AN INVESTIGATION OF WEIGHT MANAGEMENT INTERVENTIONS FOR EXTREME OBESITY

by

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ABSTRACT

The increasing prevalence of obesity has been accompanied by an increase in the number of individuals at the extreme end of the obesity spectrum. The detrimental impacts of extreme obesity, defined as BMI $\geq$40.0kg/m^2, on affected individuals' physical and psychological health have not been fully established. Furthermore, it remains unclear whether medical and behavioural interventions are effective at facilitating weight loss for individuals with extreme obesity. The efficacy of two treatment pathways within the Heart of England NHS Foundation Trust Specialist Weight Management Service were examined, with both demonstrated to facilitate clinically and statistically significant weight loss. A detailed profile of the characteristics of individuals entering the service highlighted the substantial physical and psychological co-morbidity associated with extreme obesity, revealing widespread impairment in quality of life and mental health. A systematic review of primary research examining the efficacy of medical and behavioural weight management interventions within lesser-researched extreme obese populations demonstrated the value of medically-supported programmes and also revealed the limited body of good quality research. This thesis has enhanced current understanding of extreme obesity, and recommendations generated from this work have been made in order to improve primary research examining weight management interventions and service provision for affected individuals.

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LIST OF ABBREVIATIONS

AHI	Apnoea hypopnea index
AMSTAR	Assessment of Multiple Systematic Reviews
BBC	Birmingham and Black Country
BBC	British Broadcasting Corporation
BDI	Beck Depression Inventory
BDI-II	Beck Depression Inventory-Second edition
BOCF	Baseline observation carried forward
BOMSS	British Obesity and Metabolic Surgery Society
BMI	Body mass index
BSI	Brief Symptom Inventory
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CES-D	Center for Epidemiological Studies Depression Scale
CI	Confidence interval
CLAHRC	Collaborations for Leadership in Applied Health Research and Care
CONSORT	Consolidated Standards of Reporting Trials
CVD	Cardiovascular disease
CWMS	Community Weight Management Service
DARE	Database of Abstracts and Reviews of Effects
DASS-21	Depression Anxiety Stress Scales
DBP	Diastolic blood pressure
DEBQ	Dutch Eating Behaviour Questionnaire

DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EDI-2	Eating Disorder Inventory
EI	Eating Inventory
EQ5D-3L	EuroQol health-related quality of life measure
ESS	Epworth Sleepiness Scale
FFIT	Football Fans In Training programme
FPAI	Framingham Physical Activity Index
GHRI	General Health Rating Index
GLS	General Lifestyle Survey
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HEFT	Heart of England NHS Foundation Trust
HR	Hazard ratio
HSE	Health Survey for England
HTAD	Health Technology Assessment Database
IMD	Indices of Multiple Deprivation
IPAQ	International Physical Activity Questionnaire
IQR	Inter-quartile range
IWQOL-Lite	Impact of Weight on Quality of Life Questionnaire
LELD	Low Energy Liquid Diet
LOCF	Last observation carried forward
MACL	Mood Adjective Check List
MDT	Multi-disciplinary team
MeSH	Medical subject heading

MET	Metabolic equivalent
MHI	Mental Health Inventory
MIDUS	Midlife Development in the United States survey
MRC	Medical Research Council
NBSR	National Bariatric Surgery Registry
NEQ	Night Eating Questionnaire
NHANES	National Health and Nutrition Examination Survey
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
OAS	Obesity Adjustment Survey
OP	Obesity-related Problems scale
OR	Odds ratio
ORWELL	Obesity Related Well-being questionnaire
OSA	Obstructive sleep apnoea
PCT	Primary Care Trust
PICOS	Population, intervention, comparator, outcome, study design
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSC	Prospective Studies Collaboration
PSQI	Pittsburgh Sleep Quality Index
QWB	Quality of Well-Being measure
RCT	Randomised controlled trial
RSE	Rosenberg Self-Esteem scale
SBP	Systolic blood pressure

SBQ-R	Suicidal Behaviours Questionnaire-Revised
SD	Standard deviation
SDB	Sleep disordered breathing
SE	Standard error
SES	Socioeconomic status
SF-12	Medical Outcomes Study Short Form Health Survey (12 item)
SF-36	Medical Outcomes Study Short Form Health Survey (36 item)
SIMD	Scottish Index of Multiple Deprivation
SIP	Sickness Impact Profile
SLiM	Specialist Lifestyle Management programme
SMART	Specific, measurable, attainable, relevant, time sensitive
SPSS	Statistical Package for the Social Sciences
SSQ	Stigma Situations Questionnaire
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
TFEQ	Three-Factor Eating Questionnaire
UK	United Kingdom
US	United States of America
VAS	Visual analogue scale
WALI	Weight and Lifestyle Inventory
WHO	World Health Organisation
WSCS	Wisconsin Sleep Cohort Study

CHAPTER ONE

1.0 INTRODUCTION

1.1 INTRODUCTION TO THE THESIS

1.1.1 Research setting

1.1.1.1 Collaborations for Leadership in Applied Health Research and Care for Birmingham and Black Country (CLAHRC-BBC)

The CLAHRC-BBC programme was one of nine pilot CLAHRCs established across England funded by the National Institute for Health Research (NIHR). The programme ran for five years from October 2008 to December 2013 and was a collaborative partnership between the University of Birmingham and healthcare service organisations across Birmingham and the Black Country. The aim of the programme was to conduct applied healthcare research across nine themes which addressed both national and local health policy initiatives, focusing on the needs of patients and supporting the translation of research evidence into clinical practice within the National Health Service (NHS) (1).

1.1.1.2 CLAHRC-BBC Theme 8: Implementation of effective community care for diabetes

This research project was conducted as part of a body of work under the CLAHRC-BBC Theme 8: Implementation of effective community care for diabetes. Theme 8 incorporated a range of research projects following the theme of care implementation for diabetes and weight management, conducted in partnership with Heart of England NHS Foundation Trust (HEFT) and the former South Birmingham Primary Care Trust (PCT). In particular this focussed on an evaluation of the efficacy of the Specialist Weight Management Service operated by HEFT.

1.1.2 Research project

My research project was conducted to establish the efficacy of the Specialist Weight Management Service, whilst additionally gleaning a deeper understanding of the extreme obese (BMI $\geq$40.0kg/m^2) patient population entering the service. The specific aims of the project were:

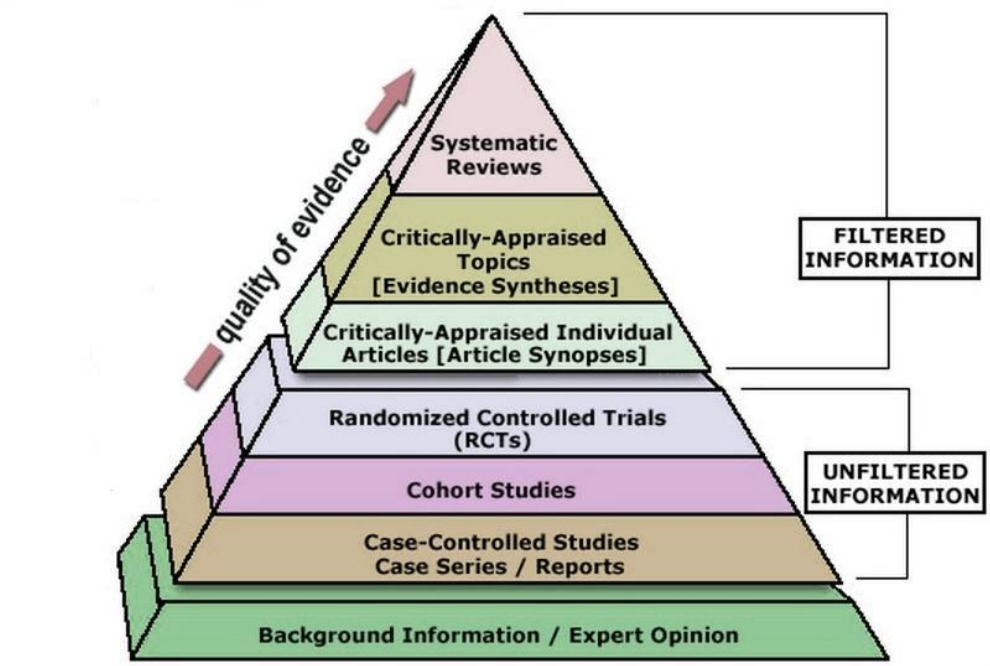
- To explore the clinical, demographic and mental well-being characteristics of extreme obesity, specifically of those individuals entering the weight management service operated by HEFT,
- To conduct a detailed examination of the psychological characteristics of individuals entering the service, incorporating an investigation of the relationship between adiposity and quality of life and mental health in extreme obesity,
- To examine the physical and psychological outcomes following attendance at the two treatment pathways currently operating within the service; the Community Weight Management Service (CWMS) and the Specialist Lifestyle Management (SLiM) programme,
- To better understand the physical and psychological impact of extreme obesity and the efficacy of this weight management service for the extreme obese patient population.

1.1.3 Research design

To achieve these aims, a pragmatic evaluation of the efficacy of the service was conducted. This pragmatic approach enables the researcher to investigate healthcare services within the complex real-world settings in which they currently operate. Indeed, one of the primary objectives of evaluations is to contribute to the knowledge base of currently operating

services, with the aim of providing feedback to improve care provision. However, this approach is not without limitation, and there has been much debate over the credibility and relevance when interpreting different types of evidence (2). Evidence-based practice has become a cornerstone of healthcare in the UK (3), with hierarchies of evidence developed to facilitate healthcare professionals, researchers and other stakeholders in the interpretation of studies and their findings. Figure 1.1 illustrates the hierarchy of evidence, which ranks a range of study designs in order of decreasing internal validity.

Figure 1.1: Hierarchy of evidence



Source: EBM Pyramid (4).

Within the hierarchy of evidence the Randomised Controlled Trial (RCT) and systematic reviews of RCTs are traditionally considered to be the gold-standard for determining the effectiveness of interventions (5). However, it has been argued that the application of the hierarchy may be problematic when appraising public health research due to the fact that

healthcare interventions are often complex and context-dependent (6, 7). Indeed there are other types of research obtained from observational and qualitative methods which although further down the hierarchy of evidence can be valuable in understanding the efficacy of interventions (7). Furthermore, triangulation approaches are also adopted whereby data is gathered using multiple methods in order to provide the best quality evidence to address a research question (8). Strengths and limitations are present in each research design and methodology, and it seems likely that the debate will continue. However, it is essential that the limitations of research design and methodology are considered when evaluating evidence and interpreting findings. In light of this evidence debate, the pragmatic approach to the evaluation of the efficacy of the service was selected in the present research study, as the best method for the investigation of the efficacy of a service currently in operation in a 'real-world' setting.

1.1.4 Research methods

The evaluation involved a close collaboration with healthcare professionals and administrative staff responsible for the delivery, organisation and operation of the Specialist Weight Management Service.

1.1.4.1 Data from the Community Weight Management Service (CWMS)

Data obtained for those individuals attending the CWMS pathway was extracted from patient records stored electronically and on paper and from completed self-report questionnaires. This involved extracting clinical and demographic data as well as questionnaire responses, and collating this information in an anonymised database. The questionnaire items were also scored and processed according to standardised protocols

issued by the developers of each scale. The data collection and entry into the database was undertaken in collaboration with two doctoral researchers, whilst the database management, data screening and analyses were undertaken independently. A secondary round of data collection was undertaken one year subsequently, in order to obtain updated weight outcome data for all individuals attending the CWMS, and expand upon the weight outcome data which was initially collected, which included weight and BMI measures at baseline and last point of contact only. The secondary round of data collection was conducted independently and involved obtaining weight and BMI outcome data at 3-month intervals throughout individuals' duration of attendance, from electronic patient records.

1.1.4.2 Data from the Specialist Lifestyle Management (SLiM) programme

Data was obtained for individuals attending the SLiM programme from the electronic database used by the healthcare professionals responsible for the delivery of the programme. Data processing was undertaken independently. This included screening the data, which involved the removal of duplicate cases, scoring the self-report questionnaire items, and transferring the data to an anonymised database to be analysed in conjunction with the CWMS data.

1.1.5 Outline of the thesis

The next section of this introductory chapter, Chapter 1.2 will provide contextual information on current understanding of the measurement, outcomes and prevalence of obesity, with a specific focus on extreme obesity. Subsequently the next section, Chapter 1.3 will give a detailed description of weight management strategies to address the increasing prevalence of obesity, including an introduction to the HEFT Specialist Weight

Management Service and its two constituent treatment pathways; the Community Weight Management Service (CWMS) and the Specialist Lifestyle Management (SLiM) Programme.

Chapter two provides a detailed characterisation of individuals entering the CWMS pathway of the service, however detailed baseline demographic and clinical information for the SLiM sample were unfortunately not routinely collected and thus were not available for analyses. The chapter examines the baseline quality of life, mental health, perceived sleep quality and physical activity levels, offering a thorough account of the baseline features of individuals entering this specific treatment pathway. The implications of the findings will be considered, with recommendations generated from the findings offered for the potential improvement of weight management services.

Chapter three presents a more detailed account of the quality of life and mental health characteristics of the individuals entering both the CWMS and SLiM treatment pathways. In addition, the cross-sectional association between baseline quality of life, mental health and adiposity will be explored in the lesser-researched extreme obese population, in order to determine the burden of psychological factors in this population. Based on the findings of the analyses, further recommendations for weight management services will be made.

Chapter four is a literature review which provides a comprehensive overview of the body of research literature examining the efficacy of weight management interventions currently offered to obese individuals in the UK. The literature review will encompass a range of intervention approaches including primary care-led, commercially provided, sporting club-based and specialist weight management services, in order to place the outcomes of the two treatment pathways demonstrated in the present evaluation in context.

Chapter five evaluates the longitudinal weight outcomes of individuals attending the CWMS and SLiM pathways, offering comparison between the effectiveness of the two services. Additionally, factors associated with weight loss and weight gain will be identified and discussed, considering the potential implications for the service, with recommendations offered to maximise the opportunity for weight loss to be achieved during attendance. There will also be an in depth analysis of the impact of the SLiM pathway on quality of life. This work will follow on from the cross-sectional investigation of quality of life and adiposity, investigating the longitudinal changes in quality of life pre- and post- attendance at the SLiM programme. The longitudinal quality of life analyses is restricted to the SLiM sample due to the fact that baseline and follow-up quality of life measures were routinely collected for individuals attending the SLiM but not the CWMS treatment pathway. The factors associated with improvement in quality of life outcomes following attendance will be explored and the longitudinal association between change in quality of life and change in BMI will also be examined.

Chapter six is a systematic review which describes the search for systematic reviews examining the effectiveness of medical and behavioural weight management interventions within exclusively extreme obese (BMI $\geq$40kg/m^2) samples. The findings of the systematic review will inform whether there is a need for a systematic review of primary research examining the efficacy of medical and behavioural weight management interventions within extreme obese samples.

Following on from the systematic review of systematic reviews, Chapter seven reports the findings of a systematic review of primary studies examining the effectiveness of medical and behavioural weight management interventions within extremely obese samples. The review will primarily examine weight and BMI outcomes, and in addition the

potential impacts of the interventions on the secondary outcomes of cardiovascular and psychological factors will also be evaluated.

Finally, Chapter eight is the thesis summary which will draw together findings from the data chapters examining the characterisation and outcomes of individuals attending the HEFT Specialist Weight Management Service and the two systematic reviews of weight management interventions for extreme obesity, discussing them in the context of the research aims and current understanding. The contribution of this programme of research and implications for weight management services will be considered, in addition to the strengths and limitations of the research study and directions for future research.

1.2 INTRODUCTION TO EXTREME OBESITY

1.2.1 Measuring and defining overweight and obesity

The most widely used measure of adiposity is Body Mass Index (BMI) which provides a measure of an individual's weight in kilograms divided by the square of their height in metres (9). BMI is used to estimate whether individuals are overweight or obese, and are subsequently more likely to experience increased risk of morbidity and mortality (10, 11). Figure 1.2 illustrates the international classification of adult underweight, overweight, and obesity as outlined by the World Health Organisation (WHO) consultation report 'Obesity: preventing and managing the global epidemic' published in 2000 (10). The figure shows that using this classification system, those individuals with BMI ≥40.00kg/m^2 classed as extremely obese or 'Obese class III' experience the greatest increased risk of morbidity, relative to those of normal BMI.

Figure 1.2: World Health Organisation (WHO) classification of BMI

Classification	BMI (kg/m^2)	Risk of co-morbidities
Underweight	<18.50	Low (but risk of other clinical problems increased)
Normal range	18.50-24.99	Average
Overweight	≥25.00	
Pre-obese	25.00-29.99	Increased
Obese class I	30.00-34.99	Moderate
Obese class II	35.00-39.99	Severe
Obese class III	≥40.00	Very severe

Source: WHO (10).

However, it is important to acknowledge that the cut-points shown in Figure 1.2 are arbitrary and should be interpreted with caution as the health risks associated with increasing adiposity are continuous and evidence suggests that the threshold at which increased health risks are experienced varies across different populations, with Asian

populations experiencing increased risk of morbidity at lower BMI levels (12). As such, cut-points at the lower BMI levels of ≥23.0kg/m^2 and ≥25.0kg/m^2 have been used to identify overweight and obesity, respectively, among Asian populations (12).

Although BMI is the most commonly used measure to indicate risk of morbidity associated with obesity, it is not a direct measure of adiposity, rather it is a proxy measure of total excess body fat distributed around the body. Alternative measures of excess body fat including waist circumference, waist to hip ratio, and skin fold thickness have been used to measure the distribution of excess weight specifically around the abdomen, providing an indication of central adiposity (13). As such, the National Institute for Health and Care Excellence (NICE) has recommended that additional measures of obesity such as waist circumference should be used in the assessment of the health risks of obesity for those with a BMI <35.0kg/m^2, as illustrated in Figure 1.3. However this suggests that individuals with BMI ≥35.0kg/m^2 experience very high risk of morbidity regardless of waist circumference (14).

Figure 1.3: Assessment of the health risks associated with overweight and obesity as recommended by the National Institute for Health and Care Excellence (NICE)

BMI classification	**Waist circumference**		
	Low	**High**	**Very high**
Overweight	No increased risk	Increased risk	High risk
Obese class I	Increased risk	High risk	Very high risk
Obese class II	Very high risk	Very high risk	Very high risk
Obese class III	Very high risk	Very high risk	Very high risk

For men, waist circumference <94cm = low, 94-102cm = high and >102 cm = very high
For women, waist circumference <80cm = low, 80-88cm = high and >88cm = very high

Source: NICE (14).

1.2.2 Health outcomes of obesity and extreme obesity

Obesity is a major public health concern due to its association with co-morbid health conditions. Figure 1.4 illustrates the increased risk of experiencing a range of health conditions faced by those who are obese, relative to those who are non-obese. The data which were obtained in a review conducted by the National Audit Office to provide estimates of risk for the population in England, indicate that the risk of developing type 2 diabetes is especially high for obese individuals, with males over five times as likely and females over 12 times as likely to develop the condition relative to those with a BMI <30.0kg/m^2.

Figure 1.4: Increased risk of co-morbid health conditions experienced by obese (≥30.0kg/m^2) relative to non-obese (<30.0kg/m^2) individuals in England

Condition	Males	Females
Type 2 diabetes	5.2	12.7
Hypertension	2.6	4.2
Myocardial infarction	1.5	3.2
Cancer of the colon	3.0	2.7
Angina	1.8	1.8
Gall bladder diseases	1.8	1.8
Ovarian cancer	-	1.7
Osteoarthritis	1.9	1.4
Stroke	1.3	1.3

Source: Health and Social Care Information Centre (15).

In addition to experiencing increased risk of co-morbid health conditions, obesity has also been demonstrated to be associated with mortality. Findings from the Prospective Studies Collaboration (PSC) which analysed data from 57 international prospective studies, suggest that moderate levels of obesity (BMI 30.0-35.0kg/m^2) are associated with a reduction in life expectancy of between 2 and 4 years, whilst extreme obesity (BMI ≥40.0kg/m^2) is associated with an 8 to 10 year reduction in life expectancy, similar to that

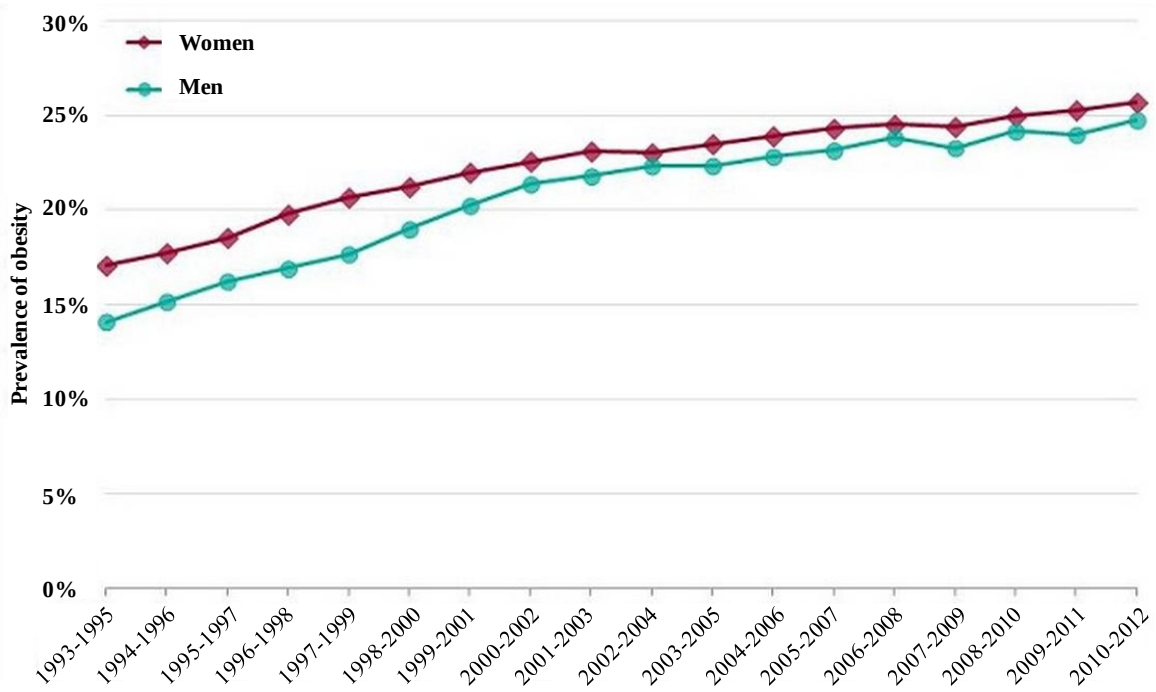
observed with life-long smoking (11). The health outcomes and clinical characteristics of extreme obesity are explored in greater detail in Chapter two.

1.2.3 The prevalence of obesity and extreme obesity

Globally, the prevalence of obesity defined as BMI ≥30.0kg/m^2, has nearly doubled since 1980, and in 2008 over 200 million men and nearly 300 million women were classed as obese, equating to over 10% of the global adult population (16). The trend of increasing prevalence of obesity among adults in England has been demonstrated using data obtained from the Health Survey for England (HSE) (15, 17). Figure 1.5 shows the three-year average prevalence of obesity defined as BMI ≥30.0kg/m^2, over a 19-year period from 1993 to 2012, for those aged 16 years or older living in England. The graph illustrates that the prevalence of obesity gradually increased from 13.2% for males and 16.4% for females in 1993 to 24.4% for males and 25.1% for females in 2012.

When considering the specific population of Birmingham, data on the prevalence of obesity are conflicting. The Birmingham unitary authority health profile published by Public Health England in 2014 indicated an obesity prevalence rate obtained using data from the Active People Survey, 2012, of 23.0% which was the same as the average rate for England of 23.0% (18). However, previous health profile reports published by Public Health England in 2011 (19), 2012 (20) and 2013 (21) used modelled estimates based on the 2006-2008 HSE data, which gave obesity prevalence rates of 26.2% for Birmingham and 24.2% for England. This suggests that previously released data modelled on estimates may have overestimated the discrepancy between the prevalence of obesity in Birmingham relative to the average prevalence for England, or alternatively may suggest that the gap between the obesity prevalence for Birmingham and England has decreased.

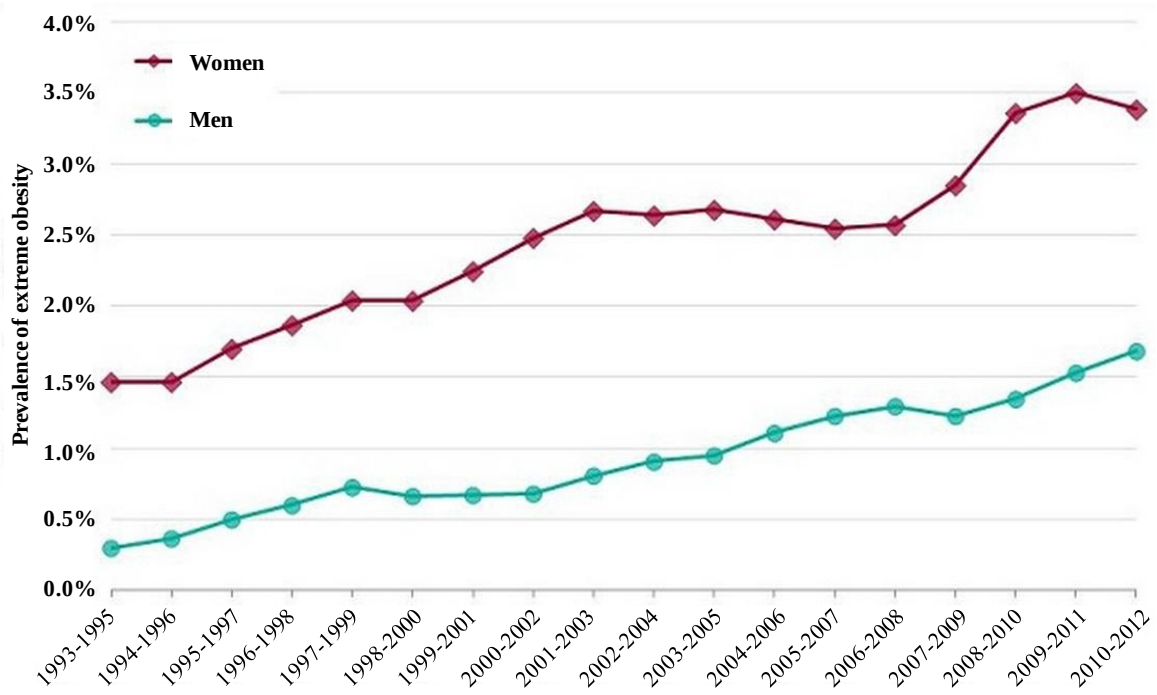
Figure 1.5: The prevalence of obesity (BMI ≥30.0kg/m^2) in England from 1993 - 2012



Source: Public Health England (22).

In addition to the trend of increasing prevalence of obesity among adults in England, HSE data (15, 17) also demonstrate that the prevalence of extreme obesity defined as BMI ≥40.0kg/m^2, increased over the same period from 1993 to 2012. Figure 1.6 demonstrates the increase in extreme obesity from 0.2% for males and 1.4% for females in 1993 to 1.7% of males and 3.1% of females in 2012 (15, 17).

Figure 1.6: The prevalence of extreme obesity (BMI ≥40.0kg/m^2) in England from 1993 - 2012



Source: Public Health England (23).

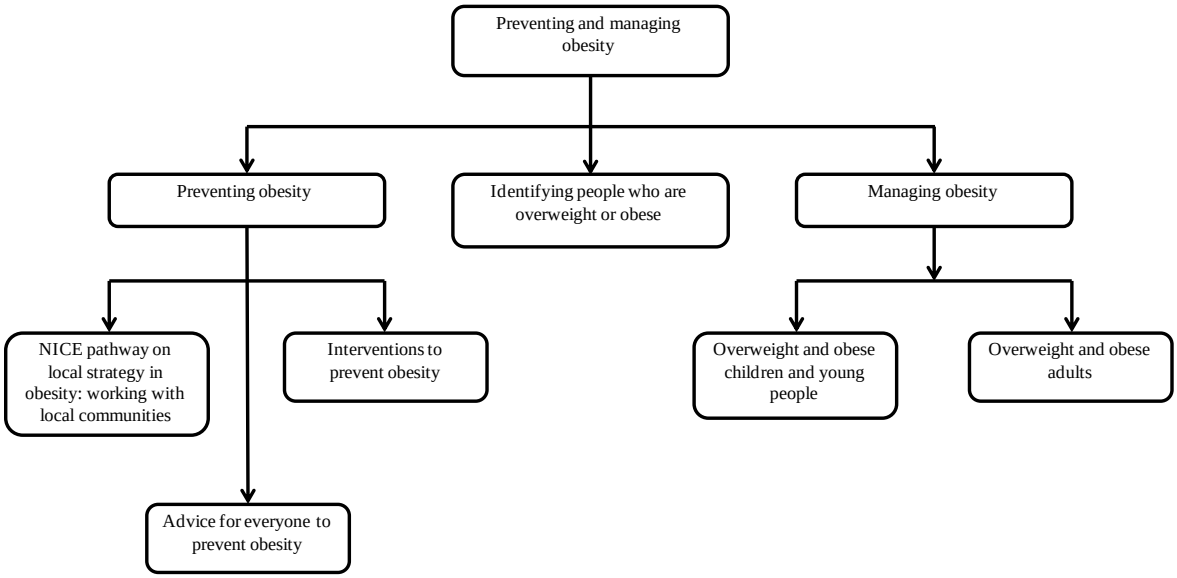
The increase in levels of extreme obesity have also been observed in the US, with a 70% increase over the last decade between 2000 and 2010 and a current prevalence rate of 6.6% (24). Furthermore, recent estimates predict that the proportion of individuals of BMI ≥40kg/m^2 will continue to increase, reaching 9% in the US by 2030 and 5% in the UK by 2033 (25). Given the current levels of extreme obesity and the fact that these levels are expected to rise, weight management strategies will play a crucial role in slowing the increasing prevalence and providing care to those individuals affected by extreme obesity.

1.3 INTRODUCTION TO WEIGHT MANAGEMENT

1.3.1 Strategies to address obesity

Chapter 1.2 has identified the challenging demand for strategies to address the increasing obesity epidemic. In 2006 NICE published Clinical guideline 43 which outlined recommendations for healthcare professionals on 'the prevention, identification, assessment and management of overweight and obesity in adults and children' (14). The clinical guideline which was last modified in May 2014, was used to create treatment pathways as illustrated in Figures 1.7 and 1.8.

Figure 1.7: NICE treatment pathway for preventing and managing obesity

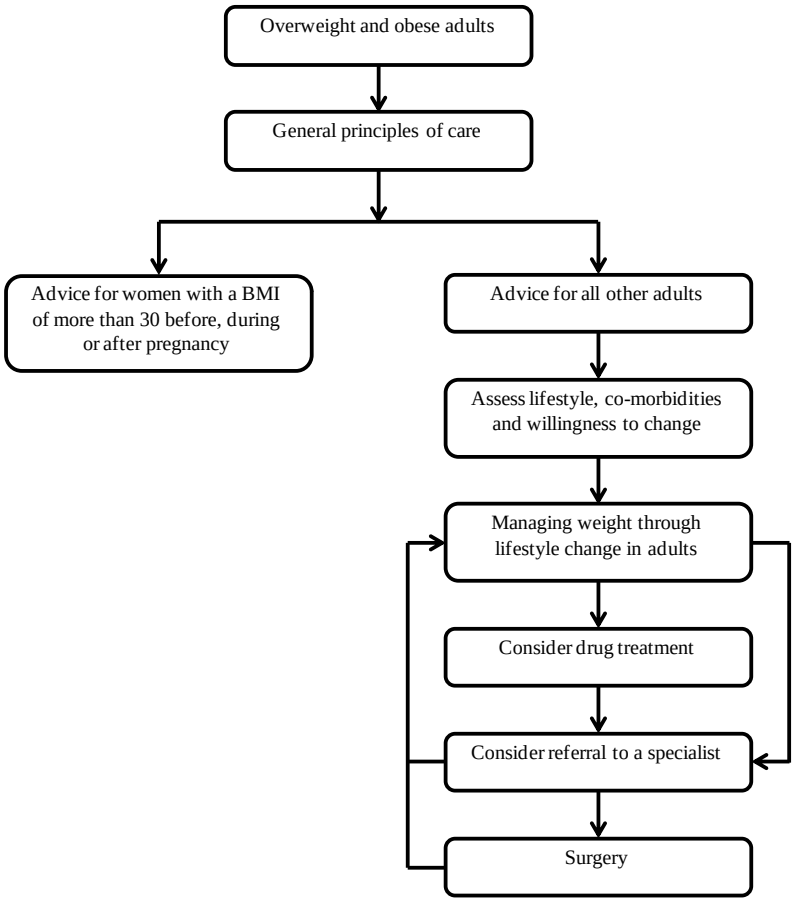


Source: NICE (26).

Figure 1.7 illustrates the care pathway developed by NICE and covers the prevention of obesity, the identification of individuals who are overweight or obese, and the management of obesity. The pathway and associated NICE guideline outline a whole-system approach, acknowledging that strategies to prevent and manage obesity require collaboration and

prioritisation of the issue from local authorities, schools, early years settings, workplaces, community and voluntary organisations, as well as the NHS (14). Prevention, identification and management are all crucial aspects in stemming the rising prevalence of obesity and its associated co-morbid health conditions. Figure 1.8 illustrates the management of obesity pathway in greater detail and is designed to improve the care provided to obese adults, particularly in primary care settings. The guideline recommends that a person-centred approach should be taken, with the choice of intervention for weight management whether pharmaceutical through the provision of weight loss medication, the initiation of a lifestyle change weight management programme or referral to a specialist weight management service, discussed and made in negotiation between the individual and healthcare professional (14). The pathway in Figure 1.8 illustrates the cyclical nature of weight management whereby individuals receive continued support as long as it is required, with the level provided depending on individuals' specific care needs.

Figure 1.8: NICE Pathway for the care of overweight and obese adults



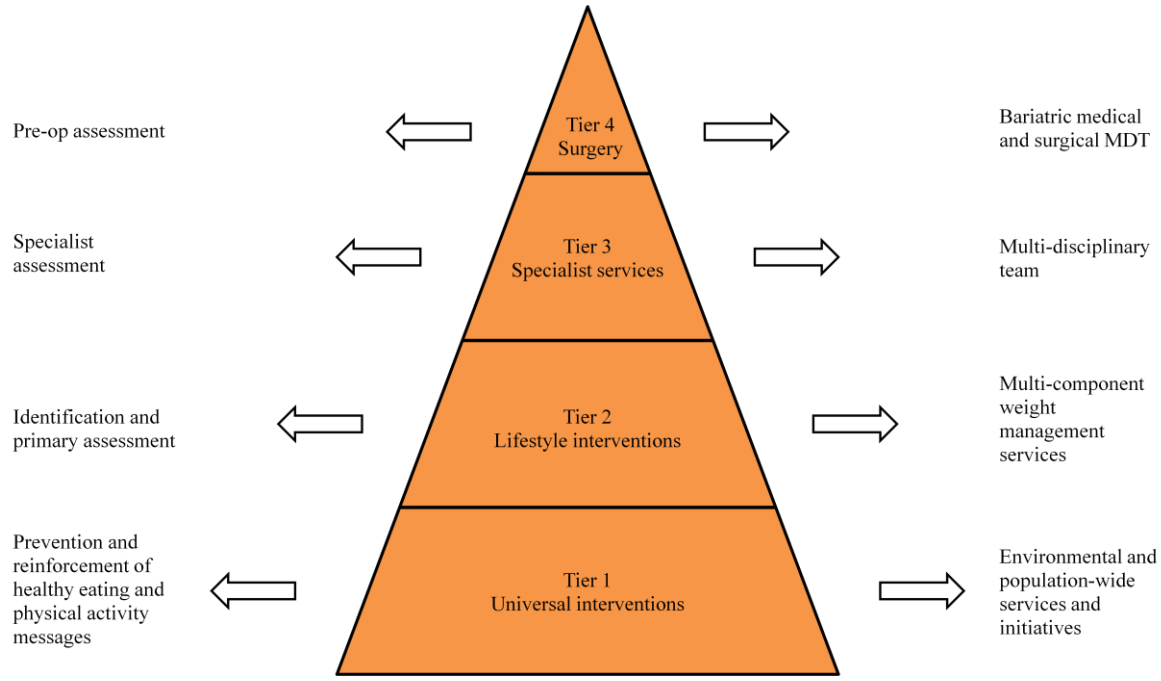
Source: NICE (27).

1.3.2 Weight management

1.3.2.1 Hierarchy of UK weight management services

Weight management care available through the NHS is organised in a hierarchical structure with the provision of increasing support for more complex and extreme levels of obesity. Figure 1.9 illustrates the hierarchy as outlined in the British Obesity and Metabolic Surgery Society (BOMSS) Commissioning guide for weight assessment and management clinics published in 2014 (28). The hierarchical model of weight management services facilitates the transition of individuals between the levels of care, with the aim that individuals receive the most appropriate service according to their needs.

Figure 1.9: Weight management levels of care



Source: BOMMS (28).

The first level of care, tier 1 incorporates health promotion at a population-level and is suitable for individuals of all weight levels. The next level of care, tier 2 incorporates lifestyle interventions such as those provided by primary care services or the commercial sector. Tier 3 and 4 services are available for individuals with higher BMI and associated complex medical needs who require more specialist services from multi-disciplinary teams, which may involve bariatric procedures and surgery.

1.3.2.2 Tier 2: Commercial and primary care-led weight management services

A detailed examination of the efficacy of primary care-led and commercial services is provided in Chapter four, however a brief introduction is provided here. The primary care-led weight management programme that has been most widely adopted is the Counterweight programme which delivers a nurse-led lifestyle intervention in group or individual sessions to obese individuals over a 3-month period, with individuals encouraged to achieve 5-10% loss of their baseline weight (29). As an alternative to Counterweight, several primary care teams have delivered their own 'in-house' services (30-32). Whilst the majority of primary care-led interventions focus on the provision of lifestyle and behaviour change advice, a Low Energy Liquid Diet (LELD) approach may also facilitate greater weight loss (33). Primary care services may also refer individuals who are overweight or obese to commercial weight management providers such as Weight Watchers, Rosemary Conley, and Slimming World through 'Slimming on referral' schemes or through participation in RCTs such as the Lighten Up study (34, 35). Alternatively individuals may also self-refer to commercial services. A substantial number of commercial interventions have demonstrated clinically significant weight losses of ≥5% of individuals' baseline body weight (36, 37).

1.3.2.3 Tier 3: Specialist weight management services

Specialist weight management services operate at the tertiary level of care, as demonstrated in Figure 1.9. Tier 3 services are usually available for individuals with BMI ≥40.0kg/m^2 or BMI ≥35.0kg/m^2 with co-morbid health conditions. It is likely that those presenting for treatment at tertiary services, may have made multiple previous attempts to lose weight through primary care or commercial programmes, potentially achieving limited

weight loss success (28). The aim of specialist weight management services is to offer these individuals more intensive support through a multidisciplinary team approach which may include input from specialist physicians, dietitians, psychologists and exercise specialists. Tier 3 services may operate in community settings or be hospital-based, delivering medically-led pharmaceutical and or behavioural interventions encompassing education, dietary and activity advice and support for lifestyle change, and the provision of anti-obesity medication. Through continued support, tier 3 services aim to facilitate not only weight loss but also the long-term maintenance of weight loss. In addition, tier 3 services evaluate co-morbid health conditions and relevant psychological factors, exclude underlying contributory diseases, whilst also evaluating attendance and engagement with the service (38). Individuals may then be referred from tier 3 services to be considered for assessment to receive bariatric surgery within a specialist tier 4 bariatric surgery service. Following bariatric surgery procedures individuals may then access tier 3 services to receive post-surgery support.

1.3.2.4 Tier 4: Multidisciplinary specialist bariatric surgical services

Surgical weight management may be considered as a treatment option for those individuals with BMI $\geq$40.0kg/m^2 or BMI $\geq$35.0kg/m^2 with co-morbid health conditions, who have received and engaged with medical weight management for a minimum period of 6 months (38). Tier 4 services are available to individuals who meet eligibility criteria which is assessed on an individual basis, with procedures carried out subject to the additional criteria of meeting funding requirements. Data released from the UK National Bariatric Surgery Registry (NBSR) indicated that in the financial year 2013/14, the 106 surgeons who contributed to the registry completed 4,389 NHS bariatric procedures across England

(39). Data provided by those who consented to the release of patient outcome data (95%), indicated that the mean baseline BMI was 50.6kg/m^2 and 72.8% were female, with a survival rate of 99.9% and an average hospital stay of 2.5 days. Furthermore, estimates obtained using hospital episode statistics suggest that a total of 5,656 operations were conducted by 138 NHS surgeons during the same period, indicating that the majority of surgeons (77%) entered data to the registry and that these estimates are representative of the provision of bariatric surgery delivered through the NHS in England.

A systematic review assessing the effectiveness of bariatric surgery published in 2009 revealed that of the 26 included studies only 3 RCTs and 3 prospective cohort studies compared surgical and non-surgical management of obesity, with findings suggesting that surgery resulted in greater weight loss, with results maintained for a minimum of ten years (40). However, the authors also concluded that surgical procedures can also be associated with adverse effects and additionally carry the risk of post-operative mortality. Whilst the estimates of weight loss and survival rates for bariatric surgery are encouraging, there is a discrepancy between the number of procedures conducted and the number of eligible individuals, thus bariatric surgery procedures are not available or suitable for all individuals affected by extreme obesity.

1.3.3 Heart of England NHS Foundation Trust Specialist Weight Management Service

The Specialist Weight Management Service is operated by the Heart of England NHS Foundation Trust (HEFT), which is one of the largest hospital trusts within England (41). The Specialist Weight Management Service was established in 2000 and provides both tier 3 and 4 medical and surgical weight assessment and management services. The provision

of bariatric surgical services incorporates comprehensive pre- and post-surgery assessment and care from specialist multi-disciplinary teams, whilst the medical services incorporate pharmaceutical, educational and behavioural interventions delivered on an individual or group basis.

Individuals are referred to the care of the service from primary care settings across the West Midlands and as such, it serves an ethnically and socioeconomically diverse population. The criteria for referral to the service is a BMI of $\geq$40.0kg/m^2 or BMI of $\geq$35.0kg/m^2 for individuals with a co-morbid health condition such as type 2 diabetes or hypertension. On referral to the service individuals are invited to attend an appointment with a physician from the specialist weight management team, during which any potential undiagnosed underlying conditions such as hypothyroidism and Cushing's syndrome or potential undiagnosed co-morbid health conditions such as type 2 diabetes are investigated. Individuals decide in collaboration with the physician which of the two treatment pathways offered by the service that the individual will proceed on; the Community Weight Management Service (CWMS) or the Specialist Lifestyle Management (SLiM) programme.

1.3.3.1 Community Weight Management Service (CWMS)

The CWMS provides support to individuals from a multi-disciplinary team (MDT) incorporating one-to-one appointments with physicians, dieticians and a psychologist. The aim of the CWMS is to support and facilitate individuals in making lifestyle changes and achieving a weight loss of at least 5% of their baseline weight. The CWMS clinic sessions operate from community settings such as General Practitioner (GP) practices in collaboration with local primary care providers. This approach allows individuals to

receive specialist care from the clinical team at local primary care centres without having to go to hospital, thus increasing access to the service. Those individuals who do not speak English can request to attend clinic sessions with a language interpreter provided by the service where available.

Individuals attend an initial CWMS appointment, which lasts for between two and three hours, and is designed to be an intensive introductory session. During the initial appointment, individuals will receive one-to-one consultations with each member of the MDT, addressing a range of topics as outlined in Table 1.1. After the initial appointment individuals are invited to contact the service to arrange a suitable time for their subsequent appointments, which can be made with each member of the MDT, or alternatively with one or two team members only. The frequency of contact varies as a result of individual requirements and session availability, with individuals attending subsequent appointments every two to three months or more frequently if needed. Individuals receive support through appointments within the service for a period of 12 months, after which individuals are discharged back to the care of their GP. However, some individuals choose to continue attending regular appointments within the service for longer durations depending on specific requirements.

Table 1.1: Outline of the Community Weight Management Service (CWMS) sessions

Member of multi-disciplinary team	Topics covered during appointment
Physician	During the initial appointment weight and BMI are recorded and discussed with the individual. Individuals' weight history and previous weight loss efforts are discussed including age of current obesity onset. The completed self-report questionnaires are reviewed, during which quality of life and mental well-being are discussed and if appropriate individuals may be recommended to attend regular appointments with the psychologist. The self-reported sleep quality of individuals is also discussed, with investigation of potential undiagnosed co-morbid conditions such as obstructive sleep apnoea, through referral to a sleep specialist for an overnight sleep study if appropriate. Previous use of anti-obesity medication is also reviewed, with medication prescribed if appropriate. Subsequent appointments incorporate a 'weigh-in' and discussion of weight loss progress, identifying barriers to changing behaviours where appropriate. Management of co-morbid health conditions such as type 2 diabetes is also discussed, with alterations made to treatment and medication as appropriate.
Dietitian	During the initial appointment, the dietitian will review the 3-day food diary which individuals receive by post and are asked to complete before attending their first appointment, identifying areas for improvement including consumption of specific foods and drinks, portion sizes, missing meals and night-eating. Recommendations will be discussed with individuals for making dietary changes. Subsequent appointments discuss progress and individuals' experiences of adopting new dietary behaviours.
Psychologist	During the initial appointment, individuals discuss factors influencing their weight and dietary and activity behaviour. Topics may include individuals' support structure including current and previous relationships with spouses or partners and family and friends, whether there is a history of abuse, diagnosis of depression or other mental health condition, or alcohol or drug addiction. Subsequent appointments will incorporate discussion of topics in greater detail if desired by the individual, or alternatively no further appointments are attended.

1.3.3.2 Specialist Lifestyle Management (SLiM) Programme

The SLiM programme is a medically-supported weight management patient education programme. The SLiM programme provides patients with a structured group-based educational curriculum encompassing advice and techniques for changing health behaviour and self-management. Table 1.2 details the content of each of the sessions and the specific behaviour change techniques which are employed. The sessions are facilitated by a dietetic assistant who received training in the delivery of the programme from the team of specialist weight management dietitians at Heartlands Hospital who developed the programme curriculum.

The key aims of the SLiM programme are to provide advice and guidance through structured education, to provide techniques and skills for long-term self-management of weight, and to facilitate individuals in achieving a weight loss of at least 5% of their baseline weight over the course of the programme. Individuals attend six sessions, attending one session per month over a total period of six months. The SLiM programme operates from the Heartlands Hospital site, on a rolling basis, with several concurrent groups, thus enabling individuals to attend an alternate group session if they are unable to attend their regular group session.

Table 1.2: Outline of the SLiM programme sessions

	Content of session	Behaviour change techniques
1	Getting to know each other, discussing weight loss expectations and introducing topics including: Healthy eating, Ideas for including activity in daily life.	Goal setting: Individuals are encouraged to make SMART goals (Specific, measurable, achievable, relevant, time-bound) for diet and activity changes. In addition to personalised goals, a weight loss goal of 5% over the programme is set. Self-monitoring: Individuals receive a 'food and mood diary' to record foods eaten, time, place, who they were with and current mood, to promote awareness of eating behaviour. Homework: Individuals asked to complete the food and mood diary, to work towards their personal dietary SMART goal and to increase their intake of water.
2	Discussion of progress from previous session and application of techniques during the month. Topics include: Eating regular meals, Achieving a balanced diet, Healthy cooking methods.	Education: Individuals given information on healthy eating using principles of the 'Eatwell plate' which was devised by the Department of Health in association with the Welsh Assembly Government, the Scottish Government and the Food Standards Agency in Northern Ireland. In addition, individuals discuss the importance of eating regular meals to achieve stabilisation of eating, controlling portion sizes, menu planning and healthy cooking methods. Homework: Individuals asked to work towards their personal activity SMART goal, make their meals balanced and reduce portion sizes by 25%.
3	Discussion of progress from previous session and application of techniques during the month. Topics include: Conscious eating, Changing negative thoughts, Trying new foods.	Stimulus control: Individuals play a game designed to increase awareness of external and internal triggers for eating, in order to promote conscious eating. Cognitive restructuring: Individuals discuss how negative thoughts can affect efforts to change behaviour, and how they can change negative unhelpful thoughts for positive ones to help them to achieve their goals. Individuals asked to challenge their 'all or nothing' beliefs, such as avoiding use of unhelpful words like 'always, never, I have to' when thinking about food and activity. Individuals are introduced to the idea of practicing 'positive self-talk' and are given a diary to encourage putting this into practice. Homework: Individuals complete a 'positive self-talk diary' substituting negative for positive thoughts, to identify their eating triggers and use techniques to avoid them, and to work towards increasing variety of fruit and vegetable intake.
4	Discussion of progress. Topics include: Interpreting food labels, Portion size control.	Education: Individuals taught to read and interpret food labels, recommended serving sizes, and put this into practice using resources and playing a labelling game. Homework: Individuals asked to use these techniques for reading labels when selecting foods whilst shopping.
5	Discussion of progress, including a virtual shopping trip employing label-reading skills. Topics include: Shopping for food, Support and reward.	Support and Reward: Individuals are encouraged to use non-food rewards to aid motivation and to avoid thinking of food as a reward. Individuals are encouraged to ask for support from family and friends. Homework: Individuals asked to reflect on last 6 months and the skills they have learnt that have helped them to achieve their goals.
6	Reflection on progress from the start of the programme, and giving thanks to each other. Topics include: Problem-solving, Maintenance, Self-esteem.	Problem-solving: Individuals are given skills and techniques to help with recognising high risk situations that may lead to 'slip-ups' in behaviour and put plans in place to avoid this. Maintenance: Individuals discuss 'slip-ups' in behaviour and learn techniques such as avoiding negative self-talk to help prevent a 'slip-up' leading to a relapse in previous behaviours. Boosting self-esteem: Brief discussion about how to improve self-esteem and feel good themselves.

The format of the sessions follows a model whereby each session begins with a discussion of individuals' experiences of adopting and employing the skills and techniques they have learned, which is primarily a peer-group discussion facilitated by the programme leader. The core material is then delivered incorporating interactive games and activities, and the session finishes with the setting of 'homework' activities to promote the adoption of new techniques and a 'weigh-in' to monitor weight loss progress. The 'weigh-in' is conducted without sharing individuals' weight and progress with other group members unless individuals choose to do so. The timing of the 'weigh-in' at the end rather than the start of the session was selected as a pilot session had revealed that some individuals experienced negative emotions following the 'weigh-in' which influenced engagement with the remainder of the session.

The curriculum of the programme is designed to equip individuals with the knowledge and skills to be able to achieve long-term self-management of their weight, and after completion of the programme individuals are discharged back to the care of their GP. Alternatively, some individuals may choose to repeat the programme in order to continue receiving guidance and support.

1.3.3.3 Comparison of the CWMS and SLiM treatment pathways

The nature of the two treatment pathways greatly differ in terms of both the duration and intensity of support provided, as well as differences in the numbers and types of staff involved in delivering the CWMS and SLiM pathways. Table 1.3 displays a comparison of the scale and costs associated with the provision of both treatment pathways.

The comparison illustrates that the estimated annual staff-related costs associated with the CWMS are over five times greater than those associated with the SLiM pathway,

due to the greater number and expertise of staff providing support through the CWMS pathway. However it should also be noted that a greater number of individuals attend the CWMS pathway during each clinic session and during each week, relative to the SLiM pathway. Nevertheless the estimated weekly cost per individual suggests that the multidisciplinary team (MDT) approach employed by the CWMS pathway is likely to be more expensive, with an estimated cost of £75 - £90 per individual per week, whilst the SLiM pathway provides support at a lower estimated cost of between £31 per individual per week when sessions are fully attended and up to £155 per individual when attendance is at the minimum level of 2 individuals per session. Thus the SLiM pathway is likely to be the more cost-effective pathway, except in instances where attendance at the SLiM sessions is low and the pathway operates at minimum capacity. Regardless of attendance, when examining the fixed weekly staff costs alone, the estimated cost associated with the CWMS is much greater at £1,789 than that of the SLiM pathway at £310, which represents expenditure which would be incurred irrespective of attendance.

The estimates are provided as a guide to facilitate comparisons of the scale and the costs associated with each pathway, however there are additional costs associated with the operation of both pathways including venue costs, provision of printed materials and resources, as well as the costs associated with the initial setting-up of each treatment pathway. A formal cost-effectiveness evaluation taking into consideration all of these factors would need to be performed in order to enable more accurate comparisons of the total costs associated with each pathway. Given that the actual number of individuals attending at each pathway greatly impacts upon the cost-effectiveness, this detailed level of data should also be incorporated. Thus a more robust health economic evaluation would be

necessary in order to generate firm conclusions as to the cost-effectiveness of the CWMS and SLiM treatment pathways.

Table 1.3: Comparison of the scale and costs associated with the CWMS and SLiM treatment pathways

	CWMS	**SLiM**
Duration of attendance	12 months	6 months
Frequency of contact	Every 3 months	Every month
Total number of contact points	Range 5 - 13	6
Time at each contact point	First contact 2 - 3 hours, subsequent 0.5 hours	1.5 hours
Total contact time	Range 4 - 9 hours	9 hours
Weekly service provision	2 x 6.5-hour clinic sessions	1 x 1.5-hour session
Number attending each session	Range 10 - 12	Range 2 - 10
Number attending each week	Range 20 - 24	Range 2 - 10
Number of staff	3	1
Type of staff	Consultant Physician, Psychologist, Dietitian	Dietetic assistant
Annual staff salary:		
Consultant Physician	£77,850	-
Psychologist	£35,536	-
Dietitian	£29,759	-
Dietetic assistant	-	£20,638
Staff cost subtotal	£143,145	£20,638
WTE for staff	0.5	0.6
Annual staff cost estimate	£71,573	£12,383
Weekly staff cost estimate*	£1,789	£310
Weekly cost per individual†	Range £75 - 90	Range £31 - £155

Note: Annual staff salary values obtained from NHS terms and conditions of service handbook (42) based on the following pay bands and pay points: Consultant Physician Band 9 Point 49, Dietitian Band 6 Point 25, Psychologist Band 7 Point 30, Dietetic assistant Band 4 Point 14
WTE= Whole Time Equivalent (dedicated to service provision including workload outside of contact hours)
** Weekly staff cost estimate based on a 40-week year*
† Weekly cost per individual based on range of minimum-maximum attendances of 20-24 and 2-10 per week at the CWMS and SLiM pathways, respectively.

1.4 SUMMARY

This chapter has discussed the increasing prevalence of obesity and specifically extreme obesity and the major challenge for healthcare services that this represents. The current structure of provision of weight management services that have been employed in the NHS to address the obesity epidemic have also been reviewed, with a detailed focus on specialist weight management services. In addition to outlining the rationale for the investigation of specialist weight management services for extreme obesity, this chapter has also introduced the aims and setting of the research project, placing it in the context of the healthcare setting and broader research design framework within which it is based. Chapter two discusses the clinical, demographic and mental well-being characteristics of extreme obesity, specifically of those individuals entering the CWMS pathway of the HEFT Specialist Weight Management Service in greater detail, giving insight to the individual experience of extreme obesity.

CHAPTER TWO

2.0 CHARACTERISTICS OF EXTREME OBESITY: A STUDY OF INDIVIDUALS ENTERING THE COMMUNITY WEIGHT MANAGEMENT SERVICE (CWMS)

2.1 INTRODUCTION

2.1.1 Clinical characteristics associated with extreme obesity

It has been established that obesity and particularly extreme obesity is associated with increased risk of developing co-morbid health conditions including type 2 diabetes mellitus and insulin resistance, hypertension, cardiovascular disease, osteoarthritis, gallbladder disease, hyperuricaemia and gout, with additional increased risk of developing certain cancers, including colorectal and prostate cancer amongst men and breast and endometrial, cancer in women (43, 44). Furthermore, improvement in co-morbid health conditions including hypertension, dyslipidaemia, type 2 diabetes and impaired glucose tolerance, as well as improvements in fertility have been observed within extreme obese individuals when weight loss is achieved (45, 46). As well as being associated with increased prevalence of chronic health conditions, extreme obesity is also associated with increased mortality (11).

The association between baseline BMI and mortality was examined by the Prospective Studies Collaboration (PSC), analysing data from 57 prospective studies including 900,000 individuals (11). The sample was recruited mostly from Europe and North America and was 61% male, with a mean age of 46 years and mean BMI of 25.0kg/m^2. The analyses which adjusted for age, sex, study and smoking status, revealed that after a mean follow-up period of 8 years, 66,552 deaths of known cause were recorded, and mortality was lowest in the upper-normal (22.5 - 25.0kg/m^2) BMI range. BMI >25.0 kg/m^2 was strongly positively associated with several specific causes of death including ischemic heart disease (Hazard Ratio: HR= 1.39, 1.34 - 1.44), stroke (HR= 1.39, 1.31 - 1.48), diabetes (HR= 2.16, 1.89 - 2.46), non-neoplastic kidney disease (HR= 1.59, 1.27 - 1.99), and non-neoplastic liver disease (HR= 1.82, 1.59 - 2.09). Furthermore, each

5kg/m^2 increase in BMI was associated with an average increase of 29% overall mortality (HR= 1.29, 1.27 - 1.32), and specific increases in vascular mortality (HR= 1.41, 1.37 - 1.45); diabetic mortality (HR= 2.16, 1.89 - 2.46), renal mortality (HR= 1.59, 1.27 - 1.99), hepatic mortality (HR= 1.82, 1.59 - 2.09), respiratory mortality (HR= 1.20, 1.07 - 1.34) and all other cause mortality (HR= 1.20, 1.16 - 1.25). Obesity and particularly extreme levels of obesity were also demonstrated to be associated with a reduction in median survival, with a BMI between 30.0 and 35.0kg/m^2 associated with a reduction of between 2 and 4 years, and an 8 to 10 year reduction in survival within the extremely obese 40.0 to 45.0kg/m^2 BMI range. It is important to note that the PSC study excluded those individuals with BMI >50.0kg/m^2 meaning that the detrimental health impacts of extreme obesity may have been underestimated in the analyses, and thus may be even more damaging than those reported.

2.1.2 Demographic characteristics associated with extreme obesity

The capacity for social relationships to have an impact on individuals' state of health has been demonstrated (47). Specifically marital status has been demonstrated to be associated with morbidity and mortality, with those individuals in relationships experiencing lower risk of poor health and death. Findings from the National Longitudinal Mortality Study demonstrated that those who were non-married experienced increased risk of mortality across ethnicity and gender groups (48). However, a different pattern of association has been observed in the relationship between marital status and obesity (49). The findings of a cross-sectional telephone survey of 3,025 US adults which adjusted for demographic, social, and physical factors, indicated that married men were significantly more likely to be obese than men who were previously married or never married. Interestingly, this

association was not observed in females, whereby marital status was not significantly associated with obesity. This pattern of observation has been shown in another study which assessed the association between relationship status and a range of health behaviours in young adults conducted in the US (50). The findings indicated that married men were more likely to be overweight or obese relative to males who were single, in casually-dating relationships or in committed-dating relationships, whereas no association between relationship status and weight was observed amongst females. Taken together these findings suggest that marital status may exert a negative impact on weight and obesity in males but not females. Gender thus plays a key role in the association, and further research required in order to identify the complex mechanisms underlying the relationship. In addition to marital status, the association between obesity and socioeconomic status (SES) has also been demonstrated.

A seminal review of the literature examining the association between SES and obesity including 144 studies was published in 1989 (51). The review identified that within developed societies there was a strong inverse relationship among females, with a higher likelihood of obesity among females of lower SES, whereas a consistent relationship for males and children was not observed. In contrast, within developing societies a strong direct relationship was observed for females, males, and children, with a higher likelihood of obesity among those of higher SES. A subsequent systematic review of the literature examining the association between SES and obesity was published in 2007 to update the review, incorporating data from 333 studies (52). The systematic review classified the level of development for each of the study samples as either high, medium, or low using the United Nations Development Program 2003 Human Development Index. As with the prior literature review, findings indicated that within the more highly developed samples of

females it was commonly observed (63% of all associations) that lower SES was associated with greater weight and body size. The effect was not quite as marked in male samples, with 50% of observed associations indicating a relationship between lower SES levels and greater weight. The findings of the systematic review suggest that there are complex socio-economic and cultural factors that influence weight and body size, and that within highly developed countries such as the UK, this relationship is influenced by gender.

The mechanism behind the SES and obesity association within developed societies may be attributable to diet, whereby individuals in higher SES groups are more likely to have a healthier diet incorporating increased consumption of fruit and vegetables and decreased consumption of fats (53). This may be due to the fact that economic income impacts upon food purchasing choices, with healthier foods demonstrated to be more expensive than less nutritious foods (54). Furthermore, those living in more affluent areas may experience increased access and opportunity to undertake physical activity and make healthier food choices (55). The SES and obesity association may be less consistent among males due to the conflict between the proposed societal phenomenon of thinness as an ideal to be pursued and valued (56), which although may be more salient among females remains omnipresent within society, and the perceived ideal of larger muscular body sizes indicating dominance and power among males (57).

An additional potential contributing factor to the association between lower levels of SES and increasing BMI levels may be the presence of weight-related discrimination. The relationship between weight and experience of discrimination has been examined in the Midlife Development in the United States (MIDUS) survey which included a randomly selected sample of over 3,000 US adults aged between 25 and 74 (58). Findings indicated

that those with BMI ≥35.0kg/m^2 were significantly more likely to report experiencing major lifetime discrimination (OR= 1.51, p <0.01), major job-related discrimination (OR= 1.84, p <0.001), day to day discrimination (OR= 1.66, p <0.001), and experience of being denied medical care (OR= 2.98, p <0.001), than normal weight individuals. However, the cross-sectional association does not establish causality of whether obesity leads to discrimination affecting SES or vice versa.

2.1.3 Psychological characteristics of extreme obesity

The quality of life and mental health characteristics associated with extreme obesity are discussed in detail in Chapter three, however a brief introduction is provided here. Evidence has supported an association between increasing adiposity and depression (59), anxiety (60) and reduced quality of life (61). Furthermore, a link has been demonstrated between obesity and broader psychopathology with obese individuals more likely to attempt suicide and demonstrate suicidal behaviour, with an even greater risk observed in extreme obesity (62). However, there is a lack of consensus and inconsistencies in the literature, with some studies providing support for an association between obesity and physical, but not mental quality of life domains (63-65). Whilst the cross-sectional association between obesity and psychological characteristics has been debated, several studies have demonstrated a marked improvement in quality of life and mental health with weight loss achieved through both surgical (46, 66-71) and behavioural (32, 72-74) weight management interventions.

2.1.4 Sleep in extreme obesity

The sleep characteristics of a sample of 1,550 US adults have been examined in the Wisconsin Sleep Cohort Study (WSCS), a population-based longitudinal study of sleep habits, sleep disorders and health, utilising data from self-report questionnaires, 6-day sleep diaries and overnight laboratory polysomnography studies (75). The association between sleep duration and BMI has been demonstrated in a study of 1,024 participants from the WSCS for whom polysomnography data was available. The findings indicated a U-shaped curvilinear association between BMI and sleep duration, whereby a minimum BMI was predicted when an average of 7.7 hours of sleep per night was achieved (76). Furthermore, a considerable proportion of the sample (74.4%) achieved less than eight hours sleep, with increased BMI shown to be proportional to decreased sleep within these individuals.

Longitudinal data from the WSCS has also demonstrated that overweight and obesity are strong causal factors of certain sleep disorders, specifically sleep disordered breathing (SDB) (77). In a study which combined data from the US National Health and Nutrition Examination Survey (NHANES) with data from the WSCS, models of the prevalence of SDB were computed, giving estimates for two time periods, from 1988 - 1994 and 2007 - 2010. Data was available for 1,520 participants of the WSCS, 47.0% of whom were obese (BMI $\geq$30.0kg/m^2) including 10.8% of the sample who were classed as extremely obese (BMI $\geq$40.0kg/m^2). The estimated prevalence rates of SDB increased across all age and sex subgroups between the two time points. The largest prevalence increases were observed among the younger age category of individuals aged 30 - 49 years, with the proportion of individuals with the most severe SDB symptoms defined as Apnoea Hypopnea Index (AHI) score $\geq$15 with Epworth Sleepiness Scale (ESS) score >10

increasing from 3.1% to 4.8% in males and from 0.6% to 0.8% in females, while mild SDB (AHI score ≥5) also increased from 20.0% to 26.6% in males and from 6.6% to 8.7% in females. The findings of the study suggest that the prevalence rates of SDB have increased substantially over the recent decades. The authors suggest that the current obesity epidemic will result in so-called "offspring epidemics", with the increased prevalence of obesity-related conditions such as obstructive sleep apnoea (OSA) associated with the rise in the prevalence of obesity.

In addition to US population-based studies, the sleep characteristics of extremely obese individuals have also been studied in a sample of individuals entering the University Hospital Aintree Specialist Weight Management Service in the UK (78). The sample of 144 individuals completed the following self-report questionnaires in order to assess the association between night eating, sleep quality, and excessive daytime sleepiness; the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Score (ESS), and Night Eating Questionnaire (NEQ). The sample were predominantly female (68%), with a mean BMI of 46.9kg/m^2 and a mean age of 44.6 years, with findings indicating that 73.0% of the sample had poor sleep quality (PSQI >5), 30.8% had suspected OSA (ESS ≥10), and 2.8% showed symptoms of night-eating behaviour (NEQ ≥30). The findings indicated that poor sleep quality was significantly associated with night-eating, with a strong correlation observed between PSQI and NEQ scores ($r= 0.54$, $p <0.001$), which remained after controlling for excessive daytime sleepiness. The study suggests that among the sample of extremely obese individuals seeking weight management, the prevalence of night-eating was low whilst the prevalence of poor sleep quality was widespread across the sample.

Whilst the evidence suggests that obesity and particularly extreme levels of obesity are associated with sleep dysfunction, weight loss has been shown to reduce the harmful

impact of excess weight on sleep. The findings of a systematic review and meta-analysis have demonstrated that lifestyle interventions are able to reduce the severity of OSA (79). The review highlighted that whilst the levels of SDB were not normalised after intervention, modest interventions were able to yield a reduction in the severity of OSA and that further exploration of the impact of weight loss on OSA after more intensive interventions is required. Indeed, it has been suggested that whilst lifestyle interventions offer the safest approach to reducing the severity of OSA, bariatric surgery may provide more immediate and long-lasting alleviation of conditions such as OSA as well as improving individuals' overall sleep function and quality (46, 80, 81).

2.1.5 Rationale for the characterisation of extreme obesity

The prevalence of extreme obesity is increasing (82), and as such the co-morbid health conditions associated with excess body weight are also increasing (77), placing increased burden on healthcare services and reducing the quality of life of those affected. Given the rising prevalence of obesity and in particular the rising prevalence of extreme obesity, there is an essential need to ensure greater understanding of this population. Whilst several studies have documented the sleep characteristics associated with obesity within population-based studies across the BMI range, the impact of extreme obesity on sleep within clinical extreme obese samples is less understood. Furthermore, the impacts on quality of life and mental health also require further investigation due to inconsistencies in the body of literature. The construction of a detailed picture of the demographic and clinical characteristics including the sleep and psychological features, of the extremely obese population will enhance our understanding of this at-risk group. The knowledge gained can then be fed back into service design and delivery, thus improving service

provision and ensuring that extreme obese individuals receive the most effective weight management services and thus are given the greatest opportunity to achieve weight loss.

2.1.6 Aims

This chapter aims to explore the characteristics of individuals attending the Community Weight Management Service (CWMS) which runs within the HEFT Specialist Weight Management Service. The baseline demographic and clinical characteristics of participants will be examined in this exploratory analysis in order to construct a detailed profile of the individuals attending the service, with no pre-defined hypotheses investigated. The factors which will be examined include the demographic characteristics, incorporating age, sex, ethnicity, marital status and occupation, and a range of clinical characteristics including waist circumference, systolic and diastolic blood pressure, smoking status, and alcohol consumption, as well as presence of obesity-related co-morbid health conditions including type 2 diabetes, cardiovascular disease (CVD), hypertension, OSA, and arthritis. Further analyses will also examine the self-reported measures of sleep quality, sleepiness, quality of life and mental health within the sample. The chapter concludes with a detailed summary of the characteristics of the extreme obese population attending the service, and in light of these findings recommendations to further enhance the design and delivery of the service will be presented.

2.2 METHODS

2.2.1 Research design

The characteristics of a sample of extreme obese individuals entering the CWMS pathway were explored as part of an evaluation of the efficacy of the Specialist Weight Management Service. The baseline demographic and clinical information for individuals entering the alternate treatment pathway, the SLiM programme are not included, as this information was not routinely collected and thus was not available for analyses. Individuals attending the CMWS pathway were referred from primary care by their GP if they had a BMI $\geq$40.0kg/m^2 or alternatively BMI $\geq$35.0kg/m^2 with a weight-related health condition, such as type 2 diabetes or hypertension. The study included a sample of 262 individuals aged 19 to 76 years, who entered the CWMS between February 2008 and August 2012.

2.2.2 Community Weight Management Service (CWMS)

The CWMS has been described in detail in Chapter one, however a brief description of the service is provided for reference. The CWMS is a medically supported specialist weight management service providing comprehensive multidisciplinary care for a 12 month period from a team of specialist physicians, dietitians, and psychologist, delivered through individual appointments at GP practices in the community.

2.2.3 Demographic and clinical information

Demographic details including participants' age, gender, and ethnicity were routinely collected at baseline, along with additional details including marital status, employment

status and whether participants had children. Participants' initial weight and height data were recorded at baseline and BMI was calculated by dividing participants' weight in kg by height in meters squared. Details of obesity-related co-morbid health conditions focussing specifically on type 2 diabetes, CVD, hypertension, OSA, and arthritis were also recorded from health records. Participants' waist circumference, systolic and diastolic blood pressure, smoking status, alcohol consumption, and use of weight medication were routinely recorded prior to treatment commencement. Additionally, subsequent referral to bariatric surgery after attendance at the service was recorded. It is important to note however, that referral of an individual to the bariatric surgery team indicated that the case was reviewed but may not have resulted in the performance of a surgical procedure.

Questionnaire booklet

Upon referral to the CWMS, participants were sent a questionnaire booklet by post which they were asked to complete before attending their first appointment. The questionnaire booklet comprised the following previously validated self-report questionnaires:

Table 2.2.1: Self-report questionnaire administered to individuals entering the CWMS

Domain assessed	Questionnaire
Quality of life- weight specific	Impact of Weight on Quality of Life (IWQOL-Lite)
Quality of life- general	EQ5D-3L
Mental health	Hospital Anxiety and Depression Scale (HADS)
Sleep	Pittsburgh Sleep Quality Index (PSQI short-form)
Sleep	Epworth sleepiness scale (ESS)
Activity	International Physical Activity Questionnaire (IPAQ long-form)

2.2.4 Quality of life and mental health measures

Quality of life and mental health were assessed using three measures, the obesity-specific Impact of Weight on Quality of Life (IWQOL-Lite) questionnaire, the EQ5D-3L, which is a general quality of life measure, and the Hospital Anxiety and Depression Scale (HADS) which is a screening tool widely used in both clinical and research settings.

The IWQOL-Lite consists of 31-items which measure the impact of obesity on an individual's physical function, self-esteem, sexual life, public distress and work (83). Respondents are asked to rate the extent to which a series of statements is applicable to them using a Likert scale ranging from 5 'Always true' to 1 'Never true'. Responses to the questionnaire items yield a total score as well as individual subscale scores for each of the five domains.

The EQ5D-3L consists of five-items relating to five dimensions of health; mobility, self-care, usual activities, pain and discomfort and anxiety and depression (84). Respondents are asked to indicate which of three statements best describe their current health state. A 'level 1' response indicates that the respondent has no problem in the specific dimension, a 'level 2' response indicates some problems, and a 'level 3' response indicates extreme problems. Respondents are asked to repeat this process for the five dimensions. Perceived current health state is measured by asking respondents to indicate their current health state on a Visual Analogue Scale (VAS) with endpoints labelled 0 'Worst imaginable health state' and 100 'Best imaginable health state'.

The Hospital Anxiety and Depression Scale (HADS) comprises 14-items, 7 relating to anxiety, and 7 to depression (85). Respondents are asked to rate the extent to which a series of statements represents how they currently feel using a Likert scale ranging from 0-3. The scale yields individual anxiety and depression scores as well as an overall HADS

score. Individual subscale scores range from 0-21, with a score of ≥8 established as a cut-point for identifying presence of symptoms of anxiety and depression (86) and ≥11 identifying severe symptoms (87).

2.2.5 Sleep and physical activity measures

Two sleep measurements were used to assess feelings of sleepiness and perceived sleep quality, the Epworth Sleepiness Scale (ESS) (88) and the Pittsburgh Sleep Quality Index (PSQI) short-form version (89). The ESS is an 8-item self-report tool which measures individuals' general levels of daytime sleepiness, by asking respondents to rate their usual chance of falling asleep during a range of situations, using a 4-point scale ranging from 0 'Would never doze' to 3 'High chance of dozing'. The eight different situations and daily life activities are those that most people would engage in, including sitting and reading, watching television, sitting inactive in a public place such as a theatre, as a passenger in a car for an hour without a break, lying down to rest in the afternoon when circumstances permit, sitting and talking to someone, sitting quietly after a lunch without alcohol, and in a car while stopped for a few minutes in traffic. The tool yields a total ESS score ranging between 0-24, with higher scores indicating higher levels of daytime sleepiness, and scores ≥11 indicating symptoms of excessive daytime sleepiness (90).

The PSQI is a self-reported measure of perceived sleep quality, comprising 19-items which generate scores for the following seven components; subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. Respondents are asked to rate their sleep habits and difficulties over the past month on a 4-point scale ranging from 0 'Not during the past month' to 3 'Three or more times a week'. Responses to the items yield seven mean

component scores ranging between 0-3 and a global PSQI score ranging between 0-21, with higher scores indicating worse levels of sleep quality, and PSQI global scores ≥6 indicating poor sleep quality (89).

To measure sedentary time, the International Physical Activity Questionnaire (IPAQ long-form) (91) was used. The IPAQ long-form version comprises 31-items relating to the following five domains; job-related activity, transportation, housework, house maintenance and caring for family, recreation, sport and leisure-time, and time spent sitting. Responses to the items are summed to yield estimates of weekly activity within each activity domain, and yield an estimate of total weekly physical activity, in hours and minutes. An error in the reproduction of the questionnaire administered to individuals entering the service, whereby sections of the items were missing or were duplicated, led to invalidation of the tool and a low completion rate. However data from the last domain of the questionnaire, time spent sitting, had been completed by a larger number of participants, with 64.9% and 62.6% of the sample completing estimates of sedentary time during weekdays and weekend days, respectively. As such, data from the sedentary activity domain was used in isolation as a reliable and valid estimate of sedentary activity.

2.2.6 Statistical analysis

Anonymised data were analysed using IBM SPSS Statistics (version 21.0). Independent t-test calculations were conducted to compare the mean demographic and clinical characteristics of males and females at baseline, with mean and standard deviation values also provided for the combined sample. Cross-tabulation and Chi^2 analyses were conducted to compare the prevalence of the co-morbid health conditions between gender groups. The following categories of baseline BMI were created; 30.0-39.9kg/m^2, 40.0-49.9kg/m^2,

50.0-59.9kg/m^2, and ≥60.0kg/m^2. The proportions of individuals in each BMI category were compared for the gender groups using cross-tabulation, and Chi^2 calculations. The proportions of individuals within different occupation, marital status, smoking status, and ethnicity groups were also compared using the same method. Additionally, analyses were repeated to compare the baseline demographic and clinical characteristics across the following BMI groups; BMI <40.0kg/m^2, 40.0 <50.0kg/m^2, and ≥50.0kg/m^2 and the following age groups; <40 years, 40 <50 years, and ≥50 years. The self-report measures were scored following the standardised protocols outlined for each tool. Means and standard deviations were presented for subscales and total scores, along with proportions of individuals scoring above established cut-points, in order to aid interpretation of the measures.

2.3 RESULTS

2.3.1 Characteristics of the general relative to the study populations

Table 2.3.1 shows the demographic, lifestyle and clinical characteristics of the general population. The prevalence of married individuals within the general population (49% females and 52% males) is similar to that observed in the sample attending the CWMS (52.5% females and 46.5% males). However the proportion of White British individuals in England (79.8%) is lower than the proportion within the CWMS (90.8%), suggesting that this ethnicity group may be over-represented. Furthermore, examination of the general population ethnicity data highlights the fact that Birmingham is a super-diverse city with residents from a wide range of national, ethnic and religious backgrounds and thus has a lower prevalence of individuals of White British ethnicity (53.1%). Additionally, the unemployment rate of the West Midlands (9.8%) is higher than that of the UK (5.3% in 2008 and 7.9% in 2012), reflecting the trend of higher unemployment and lower gross weekly earnings experienced by individuals in the region compared to the rest of the UK.

In addition to the demographic characteristics, differences in the lifestyle characteristics of the general population and those reported by the CWMS sample are also observed. Whilst the proportion of males within the CWMS sample that consumed alcohol (62.7%) was consistent with the proportion of males within the general population who reported consuming alcohol in the past week (64%), the proportion of females consuming alcohol was higher within the CWMS (65.5%) than the general population (52%). Both gender groups were also more likely to spend more time engaged in sedentary activity than the general population, during both weekdays (females 6.5 vs 4.7 hours; males 7.6 vs 4.9 hours) and during weekend days (females 6.2 vs 5.1 hours; males 7.6 vs 5.4 hours).

Table 2.3.1: Characteristics of the UK general population by gender and combined

	Genders combined	Females	Males
[1] Single marital status (%)	-	21	27
Married marital status (%)	-	49	52
[2] White British ethnicity (within England, %)	79.8	-	-
[2] Ethnicity (within Birmingham, %)			
White British	53.1	-	-
Pakistani	13.5	-	-
Indian	6.0	-	-
Black Caribbean	4.4	-	-
[3] Current smoking (%)	-	19	22
[4] Alcohol consumption (%)	-	52	64
[5] Weekday sedentary activity (hours)	-	4.7	4.9
[5] Weekend sedentary activity (hours)	-	5.1	5.4
[6] Mean sleep duration per night (hours)	7.0	-	-
[7] Anxiety (%)	33.0	-	-
[7] Depression (%)	11.4	-	-
[8] Type 2 diabetes (%)	6.0	-	-
[9] OSA (%)	-	2.0	4.0
[10] Hypertension (%)	-	28.0	31.0
[11] Cardiovascular disease (%)	-	13.4	13.9
[12] Arthritis of the hip (%)	11	-	-
[12] Arthritis of the knee (%)	24.0	-	-
[13] UK employment: Feb-April 2008 (%)	74.9	-	-
[14] UK employment: June-August 2012 (%)	71.3	-	-
[13] UK unemployment: Feb-April 2008 (%)	5.3	-	-
[14] UK unemployment: June-August 2012 (%)	7.9	-	-
[15] Regional employment and earning 2010:			
West Midlands unemployment	9.8	-	-
West Midlands median gross weekly earnings (£)	456	-	-
UK median gross weekly earnings (£)	489	-	-

Data are percentages and means unless otherwise stated
[1]Office for National Statistics(ONS): General Lifestyle Survey 2011 (92). [2]ONS: 2011 UK census (93). [3]ONS: Opinions and lifestyle survey 2012 (94). [4]ONS: Opinions and lifestyle survey 2012 (95). [5]Health and Social Care Information Centre (HSIC): Health Survey for England (HSE) 2012 (96). [6]Survey of 1997 adults 2003 (97). [7]Survey of 1792 adults 2001 (98). [8]Diabetes UK 2014 (99). [9]Sleep Apnoea Trust Association 2013 (100). [10]HSIC: HSE 2011 (101). [11]HSIC: HSE 2011 (102). [12]Systematic review of osteoarthritis in the general population (103). [13]ONS: Labour market statistical bulletin 2008 (104). [14]ONS: Labour market statistical bulletin 2012 (105). [15]ONS: Regional Trends: Portrait of the West Midlands 2011 (106).

2.3.2 Demographic characteristics

Table 2.3.2 shows the demographic characteristics of the sample. Males were significantly older than females at baseline (48.0 vs 41.5 years). However there were no other significant differences in demographic characteristics between males and females. The sample was predominantly female (74.8%), White European (90.8%), with a substantial proportion reporting that they have at least one child (88.1%). A large proportion of the sample (62.0%) were employed, whilst 22.3% were unemployed.

Table 2.3.2: Demographic characteristics of the CWMS sample by gender and combined

	Whole sample	Females	Males	P
N (%)	262	196 (74.8)	66 (25.2)	
Age (years)	43.1±11.8	41.5±11.0	48.0±12.9	<0.001
Ethnicity (%)				0.068
White European	90.8	89.0	97.0	
Asian	5.6	7.3	0.0	
Black African/Caribbean	2.8	3.7	0.0	
Other	0.8	0.0	3.0	
Marital status (%)				0.613
Single	24.2	23.0	27.9	
Married	50.9	52.5	46.5	
Living with partner	14.5	15.6	11.6	
Divorced	6.7	6.6	7.0	
Widowed	3.6	2.5	7.0	
Occupation (%)				0.117
Employed	62.0	61.7	63.0	
Unemployed	22.3	23.3	19.6	
Retired	8.4	6.0	15.2	
Studying	7.3	9.0	2.2	
Children (%)	88.1	88.0	88.2	0.975

Data are percentages and means ± standard deviations.

2.3.3 Clinical and lifestyle characteristics

Table 2.3.3 shows the clinical and lifestyle characteristics of the CWMS sample. Males were significantly heavier (146.4 vs 127.2kg), with greater waist circumference (143.0 vs 127.7cm), however there was no significant difference in BMI between the gender groups. The majority of the sample (53.4%) were in the 40.0-49.9kg/m^2 BMI range, however 23.3% of the sample had a baseline BMI of 50.0-59.9kg/m^2, with a further 6.1% of the sample with baseline BMI ≥60.0kg/m^2. The prevalence of several co-morbidities were significantly greater in males than females, including type 2 diabetes (43.9 vs 20.4%), hypertension (60.6 vs 25.5%), OSA (39.4 vs 20.9%), and CVD (27.3 vs 5.6%). The majority of the sample reported experiencing at least one of the above co-morbidities, with 42.7% of the sample reporting either one or two and 17.6% reporting the presence of at least three co-morbidities. Hypertension was the most commonly reported co-morbidity by 34.4% of the sample. There was a high prevalence of type 2 diabetes (26.3%), OSA (25.6%), arthritis (24.0%) and cardiovascular disease (11.1%). Thus the individuals attending the service have multiple health concerns contributing to poor overall health status and as a result have complex medical needs.

The lifestyle characteristics indicate that the sample were predominantly non-smokers (60.7%), whilst 64.7% of the sample reported regular consumption of alcohol. There was a high level of sedentary activity among the sample at baseline, with a mean of 6.7 hours spent sedentary during weekdays and 6.5 hours during weekend days, with males spending significantly more sedentary time at the weekend than females (7.6 vs 6.2 hours).

Table 2.3.3: Clinical and lifestyle characteristics of the CWMS sample by gender and combined

	Whole sample	Females	Males	P
N (%)	262	196 (74.8)	66 (25.2)	
Weight (kg)	132.1±24.7	127.2±23.6	146.4±22.6	<0.001
Body mass index (BMI, kg/m^2)	47.0±7.9	47.4±8.4	46.0±6.3	0.211
Proportion in BMI group (%)				0.113
BMI 30.0-39.9kg/m^2	17.2	16.3	19.7	
BMI 40.0-49.9kg/m^2	53.4	53.1	54.5	
BMI 50.0-59.9kg/m^2	23.3	22.4	25.8	
BMI ≥60.0kg/m^2	6.1	8.2	0.0	
Waist circumference (cm)	131.6±14.5	127.7±12.4	143.0±14.7	<0.001
Systolic blood pressure (mmHg)	140.9±17.7	140.7±18.4	141.3±15.5	0.849
Diastolic blood pressure (mmHg)	85.2±11.7	85.3±11.8	84.7±11.5	0.773
Type 2 diabetes (%)	26.3	20.4	43.9	<0.001
Hypertension (%)	34.4	25.5	60.6	<0.001
Arthritis (%)	24.0	24.5	22.7	0.772
Obstructive sleep apnoea (OSA, %)	25.6	20.9	39.4	0.003
Cardiovascular disease (CVD, %)	11.1	5.6	27.3	<0.001
Number of (above) co-morbidities (%)				<0.001
0	39.7	48.0	15.2	
1-2	42.7	40.3	50.0	
≥3	17.6	11.7	34.8	
Alcohol consumption (%)	64.7	65.5	62.7	0.728
Weight medication (%)	80.4	79.7	82.6	0.667
Referral to surgery (%)	14.5	13.3	18.2	0.327
Smoking status (%)				0.352
Non-smoker	60.7	62.8	54.9	
Current smoker	25.5	25.5	25.5	
Former smoker	13.8	11.7	19.6	
Weekday sedentary time (hours)				
Mean	6.7±3.9	6.5±3.8	7.6±4.1	0.118
IQR	6.0	5.3	7.5	
Range	20.0 (0 - 20)	20.0 (0 - 20)	15.0 (2 - 17)	
Weekend sedentary time (hours)				
Mean	6.5±3.6	6.2±3.5	7.6±3.5	0.027
IQR	4.0	4.0	5.0	
Range	17.0 (1 - 18)	15.0 (1 - 16)	16.0 (2 -18)	

Data are percentages and means ± standard deviations
IQR= Interquartile range.

2.3.4 Quality of life and mental health characteristics

Table 2.3.4 shows the quality of life and mental health characteristics of the sample at baseline. Quality of life was markedly impaired across all IWQOL-Lite domains, with scores ranging from 26.2 (self-esteem) to 51.2 (work), whereby 100 represents optimum quality of life. Males had significantly higher IWQOL-Lite scores on several of the subscales including self-esteem (36.5 vs 22.5), sexual life (50.3 vs 38.8) and IWQOL-Lite total score (44.2 vs 37.8), indicating that perceived quality of life was better for males than females. The prevalence of symptoms of anxiety (70.3%) and depression (66.2%) was high, with a significantly greater proportion of females than males reporting symptoms of anxiety (75.4 vs 55.7%). Scores on the EQ5D-3L general quality of life measure show anxiety and depression, pain and discomfort, and performing usual activities were areas that were more widely perceived as extremely problematic by 18.7%, 28.0% and 8.8% of the sample, respectively. The mean EQ5D-3L Perceived health status score of 44.0 indicates that the perceived health of the sample was poor, with 100 representing best and 0 representing worst possible health state. The psychological characteristics of the sample are examined in greater detail in Chapter three.

Table 2.3.4: Quality of life and mental health characteristics of the CWMS sample by gender and combined

	Whole sample	Females	Males	P
N (%)	262	196 (74.8)	66 (25.2)	
Baseline IWQOL-Lite				
Physical function	42.4±25.3	41.7±24.2	44.6±28.3	0.433
Self-esteem	26.2±27.5	22.5±24.5	36.5±32.6	<0.001
Sexual life	41.9±35.9	38.8±35.7	50.3±35.6	0.039
Public distress	40.5±28.9	39.9±28.6	42.3±30.0	0.570
Work	51.2±30.3	49.9±30.0	55.4±31.4	0.244
IWQOL-Lite total	39.5±22.1	37.8±21.2	44.2±24.0	0.047
HADS				
HADS anxiety	10.4±4.5	10.9±4.3	9.2±5.0	0.012
HADS depression	9.1±4.0	9.2±4.0	8.7±4.0	0.388
HADS Total	19.6±7.7	20.1±7.5	17.9±8.2	0.064
Anxiety present % (≥8)	70.3	75.4	55.7	0.004
Depression present % (≥8)	66.2	66.3	66.1	0.978
Severe Anxiety present % (≥11)	48.3	50.9	41.0	0.184
Severe Depression present % (≥11)	40.4	42.0	35.7	0.405
EQ5D-3L Mobility				0.219
No problems %	33.3	34.3	30.5	
Some problems %	66.3	65.7	67.8	
Extreme problems %	0.4	0.0	1.7	
EQ5D-3L Self-care				0.181
No problems %	64.3	66.1	59.3	
Some problems %	35.3	33.9	39.0	
Extreme problems %	0.4	0.0	1.7	
EQ5D-3L Anxiety/depression				0.196
No problems %	24.7	21.7	32.8	
Some problems %	56.6	57.8	53.4	
Extreme problems %	18.7	20.5	13.8	
EQ5D-3L Pain/discomfort				0.510
No problems %	14.7	13.8	17.3	
Some problems %	57.3	56.3	60.3	
Extreme problems %	28.0	29.9	22.4	
EQ5D-3L Usual activities				0.970
No problems %	31.0	30.5	32.2	
Some problems %	60.2	60.5	59.3	
Extreme problems %	8.8	9.0	8.5	
EQ5D-3L Perceived health status	44.0±20.1	43.1±20.2	46.8±20.0	0.250

Data are percentages and means ± standard deviations.

2.3.5 Sleep characteristics

Table 2.3.5 shows the sleep characteristics of the sample. The mean Global PSQI score of 8.3 indicates poor sleep quality, with 65.1% of the sample achieving scores ≥6 which indicate poor quality. The sample estimated a mean of 8.6 hours spent in bed and 6.4 hours of sleep per night, suggesting that individuals in the sample may have perceived difficulty in maintaining sleep, with only 34.0% of the sample achieving a habitual sleep efficiency score ≥85%. Indeed, slightly less than half of the sample (49.8%) reported sleeping for ≥7 hours per night, whilst 12.0% reported achieving <5 hours of sleep per night, and 38.2% of the sample reported sleeping 5-7 hours per night, indicating that a substantial proportion may not be meeting their sleep needs. Furthermore this was reflected in participants' subjective ratings of sleep quality, with 60.7% of the sample rating their sleep as either fairly or very bad and 13.6% of the sample reporting the regular use of sleep medication ≥3 times per week.

The mean ESS score of 8.8, which is within normal limits indicates that the experience of symptoms of sleepiness was not widespread across the sample. Indeed, males achieved significantly greater mean ESS scores (10.2 vs 8.3), indicating higher levels of sleepiness than reported by females. Furthermore 39.7% of the sample achieved ESS scores ≥11, which indicate presence of excessive daytime sleepiness symptoms. Together the findings of the PSQI and ESS measures indicate that perceived sleep quality is low, however this is not reflected in the experience and reporting of symptoms of sleepiness.

Table 2.3.5: Sleep characteristics of the CWMS sample by gender and combined

	Whole sample	Females	Males	P
N (%)	262	196 (74.8)	66 (25.2)	
PSQI-1 Subjective sleep quality				
Mean score (0-3)	1.7±0.9	1.8±0.9	1.6±1.1	0.326
Proportion (%)				0.014
Very/fairly good	39.3	35.5	51.8	
Very/fairly bad	60.7	64.5	48.2	
PSQI-2 Sleep latency				
Mean score (0-3)	1.4±1.0	1.4±1.0	1.1±1.0	0.022
PSQI-3 Sleep duration				
Mean score (0-3)	1.3±1.1	1.3±1.1	1.3±1.1	0.636
Proportion (%)				0.787
≥7 hours	49.8	50.6	47.5	
6-6.9 hours	21.9	20.7	25.4	
5-5.9 hours	16.3	17.2	13.6	
≤4.9 hours	12.0	11.5	13.6	
PSQI-4 Habitual sleep efficiency				
Mean score (0-3)	1.4±1.2	1.4±1.2	1.3±1.2	0.655
Proportion (%)				0.939
>85%	34.0	33.8	34.7	
75-84%	21.8	21.0	24.5	
65-74%	17.0	17.2	16.3	
<65%	27.2	28.0	24.5	
Estimated time in bed (hours)	8.6±1.5	8.6±1.5	8.5±1.4	0.487
Estimated time asleep (hours)	6.4±1.6	6.4±1.6	6.5±1.6	0.853
PSQI-5 Sleep disturbances				
Mean score (0-3)	1.6±0.8	1.7±0.8	1.5±0.9	0.219
PSQI-6 Use of sleep medication				
Mean score (0-3)	0.6±1.1	0.6±1.1	0.4±1.0	0.152
Proportion (%)				0.302
Not during past month	77.9	75.2	86.5	
Less than once a week	2.3	3.1	0.0	
Once or twice a week	6.1	6.8	3.8	
Three or more times a week	13.6	14.9	9.6	
PSQI-7 Daytime dysfunction				
Mean score (0-3)	1.2±0.9	1.3±0.9	1.1±1.0	0.276
Global PSQI score	8.3±5.3	8.7±5.5	7.0±4.6	0.024
Proportion PSQI ≥6 (%)	65.1	66.3	61.5	0.483
ESS Mean score	8.8±5.7	8.3±5.6	10.2±6.0	0.025
Proportion ESS ≥11 (%)	39.7	36.8	48.3	0.121

Data are percentages and means ± standard deviations.

2.3.6 Characteristics of the CWMS sample by BMI group

Table 2.3.6 shows the characteristics of the sample by BMI group. There were no significant differences in demographic characteristics between the groups. Those in the BMI ≥50.0kg/m^2 group were more likely to have hypertension (44.2%) and report the presence of ≥3 co-morbidities (26.0%), whilst a considerable proportion of those in the ≤40.0kg/m^2 group (22.3%) also reported the presence of ≥3 co-morbidities, due to the service referral criteria.

Table 2.3.6: Characteristics of the CWMS sample by BMI group

	Whole sample	BMI <40.0	BMI 40.0 <50.0	BMI ≥50.0	P
N (%)	262	45 (17.2)	140 (53.4)	77 (29.4)	
Age (years)	43.1±11.8	44.4±13.7	42.2±11.3	44.0±11.6	0.427
Sex (% female)	74.8	71.1	74.3	77.9	0.690
Systolic blood pressure (mmHg)	140.9±17.7	137.1±17.5	138.7±15.7	147.8±20.0	0.007
Diastolic blood pressure (mmHg)	85.2±11.7	82.7±8.8	84.8±11.2	87.6±13.8	0.192
Type 2 diabetes (%)	26.3	22.2	22.1	36.4	0.059
Hypertension (%)	34.4	37.8	27.9	44.2	0.047
Arthritis (%)	24.0	24.4	20.0	31.2	0.183
Obstructive sleep apnoea (OSA, %)	25.6	17.8	24.3	32.5	0.175
Cardiovascular disease (CVD, %)	11.1	8.9	8.6	16.9	0.153
Number of co-morbidities ≥3 (%)	17.6	22.3	11.4	26.0	0.033
Weekday sedentary time (hours)	6.7±3.9	6.1±4.4	6.5±3.6	7.6±3.9	0.142
Weekend sedentary time (hours)	6.5±3.6	5.2±3.2	6.4±3.3	7.6±4.0	0.011
Baseline IWQOL-Lite					
Physical function	42.4±25.3	56.1±25.0	42.7±24.7	35.1±24.0	<0.001
Self-esteem	26.2±27.5	34.7±31.8	24.1±25.9	25.6±27.6	0.116
Sexual life	41.9±35.9	50.4±35.9	41.5±36.5	38.4±34.6	0.310
Public distress	40.5±28.9	66.4±30.0	40.5±27.0	27.4±22.3	<0.001
Work	51.2±30.3	64.6±26.5	49.3±30.3	48.2±30.8	0.022
IWQOL-Lite total	39.5±22.1	53.4±21.6	39.1±21.8	33.3±20.2	<0.001
Mean ESS score	8.8±5.7	5.9±4.9	9.7±5.9	8.7±5.3	0.001
Proportion ESS ≥11 (%)	39.7	23.1	45.5	38.6	0.043
Mean global PSQI score	8.3±5.3	7.4±4.5	8.5±5.0	8.6±6.2	0.408
Proportion PSQI ≥6 (%)	65.1	62.2	67.9	61.8	0.610

Data are percentages and means ± standard deviations.

Those in the BMI ≥50.0kg/m^2 group reported experiencing significantly worse physical function, public distress, and work, as well as total quality of life as measured by IWQOL-Lite. Those in the BMI ≥50.0kg/m^2 group also spent significantly more time engaged in sedentary activity at the weekend (7.6 hours) compared to the other BMI groups. Interestingly, those in the BMI 40.0 ≥50.0kg/m^2 group reported the greatest amount of sleepiness, with 45.5% of the group reporting ESS scores indicative of excessive daytime sleepiness, however there was no significant difference in the self-reported sleep quality across by the BMI groups.

2.3.7 Characteristics of the CWMS sample by age group

Table 2.3.7 shows the characteristics of the sample by age group. The ≥50 year age group comprised a significantly smaller proportion of females (57.5%) compared to the younger age groups. Those in the ≥50 year age group also had a significantly greater waist circumference and were more likely to experience co-morbid health conditions than those of younger age. Interestingly, those in the youngest <40 year age group reported significantly worse anxiety, self-esteem and public distress, but better physical function and fewer problems relating to mobility and self-care than the older age groups.

Table 2.3.7: Characteristics of the CWMS sample by age group

	Whole sample	Age <40 years	Age 40 <50 years	Age ≥50 years	P
N (%)	259	96 (37.1)	90 (34.7)	73 (28.2)	
Sex (% female)	74.9	81.3	82.2	57.5	<0.001
Weight (kg)	132.0±24.8	134.9±28.9	126.8±21.5	134.5±22.0	0.051
Body mass index (BMI, kg/m^2)	47.1±8.0	47.6±8.9	46.2±6.9	47.4±7.9	0.477
Waist circumference (cm)	131.6±14.5	129.5±14.8	129.0±13.0	137.5±14.5	0.022
Systolic blood pressure (mmHg)	140.9±17.7	137.8±14.4	141.5±18.1	143.9±20.4	0.194
Diastolic blood pressure (mmHg)	85.3±11.8	85.3±10.7	87.9±11.5	82.2±12.7	0.043
Type 2 diabetes (%)	26.3	8.3	23.3	53.4	<0.001
Hypertension (%)	34.4	11.5	34.4	64.4	<0.001
Arthritis (%)	23.9	6.3	25.6	45.2	<0.001
Obstructive sleep apnoea (OSA, %)	25.9	16.7	28.9	34.2	0.025
Cardiovascular disease (CVD, %)	11.2	2.1	6.7	28.8	<0.001
Number of co-morbidities ≥3 (%)	17.8	2.1	14.4	42.5	<0.001
Baseline IWQOL-Lite					
Physical function	42.0±25.2	48.4±23.1	42.1±24.5	33.3±26.5	0.001
Self-esteem	26.1±27.5	15.9±19.6	26.6±26.6	39.1±32.2	<0.001
Sexual life	41.9±36.0	44.5±35.9	40.3±36.0	40.1±36.5	0.704
Public distress	40.2±28.8	31.6±25.4	44.9±29.8	45.9±29.6	0.001
Work	51.1±30.3	47.0±28.6	54.4±32.1	52.7±30.2	0.272
IWQOL-Lite total	39.2±22.1	37.4±19.8	40.2±22.8	40.3±24.5	0.631
EQ5D-3L					
Mobility (% problems)	67.1	53.5	70.3	82.3	0.001
Self-care (% problems)	35.7	23.0	31.5	59.0	<0.001
Anxiety/depression (% problems)	75.1	78.6	70.8	75.4	0.536
Pain/discomfort (% problems)	85.6	79.3	90.4	88.7	0.098
Usual activities (% problems)	69.5	64.8	67.6	78.7	0.175
HADS					
HADS anxiety	10.4±4.6	11.2±4.1	10.5±4.4	9.3±5.1	0.046
HADS depression	9.1±4.0	9.6±4.2	9.1±3.6	8.5±4.3	0.264
Anxiety present % (≥8)	70.4	75.6	72.5	60.3	0.111
Depression present % (≥8)	66.2	69.4	67.1	60.3	0.520
Severe Anxiety present % (≥11)	48.5	57.8	46.3	38.1	0.050
Severe Depression present % (≥11)	40.5	47.1	39.2	32.8	0.222

Data are percentages and means ± standard deviations.

2.4 DISCUSSION

Examination of the demographic characteristics revealed that there were no significant gender differences in marital status, and that the findings are consistent with the general population rates for adults living in England and Wales obtained by the General Lifestyle Survey (GLS) in 2011 (92). Indeed within the current sample 52.5% of females and 46.5% of males reported to be married compared to 49% of females and 52% of males in the GLS, whilst 23.0% of females and 27.9% of males were classed as single within the current sample compared to 21% of females and 27% of males in the GLS. It is surprising that married marital status was not more highly prevalent amongst males within this extremely obese sample relative to the general population, as two studies have demonstrated an association between obesity and marital status in males whereby overweight and obese men were more likely to be married (49, 50). However, the two previous studies did not specifically address extreme levels of obesity, with findings from the current sample suggesting a different pattern of association between marital status and obesity at the extreme end of the BMI spectrum, which more closely resembles the marital status of the general population.

A large proportion of the sample attending the CWMS were White European (90.8%), with the remaining sample classed as Asian (5.6%), Black African or Caribbean (2.8%) and other ethnic background (0.7%). The ethnicity data highlights that individuals of White European ethnicity were over-represented in the sample, with the sample prevalence rate of 90.8% higher than the rate of 79.8% of individuals in England reporting to be of White British ethnicity as detailed in the UK 2011 census, and considerably higher than the rate of 53.1% of Birmingham residents reporting to be of White British ethnicity (93). Indeed, Birmingham is a super-diverse city with residents from a wide range of

national, ethnic and religious backgrounds, with large proportions of individuals reporting their ethnicity as Pakistani (13.5%), Indian (6.0%), and Black Caribbean (4.4%) (93). The ethnicity data reported in the present sample, suggests that individuals from minority ethnic groups may not be accessing the specialist weight management service. This would indicate a need to take action in order to identify potential shortcomings in the referral process and in the delivery of the service, which may be limiting inclusivity. However, it is important to note that the over-representation of White European individuals may also be due to errors in the collection of ethnicity data, with a high proportion of missing ethnicity data (45.8%), and due to the fact that White British could not be differentiated from White European status.

There were no gender differences in the occupational status reported by the sample. However the level of employment reported by the sample (62.0%) was below the UK national averages, of 74.9% for the period February-April 2008 (104), and 71.3% for the period June-August 2012 (105), which correspond to the first and last 3-month periods of individuals commencing attendance at the service. In addition, the levels of unemployment (22.3%) reported by the sample exceeded the national averages of 5.3% (104) and 7.9% (105), suggesting that unemployment was significantly greater amongst the sample attending the CWMS than in the general UK adult population. Furthermore when the unemployment rate of the sample is compared to the regional unemployment figures for the West Midlands, a large discrepancy remains. Since 2005 there has been a persistent trend of higher unemployment rates in the region compared to the UK, with the West Midlands having the second highest unemployment rate (9.8%) of all the UK regions and countries compared with the UK average of 7.9% in the fourth quarter of 2010 (106). The impact of the lower employment level is reflected in the fact that median gross weekly

earnings were also lower in the region (£456) than for the UK (£489) (106). Despite the higher regional rate of unemployment, the rate observed in the current sample of individuals attending the CWMS (22.3%), can still be considered to be markedly higher than the West Midlands average.

The higher levels of unemployment within the sample attending the service could be due to a number of factors including reduced physical and psychological capacity thus reducing ability to work, and limited employment opportunities due to weight-related discrimination from existing or potential employers. This is supported by a study of over 3,000 adults which found that those with BMI $\geq$35.0kg/m^2 were significantly more likely to report experiencing major job-related discrimination (58). The higher level of unemployment in the sample may also be a reflection of the fact that the service operates clinic sessions during normal working hours on weekdays, thus making the service less accessible to those in full-time employment who are not able to attend during the time the service runs clinics.

It is also conceivable that the higher level of unemployment observed in the sample is a reflection of the social gradient phenomenon whereby the poorest individuals with the lowest SES have the worst health status (107). The phenomenon is observed in low, middle and high income countries, with the gradient running across the entire SES spectrum, with health inequities affecting everyone. The conditions in which individuals live and work are determinants of health, directly impacting upon well-being, and thus SES and health status are inextricably linked (108). Further investigation of these issues would be facilitated by the routine collection of more robust SES measures for individuals commencing attendance at the CWMS, including current income, educational attainment and specific occupation details, rather than employment status alone (109). Additionally, Indices of

Multiple Deprivation (IMD) data for participants' area of residence could also be examined, in order to determine if there are certain specific highly deprived local areas from which participants are more commonly referred to the service.

SES has also been demonstrated to be related to lifestyle characteristics such as smoking status (110) and alcohol consumption (111) with lower SES groups more likely to engage in these behaviours. A slightly greater proportion of the sample (25.5% for both males and females) reported to be current smokers, compared to 19% of females and 22% of males in the UK general population over age 16 (94). The proportion of males within the sample that consumed alcohol (62.7%) is in line with data from the Opinions and Lifestyle Survey in which 64% of males in the UK general population reported drinking alcohol in the previous week. However the proportion of females consuming alcohol within the sample exceeded the UK general population prevalence (65.5% vs 52%) (95).

In addition to females within the sample consuming more alcohol than those in the general population, females spent more time engaged in sedentary behaviour than those in the general UK adult population, during weekdays (6.5 vs 4.7 hours) and during weekend days (6.2 vs 5.1 hours), as did males during both weekdays (7.6 vs 4.9 hours) and weekend days (7.6 vs 5.4 hours) (96). The sample reported that their level of activity was markedly sedentary, with males spending significantly more sedentary time at the weekend compared to females. These findings are consistent with a study of ten extremely obese individuals in the US seeking weight management. Activity was measured using an arm-based activity sensor over a 72-hour period, which showed that the sample engaged in an average of 8.4 minutes of moderate activity per day, defined as 3-6 metabolic equivalents (METs), with the remainder spent engaged in sedentary activity, defined as (<3 METs) (112). Furthermore, the study indicated that participants took an average number of 3,763

daily steps, which is considerably less than the target of 10,000 steps per day which has been widely utilised as a goal in health promotion interventions (113). These findings indicate that physical activity is limited within populations of extremely obese individuals. However further investigation of the physical and sedentary activity levels of individuals entering the service is required. The collection and utilisation of the complete IPAQ measure rather than a single domain (sedentary time) and the additional inclusion of an objective measure of physical activity using pedometers or sensors to record data in addition to self-reported measures, would facilitate more detailed examination of the baseline physical activity levels of the sample and identify areas for improvement. Given the contribution of physical inactivity to cardiovascular disease (114), type 2 diabetes (114), cancers (114) and impairment in mental health (115, 116) it is important to understand the full extent of sedentary activity within this at-risk patient population.

In addition to low levels of physical activity, the sample also demonstrated low levels of perceived sleep quality, with a substantial proportion (65.1%) achieving PSQI scores indicative of poor sleep quality and providing subjective ratings that their sleep was fairly or very bad (60.7%). The observation of poor sleep quality within the sample is consistent with a study which has also demonstrated widespread poor sleep quality in a sample attending the University Hospital Aintree weight management service, whereby 73.0% of the sample achieved global PSQI scores >5. However it is important to note that the larger proportion of 73.0% may be due to the fact that a lower threshold (>5) was utilised than the cut-point utilised in the present study (≥6), with the developers of the PSQI instrument recommending a threshold of scores ≥6 to indicate poor sleep quality (89). Despite the methodological differences, these findings provide further support that

poor sleep quality is experienced in extremely obese individuals attending weight management services.

The present sample reported a mean of 6.4 hours of sleep per night, which is lower than the mean of 7.0 hours per night reported in a study of 1,997 adults recruited from the UK general population (97). Indeed, findings from the Hordaland Health Study, a large scale cross-sectional study of 8,860 individuals living in Norway have also demonstrated longer mean self-reported sleep durations of 7 hours 11 minutes for females and 6 hours and 52 minutes for males, than those observed in the present sample (117). Furthermore, slightly less than half of the present sample (49.8%) reported sleeping ≥7 hours per night, indicating that a considerable proportion of the sample may not be meeting their sleep requirements. It has been demonstrated that there are individual differences in habitual sleep duration (118) and in subjective sleep need (119), suggesting that individuals require and take varying amounts of sleep per night. However, the fact that a considerable proportion of the sample (28.3%) report a mean <6 hours per night gives cause for concern. A systematic review and meta-analysis has established that individuals who report short sleep duration and indeed also those who are long-sleepers are at increased risk of all-cause mortality (120).

It is of interest that the reporting of poor sleep quality was not reflected in the experience of symptoms of sleepiness. Indeed, whilst 65.1% of the present sample obtained poor sleep quality scores, only 39.7% of the sample achieved scores indicative of excessive daytime sleepiness. A similar pattern of results was observed in the study of individuals attending the University Hospital Aintree weight management service, whereby 30.8% of the sample reported scores indicative of excessive daytime sleepiness, whilst a much higher proportion (73.0%) of the sample reported poor sleep quality. These findings

suggest that some of the participants either were not experiencing negative impacts of their poor sleep or alternatively that these symptoms were instead attributed to generalised low mood and quality of life rather than to sleepiness.

Quality of life has been demonstrated to be markedly low within the sample, with mean total IWQOL-Lite scores of 37.8 for females and 44.2 for males, with females experiencing significantly poorer quality of life than males. In addition, widespread high prevalence of symptoms of anxiety (70.3%) and depression (66.2%) were observed across the sample, which greatly exceeds the prevalence in the UK general population of 33.0% for anxiety and 11.4% for depression, also measured using the HADS tool (98). The findings indicate that the mental well-being of females was more severely impacted, with a significantly greater proportion experiencing anxiety (75.4 vs 55.7%) and greater impairment across several quality of life domains, relative to males. The level of impairment observed in the present sample is consistent with a study of extremely obese individuals in the US seeking bariatric surgery which also demonstrated widespread reduction in quality of life, with IWQOL-Lite scores ranging from 40.4-46.2 across domains (61). However, it is important to note that obese individuals who are not seeking treatment have been demonstrated to report lower levels of psychological distress (121) and impairment in quality of life (61) than those who are treatment-seeking. As such, the findings of the present sample reflect the mental well-being of a treatment-seeking population and may not be representative of extremely obese non-treatment-seeking individuals. Furthermore, obese individuals, incorporating both treatment-seeking and non-treatment-seeking individuals, have been demonstrated to report greater use of maladaptive coping strategies which avoid thinking about and actively facing stressful events, relative to normal weight individuals who are more likely to employ coping styles which actively

address stressors (121). This may be a potential mechanism behind the impairment in mental well-being among the extremely obese patient population.

In addition to psychological co-morbidity, the findings have highlighted the pervasiveness of co-morbid physical health conditions. These findings are consistent with the literature which has previously documented the co-morbid health conditions commonly associated with obesity (43, 44). Indeed, studies have also demonstrated that the negative health impacts of obesity are alleviated with weight loss (45, 46), with findings of the Look AHEAD study demonstrating that those overweight and obese individuals with type 2 diabetes achieving modest losses of 2-5% baseline body weight were more likely to experience clinically significant improvement in systolic blood pressure (OR= 1.24, 1.02 - 1.50), HbA1c (OR= 1.80, 1.44 - 2.24), and triglycerides (OR= 1.46, 1.14 - 1.87), relative to those who did not lose weight (122).

A greater prevalence of several conditions was observed within the sample compared to the general population, including type 2 diabetes (26.3 vs 6.0%) (99), OSA (39.4 vs 4.0% males, and 20.9 vs 2.0% females) (100), hypertension amongst males (60.6 vs 31.0%) (101), cardiovascular disease amongst males (27.3 vs 13.9%) (102), and arthritis 24.0% within the present sample vs 11% (arthritis of the hip) observed in the general population (103). Interestingly, the prevalence of arthritis within the sample was the same as the general population prevalence of arthritis of the knee 24.0% (103), thus an increased prevalence within this clinical sample was not observed. This may be due to the fact that the general population prevalence rates are elevated due to an increased prevalence of arthritis observed in older age groups. It is also of interest that the prevalence of hypertension among females of the sample was similar to the UK female prevalence (25.5 vs 28.0%) (101), and the prevalence of cardiovascular disease among females of the

sample was considerably lower than that of the general female population (5.6 vs 13.4%) (102). Interestingly, further gender differences were observed in the present sample whereby all of the co-morbid conditions except arthritis were demonstrated to be more widespread amongst males than females, with a significantly greater proportion of males (slightly more than a third of all male participants) reporting the presence of ≥3 co-morbid conditions. These findings demonstrate that the physical health of the individuals attending the service was considerably poorer amongst the male participants. This may reflect gender differences in individuals' motivation for attending the service, with males being prompted to seek help as a result of physical symptoms and difficulties, whilst females may have been motivated as a result of the experience of psychological symptoms.

Further potential motivation for attendance was identified in the analyses demonstrating the characteristics of the sample stratified by BMI and age group. The findings indicate that those in the BMI ≤40.0kg/m^2 and ≥50.0kg/m^2 groups were more likely to report the presence of ≥3 co-morbidities, which is likely due to the service referral criteria which specify that those with BMI ≤40.0kg/m^2 must also have a co-morbid health condition in order to be eligible to attend the service. Furthermore, those in the older (≥50 year) age group were more likely to experience physical co-morbidities and as a result report problems in mobility and self-care than those of younger age. The findings suggest that those in the younger (≤40 year) age group were potentially motivated to attend the service due to the greater reported experience of psychological co-morbidities including experience of anxiety, public distress and low self-esteem, rather than physical co-morbidities which appear to be less pertinent.

This chapter has constructed a detailed profile of individuals attending the CWMS, however it is important to highlight the limitations of this work. Firstly, caution must be

taken when generalising the findings of this study to the broader extreme obese population, as the sample described are those who were seeking weight management support. This study does not shed light on the health and well-being of non-treatment-seeking extreme obese individuals, with the possibility that these individuals experience better mental well-being than the present sample and thus have not been compelled to seek help. Conversely, it is conceivable that the well-being of those not seeking treatment could be considerably worse than the present sample, with these individuals not seeking support as a consequence of their extremely poor mental and physical health and potentially due to a greater number of unsuccessful prior weight loss experiences. In addition, the study is also limited by the relatively small sample size and due to the fact that detailed demographic, clinical and self-report questionnaire data were only available for those individuals attending the CWMS and not those attending the SLiM pathway which also operates within the Specialist Weight Management Service. Whilst there was not the same level of detailed information collected for the SLiM sample, additional longitudinal quality of life data for those attending the SLiM programme were obtained and are examined in Chapter three. Despite the discussed limitations, there are several notable strengths of the work including the measurement of a wide range of factors affecting individuals' lives, the use of validated and reliable self-report measures, the investigation of an under-researched group, the clinical utility of examining a service currently in operation, and the potential to impact service development.

2.4.1 Summary of findings

This chapter has provided a detailed profile of the characteristics of the individuals attending the CWMS pathway of the specialist weight management service. The

characterisation of individuals in the patient population has enhanced current understanding of individuals attending the service and more broadly of individuals with extreme obesity. Key findings include the over-representation of individuals of White European ethnicity as well as those who were unemployed, in addition the presence of co-morbid health conditions were also demonstrated to be highly prevalent. Furthermore, the study has highlighted the poor sleep quality and impaired quality of life experienced by the individuals in the sample, as well as the widespread prevalence of anxiety and depression. These findings have highlighted that the individuals entering the CWMS are a sample with very complex medical and psychological needs, whereby quality of life is substantially reduced.

2.4.2 Recommendations

The findings outlined in this chapter have enhanced current understanding of this patient population and the following recommendations are supplied in order to improve weight management services which currently provide vital care and support to individuals with extreme obesity, to aid them in making changes and commencing weight loss. The high proportion of females, White European individuals and those who are unemployed, indicates that consideration may need to be taken in the referral and commencement procedures of the service. Action may be required in order to reach those individuals who are not accessing the service, such as events to raise awareness held in local communities in order to promote the service and engage with individuals from minority ethnicity communities. Further contact such as follow-up telephone calls may also be required with individuals who do not respond to initial communications regarding appointments and commencement at the service. Alternative commencement approaches could also be

considered including informal information sessions whereby individuals who have been referred can receive information about the service and have their queries answered before committing to attend. Additional consideration may also be needed for those individuals who cannot attend due to employment commitments, such as the provision of 'out of hours' clinic sessions. Through the modification of existing service referral and delivery processes or the trial of new approaches, it is anticipated that the service could be accessible to a greater number of individuals of all backgrounds, thus increasing the inclusivity of the service and maximising the opportunity for weight loss for all of those individuals who would benefit from attendance.

The findings highlight additional areas to potentially be addressed in the multidisciplinary management of these individuals, including the psychological and physical co-morbidities faced by a large proportion of those attending the service. Consideration should be given to individuals with co-morbid psychological and physical conditions, which may potentially affect ability to achieve weight loss. These individuals may potentially require additional support, which could be provided through one-to-one clinic sessions. Additionally, targeted support groups could be operated which are tailored to specific areas of concern such as improving mental health and well-being, or support in managing the demands of chronic conditions such as type 2 diabetes and OSA. Those individuals with multiple co-morbidities may also potentially benefit from receiving further tailored support and specific advice in managing and coping with the burden of facing multiple threats to health. Whilst the prevalence levels of co-morbidities observed in this chapter have highlighted areas of concern, further investigation of the physical and psychological impact of extreme obesity will be required in order to advise more detailed recommendations. Furthermore, the introduction of any new additional support

interventions would need to be trialled in a small-scale pilot intervention study and thoroughly evaluated to ensure clinical efficacy and acceptability with participants. It is anticipated that in light of the findings demonstrated in this chapter and through the consideration of recommendations, that the design and delivery of specialist weight management services will be enhanced.

CHAPTER THREE

3.0 QUALITY OF LIFE AND EXTREME OBESITY: A STUDY OF INDIVIDUALS ENTERING THE COMMUNITY WEIGHT MANAGEMENT SERVICE (CWMS) AND SPECIALIST LIFESTYLE MANAGEMENT (SLIM) PROGRAMME

3.1 INTRODUCTION

3.1.1 Extreme obesity and quality of life: Literature search procedure

The physical co-morbidities of extreme obesity are well documented and research suggests that there are also substantial negative impacts on quality of life and mental health, as such a systematic literature search was conducted focusing on quality of life and mental health in extreme obesity in adult populations. A search of the literature was conducted using free text terms, of the PubMed database for articles published in English up to and including September 2013. The search strategy is displayed in Table 3.1.1.

Table 3.1.1: Search strategy

1	Extreme obes*
2	Quality of life
3	Mental health
4	Mental well-being
5	Depression
6	Anxiety
7	2 or 3 or 4 or 5 or 6
8	1 and 7

A total of 37 articles were identified, through the database, hand-searching reference lists and relevant journals. Of the identified studies, 20 were cross-sectional, 7 intervention studies and 10 review articles.

3.1.2 Cross-sectional studies

The 20 cross-sectional studies included in this review are described in Table 3.1.2. The cross-sectional data included 200,778 individuals, conducted between 1998 and 2013, within Western population samples, namely the UK, US, Canada, Germany, Spain, and Australia. Whilst the majority of studies identified in the present literature search have exclusively studied extreme obese samples, several studies have focussed on the cross-sectional relationship between quality of life and obesity in the non-clinical general population. These studies have facilitated comparisons between those individuals that are normal weight, overweight and within the various classes of obesity, including extreme obese (BMI $\geq$40kg/m^2) samples.

The first population-based study conducted in the UK was a postal-survey whereby questionnaires were received from 8,889 randomly-selected adults living in four English counties in 1997 (63). Data collected included self-reported height and weight, chronic illness status and the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36). Of the sample, 11% were categorised as obese (BMI 30.0-39.9kg/m^2), with a further 1% categorised as extreme obese (BMI $\geq$40.0kg/m^2). Findings showed that there were significant differences in all dimensions of the SF-36 between the BMI categories, with those with extreme obesity scoring the lowest across both the physical and mental dimensions. Extreme obese individuals also had the lowest physical component score, which was significantly lower than the normal weight score (40.6 vs 51.2, $p < 0.001$), whilst for the mental component score, the underweight group had the lowest score, with the extreme obese score being second lowest and significantly lower than that of normal weight individuals (48.1 vs 50.1, $p < 0.001$). Furthermore, those with obesity and additional co-morbid chronic health conditions, which accounted for 56% of those with obesity,

reported further impairment in both physical and mental health. However, the authors note that the deterioration in health status seen with increasing adiposity was more marked in the physical than in the mental components, whereby in the mental and social dimensions those individuals in the overweight and obese categories reported a similar level of impairment to those in the underweight category. The authors concluded that in this population-based sample, obesity was associated with greater impairment in physical than mental quality of life, suggesting that the presence of co-morbid health conditions may mediate the relationship between obesity and impairment in mental quality of life. Results of the study should be interpreted with caution as the study was limited by the use of self-reported weight and height measures, rather than a more accurate physical measurement, which may have resulted in erroneous data as it has been widely reported that individuals underestimate their weight. Thus the potential measurement and reporting bias may result in misinterpretation of the relationship between adiposity and the psychosocial variables.

The second and most recent cross-sectional study conducted in a UK population-based sample utilised data from the 2003 Health Survey for England (HSE) (123). The sample comprised 14,416 randomly selected adults, with whom questionnaire-based face-to-face interviews were conducted, which included the EQ-5D quality of life measure, and height and weight measurements were obtained. Prevalence of extreme obesity was slightly higher in females (2.9%) than males (1%), and after adjusting for confounding factors, analyses showed a clear association between being underweight or obese and impairment in quality of life as measured by EQ5D in both males and females. Those in the overweight, obese or extreme obese categories reported increased problems in all dimensions of the EQ-5D (mobility, self-care, anxiety and depression, pain and discomfort, and performing usual activities), with the exception of anxiety and depression

for which the prevalence was the same for overweight and normal weight individuals. The study utilised a large sample size and reliable physical measurements, which enables confidence in the observed strong association between above and below normal BMI and decreased quality of life.

The final cross-sectional study conducted in the UK was a small sample (N=179) questionnaire survey completed by BMI ≥30.0kg/m^2 female magazine subscribers (64). Findings indicated that those in the extreme obese category reported significantly poorer self-esteem as measured by the Rosenberg Self-Esteem scale, compared to those with BMI 30.0-39.0kg/m^2, however there were no significant differences between the groups regarding mental health as measured by the Mental Health Inventory. The authors conclude that in this sample of obese females the relationship between obesity and psychological well-being is complex, with those extreme obese individuals reporting the greatest dissatisfaction with their body weight, shape and appearance. However, the sample did not differ significantly in terms of mental health, a finding which is in contrast to some previous population-based studies. The study benefits from the inclusion of a sample recruited from a non-clinical setting, thus capturing the experiences of non-treatment-seeking individuals. However, the fact that individuals were recruited from a population of subscribers to a magazine focusing on ladies fashion for clothes sizes ≥16 means that the sample is not representative of all individuals. In addition, the small sample size is likely underpowered and the use of self-reported weight and height measures introduces the potential for measurement error as previously described.

Several cross-sectional population-based studies have been conducted in the US (124-126), the largest of which utilised data from the 1999 Behavioural Risk Factor Surveillance Survey (124). The study sample comprised 155,989 adults who completed

self-reported height and weight data along with four questions designed to assess individuals' perceived health-related physical and mental quality of life over the past 30 days. A J-shaped association between BMI and quality of life was observed, whereby compared to those in the BMI 18.0-24.9kg/m^2 group, those who were underweight, overweight, and in obesity classes I, II, and III were significantly more likely to report fair/poor general health status, with respective odds ratios of 1.57 (1.39 - 1.76), 1.19 (1.14 - 1.24), 1.95 (1.85 - 2.05), 2.72 (2.53 - 2.93) and 4.36 (3.97 - 4.80), $p < 0.001$. The findings of this large scale population-based study indicate that the health-related quality of life was poorest for those in the extreme obese category. However the use of self-reported height and weight measures is a limitation despite the overall high methodological rigour of the study.

Another large sample, US population-based study utilised data from the third National Health and Nutrition Examination Survey (NHANES) collected between 1988 and 1994 (125). The sample comprised 8,410 individuals aged 15-39 years who completed weight and height measures as well as a structured diagnostic interview which was used to assess the presence of major depression according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) criteria. Analyses assessing risk of experiencing depression over the past month were conducted adjusting for age, gender and socioeconomic status. These findings indicated a dose-response relationship between depression and adiposity, with extreme obese individuals having greater odds of experiencing depression in the past month (OR= 4.63, 2.06 - 10.42) than those with BMI 35.0-39.9kg/m^2 (OR= 1.90, 0.79 - 4.60) and BMI 30.0-34.9kg/m^2 (OR= 1.33, 0.57 - 3.13), relative to those of BMI 24.9-29.9kg/m^2. Furthermore, the authors identified that across the sample the prevalence of past-month major depression was approximately 2.5-fold higher

in females than males, a finding which is consistent with other population-based studies. Within extreme obese individuals specifically, the prevalence of past-month major depression was higher in females (13.03%) than males (11.54%). The authors conclude that the association between obesity and depression varies with the severity of obesity, with the prevalence of depression being highest in the extreme obese category.

Only one population-based study was conducted outside of the UK and US, which was conducted in Germany. The study examined the association between obesity and suicidal behaviour which was assessed using the revised Suicidal Behaviours Questionnaire in a sample of 2,436 individuals (62). Findings indicate that those with BMI 30.0-34.9kg/m^2 were significantly more likely to attempt suicide (OR= 3.49, 1.76 - 6.90, p <0.001) relative to overweight (BMI 24.9-29.9kg/m^2) individuals, with extreme obese individuals at even greater risk (OR= 12.43, 3.87 - 39.86, p <0.001). Furthermore, extreme obese individuals are also at greater risk of suicidal behaviour (OR= 21.22, 6.51 - 69.20) than those with BMI 30.0-34.9kg/m^2 (OR= 3.02, 1.50 - 6.08), relative to overweight (BMI 24.9-29.9kg/m^2) individuals. This novel study benefits from the use of a tool which goes beyond the measurement of emotion and examines the consequences of mood disturbance on individuals' actions in terms of both suicidal ideation and actions. The study also highlights the obese and specifically extreme obese population as an at-risk group and indicates that there is potentially a need for the introduction of screening to identify and provide support for vulnerable individuals.

The following studies have been conducted in treatment-seeking extreme obese samples. Only one treatment-seeking cross-sectional study has examined the relationship between quality of life and extreme obesity in a UK sample (127). The study examined baseline data from 253 individuals entering one of two specialist weight management

centres, Luton and Dunstable Hospital NHS Trust, Luton and Addenbrooke's Hospital NHS Trust, Cambridge. The authors did not detail the nature of the service delivered at the centres. Self-report questionnaire data were collected at baseline including the Hospital Anxiety and Depression Scale (HADS), the Eating Disorder Inventory (EDI-2), and the Impact of Weight on Quality of Life scale (IWQOL-Lite). Analysis of the baseline data revealed that within the sample entering the specialist weight management centres, 56% achieved a HADS score indicative of anxiety and 48% for depression. Furthermore, gender differences were observed, whereby the prevalence of anxiety was higher in females (60.5%) than males (42%, $p < 0.01$). Interestingly, the authors reported no significant gender difference in prevalence rates of depression, which were 47.8% for females and 47.5% for males. Analysis of the EDI-2 data revealed that 11.5% of the sample demonstrated a score indicative of presence of bulimia nervosa. The IWQOL-Lite data revealed widespread reduction of quality of life in the sample, with substantial proportions scoring within 10% of the lowest possible score, indicating the poorest quality of life. In males, sexual life was the most affected area with 32.8% of the sample scoring within the lowest 10%, whilst in females self-esteem was the most affected domain, with 20.5% of the sample achieving a score within 10% of the lowest possible score. The authors concluded that their findings demonstrate a high prevalence of psychological co-morbidities, including anxiety, depression, and eating disorders, as well as marked impairment in quality of life within the sample, proposing that psychological diagnoses should be considered prior to commencement on weight management programmes in order to increase the effectiveness of treatment. However, it is important to note that the high prevalence of psychological co-morbidity was observed in a treatment-seeking sample and may not be representative of non-treatment-seeking individuals.

One study comprising a treatment-seeking sample has been conducted in Germany. The study assessed health-related quality of life utilising the SF-36, in a sample of 640 adults attending one of four obesity treatment centres (65). BMI was shown to be significantly associated with the physical but not the mental component of the SF-36. Those with extreme obesity scored significantly lower than the other obese groups on the physical component subscale and correspondingly a significant negative association was observed between BMI and the physical component score ($r= -0.56$, $p <0.001$). However, there were no significant differences between the BMI groups in terms of mental component score, likewise, there was no association between BMI and the mental component score. The absence of an observed relationship between BMI and mental health is in contrast to the previously discussed studies, and could be due to limitations in the capabilities of the SF-36 tool in detecting the mental health issues of this population, rather than due to the fundamental absence of an association with BMI. The inclusion of additional mental health measures is necessary in order to further assess the relationship between adiposity and adverse mental health within this population.

Additional cross-sectional design studies are those that have examined the use of assessment tools such as validation of the IWQOL-Lite in non-English languages (128), development of new tools such as the Obesity Adjustment Survey (129), and the comparison of a selection of assessment tools such as the EQ5D and SF-36 (130).

One study did not use quantitative assessment tools, instead opting for a qualitative approach conducting in-depth semi-structured interviews with 76 obese Australian adult participants (131). Although the study included participants across the spectrum of obesity, the mean BMI of the sample ($42.5 kg/m^2$) was within the extreme obese category. Capturing the social experiences of obesity and the effects on daily life was a key topic of

enquiry in this study and findings indicated that nearly all of the participants reported that they had experienced stigma and discrimination because of their weight. Interestingly, a small proportion of the sample also reported feelings of social isolation, rarely interacting with others. The authors conclude that whilst there was variation in the lived experiences of obesity reported by the study participants, several recurring themes were identified, including experience of discrimination, stigma and social isolation, repeated unsuccessful attempts at weight loss, and the perception of being misunderstood by healthcare professionals. The authors propose that weight management interventions should recognise the common enduring themes as well as the variation in the experience of obesity and its impact on daily life. Interestingly, this was the only study within the present literature review to adopt a qualitative approach to examine the relationship between adiposity, quality of life and mental well-being. The lack of qualitative studies highlighted by the present literature review, is surprising given that this methodology facilitates the exploration of lived experiences and has the potential to add to our understanding of the relationship.

Several quantitative studies have been published examining the impact of social stigma in obesity (132-134). The most recently published study comprised a sample of 574 individuals seeking treatment at two bariatric surgery centres in the US (132). A telephone survey was conducted with participants whereby self-reported weight and height data were collected along with data from two questionnaires, the SF-36 and the IWQOL-Lite. A preference-based quality of life measure was also used to assess individuals' health utility through a series of gambling scenarios which assessed willingness to risk death in order to lose various amounts of weight or achieve their most valued health and weight state. The health utility score indicated that the sample were willing to accept a 13% risk of death in

order to achieve their most desired health and weight state. The most prominent predictors of health utility were public distress as measured by IWQOL-Lite, which accounted for 5.4% of the variance in health utility and role limitations due to physical health as measured by SF-36, which accounted for 6.0% of the variance. The study highlights that as well as having a detrimental effect on individuals' mental well-being, the experience of stigma and public distress may have further implications as these experiences could deter individuals from seeking contact with healthcare professionals.

Indeed, another study has focussed on the experience of weight-related stigma and its association with quality of life and depressive symptoms in a sample of extreme obese individuals seeking bariatric surgery (133). The sample comprised 117 extreme obese individuals (mean BMI 48.2kg/m^2) who completed baseline self-report questionnaires including the Stigma Situations Questionnaire, IWQOL-Lite, and the Beck Depression Inventory, second edition (BDI-II). The findings indicate that participants reported relatively minimal weight-related stigma experienced 'several times' in participants' lives. Several specific forms of stigmatisation were related to BMI including 'Being stared at' ($r= 0.43$, $p <0.001$), 'Comments from children' ($r= 0.36$, $p <0.001$), 'Physical barriers' ($r= 0.45$, $p <0.001$), and 'Loved ones embarrassed by your size' ($r= 0.26$, $p <0.01$). BMI was not significantly associated with total experiences of stigmatisation or experience of depressive symptoms, however, BMI was significantly associated with lower quality of life as measured by IWQOL-Lite total scores ($r= 0.41$, $p <0.01$). Interestingly, those participants who reported more frequent experience of stigma also reported poorer quality of life across all IWQOL-Lite domains; physical function ($r= 0.26$, $p <0.01$), self-esteem ($r= 0.48$, $P <0.001$), sexual life ($r= 0.28$, $p <0.01$), public distress ($r= 0.52$, $p <0.001$), and work ($r= 0.42$, $p <0.001$). The findings of the study demonstrate that the sample reported

experiencing a surprisingly low level of stigmatisation. However, where stigmatisation was present, this was linked to more widespread negative emotional state including depressive symptoms and impairment in quality of life.

The link between depression and quality of life in extreme obesity was also studied by the same group in a separate sample of 306 individuals seeking bariatric surgery at the same institution (134). This study measured quality of life using the SF-36 and BDI-II. Significant negative associations between BMI and the physical functioning, physical role limitations, and bodily pain domains of the SF-36 were observed, with higher BMI being associated with lower physical quality of life. BMI was also demonstrated to be significantly associated with symptoms of depression however, the correlation was weak ($r= 0.11$, $p \leq 0.05$). Regression analyses between these variables revealed that physical role limitations and bodily pain each contributed significantly to the experience of symptoms of depression with these predictors accounting for 15.9% and 4.3% of the variance in depression, respectively. Interestingly, the physical function variable and BMI each explained less than 1% of the remaining variance in depression scores indicating that these factors play less of an important role in the relationship between depression and quality of life in extreme obesity.

Several studies conducted in the US have examined the relationship between extreme obesity and quality of life among various subgroups of treatment-seeking individuals such as ethnic group and gender (135), ethnic group and treatment status (61), gender and treatment status (136), and across BMI categories and treatment status (137). Findings of the treatment-seeking extreme obese sample sub-group analysis revealed that African-American males reported significantly less impairment in quality of life than the other ethnicity groups, despite having the highest BMI levels. Additionally, White females

reported the greatest impairment in quality of life ($p < 0.05$), despite having the lowest BMI levels when compared to the other ethnicity groups ($p < 0.05$) (135), suggesting that ethnicity and gender factors impact upon the self-reported experience of obesity among extreme obese samples. Whilst a significant negative association was observed between BMI and quality of life, both within the overall sample and ethnicity and gender subgroups, analyses was limited to correlation and a regression analyses would be required in order to account for potential confounding variables. These studies support the use of the IWQOL-Lite tool in assessing the quality of life of extreme obese samples and have highlighted its efficacy (135).

Table 3.1.2: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Doll, 2000	UK	8,889	General population: Residents of four counties in southern and central England (mean BMI= 24.9kg/m^2)	SF-36	Self-reported height and weight, chronic illness status	Extreme obese had significantly lower SF-36 physical component scores compared to normal BMI group (40.6 vs 51.2, p <0.001), as well as significantly lower mean mental score than normal weight group (48.1vs 50.1, p <0.001).
Soltoft, 2009	UK	14,416	General population: The Health Survey for England (2003) (mean BMI= 27.2kg/m^2 for males, 27.0kg/m^2 for females)	EQ-5D	Nurse-measured weight and height	Significant negative association between BMI and quality of life. Extreme obese reported increased problems in all EQ-5D dimensions relative to 24.9-29.9kg/m^2 BMI group (mobility problems in 35.4% of extreme obese women vs 10.1% of normal BMI women, self-care 9.8% vs 2.6%, usual activities 22.6% vs 11.2%, pain 48.0% vs 25.4%, and anxiety problems in 30.6% vs 21.3%).
Hill, 1998	UK	179	General population: Survey of female magazine subscribers clothes size ≥16 (mean sample BMI not given, 39% BMI ≥40.0kg/m^2)	RSE, MHI	Body shape assessment, Body shape satisfaction, DEBQ	Extreme obese had significantly lower self-esteem scores compared to Class II and I obese groups, 26.6 vs 29.0 and 30.2, p <0.01, respectively. No significant difference in mental health between class I-III groups.
Heo, 2003	US	155,989	General population: The Behavioural Risk Factor Surveillance Survey, 1999 (mean BMI= 26.3kg/m^2)	Four questions assessing perceived health-related physical and mental quality of life over past 30 days	Self-reported height and weight	J-shaped association between BMI and quality of life. Underweight, overweight, and class I to III obese groups significantly more likely to report fair/poor general health, relative to normal weight. Extreme obese most likely to report fair/poor health (OR= 4.36, 3.97 - 4.80)

SF-36= Medical Outcomes Study Short Form Health Survey, RSE= Rosenberg self-esteem scale, MHI= Mental Health Inventory, DEBQ= Dutch Eating Behaviour Questionnaire .

Table 3.1.2 Continued: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Onyike, 2003	US	8,410	General population: The third National Health and Nutrition Examination Survey (NHANES). Aged 15-39 years (mean BMI not given, 16.3% BMI ≥30.0kg/m^2)	Structured diagnostic interview assessing presence of major depression using DSM-IV criteria	Researcher-measured weight and height	Dose-response relationship between depression and adiposity with extreme obese at greater risk of depression in the past month (OR= 4.63, 2.06 - 10.42) than class I obese (OR= 1.33, 0.57 - 3.13) and class II obese (OR= 1.90, 0.79 - 4.60), relative to normal weight.
Yancy, 2002	US	1,168	General population: males attending one Veterans' primary care medical centre (mean BMI not given, 3.0% BMI ≥40.0kg/m^2)	SF-36, CES-D, FPAI	Researcher-measured weight and height	Extreme obese had significantly lower scores on the physical functioning (35.0 vs 56.7, p <0.001), role-physical (27.5 vs 50.8, p <0.05), bodily pain (38.8 vs 53.1, p <0.01) and vitality (33.0 vs 50.0, p <0.05) SF-36 subscales, relative to normal weight individuals. However there were no significant differences in the SF-36 mental component scores.
Wagner, 2013	Germany	2,436	General population: randomly generated sample (mean sample BMI not given, 8.1% BMI ≥30.0kg/m^2, 0.6% BMI ≥40.0kg/m^2)	SBQ-R	Self-reported weight and height	Extreme obese at greater risk of attempting suicide (OR= 12.43, 3.87 - 39.86) than Class I obese (OR= 3.49, 1.76 - 6.90), relative to normal weight. Extreme obese at greater risk of suicidal behaviour (OR= 21.22, 6.51 - 69.20) than Class I obese (OR= 3.02, 1.50 - 6.08), relative to normal weight.
Tuthill, 2006	UK	253	Extreme obese seeking treatment at two specialist weight management centres (mean BMI= 45.8kg/m^2 for males, 46.4kg/m^2 for females)	HADS, EDI-2, IWQOL-Lite	Nurse-led medical assessment including weight and height	Anxiety prevalence= 56%, depression= 48% bulimia nervosa= 11.5%. For females, self-esteem was the most impaired aspect, 20.5% scoring within 10% of the lowest possible IWQOL-Lite score. In males, sexual life was most affected, with 32.8% scoring within 10% of lowest score.

DSM-IV= Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, SF-36= Medical Outcomes Study Short Form Health Survey, CES-D= Center for Epidemiological Studies Depression Scale, FPAI= Framingham Physical Activity Index, SBQ-R= Suicidal Behaviours Questionnaire-Revised, HADS= Hospital Anxiety and Depression Scale, EDI-2= Eating Disorder Inventory, IWQOL-Lite= Impact of Weight on Quality of Life scale.

Table 3.1.2 Continued: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
de Zwann, 2009	Germany	640	Adults attending 1 of 4 obesity centres, 1 of 6 surgery units, or randomly selected general population (mean BMI= 37.3kg/m^2, 39.1% BMI ≥40.0kg/m^2)	SF-36	Researcher or clinician-measured weight and height	Significant negative association between BMI and SF-36 physical component score (r= -0.56, p <0.001). Extreme obese scored significantly lower (p <0.05) than class I and II obese groups in physical component score. No significant association between BMI and mental component scores.
Andres, 2012	Spain	109	Obese adults seeking bariatric surgery at an obesity outpatient unit (mean BMI= 47.2 kg/m^2)	IWQOL-Lite, DASS-21, BSI, items from the self-perception scale of the WALI	Weight and height, unknown whether self-reported or measured	Significant negative association between BMI and IWQOL-Lite total scores (r= −2.98, p <0.01), with BMI also accounting for 8.9% of variance in IWQOL-Lite total score. Construct validity of Spanish version supported.
Butler, 1999	Canada	89	Obese adults accepted for bariatric surgery at a health service centre (mean BMI= 48.1 kg/m^2)	OAS, MHI, SIP, EI	Pre-surgical weight and height, unknown whether self-reported or measured	OAS significantly associated with MHI (r= -0.49, p <0.001) and SIP (r= 0.43, p <0.001) but not any of the EI measures (r= -0.14, r= 0.17, r= 0.11, p >0.05).
Sach, 2007	UK	1,865	Adults aged ≥45 years recruited onto a study assessing lifestyle interventions for knee pain (mean BMI= 26.0 kg/m^2)	EQ5D and SF-6D (derived from SF-36)	Self-reported weight and height collected via questionnaire	Obese Classes I-III had significantly lower scores on EQ5D and SF-6D, relative to normal weight group. Extreme obese mean EQ5D score significantly lower (0.62 vs 0.80, p <0.001) than the normal weight group, as well as SF-6D score (0.67 vs 0.78, p <0.001).

SF-36= Medical Outcomes Study Short Form Health Survey, IWQOL-Lite= Impact of Weight on Quality of Life scale, DASS-21= Depression Anxiety Stress Scales, BSI= Brief Symptom Inventory, WALI= Weight and Lifestyle Inventory, OAS= Obesity Adjustment Survey, MHI= Mental Health Inventory, SIP= Sickness Impact Profile, EI= Eating Inventory.

Table 3.1.2 Continued: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Thomas, 2008	Australia	76	General population: Obese aged ≥16 years (mean BMI= 42.5kg/m^2)	In-depth semi-structured interviews	Self-reported weight and height	Majority of sample reported weight-related stigma and discrimination. Small proportion reported social isolation and lack of interaction.
Wee, 2013	US	574	Extreme obese seeking treatment at two bariatric surgery centres (mean BMI= 46.5kg/m^2)	Collected via telephone survey: IWQOL-Lite, SF-36 and willingness to risk death in order to lose weight items	Self-reported weight and height collected via telephone survey	Sample willing to accept a 13% risk of death in order to achieve most desired health and weight state. Public distress and physical limitations predicted willingness to risk death, each accounting for 5.4% and 6.0% of the variance in health utility, respectively.
Sarwer, 2008	US	117	Extreme obese seeking bariatric surgery at Pennsylvania University Hospital (mean BMI= 48.2 kg/m^2)	IWQOL-Lite, SSQ and BDI-II	Weight measured at pre-surgery evaluation, height self-reported	BMI significantly negatively associated with IWQOL-Lite (r= 0.41, p <0.01). BMI significantly associated with several stigmatisation subscales (r= 0.43, 0.36, 0.45, 0.26, p <0.001). BMI not significantly associated with depressive symptoms. Low levels of weight-related stigma experienced by sample. Stigma significantly negatively associated with quality of life.
Fabricatore, 2005	US	306	Extreme obese seeking bariatric surgery at Pennsylvania University Hospital (mean BMI= 52.8 kg/m^2)	SF-36 and BDI-II	Weight measured at pre-surgery evaluation, height self-reported	BMI significantly negatively associated with physical functioning (r= -0.36, p <0.001), physical role limitations (r= -0.21, p <0.001), and bodily pain (r= -0.23, p <0.001) of the SF-36. BMI significantly positively associated with symptoms of depression (r= 0.11, p ≤0.05).

IWQOL-Lite= Impact of Weight on Quality of Life scale, SF-36= Medical Outcomes Study Short Form Health Survey, SSQ= Stigma Situations Questionnaire, BDI-II= Beck Depression Inventory, Second Edition.

Table 3.1.2 Continued: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
White, 2004	US	512	Extreme obese seeking bariatric surgery (mean BMI= 53.3 kg/m^2) at a medical unit	IWQOL-Lite and BDI	Pre-surgical weight and height, unknown whether self-reported or measured	BMI significantly negatively associated with total IWQOL-Lite (r= -0.22, p <0.01) and subscales physical function (r= -0.21, p <0.01), public distress (r= -0.39, p <0.01) and work (r= -0.18, p <0.01), but not sexual life and self-esteem. BMI not significantly associated with depression score. African-American males had highest BMI and reported significantly less impairment in quality of life than other ethnicity groups. White females had lowest BMI and reported greater impairment in quality of life than other ethnicity groups.
Kolotkin, 2002	US	3,353	Individuals not enrolled in weight-loss treatment BMI ≥25kg/m^2, participants of obesity medication clinical trials, individuals attending a weekly weight-loss programme, individuals attending a daily intensive programme, individuals seeking bariatric surgery, (mean BMI= 36.1kg/m^2 for males, 36.8kg/m^2 for females)	IWQOL-Lite	Weight and height, unknown whether self-reported or measured.	BMI significantly negatively associated with quality of life, IWQOL-Lite total (r= -0.53, p <0.001), with BMI accounting for almost 28% of the variance in IWQOL-Lite total score. White females scored significantly lower than African American females on all IWQOL-Lite subscales. White males scored significantly lower than African American males on all IWQOL-Lite subscales except 'work'. Significant effect of treatment modality, with those seeking bariatric surgery and intensive daily obesity treatment programme reporting the lowest quality of life scores across all domains (p <0.001).

IWQOL-Lite= Impact of Weight on Quality of Life scale, BDI= Beck Depression Inventory.

Table 3.1.2 Continued: Cross-sectional studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Kolotkin, 2006	US	1,158	Individuals not enrolled in weight-loss treatment BMI ≥30kg/m^2, individuals seeking bariatric surgery, individuals attending an intensive programme (mean BMI of all samples ≥40kg/m^2)	IWQOL-Lite, with specific focus on the 'sexual life' component	Researcher or clinician-measured weight and height	Participants in the Class III obesity group reported less sexual enjoyment ($p < 0.01$), more difficulty with sexual performance ($p < 0.01$), and greater avoidance of sexual encounters ($p < 0.05$), relative to class I and II obese individuals. Gender effects were also observed whereby in the class III obese group, women reported significantly less sexual enjoyment ($p < 0.01$), less sexual desire ($p < 0.01$), and greater avoidance of sexual encounters ($p < 0.01$), relative to males.
Wadden, 2006	US	239	Females seeking bariatric surgery (mean BMI= 52.6kg/m^2) or behavioural weight-loss programme (mean BMI= 33.8kg/m^2)	BDI-II, WALI, RSE	Weight and height, unknown whether self-reported or measured.	Women with class III obesity, reported significantly more symptoms of low self-esteem (19.9 vs 16.6, $p < 0.01$) and more symptoms of depression (13.2 vs 8.1, $p < 0.01$), relative to class I-II obese individuals. 25% of class III group had BDI-II scores which indicated that they would benefit from treatment. Class III obese also significantly more likely to report a history of physical abuse (24.3 vs 6.6%, $p < 0.01$) and sexual abuse (19.9 vs 8.9%, $p < 0.05$), relative to class I-II individuals.

IWQOL-Lite= Impact of Weight on Quality of Life scale, BDI-II= Beck Depression Inventory-Second edition, WALI= Weight and Lifestyle Inventory, RSE= Rosenberg self-esteem scale.

3.1.3 Intervention studies

The seven intervention studies included in this review are described in Table 3.1.3. The intervention data were from 2,859 individuals, conducted between 2005 and 2013, within predominantly European population samples, namely the UK, Germany, France, Sweden and Norway, with only one study outside of Europe, which was conducted in the US.

Whilst the majority of the intervention studies focus on the impact of surgical interventions on quality of life outcomes, one UK study has detailed the quality of life outcomes of a medical weight management intervention (74). The sample comprised 199 adult individuals of BMI $\geq$30.0kg/m^2 with co-morbidities or BMI $\geq$35.0kg/m^2. The intervention consisted of a group-programme led by a dietician with input from a clinical psychologist, comprising nine fortnightly-sessions (lasting 1.5 hours) focussing on diet and activity lifestyle advice and behavioural change strategies. Quality of life and mental health were assessed by the IWQOL-Lite and HADS, pre- and post- intervention. Findings indicated that both weight loss (OR= 0.85, 0.75 - 0.95) and changes in depression (OR= 0.78, 0.65 - 0.93) were significant predictors of improvement in post-intervention quality of life scores. For those individuals losing $\geq$5kg, improvement in quality of life was predicted by weight loss. However, for those losing smaller amounts of weight <5kg, improvement in quality of life was predicted by positive changes in depression scores. The findings demonstrate that a clinically meaningful improvement in quality of life was achieved through this group-based medical weight management intervention. The authors suggest that the improvement in depression scores seen in those losing smaller amounts of weight could be due to the social interaction within the group having a positive effect on well-being and quality of life. However, for those individuals losing greater amounts of

weight, the improvement in quality of life was attributable to weight loss rather than the group-based nature of the intervention.

The remaining intervention studies focused on surgical intervention. A review of the impact of bariatric surgery on psychosocial functioning was conducted in 2003 (138). The review included 40 studies involving 3,739 patients which detailed psychosocial and mental health outcomes following bariatric surgery. The review concluded that for the majority of individuals undergoing bariatric surgery, mental health and psychosocial status are improved post-intervention. Specifically, psychiatric co-morbidity, affective disorders including anxiety and depression and psychopathologic symptoms were shown to decrease following surgical intervention, with post-surgery Axis I DSM-III psychiatric disorder prevalence rates ranging from no diagnosis, to half and a third of the pre-surgical rates which ranged between 27.4-41.8%. Other subsequent studies detailing the impact of bariatric surgical interventions on quality of life outcomes among extreme obese individuals have shown similar results (66-71). In a small sample study of 50 extreme obese females undergoing gastric banding, 3 year post-surgery BMI reduction was shown to be associated with reduced depression ($r= -0.61$, $p <0.05$) and improvement in quality of life as measured by the SF-36 subscales: physical functioning ($r= -0.71$, $p <0.01$), role physical ($r= 0.59$, $p <0.05$), mental health ($r= 0.62$, $p <0.05$) and vitality ($r= 0.57$, $p <0.05$). A subsequent follow-up of the same sample after a further three years, revealed that 6-years post-baseline, the reduction in BMI and improvement in depression and quality of life remained (67). The Swedish Obese Subjects study also examined the long-term effects of bariatric surgery on quality of life outcomes (68). The study included a large sample size of 1,276 individuals and incorporated a control group comparator receiving medical weight management, with significant improvements in all quality of life measures from baseline to

10-years for the surgical group, whereas most initial significant improvements in quality of life for the medical group were lost by 2-years, with the exception of anxiety, which remained significantly reduced from baseline to 10-years. The final large sample size intervention study included 1,156 extreme obese individuals, receiving Roux-en-Y gastric banding or non-surgical care (71). Six-year post-baseline mean weight change was -27.7% for the group receiving surgery, +0.2% for those seeking but not receiving surgery and 0% change in those not-seeking surgery. There were significant improvements in SF-36 and IWQOL-Lite scores from baseline to 6-years for all groups. The improvement in quality of life as measured by IWQOL-Lite was significantly greater for the surgery group than the control group, with a mean difference of 34.2 (28.7 - 39.7), $p < 0.001$, as well as the SF-36 physical function score, with a mean difference of 11.2 (8.2 - 14.3), $p < 0.001$. However, the improvement in mental component score was not significantly different between the surgical and control group, with a mean difference of 0.6 (-2.6 - 3.9), $p > 0.05$, indicating that the psychological co-morbidities had remained independent of weight loss.

This review has highlighted the limited number of studies which report the impact of medical weight management interventions on the quality of life and mental health of individuals with extreme obesity, with the majority of the evidence base originating from surgical interventions. Future studies examining the efficacy of medical weight management interventions should incorporate psychological outcome measures, in order to improve understanding of the role of psychological factors in extreme obesity.

Table 3.1.3: Intervention studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Wright, 2013	UK	199	Extreme obese receiving a non-surgical medical weight management intervention (mean BMI ≥30kg/m^2, mean weight= 114.5kg)	IWQOL-Lite, HADS	Dietitian-measured weight and height	Baseline BMI significantly positively correlated with depression (r= 0.16, p <0.05) but not anxiety (r= 0.10, p >0.05). Baseline BMI significantly negatively correlated with all subscales and total IWQOL-Lite (r= -0.43, p <0.001), physical function (r= -0.43, p <0.001), self-esteem (r= -0.19, p <0.01), sexual life (r= -0.18, p <0.05), public distress (r= -0.58, p <0.001), and work (r= -0.30, p <0.001). Post-intervention weight loss (OR= 0.85, 0.75 - 0.95) and improvement in depression (OR= 0.78, 0.65 - 0.93) were significant predictors of quality of life improvement.
Nickel, 2005	Germany	50	Females seeking gastric banding procedure. 21 had procedure (mean BMI= 47.4kg/m^2), 29 opted out of procedure (mean BMI= 45.1kg/m^2)	TFEQ, HADS, SF-36	Researcher or clinician-measured weight and height	Three-year post-surgery reduction in BMI was significantly associated with reduction in depression (r= -0.61, p <0.05) and the SF-36 subscales: physical functioning (r= -0.71, p <0.01), role physical (r= 0.59, p <0.05), mental health (r= 0.62, p <0.05) and vitality (r= 0.57, p <0.05).
Nickel, 2007	Germany	50	Females seeking gastric banding procedure. Sample same as reported 2005. 21 had procedure (mean BMI= 47.4kg/m^2), 29 opted out of procedure (mean BMI= 45.1kg/m^2)	TFEQ, HADS, SF-36	Researcher or clinician-measured weight and height	Six-year post-surgery reduction in BMI was significantly associated with improvements on all TFEQ scales (p <0.01), on HADS anxiety (p <0.05), depression (p <0.05), and on all SF-36 scales (p <0.01).

IWQOL-Lite= Impact of Weight on Quality of Life scale, HADS= Hospital Anxiety and Depression Scale, TFEQ= Three-Factor Eating Questionnaire, SF-36= Medical Outcomes Study Short Form Health Survey.

Table 3.1.3 Continued: Intervention studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Karlsson, 2007	Sweden	1,276	Individuals taking part in the Swedish obese subjects (SOS) intervention. 655 receiving banding or bypass bariatric surgery (mean BMI= 41.9kg/m^2), 621 receiving medical weight-management (mean BMI= 39.9kg/m^2)	SOS Quality of Life Survey, items of the CH selected from the GHRI, MACL, HADS, SI category from the SIP, OP scale	Researcher or clinician-measured weight and height	Ten-year post-intervention mean BMI change was -6.7kg/m^2 for the surgical group and +0.7kg/m^2 for the medical group. In the surgical group, there were significant improvements in all quality of life measures from baseline to 10 years. In the medical group, there were significant improvements in quality of life measures, with most lost by two years, however anxiety remained significantly reduced from baseline to 10 years.
Andersen, 2010	Norway	50	Individuals receiving duodenal switch bariatric surgery (mean BMI= 51.7kg/m^2)	HADS, SF-36	Researcher or clinician-measured weight and height	At baseline 50% of sample showed presence of anxiety (≥8) and 36% presence of depression. Two-year post-surgery mean BMI change was -20.0kg/m^2. Anxiety prevalence reduced to 22.7% at 2 years, and depression reduced to 4.5%. BMI change was not significantly associated with change in HADS scores, but was significantly associated with improvement in PCS scores. MCS change scores were not presented.
Fezzi, 2011	France	78	Individuals receiving laparoscopic sleeve gastrectomy bariatric surgery (mean BMI= 47.0kg/m^2)	SF-36, IWQOL-Lite	Researcher or clinician-measured weight and height	One-year post-surgery mean BMI change was -14.0kg/m^2. There were significant improvements in all SF-36 and IWQOL-Lite domains from baseline. One-year change in quality of life was not significantly associated with change in weight.

CH= Current Health scale, GHRI= General Health Rating Index, MACL= Mood Adjective Check List, SI= Social Interaction, SIP= Sickness Impact Profile, OP= Obesity-related Problems Scale, HADS= Hospital Anxiety and Depression Scale, SF-36= Medical Outcomes Study Short Form Health Survey, IWQOL-Lite= Impact of Weight on Quality of Life scale.

Table 3.1.3 Continued: Intervention studies examining the relationship between psychosocial variables and adiposity

First author, year	Country	Sample size	Sample	Psychosocial measures	Other measures	Findings
Adams, 2012	US	1,156	418 individuals receiving Roux-en-Y gastric bypass (RYGB), 417 individuals seeking but not receiving surgery, 321 extreme obese individuals not-seeking surgery (mean BMI= 45.9kg/m^2)	SF-36, IWQOL-Lite	Researcher or clinician-measured weight and height	Six-year post-baseline mean weight change was -27.7% for the group receiving surgery, +0.2% for those seeking but not receiving surgery and 0% in those not-seeking surgery. The improvement in IWQOL-Lite was significantly greater for the surgery group than the control group, mean difference= 34.2, 28.7 - 39.7, $p < 0.001$, as well as the SF-36 physical function score mean difference= 11.2, 8.2 - 14.3, $p < 0.001$. The improvement in mental component score was not significantly different between the surgical and control group, mean difference= 0.6, -2.6 - 3.9, $p > 0.05$.

SF-36= Medical Outcomes Study Short Form Health Survey Questionnaire, IWQOL-Lite= Impact of Weight on Quality of Life scale.

3.1.4 Reviews

The ten review articles included in this review are identified in Table 3.1.4. The reviews which were published between 1985 and 2012 encompassed data from 699 papers. Whilst the number of included participants could only be ascertained for four of the review articles, this gives rise to the following minimum number of included participants N=517,456. However, it is anticipated that the actual number of included individuals is considerably larger.

The first review to encompass the association between quality of life and obesity published in 1985, focused on the associated health complications of extreme obesity (139). The authors commented that whilst "functional impairment of activities of daily living" was an area that had been greatly ignored when considering health complications, several studies had however, reported an association between increasing weight and impairments in physical ability, ability to participate in recreation, work and social interaction. This narrative review provides a useful insight into the developing field of the study of extreme obesity including the terms and definitions utilised. Indeed, extreme obesity was termed by the authors as "morbid obesity" and defined as "an absolute (45.4kg i.e. 100lb) or relative (60%) excess in weight above desirable weight associated with maximum life expectancy". This is in contrast to the subsequent World Health Organisation (WHO) classification based on BMI which proposed the cut-points of 25.0-29.9kg/m^2 for overweight, 30.0-34.9kg/m^2 for obese class I, 35.0-39.9kg/m^2 for class II obese, and a cut-point of $\geq$40.0 kg/m^2 for class III obesity (10, 140, 141).

The first literature review which focussed specifically on the psychological characteristics of extreme obese individuals seeking bariatric surgery published in 1992, concluded that the patient population did not report greater levels of psychopathology than

average-weight individuals (142). However, this narrative non-systematic review included only eight papers studying extreme obese individuals (N=366 included individuals), with the remaining papers comprising samples of unknown weight. A more recent review published in 2004 (143) which also detailed the baseline psychological characteristics of extreme obese bariatric surgery-seeking individuals utilised a systematic literature review approach. This review contrasted with the previous review, concluding that most studies within the body of literature indicate that those surgery-seeking extreme obese individuals report significantly poorer quality of life. The stronger methodological rigour provides greater support for the findings of the later review. Two additional reviews published by the same author in 2005 (144) and 2008 (145) have focused on the pre- and post-operative psychosocial status of bariatric surgery-seeking extreme obese individuals. Indeed, the impact of bariatric surgery on psychosocial outcomes was also reviewed in 2002 by a different research group (146), concluding that bariatric surgery has been shown to improve psychosocial outcomes through improvement in mood and reduction in depression and anxiety. However the reviews also conclude that the extent of the impact of obesity on psychosocial functioning and the impact of psychosocial factors on post-intervention success remain unclear.

The most recent systematic review published in 2012 focussed on the relationship between extreme obesity, quality of life and specifically sexual quality of life, with the authors proposing that sexual function is an important yet under-researched aspect contributing to quality of life (147). The review details the small body of literature which suggests that extreme obese individuals report experiencing greater difficulties in sexual functioning than their normal weight counterparts. It was suggested that these difficulties may be a consequence of the changes in reproductive hormones associated with excess

body weight, the presence of obesity-related co-morbidities including hypertension and type 2 diabetes and additionally due to psychosocial factors including poor body image and depression. Other reviews which have focused on specific aspects of mental well-being are the 2008 systematic review which examined the literature investigating the association between obesity and depression (59) and the 2010 systematic review and meta-analysis which examined the association between obesity and anxiety (60), both in non-clinical general population samples. The authors conclude that evidence supporting the association between obesity and depression is inconclusive with cross-sectional studies reporting varied effects of no significant increased likelihood of depression (OR= 0.60, -1.55 - 1.70), and increased likelihood of depression (OR= 1.50, 1.1 - 2.1) in obesity. Unfortunately a meta-analysis was not conducted, with analyses restricted to a narrative synthesis (59). The systematic review and meta-analysis examining the association between obesity and anxiety concluded that there is a moderate level of evidence supporting the association between obesity and anxiety disorders, with pooled cross-sectional data indicating that obese individuals are more likely to experience anxiety (OR= 1.4, 1.2 - 1.6) than non-obese individuals, however, the role of obesity severity has not yet been established (60). We can accept the conclusions of the two reviews with confidence, incorporating data from 24 studies and 167,062 individuals within the obesity and depression review (59) and data from 16 studies and 346,289 individuals for the review focussing on obesity and anxiety (60).

The systematic literature search conducted and reported within this chapter has highlighted that within the body of literature examining the relationship between psychological factors and adiposity, there is a need for greater methodological rigour within review articles. Of the ten reviews discussed, only two reported the number of

studies included in the reviews (59, 60), with the remaining reviews not providing this information. Additionally, many of the identified reviews utilised a non-systematic approach which means that any reported results should be interpreted with caution. Furthermore, a narrative rather than statistically-based approach was widely used, with only one of the reviews including a meta-analysis providing an estimate of the effect of obesity on mental health, indicating a gap in the body of literature.

Table 3.1.4: Reviews examining the relationship between psychosocial variables and adiposity

First author, year	Sample size	Focus of review	Conclusions
Kral, 1985	32 papers referenced, number of individuals unknown	Narrative, non-systematic review, focussing on defining and characterising the health risks of "morbid obesity", defined as "an absolute (45.4kg or 100lb) or relative (60%) excess in weight above desirable weight associated with maximum life expectancy".	Extreme obesity is associated with dramatic increases in mortality relative to the normal-weight population. The health risk of extreme obesity is well recognized. Decreased quality of life, specifically functional limitations and impairment of daily activities are evident and should be quantified in the same way as morbidity and mortality.
Stunkard, 1992	82 papers referenced, total number of individuals unknown	Narrative, non-systematic review, focussing on the psychological aspects of severe obesity. Specifically, baseline associations and changes following weight loss after bariatric surgery are examined.	Severe obesity is not associated with any single personality type or trait and is not associated with greater levels of psychopathology than average-weight individuals. Complications which are associated with severe obesity include body image disturbance and binge eating. Post-surgery studies have shown improvements in self-esteem, body image, eating behaviour, positive emotion and marital satisfaction. Greater improvements are seen for those receiving surgery relative to dietary treatment alone.
Herpertz, 2003	40 papers referenced, number of individuals N=3,739	Narrative, non-systematic review, focussing on the psychosocial and mental health outcomes following bariatric surgery	Mental health and psychosocial status are improved post bariatric surgery intervention for the majority of individuals, with psychiatric co-morbidity, affective disorders including anxiety and depression and psychopathologic symptoms shown to decrease following surgery.
van Hout, 2004	75 papers referenced, number of individuals unknown	Systematic literature search, focussing on defining the psychological profile of the morbidly obese.	"Morbid obesity" is associated with impaired quality of life, depression, anxiety, low self-esteem, poor impulse control and eating behaviour which includes rigid control, dieting and disinhibition. These characteristics are more pronounced in surgery-seeking individuals. The literature is not conclusive and assessment methods require improvement.
Sarwer, 2005	128 papers referenced, number of individuals unknown	Non-systematic literature review, focussing on the psychosocial and behavioural aspects of individuals seeking bariatric surgery. Specifically, baseline associations and changes following weight loss after bariatric surgery are examined.	Surgery-seeking individuals are at increased risk of psychosocial complications, suggesting an increased prevalence of psychiatric symptoms and psychopathology, including mood and anxiety disorders and binge-eating disorders, as well as impairments in quality of life encompassing physical health, body image, and relationship functioning. Whilst numerous studies have shown post-surgery psychosocial improvements, conclusions are limited by lacking standardised measurements and control groups. Some studies have shown improvements decrease with time and post-surgery deterioration in psychosocial status.

Table 3.1.4 Continued: Reviews examining the relationship between psychosocial variables and adiposity

First author, year	Sample size	Focus of review	Conclusions
Sarwer, 2008	123 papers referenced, number of individuals unknown	Non-systematic literature review, focussing on the psychosocial and behavioural changes following weight loss after bariatric surgery and after body-contouring post-weight loss.	Post-surgery weight loss is associated with psychosocial improvements including quality of life, depression, self-esteem and body image, however this may be limited to the first few years. It is unclear whether baseline characteristics impact on post-surgery outcomes. There is limited research examining associations between psychosocial characteristics and body-contouring surgery.
Bocchieri, 2002	79 papers referenced, number of individuals unknown	Systematic literature review of the psychosocial outcomes of bariatric surgery for morbid obesity, with an assessment of the theoretical and methodological issues.	Post-surgery weight loss appears to be associated with improvements in mood, depression and anxiety, however more research is needed to understand surgery outcomes, specifically relating to the impacts on psychological distress and discrimination, general quality of life, obesity-related pain and gender differences. More consistency in research methodology is required.
Sarwer, 2012	100 papers referenced, number of individuals unknown	Non-systematic literature review, focussing on the relationships between extreme obesity and quality of life, with specific emphasis on sexual function, examining baseline characteristics and post-surgery changes.	Extreme obesity appears to be associated with difficulties in sexual functioning and impairment in sexual quality of life. The relationship between sexual quality of life, obesity and other related psychosocial constructs including body image dissatisfaction and depression is complex. The association between sexual quality of life and extreme obesity is under-researched and requires further investigation.
Atlantis, 2008	24 studies included, 4 prospective cohort, 20 cross-sectional studies. Number of individuals N=167,062	Systematic literature review of epidemiological studies, focussing on the effects of obesity on depression.	Obesity appears to increase the odds of future depression outcomes, with consistent effect sizes reported in prospective cohort studies however, those reported in some cross-sectional studies showed the association in females but not males, and some studies showed no association in combined samples. Obesity appears to be related to depression, however evidence is weak as good-quality prospective studies are limited and cross-sectional studies cannot confirm causality.
Gariepy, 2010	16 studies included, 2 prospective cohort, 14 cross-sectional studies. Number of individuals N=346,289	Systematic review and meta-analysis focussing on the association between obesity and anxiety disorders in the general population.	There appears to be a positive association between obesity and anxiety amongst males and females, with pooled cross-sectional studies suggesting obesity is associated with increased risk of anxiety (OR= 1.4, 1.2 - 1.6). Effect sizes from prospective data were varied and a causal relationship cannot be inferred. However, there is a moderate level of evidence for a positive association between obesity and anxiety. Further research is needed to determine causality through prospective studies and determine the role of obesity severity which is as yet not established.

3.1.5 Rationale for the assessment of quality of life in extreme obesity

Evidence suggests an association between increasing adiposity and depression (59), anxiety (60) and reduced quality of life (61). Indeed, obesity has been linked to widespread psychopathology with obese individuals more likely to attempt suicide and demonstrate suicidal behaviour, and an even greater risk is observed in extreme obesity (62). However, there are inconsistencies in the research literature, with some studies supporting an association between obesity and physical but not mental quality of life (63-65). Furthermore, current understanding is limited as studies have focused on those extreme obese individuals who are specifically seeking bariatric surgery (68) and with the exception of one study (74), have not encompassed those individuals attending medical weight-management services.

3.1.6 Aims

This chapter aims to explore the quality of life and mental health characteristics of a sample of extreme obese individuals attending two different treatment pathways offered by the HEFT Specialist Weight Management Service; the Community Weight Management Service (CWMS) and the Specialist Lifestyle Management (SLiM) programme. The cross-sectional association between adiposity and quality of life will be examined using baseline clinical examination and self-report data collected from individuals seeking treatment at the service prior to treatment commencement. Additional subsample analysis will examine the quality of life and mental well-being characteristics of the CWMS subsample in greater detail. The chapter concludes with a summary of the observed relationship between adiposity, mental health and quality of life, and finally recommendations to enhance specialist weight management services are presented.

3.2 METHODS

3.2.1 Research design

The study explored the mental health and quality of life characteristics of a sample of extreme obese individuals entering the Specialist Weight Management Service, conducted as part of an evaluation of the efficacy of the service. All patients were referred to the service by their GP as a result of fulfilling the criteria of having BMI $\geq$40.0kg/m^2 or alternatively BMI $\geq$35.0kg/m^2 with a weight-related health condition, such as type 2 diabetes or hypertension. The study included a sample of 414 individuals aged 19 to 76 years, 262 of whom entered the Specialist Community Weight Management Service (CWMS) between February 2008 and August 2012 and 152 of whom entered the Specialist Lifestyle Management (SLiM) programme between August 2009 and February 2013.

3.2.2 Specialist Weight Management Service

The two medically supported treatment pathways delivered within the Specialist Weight Management Service operated by HEFT have been described in Chapter one; however the following brief description is for reference. The CWMS provides comprehensive multidisciplinary care for a 12-month period from a team of specialist physicians, dietitians, and psychologist, delivered through one-to-one appointments in the community. The SLiM programme provides patient education, peer-support and self-management through a structured programme of six consecutive monthly weight management group-sessions.

3.2.3 Demographic and clinical information

Participants' initial weight and height data were recorded at baseline and BMI was calculated by dividing participants' weight in kg by height in meters squared. Demographic details including participants' age, gender, and ethnicity as well as clinical details including whether participants had co-morbid type 2 diabetes were routinely recorded prior to treatment commencement for individuals attending both the CWMS and SLiM pathways. The use of insulin was routinely collected for those entering the SLiM pathway only. Additional data were routinely collected for those entering the CWMS pathway including waist circumference, blood pressure, smoking status and alcohol consumption. Details of obesity-related co-morbid health conditions were also recorded focussing specifically on type 2 diabetes, CVD, hypertension, OSA, and arthritis. Additional demographic details were also routinely collected for those attending the CWMS, including marital status, employment status and whether participants had children.

3.2.4 Quality of life and mental health measures

The quality of life and mental health measures have been described in detail in Chapter two, however the following brief description is provided for reference. Upon entering both treatment pathways, participants were asked to complete validated self-report questionnaires before attending their first service appointment. Quality of life and mental health were assessed using three measures, an obesity-specific quality of life measure, the IWQOL-Lite (83), a general quality of life measure, the EQ5D-3L (84), and the HADS anxiety and depression screening tool (85). The IWQOL-Lite was administered to individuals entering the CWMS and SLiM pathways, whilst the EQ5D-3L and HADS were administered to individuals entering the CWMS only.

3.2.5 Statistical analysis

Data were analysed using IBM SPSS Statistics (version 21.0). T-tests, cross-tabulation, Chi^2 and analysis of variance (ANOVA) were conducted to examine the associations between variables. BMI tertile groups were created for the CWMS and the SLiM samples separately. This gave rise to the following groups for the CWMS sample: first, BMI tertile $\leq 42.99 kg/m^2$; second, BMI tertile $43.00 \leq 48.61 kg/m^2$; third, BMI tertile $\geq 48.62 kg/m^2$. The following groups were created for the SLiM sample: first, BMI tertile $\leq 46.85 kg/m^2$; second, BMI tertile $46.86 \leq 53.82 kg/m^2$; third, BMI tertile $\geq 53.83 kg/m^2$. Linear regression coefficients were calculated to assess the relationship between BMI and quality of life as measured by IWQOL-Lite scores and overall perceived health status as measured by EQ5D-3L VAS. Analyses were conducted for the whole sample and repeated in gender-stratified sub-groups. Three hierarchical models are presented: crude; adjusting for age and sex and interaction between sex and BMI; and additionally adjusting for the presence of co-morbid type 2 diabetes, hypertension, arthritis, OSA and CVD.

Within the CWMS subsample, logistic regression models were constructed to assess the association between BMI and presence of anxiety and depression as measured by HADS, and presence of problems in mobility, self-care and performing usual activities as measured by EQ5D-3L, with the first BMI tertile group as the reference. The odds ratios (ORs) and 95% confidence intervals (CIs) for three hierarchical models are presented: crude; adjusting for age and sex; and additionally adjusting for the co-morbidities; diabetes, hypertension, arthritis, OSA and CVD.

3.3 RESULTS

3.3.1 Demographic, clinical and quality of life characteristics

Table 3.3.1 shows the comparison between the samples entering the CWMS and the SLiM pathways. Those attending the CWMS were significantly younger with a mean age of 43.1 vs 48.5 years ($p < 0.001$), of lower BMI with a mean of 47.0 vs 51.3 kg/m^2 ($p < 0.001$), less likely to have type 2 diabetes: 26.3 vs 35.5% ($p < 0.05$) and less likely to be referred for bariatric surgery: 14.5 vs 30.9% ($p < 0.001$), than those attending the SLiM programme. Those attending the CWMS also reported significantly better physical function, with mean IWQOL-Lite physical function scores of 42.4 vs 32.3 ($p < 0.001$), than those attending the SLiM programme, whilst there were no significant differences in other IWQOL-Lite scores between the two samples. Data indicate that within both samples quality of life was low, with sample mean IWQOL-Lite scores ranging from 26.2 (self-esteem) to 51.2 (work) for the CWMS sample, and 28.5 (self-esteem) to 50.3 (work) for the SLiM sample, whereby 100 represents optimum quality of life.

Table 3.3.1: Comparison of the demographic and clinical characteristics of the CWMS and SLiM samples

	CWMS	SLiM	P
N	262	152	
Age (years)	43.1±11.8	48.5±11.1	<0.001
Sex (% female)	74.8	73.0	0.690
Ethnicity (%)			0.069
White European	90.8	80.3	
Asian	5.6	9.9	
Black African/Caribbean	2.8	8.6	
Other	0.7	1.3	
Weight (kg)	132.1±24.7	140.0±28.3	0.003
Body mass index (BMI, kg/m^2)	47.0±7.9	51.3±9.9	<0.001
Type 2 diabetes (%)	26.3	35.5	0.049
Referral to surgery (%)	14.5	30.9	<0.001
Baseline IWQOL-Lite			
Physical function	42.4±25.3	32.3±22.1	<0.001
Self-esteem	26.2±27.5	28.5±27.8	0.424
Sexual life	41.9±35.9	46.5±31.1	0.219
Public distress	40.5±28.9	36.3±26.7	0.154
Work	51.2±30.3	50.3±28.3	0.760
IWQOL-Lite total	39.5±22.1	36.1±19.9	0.130

Data are percentages and means ± standard deviations.

Table 3.3.2 illustrates that within the CWMS sample those with increasing levels of adiposity were more likely to have type 2 diabetes mellitus, hypertension, CVD and OSA and were also more likely to be referred to receive bariatric surgery. Table 3.3.3 shows that in the CWMS sample those with increasing levels of adiposity also experienced significantly more problems in mobility, self-care and performing usual activities. Increasing levels of adiposity were also associated with poorer scores on the IWQOL-Lite subscales, physical function, public distress, work and IWQOL-Lite total score. Perceived health status as measured by EQ5D-3L was also poor with a sample mean of 44.0, whereby 100 represents best possible health state; which is considerably worse than the UK general population mean score of 82.8 (148). There were no significant differences in

anxiety and depression scores, with prevalence of anxiety and depression consistently high across the BMI groups. Data for the whole CWMS sample indicate that the prevalence rates of symptoms of anxiety (70.3%) and depression (66.2%) are very high. Indeed, levels of severe anxiety and depression symptoms defined by the higher cut-point of scores ≥11 are also substantial, with severe anxiety symptoms experienced by 48.3% of the sample and 40.4% of the sample experiencing symptoms of severe depression.

Table 3.3.2: Demographic and clinical characteristics of the CWMS sample across BMI tertiles

	Whole sample	**1st BMI tertile ≤42.99**	**2nd BMI tertile 43.00 ≤ 48.61**	**3rd BMI tertile ≥48.62**	**P**
N	262	87	87	88	
Age (years)	43.1±11.8	43.0±13.2	41.7±10.2	44.7±11.8	0.234
Sex (% female)	74.8	72.4	77.0	75.0	0.783
Ethnicity (%)					0.585
White European	90.8	90.0	95.5	87.9	
Asian	5.6	5.0	2.3	8.6	
Black African/Caribbean	2.8	2.5	2.3	3.4	
Other	0.7	2.5	0.0	00	
Weight (kg)	132.1±24.7	112.6±14.7	129.1±15.6	154.2±22.3	<0.001
Body mass index (BMI, kg/m^2)	47.0±7.9	39.4±2.6	45.8±1.6	55.8±6.6	<0.001
Waist circumference (cm)	131.6±14.5	123.8±11.8	128.6±12.7	142.4±12.5	<0.001
Systolic blood pressure (mmHg)	140.9±17.7	136.0±14.5	140.4±17.0	146.4±20.0	0.009
Diastolic blood pressure (mmHg)	85.2±11.7	83.3±9.7	85.5±11.4	86.9±13.6	0.263
Type 2 diabetes (%)	26.3	24.1	18.4	36.4	0.022
Hypertension (%)	34.4	31.0	26.4	45.5	0.022
Arthritis (%)	24.0	21.8	19.5	30.7	0.190
OSA (%)	25.6	16.1	26.4	34.1	0.024
CVD (%)	11.1	9.2	5.7	18.2	0.026
Smoking (%)	25.5	31.7	23.0	22.2	0.655
Alcohol consumption (%)	64.7	62.9	81.0	52.9	0.004
Referral to surgery (%)	14.5	10.3	10.3	22.7	0.027

Data are percentages and means ± standard deviations
OSA= Obstructive Sleep Apnoea, CVD= Cardiovascular disease.

Table 3.3.3: Quality of life and mental health characteristics of the CWMS sample across BMI tertiles

	Whole sample	1st BMI tertile ≤42.99	2nd BMI tertile 43.00 ≤ 48.61	3rd BMI tertile ≥48.62	P
N	262	87	87	88	
Baseline IWQOL-Lite					
Physical function	42.4±25.3	54.1±24.9	40.4±23.6	34.1±23.7	<0.001
Self-esteem	26.2±27.5	30.4±30.5	24.1±24.4	24.5±27.5	0.286
Sexual life	41.9±35.9	47.3±36.9	43.5±35.6	35.2±34.7	0.128
Public distress	40.5±28.9	56.6±31.5	38.9±25.2	27.7±22.7	<0.001
Work	51.2±30.3	61.6±30.4	46.1±27.4	47.1±31.3	0.003
IWQOL-Lite total	39.5±22.1	49.0±23.3	38.5±19.9	32.1±20.2	<0.001
EQ5D					
Mobility problems %	66.7	55.9	63.0	80.3	0.006
Self-care problems %	35.7	29.9	27.2	50.0	0.006
Anxiety/depression problems %	75.3	73.1	75.6	77.0	0.864
Pain/discomfort problems %	85.3	80.0	86.3	89.3	0.272
Usual activities problems %	69.0	58.0	70.4	77.6	0.036
Perceived health status	44.0±20.1	47.4±19.4	42.4±19.0	42.9±21.8	0.303
HADS					
HADS anxiety	10.4±4.5	10.5±4.3	10.7±4.8	10.2±4.5	0.780
HADS depression	9.1±4.0	8.6±4.0	9.3±3.9	9.3±4.1	0.436
HADS Total	19.6±7.7	19.0±7.6	20.2±7.8	19.6±7.9	0.654
Anxiety symptoms % (≥8)	70.3	74.0	68.7	68.8	0.716
Depression symptoms % (≥8)	66.2	62.3	72.5	63.2	0.333
Severe Anxiety symptoms % (≥11)	48.3	50.7	48.2	46.3	0.860
Severe Depression symptoms % (≥11)	40.4	33.3	42.5	44.7	0.338

Data are percentages and means ± standard deviations
HADS= Hospital anxiety and depression scale.

Table 3.3.4 shows that within the SLiM sample those with increasing levels of adiposity were more likely to be referred to receive bariatric surgery, with 54.0% of the third BMI tertile being referred (p <0.001). Those participants with increasing levels of adiposity attending the SLiM programme also reported significantly poorer baseline physical function, public distress, work and IWQOL-Lite scores.

Table 3.3.4: Demographic, clinical and quality of life characteristics of the SLiM sample across BMI tertiles

	Whole sample	1st BMI tertile ≤46.85	2nd BMI tertile 46.86 ≤ 53.82	3rd BMI tertile ≥53.83	P
N	152	51	51	50	
Age (years)	48.5±11.1	46.8±11.6	51.4±10.3	47.3±11.1	0.071
Sex (% female)	73.0	62.7	76.5	80.0	0.118
Ethnicity (%)					0.678
White European	80.3	80.4	82.4	78.0	
Asian	9.9	11.8	9.8	8.0	
Black African/Caribbean	8.6	5.9	5.9	14.0	
Other	1.3	2.0	2.0	0.0	
Weight (kg)	140.0±28.3	118.4±16.3	137.1±18.0	164.9±27.1	<0.001
Body mass index (BMI, kg/m^2)	51.3±9.9	41.8±3.7	50.2±2.0	62.2±8.2	<0.001
Type 2 diabetes (%)	35.5	39.2	31.4	36.0	0.707
Insulin use (%)	9.2	13.7	5.9	8.0	0.367
Referral to surgery (%)	30.9	5.9	33.3	54.0	<0.001
Baseline IWQOL-Lite					
Physical function	32.3±22.1	41.2±23.3	32.6±22.3	22.8±16.5	<0.001
Self-esteem	28.5±27.8	28.6±28.1	28.4±28.3	28.4±27.3	0.999
Sexual life	46.5±31.1	48.4±29.1	50.3±32.1	40.7±31.9	0.292
Public distress	36.3±26.7	47.5±27.1	35.5±27.6	25.5±20.6	<0.001
Work	50.3±28.3	58.4±29.0	48.4±30.2	43.0±23.3	0.026
IWQOL-Lite total	36.1±19.9	41.9±19.8	36.5±19.9	29.6±18.2	0.008
Follow-up IWQOL-Lite					
Physical function	39.5†±24.0	51.4±24.2	40.4±23.9	28.9±19.2	<0.001
Self-esteem	34.7*±29.5	36.6±32.1	33.8±30.3	33.9±26.9	0.894
Sexual life	55.9*±34.4	56.6±34.4	62.9±34.2	49.3±34.0	0.221
Public distress	37.7*±29.5	49.3±28.1	39.2±33.4	27.9±24.1	0.020
Work	55.2†±30.6	65.8±31.1	57.8±30.9	43.6±26.2	0.003
IWQOL-Lite total	42.9†±22.3	51.2±23.6	43.3±22.1	35.4±18.9	0.005

Data are percentages and means ± standard deviations
**Indicates value is significantly different from baseline value, p <0.05, † p <0.001.*

3.3.2 Gender differences in quality of life

Table 3.3.5 shows the mean baseline IWQOL-Lite data for both samples split by gender. Within the CWMS there were significant gender differences in the self-esteem (p <0.001), sexual life (p= 0.039) and total IWQOL-Lite scores (p= 0.047), whereby scores indicated significantly poorer quality of life in females. There were more widespread gender differences within the SLiM sample, with significant differences observed in all subscales; physical function (p= 0.001), self-esteem (p= 0.001), sexual life (p= 0.035), public distress (p= 0.001), work (p= 0.020) and total IWQOL-Lite scores (p <0.001). As with the CWMS sample, scores within the SLiM sample indicated significantly poorer quality of life for females.

Table 3.3.5: Mean IWQOL-Lite quality of life scores in CWMS and SLiM samples split by gender

	Gender		P
	Males	**Females**	
CWMS:			
N	66	196	
Physical function	44.6±28.3	41.7±24.2	0.433
Self-esteem	36.5±32.6	22.5±24.5	<0.001
Sexual life	50.3±35.6	38.8±35.7	0.039
Public distress	42.3±30.0	39.9±28.6	0.570
Work	55.4±31.4	49.9±30.0	0.244
Total	44.2±24.0	37.8±21.2	0.047
SLiM:			
N	41	111	
Physical function	42.4±22.1	28.6±21.0	0.001
Self-esteem	40.9±29.9	23.9±25.6	0.001
Sexual life	55.3±25.5	43.0±32.4	0.035
Public distress	48.1±25.6	32.1±26.0	0.001
Work	59.3±26.5	46.9±28.4	0.020
Total	46.8±18.8	32.2±18.9	<0.001

Data are means ± standard deviations.

Table 3.3.6 shows the EQ5D-3L scores for the CWMS sample split by gender, with the proportion of individuals reporting the experience of 'some problems' or 'extreme problems' for each quality of life domain. There were no significant gender differences observed in EQ5D-3L scores. Table 3.3.7 shows the mean HADS scores for the CWMS sample split by gender. There were significant gender differences in HADS anxiety scores with a greater mean score for females (p= 0.012) and presence of anxiety in a greater proportion of the female sample (p= 0.004). Interestingly, there were no significant gender differences observed in mean total HADS scores (p= 0.064) and in HADS depression scores (p= 0.388). There were also no significant gender differences in presence of severe anxiety (p= 0.184) and severe depression (p= 0.405).

Table 3.3.6: Proportion of individuals reporting problems in EQ5D-3L quality of life in CWMS sample split by gender

	Gender		P
	Males	**Females**	
CWMS:			
N	66	196	
Mobility problems (%)	69.5	65.7	0.592
Self-care problems (%)	40.7	33.9	0.354
Anxiety/depression problems (%)	67.2	78.3	0.095
Pain/discomfort problems (%)	82.8	86.2	0.520
Usual activities problems (%)	67.8	69.5	0.812

Data are percentages
Presence of problems defined as level 2 (some problems) and level 3 (extreme problems) scores on EQ5D-3L

Table 3.3.7: Mean HADS anxiety and depression scores in CWMS sample split by gender

	Gender		P
	Males	**Females**	
CWMS:			
N	66	196	
HADS anxiety	9.2±5.0	10.9±4.3	0.012
HADS depression	8.7±4.0	9.2±4.0	0.388
HADS Total	17.9±8.2	20.1±7.5	0.064
Anxiety symptoms % (≥8)	55.7	75.4	0.004
Depression symptoms % (≥8)	66.1	66.3	0.978
Severe Anxiety symptoms % (≥11)	41.0	50.9	0.184
Severe Depression symptoms % (≥11)	35.7	42.0	0.405

Data are percentages and means ± standard deviations
Presence of anxiety and depression symptoms defined as HADS subscales Anxiety ≥8, Depression ≥8
Presence of severe anxiety and depression symptoms defined as HADS subscales Anxiety ≥11, Depression ≥11.

3.3.3 Linear regression: BMI, IWQOL-Lite and perceived health status

The IWQOL-Lite total measure and the subscales physical function, self-esteem, public distress and work were significantly negatively associated with increasing BMI in the CWMS sample, as illustrated in Table 3.3.8. An increase in one BMI unit was associated with a decrease of 1.93 in physical function, 1.62 in self-esteem, 2.69 in public distress, 1.33 in work, and 1.79 in total scores for the CWMS sample. Stratification by gender revealed that the observed effect sizes were greater in males for the physical function, public distress and total scores, indicating that within the male sample, BMI was more strongly negatively associated with these measures. Interestingly, BMI was not significantly associated with the sexual life subscale. The perceived health status measure (EQ5D-3L VAS) was also not significantly associated with BMI in the linear regression analysis.

Table 3.3.8: Linear regression of BMI predicting IWQOL-Lite subscale and total scores and perceived health status (EQ5D-3L VAS) in the CWMS sample stratified by gender

	Univariate		Model 1		Model 2	
	U.B.	**S.E.**	**U.B.**	**S.E.**	**U.B.**	**S.E.**
Physical function (N=238)	-0.83†	0.20	-1.95†	0.48	-1.93†	0.47
Male § (N=62)	-1.66*	0.54	-1.92*	0.53	-2.00†	0.50
Female § (N=176)	-0.66*	0.21	-0.56*	0.20	-0.51*	0.21
Self esteem (N=239)	-0.34	0.22	-1.53*	0.53	-1.62*	0.53
Male § (N=62)	-1.80*	0.63	-1.39*	0.60	-1.19	0.63
Female § (N=177)	0.01	0.22	-0.06	0.22	-0.11	0.22
Sexual life (N=213)	-0.56	0.32	-1.55*	0.77	-1.45	0.79
Male § (N=57)	-1.47	0.75	-1.55*	0.76	-1.21	0.81
Female § (N=156)	-0.33	0.35	-0.27	0.35	-0.29	0.36
Public distress (N=240)	-1.44†	0.22	-2.82†	0.53	-2.69†	0.54
Male § (N=62)	-3.00†	0.49	-2.76†	0.48	-2.48†	0.51
Female § (N=178)	-1.14†	0.24	-1.19†	0.24	-1.18†	0.25
Work (N=219)	-0.83*	0.25	-1.34*	0.65	-1.33*	0.66
Male § (N=53)	-1.39*	0.67	-1.23	0.68	-1.22	0.73
Female § (N=166)	-0.70*	0.27	-0.70*	0.28	-0.68*	0.28
IWQOL-Lite total (N=235)	-0.79†	0.17	-1.84†	0.43	-1.79†	0.44
Male § (N=62)	-1.82†	0.44	-1.78†	0.45	-1.60*	0.46
Female § (N=173)	-0.56*	0.19	-0.54*	0.19	-0.52*	0.19
Perceived health status (N=205)	-0.17	0.18	-0.12	0.49	-0.07	0.49
Male § (N=51)	-0.12	0.48	-0.11	0.50	-0.08	0.50
Female § (N=154)	-0.18	0.19	-0.18	0.20	-0.12	0.20

*U.B.= Unstandardised Beta, S.E.= Standard error, * p <0.05, † p <0.001*
Model 1 adjusting for age, gender and interaction between BMI and gender. Model 2 additionally adjusting for diabetes, hypertension, arthritis, obstructive sleep apnoea, cardiovascular disease
§ *Model 1 and 2 adjusting for age only.*

Table 3.3.9 shows the association between IWQOL-Lite scores and increasing adiposity in the SLiM sample. Interestingly, there was a different pattern of association between BMI and IWQOL-Lite compared to that observed in the CWMS sample. Physical function and public distress were significantly negatively associated with increasing BMI in the female subgroup, with an increase in one BMI unit associated with a decrease of 0.67 in physical function and 0.91 in public distress for females in the SLiM sample.

Table 3.3.9: Linear regression of baseline BMI predicting baseline IWQOL-Lite subscale and total scores in the SLiM sample stratified by gender

	Univariate		Model 1		Model 2	
	U.B.	**S.E.**	**U.B.**	**S.E.**	**U.B.**	**S.E.**
Physical function (N=152)	-0.61*	0.18	-0.42	0.27	-0.42	0.27
Male § (N=41)	-0.42	0.29	-0.42	0.29	-0.41	0.29
Female § (N=111)	-0.67*	0.21	-0.66*	0.21	-0.67*	0.21
Self esteem (N=149)	0.28	0.23	0.45	0.35	0.45	0.35
Male § (N=40)	0.45	0.40	0.44	0.36	0.44	0.36
Female § (N=109)	0.23	0.27	0.22	0.27	0.19	0.27
Sexual life (N=139)	0.06	0.26	-0.27	0.42	-0.27	0.41
Male § (N=39)	-0.27	0.35	-0.27	0.35	-0.28	0.32
Female § (N=100)	0.31	0.35	0.32	0.35	0.28	0.35
Public distress (N=148)	-0.68*	0.22	-0.26	0.33	-0.25	0.33
Male § (N=39)	-0.25	0.35	-0.27	0.34	-0.26	0.34
Female § (N=109)	-0.90*	0.26	-0.90*	0.26	-0.91*	0.26
Work (N=141)	-0.39	0.24	-0.15	0.37	-0.15	0.37
Male § (N=38)	-0.15	0.36	-0.14	0.31	-0.13	0.31
Female § (N=103)	-0.52	0.31	-0.52	0.31	-0.49	0.31
IWQOL-Lite total (N=146)	-0.28	0.16	-0.11	0.25	-0.10	0.25
Male § (N=39)	-0.11	0.25	-0.12	0.25	-0.11	0.24
Female § (N=107)	-0.35	0.20	-0.35	0.20	-0.37	0.20

*U.B.= Unstandardised Beta, S.E.= Standard error, * p <0.05, † p <0.001*
Model 1 adjusting for age, gender and interaction between BMI and gender
Model 2 additionally adjusting for diabetes
§ *Model 1 and 2 adjusting for age only.*

3.3.4 Logistic regression: BMI, EQ5D-3L and HADS anxiety and depression

Table 3.3.10 shows the logistic regression analyses of the EQ5D-3L subscales mobility, self-care and usual activities which were significantly associated with BMI. The fully adjusted model revealed an increased risk of mobility problems with increased BMI, with the odds ratios of 1.64 (0.78 - 3.44) and 3.44 (1.47 - 8.05) for second and third BMI tertile groups (P for trend <0.05) respectively, compared to those in the first BMI tertile group. There was a non-significant increased risk of self-care problems in the upper BMI tertile group, with an odds ratio of 1.87 (0.86 - 4.09) (P for trend= 0.104). The fully adjusted

model also revealed an increased risk of problems performing usual activities, with the odds ratios of 2.04 (0.98 - 4.26) and 2.45 (1.10 - 5.46) for second and third BMI tertile groups (P for trend <0.05) respectively, compared to those in the first BMI tertile group. Interestingly, the logistic regression analyses of presence of anxiety and depression symptoms as defined as HADS subscale score ≥8 revealed that anxiety and depression were not significantly associated with BMI across the range encountered in the sample of individuals attending the CWMS.

Table 3.3.10: Logistic regression of presence of problems in mobility, self-care and usual activities (EQ5D) and presence of anxiety and depression (HADS) in the CWMS sample by BMI tertiles

		1st tertile (≤42.99)	2nd tertile (43.00 ≤ 48.61)	3rd tertile (≥48.62)	P for linear trend
		Odds ratio (95% CI)			
Mobility problems (N=222)	**Univariate**	1.00	1.25 (0.64 – 2.44)	2.95 (1.40 – 6.22)*	0.004
	Model 1	1.00	1.32 (0.66 – 2.63)	2.83 (1.31 – 6.15)*	0.008
	Model 2	1.00	1.64 (0.78 – 3.44)	3.44 (1.47 – 8.05)*	0.009
Self-care problems (N=221)	**Univariate**	1.00	0.84 (0.41 – 1.72)	2.19 (1.09 – 4.39)*	0.018
	Model 1	1.00	0.88 (0.42 – 1.88)	2.05 (0.98 – 4.27)	0.044
	Model 2	1.00	0.89 (0.41 – 1.96)	1.87 (0.86 – 4.09)	0.104
Problems performing usual activities (N=223)	**Univariate**	1.00	1.71 (0.86 – 3.37)	2.65 (1.27 – 5.52)*	0.008
	Model 1	1.00	1.73 (0.86 – 3.44)	2.48 (1.17 – 5.23)*	0.016
	Model 2	1.00	2.04 (0.98 – 4.26)	2.45 (1.10 – 5.46)*	0.040
Anxiety (N=233)	**Univariate**	1.00	0.75 (0.37 – 1.51)	0.73 (0.36 – 1.45)	0.409
	Model 1	1.00	0.68 (0.33 – 1.42)	0.74 (0.35 – 1.54)	0.460
	Model 2	1.00	0.71 (0.34 – 1.50)	0.81 (0.37 – 1.74)	0.633
Depression (N=222)	**Univariate**	1.00	1.57 (0.78 – 3.15)	1.00 (0.51 – 1.98)	0.958
	Model 1	1.00	1.59 (0.79 – 3.20)	1.06 (0.53 – 2.11)	0.910
	Model 2	1.00	1.65 (0.80 – 3.40)	1.26 (0.61 – 2.62)	0.550

*Presence of problems defined as level 2 (some problems) and level 3 (extreme problems) scores on EQ5D-3L; Presence of anxiety and depression symptoms defined as HADS anxiety and depression subscale scores ≥8. * p <0.05, † p <0.001*
Model 1: adjusting for age and sex
Model 2 additionally adjusting for diabetes, hypertension, arthritis, obstructive sleep apnoea, cardiovascular disease.

3.4 DISCUSSION

The findings demonstrated that quality of life was markedly impaired in this sample of extreme obese individuals entering the CWMS and SLiM pathways of the service. Furthermore, gender differences were observed whereby quality of life was significantly poorer and prevalence of anxiety was greater for females. Whilst much of the research investigating the association between adiposity, quality of life and mental well-being has incorporated individuals across the spectrum of obesity, the present study is of particular importance as it focuses on the lesser-researched extreme obese population. Indeed, a significant negative association between increasing BMI and reduced quality of life was also observed, however this association was not observed for anxiety and depression, whereby the prevalence was consistently high across the sample.

The extreme obese individuals attending the service are those who have chosen to seek weight management support. It appears that those attending the SLiM programme are an even more complex group than those attending the CWMS, with a higher BMI and a greater proportion facing threats to health through type 2 diabetes. Indeed the SLiM group are also older than those individuals attending the CWMS, suggesting that they may have been facing the challenges of weight management for a longer period of time and may not have succeeded with previous weight loss and weight loss maintenance efforts.

A significant negative association was observed between increasing adiposity at these extreme BMI levels and quality of life, specifically in the areas of physical function, self-esteem, public distress, work and overall quality of life as measured by IWQOL-Lite scores, with increased adiposity associated with reduced quality of life in the CWMS sample. However, a different pattern of association was observed in the SLiM sample,

whereby a significant negative association between adiposity and quality of life was observed in the physical function and public distress areas of life for females only. Despite the fact that the association with adiposity was not significant in all subscales, the quality of life scores were markedly low, indicating substantial impairment. The association between adiposity and weight-specific quality of life as measured by IWQOL-Lite has been established, with the findings of one study indicating that BMI accounts for approximately 28% of the variance in total IWQOL-Lite scores (61). Previous research has shown that scores vary with degree of adiposity and treatment status, with those of higher BMI and those seeking treatment reporting significantly worse quality of life (61). In addition, changes in IWQOL-Lite score from baseline to follow-up post weight management intervention have been shown to correlate significantly with percentage of weight loss (149). The results obtained in the present study show a similar level of impairment in quality of life to those obtained in a study of bariatric surgery-seeking individuals, which reported scores ranging from 40.4 (work) to 46.2 (self-esteem) across IWQOL-Lite subscales (61). Interestingly, the present study reported one subscale, sexual life which was not shown to be significantly associated with adiposity. A similar pattern of results whereby significant association was not observed between BMI and sexual life has also been reported in a sample of over 400 bariatric surgery-seeking extreme obese individuals (135). The authors conclude that the lack of observed association is due to the high level of co-morbidities which may diminish the association between quality of life and BMI at the level of extreme obesity. However, the results of the present study show that the association between BMI and quality of life remains when controlling for co-morbid health conditions, suggesting that obesity negatively impacts on quality of life independently of the co-morbidities associated with extreme obesity. The fact that the

expected association between adiposity and sexual life was not observed in the present study and previous studies (135) indicates that there are additional factors outside of those measured which contribute to the reduced level of quality of life in the specific domains such as sexual life. Indeed, the substantial impairments in sexual quality of life in this population have been suggested to be greatly under-researched (136) and are thought to be associated with the broader aspects of stigmatisation and discrimination (150) as well as negative perceived body image (136, 151) experienced by this population.

Scores on the self-esteem subscale were notably lower than the other subscales, indicating specific impairment in this quality of life domain. The observed low level of self-esteem is consistent with findings from a comparison of White and African American US women, whereby White women scored significantly lower on self-esteem and sexual life compared to their African American counterparts in both class II and III obesity groups (152). These findings suggest that ethnic and cultural factors play a large role in the relationship between adiposity and quality of life and that self-esteem is an area which is particularly impaired in extreme obese individuals.

A similar pattern of association was observed for the EQ5D-3L, whereby significant associations were observed between adiposity and some, but not all of the EQ5D-3L subscales. Adiposity was associated with experience of problems in mobility, self-care and performing usual activities, with those in the upper BMI tertile more likely to experience problems in these areas. Whilst the fully adjusted models remained significant for the mobility and performing usual activities analyses, the self-care model was no longer significant. These findings are consistent with the limited previous studies that have shown general quality of life as measured by EQ5D-3L being poorest for individuals with extreme obesity, compared to those of BMI 30.0-34.9kg/m^2 and 35.0-39.9kg/m^2, as well as

overweight and underweight groups, relative to those of normal weight where quality of life scores are optimum (130, 153). Interestingly, the present study reported no significant association with adiposity for the other two EQ5D-3L subscale scores, pain and discomfort and anxiety and depression, despite individuals reporting the greatest amount of problems in these domains. The observed lack of association between anxiety and depression and adiposity is in contrast to previous research which has identified that individuals who are obese are at greater risk of experiencing depression (59), anxiety (60), and pain (130), relative to normal weight individuals. Likewise, no significant association between adiposity and perceived health status as measured by EQ5D-3L VAS was observed which is again in contrast to the findings of previous studies (130). There was however, a non-significant trend whereby perceived health status was highest for the first BMI tertile group (47.4) and lowest for the third BMI tertile group (42.9). Together, these findings suggest a possible ceiling effect for the EQ5D-3L tool being unable to detect differences within such a homogeneous group as the present sample in which the quality of life is consistently low. An additional aspect is the absence of normal weight individuals which truncates the BMI range, reducing the opportunity to identify an association, with those studies identifying an association usually including non-obese comparator groups.

The expected significant associations between adiposity and presence of anxiety and depression as measured by HADS were also not observed in the present study. However, it was evident that the prevalence rates of these psychological symptoms, indicated by scores ≥8, were consistently high across the sample (anxiety, 70.3% and depression, 66.2%) and are far greater than the UK general population rates of 33.0% for anxiety and 11.4% for depression (98). Indeed, the adjustment of cut-points to indicate severe levels of anxiety and depression (scores ≥11), revealed that these levels remained

high with 48.3% experiencing severe symptoms of anxiety and 40.4% severe symptoms of depression. The relationship between depression and obesity has been widely documented in the literature, with results from prospective studies indicating that obesity is associated with future incidence of depression and cross-sectional studies revealing significant positive associations between adiposity and depression, particularly in females (59). Data from the NHANES study demonstrated a dose-response relationship between depression and adiposity, with extreme obese individuals facing greater odds of experiencing lifetime major depression (OR= 2.60, 1.38 - 4.91), recurrent major depression (OR= 2.28, 0.93 - 5.60), depression in the past month (OR= 4.63, 2.06 - 10.42) and past year (OR= 2.92, 1.28 - 6.67) than those of BMI 30.0-34.9kg/m^2 and 35.0-39.9kg/m^2, relative to those of normal BMI (125). However, no significant variation in prevalence of anxiety and depression was observed across the levels of adiposity in the current sample, probably due to the truncated BMI range and homogeneity of the sample caused by the overall high prevalence of these conditions. Whilst much research has demonstrated evidence for an association between adiposity and both depression and anxiety (59, 60, 125) it is important to note that some studies have reported no significant association (154) or have reported non-significant trends (155-158). A systematic review and meta-analysis of the association between obesity and anxiety concluded that there is evidence in support of a positive association between obesity and anxiety, with pooled cross-sectional data indicating that obese individuals are more likely to experience anxiety (OR= 1.4, 1.2 - 1.6) (60). The results of the present study did not concur as no relationship was observed within this extreme obese sample, however the consistently high levels of anxiety and depression highlight that these conditions are widespread in this population. Furthermore, the truncation of the adiposity range is likely to contribute to the lack of observed association despite the high prevalence

of anxiety and depression symptoms within the sample. It is also of interest that the findings of the present study indicate that anxiety was more prevalent in the sample than depression, which reflects the UK general population prevalence rates which are also greater for anxiety than depression.

The mechanism of the association between adiposity, impairment in quality of life and presence of anxiety and depression is not yet established, with several proposed pathways through which obesity may lead to psychological co-morbidity and vice versa. Firstly, through the multiple health threats associated with obesity acting as stressors, and secondly through the negative effects of stigma and weight-related discrimination. Indeed frequency of stigmatisation and inability to adopt effective coping strategies have been shown to result in depressed mood (158). The relationship between obesity and depression specifically, appears to be bi-directional with obesity associated with increased experience of depression, and depressive episodes associated with further weight gain. Indeed, obese individuals are more likely to over-eat and gain weight relative to non-obese individuals during an episode of depression (159). A systematic review of the literature on the relationship between depression and adiposity reported however, that the majority of the evidence base was cross-sectional and thus causality could not be established (59).

Previous research has been criticised for the inclusion of only one measure of quality of life (130), and as such the inclusion of several quality of life measures is a novel aspect of the present study. Previous studies have utilised either general measures such as the EQ5D-3L (130, 153), and the SF-36 (134, 160), or condition-specific measures such as the Obesity Adjustment Survey (OAS) (129) and the Obesity Related Well-being (ORWELL 97) questionnaire (161); however, the IWQOL-Lite measure is the most widely used weight-specific measure (162). Findings of the present study suggest that in the

assessment of quality of life in the extreme obese patient population, both weight-specific and general quality of life measures can be utilised. Interestingly, the IWQOL-Lite and EQ5D-3L measures and the HADS mental health screening tool all contained subscales that were not associated with adiposity. Indeed, the specific domains which were not associated with adiposity; pain and discomfort, anxiety and depression, and sexual life were in fact the more severely affected aspects of life, likewise, none of the components of the HADS mental health screening tool were associated with adiposity, despite the fact that the tool determined the high prevalence of anxiety and depression in this extreme obese sample. Thus, the overall low quality of life and high prevalence of anxiety and depression symptoms and the BMI truncation are more likely to be responsible for masking the association with adiposity, rather than there being no association. This suggests that each of the tools may have limitations in capability of identifying differences between levels of extreme adiposity. Future studies likewise should utilise several quality of life measures, including those that are weight-specific and general in order to establish the responsiveness and validity of the measures in this minority patient group (163), as well as enabling deeper understanding of the additional factors which may influence the complex relationship between adiposity, quality of life and mental well-being.

A key strength of the present study is that it demonstrates that the negative impact on quality of life associated with increasing BMI remains even when controlling for the presence of co-morbid health conditions commonly experienced by the extreme obese population. Previous studies have concluded that the association between adiposity and quality of life is mediated by co-morbid health conditions such as chronic pain, cardiovascular disease and type 2 diabetes (63, 124, 164). However, the present study supports that the association is independent of co-morbid health conditions and suggests

that the role of co-morbidities in the relationship may have previously been over-estimated, while the impact of adiposity itself may have been underestimated in extreme obesity.

An additional strength of the present study is that it facilitates greater understanding of the quality of life and mental health characteristics of this lesser-researched extreme obese population. However, the present study has several limitations. The individuals characterised in the sample are those that had sought assistance in managing their weight and as a consequence it may not be appropriate to extrapolate these findings to the general extreme obese population. There are many extreme obese individuals who do not seek treatment and evidence suggests that non-treatment-seeking obese individuals experience lower levels of psychological distress (121) and impairment in quality of life (61) than those treatment-seeking individuals. The cross-sectional design of the present study means that it has not been possible to confirm a causal relationship between adiposity and the quality of life measures, however, the following longitudinal analyses chapter examines the association between change in BMI and change between pre- and post-intervention quality of life scores. The present study was also conducted as part of a pragmatic evaluation which meant that it was not possible to compare the characteristics of the extreme obese treatment-seeking group with a non-obese control group or an extreme obese non-treatment-seeking group for comparison. As such the findings of the present study should be interpreted with consideration of these factors, and future studies adopting a controlled design should be utilised in further investigation of the psychological co-morbidities of extreme obesity.

3.4.1 Summary of findings

The present chapter has highlighted the substantial psychological co-morbidity associated with extreme obesity. Among this sample of extreme obese individuals seeking treatment at the service there is a high prevalence of psychological co-morbidity, including presence of anxiety and depression symptoms and markedly impaired quality of life. Increasing adiposity was associated with a reduction in several areas of quality of life, but was not significantly associated with prevalence of anxiety and depression, although the lack of an observed association may be the result of limitations in study design.

3.4.2 Recommendations

Individuals attending weight management services have complex psychological needs and as such should receive support in managing the physical as well as mental co-morbidities of extreme obesity. If obesity is driven by underlying psychological issues, it is essential that support is given to address these factors if long-term weight loss is to be achieved. Support should be provided through tailored weight management interventions which focus on enhancing mental health and well-being, with a specific emphasis on self-esteem as an area for improvement, as this was the domain within which individuals showed the greatest impairment in quality of life. These strategies should be incorporated into the multi-disciplinary care of extreme obese individuals in order to minimise the harmful impact of the impairment in quality of life and mental well-being faced by these individuals.

CHAPTER FOUR:

4.0 LITERATURE REVIEW OF UK WEIGHT MANAGEMENT INTERVENTIONS FOR OBESITY

4.1.1 Literature review of UK weight management interventions for obesity: Literature search procedure

In order to place the outcomes of the Specialist Weight Management Service demonstrated in the present evaluation in context, the body of research literature examining the efficacy of other weight management approaches offered to obese individuals in the UK is reviewed. A literature search was conducted using the PubMed database, hand-searching reference lists of relevant articles and searching research project websites. The search included articles that detailed interventions aimed at achieving weight loss with or without weight maintenance components, delivered by individuals from healthcare or non-healthcare background, to an obese sample, defined as mean BMI ≥30.0kg/m^2. The review excluded studies describing surgical interventions and those which described baseline characteristics without outcome data. Articles were included if they were published up to and including March 2014, written in English and included an adult study population. A total of 25 studies were identified, 11 of which were primary care-led (Table 4.1.1), 5 specialist weight management services (Table 4.1.2), 8 commercial weight management programmes (Table 4.1.3) and the remaining study related to a sporting club-based programme (Table 4.1.4).

4.1.2 Primary care programmes

The most widely adopted primary care-led weight management programme is the Counterweight programme which was developed and launched in 2000 and provides training for primary care staff to implement and deliver a structured and evidence-based programme to obese individuals. The aims of the Counterweight programme were to 1) conduct a needs assessment and evaluate current service provision in primary care practice,

2) provide support and training to practice staff, 3) implement structured, theoretically- and evidence-based weight management interventions in the primary care setting, and 4) to evaluate the programme through a UK-wide trial (29). A total of 70 primary care practices took part, of which 58 were randomised to implement the Counterweight programme and 12 were randomised to act as a control comparator group, who would deliver the programme after a deferred period of two years once the second audit of practice activity had been completed. Practices of varying sizes were recruited from seven centres; Hammersmith, Luton, Bath, Birmingham, Leeds, Glasgow and Aberdeen, enabling variation in geographical location and levels of deprivation across the UK.

The initial audit collected information on the baseline approaches to weight management in the primary care practices, which was analysed in order to identify potential gaps in the provision of weight management care (165). This large-scale survey comprised anonymously-completed questionnaires and structured interviews conducted with 141 General Practitioners (GPs) and 66 practice nurses from 40 primary care practices in order to examine healthcare professionals' accounts of the service delivered under their care. Additionally the proportion of patients who had a weight or BMI ever recorded was obtained for the total patient population for each practice. A randomly selected sample of 100 medical records of obese patients were also reviewed from each practice to establish the use of anti-obesity medication and rates of referral to specialist weight management services.

The 40 practices recruited to the baseline audit were selected from within the seven Counterweight sites across the UK. Findings from the survey revealed that BMI was recorded for 64.2% of patients, suggesting that obesity may have been under-reported and under-diagnosed in primary care. The results of the self-reported questionnaires indicated

that the majority of GPs (83%) and nearly all nurses (97%) reported that they would raise the issue of weight with obese patients, with significantly more nurses discussing the issue ($p < 0.05$). Furthermore, the findings indicated that nurses spent more time discussing weight issues with patients, with 15% of GPs and 76% of nurses spending up to 10 minutes in consultations discussing weight-related issues ($p < 0.001$). Practice-based dietary counselling was the most common referral for obese patients (20%), with relatively few referrals to dietetic centres (4%) and obesity centres (1%), with prescription of anti-obesity medication also low (2%). The investigators concluded that the findings of the baseline audit indicated that there was a need for better recording and diagnosis of obesity. Where obese patients received an intervention this was most likely to take the form of brief opportunistic consultations with practice nurses. Furthermore, healthcare professionals tended to favour practice-based weight management interventions, with relatively few patients referred to external weight management services. As such the authors highlighted that these findings demonstrate the importance of establishing effective weight management interventions to be delivered in the primary care setting. Data collected from the baseline audit demonstrated that the annual healthcare expenditure of the patient sample increased by £16 for each obese individual with every increase in BMI unit, providing further evidence of the need for effective weight management interventions (166).

The findings of the baseline audit were primarily used to inform the development of a training programme to equip the practice nurses with the skills required to deliver the individual and group-based interventions. The aim of the programme was to introduce a new model of weight management in primary care incorporating complex patient interventions, modification of healthcare professionals' behaviour and practice screening

and referral systems. The outcomes of the first 12-month period of the Counterweight programme indicated that the majority of the recruited practices had received the training programme (93.5%), and a considerable proportion of practices were actively implementing the new weight management model (75.8%) (167). At 12 months a total of 1,549 patients had been recruited, with a mean BMI of 36.9kg/m^2, with 26% of those recruited classed as extremely obese with a BMI ≥40.0kg/m^2. Of those who had completed the minimum number of appointments (49% of those recruited), receiving the lifestyle intervention either in the group or individual consultation format, a substantial proportion (40%) had achieved weight losses of ≥5% of their baseline body weight at 12 months. The preliminary results indicated that the Counterweight programme was effective at facilitating weight loss in a primary care setting. However, it is important to note that when including all individuals who commenced the programme, thus including those who did not complete, a more modest proportion (16.2%) achieved weight losses of ≥5% body weight. Furthermore, during the initial 12-month evaluation period four practices withdrew prior to healthcare professional staff training and 11 practices stopped recruiting additional patients, with the authors suggesting that this was due to difficulties incorporating the programme into routine practice without additional funding resources.

A subsequent evaluation has also reported final outcomes of the five-year evaluation phase of the Counterweight programme (168). At the end of the evaluation period 2,095 patients were identified for inclusion, of which 1,906 were eligible across the 56 participating practices. Weight data was obtained for 642 individuals who completed a minimum of 12 months attendance, and 357 individuals who completed 24 months attendance. The characteristics of the total sample entering the programme (N=1,906) indicated that the sample were predominantly female (77%) with a mean age of 49.4 years

and mean BMI of 37.1kg/m^2, with 25.4% of the sample classed as extremely obese. The mean weight loss for those attending a minimum of 12 months was -3.0±6.6kg with a mean BMI reduction of -1.1±2.4kg/m^2, with weight losses of ≥5% baseline body weight achieved by 30.7% of the sample attending at 12 months. For those attending a minimum of 24 months, a mean weight loss of -2.3kg was achieved, with weight losses of ≥5% baseline body weight achieved by 31.9% of the sample. It is important to note that the reported outcomes were achieved via a variety of treatments which comprise the complex multi-component programme. For instance, of those completing 12 months attendance, 70% received the lifestyle intervention through individual consultations, 34% through group interventions, and 19% were prescribed anti-obesity medication, with some individuals receiving these treatments in combination and others in isolation. With such a complex intervention it is imperative to establish which components are the 'active ingredients' that contribute to the observed intervention effects. However these analyses were not conducted, meaning that such conclusions cannot be drawn. The initial publication (29) outlining the programme design stated that 18 practices were randomised to act as control comparators in the evaluation. However, the subsequent evaluations (167, 168) make no reference to the control practices, which is a major flaw in the implementation of the study design and reporting of outcomes.

A cost-effectiveness analysis of the Counterweight programme has been conducted (169), which suggested that the weight losses of -3.0kg and -2.3kg achieved by those attending the programme, at 12 and 24 months respectively, is a significant improvement relative to the estimated population rate of weight gain of +1kg per year. The estimated cost of delivery of the Counterweight programme was £59.83 per individual entered onto the programme, and was cost-saving, assuming that the 12-month weight loss of -3.0kg

achieved by 45% of the sample was completely regained over the following two-year period and assuming that non-attenders (55% of the sample) gained weight at the rate of +1kg per year. Evaluation of the Counterweight programme has demonstrated the efficacy of a novel weight management model implemented in primary care settings on a large scale across the UK. However, the observed weight losses were relatively small.

In order to increase individuals' access to the programme, a pilot service operating the programme from pharmacies was introduced to areas where the programme was not available at GP practices (170). Sixteen community pharmacies took part in the pilot study in Fife, Scotland, recruiting a total of 458 individuals. The sample was predominantly female (74.7%), with a mean age of 54 years and mean BMI of 36.1kg/m^2, with 21.2% of the sample classed as extreme obese at baseline. The Counterweight lifestyle intervention was delivered by pharmacy staff through one-to-one appointments, with initial appointments lasting between 10-30 minutes in duration and taking place monthly for the first six months, with follow-up appointments at 6, 9 and 12 months. Total patient contact time was estimated to be approximately 130 minutes for the entire duration of the programme. Follow-up data was available for 314 individuals at 12 months post-baseline, with these individuals achieving a mean weight loss of -4.1kg (-2.8 - -5.4), with 41.6% of individuals attending at 12 months achieving losses of ≥5% of their baseline body weight. In addition to analysing available case data the authors also reported 12-month weight outcomes calculated through analysis of Last Observation Carried Forward (LOCF) data. This demonstrated a more conservative mean weight loss of -1.7kg (-1.3 - -2.1), with a reduced proportion of the sample, 15.9% achieving ≥5% loss of baseline body weight. Furthermore, subgroup analyses of 64 extreme obese individuals with baseline BMI ≥40.0kg/m^2 were conducted, with those completing 12 months of attendance achieving a

mean weight loss of -7.4kg (-3.1 - -11.6), with 46.7% achieving ≥5% loss of baseline body weight. Similarly, analyses of the LOCF data indicated more conservative weight losses for the BMI ≥40.0kg/m^2 subgroup, with a mean loss of -2.4kg (-1.1 - -3.7), with 15.6% achieving ≥5% weight loss. Interestingly, there were no significant differences in the weight loss achieved by individuals across the baseline BMI range, supporting that the Counterweight programme as delivered in a community pharmacy setting was able to facilitate weight loss across the spectrum of overweight and obesity. However, when considering all of those enrolled on the programme, analysis of Baseline Observation Carried Forward (BOCF) data demonstrated much more conservative losses at 12 months, with a mean weight loss of -1.0kg (-0.6 - -1.4), with 10.2% achieving ≥5% baseline body weight loss. A key strength of the study is that it effectively demonstrated the implementation of an established weight management model in a new setting, delivered by a different group of healthcare professionals, namely pharmacists and predominantly pharmacy-assistants, rather than by trained nurses. The study also included a detailed level of reporting of outcome measures, enabling comparison between those completing the programme for whom data were available and those with missing data whereby imputation of last and baseline observations was used. Whilst the study included 12-month outcome data for individuals, longer-term data would be necessary in order to demonstrate whether the initial weight loss achieved could be maintained beyond the initial one year period.

A different weight management approach combining lifestyle education with a Low Energy Liquid Diet (LELD) approach has also been implemented in 25 practices delivering the original Counterweight programme in Scotland (33). A total of 91 patients with a BMI ≥40.0kg/m^2 were recruited to the feasibility study assessing the effectiveness of a LELD intervention in extreme obese individuals in a primary care setting. The sample was

predominantly female (81.3%), with a mean BMI of 48.0kg/m^2, and a mean age of 45.7years. The intervention was delivered by primary care nurses and dietitians who had received specialist training in the use of LELD, and the aim of the intervention was to facilitate ≥15kg weight loss over the 12-month programme duration. The intervention comprised three stages, the provision and supervision of the LELD which was maintained for a period 12-weeks or until individuals had obtained ≥20kg weight loss, during which time individuals also received structured lifestyle education during fortnightly appointments. This was followed by a phase of food reintroduction lasting approximately 6-8 weeks in duration, during which time the fortnightly lifestyle education appointments continued. The final phase of the intervention was aimed at achieving weight maintenance, whereby individualised meal plans were followed in conjunction with lifestyle education at monthly appointments. The LELD phase of the intervention was completed by 64% of the sample, with a sample mean weight loss at 14-weeks of -16.9±6.0kg, which equated to a loss of -12.6±4.5% baseline body weight, with 69% of those completing the LELD phase achieving the targeted weight loss of ≥15kg. The food reintroduction phase was completed by 41% of the sample, with a mean further weight change of -2.1±3.7kg after the 9-week period. On completion of the LELD and food reintroduction phases, a mean weight loss from baseline of -19.1±7.5kg, equating to -14.6±5.1%, was achieved, with 77% of those completing both phases achieving ≥15kg weight loss. The final phase of the intervention, weight maintenance was completed by 75% of the sample, with a mean weight change from baseline of -12.4±11.4kg, equating to -9.1±8.2%, with weight loss ≥15.0kg achieved by 44% of those completing the final phase and 33% of those recruited to the feasibility study. The feasibility study demonstrated that the LELD in combination with lifestyle education was effective at facilitating larger weight losses, as necessary for those

individuals with extreme obesity. The estimated cost of delivery of the LELD intervention was £861.05 per patient entered, a cost which is considerably larger than that of the original Counterweight programme which was delivered at a cost of £59.83 per individual. The larger cost is expected given the greater intensity of the LELD intervention and the greater amount of weight loss achieved. The LELD intervention can be implemented to large numbers of individuals in primary care settings and was demonstrated to be a cost-effective alternative to surgical intervention. For instance, for the cost of £1million a total of 1161 patients receiving LELD treatment would result in 12-month maintained ≥15kg weight losses for 383 patients, compared to 133 patients receiving laparoscopic banding, resulting in ≥15kg weight loss for 110 patients also for a cost of £1 million (171).

The outcomes of 6,715 individuals attending the Counterweight programme have been published providing an overview of the overall effectiveness of the programme (172). The evaluation comprised outcome data from the implementation of the programme in 184 general practices, 16 community pharmacies and a community-based service. Attendance for the combined implementation at 12 months was 28%, which was markedly lower than the 45% attendance rate reported in the original evaluation detailing the five-year outcomes (168). Those attending at 12 months achieved a mean weight loss of -3.7kg (-3.3 - -4.4), with 35.2% achieving ≥5% weight loss, which is a greater proportion than the 30.7% of the sample reported to achieve ≥5% weight loss in the original evaluation (168). Interestingly, the evaluation additionally reported intention to treat data detailing the outcomes for the whole sample, incorporating data from those individuals who did not attend enough sessions to classify as completers of the programme, with data indicating that of the whole sample, a more modest proportion of 10.0% achieved ≥5% weight loss at 12 months. This evaluation provides support for the efficacy of the Counterweight programme delivered in

primary care settings, with consistent weight loss achieved, and demonstrates that the greatest weight losses achieved are among those who fully attend the programme. The study highlights the importance of understanding reasons for non-attendance and strategies to overcome barriers to attendance, in order to maximise the efficacy and weight losses achieved through the implementation of the programme.

As an alternative to delivering the Counterweight programme, other primary care teams have devised and delivered their own 'in-house' services facilitated by healthcare professionals, an example of this is a programme delivered by community nurses in Camelon, a region of high socio-economic deprivation in Scotland (30). The Camelon model which was delivered by community nurses and a dietitian, focussed on weight management specifically for obese adult men. The model comprised an initial 40-minute screening appointment conducted in community settings, in which individuals were invited to join the Camelon programme, followed by a 20-minute pre-programme individual assessment appointment in which individuals were given further information about the programme, and baseline measures were obtained. The subsequent 12-week weight management programme was conducted in male-only groups, with each session lasting 60-minutes and taking place in the evening. The programme used behaviour change techniques to achieve a balanced healthy diet and increased physical activity, with an aim of facilitating between -0.5 and -1.0kg weight loss per week. The evaluation provides an extremely useful detailed description of the intervention programme, providing explicit detail of the content of each of the sessions and specifically describing the techniques used in order to tailor the lifestyle information and delivery of the information to be most appropriate for the male patient population. This detail of reporting is a major strength of the evaluation as transparency enables replication of the principles of the programme in the

design and implementation of future weight management programmes. Of the 1,855 males attending the initial health clinic visit, 105 eligible individuals took part in the programme, with analyses comparing the outcomes of those participants who attended the programme with those who chose not to join the programme. At the end of the 12-week programme, of the 105 males that took part, 80 (76.2%) completed the programme, achieving a mean weight loss of -5.0kg, with 44.3% of those completing the programme achieving a weight loss of ≥5% of their baseline weight, of whom 8.9% achieved losses of ≥10% of their baseline body weight. Post-programme follow-up was available for a very limited number of 20 individuals, obtained between 1-49 months after finishing the programme, who achieved a mean weight loss of -3.7% of their baseline weight after the longer-term follow-up. Long-term outcome data would be needed for a larger sample size in order to establish the efficacy of the programme. Furthermore, the quantitative analysis would have been improved by including comparison of the baseline characteristics and outcomes obtained between those completing the programme and those who did not, and additionally including intention to treat data detailing the outcomes for all individuals entering the programme. It is a limitation of the study that such a small proportion (13.6%) of the 770 obese individuals identified as eligible potential participants went on to attend the programme, with a total of only 110 joining the programme over the four-year period between 2003-2007. The majority of those identified as eligible (69.4%) chose not to join the programme waiting list, with this suggesting that a greater understanding of the barriers to participation are required in order to improve attendance rates and thus strengthen the intervention.

A major strength of the evaluation is the inclusion of a qualitative component, which examined individuals' experiences of attending the programme through two focus

groups conducted with separate samples of eight participants and one focus group conducted with eight partners of the participants. The qualitative work explored the participants' reasons for joining the programme, which were identified as personal health concerns, pressure from family members and the use of humour and male-only aspects of the programme. The participants also highlighted which information delivered during the programme that they had personally found to be the most helpful. These included advice about reducing portion sizes, changing cooking methods and learning about nutritional labelling. Participants' reasons for continued attendance in the programme were also shown to be enjoyment and the rapport built with facilitators of the programme. Finally, family member involvement with the programme was also discussed by both participants and partners, suggesting that the lifestyle changes had extended beyond the individual participants and were adopted by the wider family.

The effectiveness of other primary care-led interventions have been evaluated using the more rigorous Randomised Controlled Trial (RCT) design (31, 32, 173). The first of which, evaluated the impact of a brief training intervention delivered to nurses and GPs from 22 primary care practices in the north of England, in the provision of a new weight management model (173). The training consisted of three 90-minute sessions delivered to nurses. These were completed within a two-week period, detailing information on the clinical benefits associated with weight loss and a range of treatment options to be offered to patients including the prescription of an individualised 500 calorie deficit low-energy diet, guidance on increasing physical activity and pharmaceutical treatment. On completion of the training, the new model of weight management was delivered to 415 obese individuals, recruited as a result of meeting the inclusion criteria of having a BMI $\geq$30.0 kg/m^2 and being aged 16-64 years. Participants received individual fortnightly

appointments until ≥10% body weight loss was achieved, after which there was a period of weight maintenance which comprised monthly or bi-monthly appointments.

The primary care-based RCT evaluated the effectiveness of the new weight management model versus a control arm comprising 22 of the 44 recruited practices who were instructed to provide usual care to obese individuals for the duration of the 18-month study period. Weight outcomes were obtained at 3, 12 and 18 months post-intervention and whilst there were no significant differences in weight between the intervention and control arms at each time point, there was a non-significant trend for the intervention arm to be heavier than the control group by +0.6kg (-2.1 - 3.2), +1kg (-1.9 - 3.9), and +1.3kg (-1.8 - 4.4), respectively across the study duration ($p > 0.05$). There was also little change from the baseline values, with the intervention arm achieving losses of -0.4kg and -0.5kg at 3 and 12 months from baseline. However this slight weight loss was regained and at 18 months there was no change from the baseline weight of 100.8±18.1kg. The control arm of the study achieved greater weight loss than the intervention arm, with losses of -0.4kg, -0.9kg and -0.7kg at 3, 12 and 18 months post-baseline, respectively. The analyses were conducted using available case data, with 3-month data obtained for 78.8%, 12-month data obtained for 67.0%, and 18-month data obtained for 63.0% of the sample. This RCT demonstrated that the intervention did not facilitate weight loss in the sample of high BMI individuals, with mean baseline BMI values of 37.0kg/m^2 in the intervention arm and 36.9kg/m^2 in the control arm. The investigators suggested that greater weight change was not observed in individuals receiving the intervention due to low levels of implementation, with intervention practices reporting that individuals were receiving an average of eight consultations over the 12-month period, which is far less contact than the fortnightly appointments which were recommended as per study protocol, which would equate to a

minimum of 20 consultations. Indeed, individuals in the control arm of the study received a similar number of appointments, 6 over the 12-month duration, which may account for the similar weight outcomes achieved by the study arms. Whilst the RCT was not able to determine the effectiveness of the intervention, as the new weight management model was not implemented as per protocol, the trial has highlighted the difficulties of implementing new models of practice in primary care settings where training time is limited and there are competing priorities.

In a separate pilot RCT conducted in the primary care setting, the effectiveness of a structured lifestyle support intervention with and without the use of pedometers was evaluated (32). In this pilot trial 103 individuals with BMI $\geq$27 kg/m^2 were randomised to one of four arms; structured lifestyle support with pedometer, structured lifestyle support without pedometer, usual care with pedometer, and usual care without pedometer. Eight primary care practices took part, with nurses receiving training via a CD-ROM, in the delivery of the 12-week structured support intervention which comprised fortnightly group sessions. A detailed description of the material delivered during the sessions was provided by the authors, which is a major strength of the reporting of the study. In addition, the intervention was developed following the complex interventions guidance issued by the Medical Research Council (MRC). The intervention utilised behaviour change techniques including goal setting, and monitoring to improve diet and activity levels. Individuals randomised to receive usual care received a single individual 30-minute appointment during the 12-week period. Those individuals who were randomised to receive a pedometer alongside either the structured group support intervention or usual care, were provided with the device and given instructions on its use as well as a leaflet highlighting the benefits of achieving a target of 10,000 steps per day and individuals were also

instructed to record the number of steps taken per day. The authors reported 12-week intervention-end weight outcomes, with losses of -4.0±3.5kg (-4.0±3.4%) achieved by those receiving the structured support (either with or without pedometer), with 34% achieving ≥5% loss of baseline body weight. Those not receiving structured support achieved smaller losses of -1.2±3.8kg (-1.2±4.1%), with 18.9% achieving ≥5% baseline body weight loss. Analyses comparing those receiving the structured group support intervention with those who did not receive support was conducted, with findings indicating that those receiving support lost significantly more weight than those not receiving support, with adjusted mean differences of -2.6kg (-4.1 - -1.2) and -2.8% (-4.3 - -1.3) body weight. Analyses showed that there were no significant differences in weight loss between those receiving a pedometer and those who did not receive a pedometer, with mean weight losses of -2.5±4.0kg and -2.5±3.9kg, respectively. However, the findings of these analyses should be interpreted with caution due to the fact that this was a pilot RCT and was thus not sufficiently powered to detect between group differences.

Following the pilot RCT, a larger scale RCT was conducted, with a revised intervention design (31). The trial inclusion criteria was also widened to include those with BMI ≥25.0 kg/m^2, although the mean baseline BMI of 33.5kg/m^2 indicates that the sample were predominantly obese rather than overweight. The new primary care-based intervention was termed the Camwel programme and delivered in 23 practices in the Camden area of London, and was delivered on a one-to-one rather than group basis, to a much larger sample size of 381 individuals. The RCT evaluated the Camwel structured lifestyle support programme versus usual care. The intervention comprised fortnightly one-to-one appointments, each lasting 30 minutes for the first 12 weeks, after which there was a further 12 weeks of appointments which took place every 3 weeks, followed by monthly

appointments for the final 12 weeks, giving a total of 14 sessions over a 9-month period. The intervention covered diet and physical activity behaviour change and as with the pilot RCT the reporting of the intervention was a key strength of the study, describing in great detail the specific behaviour change techniques utilised in the programme and the theoretical frameworks underpinning each of the techniques. The intervention was delivered by a team of six Camwel advisors who were non-healthcare professionals who received two days of training including the CD-ROM tool utilised in the pilot study, supplemented with further quarterly meetings with the research team. The 6-month weight outcomes revealed that there was no significant difference in weight loss between the intervention and control arms. The intervention arm achieved mean losses of -1.7kg (-2.5 - -1.0) and -1.8% (-2.5 - -1.1), with 23.9% achieving ≥5% baseline body weight loss, whilst the control arm achieved mean weight losses of -1.0kg (-1.7 - -0.2) and -1.0% (-1.9 - -0.2), with 13.2% achieving ≥5% baseline body weight loss. The adjusted mean difference between intervention and control arms was 0.8kg (-1.9 - 0.3). A similar pattern of results were observed in the 12-month data, with the intervention arm achieving mean losses of -2.4kg (-3.5 - -1.3) and -2.6% (-3.7 - -1.5), with 34.0% achieving ≥5% baseline body weight loss. The control arm achieved mean weight losses of -1.3kg (-2.2 - -0.4) and -1.4% (-2.4 - -0.4), with 19.3% achieving ≥5% baseline body weight loss, with an adjusted mean difference between intervention and control arms of 1.1kg (95% CI: -2.5 - 0.3). However, the intervention arm had a significantly greater proportion of individuals losing ≥5% baseline body weight at both 6 and 12 months, with adjusted mean differences of 10.7% (1.4 - 20.0), and 14.7% (3.0 - 26.4), respectively.

In conclusion, the weight management interventions delivered in primary care settings have all focussed on the provision of lifestyle and behaviour change advice, with

the exception of one study which provided participants with an alternative Low Energy Liquid Diet (LELD) approach (33). Despite the homogeneity in intervention type, there has been great variation in the effectiveness of the interventions, with two RCTs reporting no significant differences in weight loss between intervention and control arms (31, 173). However, the studies utilising poorer quality designs have reported weight losses ranging from -5.0kg (30) and -3.0±6.6kg (168) achieved after lifestyle intervention, and a loss of -12.4±11kg obtained after completion of the LELD intervention (33). It appears that whilst the majority of the lifestyle focussed primary care-led weight management programmes have demonstrated weight loss, the weight losses achieved have been modest and may not be sufficient to produce the clinically significant improvement to health that is required.

Table 4.1.1: Studies examining the effectiveness of weight management interventions in Primary care

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Counter-weight project team, 2005	UK, 7 regions: Aberdeen, Bath, Birming-ham & Solihull, Glasgow, Hammer-smith (London), Leeds, Luton	1,549	Mean BMI=36.9kg/m^2 Age=49years 26% classed as extreme obese BMI≥40.0kg/m^2 74% had ≥1 obesity co-morbidity	Counterweight weight management model comprising changes to clinician behaviour, practice systems, and nurse training to deliver Counterweight lifestyle intervention. Nurse-led lifestyle intervention, 3 month duration aimed at achieving ≥5-10% body weight loss delivered either in: • Group sessions, lasting 1 hour, 6 total • Individual consultation, comprising 6 appointments (10-30min duration) All patients received follow-up appointments every 3 months	Interim findings: at 12 months after initiation 93.5% of practices had received the training programme, with 75.8% of practices implementing the Counterweight weight management model and 91% of patients recruited receiving lifestyle intervention. Of those completing the programme (attending ≥6 appointments in 12 months, N=445) mean weight loss -4.5kg, with 40% achieving ≥5% weight loss, Analysis of LOCF data: 16.2% achieved ≥5% weight loss (N=893) at 12 months
Counter-weight project team, 2008	As Counterweight project team, 2005	1,906	Mean BMI=37.1kg/m^2 Age=49.4years 77% female 25.4% classed as extreme obese BMI≥40.0kg/m^2	As Counterweight project team, 2005	Five-year outcomes: At 12 months (N=1,419, data available for N=642, 45%) mean weight loss of -3.0±6.6kg (-3.5 - -2.4), mean BMI loss of -1.1±2.4kg/m^2, with 30.7% achieving ≥5% weight loss Sub-group analysis of baseline BMI≥40.0kg/m^2 individuals (N=160), at 12 months: mean weight loss of -4.6±8.9kg (-6.0 - -3.2) At 24 months (N=357) mean weight loss of -2.3kg (-3.2 - 1.4), with 31.9% achieving ≥5% weight losses
Counter-weight project team, 2010	As Counterweight project team, 2005	1,906	As Counterweight project team, 2008	As Counterweight project team, 2005	Cost-effectiveness evaluation: Estimated Counterweight delivery cost of £59.83 per individual entered onto programme Weight loss of -3.0kg at 12 months and -2.3kg at 24 months, is a significant improvement relative to the expected +1kg per year weight gain. Counterweight was cost-saving, assuming 12 month loss of -3.0kg was regained over 2 years and non-attenders (55%) lost no weight and gained +1kg/year.

Table 4.1.1 Continued: Studies examining the effectiveness of weight management interventions in Primary care

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Counter-weight project team, 2012	UK	6,715	Mean BMI=37.0kg/m^2 Age=53years 74.3% female 25.8% classed as extreme obese BMI≥40.0kg/m^2	Counterweight programme implemented in 184 general practices, 16 community pharmacies and 1 community service	At 12 months attendance was 28% (lower than the 45% in original 2008 evaluation) mean weight loss of -3.7kg (-3.3 - -4.4), with 35.2% achieving ≥5% weight loss. Analysis of all eligible participants at 12 months (including those not completing full attendance, N= unknown) 10.0% achieved ≥5% weight loss.
Morrison, 2013	Fife, Scotland	458	Mean BMI=36.1kg/m^2 Age=54years 74.7% female 21.2% classed as extreme obese BMI≥40.0kg/m^2	Counterweight programme implemented in 16 community pharmacies where Counterweight not available via GP. Lifestyle intervention delivered one to one by pharmacy staff through 6 monthly appointments lasting 10-30mins, with follow-up appointments at 6, 9, 12 months. Estimated total patient contact time of 130 minutes.	At 12 months (N=314) mean weight loss of -4.1kg (-2.8 - -5.4), with 41.6% attenders achieving ≥5% weight loss Sub-group analysis of baseline BMI≥40.0kg/m^2 individuals (N=64, 23%), at 12 months: mean weight loss of -7.4kg (-3.1 - -11.6), with 46.7% achieving ≥5% weight loss. No significant difference in weight loss between baseline BMI subgroups. LOCF analyses indicated mean weight loss of -1.7kg (-1.3 - -2.1), with 15.9% achieving ≥5% weight loss. BOCF analyses indicated mean weight loss of -1.0kg (-0.6 - -1.4), with 10.2% achieving ≥5% weight loss.
Lean, 2013	UK	91	Mean BMI=48.0kg/m^2 Age=45.7years 81.3% female Only those with BMI≥40.0kg/m^2 recruited	Intervention aiming to achieve ≥15kg weight loss after 12 months total duration, delivered by primary care nurses and dietitians to patients recruited from primary care practices delivering Counterweight, comprising: • Low Energy Liquid Diet (LELD) for 12 weeks or ≥20kg weight loss, with fortnightly structured appointments • Food re-introduction for 6-8 weeks with fortnightly appointments, • Weight maintenance until 12 months with individualised meal plan and monthly appointments	LELD stage completed by 64% of the sample, mean weight change at 14 weeks -16.9 ±6.0kg, -12.6±4.5%, with 69% of those completers achieving ≥15kg weight loss Food re-introduction completed by 41% of the sample, mean further weight change -2.1±3.7kg after 9 week period. Mean difference from baseline of -19.1±7.5kg, -14.6±5.1%, with 77% of those completing achieving ≥15kg weight loss at end of food re-introduction stage. Weight maintenance completed by 75% of the sample. At end of intervention (12 month): mean weight change -12.4 ±11.4kg, -9.1 ±8.2%, with 33% of total sample achieving ≥15.0kg weight loss. Estimated cost per patient entered =£861.05 48% received Orlistat at some point during duration.

Table 4.1.1 Continued: Studies examining the effectiveness of weight management interventions in Primary care

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Gray, 2009	Camelon, Scotland	105	Males only Mean BMI=not known Age=50.9years 9.3% classed as extreme obese BMI≥40.0kg/m^2	The Camelon model delivered by community nurses and a dietitian comprised • One 40-minute appointment at a men's health clinic held in the community at a GP practice, discussing health and lifestyle where obese individuals were invited to join the Camelon programme • One 20-minute pre-programme individual assessment, describing the 12-week programme, answering questions and obtaining baseline measures • Weight loss intervention comprising a 12-week male only group programme, with each session lasting 60-minutes and taking place in the evening. The programme used behaviour change techniques to achieve balanced healthy diet and increased physical activity, with an aim of achieving -0.5 - -1.0kg weight loss per week • Post-programme meetings held every 3 months for those who completed the programme, in order to help maintain weight loss	Of the 1,855 males attending the initial men's health clinic visit, 105 eligible individuals took part in the programme. Analyses compared participants (those who began attending the programme regardless of whether they completed it) and non-participants (those who chose not to join the waiting list or subsequently decided not to join the programme). At 12-weeks, of the 105 males who took part, 80 (76.2%) completed the programme, achieving -5.0kg weight loss, with 44.3% achieving ≥5% weight loss, of whom 8.9% achieved ≥10% weight loss. At post-programme follow-up (between 1-49 months after programme-end), data was available for 20 individuals who achieved mean weight loss of -3.7% of their baseline weight. Qualitative study examining the experiences of attending the programme comprising 2 focus groups conducted with separate groups of 8 participants and 1 focus group conducted with 8 partners of the participants. Reasons for joining the programme were identified as health concerns, pressure from family and the use of humour and all-male aspects of the programme. Advice identified as most useful was reducing portion sizes, changing cooking methods and learning about nutritional labelling. Reasons for continued attendance were identified as enjoyment of the programme and rapport with facilitators. Family member involvement with the programme was also discussed by participants and partners, suggesting that the lifestyle changes had been extended to the wider family as well as the individual participants.

Table 4.1.1 Continued: Studies examining the effectiveness of weight management interventions in Primary care

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Moore, 2003	UK: Durham, Leeds, Newcastle, Scarborough	843	Intervention arm: Mean BMI=37.0kg/m^2 Weight =100.8kg Age= 48.4years 75.0% female Control arm: Mean BMI=36.9kg/m^2 Weight =100.2kg Age= 48.8years 73.0% female	Primary care RCT of new weight management model for obese individuals versus usual care. Training delivered to GPs and nurses at 22 practices, comprising three 90-minute sessions within 2 weeks, including information on benefits of weight loss, and treatment options of low energy diet (500cal deficit), increased physical activity and pharmaceutical options. The intervention comprised individual fortnightly appointments until ≥10% body weight lost, then weight maintenance appointments every 1-2 months. The 22 practices in the control arm provided usual care to patients for the 18 month study period.	There were no significant differences between intervention and control groups, however at 3, 12 and 18 months post intervention non-significant trend of the intervention arm being heavier than the control group by +0.6kg, +1kg, and +1.3kg, respectively ($p>0.05$). The following changes were obtained from baseline: At 3 months: Intervention arm -0.4kg, control -0.4kg At 12 months: Intervention arm -0.5kg, control -0.9kg At 18 months: Intervention arm 0kg, control -0.7kg Analyses conducted using available case data, with 3 month data obtained for 78.8%, 12 month data obtained for 67.0%, and 18 month data obtained for 63.0% of the sample.

Table 4.1.1 Continued: Studies examining the effectiveness of weight management interventions in Primary care

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Nanchahal 2009	UK	103	Mean BMI=35.9kg/m^2 Weight= 98.5kg Age= 47.2years 80.3% female	Primary care Pilot RCT with 4 arms: • Structured lifestyle support • Structured support with pedometer • Usual care • Usual care with pedometer Nurses from 8 practices were given a CD-ROM training tool, then structured lifestyle support delivered to individuals BMI ≥27 kg/m^2. The 12-week support intervention comprised fortnightly group sessions covering diet and activity behaviour change. Usual care comprised a single individual 30-minute appointment during the 12-week period. Those receiving pedometer were given leaflet of benefit of 10,000 steps per day and asked to record steps taken.	At 12 weeks, the following losses were obtained (available data): Structured support group achieved -4.0kg, -4.0%, with 34% achieving ≥5% baseline body weight loss. Not receiving support achieved -1.2kg, -1.2%, with 18.9% achieving ≥5% baseline body weight loss. Pedometer group achieved -2.5kg, -2.7%, with 29.2% achieving ≥5% baseline body weight loss. Not receiving pedometer achieved -2.5kg, -2.4%, with 23.6% achieving ≥5% baseline body weight loss. Those receiving structured support lost significantly more weight than those not receiving support, adjusted mean differences of -2.6kg (-4.1 - -1.2) and -2.8% (-4.3 - -1.3). No significant difference in weight lost between those receiving pedometer and those not, adjusted mean differences of -0.1kg (-1.5 - 1.3) and -0.4% (-1.8 - 1.1). Losses ≥5% baseline weight associated with improved scores on the Rosenberg self-esteem +14.1 (9.82 - 18.4), HADS anxiety -1.50 (-2.79 - -0.21) and depression -1.76 (-2.92 - -0.60), and EQ5D-VAS +12.2 (7.5 - 17.0).
Nanchahal 2012	UK, Camden, London	381	Mean BMI=33.5kg/m^2 Weight= 92.3kg Age= 48.8years 72.2% female	Primary care RCT evaluating structured lifestyle support (Camwel) versus usual care. Structured support comprised fortnightly 30-minute one to one appointments for the first 12 weeks, followed by a further 12 weeks of appointments every 3 weeks, followed by monthly appointments for 12 weeks, giving a total of 14 sessions over 9 months. Intervention covered diet and activity behaviour change and was delivered by trained Camwel advisors (non-healthcare professionals) after 2 days training including CDROM tool.	At 6 months intervention arm achieved losses of -1.7kg, -1.8% with 23.9% achieving ≥5% baseline weight loss, whilst control arm achieved -1.0kg, -1.0%, with 13.2% achieving ≥5% baseline weight loss. At 12 months intervention arm achieved losses of -2.4kg, -2.6% with 34.0% achieving ≥5% baseline weight loss, whilst control arm achieved -1.3kg, -1.4%, with 19.3% achieving ≥5% baseline weight loss. There were no significant differences between weight losses achieved by intervention and control at 6 and 12 months, adjusted mean differences -0.8kg (-1.9 - 0.3) and -1.1kg (-2.5 - 0.3). There were significant differences in proportions achieving ≥5% baseline weight loss at 6 and 12 months, with adjusted mean differences 10.7% (1.4 - 20.0), and 14.7% (3.0 - 26.4), respectively. Quality of life measures obtained at follow-up but not reported.

4.1.3 Specialist weight management programmes

The Glasgow and Clyde Weight Management Service is a specialist multidisciplinary service, similar to that described in the present evaluation, delivered by a team comprising dietitians, psychologists and physiotherapists. The weight outcomes of the service have been evaluated, incorporating data from 2,976 individuals who were referred to the service as a result of fulfilling the criteria of having a BMI ≥35.0kg/m^2 without obesity-related co-morbidities or a BMI ≥30.0kg/m^2 with co-morbidities (174). The mean BMI of the sample at baseline was not reported, however 52.3% of the sample were classed as extreme obese (BMI ≥40.0kg/m^2). The sample was also predominantly from regions of high socio-economic deprivation, with 62.1% of the sample living in areas classed within the fifth quintile of the Scottish Index of Multiple Deprivation (SIMD) index. The evaluation reported outcomes of the first phase of the intervention delivered to participants, which comprised nine fortnightly group sessions delivered over a 16-week period. The group programme sessions were delivered in community and outpatient hospital settings and focussed on facilitating lifestyle and behaviour change through the use of a cognitive behavioural approach, with input from psychologists. Participants were also provided with individually calculated 600 calorie deficit diet plans, with an overall aim of the first phase of the intervention to facilitate ≥5kg weight loss for individuals. A total of 2,976 individuals were referred to the service, of which 2,156 (72.4%) attended the service, with 809 individuals going on to complete phase one of the intervention (27.2% of those referred).

A major limitation of the study is that the mean weight and BMI outcomes achieved on completion of the programme were not reported, however the proportion of individuals achieving the target weight loss of ≥5kg was reported, with 35.5% of the 809

completers achieving this. When analysing BOCF data, thus considering all participants who entered the service, including those who did not complete phase one, 13.6% achieved the target weight loss of ≥5kg. The fact that the evaluation did not report mean weight change is a substantial flaw, however the emphasis was placed on analyses identifying the predictors of the target ≥5kg weight loss. Findings demonstrated that among all individuals referred to the service, the factors associated with successful target weight loss were age ≥40 years, male sex (OR= 1.39, 1.05 - 1.82), BMI ≥50 kg/m^2 (OR= 1.70, 1.14 - 2.54) and experiencing symptoms of depression, with depression defined as HADS score ≥12 (OR= 1.81, 1.35 - 2.44). Conversely, presence of diabetes (OR= 0.55, 0.38 - 0.81) was associated with a decreased risk of achieving ≥5kg weight loss. Separate analyses of the sub-group of intervention-completers only, indicated that males were more likely to achieve the target weight loss (OR= 1.85, 1.33 - 2.58), whilst those with diabetes were less likely to achieve ≥5kg weight loss (OR= 0.45, 0.29 - 0.68). The evaluation of the Glasgow service highlights the need for greater consistency in the reporting of outcomes within the body of weight management literature, so that there is greater transparency of intervention effectiveness and so that comparisons between services can be made.

A subsequent evaluation of the Glasgow service, has been published, describing the outcomes of a separate sample of 1,838 individuals in a much greater level of detail of reporting than in the prior publication (175). The second publication reported the mean BMI of the sample as 43.3kg/m^2, with a mean weight of 118.1kg. Whilst it is not possible to compare baseline values between the two evaluations, as this was not reported for the first evaluation, it is possible to compare the proportion of extreme obese individuals, with the second publication comprising a greater proportion, 63.1% compared to 52.3% of the first sample, classified as extreme obese. Whilst the first publication reported outcomes of

the first phase of the intervention comprising the 16-week group programme only, the second publication described outcomes obtained in the second and third phases of the intervention. The second phase of the intervention comprised three 60-minute sessions delivered monthly consisting of further lifestyle advice, a prescribed low calorie diet, and weight loss medication, whilst the third phase of the intervention comprised twelve 60-minute sessions delivered monthly, aimed at achieving weight maintenance.

Of the 6,505 individuals referred to the service, 5,637 were eligible to attend the service and 3,460 chose to opt into the service (61.4% of those who were eligible), with 1,838 attending the phase one intervention (32.3% of those who were eligible). The majority of individuals attending phase one (71.9%), completed the 16-week programme, achieving a mean weight loss of -4.0kg (-4.3 - -3.8), with 36% achieving ≥5kg weight loss and 29% achieving ≥5% weight loss. LOCF data was analysed, with this data indicating a more conservative mean weight loss of -2.9kg (-3.1 - -2.7), with 26% achieving ≥5kg weight loss and 21% achieving ≥5% weight loss. Of those completing phases one and two, mean weight loss was -6.4kg (-6.9 - -5.8), with 55% achieving ≥5kg weight loss and 49% achieving ≥5% weight loss. LOCF data again indicated more conservative weight losses of -3.6kg (-3.9 - -3.4), with 30% achieving ≥5kg weight loss and 25% achieving ≥5% weight loss. Of those completing all three phases of the intervention (N=208), mean weight loss of -8.5kg (-9.7 - -7.2) was achieved, with 58% achieving ≥5kg weight loss and 56% achieving ≥5% weight loss, with LOCF data (N=1,838) indicating mean weight losses of -3.6kg (-3.8 - -3.3), with 28% achieving ≥5kg weight loss and 24% achieving ≥5% weight loss. This evaluation is greatly strengthened by the large sample size and the detailed reporting of weight outcomes, including the reporting of weight change at each phase of the

intervention, the separate analyses of the outcomes of those individuals completing each of the phases, and the imputation of LOCF data.

In addition to the evaluation of large weight management services, smaller scale programmes have been developed and evaluated in several UK dietetic departments, with findings published as pragmatic service evaluations. One evaluation conducted at a London hospital compared the effectiveness of one-to-one appointments at a dietetic outpatient clinic with a 10-week hospital group-based dietetic weight loss programme (176). The small study included 44 individuals receiving individual consultations and 105 receiving the group programme. Analyses demonstrated that there was no significant difference ($p > 0.05$) in mean weight loss between the interventions, with mean weekly losses of -0.4kg, -0.2kg, -0.1kg and 0.0kg from sessions one to four, for the one-to-one clinic and mean weekly losses of -0.4kg, -0.2kg, -0.3kg and -0.1kg for the group-based programme. However, there was a significant difference in the proportion of individuals achieving weight loss, with 52% of those attending the one-to-one clinic achieving weight loss, and 60% of those attending the group programme achieving weight loss ($p = 0.001$). The evaluation demonstrated that the two interventions achieved a similar level of weight loss. These losses were considerably below the level of -0.5 - -1.0kg per week weight loss which is recommended by the National Institute of Health and Care Excellence (NICE) (14) in order to achieve long-term weight loss for adult individuals. This was a small pragmatic service evaluation and continued evaluation of the services incorporating a greater number of individuals would be required, in order to detect any potential differences between the weight outcomes of the two services.

In an evaluation of another London-based dietetic centre, the weight outcomes of a structured lifestyle weight management clinic were examined at 6, 9 and 12 month follow-

up (177). The clinic offered patients six monthly appointments which targeted ≥5% weight loss, which were followed by review sessions at 9 and 12 months in which weight loss maintenance was targeted. Of the 24 individuals for which 6-month data was available, 20 (83%) achieved weight loss, and at 6 months the mean weight loss for the sample was -6.2kg which equates to -5.5% baseline body weight loss. Of the patients attending the 9-month follow-up (80% of the sample), 11 individuals (92%) achieved maintenance of their weight loss, with a mean loss of -7.2kg and -5.7% of baseline body weight loss. At the 12-month follow-up 86% maintained some level of weight loss, with a mean loss of -5.1kg (-4.1%). However, the data from this service evaluation demonstrated that weight loss decreased between the 9- and 12-month follow-up sessions, indicating that some of the sample did not maintain their weight loss and indeed re-gained weight. The authors concluded that attending the structured lifestyle weight management clinic aided individuals in achieving the desired ≥5% body weight loss, which was maintained at the 9-month follow-up. However, findings indicate that further support may be required for individuals between the 9- and 12-month period in order to prevent weight re-gain and facilitate longer-term maintenance of the initial weight loss. The findings of the service evaluation must also be interpreted with caution due the small sample size and could ideally be utilised to inform the development of a larger scale evaluation of the service.

In another small-sample evaluation, the long-term effectiveness of two 6-week programmes ‘Size Down’ and ‘Post-Natal Size Down’ were examined in a multicultural, deprived inner city area of Birmingham (178). The aim of the evaluation was to establish whether the initial weight loss achieved was maintained longer-term after the community-based group programmes had finished. A total of 74 individuals completed a telephone survey after finishing the programme between 6-24 months previously in order to obtain

self-reported current weight data. On completion of the programmes, individuals who attended the Size Down programme achieved a mean weight loss of -1.7%, with the Post-Natal Size Down programme achieving a mean body weight loss of -2.2% at intervention end. At follow-up, those attending Size Down reported a mean further weight loss of -4.3%, whilst those attending the post-natal programme reported mean further losses of -9.0% baseline body weight. However, not all individuals achieved further weight losses, with 28% achieving maintenance of their original loss without further loss and 18% achieving weight gain. When data from only those individuals who had completed the programmes more than 12 months ago was analysed, the mean overall weight loss for both programmes combined was -4.1kg (-3.9%). However, the validity of reporting combined outcome data for the two programmes is questionable, as weight loss would likely occur regardless of intervention in a post-natal sample. The findings of this evaluation indicate that the majority of participants were able to maintain their initial weight loss or indeed to achieve further weight loss in the longer-term. However, the amount of weight loss maintained at 12 months was below the recommended target of ≥5% baseline weight. A major limitation of the evaluation was the use of self-reported weight outcome data at follow-up, with additional weight measures obtained through home visits in only a subset of 23% of the sample, which introduces the risk of bias and inaccurate reporting of the main outcome measure for the majority of the sample. In addition, a relatively low response rate (44%) was achieved for the follow-up telephone survey, which introduces the potential for responder bias, whereby only those with better weight outcomes may have chosen to report their weight. As a result the findings of the evaluation should be interpreted with caution and further evaluations of the service would be improved by the use of measured weight outcomes rather than self-report at follow-up.

In conclusion, the body of literature evaluating specialist weight management services highlights the poor methodology utilised in the conduct of the studies and poor reporting of baseline and outcome data (174, 176-178). The first publication to evaluate outcomes of the Glasgow and Clyde Weight Management Service (174) was flawed by not reporting baseline weight and BMI and indeed post-intervention mean changes in weight and BMI. However, the second publication evaluating the Glasgow service (175) used excellent reporting methods and was the only study included in this review of specialist programmes that included sufficiently detailed reporting of baseline weight and BMI characteristics of the sample. Furthermore, this was the only study to explicitly outline the weight outcomes obtained on completion of each phase of the intervention, and include separate analyses to demonstrate the outcomes obtained using available case data from those completing the programme and using LOCF data, thus facilitating interpretation of the results.

Table 4.1.2: Studies examining the effectiveness of weight management interventions in Specialist services

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Morrison, 2012	Glasgow and Clyde weight manage-ment service, UK	2,976	Mean BMI & weight =unknown 72.6% female 52.3% classed as extreme obese BMI ≥40.0kg/m^2 62.1% highly deprived SES	Multidisciplinary team comprising dietitians, psychologists, physiotherapists, delivered to patients referred to service with BMI ≥35 kg/m^2 or 30kg/m^2 with co-morbidities, between 2004 and 2006. Phase 1 intervention comprised 9 fortnightly 90-minute group sessions delivered over 16 weeks. Group programme of lifestyle and behaviour change using cognitive behavioural approach, and delivered in community and outpatient hospital setting, aiming to achieve ≥5kg weight loss. 600 calorie deficit diet plan provided.	Of the 2,976 referred, 2,156 opted into the service (72.4%), with 809 completing the phase 1intervention (27.2% of those referred). Of the 809 completers: Mean weight and BMI change unknown, with 35.5% achieving the target weight loss ≥5kg. Analysis of all those referred to service (N=2,976) established factors predicting ≥5kg weight loss success, with age ≥40 years, male sex (OR=1.39, 1.05 - 1.82), BMI≥50 kg/m^2 (OR=1.70, 1.14 - 2.54) and depression (OR=1.81, 1.35 - 2.44) associated with increased odds of achieving ≥5kg weight loss. Those with diabetes mellitus (OR=0.55, 0.38 - 0.81) were less likely to achieve the target weight loss. Analysis of completers only (N=809), males were more likely to achieve weight loss (OR=1.85, 1.33 - 2.58), and those with diabetes were less likely to achieve ≥5kg weight loss (OR=0.45, 0.29 - 0.68). Follow-up HADS anxiety and depression scores were not reported.
Logue, 2014	Glasgow and Clyde weight manage-ment service, UK	1,838	Mean BMI= 43.3kg/m^2 Weight= 118.1kg Age= 49.1years 72.9% female 43.3% highly deprived SES 63.1% classed as extreme obese BMI ≥40.0kg/m^2	Separate sample as Morrison, 2011, with sample attending between 2008 and 2009. Phase 1 intervention: as Morrison, 2011. Phase 2 intervention: Patients entered after completing phase 1, comprised 3 sessions each of 60-minutes duration delivered monthly. Consisted of further lifestyle advice, prescribed low calorie diet, & Orlistat weight loss medication. Phase 3 intervention: Patients entered after completing phase 1 or 1&2, or repeating phase 2, comprised 12 monthly 60-minute weight maintenance sessions.	Of the 6,505 referred, 5,637 were eligible and 3,460 opted into the service (61.4% of eligible), 1,838 attended the phase 1intervention. Of the 1,322 phase 1 completers (71.9% of those attending) mean weight change was -4.0kg (-4.3 - -3.8), with 36% achieving ≥5kg weight loss and 29% achieving ≥5% weight loss. LOCF (N=1,838) data mean weight change of -2.9kg (-3.1 - -2.7), with 26% achieving ≥5kg weight loss and 21% achieving ≥5% weight loss. Of the 639 phase 1&2 completers (34.8% of those attending) mean weight change was -6.4kg (-6.9 - -5.8), with 55% achieving ≥5kg weight loss and 49% achieving ≥5% weight loss. LOCF data (N=1,838) mean weight change -3.6 (-3.9 - -3.4), with 30% achieving ≥5kg weight loss and 25% achieving ≥5% weight loss. Of the 208 phase 1, 2 & 3 completers (11.3% of those attending) mean weight change was -8.5kg (-9.7 - -7.2), with 58% achieving ≥5kg weight loss and 56% achieving ≥5% weight loss. LOCF data (N=1,838) mean weight change -3.6 (-3.8 - -3.3), with 28% achieving ≥5kg weight loss and 24% achieving ≥5% weight loss.

Table 4.1.2 Continued: Studies examining the effectiveness of weight management interventions in Specialist services

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Mayre-Chilton, 2010	Dietetic department London, UK	149	Mean BMI & weight =unknown One-to-one clinic= 66% female Group programme= 79% female	Two interventions within a dietetic service: • One-to-one appointments at a general adult dietetic outpatient clinic. Initial 30 min appointment with 15 min follow-up appointments. N= 44 • Group-based dietetic weight loss programme 'Healthy Choice Group Programme' delivered over 10-week period at hospital setting with one 90-min session per week. N= 105	No significant difference (p>0.05) in mean weight loss between two interventions. One-to-one intervention: mean weekly losses of -0.4kg, -0.2kg, -0.1kg and 0.0kg from sessions one to four. Group intervention: mean weekly losses of -0.4kg, -0.2kg, -0.3kg and -0.1kg. Significantly greater proportion of individuals achieving weight loss in group intervention (60%) compared to one-to-one intervention (52%), p=0.001.
Forrest, 2011	Dietetic service, London, UK	24	Mean BMI & weight =unknown No baseline information	Structured lifestyle weight management clinic incorporating 6 monthly appointments which targeted ≥5% weight loss Followed by review sessions at 9 and 12 months, which targeted weight loss maintenance	At 6 months: mean weight loss of -6.2kg, -5.5%, with 83% achieving weight loss. At 9 month follow-up: mean loss of -7.2kg, -5.7%, with 92% achieving maintenance of weight loss. At 12 month follow-up: mean loss of -5.1kg, -4.1%, with 86% maintaining some level of weight loss.
Gordon, 2011	Dietetics department Birmingham UK	74	Mean BMI & weight =unknown Combined intervention sample= 97.3% female	Two interventions within a dietetic service: • Size Down programme • Post-Natal Size Down programme Both programmes community-based, group weight management programmes of 6-week duration	At 6 weeks, Size Down intervention achieved mean loss of -1.7% baseline body weight, and post-natal programme achieved mean loss of -2.2% baseline body weight. Individuals completed a telephone survey after finishing the programme 6 - 24 months prior (44% response rate). At telephone follow-up, Size Down achieved mean further weight loss of -4.3% baseline body weight, and post-natal programme achieved mean further loss of -9.0% baseline body weight. At a minimum follow-up period of 12 months, interventions combined: 28% reported achieving maintenance of their original loss without further loss, 18% achieved weight gain, with mean losses of -4.1kg, and -3.9% baseline body weight loss.

4.1.4 Commercial programmes

Individuals may gain access to a range of commercial programmes currently operating in the UK such as Weight Watchers, Rosemary Conley, and Slimming World either through self-referral or by referral from a healthcare professional. The outcomes of a model operating referrals from primary care to the commercial Slimming World 12-week programme have been evaluated in a small pilot study conducted in Derbyshire, UK (72) and subsequently in a larger scale UK-wide service evaluation comprising data from 34,271 individuals referred to the Slimming World programme (37). The pilot study which was designed to assess the feasibility of referral to the commercial programme from a primary care setting, employed a much smaller sample size of 91 obese individuals who were referred to the programme after attending a GP appointment for non-weight related reasons (72). The programme was completed by 68.1% of individuals, achieving a 12-week intervention-end mean weight loss of -5.4±3.2kg (-6.4%), with 57% of these individuals achieving ≥5% loss of baseline body weight. A substantial proportion (51.6%) of the original sample who were referred to receive the 12-week programme free of charge, elected to self-fund a further 12-week duration of programme attendance. Of those who completed 24 weeks total programme attendance, a mean weight loss of -11.1±5.5kg (-11.3%) was achieved. Of those attending for 24 weeks, the majority of the sample (86%) achieved ≥5% loss of baseline body weight, whilst 59% achieved losses in excess of 10% of their baseline body weight. The service evaluation demonstrated that referral to the commercial Slimming World programme was feasible for healthcare professionals and that the programme produced substantial weight loss for individuals after the initial 12-week programme. Further weight loss was achieved when individuals chose to continue their attendance to 24 weeks. The authors concluded that the ‘slimming on referral’ service

could be considered as a cheaper, effective alternative to pharmaceutical treatment or in-house primary care-led weight management interventions.

A larger scale Slimming World evaluation (37) was conducted in order to examine the efficacy of the 'slimming on referral' service which was rolled out across much of the UK following the feasibility study (72). The mean age of the sample included in the evaluation was 47.3 years with mean a BMI of 36.8kg/m^2. The sample was predominantly female (89.3%) and a large proportion were classed as extreme obese, with 25.4% of those referred having a BMI ≥40.0kg/m^2 at baseline. The large proportion of extreme obese individuals within the sample is likely to be due to the fact that individuals were recruited to the service via referral from primary and secondary healthcare professionals. This approach would reach a wider BMI range than had individuals been recruited from primary care alone. Of those referred, 19,907 (58.1%) completed the programme by attending a minimum of 10 sessions, with the remaining 41.9% attending 9 or fewer sessions and consequently being classed as non-completers. The mean weight change of the sample at intervention-end (3-month follow-up), incorporating all individuals entering the programme, was -4.0±3.7kg (-4.0±3.6%) and mean BMI change was -1.5±1.3kg/m^2. Analyses of the weight outcome data were limited to comparisons by gender and by programme completion status. Males achieved a significantly greater reduction in body weight and BMI from baseline than females (-5.8kg vs -3.8kg, $p < 0.001$) and (-1.8kg/m^2 vs -1.4kg/m^2), and those completing the programme achieved a significantly greater reduction in body weight and BMI from baseline than non-completers (-5.5kg vs -1.8kg, $p < 0.001$) and (-2.0kg/m^2 vs -0.7kg/m^2). In a subsequent publication, further analyses were conducted on data from the same evaluation sample (179), which enabled weight loss outcomes to be compared across baseline BMI subgroups. Across the BMI subgroups, there were

statistically significant ($p < 0.001$) differences between mean weight change values at intervention-end (3-month follow-up), of -2.9±2.8kg for the <30kg/m^2 group, -3.6±3.2kg for the 30.0-34.9kg/m^2 group, -4.1±3.7kg for the 35.0-39.9kg/m^2 group, and -4.8±4.4kg for the ≥40.0kg/m^2 group. There were also statistically significant differences ($p < 0.001$) in BMI change across the BMI groups, respectively; -1.1±1.0kg/m^2, -1.3±1.2kg/m^2, -1.5±1.3kg/m^2, -1.8±1.6kg/m^2, as well as statistically significant differences ($p < 0.001$) in percentage body weight change; -3.7±3.6%, -4.0±3.6%, -4.0±3.6%, -3.9±3.5%. Whilst the differences in outcomes between the baseline BMI groups were statistically significantly different, in real terms these were clinically small differences with a range of only 0.7kg/m^2 across all of the baseline BMI subgroups.

The results of the Slimming World evaluation demonstrate that a substantial proportion of each baseline BMI group achieved ≥5% baseline body weight loss at intervention end; 33.4%, 36.6%, 36.4% and 35.8% across the BMI groups, respectively. This indicates that lifestyle interventions such as the Slimming World programme can be as effective in extremely obese individuals as for those with lower levels of obesity and overweight. However, in order to establish the efficacy of the Slimming World programme within the extreme obese patient population, the weight outcomes must be compared against other weight management programmes, specifically within this BMI subgroup. Additionally, a comparator group, ideally within an RCT, would be necessary and extended follow-up periods would be needed in order to determine the longer-term weight outcomes. Only then can well-founded conclusions be drawn about the efficacy of such programmes for this patient population.

In addition to Slimming World, primary care providers have also made referrals to the Weight Watchers commercial programme, which has been evaluated in a large scale

UK-wide audit (180). Data were retrospectively analysed from 29,326 referrals made from primary care over a one-year period, whereby overweight and obese individuals received the Weight Watchers commercial 12-week programme free of charge. The sample were predominantly female (90.0%), with a median age of 49.0 years and median BMI of 35.1kg/m^2. The majority of the referrals (75%) were first referrals to the programme, however 19% represented individuals' second and 5% represented a third referral to the programme. Data were analysed for all first referrals in which a minimum attendance of one session was reported (N=22,519), with a median weight loss of -3.6kg (-3.6%), with 38% achieving ≥5% baseline weight loss at 12 weeks. Separate analyses including first referrals in which all programme sessions were attended (N=11,851) yielded a greater weight loss of -5.4kg (-5.6%), with 57% of the sample achieving ≥5% weight loss. Whilst these findings demonstrate that a substantial proportion of those completing the Weight Watchers programme were able to achieve a clinically significant weight loss, it highlights a low retention rate, with 46% of the commenced referral courses not being completed. A considerable proportion (24%) of those completing a first time referral were classed as extreme obese BMI ≥40kg/m^2. Analysis revealed that the subgroup experienced significantly poorer weight loss with a median percentage weight change of +0.38%, relative to an overweight BMI <30kg/m^2 subgroup ($p < 0.05$), suggesting that the programme did not meet the weight loss needs of the extreme obese subgroup.

The Slimming World and Weight Watchers interventions have also been evaluated in the Lighten Up trial which is the only RCT to compare the effectiveness of both commercial and primary care programmes within a single trial, whereas other RCT studies have compared the effects of either commercial interventions (36, 181), or primary care interventions (31, 32, 173) against control arms separately. The Lighten Up trial used

rigorous RCT methodology to evaluate the efficacy and cost-effectiveness of the commercially available and primary care-led weight management services (34, 35). The multi-arm trial compared the following six 12-week programmes; Weight Watchers, Slimming World, Rosemary Conley, Size Down group-based dietetic-led programme, general practice one-to-one counselling, pharmacy-led one-to-one counselling, or a choice of one of the six programmes, and a comparator group who were provided with exercise vouchers enabling free admission to local fitness facilities. A total of 740 individuals were randomly assigned to one of the eight arms, with follow-up data available for 658 individuals (88.9%) at 3 months and 522 individuals (70.5%) at 12 months. The mean BMI of individuals joining each arm ranged from 33.1kg/m^2 (general practice counselling arm) to 34.0kg/m^2 (Weight Watchers arm), with mean age ranging from 47.5 years (choice of intervention arm) to 50.7 years (Weight Watchers arm). At intervention-end (3-month follow-up) each of the seven intervention arms and the minimal intervention comparator arm achieved the following statistically significant weight losses from baseline; -4.4kg, $p \leq 0.001$ (Weight Watchers), -4.2kg, $p \leq 0.001$ (Rosemary Conley), -3.6kg, $p \leq 0.001$ (Slimming World), -3.3kg, $p \leq 0.001$ (choice of intervention arm), -2.4kg, $p \leq 0.001$ (Size Down dietetic group), -2.1kg, $p \leq 0.001$ (Pharmacy counselling), -2.0kg, $p \leq 0.001$ (comparator receiving exercise vouchers), and -1.4kg, $p < 0.05$ (General practice counselling). At the 12-month follow-up, the following significant weight losses from baseline were achieved; -3.5kg, $p \leq 0.001$ (Weight Watchers), -2.5kg, $p \leq 0.001$ (Size Down dietetic group), -2.2kg, $p \leq 0.001$ (choice of intervention arm), -2.1kg, $p \leq 0.001$ (Rosemary Conley), -1.9kg, $p \leq 0.001$ (Slimming World) and -1.1kg, $p < 0.05$ (comparator group receiving exercise vouchers). However, the two primary care-led intervention arms did not achieve significant weight losses from baseline at 12 months, with the General practice

counselling arm achieving a loss of -0.8kg ($p > 0.05$) and the Pharmacy counselling arm achieving a loss of -0.7kg ($p > 0.05$). Indeed, further analyses adjusting for baseline weight, physical activity, age, gender and ethnicity, revealed that when comparing the individual arms against the exercise voucher comparator arm, at intervention-end, only the Weight Watchers and Rosemary Conley arms produced significantly greater weight loss than the comparator arm, with adjusted mean differences of -2.3kg, $p \leq 0.001$ and -2.4 kg, $p \leq 0.001$, respectively. At the 12-month follow-up, only the Weight Watchers arm produced significantly greater weight loss than the comparator arm, with an adjusted mean difference of -2.5kg, $p < 0.05$. The findings of the Lighten Up trial demonstrate that the commercial weight management programmes produced better weight loss outcomes and were more cost-effective than the primary care-led weight management services. However, the weight loss achieved was modest and it is uncertain whether the mean loss of -2.5kg which was achieved by the Weight Watchers arm would be sufficient to produce the substantial health benefits required. Furthermore, the trial did not demonstrate the efficacy of the programmes for extreme obese individuals, indeed only 37 of the 740 individuals included in the trial (5%) were classed as extreme obese at baseline. In order to establish whether the weight loss outcomes achieved by the commercial programmes in the Lighten Up trial could potentially be achieved within the extreme obese patient population, a larger trial incorporating a subgroup of extreme obese individuals would be required. Additionally, whilst the Lighten Up trial included a follow-up period of one year, an extended follow-up period is necessary in order to determine whether the commercial and primary care-led programmes can produce lasting weight change and prevent the progression from mild to extreme levels of obesity.

Two additional RCTs have evaluated the effectiveness of commercial interventions, evaluating a single-intervention arm receiving the Weight Watchers programme (181), and a range of four commercial interventions (36). In a single-intervention arm RCT the effectiveness of a 12-month Weight Watchers programme versus usual care was evaluated internationally, with 772 individuals from the UK, Germany and Australia who were randomised to receive either the commercial programme or to a usual care comparator group (181). Those individuals who were randomised to the intervention arm received free access to weekly Weight Watchers group sessions for a period of 12 months. The aim of the Weight Watchers sessions which were held in the community, was to facilitate weight loss through promoting a low energy diet and increased physical activity through the provision of group support. Those individuals randomised to the control arm of the study received weight loss advice from a primary care professional in line with national clinical guidelines, during monthly appointments at their local GP practice over a 12-month period. Individuals who were aged ≥18 years with a BMI 27-35kg/m^2 and at least one co-morbidity risk factor such as dyslipidaemia, hypertension, osteoarthritis, impaired fasting glycaemia and family history of diabetes were recruited to the study from primary care practices. The primary outcome measure of the RCT was weight change post-intervention at 12 months. There was a remarkably high non-completion rate, with 12 month measures obtained for only 230 individuals (61%) of the intervention arm and 214 individuals (54%) of the control arm. Investigators reported that there were significant differences in the study completion rates between countries, with higher non-completion rates in the UK (42%) and Australia (41%) compared to Germany (25%) ($p < 0.0001$). There were no significant differences in the observed effectiveness of the intervention between countries ($p > 0.10$), with the intervention arm achieving significantly greater weight loss than the

control arm across all countries. A major strength of the study is the detailed reporting of results, with the findings reported for separate analyses using available case data for those who completed the study as well as LOCF and BOCF data. The greatest weight loss was seen in the available case data, with a mean loss of -6.7kg in the intervention arm and -3.3kg in the control arm ($p < 0.0001$), whilst the LOCF data showed more conservative losses of -5.1kg for the intervention arm and -2.3kg for the control arm ($p < 0.0001$) and the BOCF data demonstrated losses of -4.1kg for the intervention arm and -1.8kg for the control arm ($p < 0.0001$). Furthermore, those receiving the commercial programme were more likely to lose ≥5% baseline weight, OR= 3.0 (2.0 - 4.4), and ≥10% baseline weight, OR= 3.2 (2.0 - 5.3), compared to those receiving usual care. The likelihood of achieving weight loss was increased for those in the intervention arm who completed the study, for losing ≥5% baseline weight OR= 2.9 (2.1 - 3.9) and for losing ≥10% baseline weight OR= 3.5 (2.3 - 5.4), compared to those receiving usual care. The findings of this RCT demonstrated that the Weight Watchers programme is effective at facilitating weight loss across a range of economically developed countries, with those completing the intervention achieving the greatest weight loss. The development and implementation of strategies to reduce attrition would further improve its effectiveness.

The second of the two studies to utilise an RCT approach in evaluating commercial programmes was conducted as part of a UK television programme entitled ‘Diet Trials’ produced by the British Broadcasting Corporation (BBC) (36). The RCT compared the effectiveness of four commercial interventions widely available in the UK, for a period of six months, with a delayed treatment control group who were asked to maintain their current dietary patterns and physical activity levels for the duration of the study. The four intervention arms included Weight Watchers comprising weekly group support sessions,

Slim-Fast plan comprising the provision of two daily meal replacements and a support pack, Dr Atkins' 'New diet revolution' comprising the provision of a self-help dietary guidance book, and Rosemary Conley's 'Eat yourself slim' comprising weekly group exercise and dietary advice sessions. The trial which was conducted at five regional centres; Bristol University, Surrey University, Nottingham University, Queen Margaret University College Edinburgh and Ulster University, recruited 292 adult participants from community settings across the UK. The study included overweight and obese individuals who reported a BMI in the range of 27.0-40.0kg/m^2, which is reflected in the relatively low mean baseline BMI of the sample, which ranged from 31.2-32.2kg/m^2 across study arms. At six months post-baseline (intervention-end), there was no significant difference between the four intervention arms, with all interventions achieving significantly greater weight loss than the control arm ($p < 0.001$). Using 6-month LOCF data the following losses were obtained for each intervention arm; Weight Watchers -6.6kg (-7.3%), Slim-Fast -4.8kg (-4.9%), Dr Atkins' 'New diet revolution' -6.0kg (-6.2%), and Rosemary Conley's 'Eat yourself slim' -6.3kg (-7.0%). Additional analyses were conducted which demonstrated the 6-month outcomes for those completing participation in the study, using available case data which was obtained for 71.9% of sample, facilitating the following losses; Weight Watchers -8.0kg (-9.0%), Slim-Fast -6.5kg (-6.8%), Dr Atkins' 'New diet revolution' -8.5kg (-8.9%), and Rosemary Conley's 'Eat yourself slim'-8.8kg (-9.9%). Follow-up data was obtained for 54% of the sample at 12 months. However, the majority of the sample had discontinued with their allocated diet, whilst only 19% reported that they had continued. In the following six months from the end of the study period up to 12 months, individuals attending the Weight Watchers arm reported a weight gain of +0.5kg, individuals attending Rosemary Conley also reported a gain of +1.2kg, whilst those

attending Slim-Fast reported further losses of -1.7kg, and those allocated to Dr Atkins' 'New diet revolution' achieved further losses of -1.5kg between the intervention-end period and 12 months. The study which used a novel approach, was conducted as part of a television programme and used rigorous methodology employing an RCT design, with findings demonstrating the effectiveness of four commercial weight loss programmes. The study highlights that referral to commercial programmes from community settings with no primary care input can facilitate clinically significant weight losses, with the majority of programmes achieving ≥5% baseline body weight loss for participants after six months.

In conclusion, a large number of studies have evaluated the efficacy of commercial weight management programmes, with the body of literature encompassing a range of research methodologies, from a pilot trial, to a non-controlled yet large sample size evaluation of a slimming on referral scheme, to three studies which employed the gold-standard research design of RCTs. The studies reported weight losses ranging from -11.1±5.5kg achieved after 6 months attendance at Slimming World (72) to -0.7kg achieved at 12 months by individuals in the Lighten Up trial receiving 3 months of pharmacy-led counselling (34), with a substantial number of commercial interventions facilitating clinically significant weight loss of ≥5% of individuals baseline body weight (36).

Table 4.1.3: Studies examining the effectiveness of weight management interventions in Commercial programmes

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Lavin, 2006	Derbyshire UK	91	Mean BMI= 36.0kg/m^2 Age= 49.5 years 89% female 23% classed as extreme obese BMI≥40.0kg/m^2	Individuals received the 'Slimming World' commercial 12-week programme free of charge, as part of a pilot of the 'Slimming on referral' scheme whereby obese individuals are referred from primary care (GP practices). Individuals were given the option to continue the programme through self-funding beyond the 12-week period.	At 12 weeks: mean weight loss of -5.4±3.2kg, -6.4%, with data obtained for 68.1%. Programme attendance continued by 51.6% to 24 weeks. At 24 weeks: mean weight loss of -11.1±5.5kg, -11.3%, with 86% achieving ≥5% loss of baseline weight, with 59% achieving ≥10% loss. Self-rated well-being domains improved significantly from baseline, at 12 weeks: feeling calm $p<0.001$, energetic $p<0.001$, and down-hearted $p<0.05$, with these improvements maintained at 24 weeks $p<0.05$, $p<0.001$, $p<0.001$, respectively.
Stubbs, 2011	UK, across 77 PCTs	34,271	Mean BMI=36.8kg/m^2 Age=47.3 years 89.3% female 25.4% classed as extreme obese BMI≥40.0kg/m^2	Individuals received the 'Slimming World' commercial 12-week programme free of charge, in a large scale evaluation of the 'Slimming on referral' scheme whereby obese individuals are referred from primary care (GP practices).	At 12 weeks: mean weight loss of -4.0±3.7kg, -4.0±3.6% and mean BMI change -1.5±1.3kg/m^2. Those completing the programme by attending ≥10 sessions (58.1% of sample) achieved greater weight loss than non-completers: -5.5kg vs -1.8kg, $p<0.001$ and greater BMI loss -2.0kg/m^2 vs -0.7kg/m^2 than non-completers.
Stubbs, 2013	As Stubbs, 2011	As Stubbs, 2011	As Stubbs, 2011	As Stubbs, 2011	Analyses of 12-week outcomes by BMI sub-groups: <30kg/m^2: -2.9±2.8kg, -3.7±3.6%, -1.1±1.0 kg/m^2 30.0-34.9kg/m^2: -3.6±3.2kg, -4.0±3.6%, -1.3±1.2 kg/m^2 35.0-39.9kg/m^2: -4.1±3.7kg, -4.0±3.6%, -1.5±1.3 kg/m^2 ≥40.0kg/m^2: -4.8±4.4kg, -3.9±3.5%, -1.8±1.6 kg/m^2 All change values were significantly different from baseline values $p<0.001$ for each BMI sub-group. At 12 weeks, 35.8% of the BMI ≥40.0kg/m^2 group achieved ≥5% loss of baseline weight.
Ahern, 2011	UK	29,326	Median BMI= 35.1kg/m^2 Median Age=49years 90.0% female	Individuals received the 'Weight Watchers' commercial 12-week programme free of charge, as part of an NHS referral scheme whereby overweight and obese individuals are referred from primary care. Data were analysed as part of a retrospective audit.	Median weight change for all first referrals attending minimum of 1 session (N=22,519) = -3.6kg (IQR -6.4 - -1.0kg), and -3.6% (IQR -6.7 - -1.1%), with 38% achieving ≥5% baseline weight loss. Median weight change for all first referrals completing 12 sessions (N=11,851) = -5.4kg (IQR -7.8 - -3.1kg), and -5.6% (IQR -8.1 - -3.2%), with 57% achieving ≥5% baseline weight loss.

Table 4.1.3 Continued: Studies examining the effectiveness of weight management interventions in Commercial programmes

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Jolly, 2010, 2011	Birmingham UK	740	Mean values across arms: BMI=33.1-34.0kg/m^2 Weight=91.7-95.5kg Age=47.5-50.7 years 74-81% female 2-8% classed as extreme obese BMI≥40.0kg/m^2	Individuals recruited through primary care practices to Lighten Up multi-arm RCT comparing 6 programmes: • Weight Watchers • Slimming World • Rosemary Conley • Size Down, dietetic-led • Counselling, general practice • Counselling, pharmacy-led Additional arms also comprised: • Choice of one of the 6 programmes • Comparator group given exercise vouchers enabling free access to local fitness facilities Individuals were provided with free of charge access after being randomised to one of the 8 arms for a period of 12 weeks.	At 3 months follow-up data obtained for 88.9% with all arms achieving significant losses from baseline: Weight Watchers: -4.4kg, p≤0.001 Slimming World: -3.6kg, p≤0.001 Rosemary Conley: -4.2kg, p≤0.001 Size Down: -2.4kg, p≤0.001 Counselling, general practice: -1.4kg, p<0.05 Counselling, pharmacy: -2.1kg, p≤0.001 Choice: -3.3kg, p≤0.001 Comparator: -2.0kg, p≤0.001 At 12 months follow-up data obtained for 70.5% with following arms only, achieving significant losses from baseline: Weight Watchers: -3.5kg, p≤0.001 Slimming World: -1.9kg, p≤0.001 Rosemary Conley: -2.1kg, p≤0.001 Size Down: -2.5kg, p≤0.001 Choice: -2.2kg, p≤0.001 Comparator: -1.1kg, p<0.05 The two primary care arms did not achieve significant loss from baseline at 12 months: Counselling, general practice: -0.8kg, p>0.05 Counselling, pharmacy: -0.7kg, p>0.05 Adjusting for age, gender, baseline weight, ethnicity at 12 month follow-up, only Weight Watchers produced significantly greater weight loss than the comparator arm, with an adjusted mean difference of -2.5kg, p<0.05.

Table 4.1.3 Continued: Studies examining the effectiveness of weight management interventions in Commercial programmes

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Jebb, 2011	UK, Germany, Australia	772	Intervention arm: Mean BMI= 31.5kg/m^2 Weight= 86.9kg Age= 46.5years 88.0% female Control arm: Mean BMI= 31.3kg/m^2 Weight= 86.5kg Age= 48.2years 86.0% female	RCT comparing 12 months commercial Weight Watchers programme with primary care usual care comparator in overweight and obese adults. Intervention arm received 12 months of free access to weekly Weight Watchers meetings held in the community, which promote low energy diet and increased physical activity through group support. Control arm received 12 months of weight loss advice from a primary care professional in line with national clinical guidelines, at their local GP practice	At 12 months, weight outcomes were obtained for 230 individuals (61%) of the intervention arm while outcomes were obtained for 214 individuals (54%) of the control arm. Mean weight change was greater for intervention group using LOCF data: -5.1kg vs -2.3kg, p<0.0001 BOCF: -4.1kg vs -1.8kg, p<0.0001 Available case data: -6.7kg vs -3.3kg, p<0.0001 Individuals receiving the commercial programme had increased odds of losing ≥5% baseline weight: OR= 3.0 (2.0 - 4.4), and ≥10% weight: OR= 3.2 (2.0 - 5.3), compared to those receiving usual care. Odds of losing ≥5% baseline weight were increased for those completing the programme: OR= 2.9 (2.1 - 3.9), and ≥10% baseline weight: OR= 3.5 (2.3 - 5.4), compared to those receiving usual care. No significant difference in intervention effectiveness between countries, p>0.10. Baseline and follow-up IWQOL-Lite not reported.
Truby, 2006	UK, 5 regions: Bristol, Surrey, Nottingham, Edinburgh and Ulster	292	Mean values across arms: BMI=31.2-32.2kg/m^2 Weight=87.9-90.3kg Age=38.9-40.9 years 71-75% female	RCT comparing the following 4 commercial interventions for 6 months, with a control group who were asked to maintain current diet and exercise levels. • Weight Watchers comprising weekly group support sessions, • Slim-Fast plan comprising provision of two daily meal replacements and support pack, • Dr Atkins' 'New diet revolution' comprising provision of a self-help dietary advice book, • Rosemary Conley's 'Eat yourself slim' comprising weekly group exercise and diet advice sessions.	At 6 months (intervention-end), no significant difference between intervention arms, with all interventions achieving significantly greater weight loss than control (p<0.001) with the following losses (LOCF data): Weight Watchers: -6.6kg, -7.3% body weight Slim-Fast: -4.8kg, -4.9% body weight Atkins: -6.0kg, -6.2% body weight Rosemary Conley: -6.3kg, -7.0% body weight. Available data at 6 months obtained for 71.9% of sample: Weight Watchers: -8.0kg, -9.0% body weight Slim-Fast: -6.5kg, -6.8% body weight Atkins: -8.5kg, -8.9% body weight Rosemary Conley: -8.8kg, -9.9% body weight. 12 month data for 19.9% of sample who continued allocated diet, with changes from 6months: Weight Watchers +0.5kg, Slim-Fast -1.7kg, Atkins -1.5kg, Rosemary Conley +1.2kg.

4.1.5 Sporting club-based programmes

A novel sporting club-based intervention, Football Fans in Training (FFIT) was evaluated in a large scale RCT (73) by the team who devised the male-only primary care-based Camelon programme (30). The FFIT intervention was delivered in partnership with 13 Scottish professional football clubs from the Scottish Premier Football League to 747 male football fans aged 35 to 65 with a BMI ≥28 kg/m^2. The mean BMI of individuals receiving the FFIT intervention at baseline was 35.5kg/m^2, with a mean age of 47.0 years. The FFIT male-only adult group intervention comprised an initial programme of 12 weekly 90-minute sessions delivered at individuals' local football club stadiums by coaching staff who received training from the research team. The sessions were conducted in relatively large-sized groups, with up to 30 men per group, with a maximum of 15 individuals to every coach, with sessions comprising diet and activity advice using recognised behavioural change techniques, along with physical activity sessions which increased in intensity throughout the programme. On completion of the 12-week intervention, there was a weight maintenance phase comprising six email prompts delivered to participants over the following 9 month period and a final group session which was delivered 6 months after the completion of the initial 12-week programme of sessions, making the total duration of the FFIT intervention 12 months.

An additional publication describing the development of the FFIT intervention provides detail of how data gathered during the implementation of a pilot study, the p-FFIT intervention which was delivered at 11 football clubs and a feasibility study conducted in two football clubs was used to inform the design of the FFIT intervention (182). Additionally, the FFIT intervention has been described in greater detail, providing excellent description of the specific behaviour change techniques which were utilised in

the delivery of the FFIT programme. The techniques were been mapped onto the taxonomy of behaviour change techniques (version 1) which was developed in response to the need for more accurate reporting and description of complex behavioural interventions (183). This detailed reporting allows the reader to see which techniques have been used in each FFIT session and in each email communication with the participants, and additionally the theoretical constructs which underpin each of the specific techniques. The process identified that the techniques of self-monitoring, development of implementation intentions, and goal setting, which are associated with control theory and social cognitive theory were prominent in the FFIT intervention.

The findings of the RCT of the FFIT programme were published in the Lancet (73). Data were obtained for 92% of the sample at 12 months, with analyses conducted using LOCF data. On completion of the initial 12 weekly sessions, the intervention arm receiving the FFIT programme achieved mean losses of -5.8kg (-5.2%) and -1.9kg/m^2 BMI, with 47% of those receiving the intervention achieving a loss of ≥5% of their baseline body weight. The adjusted mean differences between the intervention and control arms at 12 weeks were -5.2kg (-4.7%) and -1.7kg/m^2 BMI, $p < 0.0001$, with greater losses achieved by the intervention arm. At 12 months, the intervention arm achieved mean losses of -5.6kg (-5.0%) and -1.8kg/m^2 BMI, with 39% achieving a baseline body weight loss ≥5%. The adjusted mean differences between the intervention and control arms at 12 months were -4.9kg (-4.4%) and -1.6kg/m^2 BMI, $p < 0.0001$, with greater losses in the intervention arm. The evaluation also encompassed a cost-effectiveness assessment and the inclusion of quality of life outcomes, which indicated that psychological and mental health outcomes were significantly better for those receiving the FFIT intervention rather than the control group ($p < 0.01$), with the exception of the 12 month longer-term mental health component

of the SF-12, where there were no significant differences between the intervention and control groups ($p > 0.05$).

The RCT was strengthened by the rigorous trial methodology, the detailed reporting of the intervention and its development and by the inclusion of quality of life measures and a cost-effectiveness evaluation. However it would be beneficial to include outcome data and separate analyses for those individuals who completed the programme, in addition to the LOCF data which was presented. In conclusion, the study demonstrates the effectiveness of a weight management intervention delivered to an at-risk hard to reach group of males, as an alternative to more traditional weight management interventions implemented either in healthcare or commercial settings. These are often perceived to be a female-orientated domain, with predominantly female samples, which males may consider to be an uninviting prospect. There are plans for the research group to extend the intervention to additional target groups including a female-only group for individuals recruited through football clubs and a male-only group delivered at local rugby clubs, to offer other individuals the opportunity to attend weight management programmes in settings which may be deemed to be more engaging and acceptable.

Table 4.1.4: Studies examining the effectiveness of weight management interventions in Sporting clubs

First author, year	Setting	Sample size	Sample	Intervention (Weight loss or maintenance)	Findings
Hunt, 2014	Scotland, across 13 football clubs	747	Intervention arm: Mean BMI= 35.5kg/m^2 Weight= 110.3kg Age= 47.0years 0% female Control arm: Mean BMI= 35.1kg/m^2 Weight= 108.7kg Age= 47.2years 0% female	Football Fans in Training (FFIT) 12-week male-only adult group intervention delivered at local football club stadiums. Coaching staff employed by the clubs received 2-days training from research team and delivered intervention to groups of up to 30 males, with a maximum of 15 per coach. The weekly 90-minute sessions comprised diet and activity advice using techniques including self-monitoring and goal setting, along with physical activity sessions which increased in intensity throughout the programme. Initial 12-week intervention followed by weight maintenance phase comprising 6 email prompts over the following 9 month period and a group session 6 months after 12-week session end, making total FFIT intervention duration of 12 months.	Data obtained for 688 individuals (92%) of sample at 12 months, analyses of LOCF data: At 12 weeks, FFIT achieved mean losses of -5.8kg, -5.2%, -1.9kg/m^2, with 47% achieving ≥5% weight loss. Adjusted mean difference between intervention and control: -5.2kg, -4.7% and -1.7kg/m^2, p<0.0001. At 12 months, FFIT achieved mean losses of -5.6kg, -5.0%, -1.8kg/m^2, with 39% achieving ≥5% weight loss. Adjusted mean difference between intervention and control: -4.9kg, -4.4% and -1.6kg/m^2, p<0.0001. Estimated cost of £680 per participant to receive intervention and £475 per participant to receive no intervention. FFIT associated with a gain in QALYs of 0.015 (0.003-0.027), and cost-effectiveness of £13,847 per QALY gained. Psychological and mental health outcomes significantly better for intervention arm, with adjusted mean differences in: Rosenberg self-esteem score of +0.2 at 12 weeks, p<0.0001 and +0.1 at 12 months, p<0.0001. Positive affect PANAS score of +0.4 at 12 weeks, p<0.0001 and +0.3 at 12 months, p<0.0001. Negative affect PANAS score of -0.1 at 12 weeks, p<0.01 and -0.1 at 12 months, p<0.01. Physical component SF12 score of +2.6 at 12 weeks, p<0.0001 and +1.9 at 12 months, p<0.001. Mental component SF12 score of +2.0 at 12 weeks, p<0.001 however there was no significant difference between intervention and control, with adjusted mean difference of +0.5 at 12 months, p>0.05.

CHAPTER FIVE

5.0 LONGITUDINAL WEIGHT AND QUALITY OF LIFE OUTCOMES OF THE COMMUNITY WEIGHT MANAGEMENT SERVICE (CWMS) AND SPECIALIST LIFESTYLE MANAGEMENT (SLIM) PROGRAMME

5.1 INTRODUCTION

5.1.1 Rationale

The increasing prevalence of obesity and the associated detrimental impacts on individuals' health and quality of life, have led to the development of a wide variety of weight management programmes implemented in the UK and delivered across primary care settings, specialist weight management centres, commercial group programmes and sporting club-based initiatives. The literature review presented in Chapter four has highlighted the limited availability of good quality evaluations of weight management services in the body of the literature. The majority encompass evaluations of primary care-led programmes, whilst the effectiveness of specialist weight management services has not been established.

The lack of evidence base has meant that the variation in weight management service provision available for individuals in the UK has continued. However, the increasing prevalence of obesity and subsequent demand for services means that establishing the effectiveness of weight management services is essential in order to ensure that individuals are given the best opportunity at achieving weight loss. It is therefore important to establish whether the two treatment pathways operating within the Specialist Weight Management Service; the Community Weight Management Service (CWMS) and the Specialist Lifestyle (SLiM) programme, provide effective weight loss and quality of life outcomes.

5.1.2 Aims

This chapter aims to examine the efficacy of two treatment pathways offered by the HEFT Specialist Weight Management Service; the CWMS and the SLiM programme. The baseline and longitudinal weight and quality of life outcomes of participants will be examined in order to compare the efficacy of the two medically-supported weight management pathways and establish if they can yield clinically significant weight loss outcomes. Further analyses will examine the factors associated with successful weight loss and improvement in quality of life. Additional subsample analyses will examine the association between change in BMI and change in quality of life from baseline to programme-end in further detail within the SLiM subsample. The chapter will conclude with a summary of the outcomes achieved by the services, the factors predicting changes in weight and quality of life outcomes and recommendations to further improve the service in light of these findings.

5.2 METHODS

5.2.1 Research design

The baseline determinants of longitudinal outcomes in a sample attending a Specialist Weight Management Service were analysed in order to examine the efficacy of two different treatment pathways which run within the service; CWMS and SLiM. Individuals fulfilling the eligibility criteria of having BMI $\geq$40.0kg/m^2 or alternatively BMI $\geq$35.0kg/m^2 with a weight-related health condition were referred to the service by their GP. The sample of 700 extreme obese individuals attended either the CWMS (N=262), or the SLiM programme (N=438). The sample comprised individuals aged 19 to 76, who entered the CWMS between February 2008 and August 2012, and entered the SLiM programme between August 2009 and February 2013.

5.2.2 Specialist Weight Management Service

The two medically supported treatment pathways delivered within the Specialist Weight Management Service operated by HEFT have been described in Chapter one; however the following brief description is for reference. The CWMS provides comprehensive multidisciplinary care for a 12-month period from a team of specialist physicians, dietitians, and psychologist, delivered through one-to-one appointments in the community. The SLiM programme provides patient education, peer-support and self-management through a structured programme of six monthly weight management group-sessions.

5.2.3 Weight and BMI change

Baseline weight and height were obtained from all individuals on entry to the service and BMI was calculated by dividing participants' weight in kg by height in meters squared. In addition to recording participants' initial weight and BMI data at baseline, weight and BMI data were collected at each point of contact for individuals in the CWMS for the duration of service attendance, which ranged across the sample from 3 months to 36 months. However, for individuals attending the SLiM programme, weight and BMI were collected at baseline, at 3 months post-baseline and at programme-end which was at 6 months. During the period of evaluation, the recording of weight data at each month of the SLiM programme was initiated. However as this was only available for a limited number of cases, these data were not included in the analyses in the present evaluation.

5.2.4 Predictors of weight and quality of life change

A wide range of baseline clinical and demographic data were obtained from individuals on entry to the service, including age, gender, ethnicity, self-reported quality of life as measured by IWQOL-Lite, HADS and EQ5D-3L, and co-morbid health conditions including diabetes, obstructive sleep apnoea (OSA), cardiovascular disease (CVD), arthritis and hypertension. These factors have been described in detail in Chapter two.

5.2.5 Missing data

As expected due to the pragmatic approach used to evaluate the efficacy of the service, there were instances of missing weight and BMI data, whereby for individual or practical reasons weight and BMI measures were not recorded. For the SLiM group, weight data was obtained for 86.1% of the sample at 3 months, and 100% of the sample at 6 months

post-baseline. However, for the CWMS sample, data was obtained for 62.6% of the sample at 3 months, 44.7% of the sample at 6 months, 32.1% at 12 months, 11.8% at 18 months, and 8.4% at 24 months. The observed attrition rate of 67.9% at 12 months is consistent with the rate demonstrated by the Glasgow and Clyde Specialist Weight Management Service, of 65.2% (175). Indeed, medical and behavioural weight management interventions have been demonstrated to be at risk of high attrition, with a systematic review of 13 studies demonstrating attrition rates ranging from 16-59% (184).

A high attrition rate may demonstrate a significant source of withdrawal bias and has the potential to lead to misleading results (185). It is therefore imperative to assess whether there are clinically and statistically significant differences in the characteristics of those attending and withdrawing from weight management services as this will greatly impact on the interpretation of the outcomes achieved. Thus sensitivity analyses were conducted within the present study to assess for differences between those who attended at 12 months (the minimum attendance period for the CWMS), and those who had withdrawn. There were no significant differences in the demographic characteristics of age, gender, ethnicity, marital status, occupation and children. Furthermore there were no significant differences in the baseline clinical characteristics of weight, BMI, waist circumference, systolic and diastolic blood pressure, presence of diabetes, hypertension and arthritis, use of weight medication, smoking and alcohol consumption, sedentary time as well as self-reported scores on the HADS, ESS and PSQI measures. The only significant differences identified between those attending and withdrawing were a smaller proportion of those with OSA (21.9% vs 33.3%, p= 0.048) and CVD (8.4% vs 16.7%, p= 0.047) in those withdrawing at 12 months, relative to those attending at 12 months, and a smaller proportion reporting the presence of 3 or more co-morbid health conditions (13.5% vs

26.2%, p= 0.034). Whilst there were no significant differences in continuous baseline BMI, there was a significantly smaller proportion of individuals in the BMI 50-59 category (17.4% vs 35.7%, p= 0.002) for those withdrawing at 12 months. There were also significant differences in self-reported physical function, self-care and pain and discomfort, whereby those withdrawing at 12 months reported better physical function (44.6 vs 37.7, p= 0.046), were more likely to report experiencing no problems in self-care (69.7% vs 52.2%, p= 0.018) and less likely to report experiencing extreme problems pain and discomfort (23.1% vs 39.1%, p= 0.003). Furthermore, the initial weight loss outcomes achieved during the service did not appear to impact upon attrition, with no significant differences in the weight change achieved at 3 months and 6 months between those who had withdrawn or were attending at 12 months. In summary, despite the relatively high attrition rate, there did not appear to be substantial differences in the baseline characteristics of those attending and withdrawing from the service, and importantly initial weight loss outcomes were not demonstrated to impact on attrition. Thus the outcomes demonstrated by those attending can be considered to be representative of the outcomes which could have been achieved by those individuals withdrawing from the service, had they remained and completed their attendance.

To deal with the missing data, a LOCF approach was utilised, whereby the last observed data points were imputed in cases where follow-up data for specific time points were not available, which increased the proportion of data for the CWMS sample to 100%. The analysis of LOCF data is an accepted approach that has been widely used to deal with the problem of missing outcome data in RCTs assessing treatment effects (186). In order to facilitate comparison, the findings of descriptive analyses are presented using data from available cases, which gives an indication of the outcome for individuals who attend the

service more fully, as well as data imputed using the LOCF approach which gives a more conservative outcome for all individuals attending the service for varied periods of time. All further analyses examining the predictors of weight loss and gain were conducted using LOCF data, in order to give a more conservative estimate of the outcome of all individuals entering the service, irrespective of attendance.

5.2.6 Statistical analysis

All data were analysed using IBM SPSS Statistics (version 21.0). The mean weight and BMI of the CWMS and SLiM groups at baseline were compared using independent t-test. The proportion of individuals in the following baseline BMI groups 30.0-39.9kg/m^2, 40.0-49.9kg/m^2, 50.0-59.9kg/m^2, and ≥60.0kg/m^2 were compared using cross-tabulation and Chi^2 calculations (Table 5.3.1). The mean changes in weight, BMI and change in percentage of baseline body weight lost at 3 and 6 months from baseline were analysed by paired t-test (Tables 5.3.2a and b). Linear regression was used to establish if the mean changes in weight and BMI at 3 and 6 months from baseline differed between the CWMS and SLiM samples, adjusting for age, sex and baseline weight (Tables 5.3.2a and b). The mean changes in weight, BMI and change in percentage of baseline body weight lost at 3, 6, 12, 18 and 24 months from baseline for the CWMS sample were analysed by paired t-test, indicating significant differences between baseline and follow-up values, and additionally indicating significant differences between 12 and 24 month values (Tables 5.3.3a and b). The proportion of individuals losing any amount of weight (>0%) was calculated for the SLiM and CWMS samples separately and combined, throughout service attendance, as were the proportions of the sample losing >0-4.9%, 5-9.9%, ≥5%, and ≥10% of their baseline body weight and the proportion gaining or maintaining their baseline

weight. The proportion of individuals in each category was compared for the CWMS and SLiM groups using cross-tabulation and Chi^2 calculations (Tables 5.3.4a and b). The mean weight loss and gain values for the CWMS and SLiM samples were compared using linear regression to establish if the mean weight gain and weight loss from baseline values differed between the CWMS and SLiM samples, adjusting for age, sex and baseline weight (Table 5.3.5).

Logistic regression analyses were conducted to examine factors predicting clinically significant weight loss (≥5%), and weight gain (>0kg). Predictors of ≥5% weight loss and weight gain at 6 months were examined in the CWMS and SLiM samples separately using a hierarchical approach: Model 1 included age and gender; Model 2 additionally included baseline weight, presence of diabetes, and ethnicity; Model 3 additionally included the IWQOL-Lite subscales. The factors predicting ≥5% weight loss and weight gain at 12 months (minimum attendance) in the CWMS sample comprised: Model 1 which included age and gender; Model 2 additionally included baseline weight, presence of diabetes, OSA, CVD, arthritis and hypertension; Model 3 additionally included the IWQOL-Lite subscale scores, EQ5D-3L self-reported perceived health rating and HADS anxiety and depression score. Ethnicity was not included in the factors predicting ≥5% weight loss and weight gain at 12 months as this greatly reduced the sample size and the numbers within each ethnicity group remained too small to meaningfully contribute to the analyses, despite collapsing the categories to create a binary White European and non-White European variable.

Linear regression analyses were also used to identify predictors of weight change using a continuous variable, whereby negative values indicated weight gain and positive values indicated weight loss, at 6 months in the CWMS and SLiM samples separately

using a hierarchical approach: Model 1 included age and gender; Model 2 additionally included baseline weight, presence of diabetes, and ethnicity; Model 3 additionally included the IWQOL-Lite subscales. The factors predicting weight change at 12 months (minimum attendance) in the CWMS sample comprised: Model 1 which included age and gender; Model 2 additionally included baseline weight, presence of diabetes, OSA, CVD, arthritis, hypertension and ethnicity; Model 3 additionally included the IWQOL-Lite subscale scores, EQ5D-3L self-reported perceived health rating and HADS anxiety and depression score.

Follow-up IWQOL-Lite data were obtained for a subset of the SLiM sample and the mean IWQOL-Lite subscales and total scores were analysed by paired t-test, to establish whether the 6-month follow-up scores were significantly different from baseline scores (Table 5.3.15). Additionally, a binary quality of life improvement variable was created distinguishing between those who experienced gain in IWQOL-Lite total scores between baseline and programme-end. Logistic regression analysis was then conducted to examine factors predicting quality of life improvement at 6 months using a hierarchical approach: Model 1 included age and gender; Model 2 additionally included baseline weight, presence of diabetes, and ethnicity; Model 3 additionally included baseline IWQOL-Lite subscales and total scores (Table 5.3.16). Linear regression coefficients were calculated to assess the association between change in IWQOL-Lite total and subscale scores from baseline to programme-end (dependent variable) and change in BMI from baseline to programme-end, in order to establish if change in BMI predicted change in quality of life. Three hierarchical models are presented: crude; adjusting for age and sex; and additionally adjusting for the presence of co-morbid type 2 diabetes (Table 5.3.17).

Post-hoc power calculations were conducted in order to assess whether there was sufficient power to detect the target ≥5% weight loss within both the CWMS and SLiM treatment pathways. The design was specified as a two independent study sample design with the dichotomous outcome of ≥5% weight loss, and calculations were performed using both available case and LOCF data. The post-hoc analysis indicated that on the basis of the available case data whereby ≥5% weight loss was achieved by 30.3% of the SLiM sample (N= 438) at programme completion (6 months) and by 40.5% of the CWMS sample (N= 84) at minimum attendance (12 months), the design was underpowered with 45.3% power. Similarly, when using LOCF data the design was also underpowered with 47.0% power, whereby ≥5% weight loss was achieved by 30.3% of the SLiM sample (N= 438) at 6 months and 23.7% of the CWMS sample (N= 262) at 12 months. A post-hoc power calculation was also conducted to assess whether there was sufficient power to detect differences between baseline and follow-up IWQOL-Lite quality of life scores within the SLiM sample. The design was specified as a one study group versus population design with a continuous end-point outcome of mean IWQOL-Lite total score. The post-hoc analysis indicated that on the basis of a known mean baseline score of 35.8±20.1 and an expected mean score of 42.7 (observed mean follow-up score) within the SLiM sample (N= 116), that the design was highly powered with 96% power to detect the observed difference between the baseline and intervention-end mean IWQOL-Lite total scores.

5.3 RESULTS

5.3.1 Mean weight and BMI change during service attendance

Table 5.3.1 shows the mean baseline weight and BMI of the SLiM and CWMS samples separately and combined. The SLiM sample had a significantly greater mean weight and BMI at baseline, with a greater proportion of individuals in the more extreme obese BMI $\geq$50.0kg/m^2 and $\geq$60.0kg/m^2 groups. The baseline data of the CWMS sample are described in more detail in Chapter two.

Table 5.3.1: Comparison of the baseline weight and BMI of the CWMS and SLiM samples separately and combined

	Combined	CWMS	SLiM	P
N	700	262	438	
Weight (kg)	135.2±27.2	132.1±24.7	137.1±28.5	0.018
Body mass index (BMI, kg/m^2)	48.7±9.0	47.0±7.9	49.8±9.4	<0.001
Proportion in BMI group (%)				<0.001
BMI 30.0-39.9kg/m^2	13.9	17.2	11.9	
BMI 40.0-49.9kg/m^2	49.1	53.4	46.6	
BMI 50.0-59.9kg/m^2	25.6	23.3	26.9	
BMI $\geq$60.0kg/m^2	11.4	6.1	14.6	

Data are percentages and means ± standard deviations.

Tables 5.3.2a and 2b show the mean change in weight (kg and %) and BMI across the first 6 months of service attendance for both samples separately and combined. The available case data (Table 5.3.2a) show that there were no significant differences between the SLiM and CWMS samples in the mean weight and BMI change values at both 3 and 6 months post-baseline. The LOCF data (Table 5.3.2b) show that there were significantly smaller reductions in weight (kg and %) in the CWMS sample at 3 and 6 months post-baseline relative to the SLiM sample. There was no significant difference in BMI at 3

months. However at 6 months there was a significantly smaller reduction in BMI for the CWMS sample. The significantly smaller reductions in weight and BMI observed for the CWMS sample are due to the fact that there was a greater proportion of missing data in the CWMS sample at 3 months (37.4% vs 13.9%) and at 6 months (55.3% vs 0%), with imputed LOCF values attributing to a decrease in the weight and BMI loss values for the CWMS sample. The LOCF sample combined values show mean weight reductions of -3.0kg (-2.1%) at 3 months with further reductions reaching -4.5kg (-3.2%) at 6 months post-baseline. The available case data demonstrate greater weight change, with mean losses of -3.9kg (-2.7%) and -1.4kg/m^2 at 3 months with further reductions reaching -5.2kg (-3.8%) and -1.9kg/m^2 at 6 months. The SLiM programme is a 6-month intervention, with the 6-month post-baseline outcomes demonstrating that at programme-end the SLiM programme achieved mean reductions of -5.2kg (-3.7%) body weight and -1.9kg/m^2 BMI.

Table 5.3.2a: Mean change in weight, body weight percentage and BMI throughout 6 month attendance in combined sample and by service using available case data

	Combined	CWMS	SLIM	P
N	700	262	438	
Weight change (kg)				
3 month (N=541)	-3.9†±6.1	-3.4†±5.9	-4.1†±6.1	0.546
6 month (N=555)	-5.2†±7.1	-5.4†±7.6	-5.2†±7.0	0.205
Weight change (%)				
3 month (N=541)	-2.7†±4.1	-2.4†±4.1	-2.9†±4.1	0.423
6 month (N=555)	-3.8†±4.9	-4.0†±5.5	-3.7†±4.7	0.208
BMI change (kg/m^2)				
3 month (N=541)	-1.4†±2.3	-1.2†±2.1	-1.5†±2.4	0.867
6 month (N=555)	-1.9†±2.6	-2.0†±2.7	-1.9†±2.6	0.114

Data are means ± standard deviations
Changes in body weight (kg and %) and BMI are changes from baseline values
**Indicates change value is significantly different from baseline value, $p<0.05$, † $p<0.001$, analysed by paired t-test*
P values indicate whether mean changes in weight and BMI at 3 and 6 months from baseline differ between the CWMS and SLiM samples, adjusting for age, sex and baseline weight.

Table 5.3.2b: Mean change in weight, body weight percentage and BMI throughout 6 month attendance in combined sample and by service using LOCF data

	Combined	CWMS	SLIM	P
N	700	262	438	
Weight change (kg)				
3 month (N=700)	-3.0†±5.6	-2.1†±4.9	-3.5†±5.9	0.022
6 month (N=700)	-4.5†±6.8	-3.2†±6.4	-5.2†±7.0	0.008
Weight change (%)				
3 month (N=700)	-2.1†±3.8	-1.5†±3.5	-2.5†±3.9	0.011
6 month (N=700)	-3.2†±4.7	-2.3†±4.6	-3.7†±4.7	0.004
BMI change (kg/m^2)				
3 month (N=700)	-1.1*±2.1	-0.7†±1.7	-1.3†±2.2	0.055
6 month (N=700)	-1.6†±2.5	-1.2†±2.3	-1.9†±2.6	0.032

Data are means ± standard deviations
Changes in body weight (kg and %) and BMI are changes from baseline values
**Indicates change value is significantly different from baseline value, p<0.05, † p<0.001, analysed by paired t-test*
P values indicate whether mean changes in weight and BMI at 3 and 6 months from baseline differ between the CWMS and SLiM samples, adjusting for age, sex and baseline weight.

Tables 5.3.3a and 3b show the longer-term follow-up data obtained for the CWMS sample. Data from available cases (Table 5.3.3a) indicate that significant reductions from baseline weight and BMI were achieved at each data collection point, with weight and BMI reductions increasing with longer service attendance. As anticipated, analysis of available cases data showed greater reductions of -7.0kg (-5.0%) and -2.6kg/m^2, whilst LOCF data (Table 5.3.3b) demonstrated more conservative reductions of -4.1kg (-2.9%) and -1.5kg/m^2 at 12 months post-baseline (CWMS minimum attendance). Similarly the 24 month data also showed greater reductions when analysing available cases than LOCF data, with reductions of -13.4kg (-10.2%) and -5.1kg (-3.6%), respectively. Indeed, the LOCF data demonstrated that a further significant loss of -1.0kg was obtained between 12 months and 24 months, indicating that weight loss continued with service attendance.

Table 5.3.3a: Weight change up to 24 months in CWMS sample using available case data

	Weight change (kg)	Weight change (%)	BMI change (%)
3 months (N=164)	-3.4†±5.9	-2.4†±4.1	-1.2†±2.1
6 months (N=117)	-5.4†±7.6	-4.0†±5.5	-2.0†±2.7
12 months (N=84)	-7.0†±10.8	-5.0†±8.0	-2.6†±4.0
18 months (N=31)	-10.5*±18.7	-7.2*±10.9	-3.5*±5.6
24 months (N=22)	-13.4†±15.2	-10.2†±11.8	-4.8†±5.6

Data are means ± standard deviations
Changes in body weight (kg and %) and BMI are changes from baseline values
**Indicates change value is significantly different from baseline value, p<0.05, † p<0.001, analysed by paired t-test*
≠ Indicates 24 month change value is significantly different from 12 month value, p<0.05, analysed by paired t-test.

Table 5.3.3b: Weight change up to 24 months in CWMS sample using LOCF data

	Weight change (kg)	Weight change (%)	BMI change (%)
3 months (N=262)	-2.1†±4.9	-1.5†±3.5	-0.7†±1.7
6 months (N=262)	-3.2†±6.4	-2.3†±4.6	-1.2†±2.3
12 months (N=262)	-4.1†±8.2	-2.9†±5.9	-1.5†±3.0
18 months (N=262)	-4.8†±10.2	-3.4†±6.8	-1.7†±3.5
24 months (N=262)	-5.1†≠±10.7	-3.6†≠±7.1	-1.8†≠±3.6

Data are means ± standard deviations
Changes in body weight (kg and %) and BMI are changes from baseline values
** Indicates change value is significantly different from baseline value, p<0.05, † p<0.001, analysed by paired t-test*
≠ Indicates 24 month change value is significantly different from 12 month value, p<0.05, analysed by paired t-test.

Tables 5.3.4a and 4b show the proportion of individuals in the samples gaining or losing weight throughout service attendance. There was a significantly greater proportion of individuals losing weight in the SLiM sample (78.5%) than the CWMS sample (70.1%) at 3 months when analysing available case data. This significant difference remained at 6 months, with 83.3% of the SLiM sample and 79.4% of the CWMS sample achieving weight loss. Indeed, at the point of programme-end for SLiM (6 months), 30.3% of the sample achieved a clinically meaningful weight loss of ≥5% of their baseline weight. The sample combined available case data demonstrated that attendance at the Specialist Weight

Management Service (through combined treatment pathways) resulted in weight loss for 76.0% of individuals after 3 months and 82.5% of individuals after 6 months. As duration of CWMS service attendance increased, the proportions of individuals achieving greater amounts of weight loss increased, with the proportion of individuals losing ≥5% of their baseline body weight increasing from 18.9% at 3 months, to 59.1% at 24 months.

Table 5.3.4a: Proportion of weight loss in CWMS and SLiM samples using available case data

		>0% loss	>0-4.9% loss	5.0-9.9% loss	≥10% loss	≥5% loss	Weight gain or maintain
SLiM	**3 months** (N=377)	78.5	55.4	18.6	4.5	23.1	21.5
	6 months (N=438)	83.3	53.0	21.5	8.8	30.3	16.7
CWMS	**3 months** (N=164)	70.1	51.2	14.0	4.9	18.9	29.9
	6 months (N=117)	79.4	42.7	23.9	12.8	36.7	20.6
	12 months (N=84)	77.4	36.9	16.7	23.8	40.5	22.6
	18 months (N=31)	77.4	32.2	22.6	22.6	45.2	22.6
	24 months (N=22)	77.3	18.2	22.7	36.4	59.1	22.7
Combined	**3 months** (N=541)	76.0	54.2	17.2	4.6	21.8	24.0
	6 months (N=555)	82.5	50.8	22.0	9.7	31.7	17.5

Data are percentages
†Indicates value is significantly different between SLiM and CWMS samples, p<0.001.

As expected, analysis of LOCF data demonstrated more conservative losses than available cases data, with 23.7% of the sample achieving a loss of ≥5% of their baseline body weight at the end of CWMS minimum attendance, 12 months post-baseline. These proportions remained stable at 18 and 24 months, with 24.5% and 24.8% achieving ≥5% weight loss, respectively.

Table 5.3.4b: Proportion of weight loss in CWMS and SLiM samples using LOCF data

		>0% loss	>0-4.9% loss	5.0-9.9% loss	≥10% loss	≥5% loss	Weight gain or maintain
SLiM	**3 months** (N=438)	67.6†	47.7†	16.0†	3.9†	19.9†	32.4†
	6 months (N=438)	83.3†	53.0†	21.5†	8.8†	30.3†	16.7†
CWMS	**3 months** (N=262)	43.9†	32.1†	8.7†	3.1†	11.8†	56.1†
	6 months (N=262)	53.8†	33.1†	13.4†	7.3†	20.7†	46.2†
	12 months (N=262)	58.0	34.3	10.7	13.0	23.7	42.0
	18 months (N=262)	59.5	35.0	11.5	13.0	24.5	40.5
	24 months (N=262)	58.4	33.6	10.7	14.1	24.8	41.6
Combi-ned	**3 months** (N=700)	58.7	41.9	13.3	3.5	16.8	41.3
	6 months (N=700)	72.3	45.6	18.4	8.3	26.7	27.7

Data are percentages
†Indicates value is significantly different between SLiM and CWMS samples, p<0.001.

Table 5.3.5 shows the mean weight change values, distinguishing between those who lost and gained weight across service attendance. For those who gained weight, at 3 months the combined sample mean weight gain was +0.9kg (+0.7%), and at 6 months mean weight gain was +1.8kg (+1.3%); whilst for those who lost weight, mean weight losses of -5.7kg (-4.1%) and -6.8kg (-4.9%) were achieved at 3 and 6 months, respectively. There were no significant differences in mean weight gain or loss values between the

SLiM and CWMS samples at 3 months, however at 6 months the mean weight gain values were significantly greater in the SLiM sample (+2.9kg, +2.1%) relative to the CWMS sample (+1.1kg, +0.8%).

Table 5.3.5: Mean weight loss and gain at 3, 6, and 12 months for those losing and gaining weight in combined sample and by service using LOCF data

	Combined	**CWMS**	**SLiM**	**P**
Baseline (N)	700	262	438	
Weight (kg)	135.2±27.2	132.1±24.7	137.1±28.5	0.018
Mean weight loss (kg)				
3 months	-5.7†±5.8	-5.7†±5.4	-5.7†±5.9	0.485
6 months	-6.8†±6.5	-6.9†±6.6	-6.8†±6.4	0.455
12 months	-	-8.1†±8.5	-	-
Mean weight loss (%)				
3 months	-4.1†±3.7	-4.2†±3.5	-4.0†±3.8	0.505
6 months	-4.9†±4.3	-5.1†±4.6	-4.9†±4.2	0.478
12 months	-	-5.9†±6.0	-	-
Mean weight gain (kg)				
3 months	0.9†±1.6	0.7†±1.5	1.1†±1.6	0.114
6 months	1.8†±2.3	1.1†±1.9	2.9†±2.4	<0.001
12 months	-	1.4†±2.6	-	-
Mean weight gain (%)				
3 months	0.7†±1.2	0.6†±1.3	0.8†±1.1	0.151
6 months	1.3†±1.7	0.8†±1.5	2.1†±1.8	<0.001
12 months	-	1.1†±2.1	-	-

Data are means ± standard deviations
** Indicates change value is significantly different from baseline value, p<0.05, † p<0.001, analysed by paired t-test.*

5.3.2 Predictors of ≥5% weight loss at 6 months

Table 5.3.6 displays the predictors of ≥5% weight loss at 6 months post-baseline for the SLiM sample, utilising LOCF data. A test of the fully adjusted model (Model 3) against a constant only model was not statistically significant, indicating that the predictors as a set did not reliably distinguish between those losing ≥5% weight and those who did not (Chi^2 =8.09, p =0.621). Nagelkerke's R^2 of 0.087 indicated that the model accounted for only 8.7% of the variance in weight loss status, with no significant predictors of weight loss identified.

Table 5.3.6: Predictors of ≥5% weight loss at 6 months in the SLiM sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1 N=438	Age	1.00	0.99 – 1.02
	Gender	0.61*	0.39 – 0.96
Model 2 N=436	Age	1.00	0.99 – 1.02
	Gender	0.72	0.45 – 1.16
	Baseline weight	1.01	1.00 – 1.02
	Diabetes	1.02	0.65 – 1.61
	Ethnicity (non-white)	0.78	0.45 – 1.36
Model 3 N=123	Age	1.01	0.97 – 1.05
	Gender	0.81	0.30 – 2.21
	Baseline weight	1.01	0.99 – 1.02
	Diabetes	0.44	0.18 – 1.07
	Ethnicity (non-white)	1.01	0.37 – 2.77
	IWQOL-Lite physical function	1.01	0.98 – 1.03
	IWQOL-Lite self-esteem	1.01	0.99 – 1.03
	IWQOL-Lite sexual life	0.99	0.98 – 1.01
	IWQOL-Lite public distress	1.00	0.98 – 1.03
	IWQOL-Lite work	1.00	0.99 – 1.02

* *p<0.05*
† *p<0.001.*

Table 5.3.7 shows the predictors of ≥5% weight loss at 6 months post-baseline (utilising LOCF data) for the CWMS sample. The fully adjusted model (Model 3) was not statistically significant (Chi^2 =13.39, p =0.202), with Nagelkerke's R^2 of 0.195, indicating that the model accounted for 19.5% of the variance in weight loss status. Diabetes was a significant predictor of weight loss, with the odds ratio of 0.11 indicating that the likelihood of achieving ≥5% weight loss decreases by 89% for those with diabetes relative to those without the condition. Initial weight was also a significant predictor, with the odds ratio of 1.04 indicating that for every 1kg increase in baseline weight, the likelihood of an individual achieving ≥5% weight loss is increased by 4%, with those individuals who were heavier at baseline being more likely to lose ≥5% of their baseline weight.

Table 5.3.7: Predictors of ≥5% weight loss at 6 months in the CWMS sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1 N=259	Age	1.02	0.99 – 1.04
	Gender	0.74	0.37 – 1.46
Model 2 N=140	Age	1.03	0.99 – 1.07
	Gender	0.72	0.26 – 1.97
	Baseline weight	1.02*	1.01 – 1.04
	Diabetes	0.75	0.27 – 2.12
	Ethnicity (non-white)	2.53	0.66 – 9.75
Model 3 N=106	Age	1.07	1.00 – 1.15
	Gender	1.42	0.30 – 6.81
	Baseline weight	1.04*	1.01 – 1.07
	Diabetes	0.11*	0.02 – 0.75
	Ethnicity (non-white)	1.22	0.18 – 8.15
	IWQOL-Lite physical function	1.00	0.97 – 1.03
	IWQOL-Lite self-esteem	0.98	0.94 – 1.01
	IWQOL-Lite sexual life	1.01	0.99 – 1.03
	IWQOL-Lite public distress	1.03	0.99 – 1.07
	IWQOL-Lite work	0.99	0.96 – 1.03

* *p<0.05*
† *p<0.001*.

5.3.3 Predictors of ≥5% weight loss at 12 months in the CWMS sample

Table 5.3.8 displays the predictors of ≥5% weight loss at 12 months post-baseline (utilising LOCF data) for the CWMS sample, as data for the SLiM sample were not collected at 12 months post-baseline. The fully adjusted model (Model 3) was not statistically significant (Chi^2 = 16.67, p =0.339), with Nagelkerke's R^2 of 0.166 indicating that the model accounted for only 16.6% of the variance in weight loss status. Indeed there were no significant predictors of ≥5% weight loss at 12 months, indicating that all factors: age, gender, initial weight, diabetes, OSA, CVD, arthritis, hypertension, quality of life, perceived health and anxiety and depression did not make a significant contribution to the prediction of ≥5% weight loss in the CWMS sample at 12 months.

Table 5.3.8: Predictors of ≥5% weight loss at 12 months in the CWMS sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1 N=259	Age	1.02	0.99 – 1.04
	Gender	0.51*	0.27 – 0.97
Model 2 N=259	Age	1.01	0.98 – 1.05
	Gender	0.69	0.33 – 1.43
	Baseline weight	1.02*	1.01 – 1.03
	Diabetes	0.76	0.36 – 1.61
	OSA	0.67	0.33 – 1.38
	CVD	0.84	0.31 – 2.27
	Arthritis	1.30	0.62 – 2.72
	Hypertension	1.86	0.90 – 3.86
Model 3 N=156	Age	1.03	0.97 – 1.09
	Gender	0.48	0.15 – 1.53
	Baseline weight	1.02	1.00 – 1.04
	Diabetes	0.57	0.17 – 1.84
	OSA	0.66	0.22 – 1.94
	CVD	1.12	0.23 – 5.49
	Arthritis	1.28	0.39 – 4.21
	Hypertension	1.46	0.46 – 4.65
	IWQOL-Lite physical function	1.01	0.98 – 1.03
	IWQOL-Lite self-esteem	1.00	0.98 – 1.03
	IWQOL-Lite sexual life	1.01	1.00 – 1.03
	IWQOL-Lite public distress	1.01	0.99 – 1.04
	IWQOL-Lite work	0.99	0.97 – 1.02
	EQ5D Perceived health	1.00	0.98 – 1.03
	HADS Anxiety and depression	1.03	0.94 – 1.12

* *p<0.05*
† *p<0.001.*

5.3.4 Predictors of weight gain at 6 months

Table 5.3.9 shows the predictors of weight gain at programme-end (6 months post-baseline) for the SLiM sample, utilising LOCF data. The fully adjusted model (Model 3) was statistically significant (Chi^2 =21.76, p =0.016), with Nagelkerke's R^2 of 0.310 indicating that the model accounted for 31.0% of the variance in weight gain status. Two significant predictors of weight gain were identified, age and public distress IWQOL-Lite score. The odds ratios of 0.91 and 0.95 indicate that for each increase in year of age the likelihood of gaining weight decreases by 9%, whilst for each one-point increase in public distress score the likelihood of weight gain decreased by 5%, suggesting that on completion of the 6-month SLiM programme individuals were more likely to have gained or maintained their baseline weight if they were younger and reported fewer experiences of public distress.

Table 5.3.9: Predictors of weight gain at 6 months in the SLiM sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1	Age	0.96*	0.94 – 0.98
N=438	Gender	1.46	0.77 – 2.77
Model 2	Age	0.96*	0.94 – 0.98
N=436	Gender	1.43	0.73 – 2.81
	Baseline weight	1.00	0.99 – 1.01
	Diabetes	1.05	0.59 – 1.88
	Ethnicity (non-white)	1.24	0.66 – 2.32
Model 3	Age	0.91*	0.85 – 0.98
N=123	Gender	0.30	0.05 – 1.74
	Baseline weight	0.99	0.97 – 1.01
	Diabetes	1.33	0.33 – 5.35
	Ethnicity (non-white)	2.54	0.61 – 10.59
	IWQOL-Lite physical function	0.99	0.94 – 1.03
	IWQOL-Lite self-esteem	1.02	0.98 – 1.05
	IWQOL-Lite sexual life	1.02	1.00 – 1.05
	IWQOL-Lite public distress	0.95*	0.91 – 0.99
	IWQOL-Lite work	1.01	0.97 – 1.04

* *p<0.05*
† *p<0.001.*

Table 5.3.10 shows the predictors of weight gain in the CWMS sample at 6 months post-baseline, utilising LOCF data. The fully adjusted model (Model 3) was not statistically significant (Chi^2 =15.04, p =0.131), with Nagelkerke's R^2 of 0.178 indicating that the model accounted for 17.8% of the variance in weight gain status. Two significant predictors of weight gain were identified, age and initial weight. The odds ratios of 0.95 and 0.97 indicate that for each increase in year of age the likelihood of gaining weight decreases by 5%, whilst for each 1kg increase in baseline weight the likelihood of weight gain decreased by 3%, suggesting that after 6 months attendance at the CWMS service individuals were more likely to have gained or maintained their baseline weight if they were younger and of lower baseline weight.

Table 5.3.10: Predictors of weight gain at 6 months in CWMS sample

	Predictor variables	**Odds Ratio (OR)**	**95% CI for OR**
Model 1	Age	0.97*	0.95 – 0.99
N=259	Gender	1.10	0.61 – 2.00
Model 2	Age	0.95*	0.92 – 0.98
N=140	Gender	1.25	0.47 – 3.28
	Baseline weight	0.99	0.97 – 1.00
	Diabetes	1.59	0.63 – 4.01
	Ethnicity (non-white)	0.67	0.19 – 2.33
Model 3	Age	0.95*	0.90 – 1.00
N=106	Gender	0.86	0.24 – 3.07
	Baseline weight	0.97*	0.95 – 0.99
	Diabetes	2.49	0.76 – 8.17
	Ethnicity (non-white)	1.22	0.26 – 5.76
	IWQOL-Lite physical function	1.00	0.98 – 1.02
	IWQOL-Lite self-esteem	1.03	1.00 – 1.06
	IWQOL-Lite sexual life	1.00	0.98 – 1.01
	IWQOL-Lite public distress	0.98	0.95 – 1.00
	IWQOL-Lite work	1.00	0.97 – 1.02

* *p<0.05*
† *p<0.001.*

5.3.5 Predictors of weight gain at 12 months

Table 5.3.11 shows the predictors of weight gain in the CWMS sample at 12 months post-baseline (minimum attendance at the CWMS), utilising LOCF data. The fully adjusted model (Model 3) was not statistically significant (Chi^2 =10.48, p =0.789), indicating that the predictors as a set did not reliably distinguish between those gaining or maintaining their baseline weight and those who achieved weight loss. Nagelkerke's R^2 of 0.087 indicates that the model accounted for only 8.7% of the variance in weight gain status and no significant predictors of weight gain were identified.

Table 5.3.11: Predictors of weight gain at 12 months in CWMS sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1	Age	0.98	0.96 – 1.00
N=259	Gender	0.86	0.48 – 1.56
Model 2	Age	0.98	0.96 – 1.01
N=259	Gender	0.76	0.39 – 1.48
	Baseline weight	0.99	0.98 – 1.01
	Diabetes	0.67	0.35 – 1.30
	OSA	0.99	0.54 – 1.81
	CVD	1.48	0.59 – 3.67
	Arthritis	1.06	0.55 – 2.05
	Hypertension	0.93	0.48 – 1.79
Model 3	Age	0.97	0.93 – 1.01
N=156	Gender	1.03	0.40 – 2.68
	Baseline weight	1.00	0.98 – 1.01
	Diabetes	0.90	0.37 – 2.17
	OSA	0.62	0.28 – 1.39
	CVD	1.37	0.34 – 5.57
	Arthritis	0.64	0.25 – 1.66
	Hypertension	1.26	0.50 – 3.15
	IWQOL-Lite physical function	0.99	0.97 – 1.01
	IWQOL-Lite self-esteem	1.01	0.99 – 1.03
	IWQOL-Lite sexual life	1.00	0.98 – 1.01
	IWQOL-Lite public distress	1.00	0.98 – 1.01
	IWQOL-Lite work	0.99	0.98 – 1.01
	EQ5D Perceived health	1.01	0.99 – 1.03
	HADS Anxiety and depression	0.96	0.90 – 1.03

* *p<0.05*
† *p<0.001.*

5.3.6 Predictors of linear weight change at 6 months

Table 5.3.12 shows the predictors of weight change at programme-end (6 months post-baseline) for the SLiM sample, using LOCF data. The fully adjusted model (Model 3) was statistically significant ($F_{(10, 122)} = 2.02$, $p = 0.038$), indicating that the predictors as a set reliably predicted weight change at 6 months. The Adjusted R^2 value of 0.077 indicates that the final model (Model 3) accounted for 7.7% of the variance in weight change. Increasing age and initial weight were significantly positively associated with increasing weight loss. Each increase in one year of age was associated with a weight loss of 0.17kg, whilst every 1kg increase in baseline weight was associated with a weight loss of 0.07kg.

Table 5.3.12: Predictors of linear weight change at 6 months in SLiM sample

	Predictor variables	B (SE)	95% CI for B
Model 1	Age	0.13* (0.07)	0.01 – 0.26
	Gender	-2.21 (1.54)	-5.26 – 0.84
Model 2	Age	0.15* (0.07)	0.02 – 0.28
	Gender	-1.14 (1.60)	-4.30 – 2.03
	Baseline weight	0.05* (0.02)	0.00 – 0.10
	Diabetes	-0.61 (1.47)	-3.51 – 2.30
	Ethnicity (non-white)	-2.29 (1.76)	-5.78 – 1.19
Model 3	Age	0.17* (0.07)	0.03 – 0.31
	Gender	0.77 (1.81)	-2.81 – 4.35
	Baseline weight	0.07* (0.03)	0.02 – 0.13
	Diabetes	-1.02 (1.50)	-4.00 – 1.96
	Ethnicity (non-white)	-2.55 (1.76)	-6.04 – 0.94
	IWQOL-Lite physical function	0.06 (0.04)	-0.03 – 0.14
	IWQOL-Lite self-esteem	0.03 (0.04)	-0.04 – 0.09
	IWQOL-Lite sexual life	-0.03 (0.03)	-0.08 – 0.03
	IWQOL-Lite public distress	0.04 (0.04)	-0.04 – 0.12
	IWQOL-Lite work	-0.03 (0.03)	-0.09 – 0.04

** $p<0.05$*
† *$p<0.001$.*

Table 5.3.13 shows the predictors of weight change at 6 months post-baseline for the CWMS sample, using LOCF data. The fully adjusted model (Model 3) was statistically significant ($F_{(10, 105)} = 2.13$, $p = 0.029$), indicating that the predictors as a set reliably predicted weight change at 6 months. The Adjusted R^2 value of 0.097 indicates that the final model (Model 3) accounted for 9.7% of the variance in weight change. Similarly to the SLiM sample final model (Table 5.3.12), increasing baseline weight was significantly positively associated with increasing weight loss, with each 1kg increase in baseline weight was associated with a weight loss of 0.10kg. Scores on the IWQOL-Lite self-esteem subscale were significantly negatively associated with weight change, whereby each one-point increase in self-esteem score was associated with a weight gain of 0.09kg.

Table 5.3.13: Predictors of linear weight change at 6 months in CWMS sample

	Predictor variables	B (SE)	95% CI for B
Model 1	Age	0.05 (0.06)	-0.07 – 0.16
	Gender	-2.00 (1.57)	-5.12 – 1.11
Model 2	Age	0.07 (0.06)	-0.05 – 0.20
	Gender	-0.22 (1.63)	-3.46 – 3.02
	Baseline weight	0.08* (0.03)	0.03 – 0.14
	Diabetes	-1.93 (1.66)	-5.22 – 1.37
	Ethnicity (non-white)	0.37 (2.21)	-4.01 – 4.75
Model 3	Age	0.13 (0.07)	-0.01 – 0.27
	Gender	-0.57 (1.76)	-4.06 – 2.93
	Baseline weight	0.10* (0.03)	0.04 – 0.16
	Diabetes	-2.60 (1.70)	-5.97 – 0.78
	Ethnicity (non-white)	-0.32 (2.30)	-4.90 – 4.25
	IWQOL-Lite physical function	-0.01 (0.03)	-0.08 – 0.06
	IWQOL-Lite self-esteem	-0.09* (0.04)	-0.16 – -0.01
	IWQOL-Lite sexual life	0.03 (0.02)	-0.02 – 0.08
	IWQOL-Lite public distress	0.04 (0.04)	-0.03 – 0.12
	IWQOL-Lite work	-0.01 (0.04)	-0.08 – 0.07

* *p<0.05*
† *p<0.001*.

5.3.7 Predictors of linear weight change at 12 months

Table 5.3.14 displays the predictors of weight change at 12 months post-baseline for the CWMS sample, utilising LOCF data. The fully adjusted model (Model 3) was statistically significant ($F_{(16, 83)} = 2.13$, $p = 0.011$), indicating that the predictors as a set reliably predicted weight change at 12 months. The Adjusted R^2 value of 0.194 indicates that the final model (Model 3) accounted for 19.4% of the variance in weight change. Increasing baseline weight and presence of arthritis were significantly positively associated with increasing weight loss, with each 1kg increase in baseline weight was associated with a weight loss of 0.11kg and presence of arthritis was associated with a weight loss of 4.09kg. Similarly to the CWMS 6-month final model (Table 5.3.13), scores on the IWQOL-Lite self-esteem subscale were significantly negatively associated with weight change, whereby each one-point increase in self-esteem score was associated with a weight gain of 0.10kg.

Table 5.3.14: Predictors of linear weight change at 12 months in CWMS sample

	Predictor variables	B (SE)	95% CI for B
Model 1	Age	0.03 (0.07)	-0.11 – 0.16
	Gender	-5.53* (1.84)	-9.18 – -1.88
Model 2	Age	0.04 (0.09)	-0.13 – 0.21
	Gender	-3.75 (2.19)	-8.10 – 0.61
	Baseline weight	0.09* (0.03)	0.03 – 0.15
	Diabetes	-3.39 (2.01)	-7.39 – 0.62
	OSA	-0.46 (1.71)	-3.87 – 2.96
	CVD	-1.62 (2.78)	-7.16 – 3.91
	Arthritis	3.57 (1.86)	-0.13 – 7.27
	Hypertension	2.01 (1.94)	-1.85 – 5.87
	Ethnicity (non-white)	1.19 (2.59)	-3.96 – 6.35
Model 3	Age	0.10 (0.09)	-0.09 – 0.28
	Gender	-3.45 (2.27)	-7.98 – 1.07
	Baseline weight	0.11* (0.04)	0.04 – 0.19
	Diabetes	-4.07 (2.03)	-8.13 – -0.01
	OSA	-0.44 (1.79)	-4.00 – 3.12
	CVD	0.33 (3.04)	-5.74 – 6.41
	Arthritis	4.09* (1.92)	0.26 – 7.92
	Hypertension	1.92 (2.04)	-2.15 – 5.99
	Ethnicity (non-white)	0.21 (2.75)	-5.29 – 5.71
	IWQOL-Lite physical function	0.03 (0.04)	-0.06 – 0.12
	IWQOL-Lite self-esteem	-0.10* (0.05)	-0.21 – 0.00
	IWQOL-Lite sexual life	0.04 (0.03)	-0.01 – 0.10
	IWQOL-Lite public distress	0.07 (0.05)	-0.02 – 0.17
	IWQOL-Lite work	-0.04 (0.04)	-0.13 – 0.04
	EQ5D Perceived health	0.02 (0.04)	-0.07 – 0.11
	HADS Anxiety and depression	0.06 (0.17)	-0.27 – 0.39

* *p<0.05*
† *p<0.001.*

5.3.8 Predictors of change in quality of life at 6 months

Table 5.3.15 displays the mean quality of life scores at baseline and at programme-end, 6 months post-baseline for the SLiM sample, along with the mean difference between the scores. Follow-up quality of life data were available for a subsample of the SLiM sample and were not collected for the CWMS sample. There was a significant improvement in all IWQOL-Lite subscales and total scores from baseline to programme-end. This effect was observed in both gender subgroups as well as in the overall SLiM sample, with the greatest improvement in quality of life observed in the physical function subscale. However, despite these significant improvements in quality of life, the programme-end self-reported

quality of life scores remained low, ranging from 35.0 for self-esteem and 57.4 for the work subscale, with 0 representing worst quality of life and 100 representing optimum quality of life.

Table 5.3.15: Mean change in quality of life (IWQOL-Lite) from baseline to programme-end in the SLiM sample combined and split by gender

	Baseline	Programme-end	Mean difference
Physical function	31.7±22.7	39.5±24.0	+7.8†
Male (N=34)	41.3±22.9	50.2±20.7	+8.9†
Female (N=90)	28.1±21.7	35.5±24.1	+7.4†
Self esteem	28.9±27.9	35.0±30.4	+6.1†
Male (N=33)	37.8±29.3	46.1±31.6	+8.3*
Female (N=87)	25.5±26.7	30.8±29.1	+5.3*
Sexual life	48.1±30.6	55.1±34.4	+7.0*
Male (N=31)	53.7±23.8	59.8±32.0	+6.1
Female (N=80)	46.0±32.7	53.3±35.3	+7.3*
Public distress	35.7±27.0	40.9±29.7	+5.2*
Male (N=32)	45.9±26.0	51.6±22.8	+5.6
Female (N=88)	32.0±26.6	37.1±31.1	+5.1
Work	51.2±29.1	57.4±29.6	+6.2*
Male (N=31)	57.3±27.8	63.1±28.8	+5.8*
Female (N=80)	48.8±29.5	55.1±29.8	+6.3*
IWQOL-Lite total	35.8±20.1	42.7±22.1	+6.9†
Male (N=32)	44.7±18.7	51.9±22.4	+7.2†
Female (N=84)	32.4±19.6	39.1±21.0	+6.8†

Data are means and standard deviations calculated by paired samples t-test
**P<0.05*
†P<0.001.

Table 5.3.16 displays the predictors of change in quality of life from baseline to programme-end (6 months post-baseline) for the SLiM sample. The fully adjusted model (Model 3) was not statistically significant (Chi^2 =19.52, p =0.052), with Nagelkerke's R^2 of 0.257 indicating that the model accounted for 25.7% of the variance in quality of life change.

Table 5.3.16: Predictors of change in quality of life (IWQOL-Lite total) from baseline to programme-end in SLiM sample

	Predictor variables	Odds Ratio (OR)	95% CI for OR
Model 1 N=113	Age	1.02	0.98 – 1.06
	Gender	1.18	0.47 – 2.98
Model 2 N=113	Age	1.01	0.97 – 1.05
	Gender	1.19	0.43 – 3.34
	Baseline weight	1.00	0.98 – 1.01
	Diabetes	2.12	0.78 – 5.75
	Ethnicity (non-white)	0.32*	0.11 – 0.94
Model 3 N=102	Age	0.97	0.91 – 1.02
	Gender	0.34	0.08 – 1.44
	Baseline weight	0.99	0.97 – 1.01
	Diabetes	4.06*	1.09 – 15.07
	Ethnicity (non-white)	0.27*	0.08 – 0.95
Baseline	IWQOL-Lite physical function	1.02	0.89 – 1.18
	IWQOL-Lite self-esteem	1.05	0.96 – 1.15
	IWQOL-Lite sexual life	1.04	0.98 – 1.10
	IWQOL-Lite public distress	1.02	0.96 – 1.10
	IWQOL-Lite work	1.05	1.00 – 1.11
	IWQOL-Lite total	0.82	0.55 – 1.20

**P <0.05*
†P <0.001.

Two significant predictors of change in quality of life were identified, diabetes and ethnicity. The odds ratio indicates that for those with diabetes the odds of experiencing improvement in their quality of life are 4.06 times as large as for those without the condition. For those of non-White European ethnicity, the odds of quality of life improvement decreased and were 0.27 times reduced, indicating that those of non-White European ethnicity were 73% less likely to experience improvement in quality of life compared to those of White European ethnicity. This indicates that those with diabetes are more likely to experience improvement in quality of life, whilst those of non-White European ethnicity are less likely to experience quality of life improvement following attendance at the SLiM programme. Interestingly, the baseline IWQOL-Lite subscales and total scores were not significant predictors of quality of life change, indicating that widespread change was observed for individuals across the spectrum of quality of life reported at baseline.

5.3.9 Association between change in BMI and change in quality of life

Table 5.3.17 shows the association between change in BMI from baseline to 6-months (programme-end) utilising LOCF data and change in IWQOL-Lite total and subscale scores from baseline to programme-end, within the SLiM subsample. Change in BMI significantly predicted change in the IWQOL-Lite physical function subscale, with a decrease in one BMI unit from baseline to programme-end associated with an increase of 1.06 in physical function score. A negative association was also observed between change in BMI and changes in the sexual life and public distress subscales as well as the IWQOL-Lite total score, indicating that a reduction in BMI from baseline to programme-end was associated with improvement in these quality of life areas however, this was not significant.

Table 5.3.17: Change in BMI from baseline to programme-end as a predictor of change in IWQOL-Lite scores from baseline to programme-end in the SLiM sample

	Univariate		Model 1		Model 2	
	U.B.	**S.E.**	**U.B.**	**S.E.**	**U.B.**	**S.E.**
Physical function	-0.91*	0.44	-0.85	0.45	-1.06*	0.48
Self esteem	0.41	0.48	0.61	0.49	0.36	0.53
Sexual life	-1.08	0.62	-1.08	0.64	-1.14	0.70
Public distress	-0.96	0.73	-0.44	0.73	-0.47	0.75
Work	0.45	0.52	0.36	0.54	0.12	0.57
IWQOL-Lite total	-0.10	0.39	-0.03	0.40	-0.27	0.43

U.B. =Unstandardised Beta, S.E. =Standard error
**P<0.05*
†P<0.001
Model 1 adjusting for age and gender
Model 2 additionally adjusting for diabetes and baseline BMI.

5.4 DISCUSSION

This study has highlighted the efficacy of the two treatment pathways operating within the Specialist Weight Management Service. Analysis of available case data, representing those who completed the programmes demonstrated mean losses of -5.2kg (-3.7%) for SLiM and -5.4kg (-4.0%) for CWMS after 6 months, with longer term CWMS mean losses of -7.0kg (-5.0%) and -13.4kg (-10.2%) at 12 and 24 months, indicating that 12 months of attendance at the CWMS yielded clinically meaningful weight losses of ≥5% baseline weight in the majority of participants. Indeed 40.5% of the CWMS sample had achieved ≥5% weight loss at 12 months, and 59.1% of the sample at 24 months. However as expected, analysis of LOCF data yielded more conservative weight outcomes with mean losses of -3.2kg (-2.3%) for the CWMS at 6 months, -4.1kg (-2.9%) at 12 months and -5.1kg (-3.6%) at 24 months. Analysis of LOCF data demonstrated that on completion of the 6-month SLiM programme 30.3% achieved the clinically targeted weight loss of ≥5% baseline weight, whilst after 12 months (minimum duration) attendance at the CWMS 23.7% of the sample achieved ≥5% weight loss, with available case data suggesting a greater proportion (40.5%) of the sample who attended the CWMS more fully achieved ≥5% baseline weight loss.

Analyses of available case data showed no significant differences in the weight and BMI outcomes between the CWMS and SLiM treatment pathways achieved after 3 and 6 months, despite the patient populations significantly differing at baseline, with the SLiM sample having more complex health needs. However, analyses of LOCF data demonstrated significant differences in the weight and BMI of the samples at 6 months post-baseline. This is likely to be due to the greater proportion of missing data in the CWMS sample at 3 months (37.4% vs 13.9%) and at 6 months (55.3% vs 0%), with the imputed LOCF values

potentially masking greater weight and BMI loss values for the CWMS sample, which were similar to the values attained in the SLiM sample.

The 6 month outcomes of the combined programmes demonstrated using available case data (-5.2kg, -3.8%) and LOCF data (-4.5kg, -3.2%) are greater than the mean loss observed on completion of the first four-month phase of the Glasgow and Clyde Specialist Weight Management Service using available case data (-4.0kg) and LOCF data (-2.9kg) (175). Longer term outcomes of the Glasgow service were reported, with mean losses of -8.5kg (-9.7 - -7.2) using available case data and -3.6kg (-3.8 - -3.3) using LOCF data, after a minimum period of ≥19 months. In contrast the CWMS yielded greater mean losses of -13.4kg (-10.2%) when analysing available case data and -5.1kg (-3.6%) when analysing LOCF data at 24 months. Additionally, a substantial proportion of individuals in the CWMS achieved clinically meaningful weight loss, with ≥5% baseline body weight loss achieved by 24.8% of those attending the CWMS when analysing LOCF data and 59.1% when analysing available case data at 24 months, comparable to the 24% of those entering the Glasgow service and 56% of those classed as completing attendance at the Glasgow service. However, such comparisons should be interpreted with caution, as the exact duration of attendance and frequency of contact at the Glasgow service cannot be directly compared with the CWMS, as the intervention duration and frequency of contact varies for each individual, as with the CWMS. Furthermore, the baseline BMI of the CWMS was greater than that of the Glasgow service (48.7kg/m^2 vs 43.3kg/m^2) which may have additionally contributed to the greater weight losses observed in the CWMS, however the mean percentage of baseline weight lost by individuals attending the Glasgow service was not reported and so cannot be directly compared with the CWMS. In comparison to other specialist weight management services, analysis of available case data demonstrated

greater losses in the CWMS and SLiM programmes than three other specialist weight management dietetic-led programmes which have reported weight losses ranging from -1.0 to -5.1kg using available case data (176-178).

The demonstrated weight losses of ≥5% observed in the present sample, have been shown to be associated with clinically significant improvements in a range of cardiovascular risk factors, including HbA1c, triglycerides, diastolic and systolic blood pressure, and HDL-cholesterol (122). Weight losses of ≥5% associated with these health benefits were achieved by 21.8% of the combined sample after just 3 months and 31.7% after 6 months using available case data, and 16.8% and 26.7% at 3 and 6 months using LOCF data, suggesting that the service was able to facilitate clinically meaningful weight losses for a substantial proportion of individuals after only a short period of attendance. This is a greater proportion than that achieved in primary care in an evaluation of 6,715 individuals attending 12 months of the Counterweight weight management programme (analysed using LOCF data), in which 10% of participants achieved ≥5% weight loss (172). This suggests that the specialist service was better at facilitating larger weight losses than the primary care-led Counterweight programme.

Another primary care-led weight management intervention incorporating a 12-week Low Energy Liquid Diet (LELD) approach with appointments up to 12 months was able to produce greater mean weight loss than the CWMS programme, with available case data demonstrating -12.4kg (-9.1%) loss after 12 months compared to -7.0kg (-5.0%) achieved by the CWMS (33). The Camelon primary care-led programme also yielded a greater mean loss than the CWMS and SLiM programmes after a 12-week intervention, with a mean loss of -5.0kg using available case data, compared to -3.4kg and -4.1kg achieved by the CWMS and SLiM samples after the same duration of attendance (30). Longer-term follow-up data

for the Camelon programme obtained in a smaller sample of 20 individuals obtained between 1-49 months post-programme indicated a mean loss of -3.7%, which is far less than the CWMS mean loss of -10.2% obtained at 24 months (30). A similar level of weight loss to that achieved by the CWMS and SLiM programmes after 3 months was achieved in a trial arm receiving a 12-week structured support programme as part of a primary care pilot RCT which yielded a mean loss of -4.0kg, compared to -4.1kg and -3.4kg in the SLiM and CWMS samples (32). In addition, a 12-month sporting club-based intervention yielded 12-month mean weight losses obtained using LOCF data, similar to that achieved by the CWMS (-5.6kg vs -4.1kg for the CWMS) (73).

The CWMS and SLiM programmes yielded greater weight losses than two other primary care-led programmes evaluated in RCTs (31, 173) and indeed greater 12-month weight losses than all arms of the Lighten Up RCT evaluating primary care programmes and commercial programmes (34). Indeed the CWMS demonstrated greater 12-month weight loss, than Weight Watchers as demonstrated in a 12-month RCT (-7.0kg vs -5.1kg) (181). However, another RCT yielded conflicting findings, with all commercial trial arms including Weight Watchers, Slim-Fast, Atkins diet, and Rosemary Conley yielding greater weight losses than the CWMS and SLiM programmes after 6 months using available case data (36). These findings indicate that the CWMS and SLiM programmes were able to facilitate greater weight losses than achieved by other specialist weight management services and several primary care-led and commercial programmes. However some primary care and commercial programmes have demonstrated similar and indeed better weight loss outcomes, although in generally less severely obese populations than the CWMS and SLiM programmes.

Within the Specialist Weight Management Service significant weight loss was achieved by some but not all individuals attending the SLiM and CWMS programmes. Analyses indicated that age was identified as a significant predictor of weight gain in the SLiM and CWMS samples at 6 months, indicating that older individuals were less likely to gain weight. This was also supported by the findings of the predictors of linear weight change, whereby increasing age was significantly positively associated with increasing weight loss in the SLiM sample at 6 months. The finding that increasing age was associated with increased likelihood of weight loss is consistent with the evaluation of the Glasgow service which demonstrated that relative to those <40 years of age, there was increased likelihood of achieving ≥5kg weight loss in those aged 40-49 (OR= 1.52, 1.09 - 2.12), aged 50-59 (OR= 1.47, 1.03 - 2.11) and those aged ≥60 (OR= 2.12, 1.44 - 3.14) (174). These findings suggest that older individuals may be more motivated to lose weight, with younger individuals perhaps requiring additional support in achieving weight loss when attending specialist services.

Baseline weight was also identified as a significant predictor of weight gain in the CWMS sample at 6 months, indicating that those with greater baseline weight were less likely to gain weight. Baseline weight was also a predictor of ≥5% weight loss at 6 months in the CWMS sample, with those of greater baseline weight more likely to achieve ≥5% weight loss. These findings are consistent with the Glasgow service which reported that those with baseline BMI ≥50kg/m^2 were more likely to experience ≥5kg weight loss (OR= 1.70, 1.14 - 2.54) than those with a baseline BMI ranging from 35.0-39.0kg/m^2 (174).

The only quality of life and mental health factors which significantly predicted weight change were scores on the IWQOL-Lite self-esteem and public distress subscales,

whilst none of the remaining subscales or the HADS anxiety and depression scale were significant predictors. Self-esteem was significantly negatively associated with linear weight change at 6 and 12 months in the CWMS sample, whereby greater weight loss was associated with lower self-esteem scores, indicating that those with poorer levels of self-esteem at baseline achieved greater weight loss. An opposite pattern of association was observed with the IWQOL-Lite public distress subscale, whereby public distress was a significant predictor of weight gain, with those reporting higher levels of baseline public distress being less likely to gain weight within the SLiM sample at 6 months. The fact that individuals with better self-esteem were less likely to lose weight gives cause for concern given that self-esteem was at a very low level, with mean IWQOL-Lite self-esteem scores of 26.2 and 28.9 for the CWMS and SLiM samples respectively, whereby 0 represents worst quality of life and 100 represents optimum level. One potential explanation for this observation is that low self-esteem and high levels of perceived public distress before treatment commencement may act as motivators for change during the service, thus resulting in greater weight loss among these individuals. Exploration of these complex issues through qualitative research would enhance understanding of the role of factors such as psychological and physical co-morbidities and the impact on individuals' motivation to achieve weight loss throughout attendance at the service.

Analyses indicated that the presence of co-morbid type 2 diabetes was a significant predictor of ≥5% weight loss within the CWMS sample at 6 months, whereby those with diabetes were less likely to achieve ≥5% weight loss (OR= 0.11, 0.02 - 0.75). This finding is consistent with the evaluation of the Glasgow service which demonstrated that those with diabetes were less likely to achieve the target ≥5kg weight loss (OR= 0.55, 0.38 - 0.81) (174). The finding that those with diabetes were less likely to benefit from the

service also gives cause for concern and potentially indicates the need for the provision of further support of individuals with diabetes in order to achieve weight loss. Conversely, the presence of arthritis was shown to be significantly positively associated with increased weight loss in the analyses of linear weight change in the CWMS sample at 12 months. This finding potentially suggests that those with arthritis were more likely to achieve weight loss. However, due to the magnitude of the Beta value and the large confidence interval it is probable that the observed association is a type 1 error and thus may not actually provide support for an association between weight loss and arthritis.

Analyses did not identify gender as a predictor of ≥5% weight loss, weight gain or linear weight change, which is in contrast to the evaluation of the Glasgow service which demonstrated that males (OR= 1.39, 1.05 - 1.82) were more likely to achieve ≥5kg weight loss (174). Similarly, the mental health measure of anxiety and depression was not identified as a predictor of weight change, whilst the Glasgow service demonstrated that those with depression (OR= 1.81, 1.35 - 2.44) were more likely to achieve weight loss (174). These findings potentially suggest that the CWMS and SLiM programmes were effective regardless of gender and the experience of symptoms of anxiety and depression.

Interestingly, analyses of the predictors of ≥5% weight loss at 6 months in the SLiM sample (programme-end) and at 12 months in the CWMS sample (minimum attendance) indicated that none of the demographic, clinical and self-report measures were significant predictors of weight loss. Similarly, no predictors of weight gain in the CWMS sample at 12 months were identified. The finding that none of the demographic, clinical and self-report measures were significant predictors of ≥5% weight loss at 6 months in the SLiM sample and ≥5% weight loss and weight gain at 12 months in the CWMS sample, potentially indicates that the service was successful in effectively facilitating weight loss

for participants regardless of demographic characteristics such as age, gender, and ethnicity. Furthermore the findings of some analyses indicate that participants' weight, and presence of co-morbid health conditions such as diabetes, cardiovascular disease, hypertension, arthritis and OSA also did not have an impact on whether individuals successfully achieved weight loss, as well as perceived quality of life and mental health. This suggests a positive quality of the service, indicating that the service is suitable and effective for most individuals. However, the fact that no predictors of ≥5% weight loss were identified within the 6-month SLiM and 12-month CWMS samples could also be due to homogeneity within the samples, and is in contrast to the analyses of the remaining samples within which various predictors were identified and also to the findings of the evaluation of the Glasgow service (174). This is also in contrast to a review which has demonstrated that in the successful achievement of weight maintenance following initial weight loss, there are a number of factors including magnitude of initial weight loss, attainment of weight loss goals, control of eating and self-monitoring, which are associated with successful weight maintenance (187).

Further research investigating potential factors associated with clinically significant weight loss and weight gain is required in order to definitively determine whether particular groups of individuals benefit more from attending the service than others who may require additional support, thus improving the efficacy of the programmes and increasing individuals' opportunity to achieve weight loss.

In addition to facilitating weight loss for individuals, the current evaluation has also demonstrated that attendance at the Specialist Weight Management Service facilitated improvement in individuals' quality of life, with significant improvement on all mean baseline IWQOL-Lite subscales after attendance at the SLiM programme. However,

quality of life scores remained low at programme-end, indicating that individuals were still experiencing reduced quality of life, and that further support may be required. Analyses indicated that diabetes and ethnicity were significant predictors of 6 month quality of life change in the SLiM subsample. The finding that those with diabetes were more likely to experience improvement in quality of life suggests that the presence of the condition may have motivated individuals in their weight loss efforts. Indeed, findings from the Look AHEAD RCT which randomised 5,145 overweight and obese individuals with type 2 diabetes to receive either an intensive lifestyle intervention or to receive education in the control arm, revealed that the intensive intervention facilitated weight losses of -8.6% after one year and -6.0% at study-end, as well as improvements in quality of life among individuals with the long-term condition (188). The finding that individuals of non-White European ethnicity were less likely to experience quality of life change relative to those of White European ethnicity gives cause for concern, suggesting a potential need to tailor the programmes to address and incorporate cultural and ethnic differences in food, physical activity and lifestyle practices. However, this finding should be interpreted with caution as the analyses were restricted to an over-simplistic White European and non-White European binary classification due to a large amount of missing ethnicity data. Further investigation of this issue is required in order to establish if indeed there are differences in the efficacy of the service between ethnic groups, which if present would need to be directly addressed.

Furthermore, when examining change in BMI as a predictor of change in quality of life scores, a clear association between BMI and physical function was observed, with a reduction in BMI being associated with significant improvement in the physical function quality of life domain. A non-significant negative association was also observed between change in BMI and changes in the sexual life and public distress subscales as well as the

IWQOL-Lite total score. This suggests that there may be a more widespread association between reduction in BMI and improvement across the quality of life domains, however this did not achieve significance. This is consistent with the findings reported in a study evaluating the quality of life outcomes of extreme obese individuals attending the Glasgow service, which demonstrated that weight loss was a significant predictor of IWQOL-Lite improvement (74). It is important however, to note that in the evaluation of the Glasgow service the individual IWQOL-Lite subscales were not examined and the total quality of life scores were used to assess whether individuals' quality of life had improved, deteriorated or remained unchanged with the use of an algorithm, thus utilising a different method from the present study.

The collection of pre- and post-intervention quality of life data facilitates greater understanding of the impact of the Specialist Weight Management Service and provides another dimension on which efficacy can be assessed. Future service evaluations should also incorporate the collection and analysis of a range of demographic information and self-report measures, as conducted in the present evaluation. Despite the fact that this additional patient information was not able to identify a definitive range of factors associated with weight loss success, it does however facilitate greater understanding of the patient population, and indeed the detailed characterisation of patients attending the service is a major strength of this work. The evaluation is also strengthened by the inclusion of a relatively large sample size and due to the fact that it is a pragmatic evaluation providing evidence for the effectiveness of a currently operating service, of which the efficacy has not previously been formally evaluated. However, it is important to also acknowledge the limitations of the present evaluation, chief among which is the absence of a control group, which would enable comparison between the CWMS and SLiM services and treatment-

seeking individuals not receiving intervention as well as non-treatment-seeking extreme obese individuals of the same BMI. In order to definitively compare the outcomes of the services, a different approach beyond the scope of this evaluation would be utilised, whereby an RCT with sufficient power to detect differences between the weight outcomes of the services would be conducted. A more robust study design such as an RCT would provide greater confidence in the generalisability of the findings and strengthen the capacity to draw conclusions about the efficacy of the programmes. Another limiting factor of the design of the present evaluation was the absence of an extended follow-up period, which would establish the longer-term outcomes and effectiveness of the pathways and whether weight loss outcomes are maintained. Additionally, there was a considerable proportion of missing weight outcome data in the CWMS sample, which meant that LOCF values were imputed which has the potential to attenuate the observed effects, with lower weight loss values produced when compared to available case data. This is due to the fact that the individuals providing data are those who have attended the programmes more fully and have achieved greater weight loss. However, the use of LOCF data in analyses is widely adopted in the reporting of weight management interventions (34, 36, 167, 170, 175, 181), as a process of increasing sample size and power to detect statistical differences. The inclusion of detailed description of the outcome data and how it is obtained is vital in aiding accurate interpretation and facilitating comparisons of outcomes across studies.

The present evaluation adds to the very limited body of literature examining the efficacy of specialist weight management services. Medically-supported services such as the present service are considered an essential intervention in the care of obese individuals, with NICE guidelines recommending a minimum of 6 months attendance at a specialist service before bariatric surgery is considered as a treatment option (14). The present

service delivers expert care from a multidisciplinary healthcare team available to those individuals who have been referred from primary care settings. Therefore the patient population accessing the more specialist level of care are those individuals with more complex healthcare needs who may not have succeeded with previous attempts to achieve and maintain the necessary level of weight loss through self-motivated, independent efforts or through primary care-led and commercial interventions. The sample attending the service have been demonstrated to experience substantial physical co-morbidity, with slightly less than a third (30.6%) living with type 2 diabetes, which is a long-term condition requiring careful self-management. There is also an extensive psychological co-morbidity in this sample, with 70.3% and 66.2% experiencing symptoms of anxiety and depression, respectively. Given the competing demands and anticipated additional health concerns experienced by this at-risk patient population, it is essential to continue to improve and develop services that are offered to such patients to make sure that the limited resources and capacity for weight loss within these individuals are effectively capitalised upon.

5.4.1 Summary of findings

This chapter has demonstrated the value of this medically-supported service in the care of extreme obese individuals, who are an at-risk patient population with substantial physical and psychological co-morbidities. Despite the patient populations significantly differing at baseline, with the SLiM sample having more complex needs, both treatment pathways achieved clinically significant weight loss outcomes, with a substantial proportion achieving sufficient weight loss to reduce the risk of cardiovascular disease and overall mortality. In addition, the CWMS and SLiM pathways were able to facilitate greater

weight losses than other specialist weight management services and several commercial and primary care-led programmes. However some primary care and commercial programmes demonstrated better weight loss outcomes than those achieved by CWMS and SLiM. Post-hoc analyses indicated that the study was not sufficiently powered to detect significant differences in ≥5% weight loss achieved by CWMS and SLiM, however the study was highly powered (96% power) to detect differences between baseline and intervention-end quality of life scores within the SLiM sample. Several of the analyses exploring the predictors of weight change, specifically the models examining the predictors of ≥5% weight loss in the SLiM sample at 6 months and the CWMS sample at 12 months, and weight gain in the CWMS at 12 months, indicated that there were no significant predictors of weight change. The findings of these analyses may suggest that the service is effective for all individuals regardless of demographic and clinical characteristics, however this is in contrast to the remaining samples within which predictors were identified. The other models examining predictors of weight change identified that those individuals with type 2 diabetes, of younger age, lower baseline weight, and with better self-esteem were shown to be less likely to achieve weight loss success, indicating a need for the provision of tailored support for these individuals. Additionally, individuals with type 2 diabetes were shown to be more likely to experience improvement in quality of life following attendance at the SLiM programme, whilst those of non-White European ethnicity were shown to be less likely to experience quality of life improvement. Longitudinal analyses examined the association between change in BMI and change in pre- and post-intervention quality of life scores, which showed a clear association between BMI and physical function whereby weight loss was associated with improvement in quality of life.

5.4.2 Recommendations

This evaluation demonstrates the value of medically-supported specialist weight management in the care of extremely obese patients, with both the CWMS and SLiM treatment pathways shown to facilitate clinically significant weight loss. Evaluations of weight management services should incorporate the collection of demographic information and the use of self-report measures to better understand the patient population, and identify those individuals who are benefitting most from the service, and those who may require additional support in order to fully benefit and achieve maximum potential weight change during attendance. Further support or tailoring of the programmes may be beneficial to those of younger age, those with higher levels of self-esteem, and lower baseline weight, in order to achieve their weight loss goals during attendance at the service. Further research is required in order to expand the currently limited evidence base for specialist weight management services. Future studies should utilise more methodologically rigorous designs such as RCTs in order to conclusively determine the efficacy of specialist weight management services. Such improvements to increase the efficacy and enhance understanding of the specialist weight management services and their patient populations will ensure that these individuals are given the greatest opportunity to achieve weight loss and diminish the negative health impacts of extreme obesity.

CHAPTER SIX

6.0 MEDICAL AND BEHAVIOURAL WEIGHT MANAGEMENT INTERVENTIONS FOR EXTREME OBESITY: A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS

6.1 INTRODUCTION

6.1.1 Rationale

Several reviews have examined the impact of non-surgical medical and behavioural weight management interventions within obese populations, including a narrative review focussing specifically on weight management services in the UK (189), a review and meta-analysis of interventions delivered solely to male samples (190) and a comprehensive Health Technology Assessment including a systematic review of 84 Randomised Controlled Trials (RCTs) of obesity treatments (191). The numerous reviews of weight management interventions reflect the extensive body of primary studies investigating the impact of weight management interventions in overweight (BMI $\geq$25.0kg/m^2), and obese (BMI $\geq$30.0kg/m^2) samples. However, the body of literature examining the efficacy of weight management interventions within extreme obese (BMI $\geq$40.0kg/m^2) samples is relatively limited. As such it is anticipated that the synthesis of data from primary studies investigating the impact of interventions in extreme obese samples within reviews, will consequently also be limited. Given the increasing prevalence of extreme obesity and the associated detrimental impacts on the health and quality of life of individuals (82), it is important to examine the effectiveness of treatment pathways such as medical and behavioural interventions which have been widely adopted in the care of individuals with extreme obesity (14).

This systematic review will search for systematic reviews examining the effectiveness of medical or behavioural weight management interventions within exclusively extreme obese (BMI $\geq$40kg/m^2) samples. This systematic review will summarise data from included systematic reviews, and will additionally assess the quality

of the reviews and relevance by considering date of publication and the potential need for updating due to the accumulation of new primary research since publication.

6.1.2 Objectives

The specific objectives of the systematic review are:

- To produce a systematic review of systematic reviews and health technology assessments which have examined the effectiveness of medical or behavioural weight management interventions for adults with extreme obesity (defined as baseline BMI $\geq$40.0kg/m^2) on change in weight or BMI, change in presence or severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life or change in mental health.
- To produce a summary of the evidence of the effectiveness of medical and behavioural weight management interventions for extreme obesity.
- To analyse the quality of the included reviews and provide a summary of the best evidence available.

The systematic review question was formulated using the PICOS framework as illustrated in Table 6.1.1. The explicit question which will be answered by the systematic review is: 'What is the summarised evidence for the effectiveness of medical and behavioural weight management interventions for extreme obesity?'

Table 6.1.1: Development of systematic review question using PICOS framework

Population	Adults with extreme obesity, defined as mean baseline BMI of all included primary studies ≥40.0kg/m^2.
Intervention	Medical or behavioural weight management (any non-surgical intervention which encompasses behavioural modification, medical or pharmaceutical components) of any duration.
Comparators	The reviews may incorporate a range of comparator groups including but not limited to control not receiving intervention, control receiving usual care, or alternative non-surgical intervention.
Outcomes	The reviews may include any of the following outcomes: weight and BMI change, change in presence and severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life and mental health.
Study design	Systematic reviews and health technology assessments.

6.2 METHODS

6.2.1 Protocol and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (192). A systematic review protocol was produced for use as a reference to aid the two reviewers and ensure consistency in the conduct of the review (Appendix one). The systematic review was registered on the PROSPERO international database of prospectively registered systematic reviews in health and social care, with registration number CRD42014012988.

6.2.2 Eligibility criteria

The eligibility for inclusion in the systematic review was determined by the criteria outlined in Table 6.2.1. The criteria for inclusion in the systematic review incorporated reviews solely in adult extreme obese populations, excluding those reviews examining the efficacy of interventions in child and adolescent populations, which use a different approach and address different priorities to interventions for adult populations (193). The review also focused on the general extreme obese population, thus excluding those populations recruited solely on the basis of other health conditions. For instance this incorporated the exclusion of reviews examining the effectiveness of interventions among samples of individuals specifically who have survived cancer, who have gained weight following commencement of anti-psychotic medication, or those currently receiving treatment for heart disease. The inclusion of reviews of weight management interventions targeted at such specific patient populations would be beyond the scope of the present review, and would not facilitate understanding of intervention effectiveness within the general extreme obese population.

Table 6.2.1: Eligibility criteria

Domain	Criteria
Population	• Reviews reporting intervention effectiveness exclusively in BMI ≥40.0kg/m^2 populations were included. • Reviews reporting intervention effectiveness in broader overweight and obese BMI ≥30.0kg/m^2 populations were excluded. • Reviews where included study populations are adult (≥18 years) were included. • Reviews including study populations based on health conditions other than obesity were excluded, for instance samples including solely individuals with heart disease, type 2 diabetes, cancer, or schizophrenia.
Interventions	• Reviews of non-surgical interventions providing medical and or behavioural support incorporating pharmaceutical therapies, counselling, education, and lifestyle modification incorporating diet and exercise were included. • Reviews including evaluations of bariatric procedures or surgery were excluded. • Reviews of interventions of any duration were included.
Outcomes	• Reviews which report synthesis of one or more of any of the following outcomes: weight or BMI change, change in presence or severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life or mental health, from baseline to intervention-end or post-intervention follow-up were included.
Study design	• Systematic reviews and health technology assessments were included.

6.2.3 Information sources

A search of the following three databases within the Cochrane Library was conducted: the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts and Reviews of Effects (DARE), and the Health Technology Assessment Database (HTAD), from inception to July 2014. One search was conducted using the Cochrane Library search manager, which retrieved records from the three databases simultaneously.

6.2.4 Search

The following search strategy was used to search for review articles summarising data on the effectiveness of medical or behavioural weight management interventions of any duration for samples with extreme obesity, defined as sample mean BMI ≥40.0 kg/m^2. Terms were entered as free text and MeSH (Medical Subject Heading) terms in the Cochrane Library search engine, which screened records obtained from the CDSR, DARE and HTAD. The search strategy detailing the combinations of search terms utilised is outlined in Table 6.2.2. Truncation of the free text terms 'adult' and 'obes' was used in order to include a variety of word endings such as 'adulthood' and 'obesity', thus maximising the number of relevant records returned. Those terms which were available as MeSH terms within the Cochrane Library search manager were selected using the 'explode all trees' function in order to retrieve all related terms in the search.

Table 6.2.2: Search strategy

1	Adult*
2	Overweight (MeSH) explode all trees
3	Obesity (MeSH) explode all trees
4	Obes*
5	Body Mass Index (MeSH) explode all trees
6	BMI
7	Body Weight (MeSH) explode all trees
8	2 or 3 or 4 or 5 or 6 or 7
9	1 and 8
10	Intervention
11	Life style (MeSH) explode all trees
12	Health Promotion (MeSH) explode all trees
13	Health Education (MeSH) explode all trees
14	Patient Education as Topic (MeSH) explode all trees
15	Counseling (MeSH) explode all trees
16	Behavior (MeSH) explode all trees
17	Anti-Obesity Agents (MeSH) explode all trees
18	Weight Loss (MeSH) explode all trees
19	Diet, Reducing (MeSH) explode all trees
20	Weight Reduction Programs (MeSH) explode all trees
21	Exercise (MeSH) explode all trees
22	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23	10 and 22
24	9 and 23
25	24 in Cochrane Reviews (Reviews and protocols), Other Reviews and Technology Assessments

6.2.5 Article selection

The records retrieved following the search were exported to the EndNote programme (Thomson Reuters EndNote version X7.1) and a copy of the file was made for both of the reviewers to facilitate management of the records. Two reviewers independently screened the titles and abstracts using the eligibility criteria relating to population, intervention, outcome and study design. Those records deemed to not meet eligibility criteria were removed, and the number excluded at this stage was independently recorded by each reviewer. Once the first phase of study selection, screening by title and abstract, had been completed, the two reviewers met to compare selections. Discrepancies were discussed and

consensus was reached and the final number of reviews to be screened as full text was determined. A third party was to be invited to adjudicate in instances where consensus to a disagreement was not reached, however this was not required.

After obtaining full text copies, the second phase of review selection, screening full text, was conducted by the two reviewers independently, with those not meeting the eligibility criteria excluded at this stage. The excluded records were then grouped by reason for exclusion, so that the numbers of records excluded for each reason were identified. The final number of reviews that were deemed to be eligible for inclusion in the systematic review were determined by each reviewer independently and once the second selection phase was complete the two reviewers again met to compare selections. The final number of included reviews was determined and no discrepancies in study selection were identified. However had it been necessary discrepancies would have been discussed and a third party would have been invited to adjudicate where consensus was not reached. Additionally, the reference lists of the included reviews would have been searched in order to identify any further relevant reviews, which would have been screened and subject to meeting eligibility criteria would subsequently have been added to the total number of reviews to be included in the systematic review.

6.2.6 Data collection process

The two reviewers would have independently extracted data items from the information provided in the full text articles, into a Microsoft Excel spreadsheet whereby each study would have been represented in a row of data in the spreadsheet. A detailed list of data items for extraction was developed with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0) (194), in order to facilitate the data

extraction process. A detailed list of the items specified for data extraction are outlined in Table 6.2.3, which was to be used as a point of reference when entering the data items into the spreadsheet. The two reviewers would have met once data extraction had taken place independently, in order to investigate any discrepancies, with a third party invited to adjudicate if required.

6.2.7 Data items

The data items specified for extraction from the included reviews are outlined in Table 6.2.3. Following data extraction, specific items would have been selected from the finalised extraction spreadsheet to be used in the production of review characteristics tables which would have aided in the description and qualitative analysis of the included reviews.

Table 6.2.3: Data items to be extracted from included systematic reviews

Field	Data points to be extracted
Review	Author, Publication year.
Methods	Design (state whether systematic review, Health Technology Assessment) Objectives of review.
Study characteristics	Total number of included studies within review, Participant characteristics including range of age, gender, ethnicity, co-morbid health conditions, across studies, Range of mean baseline weight of the primary studies, Range of mean baseline BMI of the primary studies.
Intervention	Range of intervention types: i.e. pharmaceutical/behavioural/combination, Range of number of intervention groups, Range of intervention settings (where intervention is delivered), Range of delivery personnel type (if healthcare professional specify which, researcher, lay public), Range of delivery personnel training (detail of training in intervention delivery received), Range of duration of interventions (number and duration of contact time, including face to face sessions, email, telephone or other contact), Intensity of interventions (frequency of sessions and contact), Theoretical basis of interventions (e.g. self-management, cognitive behavioural) Range of numbers of participants entering intervention group, Range of numbers of participants completing intervention/presenting for data collection, Range of reported loss to follow-up rate in intervention groups across primary studies.
Comparator	Range of numbers of comparator groups across primary studies, Descriptions of comparator or usual care, Range of numbers of participants entering comparator group, Range of numbers of participants completing comparator group/presenting for data collection, Range of reported loss to follow-up rate in comparator groups across primary studies.
Outcomes	Mean effect size, weighted effect size, Mean difference, standardised mean difference, weighted mean difference and p values between intervention and control groups for the following outcomes of interest: Change in weight or BMI, Change in presence or severity of co-morbid health conditions, Change in cardiovascular profile, Change in quality of life or mental health. For reviews not reporting quantitative data synthesis: Range of effects across primary studies and main conclusions of review.

6.2.8 Risk of bias in individual reviews

The included reviews would have been appraised for methodological quality using the Assessment of multiple systematic reviews (AMSTAR) measurement tool (195) as outlined in Table 6.2.4. The tool would have been used to assess the methodological quality according to the following criteria; reporting of an a priori design, duplication of study selection and data extraction, whether a comprehensive literature search is performed and whether publication status determines eligibility for inclusion, reporting of included and excluded studies and characteristics of the included studies, the assessment, reporting and use of scientific quality of the included studies, use of appropriate methods to combine study findings, and the reporting of potential publication bias and conflicts of interest. Each of the criteria specified in the AMSTAR tool would have been assessed and a judgement would have been made of 'yes', 'no', 'can't answer' or 'not applicable'. The quality assessment procedure would have been undertaken by both reviewers independently, with each included systematic review appraised. The appraisals of both reviewers would then have been compared and discrepancies discussed.

Table 6.2.4: Criteria for judging the quality systematic reviews using the AMSTAR tool

1 Was an 'a priori' design provided?	The research question and inclusion criteria should be established before the conduct of the review. Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."
2 Was there duplicate study selection and data extraction?	There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.
3 Was a comprehensive literature search performed?	At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).
4 Was the status of publication (i.e. grey literature) used as an inclusion criterion?	The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.
5 Was a list of studies (included and excluded) provided?	A list of included and excluded studies should be provided. Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."
6 Were the characteristics of the included studies provided?	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. Note: Acceptable if not in table format as long as they are described as above.
7 Was the scientific quality of the included studies assessed and documented?	'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).
8 Was the scientific quality of the included studies used appropriately in formulating conclusions?	The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.
9 Were the methods used to combine the findings of studies appropriate?	For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.
10 Was the likelihood of publication bias assessed?	An assessment of publication bias should include a combination of graphical aids (e.g. funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
11 Was the conflict of interest included?	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.

6.2.9 Synthesis of results

Qualitative analysis would have been undertaken in order to provide a narrative summary of the findings of the individual included systematic reviews for each of the outcomes of interest, with data presented in review characteristics tables. Qualitative analysis would also have provided a summary of the methodological quality of the included reviews and any potential impact on the findings of each of the constituent reviews, and potential impact on the overall conclusions of the systematic review. Additionally, the findings of the qualitative analysis would have informed recommendations for the conduct and reporting of future reviews.

The quantitative findings of the reviews would have been illustrated using forest plots without summary statistics for each of the following outcomes of interest: weight change, BMI change, change in co-morbidity presence, change in co-morbidity severity, quality of life change, mental health change and cardiovascular change following weight management intervention. The forest plots would have been used to illustrate mean difference in continuous measures such as weight or BMI change, and odds ratios for dichotomous variables such as presence of symptoms of anxiety disorder.

6.2.10 Risk of bias across reviews

Following the assessment of methodological quality of each of the included reviews using the AMSTAR tool, evaluation summaries would have been made across reviews and domains. The quality assessment information would have been used to inform the interpretation of the findings of each of the included reviews, with consideration of potential methodological factors which could introduce bias to review findings. If appropriate, recommendations to improve the methodological and reporting quality of

future reviews would have been made, highlighting areas of limitation where improvement may have been required.

6.3 RESULTS

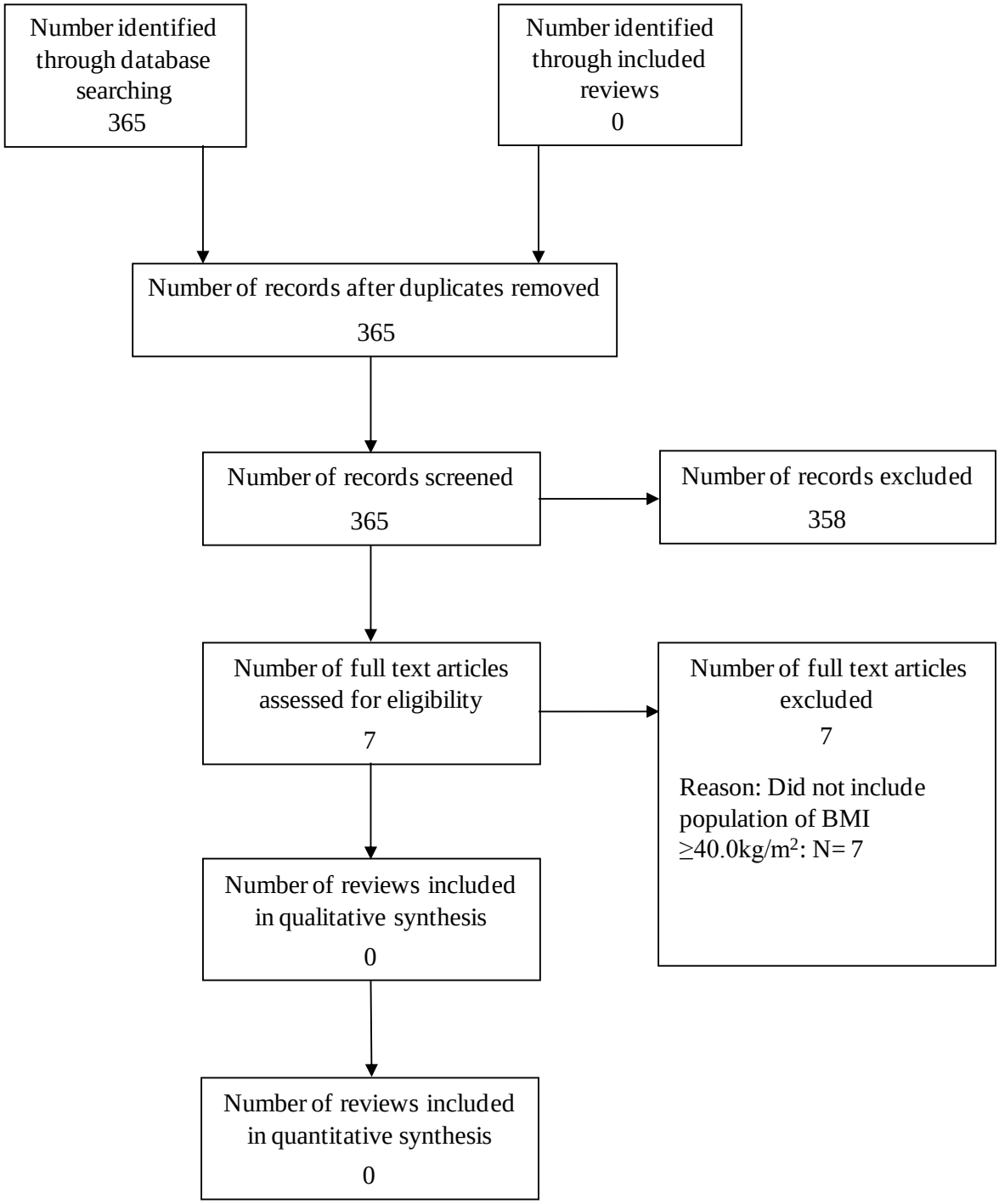
6.3.1 Article selection

The search retrieved a total of 365 records. No duplicates were identified and 358 records were excluded after screening by title and abstract. Seven full text records were screened and all seven records were excluded as they did not meet the eligibility criteria of reporting intervention effectiveness in BMI $\geq$40.0kg/m^2 individuals. Therefore no articles were identified as eligible for inclusion in the systematic review. The flow diagram (Figure 6.1) illustrates the number of records retrieved and the subsequent process of selection, as outlined in the PRISMA statement (192). The seven full text records which were screened are detailed in Table 6.3.1. Due to the fact that no systematic reviews eligible for inclusion were identified, there are no further results to report regarding review characteristics, risk of bias and analyses.

Table 6.3.1: Details of the seven reviews excluded after full text screening

Review first author and date of publication	Title of review
Anderson, 2004 (196)	Structured weight-loss programs: Meta-analysis of weight loss at 24 weeks and assessment of effects of intervention intensity
Hebden, 2012 (197)	Lifestyle intervention for preventing weight gain in young adults: a systematic review and meta-analysis of RCTs
Hutchesson, 2013 (198)	Weight management interventions targeting young women: a systematic review
Lepe, 2011 (199)	Long-term efficacy of high-protein diets: a systematic review
Perez, 2013 (200)	Evidence-based obesity treatment interventions for Latino adults in the U.S. A systematic review
Seo, 2008 (201)	A meta-analysis of psycho-behavioral obesity interventions among US multi-ethnic and minority adults
Witham, 2010 (202)	Interventions to achieve long-term weight loss in obese older people. A systematic review and meta-analysis

Figure 6.1: Flow diagram outlining the identification of included reviews



6.4 DISCUSSION

6.4.1 Summary of evidence

The present systematic review has identified that there were no systematic reviews examining the efficacy of medical and behavioural weight management interventions for extreme obese BMI $\geq$40.0kg/m^2 populations eligible for inclusion. The review has highlighted that there is a gap in the literature and indicates that there is a need for a systematic review of primary research examining the efficacy of medical and behavioural weight management interventions within extreme obese samples.

The phenomenon of empty systematic reviews, that is reviews which contain no records eligible for inclusion, has been examined in a study assessing the number of empty systematic reviews published in the Cochrane Database of Systematic Reviews (CDSR) (203). At the time of publication (August, 2010) the investigators reported a total of 376 empty reviews, which equated to 8.7% of reviews within the CDSR which reported that there were no records eligible for inclusion. The authors highlighted the fact that observed absences of evidence may help to stimulate the initiation of primary research, providing potential directions for targeted research, thus resulting in empty reviews being updated with eligible newly published studies.

It is likely that the present systematic review yielded no reviews eligible for inclusion due to the fact that the management of extreme obesity is a relatively new field, which has emerged recently with the increasing prevalence of the condition (15, 17). Thus it is possible that there is not yet a significant body of evidence to be synthesised in a systematic review of the literature.

6.4.2 Limitations

The systematic review was limited by the fact that the information sources which were searched were restricted to three databases within the Cochrane Library. There is potential for the possibility that the systematic review did not capture systematic reviews of medical and behavioural weight management interventions that were published in alternative databases. However within the scope of this body of work, the adopted approach was deemed sufficient to provide a reliable representation of the evidence for the efficacy of weight management interventions for extreme obesity within the body of literature. The present systematic review was strengthened by the duplication of the study selection process, which was conducted independently by two reviewers and was also strengthened by the use of a standardised protocol.

6.4.3 Conclusions

The results of the systematic review indicate that there is a gap in the literature, as no eligible systematic reviews summarising data from primary studies of the effectiveness of medical and behavioural weight management interventions for extreme obese populations have been published in the CDSR, DARE and HTA databases of the Cochrane Library. Given the observed increase in prevalence of extreme obesity in the UK over recent years (15, 17), and the fact that current levels are expected to rise (25), it is imperative that the efficacy of weight management interventions for the extreme obese population are established, thus enabling the best opportunity for affected individuals to achieve weight loss. The efficacy of medical or behavioural weight management interventions for extreme obesity remains unestablished, thus a systematic review of primary studies examining intervention efficacy within extreme obese populations is warranted.

CHAPTER SEVEN

7.0 MEDICAL AND BEHAVIOURAL WEIGHT MANAGEMENT INTERVENTIONS FOR EXTREME OBESITY: A SYSTEMATIC REVIEW OF PRIMARY STUDIES

7.1 INTRODUCTION

7.1.1 Rationale

The increasing prevalence of obesity and the associated detrimental impacts on individuals' health and quality of life, have led to the development of a variety of weight management programmes delivered across primary (29, 31, 32, 173) and specialist healthcare settings (174, 175), as well as commercial (36, 181) and research settings (73). Chapter four has highlighted the efficacy of such weight management interventions primarily among obese $\geq$30.0kg/m^2 populations, with the majority of the weight management programmes demonstrating modest weight losses. As such, these weight management interventions may not be sufficient to produce the clinically significant improvements to health that are required among extreme obese individuals. Furthermore whilst specialist weight management services have been demonstrated to produce modest weight losses among extreme obese (BMI $\geq$40.0kg/m^2) samples (174, 175), these studies have used non-controlled observational designs. Thus there is a lack of good quality evidence assessing the effectiveness of weight management interventions in facilitating weight loss for individuals with extreme obesity.

The findings of the systematic review described in Chapter six indicate a gap in the body of research literature, with no eligible systematic reviews summarising data from primary studies of the effectiveness of medical and behavioural weight management interventions for extreme obese populations identified. The limited evidence base has meant that the variation in weight management service provision for extreme obese individuals in the UK and internationally is continuing. However, the increasing prevalence of obesity and subsequent demand for services means that establishing the

effectiveness of weight management services is essential in order to ensure that individuals are given the best opportunity at achieving weight loss.

To address the identified gap in the literature and provide an additional contribution to the evidence base, this systematic review will search for primary studies examining the effectiveness of medical and behavioural weight management interventions within extreme obese (BMI $\geq$40kg/m^2) samples. The systematic review will summarise data from included studies, additionally assessing the quality of studies, and generating recommendations for future research.

7.1.2 Objectives

The specific objectives of the systematic review are:

- To summarise the effectiveness of medical or behavioural weight management interventions for adults with extreme obesity (defined as baseline BMI $\geq$40.0kg/m^2) on weight change, including if appropriate a meta-analysis of the effect of interventions on weight and BMI change.
- The secondary objectives are to examine the impact of these interventions on psychological profile (incorporating quality of life and mental health) and cardiovascular profile (incorporating blood pressure and lipids), with a meta-analysis if appropriate, of the effect of interventions on psychological and cardiovascular factors.
- To analyse study quality and provide a summary of the best evidence available.

The systematic review question was formulated using the PICOS framework as illustrated in Table 7.1.1. The explicit question which will be answered by the systematic review is: 'What is the effectiveness of medical and behavioural weight management interventions for extreme obesity?'

Table 7.1.1: Development of systematic review question using PICOS framework

Population	Adults with extreme obesity, defined as mean baseline BMI of $\geq 40.0 kg/m^2$.
Intervention	Medical or behavioural weight management (any non-surgical intervention which encompasses behavioural modification, medical or pharmaceutical components) of any duration.
Comparators	Control arm comprising usual care.
Outcomes	Primary outcome: Weight and BMI change at post-intervention follow-up or at intervention-end where follow-up is not available. Secondary outcome: Quality of life, mental health, and cardiovascular (blood pressure, lipids) change at post-intervention follow-up or at intervention-end where follow-up is not available.
Study design	Randomised Controlled Trials (RCTs), controlled non-randomised studies, controlled observational studies (prospective and retrospective cohort studies with concurrent controls).

7.2 METHODS

7.2.1 Protocol and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (192). A systematic review protocol was produced for use as a reference to aid the two reviewers and ensure consistency in the conduct of the review (Appendix two). The systematic review was registered on the PROSPERO international database of prospectively registered systematic reviews in health and social care, with registration number CRD42014010473.

7.2.2 Eligibility criteria

The eligibility for inclusion in the systematic review was determined by the criteria outlined in Table 7.2.1. The criteria for inclusion in the systematic review incorporated primary studies in adult extreme obese populations, excluding those studies examining the efficacy of interventions in child and adolescent populations, and those which focused on populations recruited solely on the basis of health conditions other than obesity. As such the review focussed on the general extreme obese population, excluding those studies examining the effectiveness of interventions specifically among samples of individuals receiving treatment for other diagnosed health conditions.

Table 7.2.1: Eligibility criteria

Domain	Criteria
Population	• Studies reporting intervention effectiveness in BMI ≥40.0kg/m^2 populations were included, incorporating separate BMI ≥40.0kg/m^2 subgroup samples and overall study samples. • Studies where included study populations were adult (≥18 years) were included. • Studies including study populations based on health conditions other than obesity were excluded, for instance samples including solely individuals with heart disease, type 2 diabetes, cancer, or schizophrenia.
Interventions	• Studies of non-surgical interventions providing medical and or behavioural support incorporating pharmaceutical therapies, counselling, education, and lifestyle modification incorporating diet and physical activity were included. • Studies including bariatric procedures or surgery were excluded. • Studies which incorporated interventions of any duration were included.
Outcomes	• Studies reporting weight and or BMI measures at baseline and at intervention-end, or weight and or BMI change scores were included. • Studies reporting baseline characteristics data without post-intervention follow-up or intervention-end weight or BMI outcome data were excluded.
Study design	• RCTs, controlled non-randomised studies, and controlled observational studies (prospective and retrospective cohort studies with concurrent controls) were included. • Study designs further down the hierarchy of evidence, such as observational studies without concurrent control groups were excluded. • Studies published up to and including July 2014 were included. • Peer reviewed studies and conference abstracts published in any language were included. • Review articles, editorials, commentaries and letters were excluded.

7.2.3 Information sources

A search of the following electronic databases was conducted: MEDLINE (Ovid), EMBASE (Ovid), CINAHL (Ebsco host), and Cochrane Central Register of Controlled Trials (CENTRAL) database, from inception to July 2014. In addition, grey literature

including conference abstracts and doctoral theses were searched using the OpenGrey and Zetoc databases, and reference lists of papers included in the review were hand-searched.

7.2.4 Search

The following search strategy was used to search for primary studies examining the efficacy of medical or behavioural weight management interventions of any duration for samples with extreme obesity, defined as sample mean BMI ≥40.0kg/m^2. Terms were entered as free text and MeSH (Medical Subject Heading) terms in the MEDLINE, EMBASE, CINAHL, and CENTRAL databases. The search strategy detailing the combinations of search terms utilised in each database search are outlined in Tables 7.2.2 - 7.2.5. Truncation of the free text terms 'adult' and 'obes' was used in order to include a variety of word endings such as 'adulthood' and 'obesity', thus maximising the number of relevant records returned. Those terms which were available as MeSH terms within each database were selected using the 'explode all trees' function in order to retrieve all related terms in the search. When searching the EMBASE and MEDLINE databases MeSH and free text terms were entered into multi-purpose (.mp) searches. The CINAHL database was searched by entering MeSH terms as exact major subject headings (MM), and free text terms as words in major subject headings (MJ). Limits were applied to the searches in the MEDLINE, EMBASE and CINAHL databases using the clinical query function. Specifically, the 'therapy (maximises sensitivity)' and 'therapy- high sensitivity' limits were selected in order to encompass a broad search and ensure that no relevant studies were omitted. Additionally, a 'human' limiter was applied in order to omit studies adopting animal model designs.

The following free text terms were entered into the OpenGrey database: (morbid OR extrem* OR sever*) AND obes* AND intervention. The Zetoc database was searched using the following three separate free text searches: 'morbid AND obes* AND intervention', 'extrem* AND obes* AND intervention' and 'sever* AND obes* AND intervention'. Truncation was used in order to capture a variety of word endings such as 'severely' and 'obesity', thus maximising the number of relevant records returned.

Table 7.2.2: Search strategy for MEDLINE database

1	Adult*.mp
2	Overweight/ dh, dt, rh, th, nu (MeSH)
3	Obesity/ dh, dt, rh, th, nu (MeSH)
4	Obes*.mp
5	Body Mass Index/ (MeSH) explode all trees
6	BMI.mp
7	Body Weight.mp
8	2 or 3 or 4 or 5 or 6 or 7
9	1 and 8
10	Intervention.mp
11	Life style/ (MeSH) explode all trees
12	Health Promotion/ (MeSH) explode all trees
13	Health Education/ (MeSH) explode all trees
14	Patient Education as topic/ (MeSH) explode all trees
15	Counseling/ (MeSH) explode all trees
16	Behavior/ (MeSH) explode all trees
17	Anti-obesity Agents/ (MeSH) explode all trees
18	Weight Reduction Programs/ (MeSH) explode all trees
19	Diet, Reducing/ (MeSH) explode all trees
20	Weight Loss/ (MeSH) explode all trees
21	Exercise (MeSH) explode all trees
22	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23	10 and 22
24	9 and 23
25	Limit 24 to humans
26	Limit 25 to "therapy (maximizes sensitivity)"
27	Control*.mp
28	25 and 27
29	26 or 28

.mp= title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword.
dh= diet therapy, dt= drug therapy, rh= rehabilitation, th= therapy, nu= nursing.

Table 7.2.3: Search strategy for EMBASE database

1	Adult*.mp
2	Overweight*.mp
3	Obesity/ dm, dt, rh, th (MeSH)
4	Obes*.mp
5	Body Mass/ (MeSH) explode all trees
6	BMI.mp
7	Body Weight/ co, dt, th (MeSH)
8	2 or 3 or 4 or 5 or 6 or 7
9	1 and 8
10	Intervention.mp
11	Life style/ (MeSH) explode all trees
12	Health Promotion/ (MeSH) explode all trees
13	Health Education/ (MeSH) explode all trees
14	Patient Education as topic/ (MeSH) explode all trees
15	Counseling/ (MeSH) explode all trees
16	Behavior/ dt, rh, th (MeSH)
17	Antiobesity Agent/ ct, dt (MeSH)
18	Diet Restriction/ (MeSH) explode all trees
19	Weight Reduction/ dt, th (MeSH)
20	Exercise/ (MeSH) explode all trees
21	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22	10 and 21
23	9 and 22
24	Limit 23 to humans
25	Limit 24 to “therapy (maximizes sensitivity)”
26	Control*.mp
27	24 and 26
28	25 or 27

mp= title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword.
dm= disease management, dt= drug therapy, rh= rehabilitation, th= therapy, co= complication, ct= clinical trial.

Table 7.2.4: Search strategy for CINAHL database

1	MJ Adult*
2	MJ Overweight
3	MM Obesity/ dh, dt, rh, th, nu (MeSH)
4	MJ Obes*
5	MM Body Mass Index/ (MeSH) explode all trees
6	MJ BMI
7	MM Body Weight (MeSH) explode all trees
8	2 or 3 or 4 or 5 or 6 or 7
9	1 and 8
10	MJ Intervention
11	MM Life style/ (MeSH) explode all trees
12	MM Health Promotion/ (MeSH) explode all trees
13	MM Health Education/ (MeSH) explode all trees
14	MM Patient Education/ (MeSH) explode all trees
15	MM Counseling/ (MeSH) explode all trees
16	MM Behavior/ (MeSH) explode all trees
17	MM Antiobesity Agents/ (MeSH) explode all trees
18	MM Weight Reduction Programs/ (MeSH) explode all trees
19	MM Diet, Reducing/ (MeSH) explode all trees
20	MM Weight Loss/ dh, dt, th (MeSH)
21	MM Exercise (MeSH) explode all trees
22	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23	10 and 22
24	9 and 23
25	Limiters to 24- Human
26	Limiters to 24- Clinical Queries: Therapy- High Sensitivity; Human
27	MJ Control*
28	25 and 27
29	26 or 28

MM= Exact Major Subject Headings, MJ= Word in Major Subject Headings.
dh= diet therapy, dt= drug therapy, rh= rehabilitation, th= therapy, nu= nursing.

Table 7.2.5: Search strategy for CENTRAL database

1	Adult*
2	Overweight (MeSH) explode all trees
3	Obesity (MeSH) explode all trees
4	Obes*
5	Body Mass Index (MeSH) explode all trees
6	BMI
7	Body Weight (MeSH) explode all trees
8	2 or 3 or 4 or 5 or 6 or 7
9	1 and 8
10	Intervention
11	Life style (MeSH) explode all trees
12	Health Promotion (MeSH) explode all trees
13	Health Education (MeSH) explode all trees
14	Patient Education as Topic (MeSH) explode all trees
15	Counseling (MeSH) explode all trees
16	Behavior (MeSH) explode all trees
17	Anti-Obesity Agents (MeSH) explode all trees
18	Weight Loss (MeSH) explode all trees
19	Diet, Reducing (MeSH) explode all trees
20	Weight Reduction Programs (MeSH) explode all trees
21	Exercise (MeSH) explode all trees
22	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23	10 and 22
24	9 and 23
25	24 in Trials

7.2.5 Study selection

The records were exported to the EndNote programme (Thomson Reuters EndNote version X7.1) to facilitate management of the records by both reviewers. Two reviewers independently screened the titles and abstracts using the eligibility criteria relating to population, intervention, comparator, outcome and study design. Those records deemed to not meet eligibility criteria were removed, and the number excluded at this stage was independently recorded by each reviewer. Once the first phase of study selection, screening by title and abstract was complete, the selection of the two reviewers was compared. Discrepancies were discussed, consensus was reached and the final number of studies to be screened as full text was determined.

The second phase of study selection involved obtaining full text copies of each study and screening the full text, which was conducted by the two reviewers independently. Those studies which were judged to not meet the eligibility criteria were excluded at this stage, with the excluded records grouped by reason for exclusion. The final number of studies that were deemed to be eligible for inclusion in the systematic review were determined by each reviewer independently and once the second selection phase was complete the two reviewers again met to compare selection. After discussion the final number of included studies was determined and there were no discrepancies in agreement. The reference lists of the included studies were subsequently searched in order to identify any further relevant primary studies, which were screened against eligibility criteria.

7.2.6 Data collection process

Data items were extracted from the information provided in the full text articles independently by the two reviewers, into a Microsoft Excel spreadsheet whereby each study was represented in a row of data in the spreadsheet. A detailed list of data items for extraction was developed with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0) (194), in order to facilitate the data extraction process. A detailed list of the items specified for data extraction is outlined in Table 7.2.6, which was used as a point of reference when entering the data items into the spreadsheet. The two reviewers met once data extraction had taken place independently, and discrepancies were discussed.

7.2.7 Data items

The data items specified for data extraction from the included studies are outlined in Table 7.2.6. Following data extraction, specific data items were selected from the finalised data extraction spreadsheet and were used in the production of study characteristics tables to facilitate the description and qualitative analysis of the included studies.

Table 7.2.6: Data items to be extracted from included studies

Field	Data points to be extracted
Review	Author, Publication year, Country (including city or region).
Methods	Design, (RCT, controlled non-randomised, controlled observational: prospective or retrospective cohort with concurrent control), Objectives, Randomisation method (detail method if used), Study duration (from point of recruitment to last data collection).
Study characteristics	Total number recruited, Location of recruitment (e.g. healthcare clinic/hospital, community organisation/group, specified region of healthcare organisation such as primary or specialist care), Recruitment/referral criteria, Age (mean and standard deviation years) and age range of study sample, Gender (number and proportion male and female), Ethnicity (number and proportion of each ethnic group), Weight (baseline mean and standard deviation), BMI (baseline mean and standard deviation), Whether participant data is for whole study sample (i.e. mean study sample baseline BMI is ≥40.0kg/m^2) or for a BMI ≥40.0kg/m^2 subgroup.
Intervention	Nature of intervention (i.e. behavioural, medical, education, pharmaceutical, Low Energy Liquid Diet, other, or a combination), Number of intervention groups, Intervention setting (where intervention is delivered), Delivery personnel type (if healthcare professional, researcher, lay public), Delivery personnel training (detail of training in intervention delivery received), Duration of intervention (number and duration of contact time, including face to face sessions, email, telephone or other contact), Intensity of intervention (frequency of sessions and contact), Theoretical basis of intervention (e.g. self-management, cognitive behavioural), Number of participants assigned/randomised to intervention group, Number of participants entering intervention group, Number of participants completing intervention at intervention-end, Number of participants completing intervention or presenting at time of last data collection, Loss to follow-up rate (number randomised-number completing/number randomised), Any significant differences identified between participants completing and those lost to follow-up.

Table 7.2.6 Continued: Data items to be extracted from included studies

Field	Data points to be extracted
Comparator	Number of comparator groups, Description of usual care, Number of participants assigned/randomised to comparator group, Number of participants entering comparator group, Number of participants completing comparator group at intervention-end, Number of participants completing comparator group or presenting at time of last data collection, Loss to follow-up rate (number randomised-number completing/number randomised), Any significant differences identified between participants completing and those lost to follow-up.
Outcomes	*Primary outcomes (using available case or LOCF data):* Weight change from baseline at last point of data collection (including mean and standard deviation, and time point at which obtained), BMI change from baseline at last point of data collection data (including mean and standard deviation), and time point at which obtained), Weight change from baseline at intervention-end (including mean and standard deviation), BMI change from baseline at intervention-end (including mean and standard deviation), Proportion losing weight (any amount), proportion losing ≥5% baseline weight at last point of data collection, Proportion losing weight (any amount), proportion losing ≥5% baseline weight at intervention-end, *Secondary outcomes:* Quality of life change from baseline to last point of data collection, Quality of life change from baseline to intervention-end, Detail quality of life measure used and report change for all if more than 1 measure, Mental health change from baseline to last point of data collection, Mental health change from baseline to intervention-end, State mental health measure used and report change for all if more than 1 measure, Systolic and diastolic blood pressure change from baseline to last point of data collection, Systolic and diastolic blood pressure change from baseline to intervention-end, HDL-, LDL- and total cholesterol change from baseline to last point of data collection, HDL-, LDL- and total cholesterol change from baseline to intervention-end, For all outcomes include description of confounders where adjusted-estimates are reported and include category boundaries where continuous variables are categorized.

7.2.8 Risk of bias in individual studies

The included studies were appraised for methodological quality using the Cochrane Collaboration's tool for assessing risk of bias, version 5.1.0 (204). Studies adopting both randomised and non-randomised controlled designs were assessed using the tool. However the random sequence generation domain was not completed for studies of non-randomised

design. The tool assessed the following dimensions; sequence generation, allocation concealment, blinding of participants, personnel, outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Thus the quality appraisal provided an estimate of the level of internal validity and therefore the level of risk of bias, for each study. Furthermore, the quality of reporting of RCTs was assessed with the CONSORT checklist (205), and the reporting quality of the controlled non-randomised study was assessed using the STROBE checklist (206).

7.2.9 Synthesis of results

In order for the data to be entered into meta-analyses, the outcome data were extracted as means and standard deviations. However where data were reported as standard errors and 95% confidence intervals rather than standard deviations, the data were transformed according to guidelines in the Cochrane handbook section 7.7.3.2 'Obtaining standard deviations from standard errors and confidence intervals for group means' (194). To calculate standard deviations (SD) from standard errors (SE), the following formula was used:

SD = SE x √Sample size

To calculate standard deviations from confidence intervals (CIs), the divisor was calculated using a t distribution, as the sample sizes were relatively small for both the intervention and control groups. The standard deviations were calculated using the following formula:

SD = [√Sample size x (upper 95% CI limit – lower limit)] / [2 x t value]

Once the mean and standard deviation data were obtained, they were entered in to the RevMan package for meta-analyses. Meta-analysis was conducted on only one

outcome measure, weight change from baseline to intervention-end, whereby a random-effects model was selected due to clinical heterogeneity between the studies. It was not possible to conduct meta-analyses for the other outcomes of interest; BMI, blood pressure, cholesterol and quality of life, due to inconsistencies in data collection and reporting between the included studies.

7.2.10 Risk of bias across studies

The quality assessment was used to inform the interpretation of the findings of the review, guiding the level of confidence in the study findings. The quality assessment provided evaluation summaries which were made across studies and domains, of the quality of the body of literature. This highlighted areas of strength and weakness, and facilitated the generation of recommendations for the improvement of the quality for future primary studies.

7.3 RESULTS

7.3.1 Study selection

The database search retrieved a total of 9,077 studies, 2,313 of which were retrieved from CENTRAL, 1,869 from CINAHL, 2,286 from EMBASE, and 2,609 from MEDLINE. The search of additional sources which included the Zetoc and OpenGrey databases and reference lists of included studies, yielded a total of 141 studies. A total of 1,907 studies were identified as duplicates and removed, and 7,311 studies were screened by title and abstract, with 7,232 excluded at this stage. Seventy-nine full text studies were screened and 76 studies were excluded as they did not meet the eligibility criteria. Therefore three studies were identified as eligible for inclusion in the systematic review. The flow diagram (Figure 7.1) illustrates the number of studies retrieved and the subsequent process of selection, as outlined in the PRISMA statement (192). The reasons for exclusion of the 76 full text records are detailed in Tables 7.3.1 and 7.3.2. The most common reason for exclusion was that the study did not include a population of extreme obese (BMI ≥40.0 kg/m^2) individuals.

Figure 7.1: Flow diagram outlining the identification of included studies

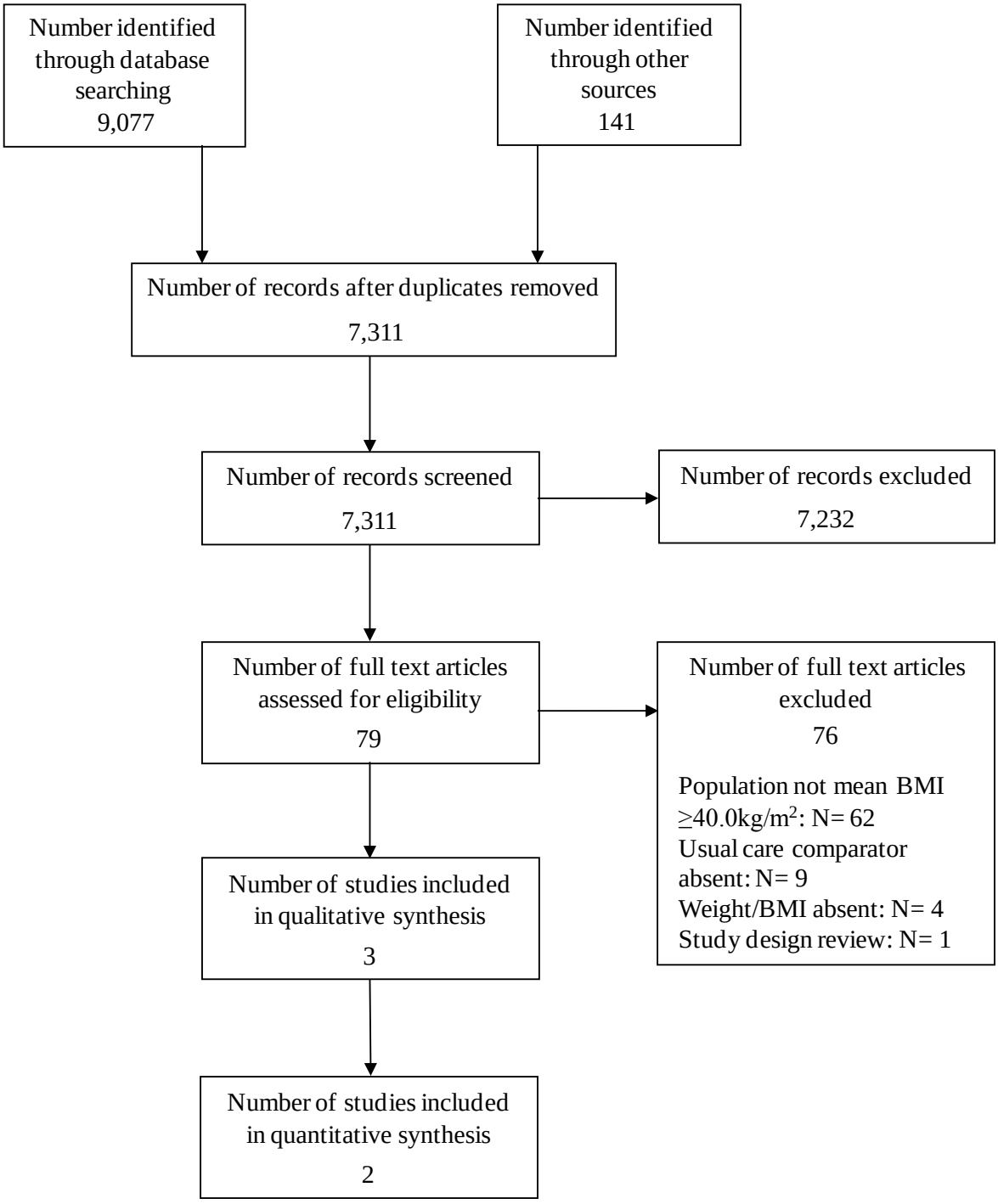


Table 7.3.1: Full text studies excluded due to not including extreme obese populations

Review first author and date of publication	
Abbenhardt, 2013 (207)	Greenway, 2009 (208)
Admiraal, 2013 (209)	Greenway, 2010 (210)
Aggel-Leijssen, 2002 (211)	Hardcastle, 2008 (212)
Arciero, 2006 (213)	Hardcastle, 2013 (214)
Aubertin-Leheudre, 2007 (215)	Ho, 2012 (216)
Bakris, 2002 (217)	Joo, 2011 (218)
Barak, 2008 (219)	Kalter-Leibovici, 2010 (220)
Bartfield , 2011 (221)	Kerksick, 2009 (222)
Berteus Forslund, 2008 (223)	Knowler, 2009 (224)
Bhutani, 2013 (225)	Lutes, 2008 (226)
Bhutani, 2013 (227)	Madsen, 2008 (228)
Blum, 2009 (229)	Martin, 2011 (230)
Brekke, 2003 (231)	Meekums, 2012 (232)
Brekke, 2005 (233)	Miller, 2002 (234)
Broom, 2002 (235)	Moore, 2013 (236)
Buscemi, 2011 (237)	Pi-Sunyer, 2006 (238)
Butsch, 2007 (239)	Poston, 2003 (240)
Cakmakçi, 2011 (241)	Research group of the Rome project of coronary heart disease prevention, 1986 (242)
Cayir, 2014 (243)	Ross, 2012 (244)
Craigie, 2011(245)	Sarsan, 2006 (246)
Davidson, 1999 (247)	Smith, 2011 (248)
Davis Martin, 2006 (249)	Sniehotta, 2011 (250)
Desouza, 2012 (251)	Stolley, 2009 (252)
Dutton, 2007 (253)	Tanco, 1998 (254)
Eiben, 2006 (255)	Tapper, 2009 (256)
Esposito, 2003 (257)	Tiikkainen, 2004 (258)
Fitzgibbon, 2010 (259)	Tsai, 2010 (260)
Folta, 2009 (261)	Tsai, 2007 (262)
Garcia, 2006 (263)	Tumiati, 2008 (264)
Gohner, 2012 (265)	Wadden, 2011 (266)
Goulis, 2004 (267)	Yancey, 2006 (268)

Table 7.3.2: Full text studies excluded due to other study factors

Review first author and date of publication	Reason for exclusion
Gantz, 2007 (269)	Mean BMI not reported (range 30-43)
Carels, 2008 (270)	Mean BMI not reported. Mean weight suggests BMI <30.0kg/m^2 based on estimation of average height
Byrne, 2012 (271)	Mean BMI not reported (range 30-56). Weight or BMI change not reported
Beresford, 1997 (272)	Mean BMI and weight not reported at baseline. Weight or BMI change not reported
Allison, 2012 (273)	Usual care comparator absent
Annesi, 2010 (274)	Usual care comparator absent
Cooper, 2012 (275)	Usual care comparator absent
Due, 2007 (276)	Usual care comparator absent
Ettinger, 2003 (277)	Usual care comparator absent
Summerbell, 1998 (278)	Usual care comparator absent
Annesi, 2013 (279)	Usual care comparator absent. Weight or BMI change not reported
Berger, 2010 (280)	Usual care comparator absent. BMI <40.0 kg/m^2
Donnelly, 1994 (281)	Usual care comparator absent. BMI <40.0 kg/m^2
Ioannides-Demos, 2005 (282)	Study design was review

7.3.2 Study characteristics

The characteristics of the three included studies are summarised in Table 7.3.3. All three studies assessed the efficacy of lifestyle interventions which adopted different approaches, and included a residential inpatient lifestyle programme promoting diet, physical activity and cognitive changes such as coping strategies, goal setting, and problem solving (283), a programme promoting physical activity (284), and a medical intervention incorporating a Low Energy Liquid Diet (LELD), pharmaceutical therapy, and a behavioural group support programme (285). Interventions also varied in duration from 10-14 weeks (283), to 24 months (285). Two of the studies were conducted in the United States of America (US), with the remaining study taking place in Norway.

Table 7.3.3: Study characteristics table

Study (location)	Design	Participants	Intervention	Comparator	Outcome measures	Main findings
Danielsen, 2013 (Norway) (283)	Study design: Non-randomised, controlled, clinical trial. Setting: NIMI Ringerike Obesity clinic. Aim: To examine the efficacy of a 10-14wk inpatient Intensive Lifestyle Intervention (ILI) in severely obese adults. Duration: 18 months, September 2010 to March 2012. Referral/recruitment: BMI ≥40.0kg/m^2 or BMI ≥35.0 kg/m^2 with co-morbidities. Aged 18-65 and capable of walking slowly for 20mins.	N= 139 Intervention: N= 100 Mean age at baseline= 45.2yrs (9.5). Females: 59.2%. Mean baseline weight= 128.9kg (19.4). Mean baseline BMI= 42.8kg/m^2 (4.6). Number entering intervention= 100 Number completing intervention= 71 Intervention loss to follow up rate= 29% Control: N= 39 Mean age at baseline= 38.5yrs (9.8). Females 63.6%. Mean baseline weight= 127.1kg (21.6). Mean baseline BMI= 42.8kg/m^2 (6.3). Number entering control= 39. Number completing control= 33. Control loss to follow up rate= 15%	Intervention group receive Intensive Lifestyle Intervention (ILI). Inpatient residential programme lasting 10-14 weeks followed by phone and email communication up to 6 months. Duration and intensity of physical activity increased from 2-3 45minute sessions per week. Energy and nutrient intake was adjusted, portion sizes restricted to 1900kcal/day for males and 1600 kcal/day for females, with additional individual dietary nutritional consultations. Intervention was a behavioural, lifestyle intervention, incorporating diet, physical activity, and cognitive components (coping strategies, goal setting, problem solving). Intervention delivered by multi-disciplinary team (MDT) including a physician, psychologist, clinical nutritionist, and nurses, exercise scientists, and physiotherapists.	Comparator group received no intervention, and were recruited from a waiting list to receive the intervention.	Intervention: Weight and BMI change at intervention-end (10-14weeks), Weight and BMI change at 12 months, Systolic and diastolic blood pressure change at 12 months, HDL-, LDL-, and total cholesterol change at 12 months. Control: Weight and BMI change at intervention-end (10-14weeks).	Mean weight change at intervention-end= Intervention: -17.5kg (6.1), Control: -0.5kg (2.8). Between group difference= -17.0kg (-18.7 - -15.3) p <0.001. Mean weight change at 12 months= Intervention: -20.3 (-23.3 - -17.3) p <0.001. Control not reported. Mean BMI change at intervention-end= Intervention: -5.8kg/m^2 (1.8), Control: -0.2kg/m^2 (1.0). Between group difference= -5.6kg/m^2 (-6.2 - -5.1) p <0.001. Mean BMI change at 12 months= Intervention: -6.7kg/m^2 (-7.6 - -5.7) p <0.001. Control not reported.

Data are means and standard deviations or 95% confidence intervals. HDL= high density lipoprotein, LDL= low density lipoprotein.

Table 7.3.3 Continued: Study characteristics table

Study (location)	Design	Participants	Intervention	Comparator	Outcome measures	Main findings
Rimmer, 2009 (Chicago, US) (284)	Study design: Randomised Controlled Trial Setting: Outpatient internal medicine clinic Aim: To examine the efficacy of a personalised exercise programme using two treatment intensities, on increasing physical activity and improving health outcomes, relative to a minimal intervention. Duration: Enrolment over a 24 month period. Total study duration not reported. Referral/recruitment: BMI >27 and receiving primary care at site. Aged ≥18 years. Sedentary with no regular physical activity in last 6 months and self-reported mobility difficulty (walking a block or more/use of mobility aid).	Total N= 96 Intervention ‘Lower’/‘Higher’: N= 31 / 30 Mean age at baseline= 58.6yrs (12.0) / 59.1yrs (10.7). Females: 94% / 97%. Mean baseline weight= 129.3kg (no sd) / 135.8kg (no sd). Mean baseline BMI= 48.5kg/m^2 (10.7) / 51.5kg/m^2 (12.1). Number entering intervention= 31 / 30 Number completing intervention= 28 / 27 Intervention loss to follow up rate= 9.7% / 10% Control: N= 31 Mean age at baseline= 58.7yrs (12.2). Females: 94% Mean baseline weight= 118.9kg (no sd). Mean baseline BMI= 43.6kg/m^2 (10.9). Number entering control= 31 Number completing control= 23 Control loss to follow up rate= 25.8%	Two intervention groups receiving 6-month personalised exercise programmes with either higher or lower support. ‘Lower’ support group receive recommendation to exercise from physician, educational brochure, device to monitor activity, monthly newsletter, weekly 5-35minute telephone consultations to develop physical activity by tailored goal-setting, and activities. ‘Higher’ support group received above plus monthly 90minute exercise support group involving participation in physical activity, encouragement from facilitator, peer discussion, education, overcoming barriers to exercise. Intervention delivered by qualified fitness professionals. Intervention was a behavioural, lifestyle intervention promoting physical activity.	Control group received recommend-ation to exercise from physician, educational brochure, and device to monitor activity. Control group received no contact or support over 6 month intervention period.	All study arms: Weight and BMI (no sd) at baseline and intervention-end. Quality of life (Quality of Well-Being QWB) scale at baseline and intervention-end. Systolic and diastolic blood pressure at baseline and intervention-end. HDL-, LDL-, and total cholesterol at baseline and intervention-end.	Mean weight change at intervention-end= ‘Lower’ intervention: 129.3 to 128.2kg, p= 0.89 ‘Higher’ intervention: 135.8 to 125.6kg, p <0.01. Control: 118.9 to 120.5kg, p= 0.89. Mean BMI change at intervention-end= ‘Lower’ intervention: 48.5 to 48.6kg/m^2, p= 0.97. ‘Higher’ intervention: 51.5 to 47.7kg/m^2, p <0.01. Control: 43.6 to 44.3kg/m^2, p= 0.85.

Data are means and standard deviations. HDL= high density lipoprotein, LDL= low density lipoprotein.

Table 7.3.3 Continued: Study characteristics table

Study (location)	Design	Participants	Intervention	Comparator	Outcome measures	Main findings
Ryan, 2010 (Louisiana, US) (285)	Study design: Randomised Controlled 'pragmatic clinical' Trial Setting: Primary care practices Aim: To examine efficacy of a primary care practice intervention on weight loss in extreme obese individuals, relative to usual care at 2 years. Duration: 2.5yrs: July 2005 to January 2008 Referral/recruitment: BMI ≥40 up to and including BMI 60. Aged 20 to 60. Enrolled in programmes of the Louisiana state employees group benefits office.	N= 390 Intervention: N= 200 Mean age at baseline= 47.2yrs (0.6)*. Females: 83.5% Mean baseline weight= 126.2kg (23.2) †. Mean baseline BMI= 45.6kg/m^2 (7.9) †. Number entering intervention= 200 Number completing intervention= 101 Intervention loss to follow up rate= 49.5% Control: N= 190 Mean age at baseline= 47.1yrs (0.6)*. Females: 83.7% Mean baseline weight= 128.4kg (28.6) † Mean baseline BMI= 46.6kg/m^2 (8.5) †. Number entering control= 190 Number completing control= 86 Control loss to follow up rate= 54.7%	Intervention group receiving Intensive Medical Intervention (IMI) for 24 months. Intervention comprised 3 phases: Phase 1 comprised Low Energy Liquid Diet (LELD) for 12 weeks. Phases 2 and 3 comprised calorie restricted diet with prescription of weight loss medication and weekly then bi-weekly behavioural 60minute group sessions, with continued meal replacement as required. Phases 2 lasted from 3 to 8 months, and phase 3 from 8 to 24 months. Intervention was medical incorporating supervised meal replacement and pharmaceutical components as well as behavioural lifestyle components.	Control group received instruction in the use of mayo clinic weight management web site. Control group received no contact or support over 24 month intervention period (except assessment at 1yr and 2yrs).	Both arms: Mean weight change from baseline to intervention-end using available case and LOCF data. Proportion losing ≥5% weight at intervention-end (using available case and LOCF data). Mean BMI change not reported. Mean change in systolic and diastolic blood pressure from baseline to intervention-end. Mean change in HDL-, and LDL-cholesterol from baseline to intervention-end. All secondary measures reported using available case data.	Mean weight change at intervention end using available case data: Intervention: -12.7kg (1.7)*. Control: -0.5 (0.9)*. Between arms comparison p <0.001. Mean weight change percentage at intervention end using LOCF data: Intervention: -8.3% (0.8)* Control: 0.0% (0.4)*. Between arms comparison p <0.001. Mean weight change percentage at intervention end using available case data: Intervention: -9.7% (1.3)* Control: -0.4% (0.7)*. Between arms comparison p <0.001.

Data are mean and standard error (SE). Data are median & IQR †. LOCF= Last observation carried forward, HDL= high density lipoprotein, LDL= low density lipoprotein.*

7.3.3 Risk of bias within studies

The included studies were appraised for quality using the Cochrane Collaboration's tool for assessing risk of bias, version 5.1.0 (204), with findings displayed in Table 7.3.4. There was a high risk of bias for several domains in two of the included studies, with Danielsen, 2013 (283) scoring high risk across four domains and Rimmer, 2009 (284), in three domains. The remaining study, Ryan, 2010 (285) scored high risk for only two domains, and low risk for three domains.

The key areas affected by risk of bias in the Danielsen, 2013 study (283) are the concealment of allocation and blinding of participants, personnel and outcome assessment, which are plausible in the evaluation of an intervention of this nature, and were similar across all studies. However there was also a high risk of bias due to the incomplete reporting of outcome data, with follow-up measures obtained for the intervention and not control arm of the study. This was a major flaw in the study design, however this was pre-specified as a study aim to investigate the long-term impact of the intervention arm only, and so consequently the selective reporting of outcomes was judged to be at low risk of bias. Rimmer, 2009 (284) was judged to be at high risk of bias in the selective reporting domain, due to the fact that measures of distribution were not reported. The incomplete reporting of such data means that as a consequence the outcomes cannot be entered into the meta-analyses. In contrast, Ryan, 2010 (285) scored as low risk for both of these domains, but scored as high risk for the blinding of participants, personnel and outcome assessment.

The assessment indicates that two of the studies were deemed to be at moderate risk of bias, although this included the performance and detection bias domains which are not necessarily pertinent to evaluations of interventions of this nature, whilst the remaining study demonstrated less risk of bias.

Table 7.3.4: Assessment of risk of bias

	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
Study	**Random sequence generation**	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective reporting**	**Other sources of bias**
Danielsen, 2013 (283)	N/A	High risk of bias: Participants and investigators could foresee assignment as control arm on waiting list for intervention.	High risk of bias: No blinding of participants or personnel	High risk of bias (all outcomes): No blinding of outcome assessment	High risk of bias (all outcomes): Outcomes not collected for control group beyond intervention end, whilst intervention group followed up at 6 and 12 months with greater range of measures.	Low risk of bias: The outcomes of interest were pre-specified, and aim identified.	Low risk of bias: The study appears to be free from other sources of bias.
Rimmer, 2009 (284)	Low risk of bias: Participants given numbered brochure outlining study arm assignment.	High risk of bias: No indication that numbered brochures were concealed.	High risk of bias: No blinding of participants or personnel.	Unclear risk of bias (all outcomes): Personnel conducting assessments not involved in intervention, but use of blinding unknown.	Low risk of bias (all outcomes): Outcome data reported for all pre-specified measures as pre- and post- intervention means (however standard deviations, standard errors or confidence intervals not reported).	High risk of bias: Outcomes of interest are missing standard deviations, standard errors or confidence intervals) thus cannot be entered into a meta-analysis.	Low risk of bias: The study appears to be free from other sources of bias.
Ryan, 2010 (285)	Unclear risk of bias: Minimisation allocation applied stratified by age, sex, BMI.	Unclear risk of bias: Insufficient information to determine whether allocation was concealed.	High risk of bias: No blinding of participants or personnel.	High risk of bias (all outcomes): No blinding of outcome assessment	Low risk of bias (all outcomes): No missing outcome data. Weight outcomes reported using available cases, LOCF and BOCF approaches.	Low risk of bias: The outcomes of interest were pre-specified, and analyses conducted and reported.	Low risk of bias: The study appears to be free from other sources of bias.

N/A: Not applicable as the study was not a randomised controlled trial.

7.3.4 Results of individual studies

Effect of intervention on weight and BMI

All three included studies reported change in weight from baseline to intervention-end, the results of which are displayed in Table 7.3.5. The greatest weight loss was observed in the Danielsen, 2013 inpatient intervention (283), achieving a significant mean loss of -17.5kg ($p < 0.001$), compared to the Ryan, 2010 medical intervention (285) which yielded a mean loss of -12.7kg (significance not reported), and the Rimmer, 2009 exercise intervention (284) with a significant mean loss of -10.2kg ($p < 0.01$) in the higher support programme and a non-significant loss of -1.1kg ($p = 0.89$) for the lower support programme, from baseline.

Table 7.3.5: Change in weight (kg) at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	128.9 (19.4)	NR	-17.5 (6.1)	127.1 (21.6).	NR	-0.5 (2.8)
Rimmer, 2009	'Lower': 129.3 'Higher': 135.8	'Lower': 128.2 'Higher': 125.6	NR	118.9	120.5	NR
Ryan, 2010	126.2 (23.2) †	NR	-12.7 (1.7*) (17.1) ≠	128.4 (28.6) †	NR	-0.5 (0.9*) (8.3) ≠

Data are means and standard deviations or standard errors (*)
† Data are median & IQR
NR= Data not reported 'Lower'= Lower support intervention, 'Higher'= Higher support intervention
Standard deviation calculated by transforming 95% CI or standard error (≠).

The mean change in BMI from baseline to post-intervention was reported in two studies and results are summarised in Table 7.3.6. Similar to the weight change findings reported in Table 7.3.5, the greatest loss of BMI was obtained through the Danielsen, 2013 inpatient

intervention (283) which yielded a significant loss of -5.8kg/m^2 (p <0.001). The Rimmer, 2009 higher support exercise programme (284) also yielded a significant mean loss of -3.8kg/m^2 (p <0.01), whilst the lower support programme resulted in a non-significant gain of 0.1kg/m^2 (p =0.97).

Table 7.3.6: Change in BMI at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	42.8 (4.6)	NR	-5.8 (1.8)	42.8 (6.3)	NR	-0.2 (1.0)
Rimmer, 2009	'Lower': 48.5 (10.7) 'Higher': 51.5 (12.1)	'Lower': 48.6 'Higher': 47.7	NR	43.6 (10.9)	44.3	NR
Ryan, 2010	45.6 (7.9) †	NR	NR	46.6 (8.5) †	NR	NR

Data are means and standard deviations
† Data are median & IQR
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention.

Only one study (Danielsen, 2013) (283) reported changes in weight and BMI at post-intervention follow-up, which was obtained at 12 months post-baseline on completion of the 10-14 week inpatient programme. However this was only reported for the intervention group, with follow-up measures not obtained for the control group. The reporting of ≥5% weight loss as shown in Table 7.3.7, was also limited, with one study (Ryan, 2010) (285) reporting proportions losing ≥5% weight loss for the intervention arm only, one study (Danielsen, 2013) (283) reporting the proportion at intervention-end only, and the remaining study not reporting any indication of ≥5% weight loss.

Table 7.3.7: Proportion of individuals in included studies achieving ≥5% weight loss

	Intervention		Control	
Study	**Intervention-end**	**Follow-up**	**Intervention-end**	**Follow-up**
Danielsen, 2013	100%	91.5%	NR	NR
Rimmer, 2009	NR	NR	NR	NR
Ryan, 2010	61%	NR	20%	NR

Data are percentages
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention.

Effect of intervention on quality of life

Only one study (Rimmer, 2009) (284) assessed the impact of the intervention on quality of life, with findings displayed in Table 7.3.8. The Quality of Well-Being (QWB) (286) 31-item self-report measure was used to assess quality of life before and after the intervention. The investigators stated that both the higher and lower support intervention groups experienced an improvement in quality of life, however the change was not significant for either group (p= 0.79) and (p= 0.24), respectively. The control group reported a mean decrease in quality of life which was also not significant (p= 0.66). Interestingly, the use of the QWB scale in the manner reported by the investigators is not the conventional way that the measure is used, as the scale authors advise that the measure should yield scores ranging between 0 to 1, whereby 0 represents death and 1 represents optimum functioning (286).

Table 7.3.8: Change in quality of life at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	NR	NR	NR	NR	NR	NR
Rimmer, 2009	'Lower': 2.4 'Higher': 2.2	'Lower': 2.5 'Higher': 2.3	NR	2.3	2.0	NR
Ryan, 2010	NR	NR	NR	NR	NR	NR

Data are mean scores on QWB scale
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention.

Effect of intervention on blood pressure

All three included studies reported either mean change in systolic and diastolic blood pressure or reported pre- and post- intervention measures and results are summarised in Tables 7.3.9 and 7.3.10. One study (Ryan, 2010) (285) reported mean percentage change in blood pressure, with both the intervention and control arms experiencing a reduction in systolic and diastolic blood pressure between baseline and intervention-end, with no significant difference between the study arms in the mean percentage reduction for both systolic ($p = 0.09$) and diastolic ($p = 0.60$) blood pressure. However, the study did not report whether the reduction from baseline was significant. No significant change in mean systolic and diastolic blood pressure for each of the study arms of the Rimmer, 2009 exercise intervention (284) were reported. Whilst the inpatient intervention (Danielsen, 2013) (283) reported a significant -6.4mmHg reduction of systolic blood pressure ($p < 0.001$), and a non-significant -1.3mmHg reduction of diastolic blood pressure ($p = 0.175$).

Table 7.3.9: Change in systolic blood pressure at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	132 (11)	NR	-6.4 (-9.1, -3.7) (11.4) ≠	NR	NR	NR
Rimmer, 2009	'Lower': 133 'Higher': 130	'Lower': 127 'Higher': 133	NR	130	137	NR
Ryan, 2010	131 (1)	NR	-14.7 (2.4)* (24.1) ≠	132 (1)	NR	-8.6 (2.6)* (24.1) ≠

Data are means and standard deviations or mean percentages with standard errors (*)
Standard deviation calculated by transforming 95% CI or standard error (≠)
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention.

Table 7.3.10: Change in diastolic blood pressure at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	83.7 (6.1)	NR	-1.3 (-3.2, 0.6) (8.0) ≠	NR	NR	NR
Rimmer, 2009	'Lower': 73.0 'Higher': 75.0	'Lower': 69.0 'Higher': 74.2	NR	72.6	71.8	NR
Ryan, 2010	79.6 (0.7)	NR	-4.4 (1.8)* (18.1) ≠	80.3 (0.7)	NR	-3.2 (1.5)* (13.9) ≠

Data are means and standard deviations or mean percentages with standard errors (*)
Standard deviation calculated by transforming 95% CI or standard error (≠)
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention.

Effect of intervention on cholesterol

The effect of the interventions on HDL-, LDL-, and total cholesterol are summarised in Tables 7.3.11, 7.3.12, and 7.3.13. The medical intervention (Ryan, 2010) (285) reported percentage increases in HDL- and LDL-cholesterol, although did not report whether the increases from baseline were significant. However the 7.9% increase in HDL-cholesterol observed in the intervention arm was significantly greater than the increase of 1.5% observed for the control arm ($p < 0.05$). The inpatient intervention (Danielsen, 2013) (283)

also reported an increase in HDL-cholesterol, with the slight increase of 0.1mmol/l representing a significant increase from baseline level ($p < 0.05$). The study examining the exercise intervention (Rimmer, 2009) (284), yielded no significant changes between baseline and post-intervention in HDL-, LDL- or total cholesterol levels, for the intervention and control arms ($p > 0.05$).

Table 7.3.11: Change in HDL-cholesterol at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	1.1mmol/l (0.3)	NR	0.1 mmol/l (0.0, 0.1) (0.2) ≠	NR	NR	NR
Rimmer, 2009	'Lower': 53.3mg/dl 'Higher': 46.0mg/dl	'Lower': 46.3mg/dl 'Higher': 43.1mg/dl	NR	49.7mg/dl	42.8mg/dl	NR
Ryan, 2010	52.4mg/dl (1.0)	NR	7.9 (1.8)* (18.1) ≠	50.6mg/dl (0.9)	NR	1.5 (1.8)* (16.7) ≠

Data are means and standard deviations or mean percentages with standard errors (*)
Standard deviation calculated by transforming 95% CI or standard error (≠)
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention
1mg/dl= 0.0259 mmol/l.

Table 7.3.12: Change in LDL-cholesterol at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	2.9mmol/l (0.9)	NR	-0.2mmol/l (-0.3, -0.1) (0.4) ≠	NR	NR	NR
Rimmer, 2009	'Lower': 123mg/dl 'Higher': 100mg/dl	'Lower': 116mg/dl 'Higher': 97mg/dl	NR	112mg/dl	114.0mg/dl	NR
Ryan, 2010	119mg/dl (2)	NR	1.8 (2.4)* (24.1) ≠	116mg/dl (2)	NR	0.7 (2.4)* (22.3) ≠

Data are means and standard deviations or mean percentages with standard errors (*)
Standard deviation calculated by transforming 95% CI or standard error (≠)
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention
1mg/dl= 0.0259 mmol/l.

Table 7.3.13: Change in total cholesterol at intervention-end for included studies

	Intervention			Control		
Study	**Baseline**	**Intervention -end**	**Change**	**Baseline**	**Intervention -end**	**Change**
Danielsen, 2013	4.7mmol/l (1.1)	NR	-0.1mmol/l (-0.3, 0.0) (0.6) ≠	NR	NR	NR
Rimmer, 2009	'Lower': 191mg/dl 'Higher': 160mg/dl	'Lower': 179mg/dl 'Higher': 164mg/dl	NR	182mg/dl	176mg/dl	NR
Ryan, 2010	202mg/dl (3)	NR	NR	199mg/dl (3)	NR	NR

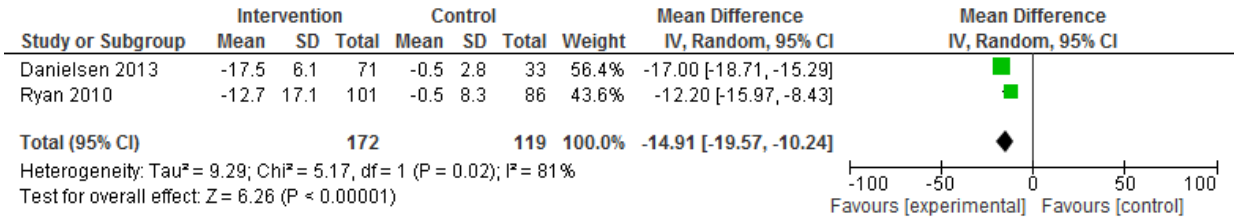
Data are means and standard deviations
Standard deviation calculated by transforming 95% CI or standard error (≠)
NR= Data not reported, 'Lower'= Lower support intervention, 'Higher'= Higher support intervention
1mg/dl= 0.0259 mmol/l.

7.3.5 Synthesis of results

Meta-analysis was conducted on only one outcome measure, weight change from baseline to intervention-end. Figure 7.2 illustrates the mean change in weight from baseline to intervention-end for two studies, Danielsen, 2013 (283) and Ryan, 2010 (285). The remaining study, Rimmer, 2009 (284) could not be included in the meta-analysis due to the fact that standard deviations or standard errors were not reported.

Both studies reported statistically and clinically significant weight losses from baseline to intervention-end. The pooled mean change in weight was -14.91kg (-19.57 - -10.24), however heterogeneity between the studies was very high (Q= 5.17, df= 1, p= 0.02, I^2= 81%. Both studies reported lifestyle interventions conducted in medical settings, however they utilised differing intensities, with Danielsen, 2013 (283) reporting a 10-14 week intervention, whilst Ryan, 2010 reported a 24-month intervention. Due to this clinical heterogeneity between the studies, a random-effects model was utilised.

Figure 7.2: Mean change in weight from baseline to intervention-end



Due to inconsistencies between the three studies in data collection and reporting, meta-analyses were not possible for the other outcomes of interest; BMI, blood pressure, cholesterol and quality of life.

7.3.6 Risk of bias across studies

The domain which was consistently at a high risk of bias was the performance bias, blinding of participants and personnel domain. However, this is plausible and reflects the nature of the studies which all examined medical and or behavioural interventions, thus are less pertinent to evaluations of interventions of this nature, for instance relative to pharmaceutical interventions.

Most of the information reported in two of the included studies, Danielsen, 2013 (283) and Rimmer, 2009 (284), is at moderately high risk of bias, whilst the remaining study, Ryan, 2010 is at a low to moderate risk of bias. Thus the proportion of information from all included studies is not deemed sufficient to affect the interpretation of the results of the systematic review. The quality assessment has highlighted the specific areas of limitation as the incomplete and selective reporting of outcome data.

7.3.7 Quality assessment of studies

The quality of reporting of the two studies adopting RCT designs, Rimmer, 2009 (284) and Ryan, 2010 (285) was assessed with the CONSORT checklist (205), and the reporting quality of the Danielsen, 2013 (283) controlled non-randomised study was assessed using the STROBE checklist (206). The assessment indicated that the reporting quality was acceptable for all studies, and the reporting forms used in the quality assessment are included in Appendix three, Tables 1-3.

7.4 DISCUSSION

7.4.1 Summary of evidence

The meta-analysis indicated that both included studies reported statistically and clinically significant weight losses from baseline to intervention-end, with a pooled mean reduction in weight of -14.9kg (-19.6 - -10.2). However heterogeneity between the studies was very high and only two studies were included due to selective outcome reporting in the remaining study (Rimmer, 2009) (284). Furthermore, the quality assessment highlighted that the incomplete and selective reporting of outcome measures was an area of limitation among the studies included in the review, and that future primary studies should improve on these specific domains in order to improve study quality and enable greater confidence in study findings. Analyses of secondary outcomes were also limited by the incomplete reporting of outcomes and between study heterogeneity in reporting. One of the aims of the systematic review was to explore the impact of interventions on psychological factors including quality of life and mental health. However, only one study (Rimmer, 2009) (284) included the use of a psychological measure, and the use of the Quality of Well-Being scale (QWB) (286) was non-conventional. This indicates that the inclusion of psychological outcomes is an area which also requires further attention. Indeed, the impacts of interventions on improvement of mental health and quality of life following intervention are an important indicator of intervention efficacy which should be assessed.

The review also highlighted the absence of long-term measures of outcomes. Only one of the included studies (Danielsen, 2013) (283) reported outcome measures obtained at post-intervention follow-up, which were obtained at 12 months post-baseline subsequent to the 10-14 week inpatient intervention. However these measures were obtained only for the intervention and not control arm of the study, thus comparison of the longer-term impacts

of the intervention could not be compared to the control arm. The remaining studies, Rimmer, 2009 (284) and Ryan, 2010 (285), reported outcome measures only at intervention-end, with no follow-up measures reported. This highlights an important area for improvement as it is essential that the long-term impacts of interventions are established. Additionally the imputation of outcome data using a LOCF approach is widely used to deal with the problem of missing outcome data in RCTs (186), however only the Ryan, 2010 study (285) reported LOCF outcomes, thus further limiting the analyses. Thus future primary studies should report outcome measures after a post-intervention follow-up period as well as at intervention-end, using both LOCF and available case data.

The literature search identified a substantial number of studies which assessed the efficacy of interventions in extreme obese samples which were not eligible for inclusion due to the use of observational non-controlled study designs. This included predominantly head to head study designs, examining for instance dietary interventions in comparison to dietary plus physical activity interventions (275, 287), behavioural interventions in comparison to behavioural interventions plus Low Energy Liquid Diet (LELD) (288, 289), comparisons of dietary interventions (278, 290, 291), and comparisons of behavioural programmes (292, 293). Additionally, several studies examined the impact of pharmaceutical interventions in extreme obese samples, however none of which included a usual care comparator and so were also not eligible for inclusion (273, 277, 294). In summary, the systematic review has highlighted that the methodological quality of the literature examining the effectiveness of interventions for extreme obesity is predominantly relatively low in the hierarchy of evidence. Thus the quality of evidence would be improved by the inclusion of studies adopting controlled study designs.

7.4.2 Limitations

The systematic review was limited by the fact that only three studies were identified which were eligible for inclusion. The fact that so few studies were included meant that the analyses and summaries of evidence were restricted. The limited body of literature highlights the need for a greater number of high quality primary studies. Indeed, the management of extreme obesity is a relatively new field, which is growing with the increasing prevalence of the condition (15, 17). This is supported by the fact that the included studies were published between 2009 and 2013, all within the last five years. Indeed, there is evidence that the body of literature is growing, as the search also identified the publication in 2013 of a study protocol for an upcoming pragmatic randomised controlled 2-arm trial of an intervention for extreme obese individuals awaiting bariatric surgery, the EVOLUTION trial (295). Thus it is possible that whilst there is not yet a significant body of evidence, the conduct of primary studies is ongoing, and an update of the review will be required in order to identify and incorporate the findings of newly published primary studies.

The present review was also limited by between study heterogeneity in the reporting of outcome measures. This restricted the quantitative analyses and as a result, only one measure was available for meta-analysis. The incomplete and selective reporting of outcome measures was a substantial flaw in the included studies and as such has been targeted as a direction for improvement. Despite these limitations, the present systematic review was strengthened by the duplication of the study selection, data extraction and quality assessment processes by two independent reviewers. Additionally the use of a standardised protocol also strengthened the methodology of the review.

7.4.3 Conclusions

The findings of the systematic review indicate that the body of literature is limited, with only three primary studies examining the effectiveness of medical and behavioural weight management interventions for extreme obese populations eligible for inclusion. Whilst the meta-analysis suggests that intensive medically-led lifestyle interventions can yield clinically and statistically significant weight loss for individuals with extreme obesity, the efficacy of these interventions remains largely unestablished. In order to establish the efficacy of weight management interventions for the extreme obese population, the conduct of further primary studies examining intervention efficacy within extreme obese populations is required. Future primary studies should use controlled designs, thoroughly report outcome measures for all study arms at intervention-end and after post-intervention follow-up using both LOCF and available case data, and also incorporating measures to assess the potential psychological impact of interventions.

CHAPTER EIGHT

8.0 THESIS SUMMARY

8.1 SUMMARY OF FINDINGS

This thesis has investigated weight management interventions for extreme obesity, specifically evaluating the efficacy of two treatment pathways within a currently operating Specialist Weight Management Service, as well as reviewing the summarised evidence and primary studies evaluating medical and behavioural interventions within extreme obese populations. This work has provided a detailed profile of the characteristics of a sample of extreme obese individuals entering the service, thus enhancing current understanding of individuals attending the service and more broadly of individuals with extreme obesity. Specifically, the poor sleep quality and poor quality of life experienced by individuals, as well as the widespread prevalence of physical and psychological co-morbid health conditions including symptoms of anxiety and depression were highlighted. Further in depth analyses examining the association between psychological characteristics and adiposity indicated a complex relationship, whereby increasing adiposity was associated with a reduction in several areas of quality of life, but was not significantly associated with prevalence of anxiety and depression.

This work has demonstrated the value of the Specialist Weight Management Service in the care of individuals with extreme obesity, with both the CWMS community-based service and SLiM group education programme achieving clinically significant weight loss outcomes. Indeed a substantial proportion of individuals attending both treatment pathways achieved weight losses ≥5% baseline body weight which have been demonstrated to reduce the risk of cardiovascular disease and overall mortality. In addition, both pathways were able to facilitate greater weight losses than demonstrated by other specialist weight management services and several but not all commercial and

primary care-led programmes. A substantial gap in the weight management literature was identified by a systematic review which demonstrated that there were no existing reviews examining the efficacy of medical and behavioural weight management interventions for extreme obese populations. Subsequently, a systematic review of primary research examining the efficacy of medical and behavioural weight management interventions within extreme obese samples was conducted, which identified the limited body of good quality research. However, the review synthesised the results of two studies which demonstrated the value of medically-supported behavioural weight management programmes in facilitating statistically and clinically significant weight loss for individuals with extreme obesity.

8.2 RECOMMENDATIONS

Recommendations have been generated from the findings of this work, including those aimed at improving both service provision and the quality of research evaluating weight management interventions.

8.2.1 Recommendations for service provision

A summary of the clinically-focussed recommendations to improve service provision is outlined in Figure 8.1. When considering the implementation of any weight management service it is essential that both the costs and outcomes associated with the service are taken into consideration. Specifically within the Specialist Weight Management Service, the nature of the CWMS and SLiM treatment pathways greatly differed in terms of duration and intensity of support. The CWMS was associated with a greater number and expertise of staff, and a greater number of individuals attending the CWMS pathway, thus making it a more expensive option relative to the SLiM pathway. The two treatment pathways both yielded clinically significant weight loss outcomes within the measured time period, thus indicating that the SLiM pathway is likely to be the more cost-effective of the two approaches. However, the longer-term weight loss outcomes of the pathways were not assessed in the present study, and would need to be taken into consideration when making conclusive recommendations regarding the cost-effectiveness of each of the treatment pathways.

Figure 8.1: Summary of recommendations for service provision

- Consider both the outcomes and costs of a weight management service:
  - The multidisciplinary team (MDT) approach provided by the CWMS is more intensive and therefore more expensive (estimated at £75 per individual per week) than the SLiM programme (estimated at £31 per individual per week)
  - Both treatment pathways yielded clinically significant weight loss outcomes within the measured time period
  - The CWMS approach offers longer-term provision of support for individuals (minimum 12 months), relative to the SLiM programme (6 months)
  - The longer-term outcomes need to be assessed, ideally after a 12 month follow-up period, in order to make conclusive cost-effectiveness recommendations for each of the pathways
- Address the complex medical and psychological needs experienced by those attending the service
  - Incorporate support in managing the mental and physical co-morbidities of extreme obesity into multi-disciplinary care
- Provide support through tailored pilot interventions focusing on:
  - enhancing overall mental health and well-being
  - improving self-esteem
  - managing specific co-morbidities such as type 2 diabetes or OSA
  - coping with multiple co-morbidities and threats to health
- Provide enhanced support for those potentially less likely to achieve weight loss; younger individuals at lower levels of baseline weight reporting better quality of life
- Improve accessibility of the service for employed individuals by potentially piloting 'out of hours' sessions held during evenings or weekends
- Consider piloting additional commencement approaches to increase access such as:
  - Providing awareness events to increase access to the service among minority ethnicity communities
  - Providing informal information sessions on referral to the service, dealing with individuals' concerns and queries
  - Increasing contact with those who do not respond to initial communication on referral to the service, through follow-up telephone calls

Recommendations also include addressing the complex medical and psychological needs experienced by those attending the service, by incorporating support in managing the mental as well as physical co-morbidities of extreme obesity into multi-disciplinary care. Specifically, support should be provided through tailored interventions which focus on enhancing mental health and well-being, with a specific emphasis on improving self-esteem, as this was an area of great impairment. Those with co-morbid health conditions such as type 2 diabetes or OSA which may potentially affect individuals' ability to achieve weight loss may also benefit from further support. A potential need was also identified for

the provision of further support for those younger individuals entering the service at lower levels of baseline weight and reporting relatively better quality of life, in order to help these individuals to achieve weight loss during attendance at the service. Tailoring of the interventions for the different needs of the individuals could be achieved by ensuring that the sessions are relevant to those attending by considering their specific priorities and resources as well as the socio-economic, religious, cultural, family and environmental factors which influence weight loss efforts. For instance sessions could focus on addressing socio-economic barriers to health through providing low-cost healthy food suggestions and recipes and providing information on local free to access physical activity opportunities. Indeed programmes tailored for low-income groups have been demonstrated to be effective in promoting healthy dietary and physical activity behaviours (296), as have those adapted to be culturally sensitive (297). For instance sessions could also be tailored at relevant times of the year coinciding with religious and cultural festivals through providing support and developing coping strategies to maintain healthy food and activity choices during more potentially challenging times where relapse to less healthy behaviours may be more likely to occur. Additionally the content of programmes should be modified to address specific issues highlighted by the individuals attending, so that targeted information can be provided and group discussion facilitated on the most relevant and important areas of concern for individuals.

In addition to the modification of support that is provided to individuals, the modification of existing service referral processes may also be beneficial. New approaches such as the provision of outreach sessions held in local communities, informal information sessions and additional follow-up communication during referral could be employed in pilot trials to assess their impacts. It is anticipated that through the adoption of improved

approaches to the service referral process that the service will be accessible to a greater number of individuals of all backgrounds, thus increasing inclusivity and maximising the opportunity for weight loss.

8.2.2 Recommendations for future research

A summary of the recommendations to improve future research is outlined in Figure 8.2. The primary recommendation is that the currently limited evidence base for the efficacy of weight management interventions within extreme obese samples needs to be expanded through the conduct of further research.

Figure 8.2: Summary of recommendations for future research

- Conduct of further research is required in order to expand the currently limited evidence base for the efficacy of weight management interventions within extreme obese samples
- Collect demographic and clinical information and self-report measures in order to:
  - Understand the specific population attending the service
  - Identify those individuals who may require additional support
- Utilise methodologically rigorous designs such as controlled studies and RCTs
- Report outcome measures fully:
  - Include LOCF data as well as available case data for outcomes so that comparisons between services can be made
  - Include outcomes for intervention and control arms
  - Include sufficient detail to enable data to be combined in a quantitative synthesis
- Include an assessment of potential differences between those withdrawing and those completing weight management interventions, in order to aid interpretation of findings and minimise the potential for withdrawal bias
- Include quality of life and mental health outcome measures in order to assess the potential psychological impacts of services
- Include the assessment of long-term outcomes ideally obtained after a 12 month follow-up period, in order to determine the impacts of the service beyond intervention-end

Future studies should incorporate the collection of a range of demographic and clinical information as well as self-report measures in order to better understand the patient population, as undertaken in the present study. The collection of such detailed measures

may potentially help to identify those individuals who require additional support in order to fully benefit from attendance at the service and have the greatest opportunity to achieve weight loss success. Additionally, future studies should also employ methodologically rigorous controlled designs such as RCTs, as well as fully reporting outcome measures by including LOCF as well as available case data for all study arms. Psychological outcome measures should also be included when assessing the impact of interventions, as the effects on individuals' quality of life and mental health are important yet lesser studied factors. Finally, it is imperative that studies include long-term outcome measures obtained after a follow-up period in order to determine any potential impacts beyond intervention-end. Through the expansion of the evidence base with the conduct of further research employing such study designs it will be possible to conclusively determine the efficacy of weight management services and interventions among extreme obese populations.

8.3 CONCLUDING REMARKS

This thesis has made a unique contribution to the limited body of research investigating weight management interventions for extreme obesity. The work has enhanced current understanding of the extreme obese population, and demonstrated the substantial psychological burden of extreme obesity. This work has investigated weight management interventions for the lesser-researched extreme obese population, through demonstrating the efficacy of two currently operating medically-supported interventions and synthesising the evidence in the body of literature. Thus the findings presented in this thesis represent a significant addition to the existing evidence base. Recommendations generated from this work have been made in order to improve service provision and research of weight management interventions. Through the adoption of the clinical and research recommendations, it is hoped that the efficacy of weight management services can be improved and understanding of specialist weight management services and their patient populations can be enhanced. This will ensure that these individuals are given the greatest opportunity to achieve weight loss and diminish the negative physical and psychological impacts of extreme obesity.

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APPENDIX ONE

1.0 PROTOCOL FOR THE SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS

MEDICAL AND BEHAVIOURAL WEIGHT MANAGEMENT INTERVENTIONS FOR EXTREME OBESITY:

A PROTOCOL FOR A SYSTEMATIC REVIEW OF SYSTEMATIC REVIEWS

Rationale

Several reviews have examined the impact of non-surgical medical and behavioural weight management interventions within obese populations, including a narrative review focussing specifically on weight management services in the UK (189), a review and meta-analysis of interventions delivered solely to male samples (190) and a comprehensive Health Technology Assessment including a systematic review of 84 Randomised Controlled Trials (RCTs) of obesity treatments (191). The numerous reviews of weight management interventions reflect the extensive body of primary studies investigating the impact of weight management interventions in obese samples. However, the body of literature examining the efficacy of weight management interventions within extreme obese (BMI $\geq$40kg/m^2) samples is relatively limited. As such it is anticipated that the synthesis of data from primary studies investigating the impact of interventions in extreme obese samples within reviews, will consequently also be limited. Given the increasing prevalence of extreme obesity and the associated detrimental impacts on the health and quality of life of individuals (82), it is important to examine the effectiveness of treatment pathways such as medical and behavioural interventions which have been widely adopted in the care of individuals with extreme obesity.

This systematic review will search for systematic reviews examining the effectiveness of medical or behavioural weight management interventions within exclusively extreme obese (BMI $\geq$40kg/m^2) samples. This systematic review will

summarise data from included systematic reviews, and if the systematic reviews identified are deemed to be of poor quality or in need of updating due to the accumulation of new primary research since publication, then a systematic review of primary studies examining intervention effectiveness within extremely obese populations will be conducted in order to fill the gap in the body of the literature. The systematic review protocol is registered on the PROSPERO international database of prospectively registered systematic reviews in health and social care, with registration number CRD42014012988.

Objectives

The specific objectives of the systematic review are:

- To produce a systematic review of systematic reviews and health technology assessments which have examined the effectiveness of medical and behavioural weight management interventions for adults with extreme obesity (defined as baseline BMI $\geq$40.0kg/m^2) on change in weight or BMI, change in presence or severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life or change in mental health.
- To produce a summary of the evidence of the effectiveness of medical and behavioural weight management interventions for extreme obesity.
- To analyse the quality of the reviews and provide a summary of the best evidence available.

Research question

The systematic review question was formulated using the PICOS format:

Population: Adults with extreme obesity, defined as mean baseline BMI of all included primary studies ≥40.0kg/m^2.

Intervention: Medical or behavioural weight management (any non-surgical intervention which encompasses behavioural modification, medical or pharmaceutical components) of any duration.

Comparators: The reviews may incorporate a range of comparator groups including but not limited to control not receiving intervention, control receiving usual care, or alternative non-surgical intervention.

Outcomes: Weight and BMI change, change in presence and severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life and mental health.

Study design: Systematic reviews and health technology assessments.

This gave rise to the following question to be answered by the systematic review: 'What is the summarised evidence for the effectiveness of medical and behavioural weight management interventions for extreme obesity?'

Eligibility criteria

- Population:
    - Reviews reporting intervention effectiveness exclusively in BMI ≥40.0kg/m^2 populations will be included.
    - Reviews reporting intervention effectiveness in broader overweight and obese BMI ≥30.0kg/m^2 populations will be excluded.

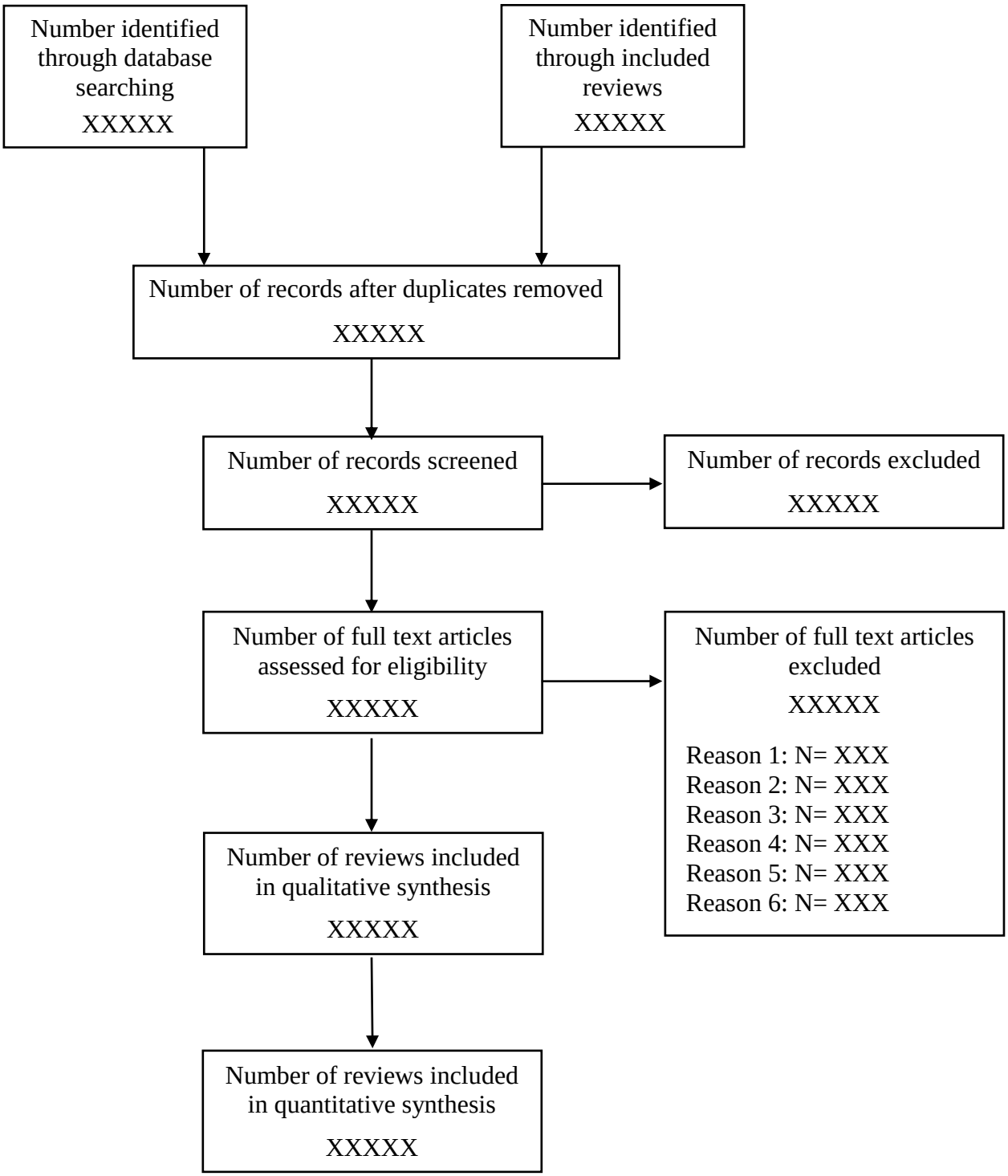
    - Reviews where included study populations are adult (≥18 years) will be included.
    - Reviews including study populations based on health conditions other than obesity will be excluded, for instance samples including solely individuals with type 2 diabetes, stroke, cancer, and schizophrenia.
- Interventions:
    - Reviews of non-surgical interventions providing medical and or behavioural support incorporating pharmaceutical therapies, counselling, education, and lifestyle modification incorporating diet and exercise will be included.
    - Reviews which include interventions of any duration will be included.
- Outcomes:
    - Reviews which report synthesis of any of the following outcomes: weight or BMI change, change in presence or severity of co-morbid health conditions, change in cardiovascular profile, change in quality of life or mental health, from baseline to intervention-end or post-intervention follow-up will be included.
- Study design:
    - Systematic reviews and health technology assessments will be included.

Information sources

A search of the following databases within the Cochrane Library will be conducted: the Cochrane Database of Systematic Reviews (CDSR), the Database of Abstracts and Reviews of Effects (DARE), and the Health Technology Assessment Database (HTAD), from inception to time of search. In addition, the reference lists of reviews included in the

systematic review will be hand-searched. A flow diagram as outlined in figure 1 will be used to demonstrate the process of study identification, as outlined in the PRISMA statement (192).

Figure 1: Flow diagram outlining the identification of included reviews



Search strategy

The following search strategy will be used to search for review articles that summarise data on the effectiveness of medical or behavioural weight management interventions of any duration, for samples with extreme obesity, defined as sample mean BMI ≥40.0 kg/m^2. Terms will be entered as free text and MeSH term searches in the Cochrane Library search engine, screening records obtained from the CDSR, DARE and HTAD.

Search terms

1. Adult*
2. Overweight (MeSH) explode all trees
3. Obesity (MeSH) explode all trees
4. Obes*
5. Body Mass Index (MeSH) explode all trees
6. BMI
7. Body Weight (MeSH) explode all trees
8. 2 or 3 or 4 or 5 or 6 or 7
9. 1 and 8
10. Intervention
11. Life style (MeSH) explode all trees
12. Health Promotion (MeSH) explode all trees
13. Health Education (MeSH) explode all trees
14. Patient Education as Topic (MeSH) explode all trees
15. Counseling (MeSH) explode all trees
16. Behavior (MeSH) explode all trees
17. Anti-Obesity Agents (MeSH) explode all trees
18. Weight Loss (MeSH) explode all trees
19. Diet, Reducing (MeSH) explode all trees
20. Weight Reduction Programs (MeSH) explode all trees
21. Exercise (MeSH) explode all trees
22. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 10 and 22
24. 9 and 23
25. 24 in Cochrane Reviews (Reviews and protocols), Other Reviews and Technology Assessments

Article selection

The number of records retrieved will be recorded in the flow diagram as illustrated in figure 1 and the records will be exported to be managed using EndNote software. The number of duplicate records will be recorded and duplicate records will then be removed. The remaining records will first be screened by title and abstract, to assess if the records meet the eligibility criteria relating to population, intervention, outcome and study design, with those records that are judged to not meet eligibility criteria removed, and the number excluded at this stage will be recorded.

The process of review selection will be conducted independently by two reviewers who will meet once the first phase of selection (screening by title and abstract) is complete. Discrepancies will be discussed and where consensus to a disagreement is not reached a third party will be invited to adjudicate on whether full text copies of reviews should be screened, after which the final number of reviews to be screened as full text will be determined.

After obtaining full text copies, the second phase of review selection (screening full text) will be conducted the reviewers, with those not meeting the eligibility criteria at this stage excluded and the excluded records will be grouped by reason for exclusion, so that the number of records excluded for each reason can be identified. The final number of reviews included in the systematic review will be recorded and the reference lists of these reviews will be searched to identify any further relevant reviews, which will then be screened and if they meet eligibility criteria will subsequently be added to the total number of reviews to be included in the systematic review of reviews. The two reviewers will meet once the second selection phase is complete. Discrepancies will be discussed and where consensus to a disagreement is not reached a third party will be invited to adjudicate on

whether reviews should be included, after which the final number of included reviews will be determined.

Data extraction

The two reviewers will independently extract data items from the information provided in the full text articles, into an Excel spreadsheet whereby each study will be represented in a row of data in the spreadsheet. Accompanying notes displayed in Table 1 were developed for use in the present review with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0) (194), which will provide further detail and be used as a reference when entering the data items into the spreadsheet. The two reviewers will meet once data extraction has taken place independently, and any discrepancies will be investigated, with a third party invited to adjudicate where consensus is not reached. Data items from the finalised data extraction spreadsheet will then be used to produce review characteristics tables as illustrated in Table 2, which will be used in qualitative analysis.

Table 1: Accompanying notes for data extraction

Field	Data points to be extracted
Review	Author, Publication year.
Methods	Design (state whether systematic review, Health Technology Assessment) Objectives of review.
Study characteristics	Total number of included studies within review, Participant characteristics including range of age, gender, ethnicity, co-morbid health conditions, across studies, Range of mean baseline weight of the primary studies, Range of mean baseline BMI of the primary studies.
Intervention	Range of intervention types: i.e. pharmaceutical/behavioural/combination, Range of number of intervention groups, Range of intervention settings (where intervention is delivered), Range of delivery personnel type (if healthcare professional specify which, researcher, lay public), Range of delivery personnel training (detail of training in intervention delivery received), Range of duration of interventions (number and duration of contact time, including face to face sessions, email, telephone or other contact), Intensity of interventions (frequency of sessions and contact), Theoretical basis of interventions (e.g. self-management, cognitive behavioural) Range of numbers of participants entering intervention group, Range of numbers of participants completing intervention/presenting for data collection, Range of reported loss to follow-up rate in intervention groups across primary studies.
Comparator	Range of numbers of comparator groups across primary studies, Descriptions of comparator or usual care, Range of numbers of participants entering comparator group, Range of numbers of participants completing comparator group/presenting for data collection, Range of reported loss to follow-up rate in comparator groups across primary studies.
Outcomes	Mean effect size, weighted effect size, Mean difference, standardised mean difference, weighted mean difference and p values between intervention and control groups for the following outcomes of interest: • Change in weight or BMI, • Change in presence or severity of co-morbid health conditions, • Change in cardiovascular profile, • Change in quality of life or mental health. For reviews not reporting quantitative data synthesis: Range of effects across primary studies and main conclusions of review.

Table 2: Review characteristics table

Review	Methods	Participants	Intervention	Comparator	Outcomes

Quality assessment

Included reviews will be appraised for methodological quality using the 'Assessment of multiple systematic reviews' (AMSTAR) measurement tool (195) as illustrated in table 3. The tool will be used to assess the methodological quality according the following criteria; reporting of an a priori design, duplication of study selection and data extraction, whether a comprehensive literature search is performed and whether publication status determines eligibility for inclusion, reporting of included and excluded studies and characteristics of the included studies, the assessment, reporting and use of scientific quality of the included studies, use of appropriate methods to combine study findings, and the reporting of potential publication bias and conflicts of interest.

Following the assessment of each of the included reviews, evaluation summaries will be made across reviews and domains. The quality assessment information will be used to inform the interpretation of the findings of each of the included reviews, with consideration of potential methodological factors which could introduce bias to review findings, which will be highlighted. If appropriate, recommendations to improve the methodological and reporting quality of future reviews will be made, highlighting areas of current limitation where improvement is required.

Table 3: AMSTAR tool

1. Was an 'a priori' design provided?	The research question and inclusion criteria should be established before the conduct of the review. Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes." □ Yes □ No □ Can't answer □ Not applicable
2. Was there duplicate study selection and data extraction?	There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work. □ Yes □ No □ Can't answer □ Not applicable
3. Was a comprehensive literature search performed?	At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary). □ Yes □ No □ Can't answer □ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit. □ Yes □ No □ Can't answer □ Not applicable
5. Was a list of studies (included and excluded) provided?	A list of included and excluded studies should be provided. Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no." □ Yes □ No □ Can't answer □ Not applicable
6. Were the characteristics of the included studies provided?	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. Note: Acceptable if not in table format as long as they are described as above. □ Yes □ No

	□ Can't answer □ Not applicable
7. Was the scientific quality of the included studies assessed and documented?	'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable). □ Yes □ No □ Can't answer □ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7. □ Yes □ No □ Can't answer □ Not applicable
9. Were the methods used to combine the findings of studies appropriate?	For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions. □ Yes □ No □ Can't answer □ Not applicable
10. Was the likelihood of publication bias assessed?	An assessment of publication bias should include a combination of graphical aids (e.g. funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies. □ Yes □ No □ Can't answer □ Not applicable
11. Was the conflict of interest included?	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies. □ Yes □ No □ Can't answer □ Not applicable

Data synthesis and analysis

Qualitative analysis will provide a narrative summary of the findings of the individual included reviews for each of the outcomes of interest, with data presented in review characteristics tables. Qualitative analysis will also provide a summary of the methodological quality of the included reviews and any potential impact on the findings of each of the reviews, and potential impact on the conclusions of the overview of systematic reviews. Additionally qualitative analysis will be used to inform recommendations for the conduct and reporting of future reviews.

The quantitative findings of the reviews will be illustrated using forest plots without summary statistics for each of the following outcomes of interest: weight change, BMI change, change in co-morbidity presence, change in co-morbidity severity, quality of life change, mental health change and cardiovascular change for BMI $\geq$40.0kg/m^2 samples.

A detailed report of the findings of the overview of systematic reviews will be written as a thesis chapter. The findings will be reported utilising the PRISMA 27-item checklist and flow-diagram illustrating the flow of information through the phases of the systematic review (192). The use of the PRISMA statement will enhance reporting by facilitating explicit description of the systematic review.

APPENDIX TWO

2.0 PROTOCOL FOR THE SYSTEMATIC REVIEW OF PRIMARY STUDIES

MEDICAL AND BEHAVIOURAL WEIGHT MANGEMENT INTERVENTIONS FOR EXTREME OBESITY:

A PROTOCOL FOR A SYTEMATIC REVIEW OF PRIMARY STUDIES

Rationale

The prevalence of obesity among adults, and in particular extreme obesity, has risen rapidly over previous decades (82). Levels of extreme obesity (BMI ≥40kg/m^2) in the US have increased 70% over the last decade (2000 - 2010), with the prevalence reaching 6.6% (24). Indeed, recent estimates predict the prevalence of extreme obesity to reach 9% in the US by 2030 and 5% in the UK by 2033 (25). The increasing prevalence of extreme obesity and associated diseases has created increased demand for weight management services in the UK. The National Institute for Health and Care Excellence (NICE) has recommended the development of multidisciplinary care teams in the management of obesity and its co-morbid complications (14). Indeed, NICE has recommended management in a specialist obesity service for a minimum period of 6 months before bariatric surgery is considered as a treatment option (14).

The increasing prevalence of obesity and the associated detrimental impacts on individuals' health and quality of life, have led to the development of a variety of weight management programmes delivered across primary and specialist healthcare settings, as well as commercial and research settings. However, there is a lack of consensus as to which weight management interventions are effective in facilitating weight loss in individuals with extreme obesity who have complex care needs. A narrative review of weight management services in the UK published in 2012, details the efficacy of services delivered to individuals with BMI ≥30kg/m^2 (189). The review encompassed a range of

programmes and services including the Counterweight primary care model of weight management (29), the Specialist Glasgow and Clyde weight management service (174) as well as the multi-arm Lighten-Up trial which incorporated commercial and primary care interventions (34). The review demonstrated that studies with a minimum of 12-month outcome data were few and that evidence is lacking for services delivered to individuals at the extreme end of the obesity spectrum. One of the studies included in the review reported data from an audit of primary care referral to the Slimming World intervention (37), which since publication of the narrative review published the findings of further analysis of the same population in an extreme obese BMI $\geq$40kg/m^2 subgroup (179).

Whilst the narrative review demonstrated an overall representation and summary of the evidence for interventions for obese individuals in the UK, it did not however advance understanding about the effectiveness of interventions specifically in the extreme obese population. Furthermore, a comprehensive Health Technology Assessment published in 2004 included a systematic review of 84 Randomised Controlled Trials (RCTs) of weight loss interventions for obese individuals with BMI $\geq$30 kg/m^2 (191), which again provided a synthesis of the evidence and recommendation in the treatment and care of obese individuals with no focus on extreme obesity.

A scoping exercise has revealed that the evidence base for medical and behavioural weight management interventions for extreme obesity is limited, and furthermore there are no protocols or review questions regarding interventions for this population registered in the Cochrane library or Prospero database. The limited evidence base has meant that the variation in weight management service provision available for extreme obese individuals in the UK and internationally is continuing. However, the increasing prevalence of obesity and subsequent demand for services means that establishing the effectiveness of weight

management services is essential in order to ensure that individuals are given the best opportunity at achieving weight loss. A systematic review will be conducted in order to provide an additional contribution to the evidence base, as there are no published systematic reviews specifically addressing interventions for extreme obesity. The systematic review protocol is registered on the PROSPERO international database of prospectively registered systematic reviews in health and social care, with registration number CRD42014010473.

Objectives

The specific objectives of the systematic review are:

- To summarise the effectiveness of medical and behavioural weight management interventions for adults with extreme obesity (defined as baseline BMI $\geq$40.0kg/m^2) on weight change, including if appropriate a meta-analysis of the effect of interventions on weight and BMI change.
- The secondary objectives are to examine the impact of these interventions on psychological profile (incorporating quality of life and mental health) and cardiovascular profile (incorporating blood pressure and lipids), with a meta-analysis if appropriate, of the effect of interventions on psychological and cardiovascular factors.
- To analyse study quality and provide a summary of the best evidence available.

Research question

The systematic review question was formulated using the PICOS format:

Population: Adults with extreme obesity, defined as BMI ≥40.0kg/m^2

Intervention: Medical and behavioural weight management (any non-surgical intervention which encompasses behavioural modification, medical or pharmaceutical components) of any duration.

Comparators: Control arm comprising usual care.

Outcomes: Primary outcome: Weight and BMI change at post-intervention follow-up, or at intervention-end where follow-up is not available.

Secondary outcomes: Quality of life, mental health, and biomedical (blood pressure, lipids) change at post-intervention follow-up, or at intervention-end where follow-up is not available.

Study design: Randomised Controlled Trials (RCTs), controlled non-randomised studies, controlled observational studies (prospective or retrospective cohort studies with concurrent controls).

This gave rise to the following question to be answered by the systematic review: 'What is the effectiveness of medical and behavioural weight management interventions for extreme obesity?'

Eligibility criteria

- Population:
    - Study samples of adults, defined as aged ≥18 years will be included.
    - Samples of individuals with extreme obesity (mean baseline BMI ≥40.0kg/m^2), will be included, incorporating separate BMI ≥40.0kg/m^2 sub-group samples and overall study samples.

- Interventions:
    - Interventions providing medical and or behavioural support, incorporating pharmaceutical therapies, counselling, education, and lifestyle modification including diet and exercise will be included.
    - Interventions of any duration will be included.
    - Studies which include surgical intervention will be excluded.
- Comparator:
    - Control arm receiving usual care or receiving no intervention.
- Outcomes:
    - Studies reporting weight and or BMI measures at baseline and at intervention-end, or weight and or BMI change scores will be included.
    - Studies which report baseline characteristics data without post-intervention follow-up or intervention-end weight or BMI outcome data will be excluded.
- Study design:
    - RCTs, controlled non-randomised studies, and controlled observational studies (prospective and retrospective cohort studies with concurrent

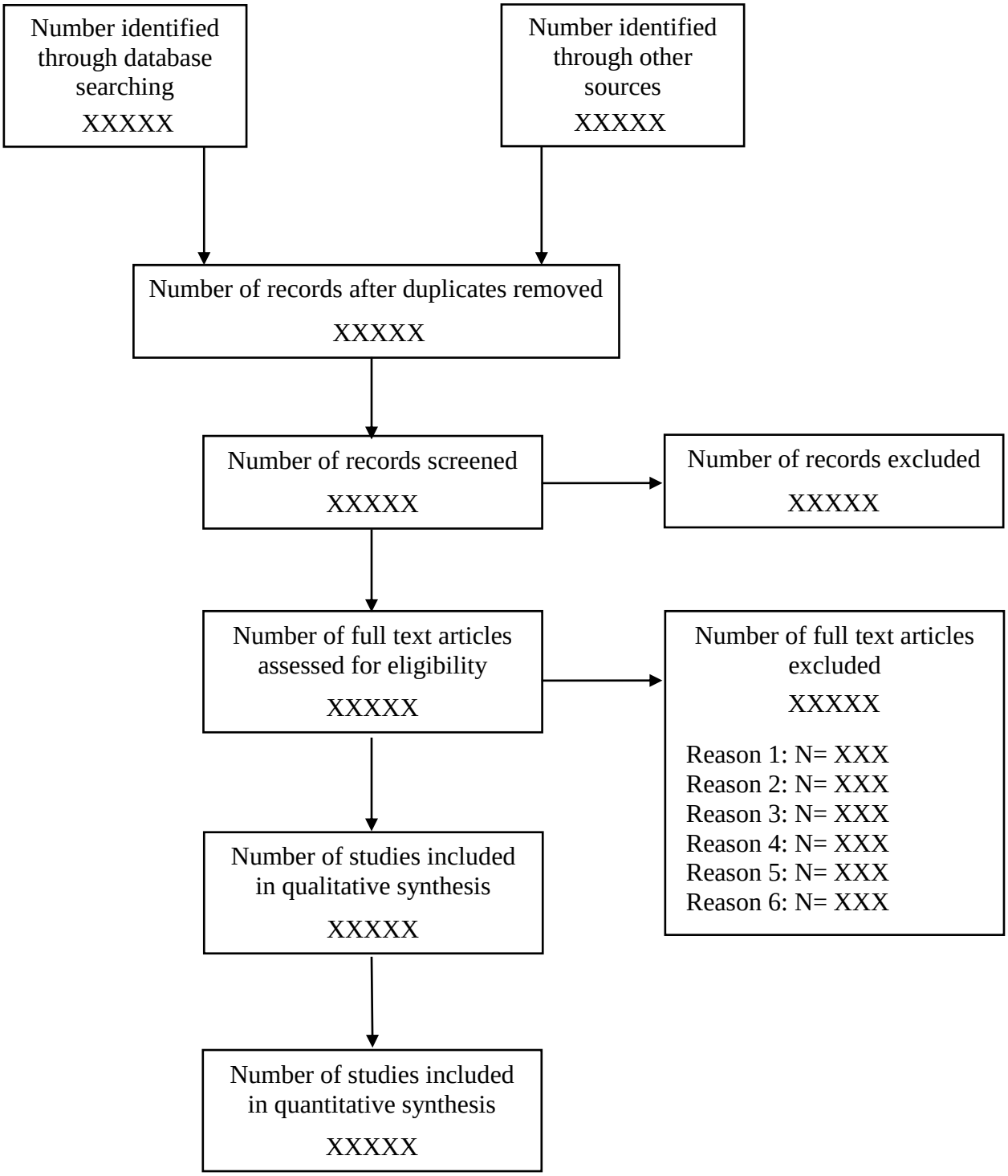
controls) will be included. Study designs further down the hierarchy of evidence, such as observational studies without concurrent control groups will be excluded.

- Studies published up to and including June 2014 will be included.
- Studies published in any language will be included.
- Review articles, editorials, commentaries and letters will be excluded.

Information sources

A search will be conducted in the area of medical and behavioural management of extreme obesity using the following electronic databases: MEDLINE (Ovid), EMBASE (Ovid), CINAHL (Ebsco host), and Cochrane Central Register of Controlled Trials (CENTRAL) database, from inception to time of search. In addition, grey literature including conference abstracts and doctoral theses will be searched using the OpenGray and Zetoc databases, and reference lists of papers included in the review will be hand-searched. A flow diagram as outlined in figure 1 will be used to demonstrate the process of study identification, as outlined in the PRISMA statement (192).

Figure 1: Flow diagram of the identification of included studies



Search strategy

The following search strategy will be used to search for articles that detail medical or behavioural weight management interventions of any duration, to samples with extreme obesity, defined as mean BMI ≥40.0kg/m^2. When searching the EMBASE and MEDLINE databases MeSH and free text terms will be entered into multi-purpose (.mp) searches. The CINAHL database will be searched by entering MeSH terms as exact major subject headings (MM), and free text terms as words in major subject headings (MJ). In the Cochrane CENTRAL database terms will be entered as MeSH and free text terms, where relevant MeSH terms are not available.

Search terms: EMBASE

1. Adult*.mp
2. Overweight*.mp
3. Obesity/ dm, dt, rh, th (MeSH)
4. Obes*.mp
5. Body Mass/ (MeSH) explode all trees
6. BMI.mp
7. Body Weight/ co, dt, th (MeSH)
8. 2 or 3 or 4 or 5 or 6 or 7
9. 1 and 8
10. Intervention.mp
11. Life style/ (MeSH) explode all trees
12. Health Promotion/ (MeSH) explode all trees
13. Health Education/ (MeSH) explode all trees
14. Patient Education as topic/ (MeSH) explode all trees
15. Counseling/ (MeSH) explode all trees
16. Behavior/ dt, rh, th (MeSH)
17. Antiobesity Agent/ ct, dt (MeSH)
18. Diet Restriction/ (MeSH) explode all trees
19. Weight Reduction/ dt, th (MeSH)
20. Exercise/ (MeSH) explode all trees
21. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. 10 and 21
23. 9 and 22
24. Limit 23 to humans
25. Limit 24 to "therapy (maximizes sensitivity)"
26. Control*.mp
27. 24 and 26
28. 25 or 27

mp= title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword.
dm= disease management, dt= drug therapy, rh= rehabilitation, th= therapy, co= complication, ct= clinical trial.

Search terms: MEDLINE

1. Adult*.mp
2. Overweight/ dh, dt, rh, th, nu (MeSH)
3. Obesity/ dh, dt, rh, th, nu (MeSH)
4. Obes*.mp
5. Body Mass Index/ (MeSH) explode all trees
6. BMI.mp
7. Body Weight.mp
8. 2 or 3 or 4 or 5 or 6 or 7
9. 1 and 8
10. Intervention.mp
11. Life style/ (MeSH) explode all trees
12. Health Promotion/ (MeSH) explode all trees
13. Health Education/ (MeSH) explode all trees
14. Patient Education as topic/ (MeSH) explode all trees
15. Counseling/ (MeSH) explode all trees
16. Behavior/ (MeSH) explode all trees
17. Anti-obesity Agents/ (MeSH) explode all trees
18. Weight Reduction Programs/ (MeSH) explode all trees
19. Diet, Reducing/ (MeSH) explode all trees
20. Weight Loss/ dt, th (MeSH)
21. Exercise (MeSH) explode all trees
22. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 10 and 22
24. 9 and 23
25. Limit 24 to humans
26. Limit 25 to “therapy (maximizes sensitivity)”
27. Control*.mp
28. 25 and 27
29. 26 or 28

.mp= title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword.
dh= diet therapy, dt= drug therapy, rh= rehabilitation, th= therapy, nu= nursing

Search terms: CINAHL

1. MJ Adult*
2. MJ Overweight
3. MM Obesity/ dh, dt, rh, th, nu (MeSH)
4. MJ Obes*
5. MM Body Mass Index/ (MeSH) explode all trees
6. MJ BMI
7. MM Body Weight (MeSH) explode all trees
8. 2 or 3 or 4 or 5 or 6 or 7
9. 1 and 8
10. MJ Intervention
11. MM Life style/ (MeSH) explode all trees
12. MM Health Promotion/ (MeSH) explode all trees
13. MM Health Education/ (MeSH) explode all trees
14. MM Patient Education as topic/ (MeSH) explode all trees
15. MM Counseling/ (MeSH) explode all trees
16. MM Behavior/ (MeSH) explode all trees
17. MM Anti-obesity Agents/ (MeSH) explode all trees
18. MM Weight Reduction Programs/ (MeSH) explode all trees
19. MM Diet, Reducing/ (MeSH) explode all trees
20. MM Weight Loss/ dh, dt, th (MeSH)
21. MM Exercise (MeSH) explode all trees
22. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 10 and 22
24. 9 and 23
25. Limiters to 24- Human
26. Limiters to 24- Clinical Queries: Therapy- High Sensitivity; Human
27. MJ Control*
28. 25 and 27
29. 26 or 28

MM= Exact Major Subject Headings, MJ= Word in Major Subject Headings.
dh= diet therapy, dt= drug therapy, nu= nursing, rh= rehabilitation, th= therapy.

Search terms: Cochrane Central Register of Controlled Trials (CENTRAL)

26. Adult*
27. Overweight (MeSH) explode all trees
28. Obesity (MeSH) explode all trees
29. Obes*
30. Body Mass Index (MeSH) explode all trees
31. BMI
32. Body Weight (MeSH) explode all trees
33. 2 or 3 or 4 or 5 or 6 or 7
34. 1 and 8
35. Intervention
36. Life style (MeSH) explode all trees
37. Health Promotion (MeSH) explode all trees
38. Health Education (MeSH) explode all trees
39. Patient Education as Topic (MeSH) explode all trees
40. Counseling (MeSH) explode all trees
41. Behavior (MeSH) explode all trees
42. Anti-Obesity Agents (MeSH) explode all trees
43. Weight Loss (MeSH) explode all trees
44. Diet, Reducing (MeSH) explode all trees
45. Weight Reduction Programs (MeSH) explode all trees
46. Exercise (MeSH) explode all trees
47. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
48. 10 and 22
49. 9 and 23
50. 24 in Trials

Study selection

The number of records retrieved will be recorded in the flow diagram as illustrated in figure 1 and the records will be exported to be managed using EndNote software. The number of duplicate records will be recorded and duplicate records will then be removed. The remaining records will first be screened by title and abstract, to assess if the records meet the eligibility criteria relating to population, intervention, outcome and study design, with those records that are judged to not meet eligibility criteria removed, and the number excluded at this stage will be recorded.

The process of study selection will be conducted independently by two reviewers who will meet once the first phase of selection (screening by title and abstract) is complete. Discrepancies will be discussed and where consensus to a disagreement is not reached a third party will be invited to adjudicate on whether full text copies of studies should be screened, after which the final number of studies to be screened as full text will be determined.

After obtaining full text copies, the second phase of study selection (screening full text) will be conducted the reviewers, with those not meeting the eligibility criteria at this stage excluded and the excluded records will be grouped by reason for exclusion, so that the number of records excluded for each reason can be identified. The final number of studies included in the systematic review will be recorded and the reference lists of these studies will be searched to identify any further relevant studies, which will then be screened and if they meet eligibility criteria will subsequently be added to the total number of studies to be included in the systematic review. The two reviewers will meet once the second selection phase is complete. Discrepancies will be discussed and where consensus to a disagreement is not reached a third party will be invited to adjudicate on whether studies should be included, after which the final number of included studies will be determined.

Data extraction

The two reviewers will independently extract data items from the information provided in the full text articles, into an Excel spreadsheet whereby each study will be represented in a row of data in the spreadsheet. Accompanying notes displayed in Table 1 were developed for use in the present review with reference to the Cochrane Handbook for Systematic

Reviews of Interventions (Version 5.1.0) (194), which will provide further detail and be used as a reference when entering the data items into the spreadsheet. The two reviewers will meet once data extraction has taken place independently, and any discrepancies will be investigated, with a third party invited to adjudicate where consensus is not reached. Relevant data items from the finalised data extraction spreadsheet will then be transferred to RevMan software for quantitative analysis and will be used to produce study characteristics tables as illustrated in Table 2, which will be used in qualitative analysis.

Table 1: Accompanying notes for data extraction

Field	Data items to be extracted into Excel spreadsheet
Study	• Author, • Publication year, • Country (including city or region)
Methods	• Design, (specify RCT, controlled non-randomised, controlled observational: prospective cohort with concurrent or historical control, retrospective cohort with concurrent control) • Objectives, • Randomisation method, (detail method or state not used) • Study duration (from point of recruitment to last data collection)
Participants	• Total number recruited, • Location of recruitment (e.g. healthcare clinic/hospital, community organisation/group, specified region of healthcare organisation such as specific Primary Care Trust), • Recruitment/referral criteria, • Age (mean and standard deviation years) and age range study sample, • Gender (number and proportion male and female), • Ethnicity (number and proportion of each ethnic group), • Weight (baseline mean and standard deviation), • BMI (baseline mean and standard deviation), • State whether participant data is for whole study sample (i.e. mean study sample baseline BMI is ≥40.0kg/m^2) or for a BMI ≥40.0kg/m^2 subgroup.
Intervention	• Nature of intervention: (i.e. behavioural, medical, education, pharmaceutical, very low calorie diet, other, or a combination), • Number of intervention groups, • Intervention setting (where intervention is delivered), • Delivery personnel type (if healthcare professional specify which, researcher, lay public),

	• Delivery personnel training (detail of training in intervention delivery received), • Duration of intervention (number and duration of contact time, including face to face sessions, email, telephone or other contact), • Intensity of intervention (frequency of sessions and contact), • Theoretical basis of intervention (e.g. self-management, cognitive behavioural) • Number of participants assigned/randomised to intervention group, • Number of participants entering intervention group, • Number of participants completing intervention at intervention-end, • Number of participants completing intervention or presenting at time of last data collection, • Loss to follow-up rate: (number randomised-number completing/number randomised), • Any significant differences identified between participants completing and those lost to follow-up (detail which factors differ, state none for specified factors if authors report this, or state not reported).
Comparator	• Number of comparator groups, • Description of comparator or usual care, • Number of participants assigned/randomised to comparator group, • Number of participants entering comparator group, • Number of participants completing comparator group at intervention-end, • Number of participants completing comparator group or presenting at time of last data collection, • Loss to follow-up rate: (number randomised-number completing/number randomised), • Any significant differences identified between participants completing and those lost to follow-up (detail which factors differ, state none for specified factors if authors report this, or state not reported).
Outcomes	*Primary outcomes using LOCF data:* • Weight change from baseline at last point of data collection calculated using last observation carried forward (LOCF) data (include mean and standard deviation, state time point at which obtained), • BMI change from baseline at last point of data collection calculated using last observation carried forward (LOCF) data (include mean and standard deviation), state time point at which obtained), • Weight change from baseline at intervention-end calculated using last observation carried forward (LOCF) data (include mean and standard deviation), • BMI change from baseline at intervention-end calculated using last observation carried forward (LOCF) data (include mean and standard deviation), • Proportion losing weight (any amount), proportion losing ≥5% baseline weight at last point of data collection calculated using last observation carried forward (LOCF) data, • Proportion losing weight (any amount), proportion losing ≥5% baseline weight at intervention-end calculated using last observation carried forward (LOCF) data,

	Primary outcomes using available case data: • Weight change from baseline at last point of data collection calculated using available case data (include mean and standard deviation, state time point at which obtained), • BMI change from baseline at last point of data collection calculated using available case data (include mean and standard deviation), state time point at which obtained), • Weight change from baseline at intervention-end calculated using available case data (include mean and standard deviation), • BMI change from baseline at intervention-end calculated using available case data (include mean and standard deviation), • Proportion losing weight (any amount), proportion losing ≥5% baseline weight at last point of data collection calculated using available case data, • Proportion losing weight (any amount), proportion losing ≥5% baseline weight at intervention-end calculated using available case data. *Secondary outcomes:* • Quality of life change from baseline to last point of data collection, • Quality of life change from baseline to intervention-end, • State quality of life measure used and report change for all if >1 used, • Mental health change from baseline to last point of data collection, • Mental health change from baseline to intervention-end, • State mental health measure used and report change for all if >1 used, • Systolic and diastolic blood pressure change from baseline to last point of data collection, • Systolic and diastolic blood pressure change from baseline to intervention-end, • HDL-, LDL- and total cholesterol change from baseline to last point of data collection, • HDL-, LDL- and total cholesterol change from baseline to intervention-end, For all outcomes include description of confounders where adjusted-estimates are reported and include category boundaries where continuous variables are categorized.

Table 2: Study characteristics table

Study	Methods	Participants	Intervention	Comparator	Outcomes

Quality assessment

It is anticipated that the review will encompass a variety of study designs, such as RCTs, controlled non-randomised studies, and controlled observational studies including prospective and retrospective cohort studies with concurrent controls. For this reason, studies adopting an RCT design will be assessed using the Cochrane Collaboration's tool for assessing risk of bias, version 5.1.0 (204) as illustrated in Table 3. Studies adopting controlled non-randomised designs, or controlled observational designs will also be assessed using the Cochrane Collaboration's tool for assessing risk of bias, version 5.1.0, however the random sequence generation domain will not be completed. Furthermore, the quality of reporting of RCTs will be assessed with the CONSORT checklist (205), and the reporting quality of studies adopting controlled non-randomised designs, and controlled observational designs will be assessed using the STROBE checklist (206).

Included studies will be appraised for quality, in order to provide an estimate of the level of internal validity and therefore the level of risk of bias, for each outcome of interest. The quality assessment will also be used to guide the interpretation of the findings of the review, for instance the level of confidence in the study findings, the explanation of heterogeneity of study findings with quality factors, or possible associations between study quality and study findings. Furthermore, the quality assessment information will be used to provide evaluation summaries which will be made across studies and domains, of the quality of the body of literature, highlighting areas of strength and limitation, and if appropriate, recommendations for the improvement of the quality of primary studies will be made.

Table 3: Reporting form for Cochrane Collaboration's tool for assessing risk of bias

	STUDY:	
DOMAIN	**SUPPORT FOR JUDGEMENT**	**JUDGEMENT**
Selection bias		
Random sequence generation		
Allocation concealment		
Performance bias		
Blinding of participants and personnel		
Detection bias		
Blinding of outcome assessment		
Attrition bias		
Incomplete outcome data		
Reporting bias		
Selective reporting		
Other bias		
Other sources of bias		

Data synthesis and analysis

Qualitative analysis will provide a narrative summary of the findings of the included studies including detail of the primary weight and BMI change outcomes and the secondary outcomes of changes in quality of life, mental health and cardiovascular factors. The qualitative analysis will also provide a summary of the methodological quality and the reporting quality of the included studies and their impact on the findings of the review, and additionally making recommendations for the conduct and reporting of future primary studies.

Quantitative analysis will be used to illustrate the findings of the studies using forest plots for the following outcomes: weight change, BMI change, quality of life change, mental health change and cardiovascular change. The forest plots will be grouped in order to reduce methodology and clinical heterogeneity caused by the differences between studies, with specific subgroup analyses conducted by study design, intervention type, intervention duration, intervention intensity, outcome measures, use of intention to treat, and length of follow-up. A judgement will be made for each subgroup regarding the clinical and methodological heterogeneity, and if the studies within the subgroup are deemed to measure the same true effect of an intervention, a fixed effects model will be used in the meta-analysis and pooled overall estimates of the effect of the weight management interventions will be reported. Alternatively, if there is deemed to be substantial clinical or methodological heterogeneity, whereby studies represent a distribution of possible effects, a random-effects model will be used. However, the heterogeneity will be further examined using the I^2 statistic, according to the guideline of I^2 values representing low levels of heterogeneity at 25%, moderate at 50% and high at 75% (298). If the level of heterogeneity between the studies is deemed to be significant then a

pooled summary statistic will either not be reported, or will be reported with emphasis on the fact that it is included for demonstration of direction of effect only and should not be interpreted as a meaningful result.

Caution will be taken in the interpretation of the findings of the meta-analysis particularly in the subgroup analyses of observational studies due to the absence of randomisation and in the analyses of subgroups based on intervention type, as the likelihood of finding a significant result increases with the number of subgroup analyses performed. Through the careful interpretation of the analyses, a summary of the best evidence available for the effectiveness of medical and behavioural weight management interventions for adults with extreme obesity will be produced.

A detailed report of the findings of the systematic review and meta-analysis will be written as a thesis chapter. The findings will be reported utilising the PRISMA 27-item checklist and flow-diagram illustrating the flow of information through the phases of the systematic review (192). The use of the PRISMA statement will enhance reporting by facilitating explicit description of the systematic review and meta-analysis.

APPENDIX THREE

3.0 QUALITY ASSESSMENT FORMS COMPLETED FOR STUDIES INCLUDED IN SYSTEMATIC REVIEW

Table 1: CONSORT checklist for Ryan, 2010 study

Section /Topic	Item No	Checklist item	Page No
Title and abstract			
	1a	Identification as a randomised trial in the title	-
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	2, 3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	2
	4b	Settings and locations where the data were collected	4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	2, 3
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	3
	6b	Any changes to trial outcomes after the trial commenced, with reasons	-
Sample size	7a	How sample size was determined	-
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	3
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	3
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	3
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	-
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	2, 3
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	3, 4
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	3, 4
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	3
	13b	For each group, losses and exclusions after randomisation, together with reasons	3, 4
Recruitment	14a	Dates defining the periods of recruitment and follow-up	1, 2
	14b	Why the trial ended or was stopped	N/A

Table 1 Continued: CONSORT checklist for Ryan, 2010 study

Section /Topic	Item No	Checklist item	Page No
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	4
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	7
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	7
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	-
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	6
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	5
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	6
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	6
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	6-8
Other information			
Registration	23	Registration number and name of trial registry	1
Protocol	24	Where the full trial protocol can be accessed, if available	-
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	3, 8

Table 2: CONSORT checklist for Rimmer, 2009 study

Section /Topic	Item No	Checklist item	Page No
Title and abstract			
	1a	Identification as a randomised trial in the title	-
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	1, 2
	2b	Specific objectives or hypotheses	2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	2, 4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	2
	4b	Settings and locations where the data were collected	2
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	2, 3
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	3, 4
	6b	Any changes to trial outcomes after the trial commenced, with reasons	-
Sample size	7a	How sample size was determined	4
	7b	When applicable, explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	2
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	-
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	2
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	2
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	2, 3
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	4
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	4
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	4
	13b	For each group, losses and exclusions after randomisation, together with reasons	4
Recruitment	14a	Dates defining the periods of recruitment and follow-up	2
	14b	Why the trial ended or was stopped	N/A

Table 2 Continued: CONSORT checklist for Rimmer, 2009 study

Section /Topic	Item No	Checklist item	Page No
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	4, 5
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	4, 5
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	-
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	-
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	5
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	-
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	6
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	6
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	6
Other information			
Registration	23	Registration number and name of trial registry	-
Protocol	24	Where the full trial protocol can be accessed, if available	-
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

Table 3: STROBE checklist for Danielsen, 2013 study

Section /Topic	Item No	Checklist item	Page No
Title and abstract			
	1	a) Indicate the study's design with a commonly used term in the title or the abstract	1
		b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1, 2
Objectives	3	State specific objectives, including any pre-specified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2, 3
Participants	6	a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	2-4
		b) For matched studies, give matching criteria and number of exposed and unexposed	2, 3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	2-4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	a) Describe all statistical methods, including those used to control for confounding	4
		b) Describe any methods used to examine subgroups and interactions	4
		c) Explain how missing data were addressed	4
		d) If applicable, explain how loss to follow-up was addressed	3, 4
		e) Describe any sensitivity analyses	4
Results			
	13*	a) Report numbers of individuals at each stage of study, e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3
		b) Give reasons for non-participation at each stage	3
		c) Consider use of a flow diagram	3
Descriptive data	14*	a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	5
		b) Indicate number of participants with missing data for each variable of interest	-
		c) Summarise follow-up time (e.g. average and total amount)	6, 7

Table 3 Continued: STROBE checklist for Danielsen, 2013 study

Section /Topic	Item No	Checklist item	Page No
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-10
Main results	16	a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-10
		(b) Report category boundaries when continuous variables were categorized	7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done, e.g. analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	5-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.	-

*Give information separately for exposed and unexposed groups in cohort studies.

APPENDIX FOUR

4.0 DISSEMINATION OF RESEARCH

Publications:

Jagielski AC, Brown A, Hosseini-Araghi M, Thomas GN, Taheri S. The association between adiposity, mental well-being, and quality of life in extreme obesity. PLoS One. 2014; 9: e92859.

Jagielski AC, Jiang CQ, Xu L, Taheri S, Zhang WS, Cheng KK, Lam TH, Thomas GN. Glycaemia is associated with cognitive impairment in older adults: the Guangzhou Biobank Cohort Study. Age Aging. 2014; [Epub ahead of print].

Jagielski AC, Neira I, Hosseini-Araghi M, Brown A, Higgs S, Thomas GN, Taheri S. Psychological co-morbidities of an extreme obese population attending a specialist Community Weight Management Service (CWMS): The impact of type 2 diabetes (T2D). Diabetes. 2013; 62, suppl 1: 2141-P

Araghi MH, Chen YF, **Jagielski A**, Choudhury S, Banerjee D, Hussain S, et al. Effectiveness of lifestyle interventions on obstructive sleep apnea (OSA): systematic review and meta-analysis. Sleep. 2013; 36: 1553-62.

Araghi MH, **Jagielski A**, Neira I, Brown A, Higgs S, Thomas GN, Taheri S. The complex associations among sleep quality, anxiety-depression, and quality of life in patients with extreme obesity. Sleep. 2013; 36 (12): 1859-65.

Conference oral presentations:

AC Cartwright, CQ Jiang, GN Thomas, WS Zhang, KK Cheng, S Taheri and TH Tam. Type 2 diabetes and memory impairment: findings from the Guangzhou Biobank Cohort Study. Diabetes UK Professional Conference. Glasgow, UK. 7-9 March, 2012.

Conference poster presentations:

Jagielski AC. Quality of life and mental health in extreme obesity: A study of individuals attending a Specialist Weight Management Service. Association for the Study of Obesity (ASO) Annual UK Congress on Obesity (UKCO) 2014. University of Birmingham, 16-17 September 2014 (upcoming).

Jagielski AC, Brown A, Gouldstone, A Wright A, Davies R, Abernethy G, Thomas GN, Taheri S. Comparison of baseline characteristics and weight loss outcomes in patients with extreme obesity attending a weight management focussed structured educational group or a specialist Community Weight Management Service. ENDO 2013, 95th Annual Meeting of the Endocrine Society. San Francisco, CA. 15-18 June, 2013.

Jagielski AC, Brown A, Hosseini-Araghi M, Wright A, Davies R, Gouldstone A, Abernethy G, Thomas GN, Taheri S. Characteristics of extreme obese patients attending a specialist Community Weight Management Service. ENDO 2013, 95th Annual Meeting of the Endocrine Society. San Francisco, CA. 15-18 June, 2013.

Jagielski AC, Brown A, Hosseini-Araghi M, Wright A, Davies R, Gouldstone A, Abernethy G, Thomas GN, Taheri S. Weight loss outcomes for an extreme obese population attending a specialist Community Weight Management Service (CWMS) - A service evaluation. American Diabetes Association, 73rd Scientific Sessions. Chicago, IL. 21-25 June, 2013.

APPENDIX FIVE

5.0 PUBLISHED PAPER 'THE ASSOCIATION BETWEEN ADIPOSITY, MENTAL WELL-BEING AND QUALITY OF LIFE IN EXTREME OBESITY'

The association between adiposity, mental well-being, and quality of life in extreme obesity

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Word count: 289 (abstract) 3,908 (main text)

Keywords: adiposity, quality of life, extreme obesity, anxiety, depression, mental well-being

Abstract

Objectives: To explore the cross-sectional association between adiposity, mental well-being, and quality of life in extreme obese individuals entering a UK specialist weight management service prior to treatment commencement.

Methods: The sample comprised 263 extreme obese individuals who were referred to the service as a result of having a body mass index (BMI) ≥40 kg/m^2 or ≥35 kg/m^2 with a co-morbid health condition. In a retrospective analysis, routinely collected baseline clinical examination data and self-report questionnaires (Impact of Weight on Quality of Life: IWQOL-Lite, EQ5D-3L, and Hospital Anxiety and Depression Scale: HADS) were analysed to examine the cross-sectional association between adiposity and quality of life.

Results: The sample was predominantly female (74.8%) with mean BMI 47.0±7.9 kg/m^2. Increasing adiposity was significantly negatively associated with quality of life, with an increase of 1 BMI unit associated with decreases of 1.93 in physical function (95% CI -2.86 - -1.00, p<0.001), 1.62 in self-esteem (95% CI -2.67 - -0.57, p<0.05), 2.69 in public distress (95% CI -3.75 - -1.62, p<0.001), 1.33 in work (95% CI -2.63 - -0.02, p<0.05), and 1.79 in total IWQOL-Lite scores (95% CI -2.65 - -0.93, p<0.001). Adiposity was associated with significantly increased risk of problems in mobility (OR=3.44, 95% CI 1.47-8.05), and performing usual activities (OR=2.45, 95% CI 1.10-5.46) in highest relative to lowest BMI tertile. The prevalence of experience of symptoms of anxiety (70.3%) and depression (66.2%) as measured by HADS was consistently high.

Conclusions: We identified a high prevalence of psychological co-morbidity, including widespread experience of symptoms of anxiety and depressive disorders and reduced quality of life among these extreme obese individuals seeking weight management

treatment. Clinical implications include the need for the incorporation of strategies to improve mental well-being into multi-disciplinary weight management interventions.

Introduction

The prevalence of obesity among adults, and in particular extreme obesity, has risen rapidly over previous decades (1). Current levels of extreme obesity (BMI ≥40 kg/m^2) in the US have increased 70% over the last decade between 2000 and 2010, with the prevalence rate reaching 6.6% (2), whilst current UK prevalence rates of extreme obesity are 3% for females and 2% for males (3). Indeed, recent estimates predict the rate of extreme obesity to reach 5% in the UK by 2033 and 9% in the US by 2030 (4). The physical co-morbidities of extreme obesity are well documented and research suggests that there are also substantial negative impacts of adiposity on depression (5), anxiety (6) and reduced quality of life (7). However, there are inconsistencies in the literature, with several reviews reporting studies demonstrating no association between adiposity and psychological health (5, 6, 8). In the extreme obese current understanding is limited as studies have focused on those individuals specifically seeking bariatric surgery (9), and have not included a range of assessments of putative psychological co-morbidities. In order to improve service provision for patients with extreme obesity, it is important to understand the extent of psychological co-morbidity and the impact on quality of life. Baseline data from treatment-seeking individuals at a community-based UK specialist weight management service were analysed in order to test the null hypothesis that there is no association between adiposity and psychological health.

Materials and Methods

Participants

This cross-sectional service evaluation study included a consecutive sample of 262 individuals with extreme obesity entering a specialist community-based weight management service (CWMS) in the West Midlands, UK. Eligible participants were referred to the CWMS by their general practitioner (GP) as a result of fulfilling the criteria of having a body mass index (BMI) $\geq$40 kg/m^2, or alternatively a BMI $\geq$35 kg/m^2 with a co-morbid health condition, such as type 2 diabetes mellitus or hypertension. Patient referral required previous unsuccessful weight loss attempts in primary care and commercial weight loss programmes. The participants entered the service between February 2008 and August 2012, with those included in the evaluation selected at random from an opportunity sample. Baseline data including adiposity, quality of life, and mental well-being were routinely collected prior to the initiation of treatment.

Demographic information

As part of routine clinical care, demographic and health details were collected including participants' age, gender, ethnicity, waist circumference, smoking status, and alcohol consumption. Details of participants' co-morbid health conditions including cardiovascular disease, hypertension, diabetes, obstructive sleep apnoea and arthritis were also recorded.

Clinical assessment

Within the CWMS, all participants underwent a comprehensive clinical history and examination by a consultant physician and specialist dietitian. A psychologist provided

further support in the service. Participants' initial weight and height data were recorded at baseline, and BMI was calculated by dividing participants' weight in kg by height in meters squared.

Quality of life and mental health measures

Questionnaires were routinely collected as part of the comprehensive clinical assessment. Quality of life and mental health were assessed using three measures, the Impact of Weight on Quality of Life (IWQOL-Lite) questionnaire, which is an obesity-specific quality of life measure, the EQ5D-3L, which is a general quality of life measure, and the Hospital Anxiety and Depression Scale (HADS) which is a screening tool widely used in both clinical and research settings. The IWQOL-Lite consists of 31 items measuring the impact of obesity on physical function, self-esteem, sexual life, public distress and work (10). Respondents are asked to rate the extent to which a series of statements is applicable to them using a Likert scale ranging from 5 'Always true' to 1 'Never true'. Responses to the questionnaire items yield a total impact of weight on quality of life score as well as individual scores for each of the five domains, with maximum scores of 100 on each subscale indicating optimum quality of life.

The EQ5D-3L consists of five questions relating to five dimensions of health; 'mobility', 'self-care', 'usual activities', 'pain and discomfort' and 'anxiety and depression' (11). Respondents indicate which of a possible three statements best describe their current health state for each dimension. A 'level 1' response indicates that the respondent has no problem in the specific dimension, a 'level 2' response indicates some problems, and a 'level 3' response indicates extreme problems. Respondents are asked to repeat this process for the five dimensions by indicating one level for each dimension,

giving rise to scores ranging from 1 to 3, with scores of 3 on each dimension indicating the most severe impairment. Binary variables were computed for each dimension dichotomising the levels into 'No problems' (level 1) and 'Problems' (levels 2 and 3). Perceived current health state is measured by asking respondents to indicate their current health state on a Visual Analogue Scale (VAS) with endpoints labelled 0 'Worst imaginable health state' and 100 'Best imaginable health state'.

The Hospital Anxiety and Depression Scale (HADS) comprises 14 items, 7 relating to anxiety, and 7 relating to depression (12). Respondents rate the extent to which a series of statements represents how they currently feel using a Likert scale ranging from 0 to 3. The scale yields individual anxiety and depression scores as well as an overall HADS score. Individual subscale for anxiety and depressive symptom scores range from 0 to 21, with a score of 8 established as a cut-point for identifying symptoms of anxiety and depressive disorders and scores of 11 established as a cut-point for identifying more severe symptoms (13). Whilst the HADS scale is widely used in clinical practice to identify the experience of symptoms of anxiety and depression, it cannot provide a confirmatory diagnosis of anxiety and depressive disorders.

Statistical analysis

All data were analysed using SPSS (version 19.0). T-tests, cross-tabulation, chi^2 and analysis of variance (ANOVA) calculations were conducted to compare the BMI tertile groups: first BMI tertile ≤42.99; second BMI tertile 43.00 - 48.61; third BMI tertile ≥48.62 kg/m^2**.** Linear regression coefficients were calculated to assess the relationship between BMI and quality of life as measured by IWQOL-Lite scores (continuous) and in separate analyses between BMI and overall perceived health status as measured by EQ5D-3L VAS.

Analyses were conducted for the whole sample and repeated in gender-stratified sub-groups.

Logistic regression models were constructed to assess the association between BMI and experience of symptoms of anxiety and depressive disorder as measured by HADS, and presence of problems in mobility, self-care and performing usual activities as measured by EQ5D-3L, with the first BMI tertile group as the reference. The odds ratios (ORs) and 95% confidence intervals (CIs) for three hierarchical models are presented: crude; adjusting for age and sex; and additionally adjusting for the co-morbidities; diabetes, hypertension, arthritis, obstructive sleep apnoea and cardiovascular disease.

Ethics statement

This was a retrospective analysis of routinely collected data to evaluate the psychological and quality of life burden of extreme obesity. Data were anonymised prior to any data analysis. The anonymised data were analysed as part of the specialist weight management service evaluation at the Heart of England NHS Foundation Trust, requiring no specific research ethics approval as recommended by the UK National Research Ethics Service (14). The analysis was registered with and approved by the local governance audit department.

Results

Demographic and clinical characteristics

The participants were aged 19 to 76 years, with a mean age of 43.1±11.8 years and a mean BMI of 47.0±7.9 kg/m^2. Table 1 shows that in those with increasing levels of adiposity, there were significantly more problems in mobility, self-care and performing usual activities, and weight was reported to have a greater impact on physical function, causing public distress, ability to work, and overall quality of life. Those with increasing BMI were also more likely to have type 2 diabetes mellitus, hypertension, obstructive sleep apnoea (OSA) and cardiovascular disease (CVD). There were no significant differences in HADS anxiety and depression scores, with prevalence of anxiety and depressive symptoms consistently high across the BMI groups, with data for the combined sample indicating prevalence rates of anxiety symptoms (70.3%) and depressive symptoms (66.2%), which are far greater than the UK general population rates of 33.0% for anxiety disorders and 11.4% for depressive disorders (15). Indeed, levels of severe anxiety and depressive symptoms defined by the higher cut-point scores of ≥11 are also substantial, with severe anxiety symptoms experienced by 48.3% of the sample and 40.4% of the sample experiencing symptoms of severe depressive disorders.

Data indicate that quality of life is impaired, with sample mean IWQOL-Lite scores ranging from 26.2 (self-esteem) to 51.2 (work), whereby 100 represents optimum quality of life. Perceived health status was also poor with a sample mean of 44.0, whereby 100 represents best possible health state; which is considerably worse than the UK general population mean score of 82.8 (16). There were no significant gender differences in EQ5D-3L. However there were gender differences in HADS anxiety, but not depression

and total scores, and gender differences in the IWQOL-Lite total and subscales self-esteem and sexual life, with significantly poorer quality of life in females (data not shown).

Linear regression: BMI, IWQOL-Lite and perceived health status

The IWQOL-Lite total measure and the subscales physical function, self-esteem, public distress and work were significantly negatively associated with increasing BMI (Table 2). Increasing BMI was associated with decreasing quality of life across the domains of physical function (1.93, $p<0.001$), self-esteem (1.62, $p<0.05$), public distress (2.69, $p<0.001$), work (1.33, $p<0.05$) and total score (1.79, $p<0.001$). Stratification by gender revealed that BMI was more strongly negatively associated with these measures in males. Interestingly, BMI was not significantly associated with the sexual life IWQOL-Lite subscale and the perceived health status measure (EQ5D-3L VAS).

Logistic regression: BMI, EQ5D-3L and HADS anxiety and depression

Table 3 shows the logistic regression analyses of the EQ5D-3L subscales 'mobility', 'self-care' and 'usual activities', which were significantly associated with BMI. The fully adjusted model revealed an increased risk of mobility problems with increased BMI, with the odds ratios of 1.64 (0.78 - 3.44) and 3.44 (1.47 - 8.05) for second and third BMI tertile groups (P for trend <0.05) respectively, compared to those in the first BMI tertile group. There was a non-significant increased risk of self-care problems, with the odds ratios of 0.89 (0.41 - 1.96) and 1.87 (0.86 - 4.09) for second and third BMI tertile groups (P for trend =0.104) respectively. However the fully adjusted model remained significant demonstrating increased risk of self-care problems in the continuous BMI model 1.05 (1.00 - 1.09). The fully adjusted model also revealed an increased risk of problems performing usual activities, with the odds ratios of 2.04 (0.98 - 4.26) and 2.45 (1.10 - 5.46) for second

and third BMI tertile groups (P for trend <0.05) respectively, compared to those in the first BMI tertile group. Interestingly, the logistic regression analyses of anxiety and depressive symptoms as defined as HADS subscale score ≥8 revealed that anxiety and depressive symptoms were not significantly associated with BMI across the range encountered in the sample.

Discussion

The findings of the present evaluation demonstrated that quality of life was markedly impaired in this sample of extreme obese individuals entering a specialist community-based weight management service having not succeeded with previous efforts at weight loss. Furthermore, we observed that the prevalence of anxiety and depressive symptoms was very high. Whilst much of the research investigating the complex association between adiposity and quality of life and mental well-being has incorporated individuals across the spectrum of obesity, the present study is of particular importance as it focuses on the escalating extreme obese population (4).

We observed a significant negative association between increasing adiposity at these extreme levels and quality of life, specifically in the areas of physical function, self-esteem, public distress and work, with increased adiposity associated with reduced quality of life as measured by IWQOL-Lite score. The association between adiposity and weight-specific quality of life as measured by IWQOL-Lite has been established, with findings indicating that BMI accounts for approximately 28% of the variance in total IWQOL-Lite scores (7). Previous research has shown that scores vary with degree of adiposity and treatment status, with those with higher BMI and those seeking treatment reporting significantly worse quality of life (7). In addition, changes in IWQOL-Lite score from

baseline to post-intervention have been shown to correlate significantly with weight loss (17). The results obtained in the present study show a similar level of impairment in quality of life to those obtained in a study of bariatric surgery-seeking individuals, which reported scores ranging from 40.4 (work) to 46.2 (self-esteem) across IWQOL-Lite subscales (7). Interestingly, the present study reported one subscale which was not shown to be significantly associated with adiposity; sexual life. This is consistent with findings from a comparison of white and African American US women, whereby white women scored significantly lower on sexual life compared to their African American counterparts, in both class II and III obesity, and BMI was significantly associated with sexual life in the white sub-group but not in the African American sub-group (18). A similar pattern of results whereby significant association was not observed between BMI and sexual life has also been reported in a sample of over 400 bariatric surgery-seeking extreme obese individuals (18). The investigators concluded that the lack of observed association is due to the high level of co-morbidities, which may diminish the association between quality of life and BMI at the level of extreme obesity. However, the results of the present study show that the association between BMI and quality of life remains when controlling for co-morbid health conditions, suggesting that obesity negatively affects quality of life, independently of these conditions. This lack of association indicates that there are additional factors outside of those measured, which contribute to the reduced level of quality of life in these specific domains. Indeed, the substantial impairments in sexual quality of life in this population have been greatly under-researched (19) and are thought to be associated with the broader aspects of stigmatisation and discrimination (20) as well as negative perceived body image (19, 21) experienced by this patient population.

Likewise, significant associations were observed between adiposity and some, but not all, of the EQ5D-3L subscales. Adiposity was associated with experience of problems in mobility, self-care, and performing usual activities, with those in the third BMI tertile more likely to experience problems in these areas. Whilst the fully adjusted models remained significant for the mobility and performing usual activities analyses, the self-care model was no longer significant when fully adjusted in the BMI tertile model. These findings are consistent with the limited previous studies which have shown that general quality of life as measured by EQ5D-3L is poorest for individuals with class III obesity, compared to class I and II obese groups, as well as overweight and underweight groups, relative to those of normal weight where quality of life scores are optimum (22, 23). Notably, the present study reported two subscale scores, which were not shown to be significantly associated with adiposity, 'pain and discomfort' and 'anxiety and depression'(data shown in Table 1). This is in contrast to previous research which has identified that obese individuals are at greater odds of experiencing anxiety and depressive disorders (5, 6), and pain (OR=1.94) relative to normal weight counterparts (23). The results of the present study indicate that individuals reported the greatest amount of problems in these domains. Likewise, no significant association between adiposity and perceived health status (EQ5D-3L VAS) was observed. Together, these findings suggest a possible ceiling effect for the EQ5D-3L tool being unable to detect differences within such a homogeneous group as the present sample in which the quality of life is consistently low. An additional aspect is the absence of normal weight individuals, which truncates the BMI range, reducing the opportunity to identify an association. There was a non-significant trend whereby perceived health status was highest for the first BMI tertile group (47.4) and lowest for the third BMI tertile group (42.9) supporting the above contentions. Unlike the

present study, previous studies have demonstrated that perceived health status significantly decreases with increasing adiposity, and is poorest for individuals with class III obesity, relative to those of normal weight (23); it is likely that the expected significant negative association was not observed in the present study due to the homogeneity in adiposity of this exclusively extreme obese sample.

The expected significant associations between adiposity and symptoms of anxiety and depressive disorder as measured by HADS were also not observed in the present study. However, it was evident that the prevalence of symptoms of psychological co-morbidities was high across the sample (anxiety, 70.3%; depression, 66.2%) and is far greater than the UK general population rates of 33.0% for anxiety and 11.4% for depressive disorder (15). The relationship between depressive disorders and obesity has been widely documented in the literature, with results from prospective studies indicating that obesity is associated with future incidence of depression and cross-sectional studies revealing significant positive associations between adiposity and depression, particularly in females (5). No significant variation in prevalence of anxiety and depressive symptoms was observed across the levels of adiposity in the current sample, probably due to the truncated BMI range and the overall high prevalence of anxiety and depressive symptoms. However, data from the NHANES (National Health and Nutrition Examination Survey) study demonstrated a dose-response relationship between depression and adiposity, with class III obese individuals having greater odds of experiencing lifetime major depression (OR=2.60), recurrent major depression (OR=2.28), depression in the past month (OR=4.98) and past year (OR=2.92) than the class I and II obesity groups relative to those of normal BMI (24).

Whilst much research has demonstrated evidence for an association between adiposity and both depressive and anxiety disorders (6, 24, 25) it is important to note that some studies have reported no significant association (8) or have reported non-significant trends (26-29). A systematic review and meta-analysis of the association between obesity and anxiety has concluded that there is evidence in support of a positive association between obesity and anxiety, with pooled cross-sectional data indicating that obese individuals are more likely to experience anxiety (OR=1.4) (6). It is also of interest that the findings of the present work indicate that anxiety was more prevalent in this sample than depression.

The mechanism of the association between adiposity, impairment in quality of life and presence of anxiety and depressive disorders is not yet established, with several proposed pathways through which obesity may lead to psychological co-morbidity and vice versa. Firstly, through the multiple health threats associated with obesity acting as stressors, and secondly through the negative effects of stigma and weight-related discrimination. Indeed frequency of stigmatisation and inability to adopt effective coping strategies have been shown to result in depressed mood (29). The relationship between obesity and depression specifically, appears to be bi-directional with obesity associated with increased experience of depressive symptoms, and depressive episodes associated with further weight gain. Furthermore, obese individuals are more likely to over-eat and gain weight compared to non-obese individuals during an episode of depression (30). A systematic review of the relationship between depression and adiposity reported that the majority of evidence was cross-sectional and thus causality could not be established (5).

Previous research has been criticised for the inclusion of only one measure of quality of life (23), and as such the inclusion of several quality of life measures is a novel

aspect of the present evaluation. Previous studies have utilised either general measures such as the EQ5D-3L (22, 23) and the Medical Outcomes Study Short Form Health Survey (SF-36) (31, 32) or condition specific measures such as the Obesity Adjustment Survey (OAS) (33) and the Obesity Related Well-being (ORWELL 97) questionnaire (34); however the IWQOL-Lite measure is the most widely used weight-specific measure (35). Present findings suggest that in the assessment of quality of life within extreme obesity, both weight-specific and general quality of life measures are effective. Notably, the IWQOL-Lite, EQ5D-3L and HADS measures all contained subscales which were not associated with adiposity indicating that each of the tools may have limitations in capability of identifying differences in extreme adiposity. The specific domains which were not associated with adiposity; pain and discomfort, anxiety and depression and sexual life were in fact the more severely affected aspects of life. Likewise, none of the components of the HADS mental health screening tool were associated with adiposity. However, the tool was shown to be effective in determining prevalence of symptoms of anxiety and depressive disorders in an extreme obese sample. Future studies should utilise several quality of life measures, including those that are weight specific and general in order to establish the validity of the measures in this patient group (36), as well as enabling deeper understanding of the additional factors which may influence the complex relationship between adiposity, quality of life and mental well-being.

A key strength of the present study is that it demonstrates that the negative impact on quality of life associated with increasing BMI remains even when controlling for the presence of obesity related co-morbid health conditions commonly experienced by the extreme obese population. Previous studies have concluded that the association between adiposity and quality of life is mediated by health co-morbidities such as pain,

cardiovascular disease and type 2 diabetes mellitus (37-39); however the present study supports that the association is independent, and that the role of co-morbidities in the relationship may have previously been over-estimated, and the impact of adiposity, underestimated.

An additional strength of the present study is that it improves understanding of the characteristics of this less-researched extreme obese population. However, the present work has several limitations. The individuals characterised in the sample are those that had sought assistance in managing their weight and as a consequence it may not be appropriate to extrapolate these findings to the general extreme obese population, as evidence suggests that non-treatment-seeking obese individuals do not experience the same psychological co-morbidities (40) and impairment in quality of life (7) as those seeking treatment. Furthermore, the fact that these findings are obtained from a single weight management service may limit their generalizability to other UK specialist weight management settings. The cross-sectional design of the present study means that it is not possible to confirm a causal relationship between adiposity and quality of life. The present work also adopted a service evaluation approach aiming to understand the psychological and quality of life burden of obesity to improve service provision, which means that it is not possible to compare the characteristics of the extreme obese treatment-seeking group, with a non-obese control group or an extreme obese non-treatment-seeking group for comparison. As such the findings of the present work should be interpreted with caution and future studies adopting a controlled design comprising a control group of extreme obese non-treatment-seeking individuals should be utilised in further investigation of the psychological co-morbidities of extreme obesity.

In conclusion, we observed that among this sample of treatment-seeking extreme obese individuals there is a high prevalence of symptoms of psychological co-morbidity, including experience of anxiety and depressive disorder symptoms and reduced quality of life. Increasing adiposity was associated with a reduction in several areas of quality of life, but was not significantly associated with symptoms of anxiety and depressive disorders. These findings are of clinical importance indicating that the impairment in quality of life and mental health challenges faced by these individuals must be addressed and incorporated into the multi-disciplinary care of these patients, in order to provide tailored weight management interventions.

Author contributions

ST developed the format and assessments for the clinical management of patients within the specialist service and was the lead clinician. AB contributed to the dietetic aspect of service provision. ACJ and MH-A collated the data. ACJ, NT, and ST developed the analysis plan. ACJ wrote the first draft. All authors contributed to the final analysis, discussion, and submitted manuscript.

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Table 1: Demographic and clinical characteristics of the sample across BMI tertiles.

	Whole sample	**1st BMI tertile ≤ 42.99**	**2nd BMI tertile 43.00 - 48.61**	**3rd BMI tertile ≥ 48.62**	**P**
N	262	87	87	88	
Age (years)	43.1±11.8	43.0±13.2	41.7±10.2	44.7±11.8	0.234
Sex (% female)	74.8	72.4	77.0	75.0	0.783
Ethnicity (%)					0.585
White European	90.8	90.0	95.5	87.9	
Asian	5.6	5.0	2.3	8.6	
Black African/Caribbean	2.8	2.5	2.3	3.4	
Other	0.7	2.5	0.0	00	
Weight (kg)	132.1±24.7	112.6±14.7	129.1±15.6	154.2±22.3	<0.001
Body mass index (BMI, kg/m^2)	47.0±7.9	39.4±2.6	45.8±1.6	55.8±6.6	<0.001
Waist circumference (cm)	131.6±14.5	123.8±11.8	128.6±12.7	142.4±12.5	<0.001
Systolic blood pressure (mmHg)	140.9±17.7	136.0±14.5	140.4±17.0	146.4±20.0	0.009
Diastolic blood pressure (mmHg)	85.2±11.7	83.3±9.7	85.5±11.4	86.9±13.6	0.263
Diabetes (%)	26.3	24.1	18.4	36.4	0.022
Hypertension (%)	34.4	31.0	26.4	45.5	0.022
Arthritis (%)	24.0	21.8	19.5	30.7	0.190
Obstructive sleep apnoea (OSA, %)	25.6	16.1	26.4	34.1	0.024
Cardiovascular disease (CVD, %)	11.1	9.2	5.7	18.2	0.026
Smoking (%)	25.5	31.7	23.0	22.2	0.655
Alcohol consumption (%)	64.7	62.9	81.0	52.9	0.004
IWQOL-Lite (%) Total	39.5±22.1	49.0±23.3	38.5±19.9	32.1±20.2	<0.001
Physical function	42.4±25.3	54.1±24.9	40.4±23.6	34.1±23.7	<0.001
Self-esteem	26.2±27.5	30.4±30.5	24.1±24.4	24.5±27.5	0.286
Sexual life	41.9±35.9	47.3±36.9	43.5±35.6	35.2±34.7	0.128
Public distress	40.5±28.9	56.6±31.5	38.9±25.2	27.7±22.7	<0.001
Work	51.2±30.3	61.6±30.4	46.1±27.4	47.1±31.3	0.003
Mobility problems %	66.7	55.9	63.0	80.3	0.006
Self care problems %	35.7	29.9	27.2	50.0	0.006
Anxiety/depression problems %	75.3	73.1	75.6	77.0	0.864
Pain/discomfort problems %	85.3	80.0	86.3	89.3	0.272
Usual activities problems %	69.0	58.0	70.4	77.6	0.036
Perceived health status	44.0±20.1	47.4±19.4	42.4±19.0	42.9±21.8	0.303
HADS Total score	19.6±7.7	19.0±7.6	20.2±7.8	19.6±7.9	0.654
HADS anxiety score	10.4±4.5	10.5±4.3	10.7±4.8	10.2±4.5	0.780
HADS depression score	9.1±4.0	8.6±4.0	9.3±3.9	9.3±4.1	0.436
Anxiety symptoms ≥8 (%)	70.3	74.0	68.7	68.8	0.716
Depression symptoms ≥8 (%)	66.2	62.3	72.5	63.2	0.333
Severe anxiety symptoms ≥11 (%)	48.3	50.7	48.2	46.3	0.860
Severe depression symptoms ≥11 (%)	40.4	33.3	42.5	44.7	0.338

Data are percentages and means ± standard deviations. HADS= Hospital anxiety and depression scale

Table 2: Linear regression of BMI predicting IWQOL-Lite subscale and total scores and perceived health status (EQ5D-3L VAS) in whole sample and stratified by gender.

	Univariate			Model 1			Model 2		
	U.B.	S.E.	S.B	U.B.	S.E.	S.B	U.B.	S.E.	S.B
Physical function	-0.83**	0.20	-0.26	-1.95**	0.48	-0.62	-1.93**	0.47	-0.61
Male †	-1.66*	0.54	-0.37	-1.92*	0.53	-0.43	-2.00**	0.50	-0.44
Female †	-0.66*	0.21	-0.23	-0.56*	0.20	-0.19	-0.51*	0.21	-0.18
Self esteem	-0.34	0.22	-0.10	-1.53*	0.53	-0.44	-1.62*	0.53	-0.47
Male †	-1.80*	0.63	-0.35	-1.39*	0.60	-0.27	-1.19	0.63	-0.23
Female †	0.01	0.22	-0.00	-0.06	0.22	-0.02	-0.11	0.22	-0.04
Sexual life	-0.56	0.32	-0.12	-1.55*	0.77	-0.34	-1.45	0.79	-0.31
Male †	-1.47	0.75	-0.25	-1.55*	0.76	-0.27	-1.21	0.81	-0.21
Female †	-0.33	0.35	-0.08	-0.27	0.35	-0.06	-0.29	0.36	-0.07
Public distress	-1.44**	0.22	-0.40	-2.82**	0.53	-0.77	-2.69**	0.54	-0.74
Male †	-3.00**	0.49	-0.62	-2.76**	0.48	-0.57	-2.48**	0.51	-0.51
Female †	-1.14**	0.24	-0.34	-1.19**	0.24	-0.35	-1.18**	0.25	-0.35
Work	-0.83*	0.25	-0.22	-1.34*	0.65	-0.35	-1.33*	0.66	-0.35
Male †	-1.39*	0.67	-0.28	-1.23	0.68	-0.25	-1.22	0.73	-0.25
Female †	-0.70*	0.27	-0.20	-0.70*	0.28	-0.20	-0.68*	0.28	-0.19
IWQOL-Lite total	-0.79**	0.17	-0.28	-1.84**	0.43	-0.66	-1.79**	0.44	-0.65
Male †	-1.82**	0.44	-0.47	-1.78**	0.45	-0.46	-1.60*	0.46	-0.42
Female †	-0.56*	0.19	-0.22	-0.54*	0.19	-0.22	-0.52*	0.19	-0.21
Perceived health status	-0.17	0.18	-0.07	-0.12	0.49	-0.05	-0.07	0.49	-0.03
Male †	-0.12	0.48	-0.04	-0.11	0.50	-0.03	-0.08	0.50	-0.03
Female †	-0.18	0.19	-0.07	-0.18	0.20	-0.07	-0.12	0.20	-0.05

U.B. =Unstandardised Beta, S.E. =Standard error, S.B =Standardised Beta.
**P<0.05, **P<0.001*
Model 1 adjusting for age, gender and interaction between BMI and gender.
† Model 1 and 2 adjusting for age only. Model 2 additionally adjusting for diabetes, hypertension, arthritis, obstructive sleep apnoea, cardiovascular disease.

Table 3: Logistic regression of presence of problems in mobility, self care and usual activities (EQ5D) and presence of anxiety and depression (HADS) by BMI tertiles and by continuous BMI.

		1st tertile (≤ 42.99)	2nd tertile (43.00 - 48.61)	3rd tertile (≥ 48.62)	P for linear trend	Continuous BMI
			Odds ratio (95% CI)			
Mobility problems	**Univariate**	1.00	1.25 (0.64 – 2.44)	2.95 (1.40 – 6.22)*	0.004	1.07 (1.02 – 1.12)*
	Model 1	1.00	1.32 (0.66 – 2.63)	2.83 (1.31 – 6.15)*	0.008	1.07 (1.02 – 1.12)*
	Model 2	1.00	1.64 (0.78 – 3.44)	3.44 (1.47 – 8.05)*	0.009	1.08 (1.03 – 1.13)*
Self-care problems	**Univariate**	1.00	0.84 (0.41 – 1.72)	2.19 (1.09 – 4.39)*	0.018	1.05 (1.01 – 1.09)*
	Model 1	1.00	0.88 (0.42 – 1.88)	2.05 (0.98 – 4.27)	0.044	1.05 (1.01 – 1.10)*
	Model 2	1.00	0.89 (0.41 – 1.96)	1.87 (0.86 – 4.09)	0.104	1.05 (1.00 – 1.09)*
Problems performing usual activities	**Univariate**	1.00	1.71 (0.86 – 3.37)	2.65 (1.27 – 5.52)*	0.008	1.05 (1.01 – 1.10)*
	Model 1	1.00	1.73 (0.86 – 3.44)	2.48 (1.17 – 5.23)*	0.016	1.05 (1.01 – 1.10)*
	Model 2	1.00	2.04 (0.98 – 4.26)	2.45 (1.10 – 5.46)*	0.040	1.05 (1.00 – 1.10)*
Anxiety	**Univariate**	1.00	0.75 (0.37 – 1.51)	0.73 (0.36 – 1.45)	0.409	0.98 (0.95 – 1.02)
	Model 1	1.00	0.68 (0.33 – 1.42)	0.74 (0.35 – 1.54)	0.460	0.98 (0.94 – 1.01)
	Model 2	1.00	0.71 (0.34 – 1.50)	0.81 (0.37 – 1.74)	0.633	0.98 (0.95 – 1.02)
Depression	**Univariate**	1.00	1.57 (0.78 – 3.15)	1.00 (0.51 – 1.98)	0.958	1.00 (0.96 – 1.03)
	Model 1	1.00	1.59 (0.79 – 3.20)	1.06 (0.53 – 2.11)	0.910	1.00 (0.96 – 1.03)
	Model 2	1.00	1.65 (0.80 – 3.40)	1.26 (0.61 – 2.62)	0.550	1.00 (0.97 – 1.04)

Presence of problems defined as level 2 (some problems) and level 3 (extreme problems) scores on EQ5D-3L; Presence of anxiety and depression defined as HADS anxiety subscale score ≥8.

** P<0.05, **P<0.001*

Model 1 adjusting for age and sex. Model 2 additionally adjusting for diabetes, hypertension, arthritis, obstructive sleep apnoea, cardiovascular disease.