormal.
   - ➔ *If yes, why did you have the medical? (For example, 'to obtain life insurance')*

☐ I had a **routine check-up** for a completely different condition (i.e. NOT my PBC) and my blood tests were found to be abnormal.
   - ➔ *If yes, why did you have the routine check-up? (For example, 'for my*

☐ I went to the doctor with **symptoms caused by a completely different condition** (i.e. symptoms that were NOT caused by my PBC) and my bloods tests were found to be abnormal.

☐ The doctor checked me for PBC because a **blood relative of mine has PBC**

☐ I went to the doctor because of **itching** and my blood tests were found to be abnormal.

☐ I went to the doctor because **I had no energy** and my blood tests were found to be abnormal

☐ I went to the doctor with **poor concentration** or **poor memory** ('brain fog') and my blood tests were found to be abnormal.

☐ I went to the doctor because of **jaundice**. (Jaundice is yellow discolouration of the white of the eye that occurs when the liver has been damaged.)

☐ I went to the doctor because **my tummy was swollen** from **ascites.** (Ascites is fluid inside the abdomen that occurs when there is severe scarring of the liver.)

☐ I went to the doctor because of **vomiting of blood** from **varices.** (Varices are swollen veins in the gullet or stomach that occur when there is severe scarring of the liver.)

☐ I went to the doctor with **severe confusion** and the doctor told me that I had **hepatic encephalopathy**. (Hepatic encephalopathy is severe confusion caused by liver disease.)

Thinking back, what symptoms did you have when you were <u>first</u> told that you have PBC?

➲ Please look at the list below and select as many options as applied to you at the time of your diagnosis with PBC.

☐ Itching of the skin
☐ Fatigue (feeling 'washed out', more than simple tiredness)
☐ Poor concentration or memory, worse than that of other people the same age ('brain-fog')
☐ Discomfort in the liver area (the right-sided upper part of the tummy)
☐ Aching of the bones
☐ Ascites (fluid inside the tummy)
☐ Bleeding from varices (swollen veins at the bottom end of the gullet)
☐ Jaundice (yellow discolouration affecting the white of the eye)
☐ Hepatic encephalopathy (severe confusion caused by liver disease)
☐ Other (please specify in the space provided below)

☐ No symptoms at all (only my blood tests were abnormal)

Thinking back, how long did you have symptoms of PBC or abnormal blood tests before you were told by the doctor that you had PBC? (That is, before your diagnosis of PBC was made.)

➲ Please tell us *the longest period* that you had any symptom of PBC before you were told by the doctor that you had PBC.

➲ If you had no symptoms of PBC but your blood tests were abnormal (i.e. the liver tests or the anti-mitochondrial antibody [AMA]), tell us how long they were abnormal before you were told by the doctor that you had PBC.

☐ I did not have symptoms or abnormal blood tests before my diagnosis was made

☐ I had symptoms/abnormal blood tests for **less than 6 months**

☐ I had symptoms/abnormal blood tests for **6 – 12 months**

☐ I had symptoms/abnormal blood tests for **1 – 2 years**

☐ I had symptoms/abnormal blood tests for **more than 2 years**

➔ *Please tell us approximately how many years you had symptoms or abnormal blood tests before your diagnosis of PBC was made*

For ☐ years before my diagnosis of PBC was

☐ I don't remember

Treatment of your PBC

Have you <u>ever</u> taken ursodeoxycholic acid (UDCA) for treatment of your PBC?

☐ **NO** ➔ Go to **Question 27** on the next page (page 13)

☐ **YES** ➔ Please complete **Section E**, below

Section E: Use of ursodeoxycholic acid (UDCA)

4. **How old were you when you first started to take ursodeoxycholic acid (UDCA)?**

I was ☐ years old when I first started to take UDCA

5. **And do you still take UDCA, nowadays?**

☐ **YES** ➔ *What is your current dose of UDCA? (e.g. 750mg once daily)*

Please ☐

➔ *What is your current weight? (e.g. 10 stone; e.g. 75kg)*

Please ☐

➔ *Since you first started UDCA, has your dose changed?*

- ☐ Increased
- ☐ Decreased
- ☐ Remained the same

☐ **NO** ➔ *How old were you when you finally stopped taking UDCA?*

I ☐ years old when I finally stopped taking UDCA

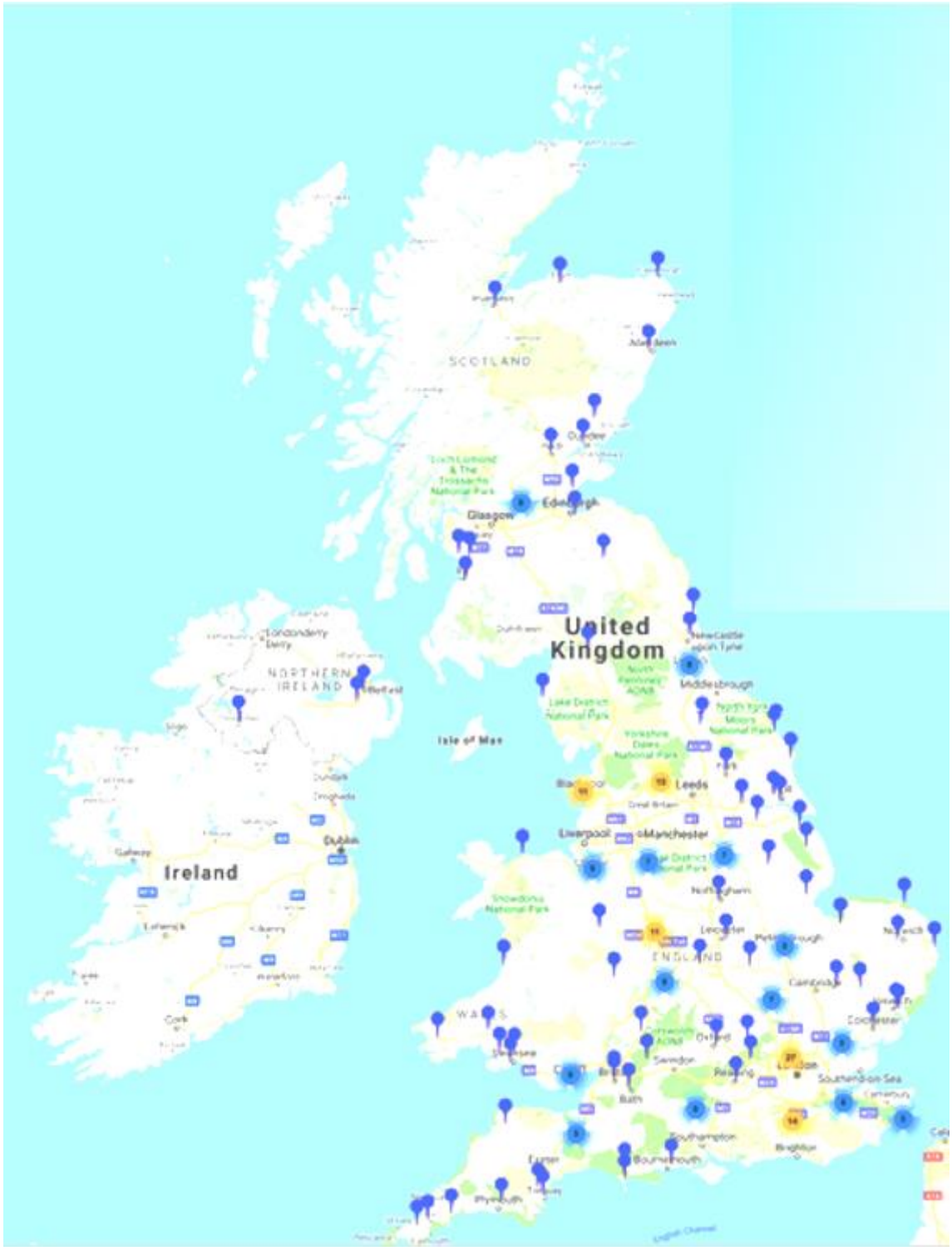
➔ *And why did you finally stop taking UDCA?*

➲ Please tick the box for as many options as apply to you

- ☐ I had unbearable side-effects (e.g. diarrhoea)
- ☐ I developed liver failure from my PBC so the UDCA was no longer useful
- ☐ I had a liver transplant
- ☐ I don't know why it was stopped
- ☐ Another reason (please specify) ☐

APPENDIX 2 – MAP OF HOSPITALS ACROSS THE UK MANAGING PATIENTS

Based on data from the UK-PBC questionnaires



APPENDIX 3 - THE UK-PBC CLINICIAN SURVEY

The following invite to take part which was sent to potential respondents via the BSG and BASL mailing lists and newsletters

Dear Colleague

Re: UK-PBC survey – Management of Primary Biliary Cirrhosis

Primary biliary cirrhosis is an area of increasing clinical research activity and our understanding of disease mechanisms, clinical care, and new potential therapies is evolving.

Through this on-line survey we aim to:

- Establish current practice in management of PBC in the UK
- Identify knowledge amongst those involved in the care of patients with PBC regarding current research and emerging therapies.

The survey will take approximately 5-10 minutes to complete and can be accessed using the link below:

https://www.surveymonkey.com/s/MGKRXL3

We very much appreciate your time in filling in this survey.

Yours, on behalf of the UK-PBC team (www.uk-pbc.com)

Dr Margaret Corrigan and Dr Gideon Hirschfield

Centre for Liver Research, Birmingham NIHR Liver BRU, University of Birmingham
[redacted]

Summary of survey questions

Q1: Which of these best describes your current professional role?

- Consultant hepatologist working in a liver transplant centre
- Consultant hepatologist working in a tertiary centre (non transplant)
- Consultant gastroenterologist with a special interest in hepatology
- Consultant gastroenterologist with other special interest
- Consultant gastroenterologist
- Registrar in gastroenterology
- Clinical nurse specialist in hepatology
- Other (please specify)

Q2/3: How many patients with PBC have you seen over the last 12 months?

- 0
- 1-10
- 11-20
- 21-50
- 51-100
- 100+

Q4: You have stated that you have not seen any patients with PBC over the last 12 months. Which answer below best describes the reason for this?

- I occasionally manage patients with PBC but have not seen any in this time period
- I do not have a specialist interest in hepatology and patients with PBC are seen by a specialist colleague
- I have a specialist interest in hepatology but not in autoimmune liver disease

Q5: In which of the following circumstances would you screen for PBC using antimitochondrial antibody (AMA)? Please tick as many as are applicable

- Patient with cholestatic liver biochemistry
- Cirrhosis of unknown aetiology
- Patient with fatigue and normal liver biochemistry
- Patient with pruritus and normal liver biochemistry
- Patient with a family history of PBC
- Patient with a strong history of other autoimmune disease
- Other (Please specify)

Q6: How confident do you feel in the interpretation of AMA results in a patient with suspected PBC?

- Not at all
-
- Moderately
-
- Highly

Q7: How often do you initiate ursodeoxycholic acid (UDCA) in a patient with confirmed PBC?

- Always
- Most of the time
- Some of the time
- Rarely
- Never

Q8: What factor/factors would lead you to not initiate UDCA at the time of diagnosis?

Free text box

Q9: How often do you use formal criteria to assess UDCA response at 12 months?

- Always
- Sometimes
- Never

Q10: What is the reason for not formally assessing UDCA response?

- Unsure what criteria is best to use
- Not aware of the criteria available
- Would refer for specialist opinion
- Other (please specify)

Q11: Please indicate which criteria you most commonly use to assess UDCA response

- Paris 1
- Paris 2
- Barcelona
- Toronto
- Combination
- Don’t use formal criteria to assess response

Q12: How confident do you feel using UDCA response criteria?

- Not at all
-
- Moderately
-
- Highly

Q13: How confident do you feel in the assessment and management of itch in PBC?

- Not at all
-
- Moderately
-
- Highly

Q14: What is your first line treatment for itch in PBC?

Free text

Q15: How confident do you feel in the assessment and management of fatigue in PBC?

- Not at all
-
- Moderately
-
- Highly

Q16: Are you aware of current and upcoming trials in PBC?

- Yes
- Somewhat
- No

Q17: Are you aware of any second line treatments (either current or upcoming) for UDCA non responders?

- Yes
- No

Q18: What second line treatments are you aware of?

Free text

Q19: How confident do you feel deciding who should be screened for cirrhotic complications? For example varices and HCC

- Not at all
-
- Moderately
-
- Highly

Q20: How often do you recommend to a patient with PBC and cirrhosis that they enter the following screening programmes?

Varices

- Never
- Rarely
- Sometimes
- Most of the time
- Always

Hepatocellular carcinoma

- Never
- Rarely
- Sometimes
- Most of the time
- Always

Osteoporosis

- Never
- Rarely

- Sometimes
- Most of the time
- Always

Q21: Do you screen non cirrhotic patients with PBC for osteoporosis?

- Yes, all patients
- Some patients
- No, never

Q22: How likely are you to discharge a patient who has responded to UDCA and is non cirrhotic to primary care follow up?

- Not at all
-
- Moderately
-
- Highly

APPENDIX 4 – DATA CAPTURE FORM FOR QEHB REFERRALS AUDIT

Case note number……..

Age at time of referral (in years) ……

Gender M/F

Date of referral

Source of referral

Primary care

Secondary care (post code) …….

Internal QE referral (department)……

Reason for referral

A – confirmed PBC – cholestatic LFTs, positive AMA
B – possible diagnosis –cholestatic LFTs, not had AMA
C – AMA positive, normal LFTs
D – possible diagnosis, AMA negative. Need for biopsy
E – symptoms of pruritus
F – HCC on background PBC
G – patient requesting review at QEHB
H – transplant assessment

I – trial inclusion

J – UDCA non responder

K – physician requesting second opinion

L – acute decompensation presenting to QEHB and In patient team requested out-patient follow up

M – pregnant patient with PBC

N – request for elastography procedure

First clinic seen in

General hepatology clinic

PBC clinic

Other (state which)

Follow up clinic seen in

General Hepatology clinic

PBC clinic

Other (state which)

Patient discharged Y/N

APPENDIX 5 – PATIENT RECRUITMENT ADVERTISEMENT

RESEARCH PARTICIPANTS NEEDED

UNIVERSITY OF BIRMINGHAM

Who is eligible to take part?

All patients with PBC are eligible to take part in this research. Ideally we are looking for patients in or near the West Midlands area.

What is the research about?

The purpose of this research is to find out more about the experiences of people who have PBC.
We are particularly interested in finding out more about patients experiences in different health care settings and with different types of healthcare professionals.

What is involved?

You will be asked to take part in a face to face interview with the researcher.
This is likely to take between 1 and 1 and a half hours
You can choose to be interviewed in your own home or at the University of Birmingham

Who is undertaking the research?

This research is being undertaken by researchers at the University of Birmingham

If you are interested in taking part in this research or would like more information please contact:
Dr Margaret Corrigan (Clinical research fellow, NIHR Liver Biomedical Research Unit
Email: m.corrigan@bham.ac.uk

Advert published in the PBC Foundation newsletter 'The Bear Facts' and on the PBC foundation website

APPENDIX 6 – CLINICIAN RECRUITMENT ADVERTISEMENT

APPENDIX 7 – CLINICIAN INVITE LETTER

UNIVERSITY OF BIRMINGHAM

Room 512, 5th Floor
Institute of Biomedical Research
College of Medical and Dental Sciences
University of Birmingham
Edgbaston
B15 2TT

Date: 18th May 2017

Dear Doctor

I am writing to invite you to take part in a research study that is being undertaken by the University of Birmingham, in conjunction with UK-PBC, looking at perspectives on management of Primary Biliary Cholangitis (formerly known as Primary Biliary Cirrhosis) or PBC.

We are looking to recruit doctors who have experience of looking after patients with PBC and are willing to take part in a face to face taped interview.

I have enclosed a copy of our participant information sheet which explains in more detail the purpose of the research and what will be required if you agree to take part.

If you are interested in taking part in this research or would like further information, please return the expression of interest slip below to Dr Margaret Corrigan (at the address given at the top of this letter) and a member of the research team will be in contact.

Many thanks in advance for your help with this research.

Yours sincerely

Dr Margaret Corrigan
Postgraduate researcher/co-investigator

Dr Gideon Hirschfield
Chief investigator

Version 1.0 30th March 2016

UNIVERSITY OF BIRMINGHAM

Expression of interest

Name: .....

Place of work: .....

Preferred contact method

Email: .....

Telephone:.....

Preferred day of the week and/or time to be contacted: .....

APPENDIX 8 – PARTICIPANT INFORMATION SHEET (PATIENTS)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis/Cirrhosis (PBC)– patient and physician perspectives on management in primary care

INFORMATION SHEET FOR PARTICIPANTS - PATIENT

Dear Participant

You are invited to take part in a research study for patients with Primary Biliary Cholangitis (PBC) formerly known as Primary Biliary Cirrhosis. Before you decide whether to take part in this study it is important that you understand why this research is being done and what you will be asked to do.

Please take time to read the following information and discuss it with others if you wish.

What is the purpose of this research?

The purpose of this research study is to explore your experience of living with PBC. We are particularly interested in your experience of being seen by doctors in different health care settings. The information gained from this research will be used to make recommendations for new ways of managing PBC and will offer insights into the experiences of patients with PBC. The overall goal of the research is to make sure that patients are treated in the right place by the right people.

Why have I been invited to take part?

You have been invited to take part as you have PBC.

Who is doing this research?

This research is being undertaken by a team based at the University of Birmingham. Dr Margaret Corrigan is conducting this study as a basis for her postgraduate degree. This research is taking place under the supervision of three senior researchers based at the University of Birmingham.

Dr Gideon Hirschfield is a Senior Lecturer at the Centre for Liver Research and an Honorary Consultant Hepatologist at the Queen Elizabeth Hospital Birmingham.
Professor Sheila Greenfield is a Professor of Medical Sociology in the Institute of Applied Health Research
Professor Jayne Parry is a Professor of Policy and Public Health in the Institute of Applied Health Research

What does the research involve?

This study involves one face to face interview with the researcher. The interview will be recorded on tape and some written notes will be taken. The interview will take between 1 hour to 1.5 hours approximately and in most cases the interview will take place in your own home. Alternatively, if you prefer, you can request to be interviewed at the University of Birmingham.

Do I have to take part in this research?

No. It is up to you to decide whether or not to take part. If you decide to take part, you will be given a copy of this information sheet to keep. You will also be asked to sign a consent form. You can change your mind at any time and withdraw from the study without giving a reason.

What are the benefits of taking part in the study?

Taking part in this study may not help you directly but the information that is gained from the study will help to increase our understanding of PBC and how it is currently managed. Information may be used to develop new care pathways for patients.

What are the disadvantages of taking part?

Some people can find it difficult to talk about their condition. If you find it difficult to talk about a specific aspect of your disease, then you can request not to answer these questions. You can ask for the interview can be stopped at any point.

What happens if I change my mind and no longer want to be involved?

Once you have agreed to take part in the study, you are entitled to change your mind about taking part in the study up. You can do this up until two weeks after the interview has taken place. You can do this by contacting the study team and letting them know that you wish to withdraw. You do not have to give a reason. If you choose to withdraw the the information collected up to that point including recordings, written notes and transcripts will be destroyed.

Will I get to see the results from this research?

You will be given the option to receive a summary of the research findings when it is completed.

Will I be paid for my involvement?

You will not be paid for your involvement. However, you will be reimbursed for any travel expenses that you may incur if you choose to be interviewed at the University of Birmingham.

Will my involvement be confidential?

Your personal details will be anonymised and will not be available to anyone outside the research team. You will be assigned a code number that will be used on all paperwork, stored data and in any publications that arise from this research. Direct quotations from interviews may be used in publication in an anonymised form.

The interview will be recorded on audio tape and then transcribed (typed out word for word) onto a computer by an external company. No identifiable information will be recorded on the tape and the transcriber will be bound by a confidentiality agreement. All paperwork related to the study and any physical recordings will be stored in a locked cabinet in a secure place within the University of Birmingham. Any electronic data stored on computer will be protected by a password. This data will be stored for up to 10 years. Only members of the direct research team will have access to this information.

In the event that information is disclosed during the study period, which in the opinion of the research team, may pose a risk to the safety of the participant or another individual then it is the obligation of the research team to pass this information on to the relevant parties.

Some patients with PBC have previously been involved with a research study called the UK-PBC research cohort. If you are already a member of this study, we will additionally ask that we can access the medical information that is held on their database. This would include information about when you were diagnosed, what medication you are on, your response to treatment, and the severity of your disease. This will allow us to make sure that we have a wide mix of patients taking part in the research. No identifiable information will be made available to anyone outside the research team. This is optional and if you do not want us to access your medical information you can still take part in the study.

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

How will the information collected be used?

At the end of the research, a report will be written which will form part of Dr Corrigan's research thesis. The results may also be published in medical journals and may be presented at conferences. The written reports and presentations may include anonymous quotes from your transcript. All published information will be anonymised and no participant will be identifiable from any publications.

Who has approved this study?

This study has been reviewed and approved by the University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee (Reference ERN_16-1030)

How is the study funded?

This research is funded with support from the National Institute of Health Research (NIHR) Birmingham Liver Biomedical Research Unit and the Queen Elizabeth Hospital Birmingham Charity.

Contact details for further information

Please do not hesitate to contact me if you need further information.

Chief investigator: Dr Gideon Hirschfield

Research fellow: Dr Margaret Corrigan email: m.corrigan@bham.ac.uk

Telephone 0121 415 8700

APPENDIX 9 – PARTICIPANT INFORMATION SHEET (CLINICIANS)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis/Cirrhosis (PBC) – patient and physician perspectives on management in primary care

INFORMATION SHEET FOR PARTICIPANTS - PHYSICIAN

Dear Doctor

You are invited to take part in a research study for Primary Biliary Cholangitis (PBC) formerly known as Primary Biliary Cirrhosis. Before you decide whether to take part in the study it is important that you understand what the research is for and what you will be asked to do. Please take time to read the following information and discuss it with others if you wish.

What is the purpose of this research?

The purpose of the research study is to explore the experiences of doctors who look after patients with PBC. The information gained from this research will offer insights into the experiences of physicians in different health care settings who look after patients with this condition. This information will be used to make recommendations for managing PBC in the future and may be used to inform the development of a care pathway.

Why have I been invited to take part?

You have been invited to take part as you may look after patients with PBC.

Version 2.0 Date: 29th June 2016
IRAS: 204690

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

Who is doing this research?

This research is being undertaken by a team based at the University of Birmingham. Dr Margaret Corrigan is conducting this study as a basis for her postgraduate degree. This research is taking place under the supervision of three senior researchers:

Dr Gideon Hirschfield is a Senior Lecturer at the Centre for Liver Research and an Honorary Consultant Hepatologist at the Queen Elizabeth Hospital Birmingham

Professor Sheila Greenfield is a Professor of Medical Sociology in the Institute of Applied Health Research

Professor Jayne Parry is a Professor of Policy and Public Health in the Institute of Applied Health Research

What does the research involve?

This study involves one face to face interview with the researcher. The interview will be recorded on tape and some written notes will be taken. The interview will take between 1 hour to 1.5 hours approximately and will be conducted in your workplace. Alternatively, if you prefer, you can request to be interviewed at the University of Birmingham.

Do I have to take part in this research?

No. It is up to you to decide whether or not to take part. If you decide to take part, you will be given a copy of this information sheet to keep. You will also be asked to sign a consent form. You can change your mind at any time and withdraw from the study without giving a reason.

What are the benefits of taking part in the study?

Taking part in this study may not help you directly but the information that is gained from the study will help to increase our understanding of PBC and how it is currently managed. Information may be used to develop new care pathways.

What happens if I change my mind and no longer want to be involved?

Once you have agreed to take part in the study, you are entitled to change your mind about taking part in the study. You can do this up until two weeks after the interview has taken place. You can do this by contacting the study team and letting them know that you wish to withdraw. You do not need to give a reason. If you choose to withdraw the information collected up to that point including recordings, written notes and transcripts will be destroyed.

Will I get to see the results from this research?

You will be given the option to receive a summary of the research findings when it is completed.

Will I be paid for my involvement?

You will not be paid for your involvement. However, you will be offered reimbursement for any travel expense that you incur if you choose to be interviewed at the University of Birmingham.

Will my involvement be confidential?

Your personal details will be anonymised and will not be available to anyone outside the research team. You will be assigned a code number that will be used on all paperwork, stored data and in any publications that arise from this research. Direct quotations from interviews may be used in publication in an anonymised form

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

The interview will be recorded on audio tape and then transcribed (typed out word for word) onto a computer by an external company. No identifiable information will be recorded on the tape and the transcriber will be bound by a confidentiality agreement. All paperwork related to the study and any physical recordings will be stored in a locked cabinet in a secure place within the University of Birmingham. Any electronic data stored on computer will be protected by a password. The data will be held for up to 10 years. Only members of the direct research team will have access to this information.

In the event that information is disclosed during the study period, which in the opinion of the research team, may pose a risk to the safety of the participant or another individual then it is the obligation of the research team to pass this information on to the relevant parties.

How will the information collected be used?

At the end of the research, a report will be written which will form part of Dr Corrigan's research thesis. The results may also be published in medical journals and may be presented at conferences. The written reports and presentations may include anonymous quotes from your transcript. All published information will be anonymised and no participant will be identifiable from any publications.

Who has approved this study?

This study has been reviewed and approved by the University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee (Reference ERN_16-0130)

How is the study funded?

This research is funded with support from the National Institute of Health Research (NIHR) Birmingham Liver Biomedical Research Unit and the Queen Elizabeth Hospital Birmingham Charity

Contact details for further information

Please do not hesitate to contact me if you need further information.

Chief investigator: Dr Gideon Hirschfield

Research fellow: Dr Margaret Corrigan email: m.corrigan@bham.ac.uk

Telephone 0121 415 8700

APPENDIX 10 – PARTICIPANT INFORMATION SHEET (PATIENT GROUP REPRESENTATIVES)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis/Cirrhosis (PBC)– patient and physician perspectives on management in primary care

INFORMATION SHEET FOR PARTICIPANTS – PATIENT GROUP REPRESENTATIVES

Dear Participant

You are invited to take part in a research study for patients with Primary Biliary Cholangitis (PBC) formerly known as Primary Biliary Cirrhosis. Before you decide whether to take part in this study it is important that you understand why this research is being done and what you will be asked to do.

Please take time to read the following information and discuss it with others if you wish.

What is the purpose of this research?

The purpose of this research study is to explore the experiences of people living with PBC. We are particularly interested in their experience of being seen by doctors in different health care settings. The information gained from this research will be used to make recommendations for new ways of managing PBC and will offer insights into the experiences of patients with PBC. The overall goal of the research is to make sure that patients are treated in the right place by the right people.

Why have I been invited to take part?

You have been invited to take part as you have PBC as you are a part of a group representing patients with PBC.

Who is doing this research?

This research is being undertaken by a team based at the University of Birmingham. Dr Margaret Corrigan is conducting this study as a basis for her postgraduate degree. This research is taking place under the supervision of three senior researchers based at the University of Birmingham.

Dr Gideon Hirschfield is a Senior Lecturer at the Centre for Liver Research and an Honorary Consultant Hepatologist at the Queen Elizabeth Hospital Birmingham.
Professor Sheila Greenfield is a Professor of Medical Sociology in the Institute of Applied Health Research
Professor Jayne Parry is a Professor of Policy and Public Health in the Institute of Applied Health Research

What does the research involve?

This study involves one face to face interview with the researcher. The interview will be recorded on tape and some written notes will be taken. The interview will take between 1 hour to 1.5 hours approximately and in most cases the interview will take place in your own home or place of work. Alternatively, if you prefer, you can request to be interviewed at the University of Birmingham.

Do I have to take part in this research?

No. It is up to you to decide whether or not to take part. If you decide to take part, you will be given a copy of this information sheet to keep. You will also be asked to sign a consent form. You can change your mind at any time and withdraw from the study without giving a reason.

What are the benefits of taking part in the study?

Taking part in this study may not help you directly but the information that is gained from the study will help to increase our understanding of PBC and how it is currently managed. Information may be used to develop new care pathways for patients.

What are the disadvantages of taking part?

Some of those taking part may have personal experience of PBC and can find it difficult to talk about the condition. Whilst the questions asked are not specifically about your personal experiences, if there are questions that you find it difficult to answer then you can request not to answer these questions. You can ask for the interview can be stopped at any point.

What happens if I change my mind and no longer want to be involved?

Once you have agreed to take part in the study, you are entitled to change your mind about taking part in the study up. You can do this up until two weeks after the interview has taken place. You can do this by contacting the study team and letting them know that you wish to withdraw. You do not have to give a reason. If you choose to withdraw the the information collected up to that point including recordings, written notes and transcripts will be destroyed.

Will I get to see the results from this research?

You will be given the option to receive a summary of the research findings when it is completed.

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

Will I be paid for my involvement?

You will not be paid for your involvement. However, you will be reimbursed for any travel expenses that you may incur if you choose to be interviewed at the University of Birmingham.

Will my involvement be confidential?

Your personal details will be anonymised and will not be available to anyone outside the research team. You will be assigned a code number that will be used on all paperwork, stored data and in any publications that arise from this research. Direct quotations from interviews may be used in publication in an anonymised form.

The interview will be recorded on audio tape and then transcribed (typed out word for word) onto a computer by an external company. No identifiable information will be recorded on the tape and the transcriber will be bound by a confidentiality agreement. All paperwork related to the study and any physical recordings will be stored in a locked cabinet in a secure place within the University of Birmingham. Any electronic data stored on computer will be protected by a password. This data will be stored for up to 10 years. Only members of the direct research team will have access to this information.

In the event that information is disclosed during the study period, which in the opinion of the research team, may pose a risk to the safety of the participant or another individual then it is the obligation of the research team to pass this information on to the relevant parties.

How will the information collected be used?

At the end of the research, a report will be written which will form part of Dr Corrigan's research thesis. The results may also be published in medical journals and may be presented at conferences. The written reports and presentations may include

anonymous quotes from your transcript. All published information will be anonymised and no participant will be identifiable from any publications.

Who has approved this study?

This study has been reviewed and approved by the University of Birmingham Science, Technology, Engineering and Mathematics Ethical Review Committee (Reference ERN_16-1030)

How is the study funded?

This research is funded with support from the National Institute of Health Research (NIHR) Birmingham Liver Biomedical Research Unit and the Queen Elizabeth Hospital Birmingham Charity.

Contact details for further information

Please do not hesitate to contact me if you need further information.

Chief investigator: Dr Gideon Hirschfield

Research fellow: Dr Margaret Corrigan email: m.corrigan@bham.ac.uk

Telephone 0121 415 8700

APPENDIX 11 – CONSENT FORM (PATIENTS)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis (PBC) – patient and physician perspectives on management in primary care

CONSENT FORM FOR PATIENTS

Participant number: _____

Please initial box

1. I confirm that I have read the information sheet dated 29th June 2016 (version 2.0.) for the above study. ☐
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
3. I understand that my participation is voluntary and that I am free to withdraw up to two weeks following my interview without giving any reason and without my medical care or legal rights being affected. ☐
4. I understand that the information collected may be used to support other research in the future, and may be published. All information obtained and/or published will be anonymised. ☐
5. I consent to direct quotations from my interview being used in publications in an anonymised form ☐
6. I wish to receive a summary of the research once it has been completed. ☐
7. I am happy for the researchers to access medical information about me that is held by UK-PBC (optional) ☐

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

8. I agree to take part in the above study ☐

Name of Participant	Date (dd/mm/yyyy)	Signature

Name of person taking consent	Date (dd/mm/yyyy)	Signature

APPENDIX 12 – CONSENT FORM (CLINICIANS)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis (PBC) – patient and physician perspectives on management in primary care

CONSENT FORM FOR PHYSICIANS

Participant number: _____

Please initial box

1. I confirm that I have read the information sheet dated 29th June 2016 (version 2.0) for the above study. ☐
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
3. I understand that my participation is voluntary and that I am free to withdraw up to two weeks following my interview without giving any reason and without my legal rights being affected. ☐
4. I understand that the information collected may be used to support other research in the future, and may be published. All information obtained and/or published will be anonymised. ☐
5. I am happy for direct quotations from my interview to be used in publication in an anonymised form ☐
6. I wish to receive a summary of the research once it has been completed. ☐

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

UNIVERSITY OF BIRMINGHAM

7. I agree to take part in the above study ☐

Name of Participant	Date (dd/mm/yyyy)	Signature
Name of person taking consent	Date (dd/mm/yyyy)	Signature

APPENDIX 13 – CONSENT FORM (PATIENT GROUP REPRESENTATIVES)

UNIVERSITY OF BIRMINGHAM

Title: Development of a stratified care pathway for Primary Biliary Cholangitis (PBC) – patient and physician perspectives on management in primary care

CONSENT FORM FOR PATIENT GROUP REPRESENTATIVES

Participant number: _____

Please initial box

1. I confirm that I have read the information sheet dated 15th March 2017 (version 1.0.) for the above study. ☐
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
3. I understand that my participation is voluntary and that I am free to withdraw up to two weeks following my interview without giving any reason and without my legal rights being affected. ☐
4. I understand that the information collected may be used to support other research in the future, and may be published. All information obtained and/or published will be anonymised. ☐
5. I consent to direct quotations from my interview being used in publications in an anonymised form ☐
6. I wish to receive a summary of the research once it has been completed ☐
7. I agree to take part in the above study ☐

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

UNIVERSITY OF BIRMINGHAM

Name of Participant	Date (dd/mm/yyyy)	Signature

Name of person taking consent	Date (dd/mm/yyyy)	Signature

University of Birmingham, Edgbaston, Birmingham, B15 2TT, United Kingdom

APPENDIX 14 – TOPIC GUIDE (PATIENTS)

Opening question

- Tell me about your PBC
- How does PBC affect you?

Diagnosis

- When, by who, how
- How did you find the process of diagnosis?
- What information were you given at the time?

Care since diagnosis

- Who and where, how often are you seen
- What treatment are you on or have been on
- Do you see your GP about issues related to PBC?
- Tell me about your experience in hospital related to PBC
- If you are unwell between appointments who would you contact?
    - How have you found that process?
    - Is that different depending on what was wrong?
- Tell me about good experiences you have had with healthcare professionals
    - What was good?
- Tell me about poor experience
    - What do you think could have been done differently?

Information seeking

- When you were first diagnosed how did you get information about PBC?
- If you want information now what resources do you use?
- Are you involved with any patient groups?
- Do you use the internet to access information?
- How do you find out about PBC if you have questions?
- Do you like to know about your disease or do you prefer to not know as much?

New care pathway

Question for responders

- How would you feel about being discharged from hospital care?
    - What would be good?
    - What would be bad?
    - How could that be improved

Question for non-responders

- How would you/ do you feel about going to a specialist centre
    - What is good
    - What is bad
    - What could be improved

Is there anything else you would like to mention?

APPENDIX 15 – TOPIC GUIDE (GPs)

Opening question – tell me about your experience of looking after patients with PBC

- How many patients have you seen/currently see?
- Over what time period have you looked after these patients?
- How many of these patients are seen in secondary/tertiary care?

Interaction with patients

- In what context do you see patients – regular review, as and when needed?
- What do they ask you about most commonly?
- What do you or don't you feel comfortable dealing with and why?

Interaction with hospital

- Tell me about your interaction with hospitals
    - Information received
    - If you had to ask for advice how would you go about this?
- What has been good?
- What has been bad?
- What could be done to improve this?

How do you access information about PBC and keep up to date?

How would you feel about looking after a patient with PBC who had been discharged from hospital?

- What challenges do you see?
- What benefits do you see?
- How do you think the process could be made better?
- If you had a patient under your care and needed advice what would be your preferred method of contact?
    - Phone, email, letter
    - Specialist nurse or consultant

Is there anything else you would like to mention?

APPENDIX 16 – TOPIC GUIDE (SPECIALISTS)

Opening question – tell me about your experience of looking after patients with PBC

- How many patients have you/do you see?
- Case mix – severity, age range

Patient interaction (for secondary and tertiary)

- How often do you see them?
- Specialist nurse involvement?
- Do patients contact you directly between appointments?
    - If so why
- Do any of them go to specialist centre?
- If so why

Interaction with between secondary and tertiary

- How does this work in practice?
- What is good?
- What has been bad?
- Specifically ask about communication
- If you needed to communicate between appointments how would you access it?
- What would be your ideal method of communication?
    - Phone, email, letter

Interaction with GP (for secondary and tertiary)

- How do you communicate with GP?
- How does GP communicate with you?
- What is good?
- What has been bad?
- What would be your ideal method of communication?
    - Phone, email, letter

How do you keep up to date with PBC?

New care pathway

- How would you feel about discharging well patients to GP?
    - What would be good?
    - What would be bad?
    - What would need to be done to make this work?
- How would you feel about specialist care looking after the complex patients?
    - What would be good?
    - What would be bad?

Is there anything else you would like to mention?