Development of predictive models for successful weight loss in people living with obesity

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Abstract

Behavioural weight management programmes are effective in helping some, but not all, patients living with obesity to lose weight. With the emerging pharmacological options for weight loss, and a range of dietary interventions available, it may be advantageous to be able to predict successful short and medium term weight loss, so patients can be moved to other therapies at an earlier stage while they are still engaged. The overall aim of this thesis was therefore to identify factors at the baseline level to predict short and medium terms successful weight loss.

In chapter 2, a hypothesis-driven questionnaire was developed after conducting a literature review to test baseline behavioural and psychological factors ability to predict successful short-term weight loss in individuals undertaking behavioural weight management programmes (in NHS GG&C region). This prospective study was not started due to the COVID-19 pandemic, but the questionnaire and study are ready to be implemented in the future.

In chapter 3, a prospective study investigated baseline clinical, sociodemographic and process factors association with weight loss (>5%) in individuals undertaking behavioural weight management programmes (in NHS GG&C region). The only variable that predicted short (16 weeks) and medium-term successful weight loss (3 years) is the early weight loss (4 weeks) in the programme. Weight loss of 0.5% at 4 weeks had sensitivity 90.4%, specificity 53.6%, PPV 32.9%, NPV 95.7% in the short term and sensitivity 89.9%, specificity 49.5%, PPV 19.6%, NPV 97.3% in the medium term.

In chapter 4, a prospective study tested behavioural and psychological factors ability to predict successful medium-term weight loss in using data from the LookAHEAD trial. Moderate predictive utility was obtained from; age, sex, randomised treatment , baseline weight, bodily pain score, diabetes medication and LDL cholesterol (AUC-ROC= 0.649)

In chapter 5, an external validation study was conducted (using the WRAP trial) to validate predictors of successful weight loss identified in Chapters 3 and 4. Strong evidence was seen that early weight loss in the programme is a strong predictor of medium-term successful weight loss (consistent with chapter 3). In contrast, only baseline weight and age were validated as predictors of successful weight loss.

In chapter 6, UK Biobank was used to test predictors of weight loss over the medium term in a general population with overweight and obesity. A large proportion(19.7%) of people with overweight or obesity lost a significant amount of weight (≥ 5%) over ~4 years even without known dietary interventions. Moderate predictive utility was obtained from sex, age, initial BMI, diastolic blood pressure, triglycerides, and time spent driving (AUC-ROC= 0.618).

In conclusion, socio-demographic, clinical, process, behavioural and psychological variables do not yield sufficient discrimination to allow prediction of successful weight loss, either in a structured weight management programme, or in the general population. However, early weight loss in the first few weeks of starting an intervention is strongly associated with short and medium term successful weight loss. A threshold of failing to achieve 0.5% body weight loss in the first 4 weeks can identify participants who are unlikely to succeed in the programme (>95% of these will not be successful completers). This approach may allow early identification of patients who might benefit more from other interventions while they are still engaged.

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Al-Ozairi Ebaa, Brown Rosemary, Hamdan Yasmine, Alabdullah Lulwa, Voase Nia, Al Kandari Jumana, Alsaeed Dalal, Al Ozairi Abdulla, Hasan Amal, Al-Mulla Fahd, Katikireddi Srinivasa, Gray Stuart, Gill Jason, Celis-Morales Carlos, Sattar Naveed, Welsh Paul. (2021) Risk of mortality among inpatients with COVID-19 and type 2 diabetes: national data from Kuwait. Endocrinology, Diabetes and Metabolism, 4(4), e00287. (doi: 10.1002/edm2.287)

Alabdullah Lulwa, Welsh Paul, Logue Jennifer. A predictive model for successful medium-term weight loss in people with type 2 diabetes engaging in weight loss interventions. (in preparation)

Alabdullah Lulwa and Welsh Paul. A predictive model for medium-term weight loss in a general population with overweight or obesity – a UK Biobank study. (in preparation)

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Presentation

The abstract below has been accepted for presentation in the 58th Annual Meeting of the European Association for the Study of Diabetes to be held in Stockholm, Sweden 19 – 23 September 2022:
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Author Contributions

Chapter 2: JL was study PI. LA wrote cover letters, a Data Protection Impact Assessment (DPIA), the content of the questionnaire, a study leaflet, a study protocol, a lay summary for public health, the statistical analysis plan, and a submission for ethics. LA also conducted the literature review and wrote the chapter and draft manuscript for the method paper of the POWER study "Predictors of WEight Reduction (POWER) – A hypothesis-driven prospective cohort study". JL checked and critically revised all documents and the first draft. PW checked statistical analyses.

Chapter 3: JL was study PI and obtained approval for data linkage from NHS GGC. LA wrote the statistical analysis plan, cleaned the data, conducted the statistical analyses and wrote the chapter and draft manuscript for "A predictive model for successful medium-term weight loss in people with type 2 diabetes engaging in weight loss interventions". PW checked statistical analyses and critically revised the first draft and the chapter. JL checked and critically revised the chapter.

Chapter 4: JL was study PI. LA started a new application to access the dataset from Look AHEAD and obtained approval. JL requested and obtained an ethical approval waiver from the College Of Medical, Veterinary & Life Sciences at the University of Glasgow. LA wrote the statistical analysis plan, cleaned the data, conducted the statistical analyses and wrote the chapter and draft manuscript for "A predictive model for successful medium-term weight loss in people with type 2 diabetes engaging in weight loss interventions". PW checked statistical analyses and critically revised the first draft and the chapter.

Chapter 5: JL was study PI. LA started a new application to access the dataset from WRAP and obtained approval. LA wrote the statistical analysis plan, cleaned the data, conducted the statistical analyses and wrote the chapter and draft manuscript for "A predictive model for successful medium-term weight loss in people with type 2 diabetes engaging in weight loss interventions". PW checked statistical analyses and critically revised the first draft and the chapter.

Chapter 6: PW was study PI. PW requested and obtained access to the UK Biobank dataset. LA wrote the statistical analysis plan, cleaned the data, conducted the statistical analyses and wrote the chapter and draft manuscript for "A predictive model for medium-term weight loss in a general population with overweight or obesity – a UK Biobank study.". PW checked statistical analyses and critically revised the chapter.

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Author's Declaration

I declare that this thesis research and written works were done by myself under my supervisors guidance. This thesis work has not been submitted previously for any degree (neither the University of Glasgow nor any other institutions).

Lulwa A A D Alabdullah
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Definitions/Abbreviations

ACC	American College of Cardiology
ADHD	Attention-deficit/hyperactivity disorder
AHA	American Heart Association
AHI	Apnoea-Hypopnoea Index
AIC	Akaike's Information Criteria
AUC-ROC	Area Under the Curve – Receiver Operating Characteristics Curve
BCT	Behavioural Change Treatment
BDI	Beck Depression Inventory
BES	Binge Eating Scale
BI	Brief Intervention
BIC	Bayesian Information Criteria
BMI	Body Mass Index
BNF	British National Formulary
BOCF	Baseline Observation Carried Forward
BP	Bodily Pain
BPD	Biliopancreatic diversion
CAPI	Computer-assisted personal interview
CBT	Cognitive Behavioural Therapy
CDC	Centers for Disease Control and Prevention
CES-D	Center for Epidemiologic Studies-Depression Scale
CHI	Community Health Index
CP12	Commercial Programme for 12 weeks
CP52	Commercial Programme for 52 weeks
CVD	CardioVascular Disease
DBP	Diastolic Blood Pressure
DES	Diabetes Support and Education
DEXA	Dual-Energy X-ray Absorptiometry
DPP	Diabetes Prevention Program
DPP-4	Dipeptidyl peptidase-4
DSMB	Data and Safety Monitoring Board
EASO	European Association for the Study of Obesity
EQ VAS	EuroQol Visual Analogue Scale
EQ-5D	EuroQol five-dimensional questionnaire
FWL	Further Lifestyle Advice
GCWMS	NHS GGC Weight Management Service
GH	General Health
GLP	Glucagon-like peptide-1
GP	General Practitioner
HbA1C	Haemoglobin A1C
HDL	High-Density Lipoprotein
HRQOL	Health-Related Quality of Life

ILI	Intensive Lifestyle Intervention
IQR	Interquartile range
IWQOL	Impact of Weight on Quality of Life
LAGB	Laparoscopic adjustable gastric banding
LCD	Low-Calorie Diet
LDL	Low-Density Lipoprotein
LOCF	Last Observation Carried Forward
LookAHEAD	Look Action for HEalth in Diabetes
MAR	Missing At Random
MCAR	Missing Completely At Random
MCS	Mental Component Summary
MET	Maximal Metabolic Equivalents
MH	Mental Health
MI	Multiple Imputations
MICE	Multiple Imputations by Chained Equations
MNAR	Missing Not At Random
MRC	Medical Research Council
MVLS	College of Medical, Veterinary and Life Sciences
NA	Not Applicable
NHS	National Health Service
NHS GGC	National Health Service - Greater Glasgow and Clyde
NICE	National Institute for Health Care Excellence
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NOCB	Next Observation Carried Backward
NPV	Negative Predictive Value
OR	Odds Ratio
OSA	Sleep apnoea
PCS	Physical Component Summary
PF	Physical Functioning
PICO	Patient/Population, Intervention, Comparison, Outcomes
POWER	Predictors OF WEight Reduction
PPV	Positive Predictive Value
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomised Control Trials
RE	Role-Emotional
RP	Role-Physical
RR	Risk Ratio
RYGBP	Roux-en-Y gastric bypass
SBP	Systolic Blood Pressure
SCI - DC	Scottish Care Information - Diabetes Collaboration
SD	Standard Deviation
SF	Social Functioning
SGLT2	Sodium/glucose cotransporter 2
SIGN	Scottish Intercollegiate Guidelines Network

SIMD	Scottish Index of Multiple Deprivation
SNP	Single Nucleotide Polymorphisms
SQL	Structured Query Language
SU	Sulfonylureas
T2MD	Type 2 Diabetes Mellitus
TFEQ	Three Factors Eating Questionnaire
TG	Triglycerides
TOS	The Obesity Society
TRE-MORE	TREatment MOtivation and REadiness
TSRQ	Treatment Self-Regulation Questionnaire
TV	Television
TZD	Thiazolidinediones
UKB	UK Biobank
USA	United States of America
USB	Universal Serial Bus
VLCD	Very-low-calorie diets
VPN	Virtual Private Network
VT	Vitality
WC	Waist Circumference
WHO	World Health Organisation
WLM	Weight Loss Maintenance
WRAP	Weight loss Referrals for Adults in Primary care
WW	Weight Watchers
YFAS	Yale Food Addiction Scale

1 General introduction

1.1 Obesity

1.1.1 Prevalence

There has been a remarkable increase in the prevalence of overweight and obesity in almost all countries in recent decades. Worldwide, the prevalence of obesity tripled between 1975 and 2016 (WHO 2018). It is reported by the World Health Organization (WHO) that there is a global obesity epidemic. In 2016, worldwide, adults (age ≥18) with body mass index (BMI) ≥25 (overweight or obesity) include more than 1.9 billion people, which accounts for 39% of people (39% of men and 40% of women). Of the total number of people living with a BMI in the overweight range, more than 650 million adults are living with obesity, which accounts for around 13% (11% of men and 15% of women) (WHO 2018). The world obesity federation estimated the prevalence of obesity in the adult population for 2025; the population who are living with overweight or obesity will rise to 2.7 billion and 1 billion, respectively, and 177 million of the adults population will have severe obesity with associated serious health problems (World Obesity Federation 2015).

The United Kingdom (UK) has the highest prevalence of obesity in Europe, with 27.8% of UK adults affected (2021 population of 68,207,116) (World Population Review 2021). Prediction for the prevalence of obesity trends in the UK showed that by 2025, the percentages of males and females who live with obesity will be 47% and 36% respectively (McPherson, Marsh, and Brown 2007). By 2050, this will rise to 60% and 50%, respectively. Moreover, by 2050, the proportion of the adult population who are within the healthy BMI range (18.5 – 25kg/m^2) will be as low as less than 10% for men and less than 15% for women. The health survey for England in 2019 showed that in total 64% of adults were living with either overweight or obesity (Health Survey for England 2019). The prevalence of obesity was slightly higher among females (29%) than males (27%). The national survey for Wales in 2019-2020 showed that 61% of adults were living with either overweight or obesity and of the total number of people who are within the overweight BMI range, 25% live with obesity (National Survey for Wales 2020). In 2019, the Healthy Ireland Survey showed that 37% of the adult population was living within overweight BMI ranges, while 23% were living within obesity BMI ranges (Healthy

Ireland Survey documents 2019). Men were more likely to live with overweight or obesity than women, 66% and 55%, respectively.

The COVID-19 pandemic has affected the prevalence of obesity. Based on the Scottish Health Survey between August to September 2020 (this report was conducted during the COVID-19 pandemic) changes to body weight were reported by more than half of adults (57%) (time: between the start of lockdown-date of the interview), 39% increased, 18% decreased and 43% remained the same. The increase in weight was more likely to be reported by women (43%) than men (34%).

1.1.2 Assessment and definition

According to WHO *"Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health"*. The human adipocyte is a specialised adipose tissue, which stores fat (Deurenberg and Yap 1999; Malone and Hansen 2019). The main function of the adipocytes is to store energy and release it to the body when needed, which creates body energy homeostasis. (Song and Deng 2020). The adipocytes in individuals living with obesity become enlarged due to the constant energy excess, which disrupts the body's energy homeostasis (Song and Deng 2020).

There are direct and indirect measures that can assess the level of adiposity in the body.

1.1.2.1 Direct measures:

The most accurate direct measure, and the least used in the clinic, is the dual-energy x-ray absorptiometry (DEXA) and imaging techniques (Adab, Pallan, and Whincup 2018). The lack of clinical use is due to their inconvenient size (i.e. large and heavy), high cost of the machine and absence of standardised thresholds to identify the severity of the risk, which makes it difficult to be used in routine clinical settings.

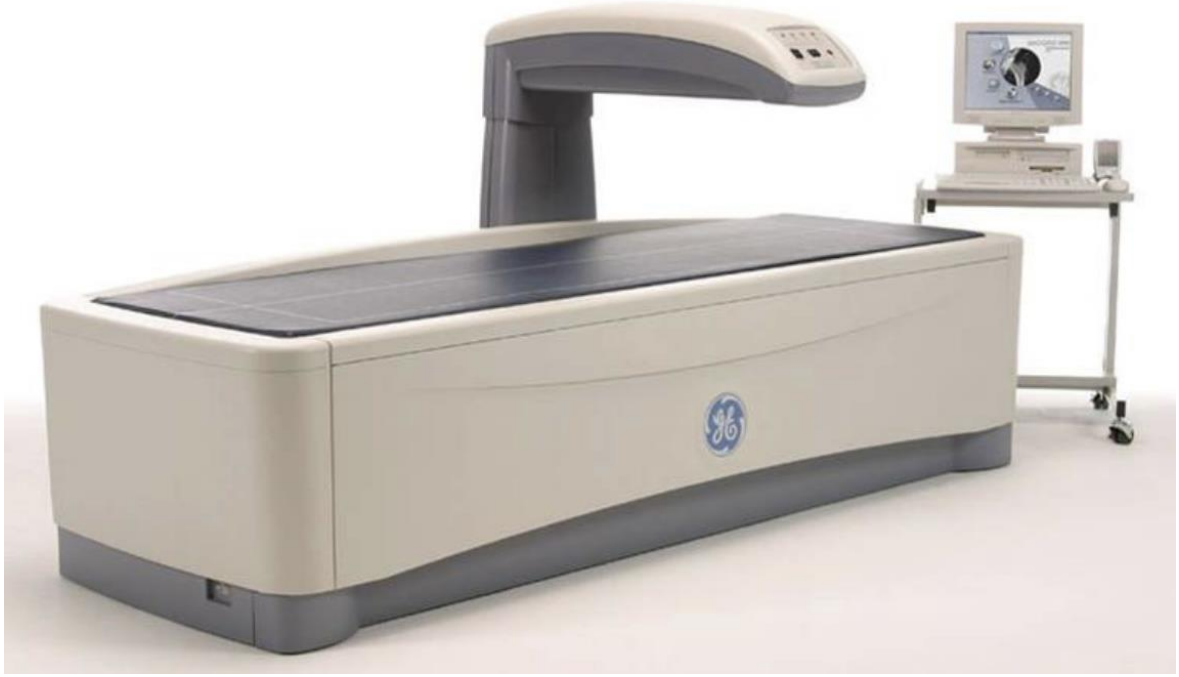

Figure 1-1: The size of dual-energy x-ray absorptiometry (DEXA) adopted from (www.doonmri.com).

1.1.2.2 Indirect measures:

Indirect measures that assess the level of adiposity are commonly used in the clinic as an alternative to DEXA. This includes BMI and waist circumference (WC) (Gažarová, Galšneiderová, and Mečiarová 2019). These measures in addition to the existence of comorbidity in patients within the overweight or obesity BMI ranges are used in the clinic to estimate the health risk status (Kushner 2012).

Body Mass Index (BMI):

BMI is a screening method used by practitioners to classify patient anthropometric health (an index of general adiposity). It is calculated by using individual weight in kilograms and dividing it by the square height in meters for the same individual (kg/m^2) (World Health Organization 2000). The advantage of this method is that it is inexpensive, straightforward and has a standardised threshold for the degree of risk (Adab, Pallan, and Whincup 2018). Regardless of the strong correlation between BMI and the gold standard body fat measures (i.e. DEXA), BMI has a drawback in that it cannot differentiate between lean and fat mass, which may ultimately result in misleading results of the distribution of the body fat (Lee et

al. 2018). Table 1-1 demonstrates the BMI categories and their correlated classifications of body weights.

Table 1-1: Classification of Body Mass Index (BMI) categories in adults (World Health Organization 2000).

BMI	Classification
< 18.5	Underweight
18.5-24.9	Normal weight
25.0-29.9	Pre-obesity or overweight
30.0-34.9	Obesity class I
35.0-39.9	Obesity class II
≥ 40.0	Obesity class III

Waist Circumference (WC):

WC is a tool used to estimate the abdominal fat amount, which is an effective tool for assessing central obesity (Yumuk et al., 2015). Cardiovascular risk factors are associated with WC and WC predicts cardiovascular risk better than BMI (Pazin et al. 2020). The International Diabetes Federation proposed different thresholds for different ethnicities (refer to Table 1-2) (Alberti, Zimmet and Shaw, 2006). The normal value of WC for Europeans is less than 94 and less than 80, for men and women, respectively.

Based on North American waist circumference values (refer to Table 1-2), central obesity is associated with major chronic diseases and all-cause mortality (independent of BMI) (Zhang et al. 2008). It is revealed from a prospective cohort study, that central adiposity is associated with the systemic inflammation of chronic diseases independent of the overall adiposity (Wedell-Neergaard et al. 2018).

Table 1-2: Ethnic-specific values for waist circumference as a measure of central obesity (Alberti, Zimmet, and Shaw 2006).

Country/Ethnic Group	Waist Circumference, cm	
	Male	Female
North American	≥ 102	≥ 88
European	≥ 94	≥ 80
South Asian/Chinese	≥ 90	≥ 80
Japanese	≥ 85	≥ 90
Ethnic South and Central American	Use South Asian recommendations	Use South Asian recommendations
Sub-Saharan Africans	Use European recommendations	Use European recommendations
Eastern Mediterranean and Middle East (Arab) populations	Use European recommendations	Use European recommendations

1.1.3 Origin

The origin of obesity is multifactorial, it involves genetic, environmental and behavioural factors (Lajunen et al. 2009; Piché et al. 2018). Due to the complex and multifactorial origin of obesity (Jih et al. 2014), it's been difficult to identify one specific major cause of the disease.

1.1.3.1 Energy balance dysregulation

At the core of the cause, long-term energy dysregulation (energy intake > energy expenditure) results in a person developing overweight or obesity (Heymsfield and Wadden 2017). In weight gain, energy intake involves excessive food intake beyond the need of the body while energy expenditure frequently involves low physical activity and low basal metabolic rate (Kimura et al. 2014). Metabolites, hormones, and neuropeptides are the regulatory pathways that are involved in regulating the energy balance (Greenwood, Bloom, and Murphy 2011).

1.1.3.2 Environment

Environmental factors that cause people to develop obesity are: 1) economic growth that raises the food supply in the country and food consumption by the population (e.g. high-calorie food and a large proportion of processed food, known as the epidemiological shift) (Hall et al. 2009; Popkin and Hawkes 2016). 2) Lack of physical activities in lifestyle circumstances (e.g. increasing sedentary behaviours like watching TV and using electronics, and low physical activity

occupations) (European Journal of Pediatrics 2000; Church et al. 2011). 3) Increased use of weight-gaining drugs (Apovian et al. 2015). 4) Poor sleeping behaviours which exacerbate the other issues (McAllister et al. 2009).

1.1.3.3 Genetic and early life factors

To explore the extent of genetic influences on medical, psychological disorders and behaviours, twin design studies are used. The statistical concept of heritability used in twin, family and adoption studies showed that 40 to 70 percent of the variation in BMI was explained by genetic causes (Bray et al. 2016). Common genetic polymorphisms such as *FTO* and *MC4R* seem to act through appetite regulation although even these commonly cited polymorphisms individually explain limited variability in adiposity (Cha et al. 2011).

1.1.4 Adverse consequences

Regardless of the origin of obesity, having a raised BMI subjects individuals to several health risks (Hruby and Hu 2015; Heymsfield and Wadden 2017). Excess body weight, especially obesity, increases the risk of non-communicable diseases such as developing type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), sleep apnoea, and musculoskeletal disorders, etc (World Health Organization 2022). Therefore, there is a linear relationship between the prevalence of obesity and the number of individuals suffering from T2DM and other risk factors (Ginsberg and MacCallum 2009). The adverse consequences of obesity are related to the accumulation of intra-abdominal and ectopic fat (i.e. the higher the amount of intra-abdominal and ectopic fat, the more the individual is prone to a high risk of metabolic and cardiovascular diseases) (World Health Organization 2000; Zhu et al. 2002; Sattar and Gill 2014).

1.1.4.1 Clinical

Type 2 Diabetes Mellitus (T2DM):

Type 2 diabetes is a metabolic disorder of relative insulin insufficiency. It is caused by either impairment of the pancreatic ß-cells to secrete insulin or the defect in the response of the insulin-sensitive tissues to insulin (Roden and Shulman 2019). Average glycaemic control (within the past 2-3 months) can be obtained through

the analysis of glycated haemoglobin (HbA1c) in blood. As standard diabetes care, diagnosis and monitoring of diabetes status are obtained through testing the HbA1c (Roden and Shulman 2019).

Currently, in the UK, there are 3.9 million people diagnosed with diabetes, of which 90% of them have T2DM (Diabetes UK 2020). The total number may rise to 4.8 million including those with undiagnosed diabetes. UK data showed a sharp increase in the number of people who have T2DM (≥ 100,000). It is suggested that by 2025 and at this rate the number will reach 5.3 million people with T2DM living in the UK (5.3 million by 2025).

There are several risk factors for diabetes, although the strongest is living with overweight or obesity. Even though not all individuals with T2DM live within overweight or obesity BMI ranges, 80-85% of the time excess body weight is responsible for developing T2DM (Diabetes UK 2020).

Factors which determine how obesity increases the risk of T2DM are the degree of disease and the location of fat accumulation. The more the body contains an excess of fat in the upper body (including visceral adiposity), the more the individual is prone to metabolic syndrome, T2DM, and CVD (Brettfeld et al. 2016; Parmar 2018).

Cardiovascular disease:

Above the healthy range, an increase in BMI is associated with an increase in the risk of CVD (Mittendorfer and Peterson 2008; Iliodromiti et al. 2018). In 2020, a Mendelian Randomisation (MR) study was done to explore the causal relationship between a high level of BMI and the increased risk of myocardial infarction (Adams, Jacocks, and Guo 2020). Independent BMI- associated single nucleotide polymorphisms (SNPs) were identified (n=72) as instruments. The results were OR for MI per 1-SD increase in BMI (or 4.5 kg/m^2): +0.8% (95% CI: 0.3%-1.2%. This infers that there is a positive causal effect of BMI on the risk of myocardial infarction.

The biological mechanism behind how obesity is causally linked to myocardial infarction and CVD is not fully understood. Regardless, it is commonly suggested through MR tests that having a higher BMI would result in hypertension (Lyall et

al. 2017; Dale et al. 2017). It is reported in these studies that the results were independent of potential confounders (e.g. age, sex, smoking and alcohol intake).

1.1.4.2 Psychosocial and Quality of life (QoL)

There are several observational studies done to investigate the relationship between BMI and QoL. The trends that were seen when analysing the continuous variable of BMI with QoL were inverse U-shaped (Laxy et al. 2018) and inverse linear relationships (Daviglus et al. 2003). In the case of the categorical variable of BMI, results showed that as the level of obesity increased the QoL decreased/impaired (Jia and Lubetkin 2005; Ul-Haq et al. 2013). The heterogeneity in the reported shape of associations was mainly due to the measure of QoL used in the study and the specific dimension the study was interested in (Zawisza et al. 2021). Commonly studies use any of the Short-Form (SF-36) Health Survey (Brazier et al. 1992) or other instruments of QoL/ Health-Related Quality of Life (HRQOL), including physical and mental health component summaries (PCS-12, MCS-12) (Ware, Kosinski, and Keller 1996), EuroQol five-dimensional questionnaire (EQ-5D) (Brooks and EuroQol Group 1996), EuroQol Visual Analogue Scale (EQ VAS) (EuroQol Group 1990), or the Impact of Weight on Quality of Life (IWQOL), which is a specific instrument that measure obesity-related QoL (Ul-Haq et al. 2013). These measurements are based on different component and weighting, and therefore it is perhaps unsurprising that different studies report different shapes of associations when different outcome measures are used.

A study done by Kearns et al. aimed to investigate the relationship between BMI and HRQoL (i.e. EQ-5D) (Kearns et al. 2013). In this study, a dataset from South Yorkshire Cohort (SYC), a large observational study (recruiting 20,000 participants) and uses a cohort multiple randomised controlled trial (RCT) design (Relton et al. 2011). Data on socio-demographics, socio-economics, co-morbidities, health resource use and HRQoL was available in the dataset, which allows testing the association between BMI and HRQoL with the possibility of testing the confounder/mediator factors that might impact the association. Results showed that having a BMI of 25 or more (i.e. individuals living with overweight or obesity) was associated with poorer HRQoL. A 1kg/m^2 BMI increase is associated with 3%, 8%, and 6% increase in odds of anxiety/depression, mobility, and self-care, usual activities, pain/discomfort, respectively. It is also revealed

that long-term conditions, including diabetes, heart disease, osteoarthritis and high blood pressure mediate the association between high BMI and all EQ-5D dimensions. There is preliminary evidence that high BMI causes a reduction in HRQoL, but a causal research design is needed to establish a true causal relationship.

A two-sample, bidirectional mendelian randomisation study was conducted to explore the existence of a causal relationship between subjective wellbeing, which includes subjective happiness and life satisfaction, and adiposity (Wootton et al. 2018). Results showed that high BMI (+1 SD) causes lower subjective wellbeing (β=−0.045 SD, 95% CI: −0.084, −0.006), which is controlled by lower satisfaction with health scores (β=−0.035 SD, 95% CI: −0.043, −0.027). In this study, the confounding effect was also explored between observed and genetic scores of BMI and the baseline confounders. In contrast, there was no effect of wellbeing on BMI or other cardiometabolic health measures. Although BMI is an indirect measure of adiposity, it is the only measure that showed a causal relationship with subjective well-being (Waist-to-Hip ratio, WC, or body fat percentage did not show any causal relationship).

1.1.4.3 Other diseases

Cancer:

An older systematic review was done to investigate the strength of the association between BMI and cancers (Renehan et al. 2008). This was explored among different sex and ethnicities. Results showed that a 5 unit (kg/m^2) increase in BMI revealed a strong association with oesophageal adenocarcinoma (RR: 1·52, p<0·0001) and thyroid (RR: 1·33, p=0·02), colon (1·24, p<0·0001), and renal (RR: 1·24, p<0·0001) cancers in men. While it was strongly associated with endometrial (RR: 1·59, p<0·0001), gallbladder (RR: 1·59, p=0.04), oesophageal adenocarcinoma (RR: 1·51, p<0·0001), and renal (RR: 1·34, p<0·0001) cancers in women. In men, a weaker association was seen (RR <1·20) between high BMI and both rectal cancer and malignant melanoma, with similar for postmenopausal breast, pancreatic, thyroid, and colon cancers in women and leukaemia, multiple myeloma, and non-Hodgkin lymphoma in both sexes. Among different populations (i.e. North America, Europe and Australia, and the Asia–Pacific region) the associations were similar. Regardless, in Asia–Pacific populations, results showed

that there was a stronger association between high BMI and premenopausal (p=0·009) and postmenopausal (p=0·06) breast cancers.

A recent study using a dataset from UK Biobank and large international consortia was done to investigate the causal relationships of body mass index, fat mass index, fat-free mass index, and height with site-specific cancer risk (Vithayathil et al. 2021). The main study findings were 1) BMI has a causal risk factor for some and not all cancers. 2) Based on the study categorisation of cancer (digestive system cancers versus non-digestive system cancers), BMI has a causal role in increasing the risk of digestive system cancers. 3) BMI has a role in sex-specific cancers with inconsistent directions of effect. 4) Consistent risk-increasing effects on overall and site-specific cancers were seen from an increased individual height.

Sleep apnoea (OSA):

Respiratory disorders including obstructive sleep apnoea (OSA) are common among people who live within overweight or obesity BMI ranges. Being older, male and having a BMI of 25 or more increases the chances of developing OSA (Senaratna et al. 2017). A systematic review and meta-analysis were conducted to identify the strength of the association between BMI scores of 25 or more and OSA, and this was explored in children and adult populations (Dong et al. 2020). Two main results were revealed from this study: 1) high BMI score was associated with increasing the risk of OSA in adults (Mean Difference = 4.67; 95% CI 2.37–6.98; p<0.0001), but not in children (Mean Difference= 0.05; 95% CI -0.33–0.43; p=0.80). 2) Using the apnoea-hypopnoea index (AHI), which is an index designed to inform about the severity of OSA. Results showed that comparing people who are living within obesity BMI ranges and those of normal weight, the individual living within the obesity BMI ranges group was significantly associated with an increased risk of AHI compared to the normal weight group in children and adults (Mean Difference = 12.29; 95% CI 8.46–16.11; p<0.00001) and (Mean Difference = 12.11; 95% CI 4.35–19.85; p=0.002), respectively.

Musculoskeletal conditions:

There is a bidirectional relationship between musculoskeletal pain and obesity (Cameron et al. 2012). In one direction, musculoskeletal conditions started with physical pain in the joints, which is a primary cause of disability (Storheim and Zwart 2014). As a result, physical activity will be avoided due to physical pain,

which eventually will result in gaining weight (Ferguson et al. 2013). On the other hand, having an excessive amount of weight gain will lead to obesity, which will eventually increase physical disability due to musculoskeletal pain (Cameron et al. 2012). One systematic review and meta-analysis study has looked at the relationship between body fat and musculoskeletal pain (Walsh et al. 2018). In this meta-analysis study, 14 studies were included. Cross-sectional studies results revealed that: 1) total body fat mass (BFM) was significantly associated with widespread pain (Standardised mean differences: 0.49, 95% CI: 0.37–0.61, p<0.001). 2) High body fat percentage was associated with single-site pain including low-back pain and knee pain when compared to control groups (Standardised mean differences: 0.34, 95% CI: 0.17–0.52, p<0.001 and Standardised mean differences: 0.18, 95% CI: 0.05–0.32, p=0.009), respectively. 3) Single-site pain, including foot pain, was positively associated with a higher fat mass index, although the association was weak (Standardised mean differences: 0.05, 95% CI: 0.03–0.06, p<0.001). Also, longitudinal studies (consisting of 8 studies) were explored in this study, although not part of the meta-analysis (unsuitable) and there was conflicting evidence regarding the association between measures of body fat and single-site pain (e.g. low-back, knee and foot). In general, those studies indicated that having a high level of body fat will increase the risk of developing joint pain.

1.1.4.4 Economic burden

The impact of overweight and obesity is not limited to health, it also affects economic factors and has a significant impact on health and care resources. Tackling obesity is problematic due to the multifactorial origin of the disease and the number of risk factors associated with obesity. This makes quantifying the cost of preventing/treating obesity to reduce the cost challenging.

The total cost of obesity reported by NHS Scotland was estimated as 60%, 30% and 10% of actual spending for prescriptions, hospital care, and GP consultations, respectively (Walker 2003). This accounted for a total of £171 million (before adjusting for inflation), or £223 million (after adjusting for inflation). It is not surprising that most of the budget specified for managing obesity is for obesity-related diseases (e.g. T2DM and CVD, etc.), rather than obesity disease management (about 2% of the total amount), since the comorbidities associated

with obesity are far more complex and likely to be managed with pharmacology and surgery (The Scottish Parliament 2015). It is worth mentioning that the estimated costs of obesity and obesity-related diseases (even after adjusting for inflation) are underestimated since the rate of obesity is increasing every year in Scotland and all over the world.

The Scottish Government (2010a) reported a total of £312 million in 2007/08 (in today's price this is £363 million) from health care costs were directed for the management of overweight and obesity and their complications (combined) (Butland et al. 2007).

Similarly, statistics from NHS England 2006/07 reported a total of £5.1 billion from health care costs were directed for overweight and obesity management (combined) (Scarborough et al. 2011). The proportion of NHS Scotland cost with regard to NHS England cost is approximated to be ≈ £600 million (Adjusting for inflation).

The purpose of these studies is to show the huge demand that overweight and/or obesity and the consequent health problems placed on the health care facilities, resources and costs on a yearly and lifetime basis are alarming recall for preventing the disease.

1.1.5 Mortality

Several studies intend to explore the association between obesity and mortality. Some studies revealed that both low and high BMI categories are associated with an increased mortality rate, which means that the relationship is either an inverse U- or J-shape (Zawisza et al. 2021). Other studies showed that being in the overweight BMI range might have either protective or neutral effects on mortality (Laxy et al. 2018; Aune et al. 2016; Bombak 2014; Cohen-Mansfield and Perach 2011; Orpana et al. 2010). A population-based cohort study (UK population) was done to investigate the association between BMI and all-cause and cause-specific mortality (Bhaskaran et al. 2018). In this detailed study, the authors found that among 3.6 million UK adults above a BMI of ≥ 25 kg/m^2, the hazard ratio per 5 kg/m^2 increase was 1·21 [95% CI 1·20–1·22]. Life expectancy (at age 40) was 4.2 years and 3.5 years shorter in men and women living within obesity BMI ranges,

respectively, when compared to men and women living within normal BMI ranges. Also, 4.3 years and 4.5 years shorter for men and women living within underweight ranges respectively, when compared to men and women with normal weights.

1.2 Management

The burden has increased on the health care system and the economy due to an increase in obesity-related morbidity. The management of obesity in the adult population is an example of a major public health problem (Y. C. Wang, McPherson, et al. 2011). Regardless of the huge efforts given by public health professionals, it is still challenging to achieve and maintain beneficial weight loss (Jensen, Ryan, Apovian, Ard, Comuzzie, Donato, Hu, Hubbard, Jakicic, and Kushner 2014; Australian Government National Health and Medical Research Council 2013). It is stated by Stubbs et al that *"weight management is a dynamic process, with a pre-treatment phase, a treatment phase (involving process) and a post-treatment maintenance or relapse period"* (J. Stubbs et al. 2011).

1.2.1 Multicomponent Lifestyle interventions

The early-stage standard behavioural treatment programs in clinical practice aim to improve dietary habits and increase the level of physical activity (Wing 1996). To get the maximal level of benefits individuals need to commit to these changes and as such to adopt these changes in their behaviours. For this reason, it is challenging for an individual living within the overweight or obesity BMI ranges to adhere to the programmes for the short or long terms (Acharya et al. 2009; Wing 2003).

A systematic review and meta-analysis aimed to explore the effectiveness of interventions provided to minimise or prevent overweight or obesity and improve diet or physical activity (Stephens, Cobiac, and Lennert 2014). The components included in the interventions provided across different settings mostly consisted of diet and physical activity. The one that has a significant effect on weight loss was diet-alone interventions, while physical activity alone showed a less significant effect on weight loss when compared to diet-alone or multicomponent interventions. The most significant benefit the individual living with overweight or obesity gets to lose weight is cognitive behavioural therapy (CBT) or

psychological therapy when added to the interventions (NHS 2022). This type of intervention is known as the lifestyle modification programme, which consists of diet, physical activity or exercise, and CBT.

Using lifestyle modification interventions has several benefits: 1) individuals attending those programmes achieved on average 7–10% weight loss. 2) prevention or reversal of obesity-related comorbidities (Thomas Wadden et al. 2012b; Baker et al. 2011). Although the lifestyle modification programmes showed a positive result for weight loss, it is still difficult to generalise study results due to the bias of high attrition rates (Jensen, Ryan, Apovian, Ard, Comuzzie, Donato, Hu, Hubbard, Jakicic, and Kushner 2014; Franz et al. 2007), and the considerable rebound rate observed during long-term follow-up (Thomas Wadden et al. 2012b; Barte et al. 2010). The drawbacks of this type of intervention are: 1) poor adherence (Burgess, Hassmen, and Pumpa 2017) 2) high dropout rate (Moroshko, Brennan, and O'Brien 2011a) 3) failure to lose significant weight 4) failure in maintaining the amount of weight loss (i.e. weight regain) (Cruwys et al. 2020).

The National Institute for Health Care Excellence (NICE) guidelines suggest physicians should use their clinical judgements alongside measurements (BMI & WC) to identify the degree of overweight or obesity (NICE 2022). Accordingly, they can prescribe a suitable intervention plan for each patient. There are several interventions for weight management of patients with obesity, including behavioural change treatments (BCTs), exercise, diet, bariatric surgery, and pharmacotherapy. The level of intervention varies according to the degree of overweight or obesity and the conjunction of comorbidities (i.e. the higher the comorbidities in people living with overweight or obesity, the higher the level of intervention). It is recommended by all guidelines to use multicomponent lifestyle interventions to treat individuals within overweight or obesity BMI ranges.

In the UK, there are two main guidelines, which are developed by NICE (NICE 2022) and the Scottish Intercollegiate Guidelines Network (SIGN 2010). The guideline used in Europe is the European Guidelines for Obesity Management in Adults (Yumuk et al. 2015a). In the United State of America, the guideline used is the US National Institutes of Health and the American Heart Association, the American College of Cardiology, and The Obesity Society (AHA/ACC/TOS) (Jensen, Ryan,

Apovian, Ard, Comuzzie, Donato, Hu, Hubbard, Jakicic, Kushner, et al. 2014). The tables below (Table 1-3, Table 1-4, Table 1-5, Table 1-6) show the weight management intervention programs that are recommended in these guidelines and highlight the multifactorial and escalating nature of the interventions.

Commercial weight management organisations (CWMOs):

Examples of CWMOs include Slimming World and Weight Watchers. Slimming World is recognised by NICE as an organisation following the guidance criteria for best practice (R. Stubbs et al. 2011). An older feasibility study was done and published in 2006, testing how implementing a Slimming World referral service by UK National Health Service (NHS) primary care benefits tackling the rise in obesity (Lavin et al. 2006). Results of the study showed that out of 107 patients 91 were offered 12 group sessions in Slimming World (Free attendance), from which 62 patients completed ≥ 10 sessions. The average weight lost by the completers was 6.4% from the baseline weight. Out of 62 patients who completed the sessions, 34 took additional 12 sessions and achieved an average weight loss of 11.3% from the baseline weight (self-funded). Based on this feasibility study, all adults attempting to change their behaviour to manage their weight were offered a referral from the NHS, as part of the referral scheme (free of charge) (R. Stubbs et al. 2011). As part of expanding the primary care services for the delivery of obesity, a partnership with CWMO is recommended as it has facilities that allow them to provide regular support. Evidence showed that commercial programmes are effective in helping and facilitating the adoption of healthy lifestyle behaviours, such as improving dietary habits and increasing the level of physical activity (Madigan et al. 2014; Ahern et al. 2011a).

Slimming World (www.slimmingworld.com) is a weight management organisation based in the UK that supports the National Institute for Health and Clinical Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) obesity guidance (NICE 2006; SIGN 2010; NICE 2022; Slimming World n.d.). It uses a lifestyle programme with a multi-component approach that is effective in helping people in changing their behaviour by adopting a healthier one, it involves reducing patients weight, preventing weight gaining and supporting longer-term weight loss. Each week, over 13,000 support groups are held across the UK and Ireland (these groups are widely accessible as it takes place in a variety of local

venues at different times and days of the week) (R. Stubbs et al. 2015). It is run by staff who are trained and received regular professional development to support the group environment and it is a self-referral programme.

Counterweight and the Diabetes Remission Clinical Trial (DiRECT):

Counterweight is another commercial weight management organisation, providing a dietary intervention, based on reducing dietary intake by total dietary replacement to 800kCal per day over the short term (3 months). A substantial weight loss to induce and sustain remission of type 2 diabetes is achievable through a structured three-phase programme 1) total diet replacement stage (liquid formula diet), 2) stepped food reintroduction (food-based diet), and 3) weight loss maintenance (Lean, Leslie, Barnes, Brosnahan, Thom, Mccombie, et al., 2018; Lean et al., 2019; Taheri et al., 2020). DiRECT is a cluster-randomized, clinical trial, conducted within routine primary care practice in the North East of England and across Scotland (Leslie et al. 2016). Participants (n=306) diagnosed with T2DM from 49 primary care practices were allocated to either continue the usual guideline-based care or to the Counterweight-Plus weight management programme. The intervention group initiated the weight loss by total diet replacement (for 12-20 weeks), followed by stepped food reintroduction (for 6-8 weeks) and ended with supported weight loss maintenance (for 2 years). Participants in the intervention group showed T2DM remission in 46% and 36% of intervention participants at 12 and 24 months, respectively (Lean, Leslie, Barnes, Brosnahan, Thom, Mccombie, et al., 2018; Lean et al., 2019). In September 2020, in a selected area in England, 5000 participants were selected to be introduced to the programme (DiRECT 2021).

National Health Service Greater Glasgow and Clyde (NHS GGC) weight management programme:

Behavioural weight management programmes are used to treat patients with T2DM and living with overweight or obesity in the NHS, although local provision of services is variable. The aim of such programmes is to assist patients to lose ≥ 5 kg of body weight to improve patients health conditions. The NHS GGC weight management programme consists of three consecutive phases, and is underpinned by a referral to Weight Watchers (NHS-GGC 2018). Details information on the programme can be found in chapter 3 (3.2.1 Intervention).

1.2.2 Bariatric surgery

Bariatric surgeries such as standard Roux-en-Y gastric bypass (RYGBP), Sleeve Gastrectomy, biliopancreatic diversion (BPD), and laparoscopic adjustable gastric banding (LAGB) have been the most effective way to reduce weight for individuals living with morbid obesity, and also can maintain weight loss for long-term (Wolfe, Kvach, and Eckel 2016). It is highly recommended to use bariatric surgery for individuals living within morbid obesity BMI ranges (BMI $\geqslant$ 40 kg/m^2) and severe obesity BMI ranges (BMI between 35.0-39.9 kg/m^2) with the co-existence of obesity-related comorbidities (NICE 2022). Despite the high cost of these surgeries, it is beneficial to use them in patients with more severe obesity for their proven effect of remission of T2DM and for minimising the possibility of developing a new case of T2DM (Gulliford et al. 2016).

1.2.3 Pharmacotherapy

It is a form of adjunctive therapy provided for individuals living with obesity (BMI of 30 or more, BMI of 27 or more with co-morbidities) undertaking multicomponent lifestyle interventions to promote weight loss, and it should not be used as replacement therapy (Wharton et al. 2020; Yumuk et al. 2015b; Garvey et al. 2016). Another form of use is to prescribe medications following the interventions (e.g. intensive dietary therapy, intragastric balloons placement, bariatric surgery) to maintain weight loss (Apovian, Garvey, and Ryan 2015; Farina et al. 2012). Due to modest efficacy, safety issues, and the high cost of the medications available, the use of the medications here has been limited (Wharton et al. 2020). More recently it is approved to use semaglutide, which is a glucagon-like peptide-1 (GLP-1) to treat adults with T2DM or T2DM accompanied by cardiovascular disease (doses up to 1 mg administered subcutaneously once weekly) (Food and Drug Administration 2020). In the phase 2 trial, semaglutide was used and it induced weight loss in individuals with T2DM and individuals living with obesity (O'Neil et al. 2018). The efficacy and safety of semaglutide in individuals living with overweight or obesity with or without complications were evaluated in the global phase 3 Semaglutide Treatment Effect in People with Obesity (STEP) (dose of 2.4 mg administered subcutaneously once weekly) (Kushner et al. 2020). A recent study was done by the same research group to test if administering semaglutide at a dose of 2.4 mg once weekly as an adjunct to lifestyle intervention in adults

living with obesity can induce weight loss (Wilding et al. 2021). The results showed that it was associated with sustained and clinically significant body weight loss (>10Kg).

Table 1-3: Weight management intervention programs recommended by NICE guidelines.

NICE (NICE 2022),(NICE 2018),(NICE 2006)	
WLM	• Multicomponent lifestyle intervention. • BCTs, increased PA, decreased sedentary behaviour, reduced energy intake, and improved diet quality.
WLM Duration	• ≥3 months on a weekly basis. • Weight measured every session.
WLM Delivery	• Individualized intervention program. • Via: face-to-face, phone, mail or internet.
Diet	• 600 kcal/day deficit diets. • LCD (800–1600 kcal/day). • VLCD.
Exercise or PA	• Increased overall PA. • 30min/5 times a week of PA. (moderate or higher) • 45–60min/day of PA. (Moderate) if not on diet. • 60–90min/day of activity to maintain weight.
Behaviour	• Modify thoughts, monitor behaviour and progress, set goals, change behaviour (e.g. slow the rate of eating), problem-solving skills and strategic plan for weight maintenance. • Stimulus control phenomena.
Target of weight loss	• Max: 0.5–1 kg/week. • 5–10% weight loss of starting weight.
Failure in Target achievements	• Pharmacological treatment. • Bariatric Surgery.

Abbreviations: WLM, Weight Loss Maintenance; BCTs, Behaviour change treatments; PA, Physical Activity; LCD, Low-calorie diets; VLCD, Very-low-calorie diets.

Table 1-4: Weight management intervention programs recommended by SIGN guidelines.

SIGN(SIGN 2010)	
WLM	• BCTs, increased PA, and improved diet quality.
WLM Duration	• 3-6 months.
WLM Delivery	• Individualized intervention program. • Vis: face-to-face, internet. • Psychological intervention: individual or group-based.
Diet	• 600 kcal deficit. • VLCD. • Reduced energy-dense foods, fast foods, and alcohol intake.
Exercise or PA	• 225-300min/week of PA. (Moderate) ≈ 1,800-2,500 kcal/week.
Behaviour	• Modify thoughts, monitor behaviour and progress, set goals, change behaviour (e.g. slow the rate of eating), problem-solving skills and strategic plan for weight maintenance. • Stimulus control phenomena.
Target of weight loss	• Max: 0.5–1 kg/week. • BMI= 25-35 kg/m^2: 5-10% weight loss. • BMI>35 kg/m^2: >15-20% weight loss.
Failure in Target achievements	• Pharmacological treatment. • Bariatric Surgery.

Abbreviations: WLM, Weight Loss Maintenance; BCTs, Behaviour change treatments; PA, Physical Activity; VLCD, Very-low-calorie diets; BMI, Body Mass Index.

Table 1-5: Weight management intervention programs recommended by European guidelines.

European (Yumuk et al. 2015a)	
WLM	• Lifelong program. • Setting a realistic weight loss goal to decrease health risks. • Improved diet, PA and behaviours. • Pharmacotherapy. • Increased weight loss and maintained weight post-intervention.
WLM Duration	• 5–15% weight loss in 6 months.
WLM Delivery	• Individualized intervention program. • EASO offered education, research initiatives and up-to-date obesity care.
Diet	• 600 kcal deficit. • 500-1000kcal/day reduction of energy intake. • 15–30% reduction of energy intake. • Daily intake of 25 kcal/kg/day.
Exercise or PA	• 150 min/week (moderate aerobic exercise) + 1-3 sessions/week (resistance exercise). • Decreased sedentary behaviours and increased daily living activities.
Behaviour	• CBT.
Target of weight loss	• 0.5–1 kg/week of weight loss • 5–15% of body weight over 6 months. • BMI>35 kg/m^2: ≥20% weight loss.
Failure in Target achievements	• BMI>30 kg/m^2 with co-morbidities: bariatric surgery.

Abbreviations: WLM, Weight Loss Maintenance; PA, Physical Activity; EASO, European Association for the Study of Obesity; CBT, Cognitive Behavioural Therapy; BMI, Body Mass Index.

Table 1-6: Weight management intervention programs recommended by AHA/ACC/TOS guidelines.

AHA/ACC/TOS (Jensen, Ryan, Apovian, Ard, Comuzzie, Donato, Hu, Hubbard, Jakicic, Kushner, et al. 2014)	
WLM	• Comprehensive lifestyle intervention. • BCTs, reduced-calorie in diet, increased PA.
WLM Duration	• Weekly on-site treatment over 6 months.
WLM Delivery	• Individualized intervention program. • Via: individual or group sessions, face-to-face, internet and telephone.
Diet	• The predictor for losing weight is the patient's adherence, regardless of what type of diet the patients undertake.
Exercise or PA	• >150min/week of PA. • 200-300min/week for long-term weight loss. • Resistance training has nothing to do with weight loss. But it may minimize health risks.
Behaviour	• ≥14 sessions in 6 months for patients living with obesity and cardiovascular disease.
Target of weight loss	• 8 kg weight loss in 6 months. • 5-10% weight loss from the initial weight.
Failure in Target achievements	• Pharmacotherapy. • BMI ≥40 kg/m^2 or ≥35 kg/m^2 with co-morbidities: bariatric surgery.

Abbreviations: WLM, Weight Loss Maintenance; BCTs, Behaviour change treatments; PA, Physical Activity; BMI, Body Mass Index.

1.2.4 Patient-centric therapy

According to the Health Foundation person-centred care is described as *"support people to develop the knowledge, skills and confidence they need to more effectively manage and make informed decisions about their own health and health care"* (The Health Foundation 2016). The concept was introduced earlier in certain countries such as Canada (Levenstein et al. 1986). An interest in creating person-centred care as part of the NHS is now evolving in the UK (NHS England 2022). The reason this concept is important is that patients living with overweight or obesity require tailored care that fits their needs and wants (Janke et al. 2016).

An International Framework for Person-Centred Obesity Care is the Canadian 5As. A personalised approach targeting and managing the complex nature of obesity has been developed by the 5As Team Research Program through collaboration between community partners and individuals living with obesity (Asselin et al. 2017). The main aim of the programme is the improvement of primary care services through the prevention and management of obesity (Ells et al. 2022). The 5As of Obesity Management™ approach based on, Ask, Assess, Advise, Agree and Assist (ObesityCanada 2022). In this approach, the individuals living with obesity developed resilience toward their health as the individuals understand the obesity complexity and the 5AsT approach considers the medical and life concerns of individuals (Ells et al. 2022).

1.3 Predictors of intentional weight loss

Despite the fact that there is a significant rise in public health concerns for managing obesity during adulthood (Y. C. Wang, Mcpherson, et al. 2011), it is still challenging to achieve and maintain substantial weight loss (SIGN 2010; Jensen, Ryan, Apovian, Ard, Comuzzie, Donato, Hu, Hubbard, Jakicic, Kushner, et al. 2014). Individuals who are living with obesity start NHS behavioural weight management programmes to lose at least 5 kg of their initial body weight to improve their health condition. Many patients fail to achieve the required weight loss, drop out, or regain that weight after completing the programme. Around 50% of drop out from lifestyle intervention programmes and poor adherence rates of participants are reported by the clinicians. In the clinic, it is hypothesized that the more patients adhere to a lifestyle modification program, the better the

outcome of the treatment (World Health Organization 2003) and the management of obesity (Burke, Wang, and Sevick 2011; Acharya et al. 2009).

Development of highly discriminatory predictive models for intentional weight loss may aid public health efforts to improve the treatment of patients with overweight and obesity. For instance, these models might:
1) Investigate factors associated with and predictive of short and longer term weight loss success would allow potentially causal factors to be highlighted which might interfere with weight loss at the time of treatment and during follow-up. Those factors include patient, process, treatment, behavioural and psychological factors (each is described below).
2) Assess the extent of behavioural change success over the short and longer terms; behavioural change therapy plays a substantial role in the lifestyle modification programme.

Different factors (patient, process, treatment, behavioural and psychological) may be associated with weight loss failure/success in both established and novel interventions, and therefore candidates for predictive models. An outline of the most prominent such factors associated with weight loss (before systematic review) is considered below.

1.3.1 Known patient factors associated with weight loss

Initial BMI:

Although the study of predictors of successful weight loss has been limited, initial BMI as a predictor of future weight loss has been frequently reported (Carraça et al. 2018). In one systematic review, initial BMI was studied in a total of 24 papers, from which ≈ 40% of the studies showed no significant association and ≈ 40% showed a positive association with the outcome (i.e. weight loss and/or maintenance) (Carraça et al. 2018). Results showed that initial BMI had a small but significant effect size at the intervention's end (r = 0.13, 95% CI: 0.02–0.24).

In DiOGenes study, an RCT of an 8-week low-calorie diet (LCD), there was a positive correlation between initial body weight, height, BMI, waist and hip circumference, sagittal abdominal diameter, fat mass and fat-free mass, and sex

(r= 0.62), (r= 0.43), (r= 0.43), (r= 0.48), (r= 0.33), (r= 0.45), (r= 0.35), (r= 0.52), (r= 0.36), respectively, with 8 weeks weight loss (all $p<0.01$) (T Handjieva-Darlenska et al. 2010). After center adjustment in multiple regression analyses, initial body weight explained 21% of the weight loss ($p=0.0001$). It is suggested that in the case of two individuals with the same energy intake, an individual with a higher body mass will lose weight faster than an individual with a lower body mass. This was explained by the greater energy gap in the individuals with higher body mass, which means higher energy expenditure (T Handjieva-Darlenska et al. 2010).

Demographic information:

In an observational study in Canada, 9,498 patients enrolled on Wharton Weight Management Clinic where patients were referred to the service by their family physician. The study aimed to identify factors associated with successful weight loss in a multidisciplinary weight management clinic. Older individuals were more likely to be successful at losing weight (≥ 5% of body weight) when compared to younger people (RR across age ranges from 1.40 to 1.65, $p<0.05$). Black females (RR [95 % CI] = 0.58 [0.37–0.94]) or ethnic minorities females (RR [95 % CI] = 0.66 [0.57–0.94]) were less likely to achieve successful weight loss when compared to White females. Males who have hypertension were less likely to achieve successful weight loss (RR [95 % CI] = 0.57 [0.40–0.81]). No difference in successful weight loss was seen in age, ethnicity, or health conditions after adjusting for treatment time in males or females, suggesting these associations are mediated by adherence (Jiandani et al. 2016a).

An observational study of 1129 participants (318 males and 811 females) engaged in Weight? Plus (WW+), which is an NHS weight management service of 12 -weeks within Shropshire County (England). The study aimed to test the sex differences in losing weight at 12 weeks, 6 and 12 months (Bhogal and Langford 2014a). Findings showed that on average men lost 1.5kg more than a woman (during a 12-week intervention). On average men lost 3kg more than women (from assessment to 6 months). On average men lost 5kg more than women (from assessment to 12 months). Both males and females lost weight during the intervention and maintain the weight loss following the intervention with males having higher weight loss at all time points. This was interpreted by men having a higher baseline weight when

compared to women at beginning of the study. Other reasons may be social norms relating to ideal 'thinness', which increases body dissatisfaction and eating disorders among females, thus greater negative effect on weight (Grossbard, Neighbors, and Larimer 2011; Furnham, Badmin, and Sneade 2002).

1.3.2 Process factors

Process factors include an individual's attendance at programme meetings/appointments, adherence, attrition, completion and being successful in the programme. It is challenging to compare studies available in the literature due to the absence of a standardised definition for each factor (Miller and Brennan 2015). Previous research suggested that the referral rate to weight management programmes varied across primary care services (Logue et al. 2014). Different reasons might explain this behaviour: 1) patients characteristics such as socioeconomic status (Sørensena, Olsena, and Vedsted 2009), 2) practitioner factors such as clinical experience and 3) system factors such as distance to services (O'Donnell 2000; Foot, Naylor, and Imison 2010). These factors might also influence attendance and/or completion of the weight management programme and whether a participant will be successful at the end of the programme or not.

Adherence:

Adherence was defined as *"the extent to which a participant's behaviour in making lifestyle changes coincided with the [intended intervention]"* (Acharya et al. 2009). In one observational study, target achievement of weight loss (5 kg or 5%) was positively affected by ≥80% completion of intervention sessions (Steinberg et al. 2013). In another, if participants (BMI ≥30 kg/m^2) in weight management interventions maintained attendance, a clinically significant weight loss (≥10% weight loss) was more likely to be achieved (at 12 months) (Avery et al. 2016).

It is also common to measure adherence in trials, as it is claimed that better clinical outcomes and management of disease complications were associated with high rates of adherence (Alhassan et al. 2008; Carels et al. 2008; TA Wadden, Crerand, and Brock 2005; Chao et al. 2000). Ideally, adherence to behavioural change programmes should be measured and account for multiple adherence components. Regardless, available studies are limited to a few adherence

components in a trial, such as attendance (Ahern et al. 2017) dietary adherence(Horne et al. 2020), or physical activity adherence (Conroy et al. 2011). In fact, trials are good sources of information but are poor at measuring effectiveness. This is because recruitment is mainly limited to highly motivated participants, which do not represent the general population (Pi-Sunyer 2014). Therefore, there is a shortage of a comprehensive understanding of adherence patterns among people attending behavioural change programmes during intervention and follow-up.

A secondary analysis of a randomized controlled trial (Johnston et al. 2019) was done to test whether adherence predicts achieving 5% to 10% weight loss in Weight Watchers (WW) over 6 months (n= 147). In this study, there were three ways to define adherence: (1) attendance of 24-weekly WW meetings over 6 months; (2) tracked WW member website usage and the number of daily logins, and (3) self-reported WW mobile application usage. Significant findings for 5% weight loss at 6 months were as follows, WW meeting attendance (threshold of 8.5 meetings, AUC= 0.770, CI= 0.654–0.885, $p<0.001$), percentage of website usage and logins (threshold of 45.5 days, AUC= 0.660, CI= 0.534–0.785, $p<0.05$), and percentage of mobile application usage and (threshold of 29 days, AUC= 0.697, CI= 0.562–0.831, $p<0.01$). In this trial, where both mode (i.e. face-to-face and digital) of attendance were assessed, attending group sessions in person were more strongly associated with weight loss than digital attendance. Despite the positive findings of the study, the results can not be generalised due to the generally small sample size, adherence monitoring was limited to 6 months while it is necessary to monitor adherence for a longer period of time to allow adopting in behaviour change.

1.3.3 Treatment factors

Treatment time and frequency:

In the observational study done by Jiandani et al (n= 9,498 patients) as part of the study aims to test factors associated with successful weight loss, it is reported that longer treatment time ($r=0.38$, $p<0.0001$) and more frequent clinical visits ($r= 0.43$, $p<0.0001$) had a positive relationship with greater weight loss (Jiandani et al. 2016a). It is suggested that individuals spending more time in the treatment

(> 6 months) lost more absolute weight than those spending less time (< 6 months) (6.1 ± 10.9 kg versus 2.8 ± 2.3 kg, p<0.0001), (4.4 ± 8.7 kg versus 2.1 ± 4.9 kg, p<0.001), male and female, respectively. Although socioeconomic status (Sørensena, Olsena, and Vedsted 2009) and system factors such as distance to services (O'Donnell 2000; Foot, Naylor, and Imison 2010) may affect weight loss success, this relationship was not explored.

Early weight loss:

A secondary analysis of an RCT of a 10-week dietary intervention of two hypoenergetic diets (Low and High fat diet) at 8 sites in 7 European countries was done to test if early weight loss (first few weeks) is a strong independent correlate of 10 weeks weight loss (Teodora Handjieva-Darlenska et al. 2012). A total of 771 participants of both sexes were included in the analysis. After combing the group and adjusting for centre and age findings showed that male (β= 1.35, p<0.001) and early weight loss in the first week (β= 1.27, p<0.001) were predictors of weight loss at week 10. Sex (β= 0.42, p=0.009) and halfway weight loss "5wk" (β= 1.38, p<0.001) were predictors of weight loss at week 10. Although the prediction model was used in this study to determine the strength of early weight loss in the final weight loss, the follow-up period was short and cannot be applied for a longer follow-up period.

1.3.4 Behavioural factors

Weight loss history:

A systematic review of 66 studies was done to explore the pretreatment factors of weight control in a lifestyle programme for individuals living with obesity (Carraça et al. 2018). Findings showed that 8 of the studies tested fewer previous weight loss attempts factor as a predictor of short and long-term weight loss. In 67% of the studies, having a history of fewer weight loss attempts was associated with a greater probability of weight loss (r = 0.10, 95% CI: 0.05–0.15) although moderate heterogeneity was seen (I^2 = 66%).

Weight loss goals:

An observational study was done using the commercial Slimming World electronic database for members joining from January to March 2012 up to September 2013 (n= 24 457) (Avery et al. 2016), The researchers aimed to test whether setting a weight loss goal at the start of the programme would influence 12 months of weight loss. Setting realistic targets/goals (5–10% weight loss) at the beginning of treatment among individuals living with obesity, showed that the likelihood of those participants to have at least 10% lower weight (at 12 months) was 10 times more than those without targets. One important limitation of this study was the incomplete data of the 12-months weight, which result in a dropping number of participants out of the analysis.

Eating behaviours:

An RCT among 86 Japanese female participants aimed to explore eating behaviour factors associated with the maintenance of weight loss success after completion of group cognitive behavioural treatment (CBT) (Ryoko Sawamoto et al. 2017). Different measures were used: 1) Japanese version of the Center for Epidemiologic Studies-Depression Scale (CES-D) for depression. 2) Binge Eating Scale (BES) for binge eating. 3) Japanese version of the Three Factors Eating Questionnaire (TFEQ) for disinhibition of eating behaviour. 4) Yale Food Addiction Scale (YFAS) for food addiction. It was reported that more weight loss during the intervention (OR: 0.69, 95% CI: 0.54–0.83, p<0.001) (OR: 0.84, 95% CI: 0.72–0.94, p<0.01), low disinhibition score (OR: 0.66, 95% CI: 0.46–0.91, p=0.017) (OR: 0.68, 95% CI: 0.48–0.94, p=0.028), and low food addiction score (OR: 0.51, 95% CI: 0.27–0.89, p=0.017) (OR: = 0.60, 95% CI: 0.34– 1.04, p=0.066) were associated with being successful at maintaining weight loss following the intervention at 12 months and 24 months, respectively. Still, these results were not suitable for generalisation for both sex, as it was limited only to female participants.

Physical activity:

In a secondary analysis of an RCT (DiOGenes study), physical activity was examined to show if it influences weight loss and minimises weight regain. A total of 1,121 participants of both sex were included in the analysis (van Baak et al. 2021). The association between baseline physical activity and weight loss at 8 weeks was positive (r= 0.132, p=0.000), meaning that participants with high baseline physical

activity will lose less weight at 8 weeks. But this was not statistically significant when applying the multiple regression analysis. Although higher baseline physical activity was not associated with subsequent weight loss it was associated with improvements in several cardiometabolic variables. The association between physical activity at 8 weeks and 6 months of weight loss were negative, suggesting that individuals with higher physical activity at the end of 8 weeks were associated with less weight regain or more weight loss. Applying multiple regression analysis showed that 8 weeks of physical activity was significantly associated with 6 months of weight loss (adjusted for body weight at 8 weeks) (B −0.675, p=0.015, N = 421). One major limitation of this study is that physical activity results were based on participants' self-reported questionnaires, which can affect the realiability.

1.3.5 Psychological factors

Social support (e.g. group support, friend and family) is an example of a psychological factor. This factor means keeping participants motivated to continue the programme, achieve the required weight loss goal, and maintain the lost weight. The MedWeight study is a Greek registry of weight loss for people who intentionally lost their weight (≥10%) and either maintain it or regain it in order to assess participants' lifestyle and dietary behaviours that are associated with weight loss maintenance. This registry was used to test the role of social support to distinguish between individuals who maintain weight loss and individuals who regain the weight after losing it (Karfopoulou et al. 2016). A total of 450 volunteers were recruited for the study. Results showed that factors (examined alone) that were significantly associated with being a weight maintainer were family support for exercise (OR= 0.59, 95 % CI 0.42–0.83), friends’ support for exercise (OR= 0.66, 95 % CI 0.48–0.91) and family support for diet (OR= 0.68, 95 % CI 0.49–0.95). In the final model of all tested variables, only exercise support was significant (OR= 0.54, 95 % CI 0.32–0.90). In a model testing combined variables of family and friends’ support, only family support was significant (OR= 0.63 OR, 95 % CI 0.41–0.96). The limitations of this study were that its participants were healthy volunteers, which might have generally healthier lifestyles when individuals living with overweight or obesity and with or without T2DM and this might limit generalisability.

1.4 The importance of using a prediction model

Prediction models are stalactitical methods developed using multivariable regression analysis. It is a combination of two or more variables (known as predictors) that can predict an outcome of interest. They have a prominent role in healthcare research and practice. It is important to use prediction models rather than associations, because prediction models can provide a tool or guidance for decision-making rather than describing relationships between an exposure and an outcome of interest (explanatory study) and understanding phenomena under study as in association models.

1.5 The need for better studies of predictors of intentional weight loss

From the literature, it is obvious that studies of predictors of weight loss have been hampered by heterogeneous definitions, lack of validation, small study bias, and short follow-up periods. Most of the studies available are mainly testing the associations between potential factors and successful weight loss, but not a prediction of successful outcome achievement. There are no current predictors of success at baseline and many people drop out before they complete as not succeeding. Few investigators have considered the issue in the general populations, observational studies of weight loss programmes and randomised controlled trials.

Currently, there is a substantial need for studies to understand why the current programme is not working for patients so that the intervention can be designed. As obesity is a complex disease and is influenced by several factors, there is a need for studies to consider a wide range of predictors (sociodemographic, clinical, behavioural, physical, psychological, and social) in the same settings and context. Also, studies looking at a range of other interventions or alternatives when the programme is not working for patients before dropout are crucial.

First, it would be useful to understand what is the most important factor to know and target before individuals start the weight loss program (at baseline). Second, using a prediction model to identify predictors of successful weight loss. Third, using a prediction model to allow for identifying who will be successful in losing

the required weight under a specific programme, and also who will fail to do so and therefore should be moved to a different intervention. Forth, provide a personalized treatment plan for individuals attending weight management programmes to reduce the medical cost of treating obesity.

1.6 Aims and objectives (pre-COVID-19)

The overall aim of this thesis is to determine predictors of weight loss success in the short and medium term for individuals living with obesity, with or without T2DM. Originally, three studies were planned to fulfil the aim of this thesis:

Study 1: Predictors Of WEight Reduction (POWER) - A hypothesis-driven prospective cohort study.

Aim 1. To identify patient-reported behavioural factors (e.g. psychological, physical activity, eating habits, self-efficacy) and sociodemographic factors that predict successful short-term weight loss in individuals undertaking behavioural weight management programmes.

Objective 1. Conduct a prospective cohort study of participants in a weight management programme (NHS GG&C weight management service). To identify baseline behavioural and sociodemographic factors to develop a predictive model for successful short-term weight loss. A questionnaire for this study was developed by conducting a narrative review of putative predictors of weight loss.

Study 2: Development of a predictive model, for successful short and medium-term weight loss in people with type 2 diabetes attending a weight management programme.

Aim 2. To identify patient factors (e.g. clinical, sociodemographic) and process factors (e.g. attendance) that will predict successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.

Objective 2. Conducting a longitudinal cohort study by using data from people with T2DM and obesity attending an NHS weight management service to identify baseline clinical and process factors to develop a predictive model for successful short (16wk) and medium-terms (3yr) weight loss.

Study 3: Validation of the model developed in study 1 and study 2 (using data from an existing cohort study Action for HEalth in Diabetes (lookAHEAD).
Aim 3. To validate newly found predictive factors of weight loss success obtained from aim 1 and aim 2.
Objective 3. Validating predictors using LookAHEAD data through replicating analysis.

Our hypothesis was that there would be common factors, even in heterogeneous studies, that would at least moderately predict successful weight loss early in programme.

1.7 Effect of COVID-19 and mitigation

Study 1: the plan was to recruit participants for a prospective cohort study. A questionnaire was developed (after literature review to generate hypotheses) with a range of validated questionnaires that had been associated with weight loss in adult patients with obesity and T2DM undertaking behavioural weight management programmes in previous studies. The questionnaire was planned to be administered to participants within a National Health Service Greater Glasgow and Clyde (NHS GG&C) funded commercial behavioural weight management programme (i.e. Weight Watchers). The questionnaire was created in the online survey system (i.e. Webropol), which is under licence by NHS GG&C. Extensive piloting took place to ensure the questionnaire was fully understandable and could be completed in a timely manner. The questionnaire was to be completed at the start of the Weight Watchers programme (i.e. baseline). Weekly weight measurements from the programme were to be collected via the NHS Safehaven (for up to 3 months). These data would have then been used to develop a predictive model for short-term (12wk) successful weight loss.

The study documents were submitted for review by the University Research Governance Office in August 2019. The University's review took longer than the expected time and consequently, official submission to the NHS GG&C Research & Development office was delayed until January 2020. The favourable opinion letter for the study application was received in February 2020 from the Research Ethics Committee (REC). The recruitment was planned to begin at the end of

March 2020. At this time, the COVID-19 outbreak started and the Weight Watchers programme has been suspended, which made recruitment impossible.

As an alternative, a pre-existing dataset from the Action for Health in Diabetes (Look AHEAD) (National Institutes of Health (NIH) 2020) was identified as being available for secondary analysis. It contained equivalent questionnaires/behavioural factors to the one used in the originally planned questionnaire. This remedial work has ensured that the majority original aims of the thesis can still be achieved.

New aims based on mitigation plan:

Study 1: To present the data and process used to derive the questionnaire intended for the POWER study, so that future work can be planned using the questionnaire.

Study 2: as originally planned in section 1.4. Development of a predictive model, for successful short and medium-term weight loss in people with type 2 diabetes attending a weight management programme.
Aim 2: To identify patient factors (e.g. clinical, sociodemographic) and process factors (e.g. attendance) that will predict successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.
Objective 2: Conducting a longitudinal cohort study by using data from people with T2DM and obesity attending an NHS weight management service to identify baseline clinical and process factors to develop a predictive model for successful short (16wk) and medium-terms (3yr) weight loss.

Study 3: Development of a predictive model for medium-term weight loss in people with type 2 diabetes – LookAHEAD randomised controlled trial.
Aim 3. To identify patient-reported behavioural factors (e.g. psychological, physical activity, eating habits, self-efficacy) and sociodemographic factors that will predict successful medium-term weight loss in individuals undertaking intensive lifestyle intervention programmes.

Objective 3. Conducting a secondary analysis of an RCT to identify baseline behavioural and sociodemographic factors to develop a predictive model for successful medium-term (4 years) weight loss

Study 4: Validation of the predictors of weight loss using Weight loss Referrals for Adults in Primary care (WRAP): data from a randomised controlled trial.

Aim 4. To validate clinical and behavioural factors that predict successful medium-term weight loss in individuals undertaking behavioural weight management programmes (from NHS-GCWMS cohort) and in individuals participating in an Intensive Lifestyle Intervention trial (from LookAHEAD cohort).

Objective 4. External validation of predictive factors identified in NHS-GCWMS & LookAHEAD (where such data overlap between studies).

Study 5: A predictive model for medium-term weight loss in a general population with overweight or obesity – a UK Biobank study

Aim 5. To identify sociodemographic, clinical, behavioural, psychological and mental health factors that will predict successful medium-term weight loss in individuals participating in a general population study.

Objective 5. To study predictors of weight loss in a general population of people with overweight or obesity, not known specifically to be engaging in weight loss activities.

2 Predictors of WEight Reduction (POWER) – A hypothesis-driven prospective cohort study

2.1 Introduction

The causes of obesity are multifaceted; a mixture of biological, psychological, socio-cultural, environmental and economic factors (Gortmaker et al. 2011). Those risk factors can be categorised into non-modifiable and modifiable risk factors (Institute of Medicine, Food and Nutrition Board, Committee on Military Nutrition Research, Subcommittee on Military Weight Management, National Academy of Sciences 2003). Non-modifiable, meaning risk factors cannot be changed with intervention, include age, sex, ethnicity, family history and genetics. Modifiable, meaning risk factors can be changed with intervention, includes physical activity levels, eating habits, and environmental and social factors. As discussed by one scientist, "Genes may co-determine who becomes obese, but our environment determines how many become obese" (Veerman 2011). This idea can be applied to other non-modifiable and modifiable factors.

In the United Kingdom (UK), commercial behavioural weight management programmes (e.g. Weight Watchers) are used to manage overweight and obesity privately and in the National Health Service. Although Weight Watchers has shown effectiveness in improving patients' health (Gillies et al. 2007a; Diabetes Prevention Program Research Group et al. 2009), half of patients who attended Weight Watchers had a successful weight loss of 5% or greater (Ahern et al. 2011a; Jebb et al. 2011) while the other half either drop out or fail to achieve 5% of weight loss despite remaining in the programme.

Structured programmes like Weight Watchers and Slimming World are based on education and various behaviour change techniques (e.g. self-monitoring and goal-setting) to promote a healthier diet and a more active lifestyle (Thomas Wadden et al. 2012b; Baetge et al. 2017a). Since behavioural weight management programmes are formed mainly from behavioural components, measuring these factors might help in detecting which behaviour is affecting patients' success in these programmes. This will allow the improvement of weight-management strategies, and may help target the right intervention to the right patient.

2.1.1 Study overview

The current study was divided into three main sections:

1- Literature review: to identify behavioural factors that had an association with successful weight loss at the follow-up were identified. A hypothesis-driven questionnaire was built based on this literature review.

2- Questionnaire development, based on the literature review: factors identified in the previous step were used to build a questionnaire based on validated questionnaires. This is a collaboration project between two PhD projects. The first project is shown in this chapter (the quantitative part, which is developing a questionnaire and building a predictive model). The second project is done by another PhD student (the qualitative part, which is conducting in-depth interviews).

3- Study protocol: a longitudinal cohort study was planned to be conducted. By recruiting patients from behavioural weight management programme (i.e. Weight Watchers). Those patients were planned to be recruited to fill questionnaire developed in this study at the baseline. Patients weight loss for up to 12 weeks will be calculated to predict if baseline behavioural factors are predictors of weight loss success at 12 weeks.

By conducting this study, a strong method to determine who is going to benefit from the behavioural weight management programme at the start of the programme will be developed, using behavioural predictors of successful weight loss. This may improve the current strategy used in Weight Watchers.

2.1.2 Study hypothesis

Baseline sociodemographic (age, gender, socioeconomic status) and behavioural factors (motivation, weight goal, self-efficacy) are predictors of weight loss success at end of treatment/programme (12 weeks). Initially, based on the literature and before conducting the literature review, older age (Svetkey et al. 2014), male (De Vet et al. 2012), least deprived areas (Saelens et al. 2018), greater motivation (Teixeira et al. 2012b), and greater self-efficacy (Byrne, Barry, and Petry 2012) are likely to be important predictors of successful weight loss.

2.1.3 Study aims

1) To identify patient-reported behavioural factors (e.g. psychological, physical activity, eating habits, self-efficacy) and sociodemographic factors that may mediate, or associate and correlate with successful weight loss in the short-term (12 weeks).

2) To test the ability of identified patient-reported behavioural factors and sociodemographic factors to predict successful short-term (12 weeks) weight loss in individuals undertaking behavioural weight management programmes.

2.1.4 Effect of COVID-19 and mitigation

The recruitment was planned to begin at the end of March 2020. At this time, the COVID-19 outbreak started and the Weight Watchers programme has been suspended, which made recruitment impossible.

As an alternative, a pre-existing dataset from the Action for Health in Diabetes (Look AHEAD) (National Institutes of Health (NIH) 2020) was identified as being available for secondary analysis. It contained many equivalent questionnaires/behavioural factors to those used in the originally planned questionnaire. An application was developed, and the College of Medical, Veterinary and Life Sciences (MVLS) Ethics Committee approved the project (ethics waiver was obtained) and full access to the dataset was granted by the (National Institute of Diabetes and Digestive and Kidney Diseases NIDDK central repository) on 05/11/2020. The positive impact of the change in plans is that the lookAHEAD trial had follow-up data for up to 4 years, which allows the development of a predictive model for medium-term (4yr) successful weight loss. This remedial work has ensured that the majority original aims of this thesis chapter can still be achieved. Data on the literature review and questionnaire development are still included for completion, and for further external use.

2.2 Methods

2.2.1 Literature review

2.2.1.1 Developing a hypothesis

A rapid review of the published literature was done to identify the behavioural factors (e.g. psychology, physical activity, eating habits, etc.) that are reported in the literature to have a relationship (mediation, association, correlation, prediction, etc.) with successful weight loss. This approach allows the derivation of testable hypotheses.

This study was intended to be a hypothesis-driven study and not to test a hypothesis or outcome. The type of literature review was chosen to gain broad coverage from the literature about known or available variables associated with weight loss and not to elicit a summary of conclusions from all available research studies. Systematic review or meta-analysis was not considered as this was a planned clinical study, which will take a great amount of time to be conducted. Therefore, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were not considered in this study.

2.2.1.2 Search strategy

The search strategy was constructed based on the Patient/Population, Intervention, Comparison, Outcomes (PICO) model. Searches are developed in OVID MEDLINE and EMBASE. The search includes published studies from 2008 to week 3 of 2019. Certain criteria were applied to define the population of interest (Table 2-1).

First, the research aims and questions were identified and listed before conducting the search. Second, based on the four elements of the PICO model, a table with the relevant keywords for each element was created. Identification of suitable keywords for the review was done in three phases. Please refer to Appendix 3 for detailed information.

Table 2-1: Inclusion and exclusion criteria developed specifically for the POWER study based on the PICO model.

Search strategy components	Inclusion	Exclusion
Patient/Population	Published studies were included only if they were done on humans and were written in the English language. Adults patients with or without Type 2 Diabetes Mellitus (T2DM) and obesity/overweight.	Published studies were excluded if they were done on pregnant women, children, adolescents, and infants.
Intervention	Patients who have undertaken any obesity treatment (e.g. behavioural weight management programmes, multi-component lifestyle interventions, weight loss programmes).	Bariatric surgery and pharmacological therapy to induce weight loss studies were excluded.
Comparison	Factors that have any relationship with weight loss success. Factors were explored at any time point (i.e. baseline, short and medium-term).	_
Outcomes	The outcome of interest was change in/achieved weight, body mass index, fat, or adiposity.	_

2.2.1.3 Study selection

All studies identified were transferred to a reference manager (Mendeley) (n= 4927). Manual screening for titles of all included studies (n= 642) was done by one reviewer to assess study eligibility. The same reviewer assessed the abstracts of the remaining studies (n= 130). The full-text screening was conducted by the same reviewer and confirmed the studies that showed an association between behavioural factors and weight change, which were included and summarised in an excel spreadsheet (n= 46).

A detailed flow chart is found in the results section (Figure 2-1).

2.2.1.4 Data extraction

Study characteristics include factors explored, study aim, sample size, participant's age, gender, country of origin, study duration, the method used to collect behavioural factors information, behavioural factors associated with

weight loss, whether the researchers used a prediction model or not, statistical analysis, type of study, weight change measurement collection, and journal article reference were extracted from each included paper (Table 2-6).

2.2.1.5 Selection of factors

The identified factors based on the literature review were a mixture of demographic, weight-related, psychological and behavioural. The summary of the behavioural factors that have shown an association with weight change is shown in the results section (Table 2-6).

In this review, a criterion was used to select a list of variables suitable for inclusion. First, priority was given to papers that used a prediction model to test the relationship with weight loss over papers that used associations. Second, a large study (a sample size of at least 450 or more) was used to select variables that have an association with or prediction of weight loss. Third, if the variable was repeatedly mentioned in the studies (at least 3-4 times), whether it was a small or a large study. Less importance was given if a variable was mentioned once in a small study.

2.2.2 Questionnaire development

From papers identified in the literature review, those that reported a relationship (mediation, association, correlation, or prediction) between behavioural factors and weight loss success, and used validated questionnaires to test the behavioural factors, were used to build the POWER study questionnaire.

Before any questionnaire or questions found in the literature were employed for the POWER study questionnare, permissions were obtained via emails by authors and original journals. The authors attempted three times in cases where authors they did not reply to the first email asking for their permission to use the questionnaire. In the third attempt, they were informed that the researcher will use the questionnaire. Some questionnaires were free to use and others asked for fees to be paid to allow using the questionnaire in this study. A description of how the questionnaire was constructed based on validated questionnaires available in the literature is shown below:

2.2.2.1 Questionnaire content

Based on the literature search results, the researchers decided to categorise the questionnaire into four main sections, which are:

“about you” (i.e. demographic information)

weight-related information

behavioural information.

For each section, specific instructions are provided to demonstrate how participants can respond to the questionnaire.

2.2.2.2 Questionnaire assessment and piloting

Two versions of the questionnaire were developed; paper copy and online. Although the online version was planned to be the main version for participants to take part in this study, a few participants were expected to complete a paper version of the questionnaire. Each version was updated several times and tested by the research team, and colleagues who were not engaged in the study, as well as family and friends to ensure the format was easy to read & understand and estimate time to complete the questionnaire.

Challenges regarding patient recruitment and completion of the questionnaire were planned to be resolved by providing incentives (£10 amazon voucher) to each participant completing the questionnaire to increase the participation rate in the study.

The final version of the questionnaire developed for the POWER study can be found in the appendix 1.

Behavioural factors related to weight loss success:

In this study, putative behavioural factors were tested for prediction of weight loss success. Therefore, the exposure of interest was behavioural predictors and weight change was the medium-term outcome. Each one is described below.

2.2.2.3 Predictors

- In this study, factors that were obtained from the literature search were hypothesised to be a baseline predictor (0m) of weight loss success at the end of the Weight Watcher programme (at 12wk).

- The demographic variables chosen for the POWER study include age, gender, education, ethnicity, diabetes status, and employment status.

Table 2-2: The definition of each variable in the demographics section.

Assumed predictor variables	Definition	Citation
Age (years).	Participants' age during questionnaire completion.	Adopted from (Logue et al. 2015)
Gender.	Gender identity during questionnaire completion.	Adopted from (Logue et al. 2015)
Marital status.	Marital status during questionnaire completion.	Adopted from (Logue et al. 2015)
Ethnicity.	Participants' ethnic group.	Adopted from (Logue et al. 2015)
Education.	Participants' most recent education level.	Adopted from (Logue et al. 2015)
Employment status.	Participants' most recent employment status.	Adopted from (Logue et al. 2015)
Diabetes status.	Current diabetes status. If participant had diabetes either Type 1 diabetes or Type 2 diabetes should be specified.	Adopted from (Welsh et al. 2019)

In the questionnaire, participants were asked about their gender based on sensitivity issues raised surrounding gender.

- The Weight-related exposure variables chosen for the POWER study include weight loss history and weight loss expectations.

Table 2-3: The definition of each variable in the weight-related section.

Assumed predictor variables	Definition	Citation
Current weight (kgs, stone, or lbs).	Participants' weight during questionnaire completion.	Adopted from (Logue et al. 2015)
Weight loss history.	An 8-item measure.	Adopted from (Myers et al. 2013a)
Weight loss expectations (kgs, stone, or lbs).	Four items: dream, happy, acceptable, and disappointing weights.	Adopted from (Foster et al. 1997)

- The Behavioural variables chosen for the POWER study include motivation, weight goal, self-efficacy, sleep and eating behaviour. This is the most important part of the questionnaire since the data collected here are not routinely collected in clinical settings.

Table 2-4: The definition of each variable in the behavioural section.

Assumed predictor variables	Definition	Citation
Motivation.	Treatment Self-Regulation Questionnaire (TSRQ), including both the autonomous and controlled motivation subscales.	((CSDT) 1989; R. Ryan, Plant, and O'Malley 1995; Williams et al. 1999)
Weight goal.	1- Target weight goal: target weight (in lbs/kgs/stone) for the present weight loss attempt. 2- Goal striving. 3- Goal commitment: a validated 5-item Hollenbeck, Williams, and Klein (HWK) scale, specified to weight goal.	1- (De Vet et al. 2013) 2- (Sheldon et al. 2004) 3- (De Vet et al. 2013; Hollenbeck, Williams, and Klein 1989)
1- Self-efficacy. 2- Self-efficacy.	1- A 4-items self-efficacy questionnaire for self-efficacy (binge drinking). Reduced to 3-items and specified for weight loss trial purposes. 2- 3-items self-efficacy scale	1- (Norman and Conner 2006; De Vet et al. 2013) 2- (McKee and Ntoumanis 2014a; Bandura 1997)
Sleep.	Pittsburgh Sleep Quality Index (PSQI) questionnaire.	(Buysse et al. 1989)
Eating behaviour.	21-item Three-Factor Eating Questionnaire (TFEQ-R21).	(Cappelleri et al. 2009)

2.2.2.4 Outcome

Short-term:

The time window for the short-term outcome variable will be 12 wk following the first week of Weight Watchers visit (i.e. baseline).

Weight change is defined as the proportion of total weight lost (in percent) at 12 wk from baseline weight (weight measurements obtained from NHS SafeHaven). This is calculated by subtracting the 12 wk weight from the baseline weight. The cut-off point for the weight change is set to be 5%. Therefore, two groups were created: 1) Successful completers, those who lost ≥ 5% from the baseline body weight at 12 wk. 2) Unsuccessful completers, those who lost < 5% from the baseline body weight at 12 wk.

Attendance outcome is defined as a binary variable to distinguish between participants based on their attendance to 12 wk visits. There were two groups: attend 12 wks and did not 12 wk visit.

2.2.3 Study protocol

2.2.3.1 Study design

A longitudinal cohort study was designed for adults referred by the National Health Service - Greater Glasgow and Clyde (NHS-GG&C) to their behavioural weight management programme (i.e. referral to Weight Watchers). Participants' eligibility criteria for the study are based on the NHS GG&C criteria used to refer participants to Weight Watchers. This includes adults aged ≥18, BMI ≥25, independently giving consent for participation in the programme, and are independently able to understand and follow Weight Watchers instructions (this is assessed by the General Practitioners as part of their usual care).

2.2.3.2 Study Procedures & Recruitment

The POWER questionnaire will be administered to participants within the weight management programme (i.e. Weight Watchers). This will be completed within the first week of starting the programme (a baseline measure) by having a study leaflet sent with the participant appointment letter. If any participants exceeded

the baseline time the survey system will not allow the participants to proceed with the questionnaire (this will be set up in the questionnaire automatically). If any participants contact the study team too late for the questionnaire and indicate that they exceeded the baseline time, the study team will not allow participation in the study. Table 2-5 shows a detailed procedure of the study.

Table 2-5: A detailed procedure of the study shows the role of NHS weight management service.

Time	Routine Care	Research study component
Week-1	Patients are referred to NHS weight management services. NHS staff telephone patient to arrange a suitable time and place for their first Weight Watcher's appointment.	NA
	Patients are sent an appointment letter.	An invitation letter for the study (with information about the questionnaire) will be included with the appointment letter.
Week-2	Patients attending first Weight Watchers session.	Patients who decide to participate will either follow the questionnaire URL provided in the invitation letter or contact the research team via the email provided in the invitation letter. The questionnaire will begin by asking whether participants wish to take part in the questionnaire. The study email will also be present on the invitation letter for any other queries or a paper copy of the questionnaire.
		Patients read the participant's information sheet and complete the consent form and questionnaire online.
Week-3	Attending Weight Watchers.	Each participant will be emailed a £10 amazon voucher for completing the questionnaire.
Week-(4-6)	Attending Weight Watchers.	NA
End of patient's active involvement in the study. At 12 weeks: weekly weight measurements will be collected via the NHS SafeHaven.		

All study documents are presented in the appendix 1 & 2.

2.2.3.3 Online survey system

All the questionnaire data (personal information, questionnaire responses) will be collected and stored on Webropol, the online survey system used under licence by NHS GG&C which fully complies with NHS data protection standards. Webropol's servers are based in the UK and provide an ISO27001, ISO9001, and GDPR compliant cloud infrastructure. It is fully compliant with Good Clinical Practice (GCP) and 21 CFR Part 11 and employs stringent security procedures to ensure protection of customers' data in the best possible way.

2.2.3.4 Data Collection

Webropol (an electronic database system: https://new.webropolsurveys.com/) will be used to build and distribute the questionnaires (v1.0, 15/10/2019). The questionnaires will be completed online, or on paper and then transcribed into Webropol. It is secure to store identifiable data by using the encryption module https://www.quest.scot.nhs.uk/hc/en-gb/articles/360002129377-What-to-put-in-an-introduction-to-a-survey-includes-guidance-to-GDPR. This module allows individual Webropol fields (study variables) to be stored in an encrypted manner. This means that the data is stored in the database in the form of a random code. To view the data that lies behind this code, the user needs to have an encryption/decryption key. Webropol is compliant with all data security standards and this study will be using NHS GGC's study licence. At the beginning of the questionnaire, patients will be asked for their Weight Watchers ID number (patients will find this information on their appointment letter, the questionnaire has an illustration to show patients where to find this) which is a unique number which is used to manage the transfer of data and for financial reimbursement by NHS-GGC and Weight Watcher but it is stored in the NHS data where the weight outcome data is recorded. Having this number will allow the study team to follow up on their attendance and weight change during their weight management programme, and link to questionnaire responses.

2.2.3.5 Data linkage

Once all the questionnaires have been completed, they will be downloaded as a single excel file from Webropol at the Safehaven offices (the study team will travel to the offices; the only 'identifier' will be Weight Watchers number; contact

details will not be downloaded). The SafeHaven will upload the results and link them to the participants' weight outcomes at the end of the programme using their Weight Watchers ID number. SafeHaven will then anonymise the results and the research team will conduct the analysis in the NHS SafeHaven via a virtual private network.

2.2.3.6 Withdrawal

During the consenting process, participants will be informed they can withdraw from the study at any time without providing a reason. They will be informed this won't affect their experience within the weight management service.

If a participant asks to stop participation in the study, they will be asked whether already collected data can still be used in the study and if they would allow us to link this data to their weight management outcomes. If they decline both options, then all their data will be deleted. If they agree data already collected with consent up to the point of withdrawal will be retained and used in the study (with data linkage to weight management outcomes if consent is given). No further data will be collected directly from the participant.

2.2.3.7 Ethics

The study documents were submitted for review by the University Research Governance Office in August 2019. The University's review took longer than the expected time and consequently, official submission to the NHS-GG&C Research & Development office was delayed until January 2020. The favourable opinion letter for the study application was received in February 2020 from the Research Ethics Committee (REC), Yorkshire and the Humber – Sheffield ethics committee.

Approval was given to inviting participants to participate in the study by giving consent to participate.

2.2.4 Sample size and power calculation

This study aims to recruit 200 adults the hypothesis was exploratory, and a number of different examples of power calculations have been modelled based on the risk factors intended to be measured. Assuming 200 participants are recruited and 45

of these successfully meet weight loss targets (the power calculation was based on data from our previous trial (Botha et al. 2018)), at alpha=0.05, 84% power was detected a difference of 10kg in starting weight between groups (120 vs 110 assuming standard deviations of 20kg in both). There would be 80% power to detect a difference of 0.48 standard deviations between groups in any continuous variable. There would be 82% power to detect a difference in success by sex if 42% of those not meeting targets are male and 66% of those who do meet targets are males. In a linear model relating predictors to continuous weight loss, 82% power is there to detect a correlation of r=0.18.

2.2.5 Statistical analysis

A predictive model will be built to allow us to identify predictors of weight loss success. Participants will first be split into binary outcome groups according to the achievement of successful weight loss targets. The null hypothesis is that risk factors (sociodemographic and behavioural) will not be associated with successful weight loss. Simple univariable tests of the null hypothesis will be conducted with independent t-tests, rank-sum tests, and chi-square tests, as appropriate depending on the nature of the risk factor. Using this information, multivariable models will be built using logistic regression to identify independent predictors of weight loss success. A final multivariable logistic regression model with the optimal fit (based on penalized likelihood criteria; Akaike and Bayesian information criterion) will be used to develop Area under the receiver operator curve (AUROC) statistics, and from there optimal cut-offs from the model for sensitivity and specificity of prediction. Analyses investigating weight loss as a continuous outcome to maximise power will also be done, using correlation and linear regression. The full analysis will be governed by a formal statistical analysis plan to be developed during the study.

- Handling of missing data for predictor variables:

Data are anticipated to be near 100% complete given that all sections of the questionnaire are mandatory. Complete case analysis therefore will be used. Any question with a less than 90% completion rate will be considered as a not suitable question for wider implementation in this population.

- Handling of missing data for outcome variable:

NHS SafeHaven weight will be used as it will provide weekly measurements of participants' weight. Two methods will be used to derive weight measurement in case it is missing: 1) last observation carried forward (LOCF). 2) baseline observation carried forward (BOCF).

2.3 Results

2.3.1 Screening

A total of 4927 unique journal studies were identified. Based on titles screening, 642 studies were identified to be relevant to the study aim. Based on abstract screening, 130 studies were identified to be relevant to the study aim. After screening full-text studies, 46 had behavioural factors related to the outcome of interest (i.e. weight loss).

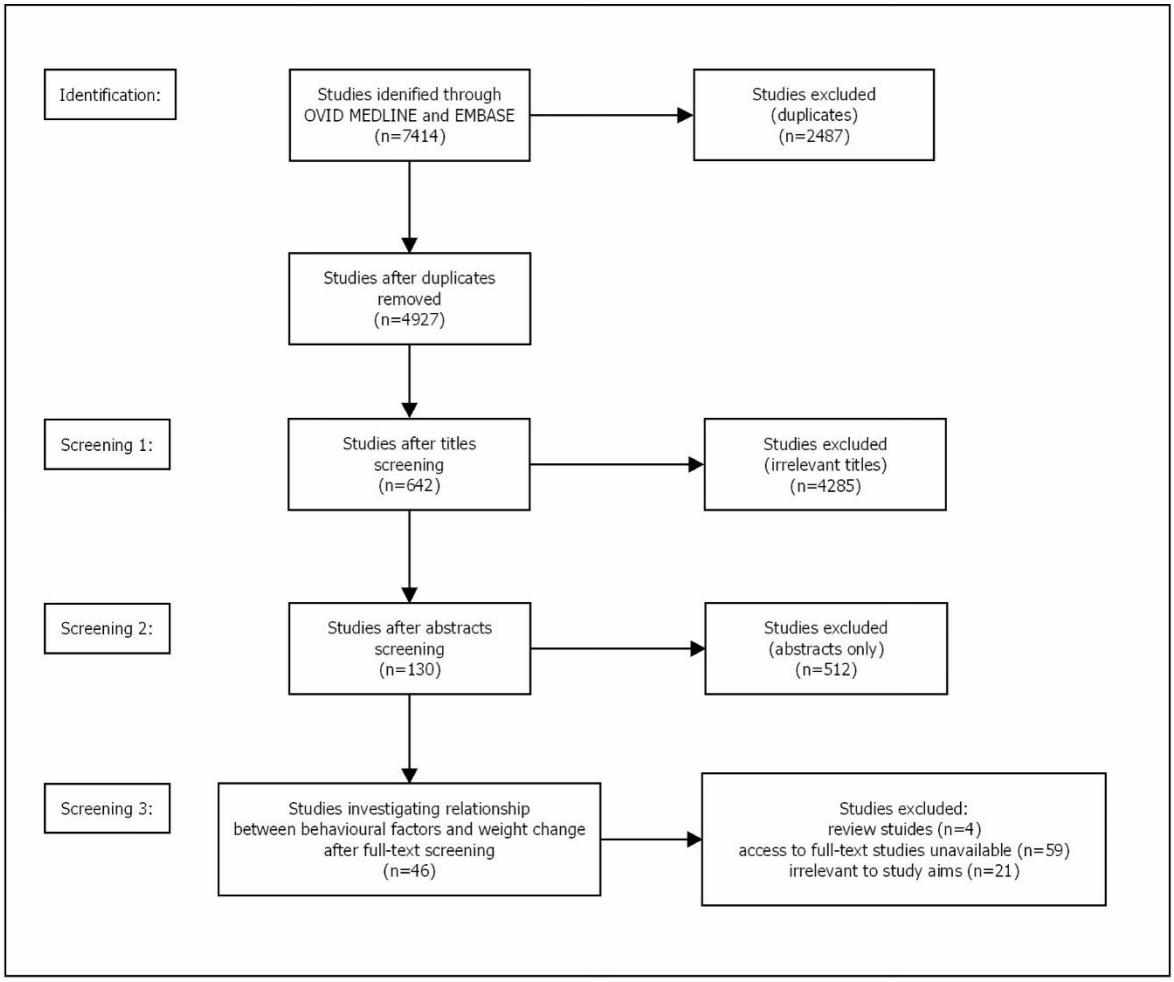

Figure 2-1: A flow chart showing the process of studies identification and screening.

2.3.2 Behavioural factors related to the weight change

Study characteristics are reported in Table 2-6. Twenty-four of the 46 studies were conducted in the USA. Further studies were conducted in the UK (Smithson and Hill 2017; Johnson and Wardle 2011; McKee and Ntoumanis 2014b; Wingo et al. 2013), Italy (Calugi et al. 2017; Rotella et al. 2014; Barbara Cresci et al. 2013; B Cresci et al. 2011), Netherlands (De Vet et al. 2012; Vinkers et al. 2014), Germany (Lahmann et al. 2011; Postrach et al. 2013), Bulgaria (Teodora Handjieva-Darlenska et al. 2012; T. Handjieva-Darlenska et al. 2010a), a collaboration between USA and UK (Myers et al. 2013b), Japan (R. Sawamoto et al. 2014), Spain (Bandín et al. 2014), Hungary (Czeglédi 2017), Georgia (Garvin, Hardy, and Xu 2016), Sweden (Elfhag and Rossner 2010), Australia (Alharbi et al. 2016), Portugal (Palmeira et al. 2010) and Israel (Greenberg et al. 2009).

Seventeen studies were longitudinal studies, fifteen were Randomised control trials (RCT), eight were secondary analysis of an RCT, four were secondary analysis of longitudinal studies, one Meta-analysis and one exploratory study. The shortest period of follow-up was 2 months while the longest was 8 years. The overall participant's ages ranged from 18 and 77 years, except for 3 studies where older ages were considered (Czeglédi 2017; Garvin, Hardy, and Xu 2016; Smithson and Hill 2017). Female participants were the majority in 29 studies, with men the majority in only 4 studies. Eight studies were conducted on the female population only. Five studies did not report proportions by sex. Weight was obtained via self-report (n= 9), measured by researchers (n= 32), using both methods (i.e. self-report & measured by researchers) (n= 2), obtained from electronic health records (n=1) and for some did not specify the way weight was obtained (n=2). Data were mostly collected via a self-report study (i.e. questionnaire).

The sample size was different across each study, the majority were below 500 (n= 36), few were between 500-999 (n= 5) and few were above 1000 (n= 5). Only 3 studies out of the 46 used a prediction model. As mentioned earlier in the method section those papers were given greater importance in the literature review as they used a prediction model.

One of those studies that used an accurate statistical method of prediction (based on this study's definition) tested the patient's motivational level for treatment as

a pre-treatment predictor of ≥5% weight loss success at the end of 6 months of treatment (B Cresci et al. 2011). After adjusting for age, sex, BMI, Binge Eating Scale, Obesity-Related Well-Being (i.e. quality of life), higher scores of TREatment MOtivation and Readiness (TRE-MORE) total (OR=29.04, p<0.001), obstacles and desire to overcome (OR= 3.82, p=0.002), and taking care of themselves and sharing the problems (OR= 2.90, p=0.03) were predictors of ≥5% weight loss at 6 months.

The other two studies were secondary analysis of an RCT (NUGENOB Project) (Teodora Handjieva-Darlenska et al. 2012) and the DiOGenes study (T Handjieva-Darlenska et al. 2010). These two studies were mentioned earlier in greater detail (section 1.3.1 Known patient factors associated with weight loss - Initial BMI and 1.3.3 Treatment factors – early weight loss)

Diabetes Prevention Program (DPP) was a multicenter RCT. It is one of the largest diabetes prevention trials (patients were from diverse ethnic groups). This study consisted of 3234 overweight participants with pre-diabetic symptoms. Out of the entire cohort, 274 participants agreed to complete a questionnaire that tested pre-treatment factors, including weight loss history, psychological and behavioural, association with a 7% weight loss outcome at 6 months of treatment (Delahanty et al. 2013a). Risk factors associated with greater success (7% weight loss at 6months) are being white (OR= 3.57, CI: 1.72 , 7.69), older age (OR= 1.05, CI: 1.02 , 1.08), baseline weight (OR= 1.02, CI: 1.01 , 1.04), older age when first overweight (OR= 1.03, CI: 1.00 , 1.05), fewer previous formal weight loss programs (OR= 1.56, CI: 1.13 , 2.12) and less frequent emotional eating (OR= 1.13, CI: 1.02 , 1.26). Risk factors associated with greater success (7% weight loss at end of study) are older age (OR= 1.06, CI: 1.03 , 1.10), fewer past weight loss attempts (OR= 1.49, CI: 1.03 , 2.12), greater exercise self-efficacy (OR= 1.60, CI: 1.11 , 2.31), greater dietary restraint (OR= 2.64, CI: 1.30 , 5.36), fewer high-fat dietary behaviors (OR= 2.94, CI: 1.29 , 6.66), and a more sedentary activity (OR= 1.01, CI: 1.00 , 1.01).

Detailed information and study characteristics found in the literature were reported in Table 2-6.

Table 2-6: Study characteristics of the 46 studies included in the literature review.

Study / Variable(s) of interest / Aim	Sample size	Participants Age	Gender	Country	Study duration	Variables associated with weight loss	Statistical analysis	Study design / Method	Weight measurement
(De Vet et al. 2012). Setting a weight loss goal. To explore the relationship between weight loss goals and successful short-term weight loss.	447	49.00 ± 12.77 (range 19-77)	F: 54.8% M: 45.2%	Netherlands	0 - 2mos	**Cross-sectional correlates of weight loss goals:** sex (β= 0.11, p< 0.001), age (β= -0.14, p< 0.001), BMI (β= 0.68, p< 0.001), Self-concordance (β= 0.08, p= 0.04). **Longitudinal risk factors of weight loss:** sex (β= 0.12, p= 0.01), BMI (β= -0.17, p= 0.01), Self-concordance (β= -0.12, p= 0.01), weight goal (β= -0.14, p= 0.03).	1-Bivariate correlations. 2-Multiple regression.	Cross-sectional and Longitudinal / Questionnaire.	Self-reported.
(McKee and Ntoumanis 2014b). Weight loss goal characteristics: self-efficacy, goal persistence. To investigate weight-loss self-regulation goal characteristics variables and their contribution to successful weight-loss attainment.	98	25.36 ± 6.9 (range 18.87–67.99)	F: 80% M: 20%	UK	_	**Weight-loss goal characteristics contribute in weight-loss attainment:** After controlling for social desirability, trait self-control and optimism/pessimism, self-efficacy (β= 0.37, p< 0.001) and goal persistence (β= 0.39, p< 0.001).	Multiple regression analyses.	Longitudinal / Web-based questionnaire.	Self-reported.
(Lahmann et al. 2011). Personality traits. To investigate the relationship between the value of personality traits and successful long-term weight loss.	54	48.4 ± 12.9 (range 21–75)	F: 66.7% M: 33.3%	Germany	0 - 52wk	**Inventory of Interpersonal Problems 8-subscales contributes in BMI reduction:** "intrusive or needy" subscale was significant at 12wk (β= 0.35, p< .01), at 26wk (β= 0.31, p= 0.02) and at 52wk (β= 0.27, p= 0.04).	Linear regression analysis.	Longitudinal / Questionnaire.	Measured by the researcher (method not specified).

(Anton et al. 2008). Psychological & behavioural factors: depression, body size and shape, current dieting, restrained eating, dietary restraint, disinhibition, perceived hunger, psychological adjustment, somatic symptoms, negative mood states, motivation and confidence for behaviour change, eating disorders, health-related quality of life, and restraint. To examine whether baseline psychological & behavioural factors were associated with weight loss over 6mos.	36	F: 37.6 ± 1.2 (range 27-45) M: 37.3 ± 1.8 (range 26-49)	F: 55.5% M: 44.5%	USA	0 - 6mos	**Psychosocial and behavioural factors contribute to percent weight loss (over 6 months):** After controlling for age, BMI, race, sex and treatment effects, higher negative mood states, poor psychosocial functioning, and somatic symptoms were associated with less weight loss (β= -0.37, p< 0.01).	1-Data reduction method. 2-Hierarchical regression analyses.	Longitudinal / Questionnaire.	Measured by the researcher (method not specified).
(J. Annesi and Gorjala 2010). Psychological factors: self-regulation, self-efficacy, mood. Physical activity. To examine the mediation effect of exercise, which induces appropriate eating habits (through self-regulation, self-efficacy, and improved mood), on weight loss.	106	43.5 ± 10.0	F: 77% M: 23%	USA	0 - 6mos	**Exercise-induced changes in psychological factors associated with appropriate eating mediate weight loss:** Changes in the Weight Efficacy Lifestyle Questionnaire (β= -0.23, p< 0.05) and self-regulation for appropriate eating (β= -0.22, p< 0.05) partially mediated the relationship between changes in physical activity and BMI.	Multiple regression.	Longitudinal / Questionnaire.	Measured by the researcher (Calibrated digital scale).
(Rotella et al. 2014). Psychological and psychopathological: general psychopathology, eating attitudes and behaviour, obesity-related quality of life, motivation, a previous attempt at losing weight.	231	F: 44.7 ± 12.7 M: 45.1 ± 13.2	F: 76.6% M: 23.4%	Italy	0 - 6mos	**Psychological and psychopathological associate with weight loss:** Hypertension [HR 0.50 (0.26–0.97)] and general psychopathology score [HR 0.53 (0.35–0.81)] were were negatively associated with success (p< 0.05).	Logistic regression for multivariate analysis.	Longitudinal / Questionnaire.	Measured by the researcher (Calibrated instruments).

To explore the association between psychological and psychopathological features and successful weight loss from a multidisciplinary program.									
(Swencionis et al. 2013b). Psychological well-being (i.e. overall well-being, anxiety, depression, self-control, general health, positive well-being, and vitality), health-related quality, physical activity. To examine which aspect of well-being would result in improving the well-being scores, which is in line with weight change.	588	52.2 ± 11.7	F: 82.3% M: 17.7%	USA	0 - 12mos	**Well-being factors associated with weight loss:** Vitality scores (at 6mo) associated with weight loss at 12 months (β= -0.21, p< 0.001).	1-Correlations analyses. 2-Multiple regression analyses.	RCT / Questionnaire.	Measured by the researcher (Balance beam scale).
(Palmeira et al. 2010). Body image, self-esteem, mood, and depression To investigate whether short-term changes in body image and psychological well-being (self-esteem, mood, and depression) are associated with short and long-term weight change.	96	38.3 ± 5.8	F: 100% M: 0%	Portugal	0 - 16mos	**Psychosocial variables associate with weight change:** After controlling for the 0–4 month's weight change; total mood disturbance (β= 0.27, p= 0.008), body size dissatisfaction (β= 0.25, p= 0.01), body attractiveness (β= -0.25, p= 0.01) were associated with weight loss (at 0-4mo). Body size dissatisfaction (β= 0.32, p= 0.002) and total mood disturbance (β= 0.30, p= 0.003) were associated with weight loss (at 0-16mo).	1-Multiple linear regression. 2-Analysis of covariance.	RCT / Questionnaire.	Measured by the researcher (Electronic scale).

(Teodora Handjieva-Darlenska et al. 2012). Pre-treatment characteristics (age, sex, body weight, height, BMI, waist and hip circumferences, waist-to-hip ratio, fat mass, and fat-free mass), and body weight losses at week 1 (early weight loss) and at week 5 (halfway weight loss).and weight loss change. To identify the pre-treatment characteristics and early weight loss as a correlate of final weight loss outcome.	771	Low fat diet : 37.0 ± 0.4 (range 20–51) High fat diet: 37.2 ± 0.4 (range 20-51)	Not reported	Bulgaria	0 - 10wk	**Early weight loss as a predictor of final weight loss (at 10wk) - combined group, adjusted for centre and age:** Male (β= 1.35, p< 0.001) and early weight loss at 1wk (β= 1.27, p< 0.001) were predictors of weight loss at week 10. Sex (β= 0.42, p= 0.009) and half-way weight loss "5wk" (β= 1.38, p< 0.001) were predictors of weight loss at week 10.	1-Correlation analyses. 2-Multivariate regression. 3-Sensitivity and specificity analyses.	Secondary analysis of an RCT / Calibrated scales.	Measured by the researcher (Calibrated scales).

(Delahanty et al. 2013a). Pretreatment characteristics (i.e. demographic and weight history) psychological (i.e. weight efficacy, self-efficacy, perceived stress, depression) & behavioural factors (i.e. emotional eating, binge eating, restraint, fat-related diet, physical activity, occupational and leisure activity. To identify the most important pretreatment characteristics and changes in psychological and behavioural factors that predict weight outcomes in the Diabetes Prevention Program (DPP).	274	52.54 ± 12.13	F: 64.6% M: 35.4%	USA	0 - 6mos	**Independent, pretreatment factors of achieving 7% weight loss at 6m:** Race (being white compared with black) (OR= 0.28, p< 0.001), older age (OR= 1.05, p< 0.001), baseline weight (OR= 1.02, p< 0.01), older age when first overweight (OR= 0.97, p< 0.05), fewer previous formal weight loss programs (OR= 0.64, p< 0.01) and less frequent emotional eating (OR= 0.88, p< 0.05) were associated with achieving 7% weight loss. **Independent, pretreatment factors of achieving 7% weight loss at end of study:** Older age (OR= 1.06, p< 0.001), fewer past weight loss attempts (OR= 0.67, p< 0.05), greater exercise self-efficacy (OR= 1.60, p< 0.01), greater dietary restraint (OR= 2.64, p< 0.01), fewer high-fat dietary behaviors (OR= 0.34, p< 0.01), and a more sedentary activity (OR= 0.99, p< 0.05) were associated with achieving 7% weight loss.	1-Multivariate models. 2-Hierarchical logistic regression.	RCT / Questionnaire.	Self-reported.
(Vinkers et al. 2014). Pre-treatment proactive coping skills, demographic, self-efficacy, and expected difficulties. To examine the interplay between pre-treatment proactive coping skills and expected difficulties during weight loss in determining successful weight management.	119	55.92 ± 5.77	F: 51.2% M: 48.8%	Netherlands	0 - 8wk	**Pre-treatment proactive coping skills and expected difficulties during weight loss and weight loss:** Females (β= 0.27, p< 0.01), higher education (β= 0.17, p< 0.05), unemployed participants (β= -0.26, p< 0.01), higher BMI (β= 0.21, p< 0.05) associated with less weight loss. the interaction between proactive coping skills and expected difficulties (β= 0.24, p< 0.01).	Hierarchical regression analysis.	Longitudinal / Questionnaire.	Self-reported.

(Alharbi et al. 2016). Self-efficacy, depression, Socio-demographic data. To identify the independent factors (i.e. exercise, self-efficacy, depression, waist circumference, Socio-demographic) of BMI at 4 and 12 months.	134	63.7 ± 8.5	F: 41% M: 59%	Australia	0 - 12mos	**Independent factors of BMI:** The variables time (4mos vs. baseline (β= –0.9, p< 0.001), 12mons vs. baseline (β= –1.0, p< 0.001)), self-efficacy (β= –0.1, p= 0.005) and depressive symptoms (β= –0.2, p= 0.03) made statistically significant contributions to BMI.	Longitudinal generalised estimating equation (GEE) models.	RCT / Questionnaire.	Measured by the researcher (Calibrated digital scale).
(Finkler, Heymsfield, and St-Onge 2012a). Study length, prescribed caloric deficit, frequency of dietary counselling, percentage of female subjects included in the study, age and initial body weight of the subjects, presence or absence of placebo, and exercise. To examine factors that influence the rate of weight loss obtained in clinical studies.	35 studies	45.6 (range 29 to 71)	Not reported	USA	≥ 6wk	**Factors influence the rate of weight loss:** Study length (β= 0.01, p< 0.0001), age (β= -0.06, p= 0.002), initial body weight (β= -0.008, p= 0.0003), prescribed energy deficit (β= -0.00005, p< 0.0001), frequency of dietary counseling (β= -0.089, p= 0.019).	Linear regression analysis.	Meta-analysis / Method not specified .	Method not specified .

(Yank et al. 2014). Baseline characteristics: **socio-demographics** (i.e. age, sex, ethnicity, education, income), **clinical measures** (BMI, prediabetes status, metabolic syndrome status, blood pressure, fasting glucose, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol), **caloric and fat gram intake, leisure-time physical activity, and psychosocial measures** (i.e. physical and mental well-being, obesity-related problems, self-efficacy and social support for diet and exercise behaviours, depression symptoms, and body size dissatisfaction). To examine baseline characteristics associated with patterns of individual week-to-week weight change trajectories over the initial 12-week intensive intervention period.	72	55.0 ± 10.8	F: 49% M: 51%	USA	**0 - 12wk**	**Factors correlate with weight loss:** Female, obesity-related problems, family & friend encouragement for dietary change, depression symptoms, body size dissatisfaction, physical well-being, physical activity overall canonical correlation p= 0.005.	Correlations analyses.	Secondary analysis of an RCT / Questionnaire & clinical.	Measured by the researcher (Calibrated balance beam).
(Calugi et al. 2017). Weight loss expectations. To assess the influence of weight-loss expectations on weight loss.	88	46.7 ± 11.1 (range 19-65)	F: 58% M: 42%	Italy	0 - 51wk	**Weight-loss expectations association with weight loss:** Weight loss at Week 27 was associated with all the expected weight targets measured in kilograms (dream weight β= 0.20, p= 0.003), happy weight (β= -0.23, p< 0.001), acceptable weight (β= -0.18, p= 0.001), disappointing weight (β= -0.21, p< 0.001).	1-Correlations analyses. 2-Linear mixed model.	Secondary analysis of an RCT / Questionnaire.	Measured by the researcher (Calibrated scale).

(Latner and Ciao 2014). Weight loss history, pretreatment BMI and treatment duration. To examine the characteristics and nature of the association of weight-loss history among participants in group behavioural self-help treatment.	128	47.21 ± 15.76	F: 83% M: 17%	USA	0 - 24mos	**Factors associate with greater weight loss at 6mos:** Greater number of past attempts (β= 0.42, p< 0.01), higher pretreatment BMI (β= 0.44, p< 0.01), longer treatment duration (β= 0.27, p< 0.01). **Factors associate with greater weight loss at 12mos:** Higher pretreatment BMI (β= 0.51, p< 0.01), longer treatment duration (β= 0.31, p< 0.05). **Factors associate with greater weight loss at 18mos:** Greater number of past attempts (β= 0.32, p< 0.05), higher pretreatment BMI (β= 0.31, p< 0.05), magnitude of largest past loss (β= 0.45, p< 0.01). **Factors associate with greater weight loss at 24mos:** Higher pretreatment BMI (β= 0.54, p< 0.05).	1-Partial correlation. 2-Multiple linear regression analyses.	Exploratory study / Questionnaire.	Measured by the researcher (Balance beam scale).
(Myers et al. 2013b). Weight loss history. To clarify the associations between weight loss history and weight loss outcomes during intensive lifestyle intervention.	1,678	54.7 ± 9.1	F: 67% M: 33%	USA & UK	0 - 6mos	**Covariates of weight loss:** Non-African American (β= -1.34, p< 0.0001), male (β= -1.18, p= 0.01), race X sex (β= -1.40, p= 0.01),never had previous weight loss attempts with assistance (β= -2.56, p= 0.02), no past use of dietary/ herbal supplements for weight loss (β= -0.83, p= 0.005) and never tried to lose weight before (β= 4.03, p< 0.0001) were significant covariates of weight loss.	Multiple regression analysis.	Longitudinal / Questionnaire.	Measured by the researcher (Calibrated digital scale).

(Forman et al. 2017). Lapse frequency. To assess the relationship between lapses and weight loss in the context of a reduced-calorie diet prescribed as part of behavioural treatment.	189	51.81 ± 9.76	F: 82% M: 18%	USA	0 - 12mos	**Lapse frequency associations with weight loss:** A model containing a number of reported lapses per week at baseline and weight change during the baseline Ecological Momentary Assessment period indicated that lapse frequency is associated with percent weight change during treatment (β= 0.34, p= 0.05) when controlling for weight change during the baseline Ecological Momentary Assessment period (β=1.49, p< 0.001).	1-Linear regressions. 2-Multiple linear regressions.	Longitudinal / Ecological Momentary Assessment Survey.	Measured by the researcher (Standardised Seca scale).
(T. Handjieva-Darlenska et al. 2010a). Early weight loss & pre-treatment characteristics. To determine whether pre-treatment characteristics and early weight change during the first weeks of a low-calorie diet (LCD) could predict weight loss outcome at the end of a carefully controlled 8-week, ~ 800 to 1000 kcal/day, weight loss period in a large cohort of adults living with overweight and obesity across Europe.	932	41.2 ± 0.21	Not reported	Bulgaria	0 - 8wk	**Predictors of weight loss outcomes:** After center adjustments, only initial body weight (β= 0.046), early weight loss (week 1) (β= -0.311) and weight loss at week 3 (β= 1.284) were significant predictors of weight loss outcome at week 8. * No p-values reported.	1-Correlation analyses. 2-Multiple regression analysis. 3-Sensitivity and specificity analyses.	RCT / method not specified.	Measured by the researcher (method not specified).

(Elfhag and Rossner 2010). Sociodemographic, lifestyle, weight-related and psychological. To identify pre-treatment factors related to weight loss in obesity treatment.	163	40.8 ± 11.8	F: 71% M: 29%	Sweden	0-12mos	**% Weight loss after 5 lectures (5 consecutive wk) correlates for weight loss:** Initial BMI (r= 0.17, p< 0.05), overweight in parent (r= -0.16, p< 0.05). **% Weight loss after treatment program (1-year group treatment) correlates for weight loss:** % weight loss after screening visit (r= 0.22, p< 0.05), % weight loss after 5 lectures (r= 0.46, p< 0.001), weight cycling 3 or more times (r= 0.28, p< 0.05), weighing oneself at least monthly (r= -0.27, p< 0.05).	1-Correlations analyses. 2-Student's t-test.	Longitudinal / Questionnaire.	Measured by researcher (Digital device) & Self-reported.
(JL Unick et al. 2015). Early weight loss. To examine whether the first 4wk weight loss is associated with weight loss following a 12wk internet program and at 6 and 12 months follow-up.	154	46.5 ± 11.4	F: 83.1% M: 16.9%	USA	0 - 12mos	**Early weight loss is associated with weight loss:** Early responders "≥2.0% weight loss" had significantly greater weight loss at all time points compared to early non-responders "<2.0% weight loss". Achieving a 5% weight loss were (OR= 8.5, 95% CI: 3.3–22.1) at 3mos, (OR= 3.4, 95% CI: 1.4–8.3) at 6mos, (OR= 2.6, 95% CI: 0.93–7.4) at 12mons. * No p-values reported.	Logistic regression.	Longitudinal / Web-based questionnaire.	Measured by the researcher (method not specified) & Self-reported.
(Garvin, Hardy, and Xu 2016). Early weight loss. To determine whether very early or early weight reduction in the weight-reduction program MOVE! is associated with later participation or achievement of weight-reduction goals.	375	56.4 ± 11.2 (range 21-81)	F: 20.5% M: 79.5%	Georgia	0 - 24mos	**Successful weight reduction of ≥5% at 6 mons:** ≥ 0.5% of weight loss at 2 weeks (OR= 5.46, p= 0.005), ≥1.0% of weight loss at 4 weeks (OR= 10.76, p= 0.001). **Successful weight reduction of ≥5% at 1 yr:** ≥1.0% of weight loss at 4 weeks (OR= 6.96, p= 0.004).	Logistic regression.	Secondary analysis of a longitudinal study / electronic health record.	Electronic health record.

(Jessica Unick et al. 2015). Early weight loss. To examine the relationship between 1- and 2-month weight loss and 8-year weight loss among participants enrolled in a lifestyle intervention.	2290	58.69 ± 6.82 (range 45-76)	F: 59.17% M: 40.83%	USA	0 - 8yr	The odds of achieving ≥ 5% weight loss at 4 yr and 8 yr were significantly greater among individuals losing the most weight at 1mos or 2mos compared to those losing the least after adjusting for clinical site, sex, race, age, and baseline BMI. **Successful weight reduction of ≥5% at 4 yr:** 1 mo "2-4% weight loss" (OR= 1.68, 95% CI: 1.36-2.08). 1 mo ">4% weight loss" (OR= 2.99, 95% CI: 3.34- 3.83). 2 mo "3-6% weight loss" (OR= 1.96, 95% CI: 1.55- 2.47). 2 mo ">6% weight loss" (OR= 4.33, 95% CI: 3.36- 5.58). **Successful weight reduction of ≥5% at 8 yr:** 1 mo "2-4% weight loss" (OR= 1.29, 95% CI: 1.04- 1.60). 1 mo ">4% weight loss" (OR= 1.99, 95% CI: 1.54-2.55). 2 mo "3-6% weight loss" (OR= 1.23, 95% CI: 0.97-1.55). 2 mo ">6% weight loss" (OR= 2.78, 95% CI: 2.15-3.57). * No p-values reported.	Logistic regression.	RCT / method not specified.	Measured by the researcher (method not specified).

(Greenberg et al. 2009). Early weight loss, 6 months of weight loss. To identify factors associated with successful weight loss in the long-term dietary intervention program.	322	52 ± 7 (range 33–64)	F: 14% M: 86%	Israel	0 - 24mos	**Successful weight reduction of ≥5% at 2 yr:** After adjusting for age, sex, baseline BMI, education, baseline smoking status and diet type, the weight loss at 6 mos of intervention (OR= 1.5, 95% CI: 1.35–1.67) was significantly associated with successful weight loss at 24 mos. * No p-values reported.	Multivariate logistic regression.	RCT / method not specified.	Measured by the researcher (method not specified).
(Volger et al. 2013). Eating behaviours, dietary habits, physical activity, completion of primary care provider visits. To examine changes in eating behaviours and physical activity, as well as factors of weight loss success.	336	51.5 ± 11.5	Not reported	USA	0 - 24mos	**6-mos change in study variables association with weight loss at 6mos:** After adjusting for sex, ethnicity, site, and baseline age, % food diaries completed (β= -0.07, p< 0.0001), Lifestyle Counseling visits during the first 6 months of treatment (β= -0.1, p= 0.009).	Multivariable regression analysis.	RCT / Questionnaire.	Measured by the researcher (Digital scale).

(Postrach et al. 2013). Early weight loss, program usage "self-monitoring (dietary and physical)" and weight entries. To investigate the weight loss dynamics of KiloCoach (i.e. a web commercial program to induce lifestyle changes that lead to weight loss) for users who used the program for at least 6 months and to associate final weight loss with the use of different program tools.	479	44.2 ± 11.8	F: 57.8% M: 42.2%	Germany	0 ≥ 6mos	**Successful weight reduction of ≥5% at 6mos:** After adjusting for sex, age, and baseline BMI, percent weight loss of week 3-4 (β= 1.57, p< 0.001), self-monitoring (β= 0.027, p< 0.001), total weight entries (β= 0.040, p= 0.001) were significantly associated with 6mos successful weight loss. **Early weight loss (%) correlates with weight maintenance - After 1 yr:** Weeks 1-2 (r= 0.249, p< 0.001), weeks 3-4 (r= 0.402, p< 0.001), after 3 months (r= 0.604, p< 0.001). **Early weight loss (%) correlates with weight maintenance - After 1.5 yr:** Weeks 1-2 (r= 0.237, p= 0.007), weeks 3-4 (r= 0.396, p< 0.001), after 3 months (r= 0.547, p< 0.001). **Early weight loss (%) correlates with weight maintenance - After 2 yr:** Weeks 1-2 (r= 0.278, p= 0.008), weeks 3-4 (r= 0.447, p< 0.001), after 3 months (r= 0.553, p< 0.001).	1- Multiple regression analyses. 2- Correlations analyses. (testing early weight loss)	Secondary analysis of an RCT / Web-based questionnaire.	Self-reported.

(Krukowski et al. 2008). Website components, website usage, dietary intake, physical activity levels, computer ability and attitudes, social influence. To explore the utilization of various weight-control website components and their impact on weight loss.	123	46.8	F: 83% M: 17%	USA	0 - 12mos	**Successful weight reduction at 6mos:** baseline weight (β= -0.136, p= 0.006), feedback factor* (β= -0.03, p= 0.003). *Past journals, progress graphs, and body mass index, waist-to-hip, and target heart rate calculators. **Successful weight reduction at (7mos-12mos):** Social support factor (β= -0.235, p= 0.01). *Social support factor: Web chats and biographical information/e-mail addresses.	1-Simple linear regression models. 2-Multiple linear regression model	Longitudinal / Web-based questionnaire.	Measured by the researcher (Beam-balance scale) & Self-reported.
(Jacobs, Radnitz, and Hildebrandt 2017). Self-monitoring components and adherence to self-monitoring. To examine adherence to self-monitoring as a factor associated with successful weight loss.	7680	Not reported	F: 72.8% M: 27.2%	USA	0 - 3mos	**Successful weight reduction of ≥5% at 3mos:** Age (β= 0.12, p= 0.003), female (β= 0.25, p< 0.001), adherence percentage (β= -0.29, p< 0.001), caloric intake (β= 0.13, p< 0.001), American (0)/African (1) (β= -0.11, p= 0.00), American (0)/European (1) (β= -0.08, p= 0.02), American (0)/Latin American (1) (β= -0.12, p= 0.00), sex X age (β= -0.15, p= 0.00), adherence X location (africa) (β= 0.10, p= 0.00), adherence X location (Europe) (β= 0.09, p= 0.02), adherence X location (Latin America) (β= 0.11, p= 0.00).	Latent growth curve modelling (LGCM) using Mplus.	Longitudinal / Participant's total amount of web log-ins.	Self-reported.
(Krukowski et al. 2013). Self-monitoring. To examine patterns of self-monitoring associated with greater weight loss at 6mos.	161	46.2 ± 9.8 (range 22–68)	F: 92% M: 8%	USA	0 - 6mos	**Successful weight reduction of ≥5% at 6mos:** After adjustment for demographic factors, overall self-monitoring log-ins (β= −0.11, p< 0.001) were significantly associated with weight loss at 6mos.	Multivariate linear regression.	RCT / Participant's total amount of web log-ins (monitored and self-reported).	Measured by the researcher (Calibrated digital scale).

(Johnson and Wardle 2011). Self-monitoring. To assess associations between engagement with self-monitoring tools and social support, and weight loss in an online weight-control programme.	3621	35.5 ± 10.5	F: 82.3% M: 17.7	UK	≥ 28 days	**Factors associated with ≥5% weight loss - women:** The odds ratios associated with clinically significant weight loss in: highest vs lowest tertile of adherence to food diaries were 5.1 (p< 0.001). highest vs lowest tertile of adherence to exercise diaries 1.5 (p< 0.05). online forum use vs not use was 1.3 (p< 0.01). **Factors associated with ≥5% weight loss - men:** The odds ratios associated with clinically significant weight loss in: highest vs lowest tertile of adherence to food diaries were 3.5 (p< 0.001). highest vs lowest tertile of adherence to exercise diaries 3.5 (p< 0.01).	Logistic regression.	Longitudinal / Number of days diet/exercise diaries used, which are adjusted for duration of programme use.	Self-reported.
(VanWormer et al. 2009). Self-weighing frequency. To examine the association between self-weighing and weight change in a cohort of individuals participating in a weight-loss program.	100	46.5 ± 8.7	F: 91% M: 9%	USA	0 - 18mos	**Successful weight reduction of ≥5% at 6mos:** The proportion of participants who lost ≥5% of their pretreatment weight was significantly higher among participants who self-weighed at least weekly than among those who self-weighed less than weekly (46% vs 8%). Participants who self-weighed at least weekly were 11 times more likely to lose at least 5% of their pretreatment weight after 6 months (OR= 11.1, p< 0.001).	General linear mixed model.	RCT / total number of days self-weighed divided by the total number of days in the active treatment phase.	Method not specified.

(Czeglédi 2017). Eating behaviours, depression, sociodemographic. To investigate factors of eating behaviours among the participants of an inpatient that is associated with weight loss treatment.	339	50.2 ± 13.47 (range 18–85)	F: 81% M: 19%	Hungary	0 - 6mos	**Factors associated with successful weight loss of ≥5% at 6mos:** Increase in cognitive restraint (OR=5.75, p< 0.001), female (OR= 2.77, p< 0.10), age (OR= 0.97, p< 0.10).	1- Correlation analysis. 2- independent-samples T-test. 3-Multiple binary logistic regression.	Longitudinal / Questionnaire.	Self-reported.

(Jessica Unick, Jakicic, and Marcus 2010). Eating behaviours, physical activity, energy intake and macronutrient composition, program participation. To examine if eating behaviours, physical activity levels, and program participation influence one's ability to achieve ≥5%, ≥7%, and ≥10% weight loss during 24 months.	170	38.3 ± 5.4 (range 23-45)	F: 100% M: 0%	USA	0 - 24mos	**Factors associated with ≥5% weight loss at 24mos:** % telephone calls completed (β= -0.010, p< 0.001), change in Eating Behaviour Inventory Questionnaire score (0–24 months) (β= -0.009, p<0.01). **Factors associated with ≥7% weight loss at 24mos:** Change in Eating Behaviour Inventory Questionnaire score (0–24 months) (β= -0.011, p< 0.01), % telephone calls completed (β= -0.007, p< 0.01). **Factors associated with ≥10% weight loss at 24mos:** Change in physical activity (0–24 months) (β= -0.0000774, p< 0.01), change in Eating Behaviour Inventory Questionnaire score (0–24 months) (β= -0.009, p< 0.01). *****Program participation was evaluated by the percentage of group meetings attended and the percentage of telephone calls completed with an interventionist.	1- Bivariate correlation coefficients. 2- Multivariate logistic regression analysis.	Secondary analysis of an RCT / Questionnaire.	Measured by the researcher (Calibrated balance beam scale).

(CHAMPAGNE et al. 2011). Dietary consumption/intake. To examine if changes to specific dietary variables were associated with weight loss and maintenance.	828	55.6	F: 63% M: 37%	USA	0 - 30mos	**Factors associated with weight change at 6mos:** **Macronutrients:** +1% carbohydrates, substitute for fat (β= -0.15, p< 0.0001). +1% protein, substitute for fat (β= -0.33, p< 0.0001). +1% protein, substitute for carbohydrate (β= -0.18, p= 0.0011). **Different food groups:** +1 fruit/vegetable serving (β= -0.29, p< 0.0001). **Factors associated with weight change at 30mos:** **Macronutrients**: +1% carbohydrates, substitute for fat (β= -0.03, p< 0.0001). +1% protein, substitute for fat (β= -0.07, p< 0.0001). +1% protein, substitute for carbohydrate (β= -0.05, p= 0.0003). **Different food groups:** +1 fruit/vegetable serving (β= -0.04, p= 0.0062). +1 dairy serving (β= -0.17, p= 0.0002).	Linear regression models.	Secondary analysis of an RCT / Questionnaire.	Measured by the researcher (Calibrated scale).
(Smithson and Hill 2017). Food craving, cognitive restraint, self-Regulatory, depression, demographic. To investigate the frequency and nature of food craving and its association with weight loss in people attending a group-based weight management programme.	2932	43.0 (range 18–91)	F: 97% M: 3%	UK	0 - 7wk	**Factors associated with weight loss at 7wk:** After controlling for baseline BMI and age, changes in weight across the study period were accompanied by changes in craving experience, such that those who lost more weight also reported a decrease in difficulty in eating control (β= 0.119, p< 0.001).	Linear regression analyses.	Longitudinal / Web-based questionnaire.	Measured by the researcher (method not specified).

(Urbanek et al. 2015). Cognitive eating restraint. To examine whether changes in cognitive eating restraint and disinhibition are associated with weight loss.	60	35.9 ± 5.8	F: 100% M: 0%	USA	0 - 18wk	**Factors associated with weight loss at 18wk - using change in hip circumference as a measure of weight loss:** Baseline BMI (β= 0.496, p= 0.03), baseline hip circumference (β= -0.232, p= 0.03), change in cognitive eating restraint score (β= -0.681, p< 0.0001), change in caloric expenditure (β= 0.005, p= 0.04), change in cognitive eating restraint score X change in disinhibition score (β= -0.123, p= 0.04).	1-Correlations analyses. 2-Multivariate linear regression.	Secondary analysis of a longitudinal study / Questionnaire.	Measured by the researcher (method not specified).
(Das et al. 2009). Energy restrictions, physical activity level, hunger, desire to eat, dietary satisfaction, and weight self-efficacy. To measure the adherence of prescribed level of energy restrictions to investigate factors of variability in individual weight loss success.	38	35 ± 6	Not reported	USA	0 - 12mos	During 6–12 mos of energy restrictions when food was self-selected, higher baseline BMI and greater 6-month disinhibition scores are associated with weight gain (adj R2= 0.71, p< 0.0001). In a separate model (not including baseline BMI) that had a slightly lower R2, a lower baseline physical activity level is associated with weight change during 6–12 months (adj R2= 0.69, p<0.0001). * No β or p-values reported.	Multiple regression model.	RCT / Doubly labelled water & food records (Energy restrictions adherence), resting metabolic rate (physical activity level), questionnaire (hunger, desire to eat, dietary satisfaction, and weight self-efficacy).	Measured by the researcher (Calibrated scale).

(Webber et al. 2010). Motivation to adhere to self-monitoring. To examine changes in motivation over time to identify periods of declining motivation and to examine the relationship of motivation to adherence to self-monitoring and weight loss.	66	50.1 ± 9.9	F: 100% M: 0%	USA	0 - 16wk	**Factors associated with ≥5% weight loss at 16wk:** Autonomous motivation (at 4wk) was correlated with 16-week weight loss. In regression analysis, autonomous motivation (at 4wk) was associated with a small but significant amount of variance in 16- week weight loss (adjusted R2= 0.06, p= 0.05). Completion of self-monitoring diaries over the entire 16-week study was strongly correlated with 16-week weight loss in the entire sample (r= 0.66, p< 0.001). Completion of self-monitoring diaries between weeks 5 and 16 was also correlated with 16- week weight loss (r= 0.63, p< 0.001). Regression analysis, using the completion of diaries between weeks 5 and 16 and controlling for previous Internet usage and treatment group, found that completion of diaries predicted a significant amount of variance in weight loss (adjusted R2= 0.44, p< 0.001). * No β or p-values reported.	1-Correlations analyses. 2-Linear regression models.	RCT / Questionnaire (motivation), online food, exercise, and weight diary forms (self-monitoring).	Measured by the researcher (Calibrated digital scale).
(B Cresci et al. 2011). Motivation. To evaluate weight loss predictability of the TREatment MOtivation and REadiness test (TRE-MORE).	129	45.7 ± 14.6	F: 79% M: 21%	Italy	0 - 6mos	**Motivation predictor of ≥5% weight loss at 6mos:** After adjusting for age, sex, BMI, Binge Eating Scale, Obesity-Related Well-Being (quality of life), higher scores of TRE-MORE total (OR=29.04, p< 0.001), obstacles and desire to overcome (OR= 3.82, p=0.002), and taking care of themselves and sharing the problems (OR= 2.90, p= 0.03) were predictors of ≥5% weight loss at 6mos.	1-Logistic Regression analysis. 2-Receiver operating characteristic curve (ROC).	Longitudinal / Questionnaire.	Self-reported.

(Barbara Cresci et al. 2013). Motivation. To explore the relationship between TRE-MORE scores and muscle mass, and their relative independent contribution to the prediction of weight loss.	266	43.2 ± 11.9	F: 73% M: 27%	Italy	0 - 6mos	**Motivation association with ≥5% weight loss at 6mos:** After adjusting for sex, age, waist and BMI, higher muscle mass (β= 0.268, p= 0.037) and higher TRE-MORE 3 scores (β= 0.200, p= 0.050) at baseline and a lower number of previous diets (β= –0,219; p= 0.031) were significantly associated with weight loss.	1-Correlations analyses. 2-Linear multiple regression.	Secondary analysis of a longitudinal study / Questionnaire.	Measured by the researcher (method not specified).
(Wingo et al. 2013). Self-efficacy, dietary behaviours, physical activity. To determine whether self-efficacy is independently associated with weight loss in behavioural intervention.	537	50 ± 8.9	F: 61% M: 39%	UK	0 - 18mos	**Change in weight and correlation with change in dietary self-efficacy at 6mos:** (r= -0.24, p< 0.01). **Change in weight and correlation with change in dietary self-efficacy at 18mos:** (r= -0.16, p< 0.01). **Change in weight and correlation with change in exercise self-efficacy at 6mos:** (r= -0.20, p< 0.01). **Change in weight and correlation with the change in exercise self-efficacy at 18mos:** (r= -0.25, p< 0.01).	Correlations analyses.	Secondary analysis of an RCT / Questionnaire.	Measured by the researcher (Calibrated scale).
(J. J. Annesi 2018). Self-regulation, mood, physical activity, consumption of fruits and vegetables. To examine whether baseline self-regulation influences participants response to behavioural treatments.	91	(range 23-60)	F: 100% M: 0%	USA	0 - 24mos	Weight loss over 6 and 24 mos was significantly greater for the responder group at 8.1% and 8.6% versus nonresponders at 4.7% and 3.8%, respectively. Changes in physical activity (β= -0.20, p= 0.049), and fruit/ vegetable consumption, (β= -0.41, p< 0.001) independently contributed in weight change.	Multiple regression test.	Secondary analysis of a longitudinal study / Questionnaire.	Measured by the researcher (Calibrated digital scale).

(J. Annesi et al. 2016). Self-regulation, mood, physical activity, consumption of fruits and vegetables, self-efficacy. To evaluate a new, theory-based protocol in which exercise support methods are employed to facilitate improvements in psychosocial predictors of controlled eating and sustained weight loss.	55	Not reported	F: 100% M: 0%	USA	0- 24mos	**Change in mediator variables (baseline-6mos) association with weight loss at 6mos:** Change in self-regulation (β= -2.13, p= 0.002). **Change in mediator variables (baseline-6mos) association with weight loss at 24mos:** Change in self-regulation (β= -5.19, p< 0.001).	Multiple regression analysis.	RCT / Questionnaire.	Measured by the researcher (Calibrated scale).
(Turner-McGrievy and Tate 2013). Social support (i.e. Twitter posting). To examine the types of online social support utilized in a behavioural weight loss intervention and the relationship between Twitter posting and weight loss.	47	42.6 ± 10.7	F: 77% M: 23%	USA	0 - 6mos	**Factors associated with weight loss at 6mos:** After adjusting for age, sex, and ethnicity, posts to Twitter were significantly associated with % weight loss at 6 mos, such that every ten posts to Twitter corresponded with approximately -0.5% weight loss (β= -0.48, p< 0.001).	Linear regression analysis.	RCT / Questionnaire.	Measured by the researcher (Calibrated digital scale).
(Bandín et al. 2014). Circadian rhythmicity. To investigate the potential relationship between weight loss and circadian rhythmicity in women undergoing a weight-loss program, in order to assess whether circadian rhythmicity could be a marker of weight-loss effectiveness.	85	39.84 ± 12.3	F: 100% M: 0%	Spain	0 - 10mos	**Factors correlated with weight loss at 10mos:** Mean wrist temperature (r= -0.239, p= 0.030), mesor (r= -0.243, p= 0.027), twelfth harmonic's accumulated power (r= 0.243, p= 0.027), first harmonic's power (r= 0.217, p= 0.049), second harmonic's power (r= 0.254, p= 0.020), hourly average during the 10 consecutive hours of minimum values (r= -0.257, p= 0.019), intradaily variability (fragmentation) (r= -0.300, p= 0.006).	Correlations analyses.	Longitudinal / Wrist temperature and actimetry measurements.	Measured by the researcher (Calibrated body scale).

(R. Sawamoto et al. 2014). Sleep fragmentation. To determine if sleep duration and quality can be associated with the magnitude of weight reduction in a weight-loss intervention program for women living with overweight and obesity.	90	47.9 ± 12	F: 100% M: 0%	Japan	0 - 7mos	**Factors associated with weight loss at 7mos - objective measure:** After adjusting for age, baseline BMI, smoking status, Center for Epidemiologic Studies-Depression Scale score and the total calorie intake per day during treatment, the number of wake episodes was the strongest associated with BMI reduction (β= -0.341, p= 0.002). **Factors correlated with weight loss at 7mos - subjective measure:** Sleep duration as measured by the PSQI, exhibited a linear relationship with sleep minutes, as measured by actigraphy (r= 0.229, P= 0.0127). The apnea subscale of the PSQI correlated only with wake after sleep onset, as assessed by actigraphy (r= 0.250, P= 0.0326).	1-Correlations analyses. 2-Simple and multiple regression analyses.	RCT / Questionnaire & actigraphy.	Measured by the researcher (method not specified).

Abbreviations: BMI, Body Mass Index; F, Female; M, Male; mos, months; wk, weeks; UK, United Kingdom; USA, United States of America; ß, beta; OR, Odds Ratio; RCT, Randomised Controlled Trial. Values of age are reported as mean ± standard deviation & range (if available) – Unit in years. Studies used a prediction model (Teodora Handjieva-Darlenska et al. 2012; T. Handjieva-Darlenska et al. 2010a; B Cresci et al. 2011).

2.4 Discussion

The Predictors OF WEight Reduction (POWER) study is a comprehensive purpose-designed study of the behavioural, psychological and clinical determinants of weight loss success. This study was planned to be conducted to identify behavioural and psychological information that predicts successful weight loss on weight management services using data that are not routinely collected.

The limitation of the existing literature based on the literature review done in this chapter is 1) the results were inconsistent and contradictory due to the diversity of the published studies. 2) The lack of generalisability as the results were variable and rarely externally validated. 3) The insufficient sample size resulting in low-powered studies (Anton et al. 2008; Finkler, Heymsfield, and St-Onge 2012a; Das et al. 2009; Turner-McGrievy and Tate 2013). 4) Limited statistical analysis methods were used to identify predictors of weight loss in almost 95% of the studies, few were using prediction models (B Cresci et al. 2011; T. Handjieva-Darlenska et al. 2010a; Teodora Handjieva-Darlenska et al. 2012). Due to these limitations, it is challenging to make the decision on which behavioural predictor of weight loss success is the most important.

2.4.1 Risk factors selected for the questionnaire

The process used in this review to identify a list of variables suitable for inclusion was that the variable that has an association with or prediction of weight loss was identified in a large study or repeatedly mentioned in the studies (at least 3-4 times). Therefore, if a variable was mentioned once in a small study, the variable was not considered for inclusion. Priority was given to papers that used a prediction model to test the relationship with weight loss. Based on the literature, risk factors were chosen to be included in the questionnaire. This includes:

1) Eight studies out of the 46 explored variables related to demographic and socio-demographic information (Delahanty et al. 2013a; Vinkers et al. 2014; Alharbi et al. 2016; Yank et al. 2014; Elfhag and Rossner 2010; Krukowski et al. 2013; Czeglédi 2017; Smithson and Hill 2017). Regardless of result variability between studies, these fundamental demographics cannot be neglected in modelling.

2) Seven studies out of the 46 emphasise the importance of early weight loss in weight loss programmes (Teodora Handjieva-Darlenska et al. 2012; T. Handjieva-Darlenska et al. 2010a; JL Unick et al. 2015; Garvin, Hardy, and Xu 2016; Jessica Unick et al. 2015; Greenberg et al. 2009; Postrach et al. 2013). Three studies out of the 46 showed the influence of weight loss history on weight loss outcome (Myers et al. 2013b; Latner and Ciao 2014; Delahanty et al. 2013a). weight-related information (i.e. current weight, weight loss history, weight loss expectations). One article reported weight loss expectations as an important variable associated with weight loss outcomes (Calugi et al. 2017).

3) Five studies out of 46 tested different forms of motivation (Anton et al. 2008; Rotella et al. 2014; Webber et al. 2010; B Cresci et al. 2011; Barbara Cresci et al. 2013). Two studies out of 46 revealed the importance of weight loss goals (De Vet et al. 2012; McKee and Ntoumanis 2014b). Nine studies out of the 46 explored self-efficacy and its relationship with weight loss outcomes (McKee and Ntoumanis 2014b; J. Annesi and Gorjala 2010; Delahanty et al. 2013a; Vinkers et al. 2014; Alharbi et al. 2016; Yank et al. 2014; Das et al. 2009; Wingo et al. 2013; J. Annesi et al. 2016). Two studies out of the 46 tested the relationship between sleep and weight loss (R. Sawamoto et al. 2014; Bandín et al. 2014). Thirteen studies out of 46 explored eating behaviour factors, including dietary habits, dieting, cognitive eating restraint, binge eating, energy intake, food craving and food consumption (Anton et al. 2008; J. Annesi and Gorjala 2010; Rotella et al. 2014; Delahanty et al. 2013a; Alharbi et al. 2016; Volger et al. 2013; Czeglédi 2017; Jessica Unick, Jakicic, and Marcus 2010; Smithson and Hill 2017; Urbanek et al. 2015; B Cresci et al. 2011; J. Annesi 2018; J. Annesi et al. 2016).

Based on the work done in this chapter, most of the important variables reported in the literature were included in the same questionnaire. Efforts have been made in this study to clarify if different questionnaires were found in the literature testing the same predictor variable. The researcher explored each questionnaire and choose the most appropriate questions/questionnaire that fulfil the aim of this study.

2.4.2 Strengths of the study

POWER can add to the literature because it tests and validates several important behavioural factors in the same study, systematically, using the same statistical analysis method. POWER study is a well-designed study with cohort specifications. It has a clear definition for dependent and independent variables. Moreover, it uses data linkage to weight management services, meaning all weight data will be available. This overcomes the loss to follow-up problem that occurs in every weight management programme, as participants may not attend follow-up study visits for weight measurements if they did not lose 'enough' weight in the early sessions.

2.4.3 Limitations

This is a narrative review and tools to assess the quality of the studies resulting from this review were not used as in a systematic review. Regardless, this study was done to identify potential predictors of weight loss success and not to elicit a summary of conclusions of all available research studies. Conducting a narrative review is more relevant to the aim of this study as it can conduct a wider exploration of the literature, which could be lost when conducting a systematic review (because of the restrictive framework).

As the main population of this study will be weight management participants (mainly white females sample), this study is prone to selection bias.

2.5 Conclusions

The POWER project is ready to be conducted. Advancing the information available in the POWER chapter by conducting the research on weight management services will help the healthcare providers to identify who will be successful in losing the required weight loss and who will fail to do so. Also, they will be able to provide more support strategies and alternative programmes for people who are not finding the current weight management programme useful for them. This will ultimately assist in providing a personalized treatment plan, which will reduce the medical cost of treating obesity.

3 Development of a predictive model, for successful short and medium-term weight loss in people with type 2 diabetes attending a weight management programme

3.1 Introduction

Overweight and obesity is a growing worldwide problem. According to the World Health Organisation (WHO), 1.9 billion adults worldwide are living with overweight or obesity. The origin of obesity is multifactorial, it involves genetic, environmental and behavioural factors (Piché et al. 2018; Lajunen et al. 2009).

Behavioural weight management programmes are effective in helping patients living with obesity to lose weight and improve their health (Knowler et al. 2009; Gillies et al. 2007b). To promote a healthy diet and lifestyle, these programmes depend mainly on education and various behaviour change techniques (e.g. self-monitoring and goal-setting) (Baetge et al. 2017b; Thomas Wadden et al. 2012a). It is suggested that in people with overweight or obesity, losing 5% of body weight would result in a variety of improved health outcomes (Franz et al. 2015; Ma et al. 2017; Wing et al. 2011; Knowler et al. 2009). In NHS GGC, Weight Watchers defines losing >5 kg of body weight as a successful outcome. Approximately 50% of the patients attending Weight Watchers achieve at least 5% weight loss of body weight (Ahern et al. 2011b; Fuller et al. 2011). However, patients' response to weight loss programmes is heterogeneous. Half of the patients get the benefit, and the other half either drop out of the programmes or fail to reach a 5% weight loss threshold despite remaining in the programme.

Several research studies have explored and suggested different clinical, demographic and process factors of success and failure to lose weight. Based on the literature review done in the previous chapter (POWER chapter), the most important clinical factor associated with successful weight loss is the early weight loss in the programme (JL Unick et al. 2015; Jessica Unick et al. 2015; Garvin, Hardy, and Xu 2016). This can be within the first weeks (1-3 weeks) or the first months (1-3 months) of the programme depending on the time point tested (short-term or medium-term, respectively. A secondary analysis of an RCT study showed that achieving a meaningful weight loss at 1 year of treatment was strongly predicted by losing at least 5% of body weight at 12 weeks in patients with/without Type 2 Diabetes mellitus (T2DM) (Smith et al. 2014). Demographic factors that are associated with successful weight loss include older age (Delahanty et al. 2013b; Mutsaerts et al. 2013), being female and having higher education (Vinkers et al. 2014). Process factors that are associated with successful weight loss include

higher program participation, engagement and attendance (Jessica Unick, Jakicic, and Marcus 2010). Research into predictors of weight loss success highlights the role of the clinical, demographic and process factors. Regardless, there are limited quantitative works done to explore predictors of weight loss success at a baseline level for individuals with obesity and T2DM, undertaking behavioural weight management programmes.

3.1.1 Study hypothesis

The previously identified proposed exposures of interest, including demographic, clinical and process factors, are associated with and predictive of successful weight loss at end of the behavioural weight management programme (i.e. short-term) and 3 years following the start of the behavioural weight management programme (i.e. medium-term).

3.1.2 Study aims

1) To identify patient factors (e.g. clinical, sociodemographic) that are associated with successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.

2) To identify process factors (e.g. attendance, completion, early weight loss) that are associated with successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.

3) To identify patient and process factors that will predict successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.

3.2 Methods

3.2.1 Intervention

3.2.1.1 National Health Service Greater Glasgow and Clyde (NHS GGC)

The National health service (NHS) in the United Kingdom is the public-funded health care system. It consists of four main systems, including Great Britain (i.e. England, Scotland, and Wales) and Northern Ireland. The NHS GGC is the largest of 14 NHS boards in Scotland (it serves a population of 1.2 million). It is the Board's responsibility to ensure the efficiency of the service (including hospitals and General Practice (GP) services) delivered to the NHS GGC patients.

3.2.1.2 NHS GGC Weight Management Service (GCWMS)

The GCWMS model was developed in 2004 and extended throughout the Health Board area in 2008. The GCWMS is a free of charge service provided by the NHS for adults who are 18 years old and above, have chronic diseases such as diabetes, heart diseases and stroke, as well as having a BMI of 35 kg/m^2 and above or a BMI of 30 kg/m^2 with serious health complications (NHS-GGC 2018). This service aims to assist patients to lose 5 kg or more of body weight to minimise or improve health conditions. Patients who fit the criteria for accessing the service can opt-in through referrals from GPs or hospital doctors. The team that participates in GCWMS consists of dietitians, psychologists, physiotherapists and administrative staff. The level of success in GCWMS and other weight management services depends on patients' motivation for changing their lifestyles. Once the eligible patients got the referral from their healthcare provider, they receive the service leaflet and are asked to phone the service within two weeks for assessment. Information about the patient's history (i.e. previous weight journey and diet, physical activity, motivations and moods) are taken during the assessment session. As part of GCWMS, the working teams such as a physiotherapist or a clinical psychologists assist patients who might need additional assessments/support by choosing the optimal treatment strategy for them to get the optimal results from the service. Moreover, the service is provided in small groups or customised to patients attending the service to fit patients' needs.

The GCWMS consists of three main phases attended one after the other:

1) 16-week / 9 fortnightly sessions of a group behavioural weight management programme meaning that the patients attend one session every two weeks. The intervention includes a deficit diet (i.e. taking 600 kcal/day less energy than the body needs to lose weight), exercise, and behavioural treatment therapy (i.e. self-monitoring, setting realistic goals, motivation techniques etc.). Education and advice by dieticians and psychologists are also provided throughout the sessions to improve healthy eating behaviours, level of physical activity, positive thinking mindset and dealing with social stress. Upon completion of this phase, patients have the option to choose between attending the second phase (immediately after the first phase) and then entering the third phase/weight maintenance or skipping the second phase and going into the third phase (immediately after the first phase).

2) 16-week / 4 monthly sessions meaning that the patients attend one session every month. The intervention includes further lifestyle advice (FWL), a low-calorie diet (LCD) or pharmacotherapy (orlistat). The intervention provided in this phase entirely depends on the patient's choice. In general, patients who achieved the required weight loss successfully from the first phase (i.e. at least 5 kg weight loss from the initial body weight) can take 3 sessions of FWL over 3 months, and patients who fail to lose the required amount of weight loss can take either the LCD or pharmacotherapy.

3) 12-month / 12 monthly sessions for weight maintenance meaning that the patients attend one session every month. Patients have the option of repeating the second phase before starting the third phase if they fail to lose the 5 kg body weight at the end of the second phase. Patients can also consider bariatric surgery if their BMI is 40 kg/m^2 or above, or 35 kg/m^2 and above with comorbidities.

3.2.2 Data Source

3.2.2.1 Patients records from NHS GGC Weight Management Service (GCWMS)

Data collection of GCWMS is obtained by the dietitians during the attendance of participants at each weight management session. The dietitians use the calibrated scales to measure and note the participant's weight and height. Then dietitians record and transfer the information into the database. The database includes participants' information (all those referred to GCWMS) for the period between 2005 to 2014. A real-time database was used for data collection and a Microsoft Structured Query Language (SQL) server was used to store the data. The data for the present work including all requested fields were extracted using a SQL query for each table by a data analyst at GCWMS. The SQL queries output was then transferred into a comma-delimited text file which was then transferred into the data development manager and sent to a Safehaven (Robertson Centre for Biostatistics).

3.2.2.2 Patients records from Scottish Care Information - Diabetes Collaboration (SCI-DC)

The SCI-DC is an integrated shared electronic patient record system that does the screening service twice a year (i.e. every 6 months) for patients who are in Scotland and have diabetes. It provides clinical (e.g. assessment and referral weight, lipid profile, hemodynamic measures etc.) and demographic data (e.g. date of birth, socioeconomic status, sex, ethnicity) and diabetes status of the patients in the NHS Scotland (e.g. diagnosis of T2DM, weight measurements, diabetes medication etc.). This register includes data from all except 5 of >1000 general practices in Scotland and was shown to detect 99.4% of patients with diabetes in Scotland.

3.2.2.3 Data linkage

The GCWMS records were then combined with SCI-DC records via the Community Health Index (CHI) number. The CHI number is a patient identifier number, where each patient gets this number upon registration into the system. The results of this linkage allow the identification/derivation of clinical, demographic and

process variables for each patient referred and attended the GCWMS and were diagnosed with T2DM.

3.2.2.4 Data access

A remote virtual private network (VPN) in the NHS GGC SafeHaven hosted by the Robertson Centre for Biostatistics was used to access the database safely, which means that any information that allows for the identification of the patient was removed before using the data. Ethical approval for this study is obtained and granted by the NHS GGC SafeHaven.

3.2.3 Design

A longitudinal cohort study. The current database was available from 2005 to 2014. This allows the follow-up period for each patient for at least 3 years (at the initiation of the project in 2017).

3.2.4 Inclusion criteria

Table 3-1: The inclusion criteria for the final analysed cohort in the study.

Criteria / Source	Definition
1) Those who were referred to the GCWMS / GCWMS.	Identifying the first recorded referral date to ensure that the patients are referred to the GCWMS.
2) Those who attend at least 1 weight loss session within the first 3 sessions of the 16-week / 9 fortnightly sessions of the group behavioural weight management programme / GCWMS.	Ideally, in this study, the date of the first 3 sessions of the behavioural weight management programme was identified. Regardless, patients should have at least one date from these 3 sessions to be considered an attendee.
3) Adult age ≥ 30 & ≤ 76 / SCI-DC & GCWMS.	The age of the participants in the first session attended in the behavioural weight management programme (calculated from the date of birth) was identified. The exclusion was then applied to exclude those <30 to >76 years.
4) Diagnosis of T2DM before attending the first weight management session of the behavioural weight management programme / SCI-DC & GCWMS.	The duration of T2DM at the patient first session attendance to GCWMS was calculated. Individuals should not exceed 30 days of T2DM diagnosis at the time of referral to GCWMS.

Abbreviations: BMI, Body Mass Index; SCI-diabetes, Scottish Care Information Diabetes; GCWMS, NHS GGC Weight Management Service.

3.2.5 Data handling

Data cleaning to detect and edit any faults in the data was performed manually. The cleaning was done for a total of 5855 patients referred and attending the GCWMS. The different datasets were merged in a sequence manner into a single dataset to allow the analysis of the data. Upon merging, there were duplicate rows for each participant which were dropped during the cleaning process.

Predetermined limit values were applied to eliminate outliers: HbA1c (30-140 mmol/mol), systolic blood pressure (SBP) (90-200 mmHg), diastolic blood pressure (DBP) (40-150 mmHg), total cholesterol (2.5-200 mmol/L) and high-density lipoprotein cholesterol (hdl) (0.5-4.0 mmol/L).

Exclusions were also applied for those who have been diagnosed with T2DM before their date of birth (n=2), those who have been diagnosed with T2DM ≥30 days after the first attendance date (n=1418), those who have missing BMI data (n=262), those with BMI <30 (n=106), those who don't have a referral or assessment height (n=1), those who aged <30 & >76 (n=194), those who have HbA1c <30 (n=6), those who have been diagnosed with T2DM on the age of <30 years old (to avoid confusion with type 1 diabetes) (n=145) and date of first attendance recorded wrongly in the dataset (n=1). After the cleaning process, 3720 participants were included.

In this study, three variables were identified: predictors, short-term outcome and medium-term outcome. Each one is described thoroughly below.

3.2.5.1 Predictors

In this study, predictor variables were classified as demographic, clinical, and process (Table 3.2 - 3.4).

The time window for predictor variables was identified at the baseline point (i.e. 0m). This was set to be the date of the first session attended in the 16-week / 9 fortnightly sessions of the group behavioural weight management programme.

- **Demographic variables** include age, sex and the Scottish Index of Multiple Deprivation (SIMD). The definition of each variable based on this study was:

- Age (Continuous, years): the age of the participants at the first session attended from the 16-week / 9 fortnightly sessions was calculated from the date of birth of participants. Only those who were at age of ≥30 to ≤75 years were included.
- Age (Categories): age categories were developed from the continuous variable of age (based on quintiles). There are five age groups: 30-39.9, 40-49.9, 50-59.9, 60-69.9 and ⩾70 years.
- Sex: there are several gender identities, in this study, two identities were explored, which are male and female.
- SIMD: the information about the patient's level of education and economic status were not available in this database. Alternatively, the SIMD was used to estimate the socioeconomic status of each participant. In Scotland, the postcode of residence is used to divide the country into 6,505 datazones. Each datazone includes ≈350 households and ≈800 people. Seven domains construct the SIMD for each datazone. Those domains are income and benefits, employment, health, education (including skills and training), housing, crime, and access to services. Therefore, the quintiles of socioeconomic status for the Scottish population using the SIMD are ranging from 1 (most deprived) to 5 (least deprived). The quintiles were as follows, Q1 (Most deprived), Q2, Q3, Q4, Q5 (Least deprived).

- **Clinical variables** and their definitions are described below:
  - Duration of T2DM (years): this variable was used to ensure that the participant did not exceed 30 days of T2DM diagnosis at the time of attending the first session of GCWMS. This was done by calculating the period between a patient's diagnosis with T2DM and the first session attended at the 16-week / 9 fortnightly sessions.
  - Initial Height (m): the patient referral height was used in this study as a baseline height.
  - Initial weight (kg): the first weight recorded in the 16-week / 9 fortnightly sessions.
  - Initial Body Mass Index (BMI, kg/m^2): person's initial weight divided by the square of the referral height.

- Initial BMI categories: BMI categories were developed from the initial BMI (based on quintiles). There are four BMI groups: 30 – 34, 35 – 39, 40 – 49, ≥ 50
- HbA1C (mmol/mol), Systolic blood pressure (SBP, mmHg), Diastolic blood pressure (DBP, mmHg), Total cholesterol (mmol/L), Triglycerides (mmol/L) and High-Density Lipoprotein (HDL) cholesterol (mmol/L): the most recent values for each variable were taken. For Low-Density Lipoprotein (LDL) cholesterol (mmol/L): friedewald formula was used to get LDL value. The time window for each variable was within 18 months before the date of first attendance of the 16-week / 9 fortnightly sessions. This time window was chosen since clinical chemistry is not taken regularly and this is the most sensible duration for getting the minimum missing values.
- % weight change: Session2 - Session1: percent of weight change between second & first attended session of the 16-week / 9 fortnightly sessions.
- % weight change: Session3 - Session1: percent of weight change between third & first attended session of the 16-week / 9 fortnightly sessions.
- % weight change: Session3 - Session2: percent of weight change between third & second attended session of the 16-week / 9 fortnightly sessions.
- % weight change: Session3 - Session1 categories (n(%)): it was developed from the continuous variable of percent weight change between Session3 - Session1. It contains three groups and was categorised in reference to zero. Those having weight change less than zero were the weight losing, those having weight change more than zero were the weight gaining and those having weight change equal to zero were the no change.
- Medications: the basis of categorising the anti-diabetic medication was adopted from Aldekhail et.al paper (Aldekhail et al. 2020). Diabetes medications classification: biguanides, dipeptidyl peptidase-4 (DPP-4) inhibitors, Glucagon-like peptide-1 (GLP-1) receptor agonists, Sodium/glucose cotransporter 2 (SGLT2) inhibitors, thiazolidinediones (TZD), sulfonylureas (SU) and insulin.

The British National Formulary (BNF) 2016 ('British National Formulary (BNF)' 2016) was used to identify the brand names and any combined medications available in the UK. The diabetes medications were then categorised into four groups based on the effect of medication on body weight.

1) **Weight loss/neutral**:
   1a. Metformin only
   1b. Metformin +DPP-IV +/OR GLP-1 +/OR SGLT2
2) **Mixed:**
   2a. **(SUs)** AND (Metformin +/OR DPP-IV +/OR GLP-1 +/OR SGLT2)
   2b. **(TZDs + SUs) OR (TZDs)** AND (Metformin +/OR DPP-IV +/OR GLP-1 +/OR SGLT2)
3) **Weight gaining:**
   3a. SUs only
   3b. SUs + TZDs
   3c. any combination including insulin
4) **No drug:** patient did not take any of the anti-diabetic medications

- The number of diabetes medications: how many anti-diabetic drugs were taken by each participant at the first session of the 16-week / 9 fortnightly sessions. There are five groups: 0, 1, 2, 3, 4.
- Any insulin: the variable was developed to identify if the participant was on insulin at the start of the programme or not. It was categorised into "Yes" and "No".

The time window used for all anti-diabetic medications was within 4 months prior first attended session.

- **Process variables** include the attendance of participants to the first three sessions of the 16-week / 9 fortnightly sessions.
  - Attendance: a categorical variable to distinguish between participants based on their attendance. There were three groups: One session (patient attend one out of the first three sessions), Two sessions (patient attend two out of the first three sessions) and Three sessions (patient attend three out of the first three sessions).

- Attendance: a binary variable where group 1 is those who attend one or two sessions of the first three sessions and group 2 is those who attended three out of the first three sessions.

- Handling of missing data:

  - Variables that have missing observations and are not associated with a definition of a primary outcome measure are retained (e.g. SIMD).

  - Variables that have missing observations and are associated with a definition of a primary outcome measure are being obtained. For the first date and weight recorded in the 16-week / 9 fortnightly sessions, Next Observation Carried Backward (NOCB) was used. This was derived by taking the first available observation immediately after the missing value and carrying it backwards. The weight of the first three sessions in the 16-week / 9 fortnightly sessions was derived using a Modified NOCB (Table 3-3, variable number 3). This was developed by the study team. If the researcher was not able to derive the observation, the entire ID was removed from the database.

Table 3-2: Data handling and description of demographic predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	age_att	Continuous	age at first attendance	Age of a participant at the start of the first attended weight management session.	age_att= (firstdate^-dob^) / 365.250 ^firstdate= date of first session ^dob= date of birth	Years	Baseline	None	SCI-diabetes
2	agegroups	Categorical	0= 30-39.9 1= 40-49.9 2= 50-59.9 3= 60-69.9 4= ≥70	Categorise of the age of a participant at the start of the first attended weight management session.	gen agegroups= 0 recode agegroups 0=1 if age_att ≥40 recode agegroups 1=2 if age_att ≥50 recode agegroups 2=3 if age_att ≥60 recode agegroups 3=4 if age_att ≥70	Years	Baseline	None	SCI-diabetes & GCWMS
3	Gender	Categorical	1= F 2= M	F refers to female M refers to male	gender= encoded into female & male.	_	Baseline	None	SCI-diabetes
4	simdrank	Categorical	1= 1-1301 2= 1302-2602 3= 2603-3903 4= 3904-5204 5= 5205-6505	Scottish Index of Multiple Deprivation, a rank used to estimate socioeconomic status by using postcodes of residence, where 1 is the most deprived area & 6505 is the least deprived area.	simdrank= recoded into categories.	Decile	Baseline	n= 7 Retained since this is not a primary outcome measure.	SCI-diabetes

Abbreviations: SCI-diabetes, Scottish Care Information Diabetes.

Table 3-3: Data handling and description of clinical predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	Firstdate	Continuous	Firstdateofprogram	First date recorded in the 16-week / 9 fortnightly sessions of weight management sessions.	firstdate= datep1s1^ replace firstdate= datep1s2^ if firstdate is missing replace firstdate= datep1s3^ if firstdate is missing ^datep1s1= 1st session date ^datep1s2= 2nd session date ^datep1s3= 3rd session date	day	Baseline	Replaced using NOCB. Date from the 16-week / 9 fortnightly sessions, session 1, session 2, session 3 (depend on availability).	GCWMS
2	Firstweight	Continuous	firstweightrecordedp1	First weight recorded in the 16-week / 9 fortnightly sessions of weight management sessions.	firstweight= weight0101^ replace firstweight= weight0102^ if firstweight is missing replace firstweight= weight0103^ if firstweight is missing replace firstweight= bweight^ if firstweight is missing ^weight0101= 1st session weight ^weight0102= 2nd session weight ^weight0103= 3rd session weight ^bweight=assessment weight	Kg	Baseline	Replaced using NOCB. Weight from the 16-week / 9 fortnightly sessions, session 1, session 2, session 3 (depend on availability).	GCWMS

3	weight0101 weight0102 weight0103	Continuous		Session 1, 2, 3 weights.	weight0101= weight0101 replace weight0101= bweight if weight0101, weight0102, weight0103 are missing replace weight0101= weight0102 if weight0101 is missing weight0102= weight0102 replace weight0102= weight0103 if weight0102 is missing weight0103= weight0103 replace weight0103= weight0102 if weight0103 is missing • **For those who did not have weight for the first 3 sessions assessment weight was used.** replace weight0102= weight0101 if weight0102 is missing replace weight0103= weight0102 if weight0103 is missing	Kg	Baseline	Replaced using a "Modified NOCB".	GCWMS
4	bweightgroups_att	Categorical	1= 50-74 2= 75-99 3= 100-124 4= 125-149 5= ≥150	Categories of first weight recorded in the 16-week / 9 fortnightly sessions of weight management sessions.	bweightgroups_att= categorised based on quintile ranges.	Kg	Baseline	None	GCWMS
5	bbmi_attc	Continuous	bbmi_firstweightrecordedp1	Body mass index, a value derived from a person first weight recorded in the 16-week / 9 fortnightly sessions of weight management	bbmi_attc= firstweight/(bheight*bheight^) ^bheight= referral height	Kg/m^2	Baseline	None Assessment height is used if referral height is missing.	GCWMS

				sessions & height.					
6	bbmigroups_att	Categorical	1= 30-34 2= 35-39 3= 40-49 4= ≥50	Categories of bbmi_attc variable.	bbmigroups_att= categorise based on quintile ranges.	Kg/m^2	Baseline	None	GCWMS
7	t2dtime_att	Continuous	t2dduration at first attendance	Time from diagnosis of T2DM to attendance of first weight management session.	t2dtimedays_att= firstdate-datet2d^ t2dtime_att= t2dtimedays_att/365.25 ^datet2d= date of t2dm diagnosis	Years	Baseline	None	SCI-diabetes & GCWMS
8	bhba1c_att	Continuous	hba1c at first attendance	Average of glycated haemoglobin concentration. Time window: within 18 months before the date of first attendance.	hba1c_att= most recent hba1c_att	mmol/mol	Baseline	n= 99 Retained since this is not a primary outcome measure.	SCI-diabetes

9	bsbp_att	Continuous	sbp at first attendance	Average of SBP. Time window: within 18 months before the date of first attendance).	bsbp_att= most recent sbp_att	mmHg	Baseline	n= 594 Retained since this is not a primary outcome measure.	SCI-diabetes
10	bdbp_att	Continuous	dbp at first attendance	Average of DBP. Time window: within 18 months before the date of first attendance.	bdbp_att= most recent dbp_att	mmHg	Baseline	n= 587 Retained since this is not a primary outcome measure.	SCI-diabetes
11	btc_att	Continuous	tc at first attendance	Average of TC. Time window: within 18 months before the date of first attendance.	btc_att= most recent tc_att	mmol/L	Baseline	n= 130 Retained since this is not a primary outcome measure.	SCI-diabetes
12	btg_att	Continuous	tg at first attendance	Average of TG Time window: within 18 months before the date of first attendance).	btg_att= most recent tg_att	mmol/L	Baseline	n= 451 Retained since this is not a primary outcome measure.	SCI-diabetes
13	bhdl_att	Continuous	hdl at first attendance	Average of HDL (time window: within 18 months before the date of first attendance.	bhdl_att= most recent hdl_att	mmol/L	Baseline	n= 454 Retained since this is not a primary outcome measure.	SCI-diabetes

14	bldl_att	Continuous	ldl at first attendance	Average LDL Time window: within 18 months before the date of first attendance.	Friedewald formula: bldl_att= btc_att-bhdl_att-(btg_att/2.2)	mmol/L	Baseline	n= 705 Retained since this is not a primary outcome measure.	SCI-diabetes
15	p1s2s1	Continuous	session2-session1	Weight change in the 16-week / 9 fortnightly sessions, between second & first attended session.	**To calculate % weight change:** p1s2s1= ((weight0102-weight0101)/firstweight) *100	%	Baseline	None	GCWMS
16	p1s3s1	Continuous	session3-session1	Weight change in the 16-week / 9 fortnightly sessions, between third & first attended session.	**To calculate % weight change:** p1s3s1= ((weight0103-weight0101)/firstweight) *100	%	Baseline	None	GCWMS
17	p1s3s2	Continuous	session3-session2	Weight change in the 16-week / 9 fortnightly sessions, between third & second attended session.	**To calculate % weight change:** p1s3s2= ((weight0103-weight0102)/firstweight) *100	%	Baseline	None	GCWMS
18	p1s3s1_cat	Categorical	0= nochange 1= weightlosing 2= weightgaining	Categories of weight change in the 16-week / 9 fortnightly sessions, between third & first attended session.	gen p1s3s3_cat= 0 replace p1s3s3_cat= 1 if p1s3s1< 0 replace p1s3s3_cat= 2 if p1s3s1> 0	-	Baseline	None	GCWMS

19	bins	Categorical	0= no 1= yes	A binary variable to distinguish whether patient took insulin within 4 months prior starting the first weight management session.	datediff_att= datemeds-firstdate baseins= meds1_ins if datediff >=-121.6 & datediff <=0 by id baseins, sort:gen nvals=1 if baseins==1 by id: egen bins = max (nvals) by id baseins, sort: gen nvalsi = _n ==1 if baseins==1 by id: egen binsn = max (nvalsi) recode binsn .=0 rename binsn bins	_	Baseline	None	SCI-diabetes
20	Bmeds	Continuous	0= using zero drugs 1= using one drug 2= using two drugs 3= using three drugs 4= using four drugs	A variable to determine how many medications were taken by each patient within 4 months before starting the first weight management session.	egen bmeds= rowtotal (bbig-bdppcom)	_	Baseline	None	SCI-diabetes

21	drug_cat	Categorical	1= weightlosing 2= mixed 3= weightgaining 4= nodrugs	A categorical variable to determine what type of medications patient was taken within 4 months before starting the first weight management session.	drug_cat= 0 recode drug_cat 0=1 if bbig==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 & bsglt==0 & bsgltcom==0 & bglp==0 & bdpp==0 & bdppcom==0 recode drug_cat 0=1 if bdppcom==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 | bsgltcom==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 | bbig==1 & bglp==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 | bbig==1 & bdpp==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 | bbig==1 & bsglt==1 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 recode drug_cat 0=3 if bsu==1 & bins==0 & bbig==0 & btzd==0 & btzdcom==0 & bsglt==0 & bsgltcom==0 & bglp==0 & bdpp==0 & bdppcom==0 recode drug_cat 0=3 if bsu==1 & btzd==1 & bbig==0 & btzdcom==0 & bsglt==0 & bsgltcom & bglp==0 & bdpp==0 & bdppcom==0 | bins==1 & bbig==0 & btzdcom==0 & bsglt==0 & bsgltcom==0 & bglp==0 & bdpp==0 & bdppcom==0 recode drug_cat 1=3 if bins==1 recode drug_cat 0=4 if bbig==0 & bins==0 & bsu==0 & btzd==0 & btzdcom==0 & bsglt==0 & bsgltcom==0 & bglp==0 & bdpp==0 & bdppcom==0 recode drug_cat 0=2 if drug_cat==0	_	Baseline	None	SCI-diabetes

Abbreviations: GCWMS, NHS GGC Weight Management Service; NOCB, Next Observation Carried Backwards; SCI-diabetes, Scottish Care Information Diabetes; T2DM, Type 2 Diabetes Mellitus; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; TC, Total Cholesterol; TG, Triglycerides; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein.

Table 3-4: Data handling and description of process predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	attend_cat	Categorical	1= onesession 2= twosessions 3= threesessions	A categorical variable to distinguish whether patient attend 1, 2 or three sessions from the first three sessions (i.e. attend session 1 or 2 or 3, attend sessions 1&2 or 1&3 or 2&3, attend sessions 1&2&3).	attend_cat=0 recode attend_cat 0=1 if attendp1s1^==1 | attendp1s2^==1 | attendp1s3^==1 recode attend_cat 1=2 if attendp1s1==1 & attendp1s2==1| attendp1s1==1 & attendp1s3==1 | attendp1s2==1 & attendp1s3==1 recode attend_cat 1=3 if attendp1s1==1 & attendp1s2==1 & attendp1s3==1 recode attend_cat 2=3 if attendp1s1==1 & attendp1s2==1 & attendp1s3==1 ^attendp1s1= 1st session attendance ^attendp1s2= 2nd session attendance ^attendp1s3= 3rd session attendance	Sessions	Baseline	None	GCWMS
2	attend_cat3	Categorical	0= other 1= threesessions	A binary variable to distinguish whether patient attend the first three sessions or not.	attend_cat3=0 recode attend_cat3 0=1 if attendp1s1==1 & attendp1s2==1 & attendp1s3==1	Sessions	Baseline	None	GCWMS

Abbreviations: GCWMS, NHS GGC Weight Management Service.

3.2.5.2 Outcome

Short-term outcome:

The time window for short-term outcome variables was identified to be 16wk following baseline, meaning at the end of 16-week / 9 fortnightly sessions of the group behavioural weight management programme (Table 3.5).

Programme completion: it is well known from studies conducted in weight management programmes that there is a direct relationship between programme attendance and weight loss. Accordingly, in this study, programme completion is set to be attending at least 80 % of the 16-week / 9 fortnightly sessions of GCWMS, meaning that the patient should attend at least seven out of nine sessions.

Weight change: is the amount of weight lost (in percent) during 16-week / 9 fortnightly sessions of the group behavioural weight management programme. This was calculated by subtracting the last weight recorded during 16-week / 9 fortnightly sessions (regardless of which session it was) from the first weight recorded in the programme (i.e. baseline weight).

All participants included in the analysis were referred to the GCWMS. Those who did not attend at least 1 weight-loss session from the 16-week / 9 fortnightly sessions were defined as **Non-attender** (removed from the entire cohort). Those who attended ≥ 1 weight-loss session from the 16-week / 9 fortnightly sessions were defined as **All-attender**.

Three outcomes of interest were derived, which are a combined variable of non-completers & unsuccessful completers, unsuccessful completers and successful completers.

- **Non-completers**: those who attended ≤ 6/9 weight loss sessions from the 16-week / 9 fortnightly sessions of GCWMS.

- Those who attended ≥ 7/9 weight loss sessions from the 16-week / 9 fortnightly sessions of GCWMS were defined as **Completers**. The completers

group were further classified into **Successful completers** and **Unsuccessful completers**.

- Successful completers: those who attended ≥ 7/9 weight loss sessions from the 16-week / 9 fortnightly sessions of GCWMS & lost ≥ 5% body weight at the end of the sessions.
- Unsuccessful completers: those who attended ≥ 7/9 weight loss sessions from the 16-week / 9 fortnightly sessions of GCWMS & lost < 5% body weight at the end of the sessions.

- Handling of missing data:
  - The last weight recorded during the 16-week / 9 fortnightly sessions is not usually recorded either because of programme discontinuation or errors during reporting of weight.

  - Two methods were used to derive weight-loss outcomes: 1) last observation carried forward (LOCF). 2) baseline observation carried forward (BOCF). The choice of model for handling data availability did not substantially impact the data. After comparing the models, and consulting with a clinician expert (Dr Logue), data were reported based on the LOCF model.

  - For LOCF, whenever there was a missing weight measurement, the value was replaced with the last observed value. This method was used in case the participant completed 80 % of the sessions from the total number of sessions provided in the 16-week / 9 fortnightly sessions. While for BOCF, whenever there was a missing weight measurement, the value was replaced with the first observed value. This method was used when a 12-week weight is not recorded.

Table 3-5: Description & derivation of outcome variables (short-term).

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Data source
1	groups2	Categorical	0= non attenders 1= all attenders	A binary variable to distinguish whether the patient attend the 16-week / 9 fortnightly sessions or not.	groups2= attendp1 attendp1= attendp1s1^ + attendp1s2^ + attendp1s3^ + attendp1s4^ + attendp1s5^ + attendp1s6^ + attendp1s7^ + attendp1s8^ + attendp1s9^ recode attendp1: (0=0) (1/9=1) • **Based on study cleaning no observations in attendp1=0** ^attendp1s1= 1st session attendance ^attendp1s2= 2nd session attendance ^attendp1s3= 3rd session attendance ^attendp1s4= 4th session attendance ^attendp1s5= 5th session attendance ^attendp1s6= 6th session attendance ^attendp1s7= 7th session attendance ^attendp1s8= 8th session attendance ^attendp1s9= 9th session attendance	Sessions	Short-term	GCWMS
2	Attendgroups	Categorical	0= non completers 1= completers	A binary variable to distinguish whether the patient complete the 16-week / 9 fortnightly sessions or not.	attendgroups= (attendp1=1) attendgroups "0"= attendp1<7 attendgroups "1"= attendp1≥7	Sessions	Short-term	GCWMS

3	lastweightp1	Continuous	lastweightrecordedp1	The last weight recorded during the 16-week / 9 fortnightly sessions, regardless of which session it was, by using Last Observation Carried Forward (LOCF).	lastweightp1= weight0109^ replace lastweightp1= weight0108^ if lastweightp1 is missing replace lastweightp1= weight0107^ if lastweightp1 is missing replace lastweightp1= weight0106^ if lastweightp1 is missing replace lastweightp1= weight0105^ if lastweightp1 is missing replace lastweightp1= weight0104^ if lastweightp1 is missing replace lastweightp1= weight0103^ if lastweightp1 is missing replace lastweightp1= weight0102^ if lastweightp1 is missing replace lastweightp1= weight0101^ if lastweightp1 is missing ^weight0109= 9th session weight ^weight0108= 8th session weight ^weight0107= 7th session weight ^weight0106= 6th session weight ^weight0105= 5th session weight ^weight0104= 4th session weight ^weight0103= 3rd session weight ^weight0102= 2nd session weight ^weight0101= 1st session weight	Kg	Short-term	GCWMS

4	lastweightp1_bcf	Continuous	lastweightrecordedp1_bcf	The last weight recorded during the 16-week / 9 fortnightly sessions, regardless of which session it was, by using Baseline Observation Carried Forward (BOCF).	lastweightp1_bcf= weight0101 replace lastweightp1_bcf = weight0102 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0103 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0104 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0105 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0106 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0107 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0108 if lastweightp1_bcf is missing replace lastweightp1_bcf = weight0109 if lastweightp1_bcf is missing	Kg	Short-term	GCWMS
5	weightlossp1	Continuous	totalweightlossp1	Amount of weight lost during the 16-week / 9 fortnightly sessions using LOCF in a kilogram.	weightlossp1= lastweightp1-firstweight	Kg	Short-term	GCWMS
6	weightlossp1_pc	Continuous	totalweightlossp1_percent	Amount of weight lost during the 16-week / 9 fortnightly sessions using LOCF in percent.	weightlossp1_pc= ((lastweightp1-firstweight)/firstweight)*100	%	Short-term	GCWMS
7	complgroups_pc	Categorical	0= unsuccessful completers_percent 1= successful completers_percent	A binary variable to distinguish whether the patient successfully completed the 16-week / 9 fortnightly sessions or not (using LOCF & the weight loss from the 16-week / 9 fortnightly sessions in percent).	complgroups_pc "0"= attendp1≥7 & weightlossp1_pc > -5 complgroups_pc "1"= attendp1≥7 & weightlossp1_pc ≤ -5	_	Short-term	GCWMS

8	Nonattendgroups	Categorical	0= not assessed 1= assessed	A binary variable to distinguish whether the patient was assessed or not.	nonattendgroups "0"= aweight^ is missing nonattendgroups "1"= aweight is available ^aweight= assessment weight • **Based on study cleaning no observations in nonattendgroups=0**	_	Short-term	GCWMS
9	groups3_pc	Categorical	1= non completers 2= unsuccessful completers_percent 3= successful completers_percent	A variable to distingiush between all three groups in the cohort (using LOCF & the weight loss from the 16-week / 9 fortnightly sessions in percent).	groups3 "1"= attendp1> 0 & attendp1< 7 groups3 "2"= attendp1≥ 7 & weightlossp1_pc≥ -5 groups3 "3"= attendp1≥ 7 & weightlossp1_pc≤ -5	_	Short-term	GCWMS
10	Complete	Categorical	0= non completers&unsuccessful completers_percent 1= successful completers_percent	A variable to distingiush between non-completers & unsuccessful completer versus successful completers.	complete= groups3_pc recode complete 1/2= 0 recode complete 3= 1	_	Short-term	GCWMS

Abbreviations: GCWMS, NHS GGC Weight Management Service.

Medium-term:

The time window for medium-term outcome variables was identified to be 3 years following baseline (Table 3.6).

Weight change: is the amount of weight lost (in percent) at 3 years from baseline weight. This was calculated by subtracting the last weight recorded in the entire programme of GCWMS (depending on available weight) from the first weight recorded in the programme (i.e. baseline weight).

The outcomes of interest in the medium-term were derived based on different scenarios. The definition for each scenario and the corresponding outcomes are shown below:

- In scenario (1) the cut-off point for successful weight loss was set to be 3%. Therefore two groups were created: 1) Successful completers, those who lost ≥ 3% from the baseline body weight at the end of the entire programme. 2) Unsuccessful completers, those who lost < 3% from the baseline body weight at the end of the entire programme.

- In scenario (2) the cut-off point for successful weight loss was set to be 5%. Therefore two groups were created: 1) Successful completers, those who lost ≥ 5% from the baseline body weight at the end of the entire programme. 2) Unsuccessful completers, those who lost < 5% of the baseline body weight at the end of the entire programme.

- In scenario (3) attendance was considered alongside scenario 1. Therefore two groups were created: 1) Successful completers, those who attended ≥ 7/9 weight loss sessions from the 16-week sessions of GCWMS, lost ≥ 5% body weight at the end of the sessions and lost ≥ 3% from the baseline body weight at the end of the entire programme. 2) Non-completers & unsuccessful completers, those who did not qualify as successful completers.

- In scenario (4) attendance was considered alongside scenario 2. Therefore two groups were created: 1) Successful completers, those

who attended ≥ 7/9 weight loss sessions from the 16-week sessions of GCWMS, lost ≥ 5% body weight at the end of the sessions and lost ≥ 5% from the baseline body weight at the end of the entire programme. 2) Non-completers & unsuccessful completers, those who did not qualify as successful completers.

Table 3-6: Description & derivation of outcome variables (medium-term).

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Data source
1	threeyrbmi_att	Continuous		Average BMI. Time window: within 30-42 months after the date of first attendance.	threeyrbmi_att= mean of BMI replace threeyrbmi_att= . If threeyrbmi_att>100 replace threeyrbmi_att= . If threeyrbmi_att<20	Kg/m^2	Medium-term	SCI-diabetes
2	threeyrweight_att	Continuous		Derived from a person's BMI recorded at 3 years from starting the first weight management session & height.	threeyrweight_att= threeyrbmi_att * (bheight*bheight^) ^bheight= referral height	Kg	Medium-term	SCI-diabetes & GCWMS
3	threeyrdiffweight_att	Continuous		Amount of weight lost in kilogram between 3 years weight and first recorded weight.	threeyrdiffweight_att= threeyrweight_att - firstweight^ ^firstweight= first weight recorded in the 16-week / 9 fortnightly sessions of weight management sessions.	Kg	Medium-term	SCI-diabetes & GCWMS
4	threeyrdiffweight_attpc	Continuous		Amount of weight loss in percent between 3 years weight and first recorded weight.	threeyrdiffweight_attpc= ((threeyrweight_att - firstweight)/ firstweight)*100	%	Medium-term	SCI-diabetes & GCWMS

5	threeyr3pcweightloss_attpc	Categorical	0= <3% 1= >=3%	A binary variable to distinguish whether the patient achieve 3 percent of weight loss at 3 years starting from first attended session.	threeyr3pcweightloss_attpc= . replace threeyr3pcweightloss_attpc= 1 if threeyrdiffweight_attpc<=-3.00 & threeyrdiffweight_attpc not missing replace threeyr3pcweightloss_attpc= 0 if threeyrdiffweight_attpc>-3.00 & threeyrdiffweight_attpc not missing	_	Medium-term	SCI-diabetes & GCWMS
6	threeyr5pcweightloss_attpc	Categorical	0= <5% 1= >=5%	A binary variable to distinguish whether the patient achieve 5 percent of weight loss at 3 years starting from first attended session.	threeyr5pcweightloss_attpc= . replace threeyr5pcweightloss_attpc= 1 if threeyrdiffweight_attpc<=-5.00 & threeyrdiffweight_attpc not missing replace threeyr5pcweightloss_attpc= 0 if threeyrdiffweight_attpc>-5.00 & threeyrdiffweight_attpc not missing	_	Medium-term	SCI-diabetes & GCWMS
7	groups2_3pc	Categorical	0= unsuccessful completers_3percent 1= successful completers_3percent	A binary variable to distinguish whether the patient achieve 3 percent of weight loss at 3 years starting from first attended session (given that the patient attend at least one weight management session in the 16-week / 9 fortnightly sessions).	groups2_3pc= . replace groups2_3pc= 0 if attendp1^>=1 & threeyr3pcweightloss_attpc=0 replace groups2_3pc= 1 if attendp1>=1 & threeyr3pcweightloss_attpc=1 ^attendp1= number of attended sessions in the 16-week / 9 fortnightly sessions	_	Medium-term	SCI-diabetes & GCWMS

8	groups2_5pc	Categorical	0= unsuccessful completers_5percent 1= successful completers_5percent	A binary variable to distinguish whether the patient achieve 5 percent of weight loss at 3 years starting from first attended session (given that the patient attend at least one weight management session in the 16-week / 9 fortnightly sessions).	groups2_5pc= . replace groups2_5pc= 0 if attendp1>=1 & threeyr3pcweightloss_attpc=0 replace groups2_5pc= 1 if attendp1>=1 & threeyr3pcweightloss_attpc=1	_	Medium-term	SCI-diabetes & GCWMS

9	allgroups_3pc	Categorical	0= non completers & unsuccessful completers_3percent 1= successful completers_3percent	A binary variable to distinguish whether the patient achieves 3 percent of weight loss at 3 years starting from first attended session (given that the patient attends at least one weight management session in the 16-week / 9 fortnightly sessions). Criteria to distinguish between successful and unsuccessful groups is to consider whether the patient lost 5 percent body weight at end of the 16-week / 9 fortnightly sessions (using LOCF).	allgroups_3pc= . allgroups_3pc= 0 if attendp1>0 & attendp1<7 allgroups_3pc= 0 if attendp1>=7 & weightlossp1_pc<=-5 & threeyr3pcweightloss_attpc=0 allgroups_3pc= 0 if attendp1>=7 & weightlossp1_pc>=-5 & threeyr3pcweightloss_attpc=0 allgroups_3pc= 0 if attendp1>=7 & weightlossp1_pc>=-5 & threeyr3pcweightloss_attpc=1 allgroups_3pc= 1 if attendp1>=7 & weightlossp1_pc<=-5 & threeyr3pcweightloss_attpc=1	_	Medium-term	SCI-diabetes & GCWMS

10	allgroups_5pc	Categorical	0= non completers & unsuccessful completers_5percent 1= successful completers_5percent	A binary variable to distinguish whether the patient achieves 5 percent of weight loss at 3 years starting from first attended session (given that the patient attends at least one weight management session in the 16-week / 9 fortnightly sessions). Criteria to distinguish between successful and unsuccessful groups is to consider whether the patient lost 5 percent body weight at end of the 16-week / 9 fortnightly sessions (using LOCF).	allgroups_5pc= . allgroups_5pc= 0 if attendp1>0 & attendp1<7 allgroups_5pc= 0 if attendp1>=7 & weightlossp1_pc<=-5 & threeyr5pcweightloss_attpc=0 allgroups_5pc= 0 if attendp1>=7 & weightlossp1_pc>=-5 & threeyr5pcweightloss_attpc=0 allgroups_5pc= 0 if attendp1>=7 & weightlossp1_pc>=-5 & threeyr5pcweightloss_attpc=1 allgroups_5pc= 1 if attendp1>=7 & weightlossp1_pc<=-5 & threeyr5pcweightloss_attpc=1	_	Medium-term	SCI-diabetes & GCWMS

Abbreviations: BMI, Body Mass Index; SCI-diabetes, Scottish Care Information Diabetes; GCWMS, NHS GGC Weight Management Service.

3.2.6 Statistical analysis

Normality of continuous variables was assessed using a normal probability plot. Descriptive statistics for each predictor variable were tabulated. For continuous variables that are normally distributed, data is presented as Mean ± Standard Deviation (SD). For continuous variables that are not normally distributed, data presented as Median & Interquartile range (IQR). For categorical variables, frequencies (n) and percentages (%) are presented. Test of association between the predictor variables and the outcome of interest (i.e. the different study groups (non-completers, unsuccessful completers and successful completers) from the same population (people who were referred and attend GCWMS)) was done by formally testing the null hypothesis of no association between predictor and outcome. For continuous variables, an independent t-test (for normally distributed data) and Rank sum test (for not normally distributed data) were used. For categorical variables, the Chi-square test was used.

Binary logistic regression analysis (a simple and multiple regression model) was used to estimate the strength of association between predictor variables and successful completion. This was done by calculating the measure of association (i.e. odds ratio (OR)) and the statistical significance (i.e. 95% confidence interval (CI) and p-value). The assumptions for logistic regression analysis were investigated: 1) binary dependent variable (i.e. a dichotomous variable that take the value 1 and 0). 2) little or no multicollinearity among the independent variables (Person's correlation test was used to investigate the association between predictor variables and any variable that showed collinearity was removed). 3) the linearity of independent variables and log odds. 4) large sample size (i.e. at least 10 observations). 5) independent observations (no repeated measures, or matched data).

After checking the assumptions, simple logistic regression was conducted for each predictor. This was done by using a null/empty model that has only the outcome of interest and adding a single predictor variable at a time to check if it improved the model fit. This technique was used to choose the models because there are many independent variables and using an automatic method like stepwise logistic regression might overlook important predictors. For continuous predictor variables, these exposures were added to the model using a natural

(untransformed scale). The reference group for binary variables was the “zero” category. The reference group for categorical variables was the most frequent category.

The next step was conducting multiple logistic regression modelling for all the accepted predictor variables from simple logistic regression with a successful completion. The model fit was optimised using model selection criteria (i.e. Akaike's Information Criteria (AIC) and Bayesian Information Criteria (BIC)). Those are measures of model performance, it accounts for model complexity to estimate how well the model fits the data. AIC estimates how much information is lost from the model, meaning that the model is a good fit if it loses less information (a lower AIC score is better). BIC estimates how many variables are included in the model and are not justified by the data (a lower BIC score is better). To choose between two models (the models should have the same number of observations and predictor variables) the scores of AIC and BIC are compared.

A value of $p \leq 0.05$ was considered a statistically significant difference in all analyses. We did not adjust for multiple comparisons in this study in order to maximise power for predictor discovery, with a view to validating positive findings in chapter 5. This increases the risk of type 1 error, but thus will be addressed by external validation (Rothman 1990).

3.2.6.1 Statistical measures performance

This study used sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) & Area Under the Curve – Receiver Operating Characteristics Curve (AUC-ROC), that are used to evaluate the success of a screening test (i.e. the predictive model). In this study, it was used to estimate/predict how each predictor variable affects the outcome of interest (i.e. successful completion). **Sensitivity:** is a test that allows for truly identifying the percentage of participants who successfully achieve the required weight loss (≥5%) at the end of the 16-week / 9 fortnightly sessions (i.e. true positive rate). **Specificity:** is a test that allows for truly identifying the percentage of participants who fail to achieve the required weight loss (≥5%) at the end of the 16-week / 9 fortnightly sessions (i.e. true negative rate). **PPV:** is the probability that participants who were defined as successful completers (based on sensitivity

results) are accurately being identified. **NPV:** is the probability that participants who were defined as unsuccessful completers (based on specificity results) are accurately being identified.

STATA-SE software version 15.0 was used in the cleaning & analysis of data.

3.3 Results

3.3.1 Patients classification

A total of 5855 patients in NHS GG&C were diagnosed with T2DM and were referred to GCWMS. A total of 2135 patients were excluded from the dataset based on the criteria used in this study. After the investigation of whether the participant attended at least 1 weight loss session within the first 3 sessions of the 16-week / 9 fortnightly sessions in the GCWMS 2062 were excluded. The remaining 1658 participants were included in the statistical analysis and were classified based on the algorithms defined above (Figure 3-1).

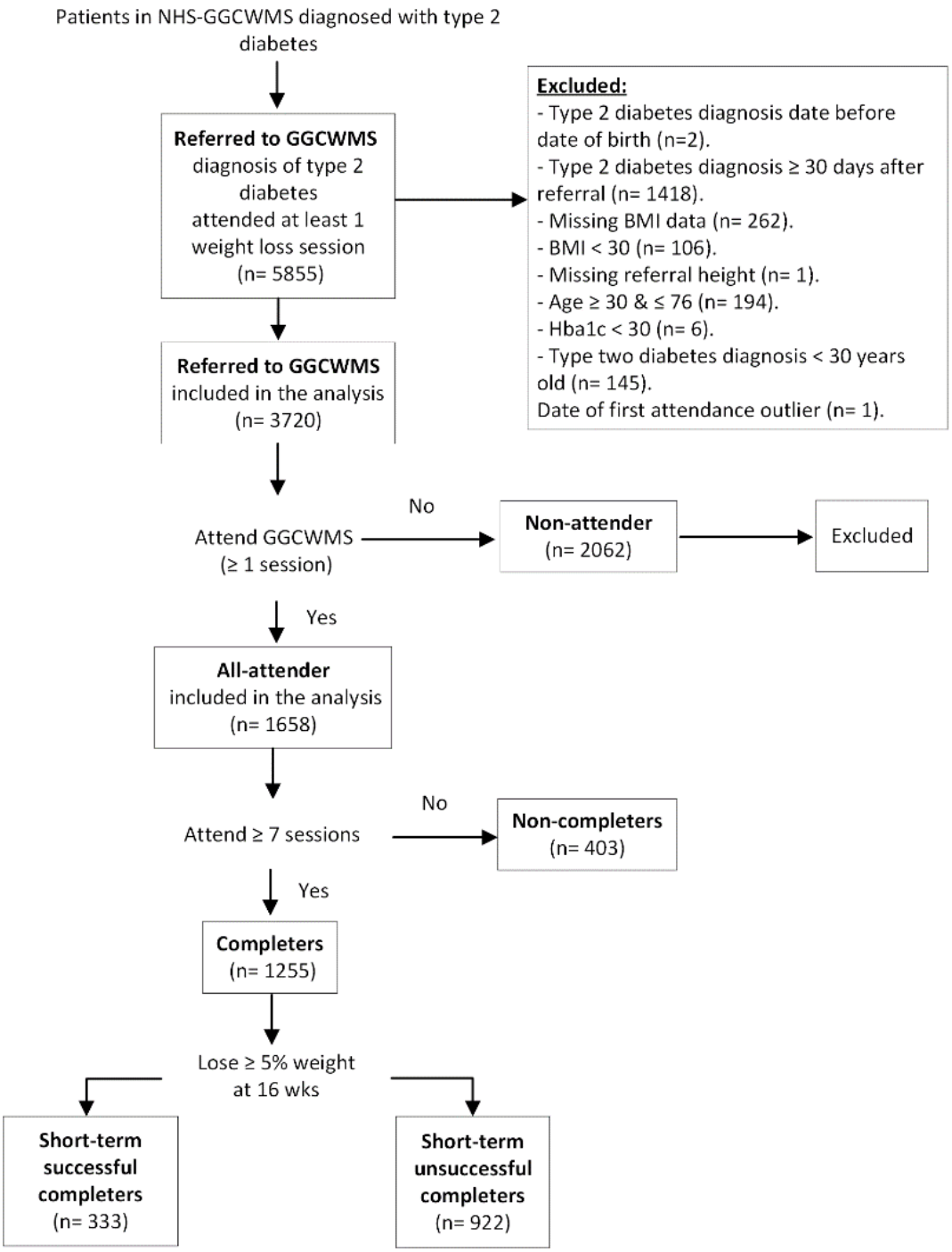

Figure 3-1: Flow chart showing cohort derivation and group classifications.

Abbreviations: NHS GG&C, National Health Service Greater Glasgow and Clyde; GCWMS, Glasgow and Clyde Weight Management Service; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin.

3.3.2 Short-term weight loss

3.3.2.1 Descriptive statistics – Complete cohort

To provide preliminary information about the proposed predictors and to examine the nature of the relationship between the predictors and outcome variables, a descriptive analysis was done.

Table 3-7 shows the baseline characteristics of the whole cohort. The mean age of the participants was 57.8 years (SD= 9.37 years) and 60% were female (n=994). According to the Scottish Index of Multiple Deprivation, a sizeable proportion are from the most socioeconomically deprived areas (n=661, 40%). Participants were generally from the White British/Scottish ethnic group: n=1526 (94.3%).

The baseline clinical variables showed that the patients have been diagnosed with T2DM for a median of 5.31 years (IQR = 2.19 – 9.77). The median BMI was 40.2 kg/m^2 (IQR = 35.9 – 44.8). The mean blood pressure was: SBP 133 mmHg (SD= 14.5 mmHg) and DBP 77.6 mmHg (SD= 9.63 mmHg). The lipid profile was as follow mean total cholesterol 4.39 mmol/L (SD= 1.06 mmol/L), median triglycerides 1.9 mmol/L (IQR= 1.4 - 2.7), mean HDL cholesterol 1.12 mmol/L (SD= 0.30 mmol/L) and mean LDL cholesterol 2.30 mmol/L (SD= 0.91 mmol/L).

The mean weight change comparisons between sessions 1-3 generally shows weight loss, and the magnitude of weight loss increases with each session. The difference was calculated between session 2 & session 1 (Mean ± SD, - 0.58% ± 1.23%), session 3 & session 2 (Mean ± SD, - 0.43% ± 0.94%) and session 3 & session 1 (Mean ± SD, - 1.01% ± 1.55%). Categorising data between session 3 & session 1 (in reference to zero), most patients were in weight losing category (n=1061, 64.0%).

Most of the patients took a mixed (weight loss and weight gain) type of diabetes medications (n=647, 39.0%), 28% of the patient did not take any medication (n=469, 28.3%), and most were not taking insulin at baseline (n= 1519, 91.6%).

The process variable for adherence showed that the vast majority of patients attended at least three weight loss sessions from active phase/phase 1 (n=1590, 95.9%).

Table 3-7: Descriptive statistics for all cohorts.

Variable	All (n=1658)	
Demographic:		
Age, years	57.8 ± 9.37	(n=1658)
Age categories, n(%)		(n=1658)
30-39.9	60 (3.6%)	
40-49.9	309 (18.6%)	
50-59.9	568 (34.3%)	
60-69.9	561 (33.8%)	
≥70	160 (9.7%)	
Sex, n (%)		(n=1658)
Female	994 (60.0%)	
Male	664 (40.0%)	
SIMD scores, n (%)		(n=1651)
Q1 Most deprived	661 (40.0%)	
Q2	289 (17.5%)	
Q3	257 (15.6%)	
Q4	202 (12.2%)	
Q5 Least deprived	242 (14.7%)	
Ethnicity, n (%)		(n=1619)
White British/Scottish	1526 (94.3%)	
Any other	93 (5.7%)	
Clinical		
Duration of T2DM, years	5.31 (2.19 - 9.77)	(n=1658)
Initial Height, m	1.65 ± 0.09	(n=1657)
Initial weight, kg	113 ± 23.21	(n=1658)
Initial BMI, kg/m^2	40.2 (35.9 - 44.8)	(n=1658)
Initial BMI categories, n (%)		(n=1658)
30 - 34	232 (14.0%)	
35 - 39	481 (29.0%)	
40 - 49	741 (44.7%)	
≥ 50	204 (12.3%)	
HbA1c, mmol/mol	56 (48 - 69)	(n=1559)
Systolic blood pressure, mmHg	133 ± 14.5	(n=1064)
Diastolic blood pressure, mmHg	77.6 ± 9.63	(n=1071)
Total cholesterol, mmol/L	4.39 ± 1.06	(n=1572)
Triglycerides, mmol/L	1.9 (1.4 - 2.7)	(n=1291)
HDL cholesterol, mmol/L	1.12 ± 0.30	(n=1295)
LDL cholesterol, mmol/L	2.30 ± 0.91	(n=1027)
% weight change: Session2 - Session1	- 0.58 ± 1.23	(n=1658)
% weight change: Session3 - Session1	- 1.01 ± 1.55	(n=1658)
% weight change: Session3 - Session2	- 0.43 ± 0.94	(n=1658)
% weight change: Session3 - Session1 categories, n(%)		(n=1658)
Weight losing	1061 (64.0%)	
Weight gaining	230 (13.9%)	
No change	367 (22.1%)	
Medications, n (%)		(n=1658)
Weight loss	448 (27.0%)	
Mixed	647 (39.0%)	
Weight gaining	94 (5.7%)	
No drug	469 (28.3%)	
Number of diabetes medications, n (%)		(n=1658)
0	469 (28.3%)	
1	492 (29.7%)	

	2	481 (29.0%)	
	3	192 (11.6%)	
	4	24 (1.4%)	
Any insulin, n (%)			(n=1658)
	Yes	139 (8.4%)	
	No	1519 (91.6%)	
Process:			
Attendance, n (%)			(n=1658)
	One session	15 (0.9%)	
	Two sessions	53 (3.2%)	
	Three sessions	1590 (95.9%)	
Attendance, n (%)			(n=1658)
	Three sessions	1590 (95.9%)	
	Other	68 (4.1%)	

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).

3.3.2.2 Descriptive statistics by short-term outcome status

Table 3-8 shows the baseline characteristics of the study groups. Successful completers were approximately a year older in general than the non-completers & unsuccessful completers. The white British/Scottish ethnicity is the dominant group in all comparable groups, although successful completers are most likely to be white. Successful completers had a slightly shorter duration of T2DM at baseline than the non-completers & unsuccessful completers (0.53 years shorter). Successful completers had around 1 kg/m^2 lower BMI than the non-completers & unsuccessful completers. Successful completers had better glycaemic control than the non-completers & unsuccessful completers (1 mmol/mol lower).

The percent weight change over the 3 first sessions was higher among successful completers. Successful completers lost more weight in the early weight loss sessions (e.g. session 3 versus session 1). When compared to other groups, successful completers lost 1.95% more weight than the non-completers & unsuccessful completers and lost 1.77% more weight than the unsuccessful completers. The proportion of participants experiencing no weight change was highest in the non-completers & unsuccessful completers group (n=360, 27.2%), and the weight gaining category was the highest in the unsuccessful completers group (n=174, 18.9%).

There was a weak trend that successful completers were more likely to be on only weight-losing T2DM drugs and as such here was a trend that successful completers were more likely to be on at least 1 type of T2DM drug (n= 118, 35.4%); most probably metformin.

All three comparison groups had the tendency to attend the first three sessions of the 16-week / 9 fortnightly sessions in the GCWMS (>95% in all groups), although of course the group including non-completers showed a trend to be least likely to attend.

Table 3-8: Descriptive statistics for study groups. The non-completers & unsuccessful completers versus the successful completers and the unsuccessful completers versus the successful completers (short-term outcome).

Variable	Non-completers & Unsuccessful completers (n=1325)	Unsuccessful completers (n=922)	Successful completers (n=333)	P-value for difference non-completers & unsuccessful completers vs. successful completers	P-value for difference unsuccessful completers vs. successful completers
Demographic:					
Age, years	57.5 ± 9.46	57.7 ± 9.21	58.8 ± 8.98	0.03	0.07
Age categories, n(%)				0.29	0.31
30-39.9	51 (3.8%)	31 (3.4%)	9 (2.7%)		
40-49.9	254 (19.2%)	165 (17.9%)	55 (16.5%)		
50-59.9	460 (34.7%)	340 (36.9%)	108 (32.4%)		
60-69.9	433 (32.7)	297 (32.2%)	128 (38.4%)		
≥70	127 (9.6%)	89 (9.7%)	33 (9.9%)		
Sex, n (%)				0.65	0.80
Female	798 (60.2%)	550 (59.7%)	196 (58.9%)		
Male	527 (39.8%)	372 (40.3%)	137 (41.1%)		
SIMD scores, n (%)				0.44	0.47
Q1 Most deprived	535 (40.6%)	349 (38.0%)	126 (37.8%)		
Q2	232 (17.6%)	169 (18.4%)	57 (17.1%)		
Q3	203 (15.4%)	145 (15.8%)	54 (16.2%)		
Q4	165 (12.5%)	126 (13.7%)	37 (11.1%)		
Q5 Least deprived	183 (13.9%)	130 (14.1%)	59 (17.7%)		

Ethnicity, n (%)				<0.001	< 0.001
White British/Scottish	1208 (93.3%)	856 (94.7%)	318 (98.1%)		
Any other	87 (6.7%)	48 (5.3%)	6 (1.9%)		
Clinical:					
Duration of T2DM, years	5.39 (2.16 - 9.76)	5.40 (2.18 - 9.39)	4.87 (2.36 - 9.81)	0.70	0.77
Initial weight, kg	113 ± 23.2	113 ± 22.0	112 ± 23.1	0.34	0.22
Initial BMI, kg/m^2	40.3 (36.1 - 45.0)	40.5 (36.4 - 44.9)	39.7 (35.4 - 44.2)	0.23	0.12
Initial BMI categories, n (%)				0.16	0.34
30 – 34	189 (14.3%)	129 (14.0%)	43 (12.9%)		
35 – 39	369 (27.8%)	240 (26.0%)	112 (33.6%)		
40 – 49	606 (45.7%)	445 (48.3%)	135 (40.5%)		
≥ 50	161 (12.2%)	108 (11.7%)	43 (12.9%)		
HbA1c, mmol/mol	56 (48 - 70)	56 (49 - 70)	55 (47.5 – 66.5)	0.08	0.05
Systolic blood pressure, mmHg	133 ± 14.6	134 ± 15.0	134 ± 13.8	0.37	0.88
Diastolic blood pressure, mmHg	77.8 ± 9.63	77.8 ± 9.66	76.9 ± 9.62	0.25	0.29
Total cholesterol, mmol/L	4.40 ± 1.07	4.40 ± 1.07	4.35 ± 1.03	0.50	0.47
Triglycerides, mmol/L	1.9 (1.4 - 2.8)	1.9 (1.4 - 2.7)	1.8 (1.4 - 2.7)	0.33	0.34
HDL cholesterol, mmol/L	1.12 ± 0.31	1.11 ± 0.29	1.12 ± 0.27	0.93	0.79

LDL cholesterol, mmol/L	2.31 ± 0.93	2.33 ± 0.94	2.27 ± 0.83	0.57	0.43
% weight change Session2 - Session1	- 0.36 ± 1.10	- 0.46 ± 1.15	- 1.42 ± 1.35	< 0.001	< 0.001
% weight change Session3 - Session1	- 0.62 ± 1.27	- 0.80 ± 1.33	- 2.57 ± 1.61	< 0.001	< 0.001
% weight change Session3 – Session2	- 0.25 ± 0.75	- 0.33 ± 0.84	- 1.15 ± 1.22	< 0.001	< 0.001
% weight change: Session3 - Session1 categories, n(%)				< 0.001	< 0.001
Weight losing	750 (56.6%)	659 (71.5%)	311 (93.4%)		
Weight gaining	215 (16.2%)	174 (18.9%)	15 (4.5%)		
No change	360 (27.2%)	89 (9.7%)	7 (2.1%)		
Medications, n (%)				0.15	0.10
Weight loss	343 (25.9%)	235 (25.5%)	105 (31.5%)		
Mixed	532 (40.2%)	377 (40.9%)	115 (34.5%)		
Weight gaining	75 (5.7%)	44 (4.8%)	19 (5.7%)		
No drug	375 (28.3%)	266 (28.9%)	94 (28.2%)		
Number of diabetes medications, n (%)				0.07	0.04
0	375 (28.3%)	266 (28.9%)	94 (28.2%)		

1	374 (28.2%)	252 (27.3%)	118 (35.4%)		
2	400 (30.2%)	278 (30.2%)	81 (24.3%)		
3	158 (11.9%)	114 (12.4%)	34 (10.2%)		
4	18 (1.4%)	12 (1.3%)	6 (1.8%)		
Any insulin, n (%)				0.28	0.40
Yes	116 (8.8%)	77 (8.4%)	23 (6.9%)		
No	1209 (91.2%)	845 (91.6%)	310 (93.1%)		
Process:					
Attendance, n (%)				< 0.001	0.65
One session	15 (1.1%)	1 (0.1%)	0 (0.0%)		
Two sessions	50 (3.8%)	5 (0.5%)	3 (0.9%)		
Three sessions	1260 (95%)	916 (99.3%)	330 (99.1%)		
Attendance, n (%)				<0.001	0.64
Three sessions	1260 (95.1%)	916 (99.3%)	330 (99.1%)		
Other	65 (4.9%)	6 (0.7%)	3 (0.9%)		

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).

3.3.2.3 Univariable risk factors for successful completion

Univariable logistic regression models were initially explored to identify exposures associated with successful completion (5% weight loss), using those who did not complete the programme or completed the programme and did not successfully lose weight as the reference group (Table 3-9). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table.

For every year increase in age, the associated odds of successful completion increased 1% (95% CI: 0,2%, p=0.02). Being in an ethnic group other than white British/Scottish was associated with decreased odds of successful completion by 74% (95% CI: -89, -40%, p<0.001). For every unit increase in HbA1c, the associated odds of successful completion decreased 1% (95% CI: -2,0%, p=0.05).

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful short-term weight loss at the end of the 16-week / 9 fortnightly sessions in the GCWMS. This means that for every 1% weight gain between session 3 and session 1, the associated odds of successful completion decreased by 64% (95% CI: -68, -60%, p<0.001). Conversely, modelling weight loss, the odds of successful completion would increase 2.78 fold for every 1% weight loss. In the categorical model for change in weight between session 3 and session 1, the weight losing group (OR: 5.94, 95% CI: 3.50,10.2, p<0.001) was 5 times higher in being successful at losing weight at end of the 16-week / 9 fortnightly sessions when compared to weight gaining group.

Another strong predictor was attendance in the first 3 sessions. Patients attending all 3 first sessions of the programme had 5 times higher odds of successful weight loss at end of the 16-week / 9 fortnightly sessions when compared to those who attend 1 or 2 sessions of the first 3 sessions (OR: 5.67, 95% Cl: 1.80,18.2, p<0.001).

Table 3-9: Unadjusted models of successful completion in the short-term, 95% confidence intervals, and p-values for each predictor variable (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Age, per year	1658	1.01	1.00-1.02	0.02
Ethnicity				
White British/Scottish	1526	**Reference**		
Any other	93	0.26	0.11-0.60	< 0.001
Clinical:				
HbA1c, per mmol/mol	1658 (1559)	0.99	0.98-1.00	0.05
% weight change Session2 - Session1, per %	1658	0.44	0.40-0.50	< 0.001
% weight change Session3 - Session1, per %	1658	0.36	0.32-0.40	< 0.001
% weight change Session3 – Session2, per %	1658	0.39	0.34-0.44	< 0.001
Session3 - Session1 weight change categories	1658			
Weight gaining	230	**Reference**		
No change	367	0.28	0.11-0.70	< 0.001
Weight losing	1061	5.94	3.50-10.2	< 0.001
Process:				
Attendance				
< 3 sessions	68	**Reference**		
= 3 sessions	1590	5.67	1.80-18.2	< 0.001

Abbreviation: N(n), number of risks (number of events); HbA1c, glycated haemoglobin.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

3.3.2.4 Univariable risk factors for successful completion (a completers-only sensitivity analysis)

Another univariable comparison was performed to identify exposures associated with successful completion (5% weight loss), in this sensitivity analysis using only those who completed the programme and did not successfully lose weight as the referent group (Table 3-10) (i.e. this sensitivity analysis does not include non-completers in the comparator group). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table. This comparison was performed in order to identify exposure associated with successful weight loss only, rather than the complicating factor of non-attendance.

The exclusion of non-completers had minimal impact on risk factors. For every year increase in age, the associated odds of successful completion increased 1% (95% CI: 0,3%, p=0.07). Being in an ethnic group other than white British/Scottish was associated with decreased odds of successful completion by 66% (95% CI: -86,

-20%, p=0.01). For every unit increase in HbA1c, the associated odds of successful completion decreased 1% (95% CI: -2, -1%, p=0.03).

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful short-term weight loss at the end of the 16-week / 9 fortnightly sessions in the GCWMS. In the categorical model for change in weight between session 3 and session 1, the weight losing group (OR: 5.47, 95% CI: 3.18,9.44, p=0.00) was 5 times higher in being successful at losing weight at end of the 16-week / 9 fortnightly sessions when compared to weight gaining group.

Attendance in the first 3 sessions was not a strong predictor of success when non-completers were omitted.

Table 3-10: Unadjusted models of successful completion in the sensitivity analysis, p-values and 95% confidence intervals for each predictor variable (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table)

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Age, per year	1255	1.01	1.00-1.03	0.07
Ethnicity				
White British/Scottish	1174	**Reference**		
Any other	54	0.34	0.14-0.80	0.01
Clinical:				
HbA1c, per mmol/mol	1255 (1183)	0.99	0.98-0.99	0.03
% weight change Session2 - Session1, per %	1255	0.49	0.44-0.56	< 0.001
% weight change Session3 - Session1, per %	1255	0.39	0.35-0.45	< 0.001
% weight change Session3 – Session2, per %	1255	0.45	0.40-0.51	< 0.001
Session3 - Session1 weight change categories				
Weight gaining	189	**Reference**		
No change	96	0.91	0.36-2.32	0.85
Weight losing	970	5.47	3.18-9.44	< 0.001
Process:				
Attendance				
< 3 sessions	9	**Reference**		
= 3 sessions	1246	0.72	0.18-2.90	0.64

Abbreviation: N(n), number of risk (number of events); HbA1c, glycated haemoglobin.
Outcome variable: unsuccessful completers versus successful completers.

3.3.2.5 Risk factors for successful completion after adjustment

In the multivariable models ethnicity, early weight loss (change between session 2 and session 1, change between session 3 and session 2) and attendance were omitted from the final model due to lack of association.

Table 3-11 shows the retained risk factors for successful completion when compared to non-completion and unsuccessful completion. It includes age, HbA1c and the continuous variable of change in weight between session 3 and session 1. Although age and HbA1c were not associated with successful weight loss, they were included in the final models to allow for minimal adjustment. The only risk factor that was associated with successful weight loss at the end of the 16-week / 9 fortnightly sessions was the weight change between session 3 and session 1. Using this model, the AUC-ROC is 0.839 and CI is 0.812,0.866 (Figure 3-2).

Table 3-11: An adjusted model of successful completion in the short-term, 95% confidence intervals, and p-values for multiple independent variables at the same time (model of continuous variable).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	1.00	0.99-1.02	0.80
HbA1c, per mmol/mol	1.00	0.99-1.01	0.68
% weight change Session3 - Session1, per %	0.35	0.31-0.40	< 0.001

Abbreviation: HbA1c, glycated haemoglobin.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
The number of risks (number of events) is 1658 (1559).

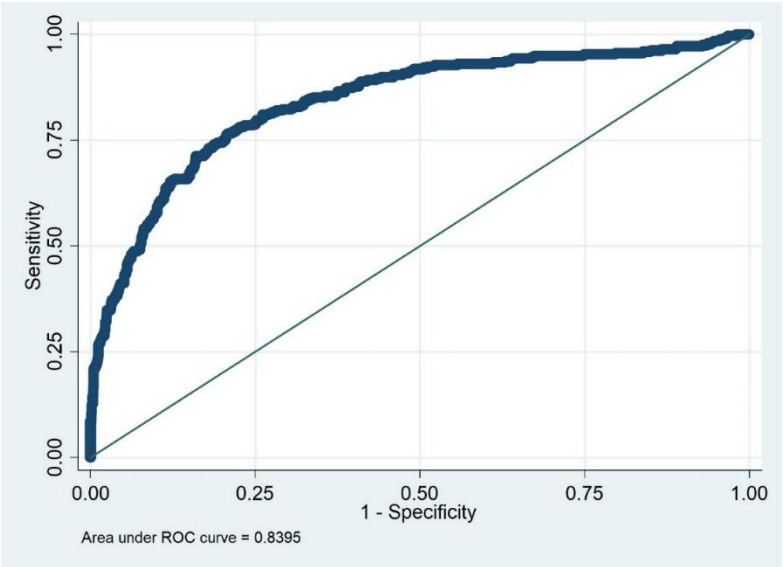

Figure 3-2: ROC curve for successful completion in the short term (model of continuous variable).

Table 3-12 shows the same comparisons but including the categorical (rather than continuous) variable of change in weight between session 3 and session 1. Using this model, the AUC-ROC is 0.700, CI is 0.672,0.728 (Figure 3-3).

Table 3-12: An adjusted model of successful completion in the short-term, 95% confidence intervals, and p-values for multiple independent variables at the same time (model of categorical variable).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	1.01	0.99-1.02	0.43
HbA1c, per mmol/mol	0.99	0.99-1.00	0.16
Session3 - Session1 weight change categories			
Weight gaining	**Reference**		
No change	0.30	0.12-0.75	0.01
Weight losing	5.77	3.30-10.1	< 0.001

Abbreviation: N(n), number of risks (number of events); HbA1c, glycated haemoglobin.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
N(n)= 1658 (1559).

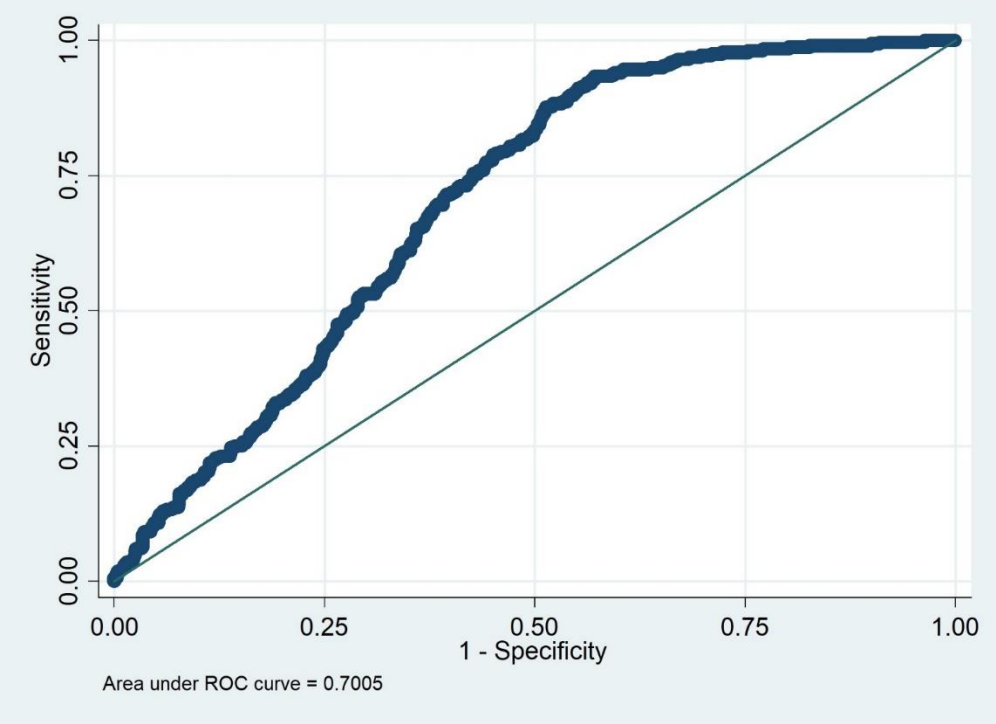

Figure 3-3: ROC curve for successful completion in the short term (model of categorical variable).

3.3.2.6 Risk factors for successful completion after adjustment (sensitivity analysis of completers only)

The exclusion of non-completers did not substantially change the associations. Table 3-13 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes age, HbA1c and the continuous variable of change in weight between session 3 and session 1. Using this model, the AUC-ROC is 0.813, CI is 0.784,0.842 (Figure 3-4).

Table 3-13: An adjusted model of successful completion in the sensitivity analysis, 95% confidence intervals, and p-values for multiple independent variables at the same time (model of continuous variable).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	1.00	0.98-1.02	0.87
HbA1c, per mmol/mol	1.00	0.99-1.01	0.89
% weight change Session3 - Session1, per %	0.39	0.34-0.44	< 0.001

Abbreviation: N(n), number of risks (number of events); HbA1c, glycated haemoglobin.
Outcome variable: unsuccessful completers versus successful completers.
N(n)= 1255 (1183).

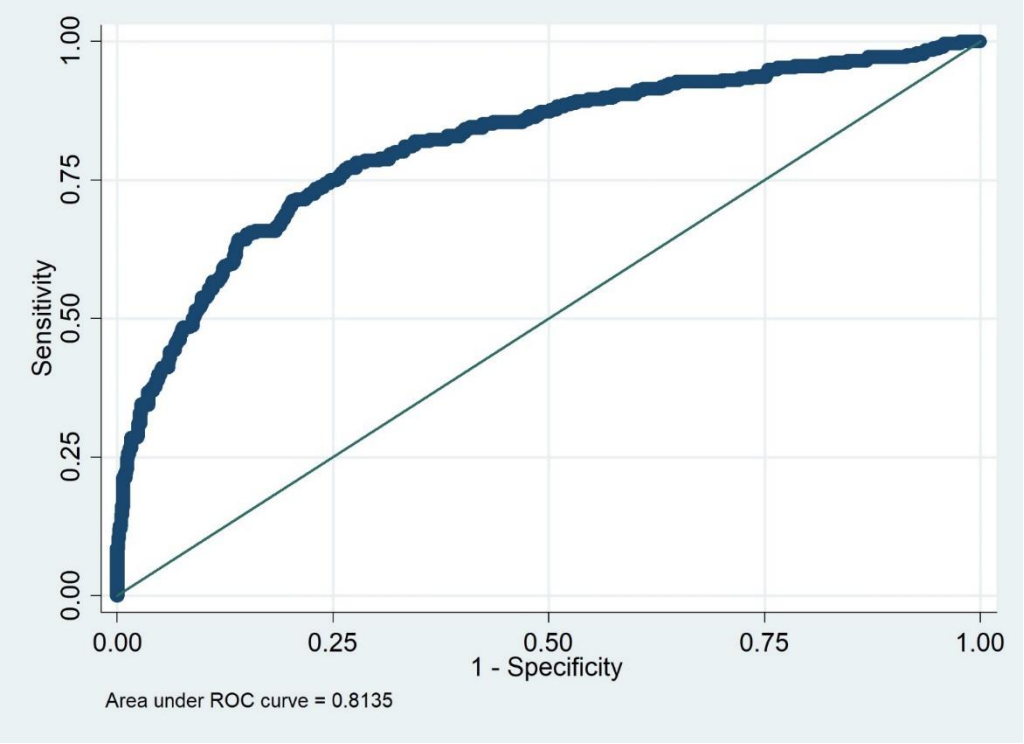

Figure 3-4: ROC curve for successful completion in the short term in the sensitivity analysis (model of continuous variable).

Table 3-14 shows the prediction of the outcome of unsuccessful completers versus successful completers. It includes age, HbA1c and the categorical variable of change in weight between session 3 and session 1. Using this model, the AUC-ROC is 0.629, CI is 0.595,0.662 (Figure 3-5).

Table 3-14: An adjusted model of successful completion in the sensitivity analysis, 95% confidence intervals, and p-values for multiple independent variables at the same time (model of categorical variable).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	1.01	0.99-1.02	0.30
HbA1c, per mmol/mol	0.99	0.99-1.00	0.12
Session3 - Session1 weight change categories			
Weight gaining	**Reference**		
No change	1.01	0.39-2.61	0.98
Weight losing	5.34	3.04-9.38	< 0.001

Abbreviation: N(n), number of risks (number of events); HbA1c, glycated haemoglobin.
Outcome variable: unsuccessful completers versus successful completers.
N(n)= 1255 (1183).

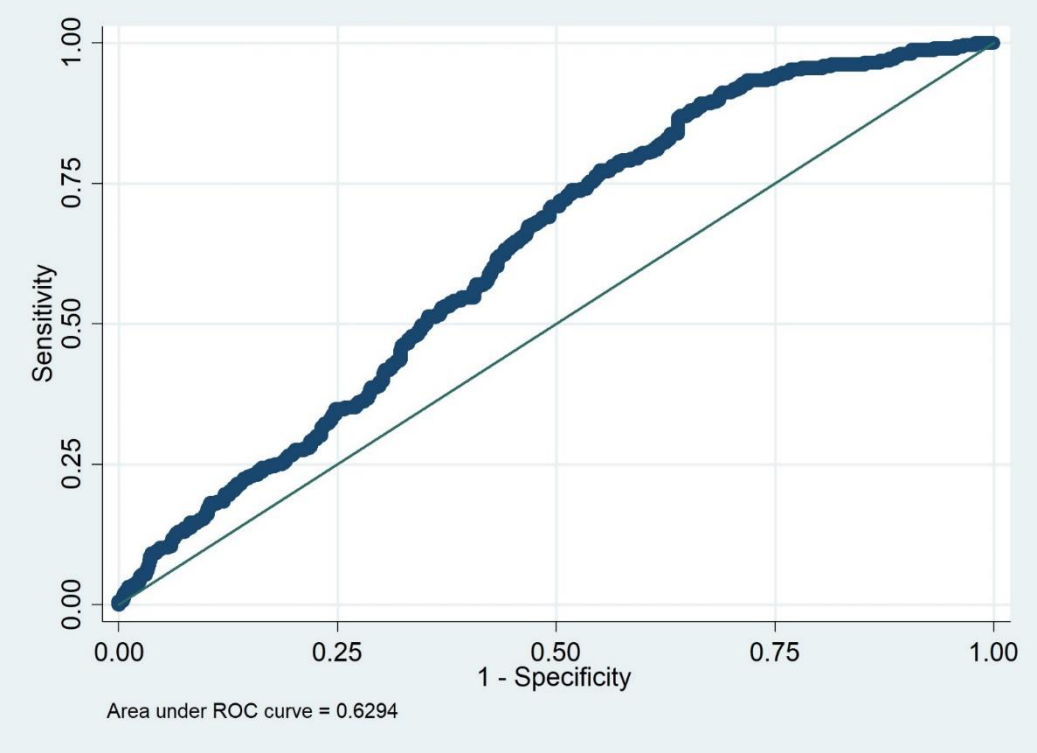

Figure 3-5: ROC curve for successful completion in the short term in the sensitivity analysis (model of categorical variable).

3.3.3 Thresholds for decision making in using the descriptive model (short-term)

3.3.3.1 Criteria for the predictive model

The baseline predictor variable of the weight change between session 3 and session 1 of the 16-week / 9 fortnightly sessions was the only independent (and the strongest) predictor of successful completion. Therefore, it was chosen to investigate the optimal definition of early weight loss to predict successful completion. Different thresholds for change in weight between session 3 and session 1 were used, using 0.5% increments from a weight change of ≤0.5% to ≥4%.

3.3.3.2 Performance of the predictive model

Table 3-15 describes the discrimination early weight change has in predicting who will complete and successfully achieve the required weight loss at end of the 16-week / 9 fortnightly sessions.

The 0.5% weight loss threshold maximises sensitivity and has a high NPV. This model would be selected for allowing the patients to continue treatment, and offer alternative interventions to a relatively small number of patients (i.e. a model predictive patients who will not succeed). In contrast, the 2.5% weight loss threshold maximises specificity, and the PPV, while still maintaining some sensitivity (51.4%). This threshold could be used to identify patients likely to succeed under this intervention.

Table 3-15: Sensitivity and specificity using a weight loss threshold based on a change in weight between session 3 and session 1 from the 16 / 9 fortnightly sessions in GCWMS to predict weight loss at 16 wks.

Weight loss threshold	Sensitivity	Specificity	PPV	NPV
≤0.5	9.6% (6.7%-13.3%)	46.4% (43.7%-49.1%)	4.3% (3.0%-6.0%)	67.1% (64.0%-70.2%)
≥0.5	90.4% (86.7%-93.3%)	53.6% (50.9%-56.3%)	32.9% (29.8%-36.0%)	95.7% (94.0%-97.0%)
≥1	85.0% (80.7%-88.6%)	65.9% (63.3%-68.4%)	38.5% (35.0%-42.1%)	94.6% (92.9%-96.0%)
≥1.5	77.8% (72.9%-82.1%)	77.8% (75.5-80.0%)	46.8% (42.6%-51.1%)	93.3% (91.7%-94.7%
≥2	65.2% (59.8%-70.3%)	86.6% (84.7%-88.4%)	55.1% (50.0%-60.1%)	90.8% (89.1%-92.4%)
≥2.5	51.4% (45.8%-56.8%)	92.2% (90.6%-93.5%)	62.2% (56.2%-67.9%)	88.3% (86.5-89.9%)
≥3	39.6% (34.3%-45.1%)	96.0% (94.8%-97.0%)	71.4% (64.3%-77.7%)	86.4% (84.5%-88.1%)
≥3.5	25.5% (20.9%-30.6%)	98.6% (97.9%-99.2%)	82.5% (73.8%-89.3%)	84.1% (82.1%-85.8%)
≥4	15.9% (12.2%-20.3%)	99.5% (98.9%-99.8%)	88.3% (77.4%-95.2%)	82.5% (80.5%-84.3%)

Abbreviation: PPV, Positive predictive value; NPV, negative predictive value.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
The ≤0.5% threshold includes zero change and weight gaining participants.

3.3.4 Medium-term weight loss

In this analysis, the follow-up period was extended for up to 3 years to investigate the effect of each predictor on the medium-term weight loss of the different scenarios.

It is shown in the previous section that early weight loss in the first few weeks is associated with and predictive of short-term weight loss. In this section, besides early weight loss in the first few weeks, additional models will also investigate early weight loss in the first few months. The correlation between % weight change Session3 - Session1 and % weight change Session9 - Session1 was tested: repeated measures correlation rho= 0.50 (moderate effect).

3.3.4.1 Descriptive statistics by medium-term outcome success (3% weight loss at 3 years)

Table 3-16 shows the baseline characteristics of the successful completers versus unsuccessful completers (based on the outcome of achieving **3% weight loss** at 3 years). From demographic data, successful completers were less than a year younger than unsuccessful completers. In ethnicity, the white British/Scottish is the dominant group in all comparable groups, although successful completers are most likely to be white. Successful completers had a slightly longer duration of T2DM at baseline than the unsuccessful completers (0.55 years longer). Successful completers were almost 3 kg heavier than the unsuccessful completers. Successful completers had around 1 kg/m^2 higher BMI than unsuccessful completers. Both groups were mostly from the 40-49 BMI category. Successful completers had a poorer glycaemic control than unsuccessful completers (2 mmol/mol higher). From the lipid profile, successful completers had slightly higher triglycerides than unsuccessful completers.

The percent weight change over the 3 first sessions was higher among successful completers. Successful completers lost more weight in the early weight loss sessions (e.g. session 3 versus session 1). Successful completers lost 0.34% more weight than unsuccessful completers. Successful completers had the highest proportion of weight-losing category (n=441, 66.1%).

There was a trend that successful completers were more likely to be on a mixed type of diabetes drugs (n=260, 39.0%) and to be on at least 1 type of T2DM drugs (n=219, 32.8%).

Both comparison groups tended to attend the first three sessions of the 16 / 9 fortnightly sessions in GCWMS (both >95%).

Table 3-16: Characteristics of participants, showing the comparison between the unsuccessful completers versus the successful completers (3% weight loss at 3 years).

Variable	Unsuccessful completers (n=485)	Successful completers (n=667)	p-value
Demographic:			
Age, years	58.0 ± 9.43	57.7 ± 8.96	0.60
Age categories, n(%)			0.50
0-39.9	16 (3.3%)	21 (3.1%)	
40-49.9	86 (17.7%)	122 (18.3%)	
50-59.9	170 (35.1%)	242 (36.3%)	
60-69.9	161 (33.2%)	231 (34.6%)	
≥70	52 (10.7%)	51 (7.6%)	
Sex, n (%)			0.30
Female	285 (58.8%)	412 (61.8%)	
Male	200 (41.2%)	255 (38.2%)	
SIMD scores, n (%)			0.22
Q1 Most deprived	196 (40.6%)	264 (39.8%)	
Q2	81 (16.8%)	124 (18.7%)	
Q3	74 (15.3%)	111 (16.7%)	
Q4	70 (14.5%)	68 (10.2%)	
Q5 Least deprived	62 (12.8%)	97 (14.6%)	
Ethnicity, n (%)			0.02
White British/Scottish	447 (92.7%)	629 (96.0%)	
Any other	35 (7.3%)	26 (4.0%)	
Clinical:			
Duration of T2DM, years	5.06 (1.87 - 10.2)	5.55 (2.66 - 9.11)	0.46
Initial weight, kg	110 ± 21.3	113 ± 23.2	0.02
Initial BMI, kg/m^2	39.5 (35.6 - 43.1)	40.7 (36.3 - 45.8)	< 0.001
Initial BMI categories, n (%)			< 0.001
30 – 34	85 (17.5%)	81 (12.1%)	
35 – 39	138 (28.5%)	189 (28.3%)	
40 – 49	226 (46.6%)	295 (44.2%)	
≥ 50	36 (7.4%)	102 (15.3%)	
HbA1c, mmol/mol	55 (48 - 68)	57 (49 – 70)	0.04
Systolic blood pressure, mmHg	133 ± 13.7	133 ± 14.7	0.83
Diastolic blood pressure, mmHg	77.8 ± 9.07	77.9 ± 10.4	0.88

Total cholesterol, mmol/L	4.37 ± 1.03	4.35 ± 1.05	0.82
Triglycerides, mmol/L	1.8 (1.3 - 2.6)	2 (1.4 - 2.8)	0.04
HDL cholesterol, mmol/L	1.14 ± 0.28	1.12 ± 0.32	0.44
LDL cholesterol, mmol/L	2.25 ± 0.86	2.24 ± 0.88	0.95
% weight change Session2 - Session1	- 0.44 ± 1.28	- 0.63 ± 1.16	0.01
% weight change Session3 - Session1	- 0.78 ± 1.56	- 1.12 ± 1.50	< 0.001
% weight change Session3 – Session2	- 0.33 ± 0.88	- 0.49 ± 0.97	0.01
% weight change: Session3 - Session1 categories, n(%)			0.01
Weight losing	297 (61.2%)	441 (66.1%)	
Weight gaining	86 (17.7%)	76 (11.4%)	
No change	102 (21.0%)	150 (22.5%)	
% weight change Session9 - Session1	- 1.80 ± 2.90	- 2.80 ± 3.50	< 0.001
Medications, n (%)			0.18
Weight loss	117 (24.1%)	195 (29.2%)	
Mixed	204 (42.1%)	260 (39.0%)	
Weight gaining	26 (5.4%)	43 (6.4%)	
No drug	138 (28.5%)	169 (25.3%)	
Number of diabetes medications, n (%)			0.50
0	138 (28.5%)	169 (25.3%)	
1	137 (28.2%)	219 (32.8%)	
2	144 (29.7%)	193 (28.9%)	
3	60 (12.4%)	76 (11.4%)	
4	6 (1.2%)	10 (1.5%)	
Any insulin, n (%)			0.28
Yes	49 (10.1%)	55 (8.2%)	
No	436 (89.9%)	612 (91.8%)	
Process:			
Attendance, n (%)			0.44
One session	3 (0.6%)	5 (0.7%)	

Two sessions	16 (3.3%)	14 (2.1%)	
Three sessions	466 (96.1%)	648 (97.2%)	
Attendance, n (%)			0.32
Three sessions	466 (96.1%)	648 (97.2%)	
Other	19 (3.9%)	19 (2.8%)	

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: achieve **3% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.

3.3.4.2 Univariable risk factors for successful completion (3% weight loss at 3 years)

Univariable logistic regression models were initially explored to identify exposures associated with successful completion, using those who complete the programme and did not successfully lose weight as the reference group (Table 3-17). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table.

Being in an ethnic group other than white British/Scottish was associated with decreased odds of successful completion by 47% (95% CI: -69, -11%, p=0.02). For every kg increase in weight, the associated odds of successful completion increased 1% (95% CI: 0,1%, p=0.02). For every kg/m^2 increase in BMI, the associated odds of successful completion increased 4% (95% CI: 2,5%, p<0.001). In the categorical model for BMI, having a BMI ≥ 50 (OR: 3.00, 95% CI: 1.83,4.84, p<0.001) was 3 times higher in being successful at losing weight at 3 years when compared to those having BMI between 30 – 34. For every mmol/L increase in triglycerides, the associated odds of successful completion increased by 10% (95% CI: 0,21%, p=0.04).

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful medium-term weight loss at the 3 years. This means that for every 1% weight gain between session 3 and session 1, the associated odds of successful completion decreased by 14% (95% CI: 20, 7%, p<0.001). Although early weight loss between session 3 and session 1 was a significant predictor of successful completion in the medium-term, the associations were a bit less strong than they were for successful completion in the short term. In the categorical model for change in weight between session 3 and session 1, the associated odds of successful completion increased by 68% in the weight losing group (95% CI: 20,40%, p<0.001) at 3 years when compared to weight gaining group.

Table 3-17: Unadjusted models of successful completion in the medium-term (3% weight loss at 3 years), 95% confidence intervals and p-values for each independent variable. (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Ethnicity				
White British/Scottish	1076	**Reference**		
Any other	61	0.53	0.31-0.89	0.02
Clinical:				
Initial weight, per kg	1152	1.01	1.00-1.01	0.02
Initial BMI, per kg/m^2	1152	1.04	1.02-1.05	<0.001
Initial BMI categories				
30 – 34	166	**Reference**		
35 – 39	327	1.44	0.99-2.09	0.58
40 – 49	521	1.37	0.97-1.94	0.78
≥ 50	138	3.00	1.83-4.84	<0.001
Triglycerides, per mmol/L	1152 (855)	1.10	1.00-1.21	0.04
% weight change Session2 - Session1, per %	1152	0.88	0.80-0.97	0.01
% weight change Session3 – Session1, per %	1152	0.86	0.80-0.93	<0.001
% weight change Session3 – Session2, per %	1152	0.84	0.74-0.95	0.01
Session3 – Session1 weight change categories				
Weight gaining	162	**Reference**		
No change	252	1.66	1.12-2.50	0.01
Weight losing	738	1.68	1.20-2.40	<0.001
% weight change Session9 - Session1, per %	1152	0.90	0.87-0.94	<0.001

Abbreviation: N(n), number of risks (number of events); BMI, Body Mass Index.
Criteria for success: achieve **3% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.

3.3.4.3 Risk factors for successful completion after adjustment (3% weight loss at 3 years)

In the multivariable model's ethnicity, initial weight, initial BMI categories and early weight loss (change between session 2 and session 1, change between session 3 and session 2, Session3 - Session1 weight change categories) were omitted from the final model due to lack of association.

Table 3-18 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes initial BMI, triglycerides, and the continuous variable of change in weight between session 3 and session 1. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 3 and session 1. Using this model, the AUC-ROC is 0.610 and CI is 0.572,648 (Figure 3-6).

Table 3-18: An adjusted model of successful completion in the medium-term (3% weight loss at 3 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.04	1.02-1.06	<0.001
Triglycerides, per mmol/L	1.12	1.02-1.23	0.02
% weight change Session3 - Session1, per %	0.83	0.76-0.92	<0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **3% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.
The number of risks (number of events) is 1152(855).

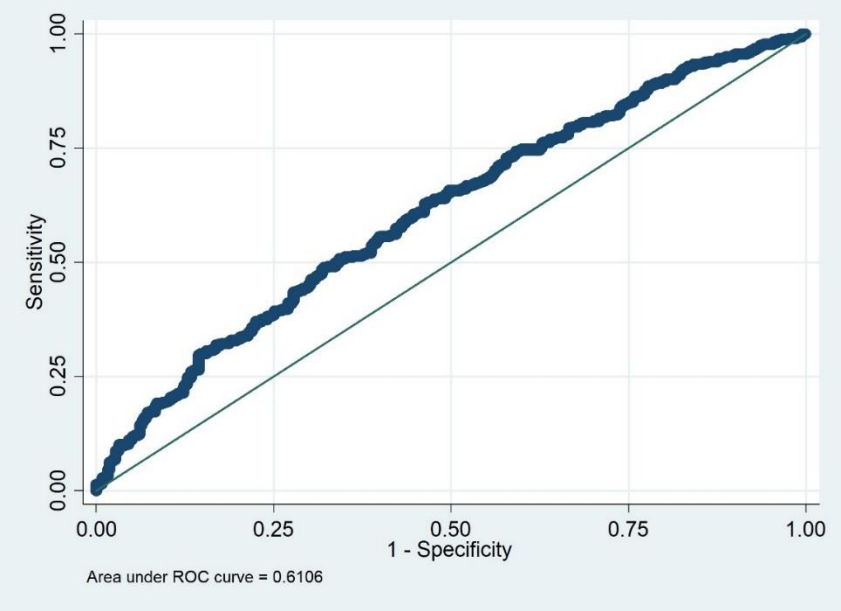

Figure 3-6: ROC curve for successful completion in the medium term (3% weight loss at 3 years).

3.3.4.4 Risk factors for successful completion after adjustment (3% weight loss at 3 years) - 16 / 9 fortnightly sessions in GCWMS weight change

Table 3-19 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes initial BMI, triglycerides, and the continuous variable of change in weight between session 9 and session 1. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 9 and session 1. Using this model, the AUC-ROC is 0.623 and CI is 0.586,660 (Figure 3-7).

Table 3-19: An adjusted model of successful completion in the medium-term (3% weight loss at 3 years) using 16 / 9 fortnightly sessions in GCWMS weight change, 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.04	1.02-1.06	< 0.001
Triglycerides, per mmol/L	1.12	1.02-1.24	0.02
% weight change ≈4months - initial, per %	0.90	0.86-0.94	< 0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **3% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.
The number of risks (number of events) is 1152(855).

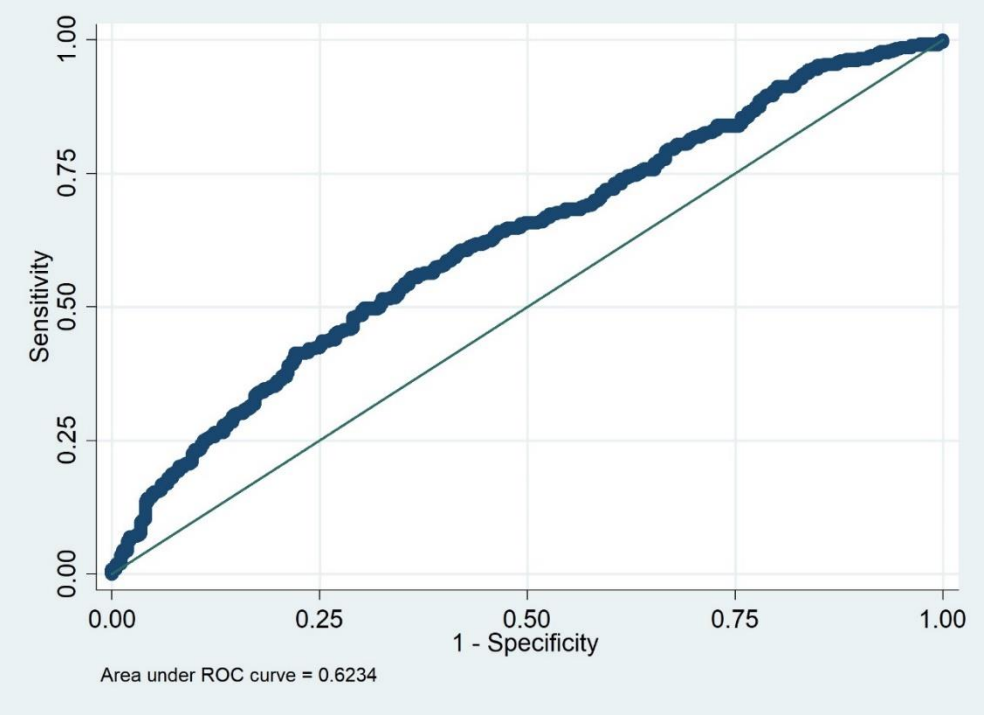

Figure 3-7: ROC curve for successful completion in the medium term (3% weight loss at 3 years) using 16 / 9 fortnightly sessions in GCWMS weight change.

3.3.4.5 Descriptive statistics by medium-term outcome success (5% weight loss at 3 years)

Table 3-20 shows the baseline characteristics of the successful completers versus unsuccessful completers (based on the outcome of achieving **5% weight loss** at 3 years). From demographic data, successful completers were less than a year younger than unsuccessful completers. In ethnicity, the white British/Scottish is the dominant group in all comparable groups, although successful completers are most likely to be white. Successful completers had a slightly longer duration of T2DM at baseline than the unsuccessful completers (0.35 years longer). Successful completers were almost 3 kg heavier than the unsuccessful completers. Successful completers had around 1.5 kg/m^2 higher BMI than unsuccessful completers. Both groups were mostly from the 40-49 BMI category. Successful completers had a slightly poorer glycaemic control than unsuccessful completers (0.25 mmol/mol higher). From the lipid profile, both groups had similar triglyceride values.

The percent weight change over the 3 first sessions was higher among successful completers. Successful completers lost more weight in the early weight loss sessions (e.g. session 3 versus session 1). Successful completers lost 0.27% more weight than unsuccessful completers. Although the same trend was shown in the previous comparison, the trend here was weaker. The proportion of weight losing category was similar among both groups, with successful completers having a slightly higher proportion).

There was a trend that successful completers were more likely to be on a mixed type of diabetes drugs (n=219, 40.7%) and to be on at least 1 type of T2DM drugs (n=176, 32.7%).

Both comparison groups tended to attend the first three sessions of the 16 / 9 fortnightly sessions in GCWMS (both >95%).

Table 3-20: Characteristics of participants, showing the comparison between the unsuccessful completers versus the successful completers (5% weight loss at 3 years).

Variable	Unsuccessful completers (n=614)	Successful completers (n=538)	p-value
Demographic:			
Age, years	58.1 ± 9.38	57.5 ± 8.90	0.30
Age categories, n (%)			0.33
30-39.9	19 (3.1%)	18 (3.3%)	
40-49.9	108 (17.6%)	100 (18.6%)	
50-59.9	213 (34.7%)	199 (37.0%)	
60-69.9	209 (34.0%)	183 (34.0%)	
≥70	65 (10.6%)	38 (7.1%)	
Sex, n (%)			0.37
Female	364 (59.3%)	333 (61.9%)	
Male	250 (40.7%)	205 (38.1%)	
SIMD scores, n (%)			0.12
Q1 Most deprived	238 (38.9%)	222 (41.5%)	
Q2	113 (18.5%)	92 (17.2%)	
Q3	91 (14.9%)	94 (17.6%)	
Q4	87 (14.2%)	51 (9.5%)	
Q5 Least deprived	83 (13.6%)	76 (14.2%)	
Ethnicity, n (%)			0.06
White British/Scottish	570 (93.4%)	506 (96.0%)	
Any other	40 (6.6%)	21 (4.0%)	
Clinical:			
Duration of T2DM, years	5.24 (2.11 - 9.95)	5.59 (2.59 - 9.23)	0.78
Initial weight, kg	111 ± 21.2	114 ± 23.6	0.03
Initial BMI, kg/m^2	39.6 (35.8 - 43.5)	41 (36.5 - 46)	< 0.001
Initial BMI categories, n (%)			< 0.001
30 – 34	99 (16.1%)	67 (12.5%)	
35 – 39	183 (29.8%)	144 (26.8%)	
40 – 49	282 (45.9%)	239 (44.4%)	
≥ 50	50 (8.1%)	88 (16.4%)	
HbA1c, mmol/mol	55.75 (48 - 69)	56 (49 – 69)	0.16
Systolic blood pressure, mmHg	134 ± 14.0	134 ± 14.5	0.92

Diastolic blood pressure, mmHg	78 ± 9.42	778 ± 10.4	0.80
Total cholesterol, mmol/L	4.37 ± 1.05	4.34 ± 1.03	0.67
Triglycerides, mmol/L	1.9 (1.3 - 2.7)	1.9 (1.3 - 2.8)	0.65
HDL cholesterol, mmol/L	1.13 ± 0.30	1.12 ± 0.30	0.72
LDL cholesterol, mmol/L	2.25 ± 0.84	2.24 ± 0.90	0.83
% weight change Session2 - Session1	- 0.49 ± 1.24	- 0.62 ± 1.18	0.08
% weight change Session3 - Session1	- 0.85 ± 1.53	- 1.12 ± 1.53	< 0.001
% weight change Session3 – Session2	- 0.35 ± 0.88	- 0.50 ± 0.99	0.01
% weight change: Session3 - Session1 categories, n (%)			0.03
Weight losing	379 (61.7%)	359 (66.7%)	
Weight gaining	102 (16.6%)	60 (11.2%)	
No change	133 (21.7%)	119 (22.1%)	
% weight change Session9 - Session1	- 1.90 ± 2.97	- 2.86 ± 3.50	< 0.001
Medications, n (%)			0.44
Weight loss	160 (26.1%)	152 (28.3%)	
Mixed	245 (39.9%)	219 (40.7%)	
Weight gaining	34 (5.5%)	35 (6.5%)	
No drug	175 (28.5%)	132 (24.5%)	
Number of diabetes medications, n (%)			0.49
0	175 (28.5%)	132 (24.5%)	
1	180 (29.3%)	176 (32.7%)	
2	175 (28.5%)	162 (30.1%)	
3	76 (12.4%)	60 (11.2%)	
4	8 (1.3%)	8 (1.5%)	
Any insulin, n (%)			0.10
Yes	64 (10.4%)	40 (7.4%)	
No	550 (89.6%)	498 (92.6%)	

Process:

Attendance, n (%)			0.46
One session	5(0.8%)	3 (0.6%)	
Two sessions	19 (3.1%)	11 (2.0%)	
Three sessions	590 (96.1%)	524 (97.4%)	
Attendance, n (%)			0.22
Three sessions	590 (96.1%)	524 (97.4%)	
Other	24 (3.9%)	14 (2.6%)	

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: achieve **5% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.

3.3.4.6 Univariable risk factors for successful completion (5% weight loss at 3 years)

Univariable logistic regression models were initially explored to identify exposures associated with successful completion, using those who complete the programme and did not successfully lose weight as the reference group (Table 3-21). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table.

Being in moderate socioeconomically status (i.e. Q3) was associated with decreased odds of successful completion by 37% (95% CI: -58, -7%, p=0.02). For every kg increase in weight, the associated odds of successful completion increased 1% (95% CI: 0,1%, p=0.03). For every kg/m^2 increase in BMI, the associated odds of successful completion increased 3% (95% CI: 2,5%, p<0.001). In the categorical model for BMI, having a BMI ≥ 50 (OR: 2.60, 95% CI: 1.63,4.14, p<0.001) was almost 3 times higher in being successful at losing weight at 3 years when compared to those having BMI between 30 – 34.

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful medium-term weight loss at the 3 years. This means that for every 1% weight gain between session 3 and session 1, the associated odds of successful completion decreased by 11% (95% CI: 18, 5%, p<0.001). In the categorical model for change in weight between session 3 and session 1, the associated odds of successful completion increased by 61% in the weight losing group (95% CI: 13,29%, p=0.01) at 3 years when compared to weight gaining group.

Table 3-21: Unadjusted models of successful completion in the medium-term (5% weight loss at 3 years), 95% confidence intervals and p-values for each independent variable. (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
SIMD scores				
Q5	159	**Reference**		
Q1 Most deprived	460	0.87	0.63-1.21	0.42
Q2	205	1.11	0.79-1.56	0.56
Q3	185	0.63	0.42-0.93	0.02
Q4	138	1.00	0.70-1.41	0.92
Clinical:				
Initial weight, per kg	1152	1.01	1.00-1.01	0.03
Initial BMI, per kg/m^2	1152	1.03	1.02-1.05	< 0.001
Initial BMI categories				
30 – 34	166	**Reference**		
35 – 39	327	1.16	0.80-1.70	0.25
40 – 49	521	1.25	0.88-1.79	0.30
≥ 50	138	2.60	1.63-4.14	< 0.001
% weight change Session2 - Session1, per %	1152	0.92	0.83-1.01	0.08
% weight change Session3 - Session1, per %	1152	0.89	0.82-0.95	< 0.001
% weight change Session3 – Session2, per %	1152	0.84	0.74-0.96	0.01
Session3 - Session1 weight change categories				
Weight gaining	162	**Reference**		
No change	252	1.52	1.02-2.28	0.04
Weight losing	738	1.61	1.13-2.29	0.01
% weight change Session9 - Session1, per %	1152	0.91	0.87-0.94	< 0.001

Abbreviation: N(n), number of risks (number of events); BMI, Body Mass Index; SIMD, Scottish Index of Multiple Deprivation.
Criteria for success: achieve **5% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.

3.3.4.7 Risk factors for successful completion after adjustment (5% weight loss at 3 years)

In the multivariable models SIMD, initial weight, initial BMI categories and early weight loss (change between session 2 and session 1, change between session 3 and session 2, Session3 - Session1 weight change categories) were omitted from the final model due to lack of association.

Table 3-22 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes initial BMI and the continuous variable of change in weight between session 3 and session 1. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 3 and session 1. Using this model, the AUC-ROC is 0.589 and CI is 0.556,0.622 (Figure 3-8).

Table 3-22: An adjusted model of successful completion in the medium-term (5% weight loss at 3 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.04	1.02-1.05	< 0.001
% weight change Session3 - Session1, per %	0.88	0.81-0.95	< 0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **5% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.
The number of risks is 1152.

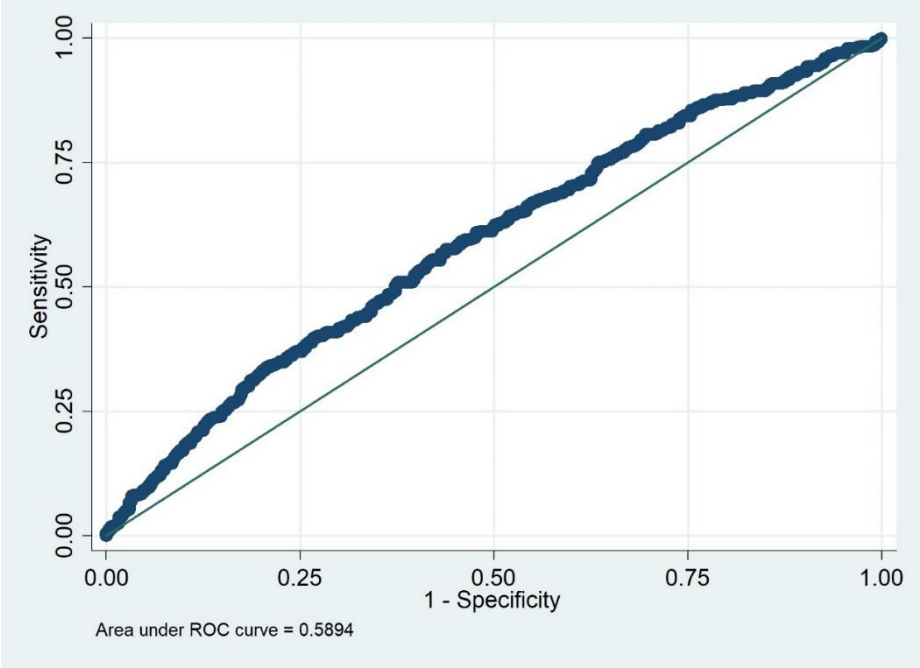

Figure 3-8: ROC curve for successful completion in the medium term (5% weight loss at 3 years).

3.3.4.8 Risk factors for successful completion after adjustment (5% weight loss at 3 years) - 16 / 9 fortnightly sessions in GCWMS weight change

Table 3-23 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes initial BMI and the continuous variable of change in weight between session 9 and session 1. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 9 and session 1. Using this model, the AUC-ROC is 0.611 and CI is 0.579,0.644 (Figure 3-9).

Table 3-23: An adjusted model of successful completion in the medium-term (5% weight loss at 3 years) using 16 / 9 fortnightly sessions in GCWMS weight change, 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.04	1.02-1.05	< 0.001
% weight change ≈4months - initial, per %	0.91	0.87-0.94	< 0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **5% weight loss** at 3 years.
Outcome variable: unsuccessful completers versus successful completers.
The number of risks is 1152.

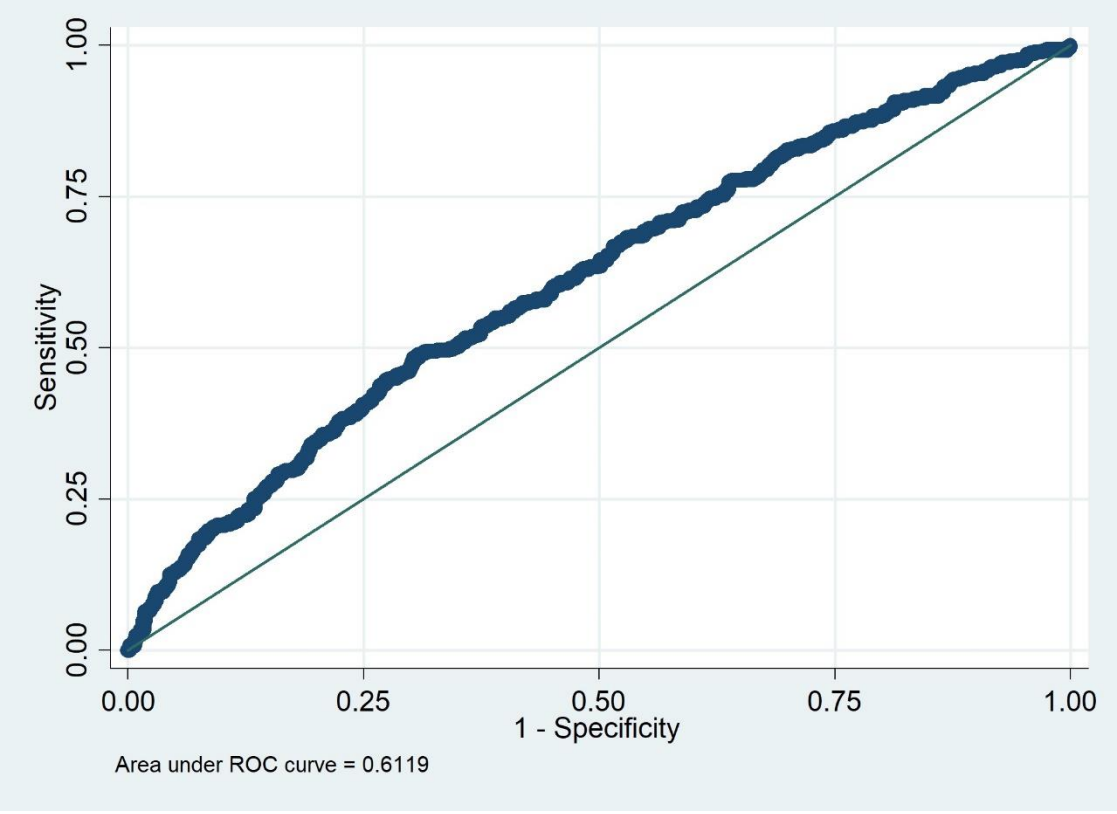

Figure 3-9: ROC curve for successful completion in the medium term (5% weight loss at 3 years) using 16 / 9 fortnightly sessions in GCWMS weight change.

3.3.4.9 Descriptive statistics by short and medium-term outcome success (5% weight loss short-term & 3% weight loss medium-term)

Table 3-24 shows the baseline characteristics of the non-completers & unsuccessful completers versus successful completers (based on the outcome of attending ≥ 7/9 weight loss sessions from the 16-week / 9 fortnightly sessions of GCWMS, losing ≥ 5% body weight at the end of the sessions and lost ≥ 3% from the baseline body weight at the end of the entire programme).

From demographic data, successful completers were a year older than the unsuccessful completers. In ethnicity, the white British/Scottish is the dominant group in all comparable groups, although successful completers are most likely to be white. Successful completers had a slightly shorter duration of T2DM at baseline than unsuccessful completers (0.53 years shorter). Successful completers were almost 2 kg lighter than the unsuccessful completers. Successful completers had around 1 kg/m^2 lower BMI than the unsuccessful completers. Successful completers were mostly from the 35-39 BMI category. Successful completers had a slightly poorer glycaemic control than unsuccessful completers (0.5 mmol/mol higher).

The percent weight change over the 3 first sessions is higher among successful completers. Successful completers lost more weight in the early weight loss sessions (specifically weight change between session 3 & session 1). Successful completers lost 1.76% more weight than unsuccessful completers. The proportion of weight losing category was high among both groups, with successful completers having a slightly higher proportion).

There was a trend that successful completers were more likely to be on a weight loss type of diabetes drugs (n=62, 38.0%) and to be on at least 1 type of T2DM drugs (n=67, 41.1%).

Both comparison groups tended to attend the first three sessions of the 16 / 9 fortnightly sessions in GCWMS (both >95%).

Table 3-24: Characteristics of participants, showing the comparison between the non-completers & unsuccessful completers versus the successful completers (5% weight loss short-term & 3% weight loss medium-term).

Variable	Non completers & Unsuccessful completers (n=989)	Successful completers (n=163)	p-value
Demographic:			
Age, years	57.7 ± 9.25	58.7 ± 8.54	0.18
Age categories, n (%)			0.62
30-39.9	34 (3.4%)	3 (1.8%)	
40-49.9	183 (18.5%)	25 (15.3%)	
50-59.9	348 (35.2%)	64 (39.3%)	
60-69.9	335 (33.9%)	57 (35.0%)	
≥70	89 (9.0%)	14 (8.6%)	
Sex, n (%)			0.45
Female	594 (60.1%)	103 (63.2%)	
Male	395 (39.9%)	60 (36.8%)	
SIMD scores, n (%)			0.47
Q1 Most deprived	400 (40.7%)	60 (36.8%)	
Q2	174 (17.7%)	31 (19.0%)	
Q3	158 (16.1%)	27 (16.6%)	
Q4	122 (12.4%)	16 (9.8%)	
Q5 Least deprived	130 (13.2%)	29 (17.8%)	
Ethnicity, n (%)			0.04
White British/Scottish	920 (94.1%)	156 (98.1%)	
Any other	58 (5.9%)	3 (1.9%)	
Clinical:			
Duration of T2DM, years	5.47 (2.31 - 9.68)	4.94 (2.46 - 8.52)	0.64
Initial weight, kg	113 ± 22.2	111 ± 23.7	0.47
Initial BMI, kg/m^2	40.3 (36.2 - 44.7)	39.3 (35.1 - 44.9)	0.54
Initial BMI categories, n (%)			< 0.001
30 – 34	145 (14.7%)	21 (12.9%)	
35 – 39	267 (27.0%)	60 (36.8%)	
40 – 49	465 (47.0%)	56 (34.4%)	
≥ 50	112 (11.3%)	26 (16.0%)	
HbA1c, mmol/mol	56 (49 - 70)	56.5 (48 – 67)	0.94

Systolic blood pressure, mmHg	133 ± 14.2	136 ± 14.0	0.08
Diastolic blood pressure, mmHg	78 ± 9.80	78 ± 10.3	0.90
Total cholesterol, mmol/L	4.36 ± 1.04	4.34 ± 1.04	0.80
Triglycerides, mmol/L	1.9 (1.3 - 2.8)	1.8 (1.3 - 2.7)	0.50
HDL cholesterol, mmol/L	1.12 ± 0.30	1.15 ± 0.30	0.33
LDL cholesterol, mmol/L	2.25 ± 0.88	2.19 ± 0.77	0.52
% weight change Session2 - Session1	- 0.42 ± 1.15	- 1.36 ± 1.26	< 0.001
% weight change Session3 - Session1	- 0.73 ± 1.39	- 2.49 ± 1.51	< 0.001
% weight change Session3 – Session2	- 0.30 ± 0.84	- 1.13 ± 1.18	< 0.001
% weight change: Session3 - Session1 categories, n (%)			< 0.001
Weight losing	586 (59.3%)	152 (93.3%)	
Weight gaining	153 (15.5%)	9 (5.5%)	
No change	250 (25.3%)	2 (1.2%)	
% weight change Session9 - Session1	- 1.50 ± 2.45	- 7.61 ± 2.61	< 0.001
Medications, n (%)			< 0.001
Weight loss	250 (25.3%)	62 (38.0%)	
Mixed	413 (41.8%)	51 (31.3%)	
Weight gaining	56 (5.7%)	13 (8.0%)	
No drug	270 (27.3%)	37 (22.7%)	
Number of diabetes medications, n (%)			0.02
0	270 (27.3%)	37 (22.7%)	
1	289 (29.2%)	67 (41.1%)	
2	295 (29.8%)	42 (25.8%)	
3	123 (12.4%)	13 (8.0%)	
4	12 (1.2%)	4 (2.5%)	
Any insulin, n (%)			0.70
Yes	88 (8.9%)	16 (9.8%)	

No	901 (8.9%)	147 (90.2%)	
Process:			
Attendance, n (%)			0.11
One session	8 (0.8%)	0 (0.0%)	
Two sessions	29 (2.9%)	1 (0.6%)	
Three sessions	952 (96.3%)	162 (99.4%)	
Attendance, n (%)			0.04
Three sessions	952 (96.3%)	162 (99.4%)	
Other	37 (3.7%)	1 (0.6%)	

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **3% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

3.3.4.10 Univariable risk factors for successful completion (5% weight loss short-term & 3% weight loss medium-term)

Univariable logistic regression models were initially explored to identify exposures associated with successful completion, using those who did not complete the programme or complete the programme and did not successfully lose weight as the reference group (Table 3-25). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table.

Being in an ethnic group other than white British/Scottish was associated with decreased odds of successful completion by 69% (95% CI: -91, -11%, p=0.05).

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful medium-term weight loss at the 3 years. This means that for every 1% weight gain between session 3 and session 1, the associated odds of successful completion decreased by 57% (95% CI: 60, 51%, p<0.001). In the categorical model for change in weight between session 3 and session 1, the weight losing group (OR: 4.41, 95% CI: 2.20,8.84, p<0.001) was almost 5 times higher in being successful at losing weight at 3 years when compared to weight gaining group.

In the categorical model of diabetes medication, being in the mixed type of diabetes drugs was associated with decreased odds of successful completion by 50% (95% CI: -67, -26%, p<0.001). Also, taking no diabetes drugs was associated with decreased odds of successful completion by 40% (95% CI: -64,-14%, p<0.001). In the categorical model of the number of diabetes medications, the associated odds of successful completion increased by 70% in 1 diabetes drug group (95% CI: 9,61%, p=0.02) at 3 years when compared to the no drug group.

Table 3-25: Unadjusted models of successful completion in the medium-term (5% weight loss short-term & 3% weight loss medium-term), 95% confidence intervals and p-values for each independent variable. (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Ethnicity				
White British/Scottish	1076	**Reference**		
Any other	61	0.31	0.09-0.99	0.05
Clinical:				
% weight change Session2 - Session1, per %	1152	0.49	0.42-0.60	< 0.001
% weight change Session3 - Session1, per %	1152	0.43	0.40-0.49	< 0.001
% weight change Session3 – Session2, per %	1152	0.50	0.40-0.53	< 0.001
Session3 - Session1 weight change categories				
Weight gaining	162	**Reference**		
No change	252	0.14	0.03-0.64	0.01
Weight losing	738	4.41	2.20-8.84	< 0.001
Medications				
Weight loss	312	**Reference**		
Mixed	464	0.50	0.33-0.74	< 0.001
Weight gaining	69	0.94	0.50-1.82	0.85
No drug	307	0.60	0.36-0.86	< 0.001
Number of diabetes medications				
0	307	**Reference**		
1	356	1.70	1.09-2.61	0.02
2	337	1.04	0.65-1.67	0.90
3	136	0.80	0.40-1.50	0.45
4	16	2.43	0.75-7.94	0.14
% weight change Session9 - Session1, per %	1152	0.40	0.35-0.46	< 0.001

Abbreviation: N(n), number of risks (number of events).
Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **3% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

3.3.4.11 Risk factors for successful completion after adjustment (5% weight loss short-term & 3% weight loss medium-term)

In the multivariable model's ethnicity, early weight loss (change between session 2 and session 1, change between session 3 and session 2, Session3 - Session1 weight change categories) and the number of diabetes medications were omitted from the final model due to lack of association.

Table 3-26 shows the retained risk factors for successful completion when compared to non-completion and unsuccessful completion. It includes the continuous variable of change in weight between session 3 and session 1 and the categorical variable of diabetes medications. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 3 and session 1. Using this model, the AUC-ROC is 0.820 and CI is 0.782,0.857 (Figure 3-10).

Table 3-26: An adjusted model of successful completion in the medium-term (5% weight loss short-term & 3% weight loss medium-term), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change Session3 - Session1, per %	0.43	0.37-0.49	< 0.001
Medications			
Weight loss	**Reference**		
Mixed	0.60	0.36-0.90	0.01
Weight gaining	1.50	0.70-3.09	0.32
No drug	0.60	0.40-0.98	0.04

Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **3% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
The number of risks is 1152.

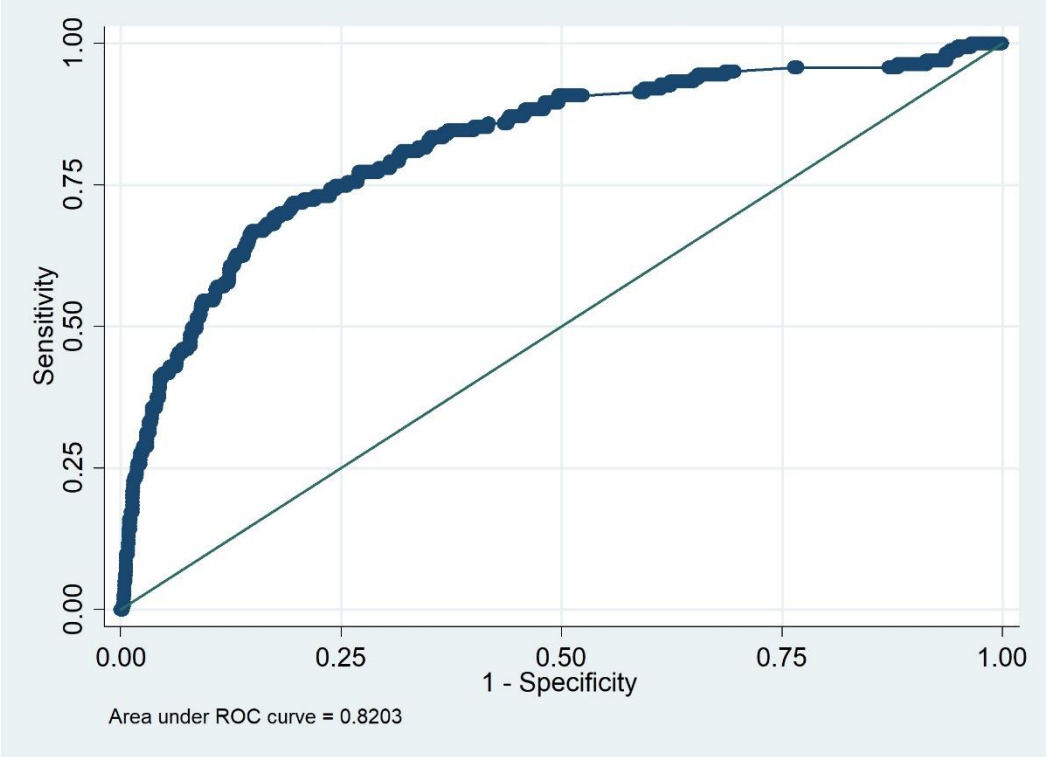

Figure 3-10: ROC curve for successful completion in the medium term (5% weight loss short-term & 3% weight loss medium-term).

3.3.4.12 Risk factors for successful completion after adjustment (5% weight loss short-term & 3% weight loss medium-term) - 16 / 9 fortnightly sessions in GCWMS weight change

Table 3-27 shows the retained risk factors for successful completion when compared to non-completion and unsuccessful completion. It includes the continuous variable of change in weight between session 9 and session 1 and the categorical variable of diabetes medications. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 9 and session 1. Using this model, the AUC-ROC is 0.972 and CI is 0.964,0.981 (Figure 3-11).

Table 3-27: An adjusted model of successful completion in the medium-term (5% weight loss short-term & 3% weight loss medium-term) using 16 / 9 fortnightly sessions in GCWMS weight change, 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change ≈4months - initial, per %	0.41	0.36-0.46	< 0.001
Medications			
Weight loss	**Reference**		
Mixed	0.71	0.40-1.30	0.27
Weight gaining	2.00	0.66-5.92	0.22
No drug	0.72	0.40-1.40	0.33

Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **3% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
The number of risks is 1152.

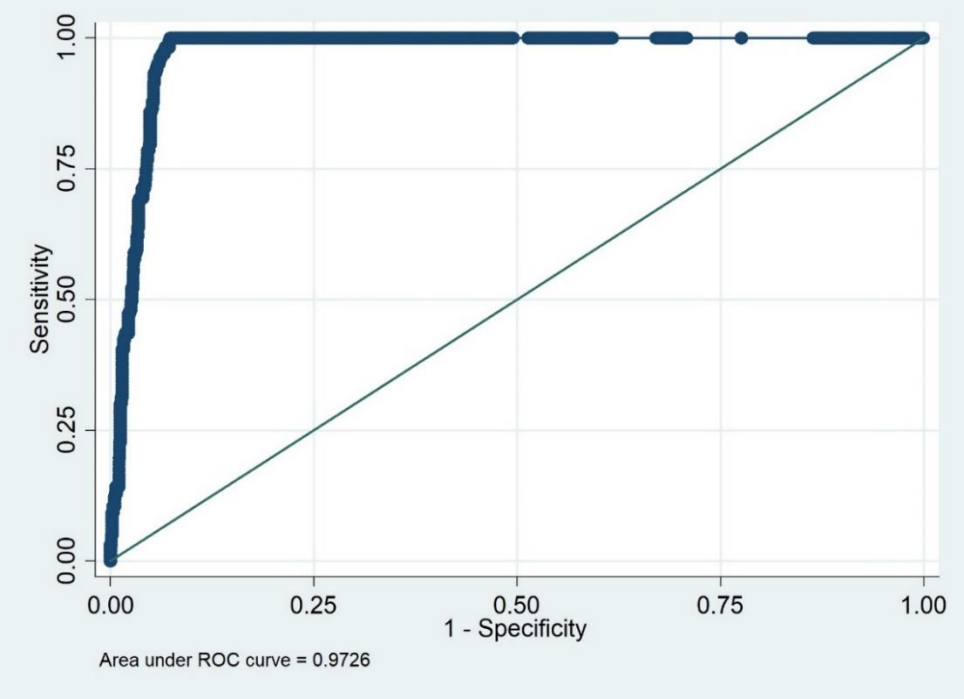

Figure -3-11: ROC curve for successful completion in the medium term (5% weight loss short-term & 3% weight loss medium-term) using 16 / 9 fortnightly sessions in GCWMS weight change.

3.3.4.13 Descriptive statistics by short and medium-term outcome success (5% weight loss short-term & 5% weight loss medium-term)

Table 3-28 shows the baseline characteristics of the successful completers versus non-completers & unsuccessful completers (based on the outcome of attending ≥ 7 sessions in phase 1 & achieving 5% weight loss at the end of the 16 / 9 fortnightly sessions & achieving 5% weight loss at 3 years). From demographic data, successful completers were less than a year older than the unsuccessful completers. In ethnicity, the white British/Scottish is the dominant group in all comparable groups, although successful completers are most likely to be white. Successful completers had a slightly shorter duration of T2DM at baseline than unsuccessful completers (0.4 years shorter). Successful completers were almost 2 kg lighter than the unsuccessful completers. Successful completers had around 0.8 kg/m^2 lower BMI than the unsuccessful completers. Successful completers were mostly from the 35 – 39 BMI category.

The percent weight change between all 3 first sessions was higher among successful completers. Successful completers lost more weight in the early weight loss sessions (e.g. session 3 versus session 1). Successful completers lost 1.74% more weight than unsuccessful completers.

There was a trend that successful completers were more likely to be on a weight loss type of diabetes drugs (n=51, 36.7%) and to be on at least 1 type of T2DM drugs (n=56, 40.3%).

Both comparison groups tended to attend the first three sessions of the 16 / 9 fortnightly sessions in GCWMS (both >95%).

Table 3-28: Characteristics of participants, showing the comparison between the non-completers & unsuccessful completers versus the successful completers (5% weight loss short-term & 5% weight loss medium-term).

Variable	Non-completers & Unsuccessful completers (n=1013)	Successful completers (n=139)	p-value
Demographic:			
Age, years	57.8 ± 9.23	58.5 ± 8.62	0.39
Age categories, n (%)			0.60
30-39.9	34 (3.4%)	3 (2.2%)	
40-49.9	186 (18.4%)	22 (15.8%)	
50-59.9	355 (35.0%)	57 (41.0%)	
60-69.9	345 (34.1%)	47 (33.8%)	
≥70	93 (9.2%)	10 (7.2%)	
Sex, n (%)			0.20
Female	606 (59.8%)	91 (65.5%)	
Male	407 (40.2%)	48 (34.5%)	
SIMD scores, n (%)			0.53
Q1 Most deprived	410 (40.7%)	50 (36.0%)	
Q2	181 (18.0%)	24 (17.3%)	
Q3	160 (15.9%)	25 (18.0%)	
Q4	123 (12.2%)	15 (10.8%)	
Q5 Least deprived	134 (13.3%)	25 (18.0%)	
Ethnicity, n (%)			0.10
White British/Scottish	944 (94.2%)	132 (97.8%)	
Any other	58 (5.8%)	3 (2.2%)	
Clinical:			
Duration of T2DM, years	5.42 (2.32 - 9.65)	5.02 (2.42 - 8.52)	0.67
Initial weight, kg	113 ± 22.3	111 ± 23.6	0.47
Initial BMI, kg/m^2	40.3 (36.2 - 44.6)	39.5 (35.1 - 45.3)	0.81
Initial BMI categories, n (%)			0.01
30 – 34	147 (14.5%)	19 (13.7%)	
35 – 39	278 (27.4%)	49 (35.3%)	
40 – 49	474 (46.8%)	47 (33.8%)	
≥ 50	114 (11.3%)	24 (17.3%)	
HbA1c, mmol/mol	56 (49 - 70)	56 (48 – 66)	0.70

Systolic blood pressure, mmHg	133 ± 14.4	136 ± 12.7	0.11
Diastolic blood pressure, mmHg	78 ± 9.83	78 ± 10.1	0.89
Total cholesterol, mmol/L	4.36 ± 1.06	4.36 ± 0.94	0.99
Triglycerides, mmol/L	1.9 (1.3 - 2.8)	1.9 (1.3 - 2.7)	0.82
HDL cholesterol, mmol/L	1.12 ± 0.31	1.14 ± 0.27	0.60
LDL cholesterol, mmol/L	2.25 ± 0.88	2.20 ± 0.78	0.64
% weight change Session2 - Session1	- 0.44 ± 1.17	- 1.36 ± 1.22	< 0.001
% weight change Session3 - Session1	- 0.77 ± 1.42	- 2.51 ± 1.49	< 0.001
% weight change Session3 – Session2	- 0.32 ± 0.85	- 1.14 ± 1.18	< 0.001
% weight change: Session3 - Session1 categories, n (%)			< 0.001
Weight losing	608 (60.0%)	130 (93.5%)	
Weight gaining	155 (15.3%)	7 (5.0%)	
No change	250 (24.7%)	2 (1.4%)	
% weight change Session9 - Session1	- 1.64 ± 2.64	- 7.60 ± 2.60	< 0.001
Medications, n (%)			0.02
Weight loss	261 (25.8%)	51 (36.7%)	
Mixed	418 (41.3%)	46 (33.1%)	
Weight gaining	58 (5.7%)	11 (7.9%)	
No drug	276 (27.2%)	31 (22.3%)	
Number of diabetes medications, n (%)			0.10
0	276 (27.2%)	31 (22.3%)	
1	300 (29.6%)	56 (40.3%)	
2	300 (29.6%)	37 (26.6%)	
3	124 (12.2%)	12 (8.6%)	
4	13 (1.3%)	3 (2.2%)	
Any insulin, n (%)			0.86
Yes	92 (9.1%)	12 (8.6%)	

No	921 (90.9%)	127 (91.4%)	
Process:			
Attendance, n (%)			0.19
One session	8 (0.8%)	0 (0.0%)	
Two sessions	29 (2.9%)	1 (0.7%)	
Three sessions	976 (96.3%)	138 (99.3%)	
Attendance, n (%)			0.10
Three sessions	976 (96.3%)	138 (99.3%)	
Other	37 (3.7%)	1 (0.7%)	

Abbreviations: SIMD, Scottish Index of Multiple Deprivation; T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **5% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

3.3.4.14 Univariable risk factors for successful completion (5% weight loss short-term & 5% weight loss medium-term)

Univariable logistic regression models were initially explored to identify exposures associated with successful completion, using those who did not complete the programme or complete the programme and did not successfully lose weight as the reference group (Table 3-29). All predictor variables were tested and the ones that did not show an association with the outcome of interest were omitted from the table.

Early change in weight between weight loss sessions was the strongest predictor among all presented independent variables. Specifically, more weight loss between session 3 and session 1 was the strongest predictor of successful medium-term weight loss at the 3 years. This means that for every 1% weight gain between session 3 and session 1, the associated odds of successful completion decreased by 55% (95% CI: 61, 48%, p<0.001). In the categorical model for change in weight between session 3 and session 1, the weight losing group (OR: 4.73, 95% CI: 2.17,10.3, p<0.001) was almost 5 times higher in being successful at losing weight at 3 years when compared to weight gaining group.

Being in a mixed type of drugs was associated with decreased the odds of successful completion by 44% (95% CI: -63, -10%, p=0.01) when compared to weight loss drugs. Being in none of the diabetes drugs was associated with decreased the odds of successful completion by 43% (95% CI: -64, -7%, p=0.01) when compared to weight loss drugs. Being on 1 type of diabetes drug was associated with increased the odds of successful completion by 66% (95% CI: 4,65%, p=0.03).

Table 3-29: Unadjusted models of successful completion in the medium-term (5% weight loss short-term & 5% weight loss medium-term), 95% confidence intervals and p-values for each independent variable. (predictor variables that did not show an association (p>0.05) with the outcome of interest were omitted from the table).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Clinical:				
% weight change Session2 - Session1, per %	1152	0.50	0.43-0.60	< 0.001
% weight change Session3 - Session1, per %	1152	0.45	0.39-0.52	< 0.001
% weight change Session3 – Session2, per %	1152	0.47	0.40-0.56	< 0.001
Session3 - Session1% weight change categories				
Weight gaining	738	**Reference**		
No change	162	0.18	0.04-0.90	0.03
Weight losing	252	4.73	2.17-10.3	< 0.001
Medications				
Weight loss	312	**Reference**		
Mixed	464	0.56	0.37-0.90	0.01
Weight gaining	69	0.97	0.50-1.97	0.93
No drug	307	0.57	0.36-0.93	0.02
Number of diabetes medications				
0	307	**Reference**		
1	356	1.66	1.04-2.65	0.03
2	337	1.10	0.70-1.82	0.72
3	136	0.90	0.43-1.73	0.70
4	16	2.10	0.60-7.61	0.30
% weight change Session9 - Session1, per %	1152	0.50	0.45-0.55	0.00

Abbreviation: N(n), number of risks (number of events).
Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **5% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

3.3.4.15 Risk factors for successful completion success after adjustment (5% weight loss short-term & 5% weight loss medium-term)

In the multivariable models, early weight loss (change between session 2 and session 1, change between session 3 and session 2, Session3 - Session1 weight change categories) and the number of diabetes medications were omitted from the final model due to lack of association.

Table 3-30 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes the continuous variable of change in weight between session 3 and session 1 and diabetes medications. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 3 and session 1. Using this model, the AUC-ROC is 0.816 and CI is 0.775,0.856 (Figure 3-12).

Table 3-30: An adjusted model of successful completion in the medium-term (5% weight loss short-term & 5% weight loss medium-term), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change Session3 - Session1, per %	0.45	0.39-0.52	< 0.001
Medications			
Weight loss	**Reference**		
Mixed	0.70	0.41-1.06	0.09
Weight gaining	1.50	0.70-3.30	0.32
No drug	0.63	0.40-1.10	0.10

Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **5% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

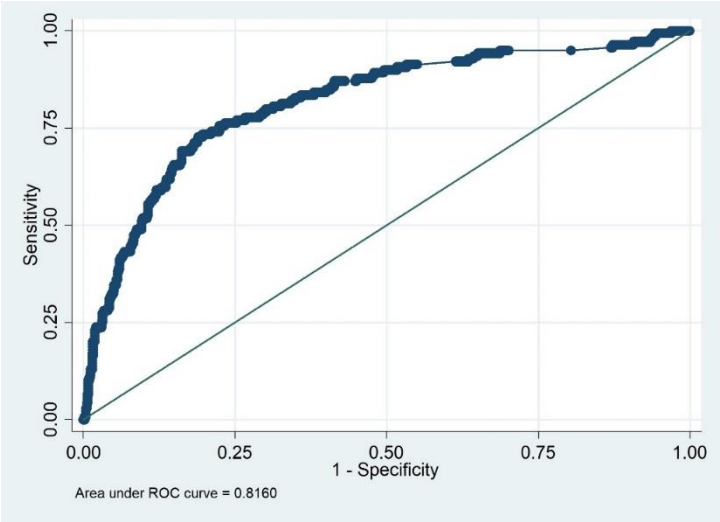

Figure 3-12: ROC curve for successful completion in the medium term (5% weight loss short-term & 5% weight loss medium-term).

3.3.4.16 Risk factors for successful completion after adjustment (5% weight loss short-term & 5% weight loss medium-term) - 16 / 9 fortnightly sessions in GCWMS weight change

Table 3-31 shows the retained risk factors for successful completion when compared to unsuccessful completion. It includes the continuous variable of change in weight between session 9 and session 1 and diabetes medications. Even though the only risk factor that was truly associated with successful weight loss at 3 years was the weight change between session 9 and session 1. Using this model, the AUC-ROC is 0.960 and CI is 0.950,0.970 (Figure 3-13).

Table 3-31: An adjusted model of successful completion in the medium-term (5% weight loss short-term & 5% weight loss medium-term) using 16 / 9 fortnightly sessions in GCWMS weight change, 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change ≈4months - initial, per %	0.50	0.45-0.56	< 0.001
Medications			
Weight loss	**Reference**		
Mixed	0.88	0.50-1.60	0.70
Weight gaining	1.80	0.65-4.90	0.26
No drug	0.80	0.42-1.52	0.50

Criteria for success: attend ≥ 7 sessions in the 16 / 9 fortnightly sessions in GCWMS + achieve 5 % weight loss at the end of the sessions + achieve **5% weight loss** at 3 years.
Outcome variable: non-completers & unsuccessful completers versus successful completers.

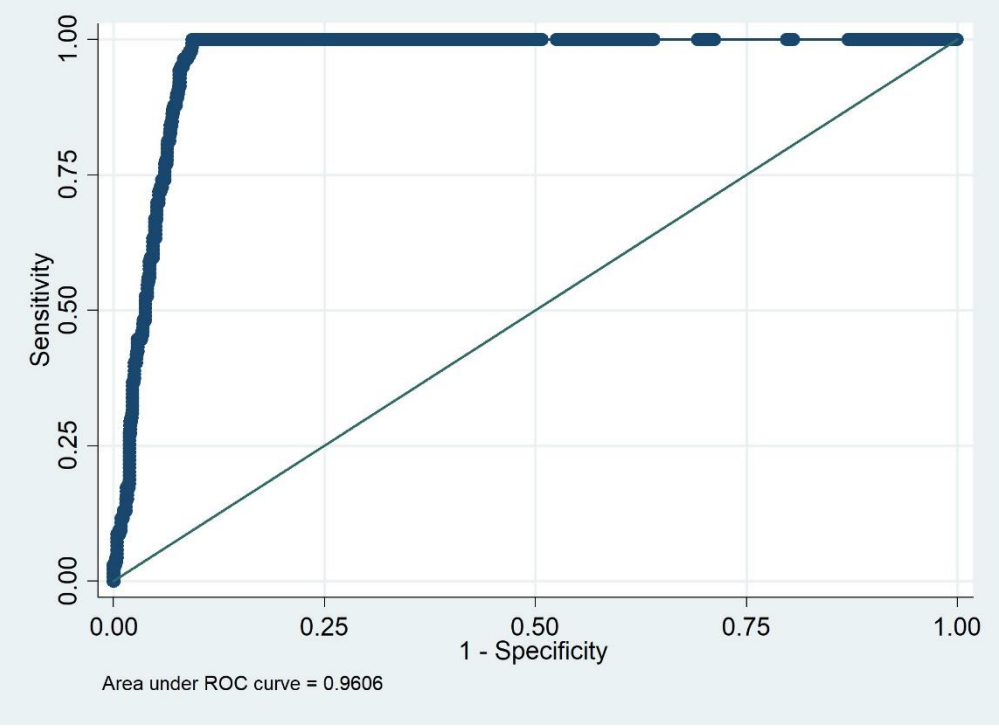

Figure 3-13: ROC curve for successful completion in the medium term (5% weight loss short-term & 5% weight loss medium-term) using 16 / 9 fortnightly sessions in GCWMS weight change.

3.3.5 Thresholds for decision making in using the descriptive model (medium-term)

Table 3-32 describes the discrimination early weight change has in predicting who will complete and successfully achieve the required weight loss at 3 years.

The >0.5% threshold maximises sensitivity for allowing the patients to continue treatment. In contrast, 2.5% maximises specificity, while still maintaining some sensitivity (52.5%).

Table 3-32: Sensitivity and specificity using a weight loss threshold based on a change in weight between session 3 and session 1 in the 16 / 9 fortnightly sessions in GCWMS to predict weight loss at 3 years (5% weight loss short-term & 5% weight loss medium-term).

Weight loss threshold	Sensitivity	Specificity	PPV	NPV
≤0.5	10.1% (5.6%-16.3%)	50.5% (47.4%-53.7%)	2.7% (1.5%-4.5%)	80.4% (77.1%-83.4%)
≥0.5	89.9% (83.7%-94.4%)	49.5% (46.3%-52.6%)	19.6% (16.6%-22.9.0%)	97.3% (95.5%-98.5%)
≥1	85.6% (78.7%-91.0%)	61.1% (58.0%-64.1%)	23.2% (19.6%-27.1%)	96.9% (95.2%-98.1%)
≥1.5	77.0% (69.1%-83.7%)	73.0% (70.1-75.7%)	28.1% (23.6%-32.9%)	95.8% (94.2%-97.1%
≥2	66.2% (57.7%-74.0%)	82.4% (79.9%-84.7%)	34.1% (28.4%-40.1%)	94.7% (93.0%-96.1%)
≥2.5	52.5% (43.9%-61.0%)	89.5% (87.5%-91.4%)	40.8% (33.5%-48.4%)	93.2% (91.5-94.7%)
≥3	37.4% (29.4%-46.0%)	93.8% (92.1%-95.2%)	45.2% (35.9%-54.8%)	91.6% (89.8%-93.2%)
≥3.5	23.7% (16.9%-31.7%)	97.0% (95.8%-98.0%)	52.4% (39.4%-65.1%)	90.3% (88.3%-92.0%)
≥4	15.1% (9.6%-22.2%)	98.7% (97.8%-99.3%)	61.8% (43.6%-77.8%)	89.4% (87.5%-91.2%)

Abbreviation: PPV, Positive predictive value; NPV, negative predictive value.
Outcome variable: non-completers & unsuccessful completers versus successful completers.
The ≤0.5% threshold includes zero change and weight gaining participants.

3.4 Discussion

This longitudinal cohort study was done to investigate patient factors (e.g. clinical, sociodemographic) and process factors predictive of successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes, specifically GCWMS.

The results of this study showed that the only variable among all tested variables associated with short-term successful completion was weight change in the first 3 sessions. This was seen when testing the successful completion model (successful completion compared to non-completion and unsuccessful completion) and the sensitivity analysis model (successful completion compared to unsuccessful completion), although the successful completion model was stronger (each 1% weight loss OR 2.86 (95%CI 2.5-3.23)) and the AUROC curve for the model was 0.839 (95%CI 0.812-0.866). Losing at least 0.5% weight in the first 3 sessions predicted successful short-term completion with a sensitivity of 90.4% and specificity of 53.6% (negative predictive value of 95.7%). From the literature, the early weight loss within a few weeks from starting the weight management programme (despite the protocol used in the programme) was associated with participants completing the programme and being successful at losing weight (Elfhag and Rossner 2010; Jessica Unick et al. 2015; Garvin, Hardy, and Xu 2016). This was also confirmed in this study. Among all tested predictor variables, early weight change (i.e. weight loss) in the programme was the most important predictor variable for the prediction of successful weight loss.

Perhaps surprisingly, the only independent predictor of medium terms weight loss was also weight change in the first three sessions (each 1% weight loss OR 2.22 (95%CI 1.92-2.56)) and the AUROC curve for the model was 0.816 (95%CI 0.775-0.856). Losing at least 0.5% of weight in the first 3 sessions predicted successful medium-term weight loss success with a sensitivity of 89.9% and specificity of 49.5% (negative predictive value of 97.3%). Extending the early weight change period to ≈ 4months was strongly associated with and predictive of medium-term successful completion (each 1% weight loss OR 2.00 (95%CI 1.80-2.22)) and the AUROC curve for the model was 0.960 (95%CI 0.950-0.970).

It is important to consider why early weight loss in the programme is associated with both short and medium term outcomes, particularly given that other data have reported similar findings. 1) Early weight loss is a subset of the outcome of interest (overall weight loss), which can be used as a predictor of short and medium term successful weight loss (James et al. 2018). 2) In Social Cognitive Theory, one of the important elements and a deriver of successful weight loss is self-efficacy (Y. Wang et al. 2017). Some studies found that's self-efficacy is associated with successful weight loss (Jennifer Linde et al. 2006). Physical activity self-efficacy (4 weeks) was associated with 8-week weight change (Nezami et al. 2017). Improvement of early weight loss self-efficacy was associated with 6 and 12 months 5% weight loss (Hays et al. 2014). Therefore, early weight loss is a marker of self-efficacy. 3) Early weight loss is likely to be greatest in those with the highest baseline BMI. Higher BMI is associated with an increased number of intentional weight loss attempts and the greater total amount of intentional weight loss (Raynor et al. 2008).

It is perhaps surprising that none of the other risk factors was associated with outcomes in multivariable models. In chapter 2, there were 8 studies out of 46 that showed an association between demographic, sociodemographic status and weight loss, but this was not confirmed in this chapter. On the other hand, chapter 2 highlighted the influence of weight measurements (e.g early weight loss etc.) on weight loss and this was confirmed in this study and other studies found in the literature. A previous longitudinal cohort study of 247 patients attending an obesity specialist clinic tested the correlation between weight-related & psychological factors and three different weight loss phases: pre-treatment (unintentional weight loss after screening visit), 5 weeks of education (weight loss after education) and 12 months of group treatment (weight loss after receiving weight loss treatment) (Elfhag and Rossner 2010). Initial BMI was associated with 5 weeks % weight loss ($r= 0.17$, $p<0.05$). Pre-treatment % weight loss after screening visit ($r= 0.22$, $p<0.05$) and 5 weeks % weight loss ($r= 0.46$, $p<0.001$) were associated with 12 months % weight loss (Elfhag and Rossner 2010). This was consistent with the short and medium-term findings of this study, where early weight loss (within the first 3 sessions or 9 sessions of the programme) were the most important predictor of successful weight loss. The new findings of this study add to the existing literature that a stronger statistical method (prediction

models) was used to identify the relationship between clinical, sociodemographic and process factors and short and medium-term successful weight loss.

It is difficult to assess how comparable our data are with other Weight Watchers programmes. In deriving this cohort, non-attenders group were excluded (this includes those who were referred) and who comprised 55.4% of referrals. The efficiency of Weight Watchers was assessed in a multicentre RCT with a parallel design by comparing commercial weight loss programmes (i.e. Weight Watchers) and standard care in a primary healthcare setting in Australia, Germany, and the UK (Jebb et al. 2011). Participants were randomised to receive either 12 months of standard care (n= 395), or 12 months of Weight Watchers (n= 377) and followed up for 12 months. Of the 772 participants, 328 (42%) dropped out of the trial at 12 months. The completion rate at the final assessment was higher among the Weight Watchers group (n= 230, 61%) than the standard group (n= 214, 54%), although the difference was not significant (p=0·06). The attrition rate differed between countries with the UK being the highest (n= 150, 64%) when compared to Australia (n= 111, 41%) and Germany (n= 67, 25%). This difference was statistically highly significant (p<0·0001). In this study, the drop-out rate was anticipated and was consistent with other weight management programme trials for people who live with overweight or obesity. Therefore the high non-attendance rate at least is comparable with other data. These analyses focus on those who do choose to attend.

Several research studies have explored and suggested different factors associated with success in losing weight. An observational study showed that on average men lost (1.5kg, 3kg, 5kg) more than the woman (during a 12-week intervention, from assessment to 6 months, from assessment to 12 months, respectively) (Bhogal and Langford 2014b). This was interpreted as being due to men having a higher average weight when compared to women at the beginning of the study. In a longitudinal study, risk factors of weight loss were female (ß= 0.12, p=0.01), BMI (ß= -0.17, p=0.01), self-concordance (ß= -0.12, p=0.01), weight goal (ß= -0.14, p=0.03) (De Vet et al. 2012). Results showed that sex and BMI at baseline are significant risk factors for weight change at follow-up. In this study, regardless of which factor was included in the final model in both the short and medium term, the only

important factor that predicts successful weight loss is early weight loss in the programme.

The sensitivity and specificity tables using the early weight loss threshold for short and medium-term weight loss presented in the results section can be used as a clinical reference. The required threshold can be selected based on the treatment goal to estimate the final results of the treatment. In the medium-term, a threshold of ≥ 0.5% weight loss in the first 3 sessions means that approximately 90% of the participants are going to be successful at losing ≥ 5% of body weight in 3 years, while approximately 50% of the participants will fail to lose ≥ 5% of body weight at 3 years. In this case, more support strategies or alternative interventions are required to assist half of the participants to lose the required weight. On the other hand, a threshold of ≥ 2.5% weight loss in the first 3 sessions means that 52.2% of the participants are going to be successful at losing ≥ 5% of body weight at 3 years, while approximately 90% of the participants will fail to lose ≥ 5% of body weight at 3 years. Using this threshold people are more likely to succeed in the programme and lose ≥ 5% of body weight in 3 years, but more support strategies or alternative interventions are required to assist a larger number of people.

3.4.1 Strengths of the study

While a comprehensive assessment of clinical sociodemographic and process factors associated with success in patients attending the behavioural weight management programme is rarely found in the literature. Most of these factors were thoroughly investigated in this study by testing associations univariably and multivariably. To the best of our knowledge, the addition of thresholds for predictive models is novel and a potentially useful clinical tool.

Moreover, the analysis of this study was done on real-world data. This means that it is a good representative clinical sample and can provide the most benefit for both clinicians and patients (because this can represent the reality of patients' journey, shows how the treatment effect patients' success and allows greater identification of who is going to benefit from the treatment).

As weekly participants' weight is missing in most weight loss programmes, the dataset used in this study provides a patient's week-to-week weight after starting the first weight management session, which allows the calculation of the accurate change in weight early in the programme.

A non-completers group (including those who attended but did not complete) were included in the referent group, while other studies consider only those who complete the programme. Our predictive model is therefore relevant to clinicians who wish to identify those who will not complete or will not be successful, rather than exclusively the latter.

3.4.2 Limitations of the study

This is an observational study and any associations cannot be taken as evidence of causality, but are investigated primarily for predictive models. Loss to follow-up (i.e. patients drop out from the programme), and some limited missingness of weight data at baseline were present. Two methods were used to obtain complete weight measurements.

Missing values are recognised in predictor variables and the outcome of interest. To overcome this limitation, missing values were retained and reported for variables that are not considered a primary outcome in the study, which helps in preserving power.

The study may not be generalizable to all weight loss interventions, or indeed of this weight loss intervention to other populations. The findings, therefore, require validation.

3.5 Conclusion

Investigating predictors of weight loss success before people start the weight management programme would allow factors to be highlighted which are impacting them at the time of treatment. Understanding how those factors influence the weight loss experience will enable behavioural interventions to be adapted in real-time. In this study, the strongest predictor of successful weight loss was early in programme weight loss, both for short (in-programme) and

medium-term (3 year) weight loss. At a threshold of 0.5% weight loss, we report that 16 weeks (sensitivity 90.4%, specificity 53.6%, PPV 32.9%, NPV 95.7%) and 3 years (sensitivity 89.9%, specificity 49.5%, PPV 19.6%, NPV 97.3%). Although simple this model may allow early identification of those least likely to benefit from continued participation in the programme. Although no other risk factors were reported to be strongly associated with weight loss, further studies of baseline behavioural and psychosocial factors in predicting weight loss success at end of the programme are needed. This will be done in the following chapter.

4 Development of a predictive model for medium-term weight loss in people with type 2 diabetes - LookAHEAD randomised controlled trial

4.1 Introduction

The previous chapter explored demographic, clinical and process factors associated with intentional weight loss, and the only important predictor was early weight change in the programme. As reported from chapter 2, there is a dearth of strongly predictive factors obtained from the literature review. There is therefore a need to explore other dimensions of weight loss.

There is a strong association between prevalent psychological problems and having overweight/obesity. There is some potential for causality and reverse causality in this context. In one direction, obesity influences mood, self-esteem, quality of life, anxiety level, eating habits and body image which all can create emotional distress. This can result in two scenarios either the patient is hindered from seeking intervention or in case the patient undertook the treatment they will be unsuccessful (i.e. fail to lose the required amount of weight or attrition from the programme) (Sarwer and Polonsky 2016). Psychological and behavioural factors were commonly reported as having a relationship with programme attrition, which is an essential reason for being unsuccessful in a weight management programme (Moroshko, Brennan, and O'Brien 2011b). On the other direction, improvements in overall well-being, depression, anxiety, self-control, and vitality were seen following the weight loss associated with cognitive–behavioural weight-loss interventions (Swencionis et al. 2013a).

Evidence reported in the literature regarding the relationship between psychological factors and successful weight loss is inconsistent and generally based on older small studies that use outdated weight-loss interventions such as diet without behavioural change treatment. Psychological aspects such as motivation (Teixeira et al. 2012a), readiness to change (Dixon et al. 2009; Teixeira et al. 2012a), locus of control (Adolfsson et al. 2005; Holt, Clark, and Kreuter 2001; Bryan and Tiggemann 2001; Nir and Neumann 1995), and empowerment (Struzzo et al. 2013) were observed to be a moderator for participants response to weight loss treatment. While self-efficacy in some studies was reported to be positively associated with the achievement of the required weight loss (McKee and Ntoumanis 2014b; Delahanty et al. 2013a), one study was reported to be negatively associated with the achievement of the required weight loss (Alharbi et al. 2016), others did not influence weight loss (Vinkers et al. 2014).

Regardless of the importance of the psychological factors in obesity-related treatment, there is a paucity of studies exploring the relationship between psychological factors and participants' response to treatment (Cargill et al. 1999; Dalle Grave et al. 2009; Presnell et al. 2008; JA Linde et al. 2004). Since the aim is to target weight loss interventions at those in whom they are most likely to succeed, it is important to better understand how psychological factors influence weight loss success.

To gain a more complete understanding of predictors of weight loss success previous work (chapter 3) must be combined with more structured systematic data collection, including psychosocial factors, such as that collected in randomised control trial (RCT) data. Look Action for HEalth in Diabetes (LookAHEAD) is the RCT used in this study to complement and expand on findings from chapter 3. As discussed, (chapter 1) this data is a replacement for the COVID-19 disrupted prospective POWER study. This study aimed to assess and understand the relationship between psychological factors and intentional weight loss from a weight management programme. This will clarify the inconsistency seen in the literature, which may be useful to develop a new perspective to be applied in the clinic.

4.1.1 Action for HEalth in Diabetes (LookAHEAD) trial

The LookAHEAD is a randomised control trial done in people with overweight/obesity and T2DM (dataset available to all researchers). Two groups were compared, 1) Intensive Lifestyle Intervention (ILI): which involved induced calorie deficit and increased physical activity levels for intentional weight loss (to achieve a long-lasting weight loss of at least 7%). 2) The control group: Diabetes Support and Education (DES). The primary goal of the comparison in the trial was to examine whether cardiovascular morbidity and mortality are improved (i.e. reduction in serious cardiovascular events incidence) following weight loss in ILI. Originally, the study was powered on at least 80% statistical power to detect an 18% difference in cardiovascular events among the two compared groups. This was done over a follow-up period of 10.5 years.

4.1.2 Current study hypothesis

Behavioural factors (e.g. psychological factors, physical activity, eating habits, self-efficacy) and sociodemographic factors, are associated with and predictive of successful weight loss at 4 years in the context of an Intensive Lifestyle Intervention trial (i.e. medium-term).

4.1.3 Current study aims

1) To identify patient-reported behavioural factors (e.g. psychological, physical activity, eating habits, self-efficacy) and sociodemographic factors that are associated with successful medium-term weight loss in individuals participating in an intensive lifestyle intervention trial.

2) To identify patient-reported behavioural factors (e.g. psychological, physical activity, eating habits, self-efficacy) and sociodemographic factors that will predict successful medium-term weight loss in individuals undertaking intensive lifestyle intervention programmes.

4.2 Methods

The LookAHEAD study design and protocol are presented in detail elsewhere (The Look AHEAD Research Group 2003), (LookAHEAD Protocol Review Committee 2012).

4.2.1 Study population

Men and women who have overweight or obesity and have Type 2 Diabetes Mellitus (T2DM) volunteered to participate in the LookAHEAD clinical trial (n= 5000 volunteers exactly). Participants were between the age of 45 and 75 years. Participants had a body mass index (BMI) of ≥27 kg/m^2, if the participants undertaking insulin BMI of ≥25 kg/m^2 was considered. They were recruited from sixteen clinical centres in the United States of America (USA). Informed consent was provided to all potential participants. Informed consent was obtained from each participant before starting screening procedures. Each clinic recruits its participants independently and should follow the requirement of its Institutional Review Board (whether to have single consent for the whole study or staged consent).

As part of inclusion criteria, the participants self-reported their T2MD status, and then the study group verified the status (via reviewing medical records, current treatment of T2DM, personal health care provider verification, or measuring fasting glucose ≥126 mg/dL, or casual or 2-hour plasma glucose ≥200 mg/dL measurements).

4.2.2 Design

A two-armed randomised, controlled clinical trial, here used as a cohort study with randomised intervention as a covariate of interest.

4.2.3 Intervention

Recruitment of participants took place over 2.5 years between January 2001 and April 2004. An educational session about diabetes management was provided for all participants recruited at the end of the screening period. Then, participants were assigned and randomized to either of the study arms. The lookAHEAD trial

had four main phases, **phase I:** year 1 after randomization; **phase II:** years 2-4 after randomization; **phase III:** Year 5 and further (i.e. follow-up for the incidence of cardiovascular events); **phase IV:** the termination of Intensive Lifestyle Intervention (September 14, 2012).

4.2.3.1 Diabetes Support and Education (DSE)

The control group of the trial received a Diabetes Support and Education (DSE) programme. The goal of this programme was to retain participants in the study by providing educational/support sessions to answer all their questions. The study group strongly encouraged participants to attend DES sessions, although it was not mandatory. Data collection and safety monitoring for DES participants were done at 6 Months/mid-assessment (via phone) and 12 Months/annual-assessment (scheduled clinic visits) for each phase.

Phase I & Phase II: participants attend 3-group educational/social support sessions per year conducted by a study team who had a background in each discussed topic. The sessions content was as followed: 1) diet/nutrition education; 2) exercise/physical activity education; 3) open discussion session to support participants who are living with diabetes. Educational topics (i.e. exercise and nutrition) varied each year.

Phase III: One educational or social support session annually will continue to be offered beginning with year 5 and beyond. Participants had the option of repeating the 3-group educational/social support sessions provided for Phase II participants.

Phase IV: One educational or social support session annually will continue to be offered as in phase III until the end of the trial.

4.2.3.2 Intensive Lifestyle Intervention (ILI)

Phase I: this is the intervention phase. The main goal was to achieve 7-10% intentional weight loss and to increase weekly physical activity to up to 175 minutes. Over the first six months, participants received 3-group sessions and 1-individualised session (seen 4 times/per month). In the following six months, participants received half the number of sessions (seen 2 times/per month) with the option of getting a more frequent follow-up.

Phase II: this is the maintenance phase. The goal was to keep participants maintaining the achieved weight loss in phase I (i.e. 7-10%) and ≥ 175 minutes/per week of physical activity.

Phase III: The main goal of this phase is the follow-up for the incidence of cardiovascular events (up to 13.5 years). Participants offered one 1-individual and one 1-group on-site session per month. Also, 1-refresher group and 1-national campaign were offered yearly.

Phase IV: Data and Safety Monitoring Board (DSMB) was assigned to review LookAHEAD data and stopped the study for futility after September 14, 2012, as no difference was detected between study arms. Participant's follow-up was continued post-intervention and both study arms received the same post-study care (i.e. general health management education).

4.2.4 Data collection

The LookAHEAD trial had a central study database. In this database, the clinical centres, central laboratory and reading centres collect data and store them in the database.

Schedule of data collection

Baseline data: done before randomisation (i.e. before the start of the intervention), which was during screening visits.
Phase I (Months 1-12): reassessment of most baseline measures at Month 12.
Phase II (Months 13-48): reassessment of most baseline measures at Month 48.
Phase III (Months ≥49): follow-up visits collecting data on the incidence of cardiovascular events.

Follow-up in the LookAHEAD trial, including medical history, the incidence of any cardiovascular disease events and collecting other measures (e.g. quality of life questionnaires), was done during the annual clinical visit. This was started after randomisation until 2014/close-out (i.e. Months 12, 24, etc.).

Progress of study

The NIDDK assigned an independent DSMB to review and evaluate the progress of the LookAHEAD trial and report it at least every year. DSMB members were independent of the study team. Their role was to assess the feasibility of the trial, time of trial termination (depending on significant differences seen between trial groups), and trial continuation based on safety measures taken by the LookAHEAD team.

4.2.5 Exclusion criteria

Exclusion criteria include anything that the recruiting team deems might influence participant adherence to the lifestyle intervention. This includes medical conditions that might not allow the participant to follow study protocol or achieve intervention goals. For instance, exclusions include, hospitalisation for depression and a full list of exclusion criteria can be found in the original study protocol (LookAHEAD Protocol Review Committee 2012).

4.2.6 Access to data

An application to access the dataset from Look AHEAD was developed, along with an analysis plan. Ethical approval waiver from the College Of Medical, Veterinary & Life Sciences at the University of Glasgow was obtained and full access to the dataset was granted by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) central repository on 05/11/2020. https://repository.niddk.nih.gov/studies/look-ahead/

4.2.7 Data handling

Due to the study design (i.e. RCT), the existing dataset had few systematic errors, which limit the need for extra exclusions or predetermined limit values. Regardless data cleaning was done by diagnosing the datasets to detect and edit any faults in the data.

In this study, two variables were identified: predictors and medium-term outcomes. Each one is described thoroughly below.

4.2.7.1 Predictors

In this study, predictor variables were chosen from the list of variables available in the LookAHEAD trial dataset. Those variables were equivalent to predictors identified from the Predictors Of WEight Reduction (POWER) study.

The time window for predictor variables was identified at the baseline visit. This was set to be before the start of the intervention in the LookAHEAD trial.

The demographic variables chosen from the LookAHEAD trial include age, sex, marital status, ethnicity, education and employment. The definition of each variable based on this study was:

- Age (Continuous, years): the age of the participants at the baseline visit.

- Sex: two identities were explored, which are male and female.

- Marital status: a binary variable with two categories was developed married and not married. The married category contains married participants and those who are living in a marriage-like relationship. The not married category contains never-married participants, divorced, widowed and separated.

- Ethnicity: a categorical variable that showed the ethnic group of each participant at the baseline visit. Three categories: white, African American / Black, and any other (e.g. American Indian / Alaskan Native, Native Hawaiian or Pacific Islander, and other).

- Education: a categorical variable that showed the level of education each participant had at the baseline visit. Three categories: higher education (e.g. some college, associate degree/junior college, bachelors degree, some graduate school, master's degree, doctorate, professional "Medical Degree, Juris Doctor Degree, Doctor of Dental Surgery Degree etc"), completed high school (e.g. high school diploma or equivalency "General Educational

Development(GED)") and any other (e.g. less than high school and some vocational school).

- Employment: a categorical variable that showed the employment of the participants at the baseline visit. Four categories: full or part-time job, full or part-time student, homemaker and not employed.

The clinical variables that were chosen from the LookAHEAD trial and their definitions are:

- Duration of T2DM (years): the duration participants had diabetes at the baseline visit (self-reported).

- Age diagnosed with T2DM (years): the age participants were diagnosed with T2DM at the baseline visit.

- Initial weight (kg): measured body weight at the baseline visit by study staff. This was done by calibrated scales and participants were asked to wear light indoor clothing.

- Initial Body Mass Index (BMI, kg/m^2): was calculated at the baseline visit using initial weight and initial height.

- Metabolic syndrome criteria: a categorical variable that showed how many numbers of metabolic syndrome criteria each participant had met at the baseline visit. Five categories: one criterion met, two criteria met, three criteria met, four criteria met and five criteria met.

- Hypertension: a binary variable that showed whether participants were diagnosed as having hypertension or not at baseline visit. Two categories: yes and no.

- Haemoglobin A1C (HbA1c, mmol/mol): the measure of glycated haemoglobin at the baseline visit.

- Systolic blood pressure (SBP, mmHg): the measure of the pressure exerted during heart contractions at the baseline visit.

- Diastolic blood pressure (DBP, mmHg): the measure of the pressure exerted during heart relaxation at the baseline visit.

- Total cholesterol (mmol/L): the total concentration amount of cholesterol in the blood at the baseline visit.

- Triglycerides (mmol/L): the concentration of the triglycerides in the blood at the baseline visit.

- High-Density Lipoprotein (HDL) cholesterol (mmol/L): the concentration of the HDL in the blood at the baseline visit.

- Low-Density Lipoprotein (LDL) cholesterol (mmol/L): the concentration of the LDL in the blood at the baseline visit.

- The number of diabetes medications: how many anti-diabetic drugs were taken by each participant at the baseline visit. Four groups: 0, 1, 2, ≥3.

- Insulin use: a binary variable to identify if the participant was on insulin at the baseline visit. Two categories: yes and no.

The behavioural variables were sub-categorised:

Selecting questions from the sleep apnoea questionnaire, the variables derived were:

- Snore: a categorical variable was derived based on the question “Have you ever snored (now or at any time in the past)?”. Three categories: yes, no, don’t know.

- Breathing: a categorical variable was derived based on the question “Are there times when you stop breathing during your sleep?”. Three categories: yes, no, don’t know.

- Sleepy: a categorical variable was derived based on the question “How often do you feel excessively (overly) sleepy during the day?”. Four categories: Almost always (16-30 days/month), Never or rarely (1 day/month or less), Often (5-15 days/month), Sometimes (2-4 days/month).

- Apnoea: a binary variable was derived based on the question “Have you ever been told by a doctor that you had sleep apnoea?”. Two categories: yes and no.

Selecting questions from the eating habits questionnaire, the variables derived were:

- Eating control: a categorical variable was derived based on the question “When you ate a really big amount of food, did you ever feel that you couldn’t stop eating?”. Three categories: yes, no, prefer not to answer.

- Eat a big amount within a short time (2 hours): a binary variable was derived based on the question “Did you ever eat a really big amount of food within a short time (2 hours or less)?”. Two categories: yes and no.

- Binge eat: a binary variable was derived based on whether participants experienced binge eating or not. Two categories: yes and no.

- Eat big amount (during the past 6 months): a binary variable was derived based on the question “Did you eat a really big amount of food (during the past 6 months)?”. Two categories: yes and no.

- Smoking: a categorical variable was derived based on the participant's smoking status. Three categories: present, past, and never.

- Maximal Metabolic Equivalents (METs): a variable that showed the participant's level of physical activity from the Maximal MET value. 1 MET can be defined as the amount of energy/calories burned or used by the body per minute in the resting state (1 metabolic equivalent = 3.5 ml of oxygen per kg of body weight per minute). As the intensity of the activity increases the level of MET increases.

- Total alcohol (oz/wk): a variable that showed the total alcohol consumption of each participant per week, including beer, wine, and liquor.

- Treatment arm: a binary variable that showed the groups in the LookAHEAD trial. Those groups were Diabetes Support and Education and Intensive Lifestyle Intervention.

The quality-of-life variables that were chosen from the LookAHEAD trial were derived from the Short Form 36 Health Survey Questionnaire (SF-36) (Ware Jr and Gandek 1998). The definitions are described below:

SF-36 quality of life classifications:

1) Thirty-six items: each item was used to score one of the eight SF-36 scales, except for self-reported health transition.

2) Eight scales: Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE) and Mental Health (MH). Each scale might contain 2–10 items.

3) Two summary measures: Physical Component Summary (PCS) and Mental Component Summary (MCS) measures. PCS contains the scales that mostly correlate with, physical components such as PF, RP, BP, and GH. MCS

contains the scales that mostly correlate with a mental component, such as MH, RE, VT and SF.

Scales and summary measures of quality of life:

- Physical function: having the lowest score means that the participant is "very limited in performing all physical activities including bathing or dressing". Having the highest score means that the participant "performs all types of physical activities including the most vigorous without limitations due to health".

- Role physical: having the lowest score means that the participant is having "problems with work or other daily activities as a result of physical health". Having the highest score means that the participant has "no problems with work or other daily activities".

- Bodily pain: having the lowest score means that the participant has "very severe and extremely limiting pain". Having the highest score means that the participant has "no pain or limitations due to pain".

- General health: having the lowest score means that the participant "evaluates personal health as poor and believes it likely to get worse". Having the highest score means that the participant "evaluates personal health as excellent".

- Vitality: having the lowest score means that the participant "feels tired and worn out all of the time". Having the highest score means that the participant "feels full of pep and energy all of the time".

- Social function: having the lowest score means that the participant has "extreme and frequent interference with normal social activities due to physical and emotional problems". Having the highest score means that the participant "performs normal social activities without interference due to physical or emotional problems".

- Role emotion: having the lowest score means that the participant has “problems with work or other daily activities as a result of emotional problems”. Having the highest score means that the participant has “no problems with work or other daily activities”.

- Mental health: having the lowest score means that the participant has “feelings of nervousness and depression all of the time”. Having the highest score means that the participant “feels peaceful, happy, and calm all of the time”.

- Physical component summary: having the lowest score means that the participant has “limitations in self-care, physical, social, and role activities, severe bodily pain, frequent tiredness, health rated (poor)”. Having the highest score means that the participant has “no physical limitations, disabilities, or decrements in wellbeing, high energy level, health rated (excellent)”.

- Mental component summary: having the lowest score means that the participant has “frequent psychological distress, social and role disability due to emotional problems, health rated (poor)”. Having the highest score means that the participant has “frequent positive affect, absence of psychological distress and limitations in usual social/role activities due to emotional problems, health rated (excellent)”.

- Health transition: the self-reported health transition has 5 levels ranging from “much better than one year ago” to “much worse than one year ago”). This item is useful to inform about the average change in the health status of a patient/participants 1 year before undertaking treatment.

The psychological variables included:

Beck Depression Inventory (BDI) (Beck et al. 1961) was used to assess depression symptoms. This questionnaire contains 21-items (each category describes attitudes and symptoms of depression). Each category had 4 to 5

graded statements (from neutral to severe) to allow patients to self-evaluate themselves and each statement had a value ranging from 0 to 3. BDI had a total score of 0–63 (i.e. the higher the BDI score the higher the depression symptoms). Item # 19 from BDI evaluates the participant's recent trial of weight loss. Since LookAHEAD a weight-loss trial and participants were overweight or obesity at entry, this item was excluded for weight stability at baseline (Faulconbridge et al. 2012). Therefore, BDI total scores had changed to 0-60. Scores were interpreted as follows: 1) Minimal/subclinical symptoms (scores of 0–9); 2) Mild symptoms (10–18); 3) Moderate symptoms (19–29); 4) Severe symptoms (≥30).

The symptom-attitude categories are as follows:

#1 Mood, #2 Pessimism, #3 Sense of Failure, #4 Lack of Satisfaction, #5 Guilty Feeling, #6 Sense of Punishment, #7 Self-Hate, #8 Self-Accusations, #9 Self-Punitive wishes, #10 Crying Spells. #11 Irritability, #12 Social Withdrawal, #13 Indecisiveness, #14 Body Image, #15 Work Inhibition, #16 Sleep Disturbance, #17 Fatigability, #18 Loss of Appetite, #19 Weight Loss, #20 Somatic Preoccupation, #21 Loss of Libido.

- Beck score (exclude weight question): a variable that showed the level of depression symptoms if any.

- Beck score (exclude weight question) categories: a categorical variable showed the level of depression symptoms if any. Four categories: minimal, mild, moderate, and severe.

- Beck total score: a categorical variable showed the level of depression symptoms if any (including weight question). Four categories: minimal, mild, moderate, and severe.

- Beck suicide indicator: a categorical variable that represents item #9 from BDI, which evaluate if participants have suicidal thought. Three categories: yes, no, and other.

- Beck severe depression >24 (exclude weight question): a binary variable that showed how many participants from all cohorts have severe symptoms of depression. Two categories: yes and no.

4.2.7.2 Outcome

Medium-term:

The time window for medium-term outcome variables was identified to be 4 years following baseline (i.e. before randomisation/the start of the intervention).

The main outcome is weight change: the amount of weight lost (in percent) at 4 years from baseline weight (i.e. initial weight). This was calculated by subtracting the 4 years weight (depending on available weight) from the baseline weight.

The cut-off point for the successful weight change was set to be 5%. Therefore, two groups were created: 1) Successful completers, those who lost ≥ 5% from the baseline body weight at 4 years. 2) Unsuccessful completers, those who lost < 5% from the baseline body weight at 4 years.

4.2.8 Statistical analysis

The normality of continuous variables was assessed using a normal probability plot and histograms. Descriptive statistics for each predictor variable were tabulated. For continuous variables that are normally distributed, data is presented as Mean ± Standard Deviation (SD). For continuous variables that are not normally distributed, data is presented as Median & Interquartile range (IQR). For categorical variables, frequencies (n) and percentages (%) are presented. Test of association between the predictor variables and the outcome of interest was done by formally testing the null hypothesis of no association. For continuous variables, an independent t-test (for normally distributed data) and a Rank sum test (for skewed data) were used. For categorical variables, the Chi-square test was used.

Binary logistic regression analysis (a simple and multiple regression model) was used to estimate the strength of the association between predictor variables and successful completion. This was done by calculating the measure of association (i.e. odds ratio (OR)) and the statistical significance (i.e. 95% confidence interval

(CI) and p-value). A value of $p \leq 0.05$ was considered a nominally statistically significant difference.

First, simple logistic regression was conducted for each predictor. This was done by using a null/empty model that has only the outcome of interest and adding a single predictor variable at a time to check if it improved the model fit. This technique was used to choose the models because there are many independent variables and using an automated method like stepwise logistic regression might overlook important predictors. For continuous predictor variables, these exposures were added to the model using a natural (untransformed scale). The reference group for binary variables was the "zero" category. The reference group for categorical variables was the most frequent category.

Second, conducting multiple logistic regression modelling for all the accepted predictor variables from simple logistic regression with a successful completion. The model fit was optimised using model selection criteria; i.e. Akaike's Information Criteria (AIC) was improved by at least 5 units (Stone 1977).

Since there were many predictor variables, this procedure was conducted in sequence to choose the final model: 1) Interactions between all predictor variables were tested (no interactions were observed). 2) Interactions between 3 main variables were tested (age, sex, and initial weight) and no interactions were observed. Therefore, a basic prediction model was developed, which contained age, sex and initial weight, and the final model will be developed after adding other predictor variables to the basic prediction model. 3) The AIC measures were obtained for all accepted predictor variables from simple logistic regression. The change in AIC was used to identify which predictor variable would improve the baseline model (at least 5 units change). The predictor variable that changes the most will go first into the basic prediction model. 4) Step 3 was repeated until no change or less than 5 units change in AIC. 5) Interactions were tested between predictor variables within the final model (no interactions were observed).

Area Under the Curve – Receiver Operating Characteristics Curve (AUC-ROC) was used to estimate/predict how each model discriminates the outcome of interest (i.e. successful completion) using the lroc command in STATA.

Handling of missing data:

After minimal data cleaning and recategorization of categorical variables with small numbers in specific groups, the variables with minimally missing data were included. Clinical variables: Total cholesterol (n=10), LDL (n=1), Number of diabetes medications (n=46), Age diagnosed with T2DM (n=36), Duration of T2DM (n=36), SBP (n=46). Behavioural variables: Snore (n=1), Breathing (n=4), Sleepy (n=16), Apnoea (n=2), Eating big amount within a short time (n=12), Binges eat (n=2), Smoking (n=9). Quality of life variables: General health (n=7), Health transition (n=3), Mental component summary (n=7). Due to the small degree of missingness, multiple imputations were not attempted, and we conducted a complete case analysis.

Single imputation:
In the context of this trial, missingness was low (470 missing follow-up weight). To derive missing values Last Observation Carried Forward (LOCF) was used.
In LOCF, whenever there was a missing weight measurement, the value was replaced with the Last observed value.
A value of $p \leq 0.05$ was considered a statistically significant difference in all analyses. We did not adjust for multiple comparisons in this study in order to maximise power for predictor discovery, with a view to validating positive findings in chapter 5. This increases the risk of type 1 error, but thus will be addressed by external validation (Rothman 1990)
STATA-SE software version 15.0 was used in the cleaning & analysis of data.

4.2.9 Power calculation

As an illustrative power calculation, assuming a sample size of 5000 participants from the initial screen of the available data and a successful completion rate of 25% (The Look AHEAD Research Group 2013), an estimation of 87% power was used (at p=0.05) to detect 5% fewer women being successful than men assuming that 55% of the unsuccessful group of women. Generically, 80% power was also used to detect a binary exposure associated with a successful outcome with an odds ratio of 1.25. For the continuous variable baseline BMI, assuming a mean BMI of 35 kg/m^2 and a standard deviation of 5.5, 80% power was there to detect if a 0.5 kg/m^2 increase in baseline BMI was associated with successful weight loss.

4.3 Results

4.3.1 Descriptive statistics

Table 4-1 shows the baseline characteristics of the whole cohort. The mean age of the participants was 58.9 years (SD= 6.74 years) and 58.9% were female (n=2724). Most participants were married (67.9%, n=3169), from a White ethnicity (70.8%, n=3304), completed higher education (74.7%, n=3487), and were in full or part-time jobs (63.0%, n=2940). The baseline clinical variables showed that the patients have been diagnosed with T2DM for a median of 5 years (IQR= 2 – 10). The mean BMI was 36.0 kg/m^2 (SD= 5.85).

General lifestyle characteristics of the cohort (aside from having overweight or obersity) were generally good. Half of the participants had never smoked (49.8%, n=2323), and the total alcohol consumption was generally low (median 0 oz/wk, IQR, 0 - 5). Participants were engaged in generally moderate levels of physical activities, and the mean Max MET was 7.20 (SD= 1.96).

The mean blood pressure was: SBP 129 mmHg (SD= 17 mmHg) and DBP 70 mmHg (SD= 9.5 mmHg) and 84.0% of the participants had hypertension. The lipid profile was as follow mean total cholesterol 4.94 mmol/L (SD= 0.96 mmol/L), median triglycerides 1.74 mmol/L (IQR= 1.22 - 2.50), mean HDL cholesterol 1.12 mmol/L (SD= 0.30 mmol/L) and mean LDL cholesterol 2.90 mmol/L (SD= 0.82 mmol/L).

The majority of the participants were taking at least one of the diabetes medications (39.5%, n=1842), and were not taking insulin (81.5%, n=3802).

SF-36 scores were generally good in all domains reflecting good quality of life. In the general population, the score for each domain is set to 50 with a standard deviation of 10. Better health status mean indicated by a higher domain score. Therefore, all SF-36 domains in LookAHEAD indicate that participants were either within the range or slightly above when compared to the general population (Scores of each domain found in Table 4-1).

The baseline psychological variables showed that participants had minimal & mild scores of depression (87.2%, n=4068), and few had suicidal thoughts (1.2%).

Table 4-1: Descriptive statistics for all cohorts.

Variable	All (n=4667)	
Demographic:		
Age, years	58.9 ± 6.74	(n=4667)
Sex, n (%)		(n=4667)
Female	2724 (58.4%)	
Male	1943 (41.6%)	
Marital status, n (%)		(n=4667)
Married	3169 (67.9%)	
Not married	1498 (32.1%)	
Ethnicity, n (%)		(n=4667)
White	3304 (70.8%)	
African American / Black	770 (16.5%)	
Any other	593 (12.7%)	
Education, n (%)		(n=4667)
Higher education	3487 (74.7%)	
Completed high school	596 (12.8%)	
Any other	584 (12.5%)	
Employment, n (%)		(n=4667)
Full or part-time job	2940 (63.0%)	
Full or part-time student	18 (0.4%)	
Homemaker	822 (17.6%)	
Not employed	887 (19.0%)	
Clinical		
Duration of T2DM, years	5 (2 - 10)	(n=4667)
Age diagnosed with T2DM, years	52.4 ± 8.06	(n=4667)
Initial Height, m	1.67 ± 0.09	(n=4667)
Initial weight, kg	101 ± 19.3	(n=4667)
Initial BMI, kg/m^2	36 ± 5.85	(n=4667)
Metabolic syndrome criteria, n (%)		(n=4667)
One criteria met	32 (0.7%)	
Two criteria met	262 (5.6%)	
Three criteria met	1249 (26.8%)	
Four criteria met	1626 (34.8%)	
Five criteria met	1498 (32.1%)	
Hypertension, n (%)		(n=4667)
Yes	3921 (84.0%)	
No	746 (16.0%)	
HbA1c, mmol/mol	54 (46 - 62)	(n=4667)
Systolic blood pressure, mmHg	129 ± 17.0	(n=4667)
Diastolic blood pressure, mmHg	70.2 ± 9.52	(n=4667)
Total cholesterol, mmol/L	4.94 ± 0.96	(n=4667)
Triglycerides, mmol/L	1.74 (1.22 - 2.5)	(n=4667)
HDL cholesterol, mmol/L	1.12 ± 0.30	(n=4667)
LDL cholesterol, mmol/L	2.90 ± 0.82	(n=4667)
Number of diabetes medications, n (%)		(n=4667)
0	612 (13.1%)	
1	1842 (39.5%)	
2	1537 (32.9%)	
≥ 3	676 (14.5%)	
Any insulin, n (%)		(n=4667)
Yes	865 (18.5%)	
No	3802 (81.5%)	
Behavioural:		
Snore, n (%)		(n=4667)

Yes	4011 (85.9%)	
No	434 (9.3%)	
Don't know	222 (4.8%)	
Breathing, n (%)		(n=4667)
Yes	588 (12.6%)	
No	3321 (71.2%)	
Don't know	758 (16.2%)	
Sleepy, n (%)		(n=4667)
Almost always (16-30 days/month)	454 (9.7%)	
Never or rarely (1 day/month or less)	2119 (45.4%)	
Often (5-15 days/month)	621 (13.3%)	
Sometimes (2-4 days/month)	1473 (31.6%)	
Apnoea, n (%)		(n=4667)
Yes	579 (12.4%)	
No	4088 (87.6%)	
Eating control, n (%)		(n=4667)
Yes	618 (13.2%)	
No	792 (17.0%)	
Prefer not to answer	3257 (69.8%)	
Eat big amount within short time (2 hours), n (%)		(n=4667)
Yes	1323 (28.3%)	
No	3344 (71.7%)	
Binge eat, n (%)		(n=4667)
Yes	603 (12.9%)	
No	4064 (87.1%)	
Eat big amount (during past 6 months), n (%)		(n=4667)
Yes	1625 (34.8%)	
No	3042 (65.2%)	
Smoking, n (%)		(n=4667)
Present	195 (4.2%)	
Past	2149 (46.0%)	
Never	2323 (49.8%)	
Max MET	7.20 ± 1.96	(n=4667)
Total alcohol, oz/wk	0 (0 – 5)	(n=4667)
Treatment arm, n (%)		(n=4667)
Diabetes support & education	2336 (50.1%)	
Weight loss intervention	2331 (49.9%)	

Quality of life (SF-36):

Health transition, n (%)		(n=4667)
1	328 (7.0%)	
2	863 (18.5%)	
3	2643 (56.6%)	
4	803 (17.2%)	
5	30 (0.6%)	
General health (Score out of 100)	47.2 ± 8.90	(n=4667)
Mental component summary (Score out of 100)	56.5 (50.9 – 59.4)	(n=4667)
Mental health (Score out of 100)	55.6 (50.0 – 58.4)	(n=4667)
Bodily pain (Score out of 100)	50.8 ± 8.63	(n=4667)
Physical component summary (Score out of 100)	49.4 (43.6 – 53.9)	(n=4667)
Physical function (Score out of 100)	50.7 (44.4 – 54.9)	(n=4667)
Role emotion (Score out of 100)	55.9 (51.9 – 55.9)	(n=4667)
Role physical (Score out of 100)	54.4 (47.0 – 56.8)	(n=4667)

Social function (Score out of 100)	56.8 (51.3 – 56.8)	(n=4667)
Vitality (Score out of 100)	53.1 ± 9.03	(n=4667)
<u>Psychological (Beck):</u>		
Beck score (exclude weight question)	4 (2 – 8)	(n=4667)
Beck score (exclude weight question) categories, n (%)		(n=4667)
Minimal	3889 (83.3%)	
Mild	683 (14.6%)	
Moderate	90 (1.9%)	
Severe	5 (0.1%)	
Beck total score, n (%)		(n=4157)
Minimal & mild	4068 (87.2%)	
Moderate	85 (1.8%)	
Severe	4 (0.1%)	
Missing	510 (10.9%)	
Beck suicide indicator, n (%)		(n=4667)
Yes	58 (1.2%)	
No	2599 (55.7%)	
Any other	2010 (43.1%)	
Beck severe depression >24 (exclude weight question), n (%)		(n=4667)
Yes	25 (0.5%)	
No	4642 (99.5%)	

Abbreviations: T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; Max MET, Maximal Metabolic Equivalent of Task; SF-36, Short Form (36) Health Survey. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).

4.3.2 Descriptive statistics by medium-term outcome status

Table 4-2 shows the baseline characteristics by the successful outcome variable. Successful completers were more likely to be in the lifestyle intervention arm of the trial (as expected). Aside from that, successful completers were approximately a year older in general than unsuccessful completers. In employment status, a full or part-time job is the dominant group in both comparison groups, although successful completers are less likely to be in a full or part-time job (60.4%).

Successful completers were approximately a year older when diagnosed with T2DM than unsuccessful completers. Successful completers were 2 Kg heavier in baseline weight and had around 0.3 kg/m^2 higher baseline BMI than unsuccessful completers. Successful completers had slightly lower cholesterol and LDL than unsuccessful completers (0.10 mmol/L and 0.15 mmol/L lower, respectively).

Both comparison groups were more likely to be on at least 1 of the diabetes medication, although successful completers are more likely to be on one of the diabetes medications (40.7%). Both comparison groups were not on insulin, although successful completers are less likely to take insulin.

Both comparison groups had a low prevalence of apnoea, although successful completers were borderline more likely to have apnoea (11.9% vs 13.6%). Both comparison groups were less likely to report their status of eating control, although successful completers are more likely to report their status.

Successful completers were less likely to have psychological distress due to emotional distress (0.7 unit higher mental component summary score). Successful completers were less likely to have limitations or pain than unsuccessful completers (1 unit higher bodily pain score). Successful completers were more likely to have a physical limitation than unsuccessful completers (1 unit lower physical component summary score). Although physical function was statistically significant, there is no clinically significant difference.

Table 4-2: Characteristics of participants, showing the comparison between the unsuccessful completers versus the successful completers (5% weight loss at 4 years).

Variable	Unsuccessful completers (n=3171)	Successful completers (n=1496)	p-value
Demographic:			
Age, years	58.6 ± 6.70	59.4 ± 6.85	< 0.001
Sex, n (%)			0.49
Female	1840 (58.0%)	884 (59.1%)	
Male	1331 (42.0%)	612 (40.9%)	
Marital status, n (%)			0.34
Married	2139 (67.5%)	1030 (68.9%)	
Not married	1032 (32.5%)	466 (31.1%)	
Ethnicity, n (%)			0.31
White	2223 (70.1%)	1081 (72.3%)	
African American / Black	537 (16.9%)	233 (15.6%)	
Any other	411 (13.0%)	182 (12.2%)	
Education, n (%)			0.64
Higher education	2370 (74.7%)	1117 (74.7%)	
Completed high school	397 (12.5%)	199 (13.3%)	
Any other	404 (12.7%)	180 (12.0%)	
Employment, n (%)			0.07
Full or part-time job	2037 (64.2%)	903 (60.4%)	
Full or part-time student	11 (0.3%)	7 (0.5%)	
Homemaker	545 (17.2%)	277 (18.5%)	
Not employed	578 (18.2%)	309 (20.7%)	
Clinical:			
Duration of T2DM, years	5 (2 - 10)	5 (2 - 10)	0.91
Age diagnosed with T2DM, years	52.2 ± 8.00	53.0 ± 8.21	< 0.001
Initial Height, m	1.67 ± 0.09	1.67 ± 0.09	0.92
Initial weight, kg	100 ± 19.0	102 ± 20	< 0.001
Initial BMI, kg/m^2	36.0 ± 5.80	36.3 ± 6.04	< 0.001
Metabolic syndrome criteria, n (%)			0.21
One criteria met	19 (0.6%)	13 (0.9%)	

Two criteria met	183 (5.8%)	79 (5.3%)	
Three criteria met	821 (25.9%)	428 (28.6%)	
Four criteria met	1128 (35.6%)	498 (33.3%)	
Five criteria met	1020 (32.2%)	478 (32.0%)	
Hypertension, n (%)			0.92
Yes	2663 (84.0%)	1258 (84.1%)	
No	508 (16.0%)	238 (15.9%)	
HbA1c, mmol/mol	54.1 (46.4 – 63.0)	53.0 (47.5 – 62.0)	0.29
Systolic blood pressure, mmHg	129 ± 17.0	129 ± 17.2	0.84
Diastolic blood pressure, mmHg	70.3 ± 9.45	70.0 ± 9.66	0.10
Total cholesterol, mmol/L	5.00 ± 1.00	4.90 ± 1.00	0.01
Triglycerides, mmol/L	1.74 (1.23 - 2.50)	1.74 (1.20 – 2.46)	0.50
HDL cholesterol, mmol/L	1.12 ± 0.30	1.13 ± 0.31	0.11
LDL cholesterol, mmol/L	3.00 ± 0.83	2.85 ± 0.80	< 0.001
Number of diabetes medications, n (%)			0.02
0	415 (13.1%)	197 (13.2%)	
1	1233 (38.9%)	609 (40.7%)	
2	1030 (32.5%)	507 (33.9%)	
≥ 3	493 (15.5%)	183 (12.2%)	
Any insulin, n (%)			
Yes	611 (19.3%)	254 (17.0%)	0.06
No	2560 (80.7%)	1242 (83.0%)	
<u>Behavioural:</u>			
Snore, n (%)			0.60
Yes	2718 (85.7%)	1293 (86.4%)	
No	304 (9.6%)	130 (8.7%)	
Don’t know	149 (4.7%)	73 (4.9%)	
Breathing, n (%)			0.23
Yes	383 (12.1%)	205 (13.7%)	
No	2262 (71.3%)	1059 (70.8%)	
Don’t know	526 (16.6%)	232 (15.5%)	

Sleepy, n (%)			0.71
Almost always (16-30 days/month)	310 (9.8%)	144 (9.6%)	
Never or rarely (1 day/month or less)	1431 (45.1%)	688 (46.0%)	
Often (5-15 days/month)	414 (13.1%)	207 (13.8%)	
Sometimes (2-4 days/month)	1016 (32.0%)	457 (30.5%)	
Apnoea, n (%)			0.09
Yes	376 (11.9%)	203 (13.6%)	
No	2795 (88.1%)	1293 (86.4%)	
Eating control, n (%)			0.02
Yes	391 (12.3%)	227 (15.2%)	
No	555 (17.5%)	237 (15.8%)	
Prefer not to answer	2225 (70.2%)	1032 (69.0%)	
Eat a big amount within a short time (2 hours), n (%)			0.24
Yes	882 (27.8%)	441 (29.5%)	
No	2289 (72.2%)	1055 (70.5%)	
Binge eat, n (%)			0.01
Yes	383 (12.1%)	220 (14.7%)	
No	2788 (87.9%)	1276 (85.3%)	
Eat big amount (during past 6 months), n (%)			0.43
Yes	1092 (34.4%)	533 (35.6%)	
No	2079 (65.6%)	963 (64.4%)	
Smoking, n (%)			0.80
Present	137 (4.3%)	58 (3.9%)	
Past	1457 (45.9%)	692 (46.3%)	
Never	1577 (49.7%)	746 (49.9%)	
Max MET, metabolic equivalents	7.24 ± 2.00	7.10 ± 2.00	0.01
Total alcohol, oz/wk	0 (0 - 6.5)	0 (0 – 5)	0.15

Treatment arm, n (%)			< 0.001
Diabetes support & education	1820 (57.4%)	516 (34.5%)	
Weight loss intervention	1351 (42.6%)	980 (65.5%)	
<u>Quality of life (SF-36):</u>			
Health transition, n (%)			0.15
1	238 (7.5%)	90 (6.0%)	
2	599 (18.9%)	264 (17.6%)	
3	1765 (55.7%)	878 (58.7%)	
4	546 (17.2%)	257 (17.2%)	
5	23 (0.7%)	7 (0.5%)	
General health (Score out of 100)	47.3 ± 9.00	47.0 ± 8.83	0.19
Mental component summary (Score out of 100)	56.3 (51.0 – 59.3)	57.0 (51.4 – 59.6)	0.04
Mental health (Score out of 100)	55.6 (50.0 – 58.4)	55.6 (50.0 – 58.4)	0.32
Bodily pain (Score out of 100)	51.1 ± 8.60	50.1 ± 8.70	< 0.001
Physical component summary (Score out of 100)	50.0 (44.0 – 54.0)	49.0 (42.6 – 53.4)	< 0.001
Physical function (Score out of 100)	51.0 (44.4 – 55.0)	51.0 (44.4 – 55.0)	< 0.001
Role emotion (Score out of 100)	56.0 (52.0 – 56.0)	56.0 (52.0 – 56.0)	0.15
Role physical (Score out of 100)	54.4 (47.0 – 57.0)	52.0 (47.0 – 57.0)	0.22
Social function (Score out of 100)	57.0 (51.3 – 57.0)	57.0 (51.3 – 57.0)	0.77
Vitality (Score out of 100)	53.2 ± 9.10	53.0 ± 9.00	0.20
<u>Psychological (Beck):</u>			
Beck score (exclude weight question)	4 (2 - 8)	4 (2 - 8)	0.55
Beck score (exclude weight question) categories, n (%)			0.88
Minimal	2637 (83.2%)	1252 (83.7%)	

Mild	467 (14.7%)	216 (14.4%)	
Moderate	64 (2.0%)	26 (1.7%)	
Severe	3 (0.1%)	2 (0.1%)	
Beck total score, n (%)			0.25
Minimal & mild	2743 (86.5%)	1325 (88.6%)	
Moderate	59 (1.9%)	26 (1.7%)	
Severe	3 (0.1%)	1 (0.1%)	
Missing	366 (11.5%)	144 (9.6%)	
Beck suicide indicator, n (%)			0.42
Yes	40 (1.3%)	18 (1.2%)	
No	1745 (55.0%)	854 (57.1%)	
Any other	1386 (43.7%)	624 (41.7%)	
Beck severe depression >24 (exclude weight question), n (%)			0.39
Yes	15 (0.5%)	10 (0.7%)	
No	3156 (99.5%)	1486 (99.3%)	

Abbreviations: T2DM, Type 2 Diabetes Mellitus; BMI, Body Mass Index; HbA1c, glycated haemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; Max MET, Maximal Metabolic Equivalent of Task; SF-36, Short Form (36) Health Survey. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: achieve **5% weight loss** at 4 years.
Outcome variable: unsuccessful completers versus successful completers.

4.3.3 Univariable risk factors for successful completion

Simple logistic regression was used to identify exposures associated with successful completion (5% weight loss), compared to those who completed the programme and did not successfully lose weight (Table 4-3). All predictor variables were tested but only ones that showed an association with the outcome of interest were reported in the table.

For context in the randomised arm variable, being in the weight loss intervention group (OR: 2.55, 95% CI: 2.25,2.90, p< 0.001) was almost 3 times higher in being successful at losing weight at 4 years when compared to those being in diabetes support & education group.

For every year increase in age, the associated odds of successful completion increased by 1% (95% CI: 0,2%, p< 0.001). Likewise, for every year increase in age diagnosed with T2DM, the associated odds of successful completion increased by 1% (95% CI: 0,2%, p< 0.001). In the employment variable, associated odds of successful completion increased by 20% in the not employed group (95% CI: 2,41%, p=0.02) at 4 years when compared to the full or part-time job group.

For every 1kg/m^2 increase in BMI, the associated odds of successful completion increased by 1% (95% CI: 0,2%, p< 0.001), and there was a similar weak but positive association with initial weight. In contrast, for the metabolic syndrome criteria variable, there was no strong association with success. For every 1mmol/L increase in total cholesterol, associated odds of successful completion decreased by 8% (95% CI: 14,2% reduction, p=0.01). For every 1mmol/L increase in LDL cholesterol, associated odds of successful completion decreased by 10% (95% CI: 18,4%, p< 0.001). In the number of diabetes medications variable, associated odds of successful completion decreased by 25% in the ≥ 3 medications group (95% CI: 39,9%, p< 0.001) at 4 years when compared to 1 medication group.

In the eating control variable, the largest response group was “prefer not to answer” which was considered the referent. Odds of successful completion increased by 25% in the “yes” group (95% CI: 4,50%, p=0.01) at 4 years when compared to the ”prefer not to answer” group.

For every unit increase in max MET, associated odds of successful completion decreased by 4% (95% CI: 7,1%, p=0.01).

In the health transition variable, associated odds of successful completion decreased by 24% in the “1” group (95% CI: 42,2%, p=0.03) at 4 years when compared to the “3” group. For every unit increase in body pain score (i.e. when pain decreases), associated odds of successful completion decreased by 2% (95% CI: 2,1%, p<0.001). For every unit increase in physical component summary, associated odds of successful completion decreased by 2% (95% CI: 3,1%, p<0.001). For every unit increase in physical function, associated odds of successful completion decreased by 1% (95% CI: 2,1%, p=0.03).

Table 4-3: Unadjusted models for odds ratios of successful completion in the medium-term, 95% confidence intervals, and p-values for each predictor variable (predictor variables that did not show an association with the outcome of interest were omitted from the table).

Variable	n	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Age, per year	4667	1.01	1.00-1.02	< 0.001
Employment				
Full or part-time job	2940	**Reference**		
Full or part-time student	18	1.43	0.55-3.71	0.45
Homemaker	822	1.14	0.97-1.35	0.10
Not employed	887	1.20	1.02-1.41	0.02
Clinical:				
Age diagnosed with T2DM, per year	4667	1.01	1.00-1.02	< 0.001
Initial weight, per kg	4667	1.00	1.00-1.01	< 0.001
Initial BMI, per kg/m2	4667	1.01	1.00-1.02	< 0.001
Metabolic syndrome criteria				
One criterion met	32	1.54	0.76-3.16	0.23
Two criteria met	262	0.97	0.73-1.30	0.87
Three criteria met	1249	1.18	1.00-140	0.04
Four criteria met	1626	**Reference**		
Five criteria met	1498	1.06	0.91-1.23	0.44
Total cholesterol, per mmol/L	4667	0.92	0.86-0.98	0.01
LDL cholesterol, per mmol/L	4667	0.90	0.82-0.96	< 0.001
Number of diabetes medications				
0	612	0.96	0.80-1.16	0.69
1	1842	**Reference**		
2	1537	0.99	0.86-1.15	0.96
≥ 3	676	0.75	0.61-0.91	< 0.001
Behavioural:				
Eating control				
Yes	618	1.25	1.04-1.50	0.01
No	792	0.92	0.77-1.10	0.33
Prefer not to answer	3257	**Reference**		
Binge eat				
No	4064	**Reference**		
Yes	603	1.25	1.04-1.50	0.01
Max MET per metabolic equivalent unit	4667	0.96	0.93-0.99	0.01
Treatment arm				
Diabetes support & education	2336	**Reference**		< 0.001
Weight loss intervention	2331	2.55	2.25-2.90	
Quality of life (SF-36):				
Health transition				
1	328	0.76	0.58-0.98	0.03
2	863	0.88	0.75-1.04	0.15
3	2643	**Reference**		
4	803	0.94	0.79-1.12	0.52
5	30	0.61	0.26-1.43	0.25
Bodily pain, per unit/100	4667	0.98	0.98-0.99	< 0.001
Physical component summary, per unit/100	4667	0.98	0.97-0.99	< 0.001
Physical function, per unit/100	4667	0.99	0.98-0.99	0.02

Abbreviation: n, number of events; T2DM, Type 2 Diabetes Mellitus; LDL, Low-Density Lipoprotein; Max MET, Maximal Metabolic Equivalent of Task; SF-36, Short Form (36) Health Survey.
Criteria for success: achieve 5% weight loss at 4 years.
Outcome variable: unsuccessful completers versus successful completers.

4.3.4 Multivariable risk factors for successful completion

In this section interactions between all predictor variables were tested and there was no interaction seen between predictor variables. This allows for building a baseline model with the most important predictor variables as seen from simple logistic regression (Table 4-4). In the basic prediction model, a priori risk factors for prediction of successful completion were sex, age and initial weight (based on chapters 2 and 3).

The associated odds of successful completion for being male decreased by 17% (95% CI: 28,5%, p<0.001) at 4 years when compared to being female. For every year increase in age, the associated odds of successful completion increased by 2% (95% CI: 1,3%, p<0.001). For every Kg increase in initial weight, the associated odds of successful completion increased by 1% (95% CI: 0,1%, p<0.001). The variables within the baseline model were also tested for interactions and no interactions were seen.

Table 4-4: An adjusted model with odds ratios, 95% confidence intervals, and p-values for the basic prediction model).

Variable	Odds ratio	95% Confidence Interval	P-value
Sex			
Female	**Reference**		
Male	0.83	0.72-0.95	< 0.001
Age, per year	1.02	1.01-1.03	< 0.001
Initial weight, per kg	1.01	1.00-1.01	< 0.001

Criteria for success: achieve 5% weight loss at 4 years.
Outcome variable: unsuccessful completers versus successful completers.
N= 4667.

All significant variables in Table 4-3 was tested stepwise for inclusion in the basic prediction model. Of the psychosocial and behavioural variables (i.e. eating control, binge eating, max MET, health transition, physical component summary and physical function) none were retained within the prediction model. Additions retained in the model include bodily pain, the categorical variable of the number of diabetes medications and LDL (Table 4-5). Using this model, the AUC-ROC is 0.567, CI is 0.550,0.584 (Figure 4-1).

Table 4-5: An adjusted model with odds ratios, 95% confidence intervals, and p-values for an expanded model predicting successful weight loss (5% weight loss at 4 years).

Variable	Odds ratio	95% Confidence Interval	P-value
Sex			
Female	**Reference**		
Male	0.84	0.73-0.97	0.01
Age, per year	1.01	1.00-1.03	< 0.001
Initial weight, per kg	1.00	1.00-1.01	< 0.001
Bodily pain, per unit/100	0.98	0.98-0.99	< 0.001
Number of diabetes medications			
0	0.97		
1	**Reference**	0.80-1.18	0.80
2	0.96	0.83-1.11	0.64
≥ 3	0.71	0.60-0.86	< 0.001
LDL cholesterol, per mmol/L	0.90	0.82-0.96	< 0.001

Abbreviation: LDL, Low-Density Lipoprotein.
Criteria for success: achieve 5% weight loss at 4 years.
Outcome variable: unsuccessful completers versus successful completers.
N= 4667.

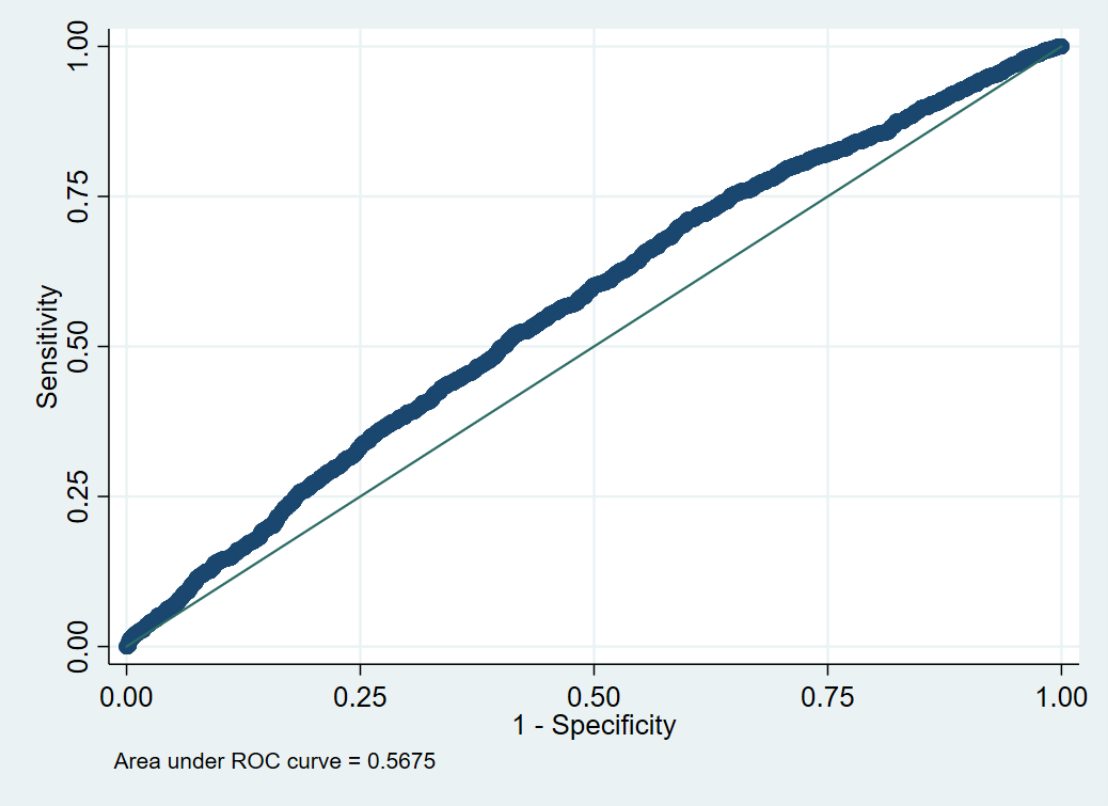

Figure 4-1: ROC curve for successful completion (Model without interaction).

A further step was taken to check the interactions of all variables with the randomised treatment arm within the final model (Table 4-6). The interaction between the treatment arm and sex was significant, which was included in the final model. The interaction effect was such that men were less likely to have successful weight loss, but weight loss success was more likely in the intervention arm in both sexes. Adding the sex-randomised treatment interaction slightly improved the model fit. The AUC-ROC was increased to 0.649, CI is 0.633,0.666 (Figure 4-2).

Table 4-6: An adjusted model with odds ratios, 95% confidence intervals, and p-values for expanded model with treatment#sex interaction (5% weight loss at 4 years).

Variable	Odds ratio	95% Confidence Interval	P-value
Sex # treatment arm			
Female # Diabetes support & education	**Reference**		
Female # Weight loss intervention	2.30	1.94-2.71	< 0.001
Male # Diabetes support & education	0.70	0.56-0.85	< 0.001
Male # Weight loss intervention	2.15	1.80-2.60	< 0.001
Age, per 5 years	1.11	1.06-1.16	< 0.001
Initial weight, per 5 kg	1.03	1.02-1.06	< 0.001
Bodily pain, per unit/100	0.99	0.98-1.00	0.01
Number of diabetes medications			
1	**Reference**		
0	0.96	0.80-1.18	0.72
2	0.95	0.81-1.10	0.50
≥ 3	0.71	0.60-0.87	< 0.001
LDL cholesterol, per mmol/L	0.90	0.82-0.97	< 0.001

Abbreviation: LDL, Low-Density Lipoprotein.
Outcome variable: unsuccessful completers versus successful completers.
N= 4667.

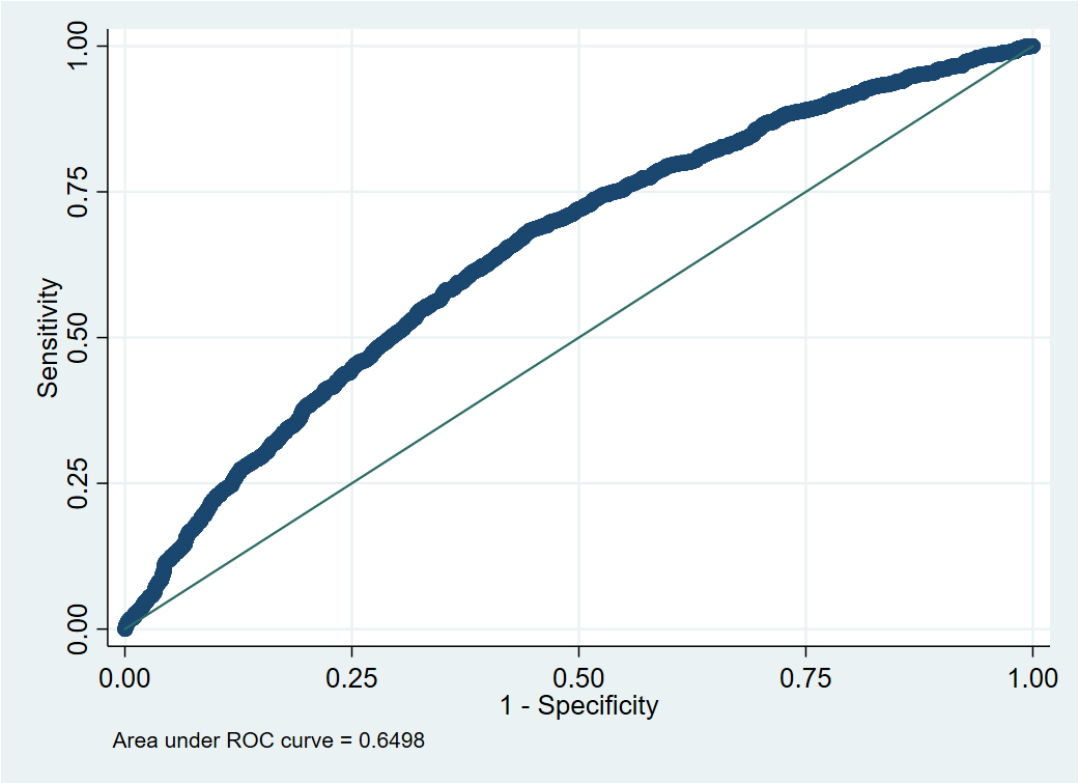

Figure 4-2: ROC curve for successful completion (Model with interaction).

4.4 Discussion

In this chapter, no psychosocial or behavioural factors tested are important except bodily pain. Predictors included basic demographics (age and sex) as well as baseline weight and bodily pain, diabetes medications and LDL cholesterol. Adding sex-randomised treatment interaction slightly improved the prediction model. However, the predictive utility of the model was generally very moderate with an area under the curve of 0.649.

The design and the cohort used in this study are different from that used in NHS GG&C. These two studies tested two different sets of variables, and this study was not intended as a validation study. In NHS GG&C, routine clinical data was used to measure the discriminative ability of clinical, process and sociodemographic factors in achieving successful weight loss. In lookAHEAD data infrequently collected in routine clinical care was used to measure the discriminative ability of behavioural, psychological and sociodemographic factors. Although this study identified several factors statistically significantly associated with successful weight loss, in general associations were weak. Model discrimination was poorer than in chapter 3, primarily due to the lack of availability of an early weight loss variable.

In general, both cohorts (NHS GG&C & LookAHEAD) were broadly comparable, and therefore the poor prediction here cannot be solely attributed to this being a substantially different cohort demographic. LookAHEAD participants were only a year older in mean than participants in the NHS GG&C cohort. The white and female populations were the predominant group in both cohorts. Although the duration of diabetes, when started the programmes, was ≥5 years, LookAHEAD participants had a slightly lower duration and lower HbA1c. Although LookAHEAD participants were mainly hypertensive, systolic and diastolic blood pressures were well managed (commensurate with the RCT design) and consequently lower than patients in NHS GG&C. Despite being in the same range of total cholesterol and triglycerides, LookAHEAD participants had lower ranges. On the other hand, LDL was higher among LookAHEAD participants. The main difference in the baseline information was the initial weight. In LookAHEAD, participants were much lighter in weight/BMI (12 Kg lighter than NHS GG&C patients/4,2 Kg/m^2 lower BMI than NHS GG&C patients).

Despite not having an identical model to NHS GG&C, the direction and the magnitude of age and initial weight associations with successful outcomes were almost identical. However, LookAHEAD showed that male participants were less likely to succeed in weight loss programmes, while sex did not show any influence on being successful in NHS GG&C.

Findings from the multivariable model showed that baseline factors of being female, older age, higher initial weight, high bodily pain, using no more than 1 diabetes medication and low LDL were associated with people being successful in the programme. It showed that none of the other psychological and behavioural factors seems to be important for being successful in the programme. Although the discrimination obtained from AUC-ROC was only moderate

The interaction was added to the model to test its effect and it can be concluded that men can do worse than women in the intervention arm and the usual care arm.

The results of this chapter were inconsistent with the observational study done to test the influence of baseline pain levels (tested via the SF-36 scale) in weight loss in patients undergoing specialist weight management within the NHS (All covariates were adjusted) (C. Ryan et al. 2017). Results of covariate-adjusted mean weight loss in that study showed similar weight loss in those with no-to-mild pain (8.1kg, 95% CI: 4.2,12.0kg) and moderate pain (8.3kg, 95% CI: 4.9,11.7kg) compared to severe pain group (3.0kg, 95% CI: -0.4,6.4kg) (p=0.08). The severe pain group lost less weight than the no-to-mild pain and moderate pain groups. This might be explained by the published study using thresholds for pain scores whereas we used a continuous model because there were few people with severe pain. It may be the association is non-linear once patients have severe pain and physical activity becomes difficult. In contrast, in this study, mild pain may provide patients with incentives to lose weight.

Another study found, when testing the entire cohort, a negative correlation between total pain score and weight loss (kg) ($r=-0.31$, $p<0.001$) (Wachholtz et al. 2010); i.e. pain is associated with poorer weight loss. After controlling for pretreatment BMI, age, depression, and anxiety, depression ($\beta= -0.19$, $p\leq0.05$) and joint pain ($\beta= -1.43$, $p\leq0.05$) were significantly associated with short-term weight

loss in females, while age (ß= 0.08, p≤0.05) and depression (ß= -0.37, p≤0.05) were significantly associated with short-term weight loss in males.

No studies were found testing the number of diabetes medications or LDL cholesterol as factors of association or prediction of successful weight loss. Based on UK guidelines, a healthy level of LDL cholesterol should be <3 mmol/L (NHS 2019). In this study, successful and unsuccessful completers were both in the healthy ranges. Although successful completers had a slightly lower LDL cholesterol it is possible that these associations (as well as associations of blood pressure and triglycerides with the successful outcome) are driven by the association with baseline weight, and thus were not significant in the adjusted model. In addition, successful completers were mostly prescribed only one type of diabetes medication and were less likely to be in ≥ 2 of diabetes medications. A possible explanation is that a successful completer engages more in their health care, which causes less severe hyperglycaemia, and makes them more likely to take ≤1 of diabetes medication. Moreover, if they were in 1 type of diabetes medication it is more likely to be from the weight loss category medications (Chapter 3).

In this chapter, being an older participant predict successful weight loss at the follow-up. This was consistent with the study done by Jiandani et al that older individuals were more likely to be successful at losing weight at follow-up (≥ 5% of body weight) when compared to younger people (RR across age ranges from 1.40 to 1.65, p<0.05) (Jiandani et al. 2016b). Possible reasons for that are older individuals experience low early attrition from weight loss programmes(Jiandani et al. 2016b), which means greater attendance and therefore better adherence. Older individuals might have better financial stability, more likely not to be employed, less stress about childcare (Honas et al. 2003), more motivation to improve general health status (Fabricatore et al. 2009).

Moreover, participants with higher baseline BMI predict successful weight loss. This was also found in a previous cross-sectional study done using the LookAHEAD dataset (Raynor et al. 2008). Their results showed that higher BMI was associated with a large amount of overall intentional weight loss (B= 0.01), practising self-weighing for <1 time per week (B= 0.83), and higher consumption of fast-food meals per week (B= 0.15) (p<0.05) (unadjusted model). After adjustment for the

duration of use of the weight control strategy included in the model, the duration of weight control practices that are suggested to be an indicator of successful weight control in adults was no longer related to BMI.

Spectrum effect, which is defined as the variation in performance of tests of prediction (i.e. PPV, and NPV) among different populations or settings depending on the proportion of patients that achieve weight loss (Usher-Smith, Sharp, and Griffin 2016). Therefore, in LookAHEAD, a validation study needs to be conducted and considered, since the results in this cohort are not generalisable to other cohorts.

4.4.1 Strengths of the study

LookAHEAD is an RCT and although real-world data, such as NHS GG&C, is the better reflection of a real population and the applied intervention (i.e. better external validity), biases cannot be avoided which reduces the internal validity of the research. Bias issues can be overcome by managing the dropout number, which can be achieved better within the controlled process of an RCT (Kim, Lee, and Kim 2018). Advantages of using LookAHEAD as a cohort study include: 1) a more wide and better standardised panel of measurements/exposures were taken (e.g. psychological/behavioural factors), 2) a long period of follow-up, 3) clear selection criteria for the population of interest, and 4) standardised controlled settings that motivate participants to lose weight.

4.4.2 Limitations

Weekly or monthly weight change or attendance as baseline factors were not measured (data were not permitted for research use). Access to the type of diabetes medications that were taken by each participant was not permitted. Accordingly medication effects were not explored. The extent of generalisability of LookAHEAD is generally limited. The cohort used in LookAHEAD is less representative of a population with overweight or obesity than NHS GG&C because healthier people, more affluent than the general population and less racial diversity would be recruited to the trial. Moreover, the intensive lifestyle intervention used in the LookAHEAD trial is a rigorous mode of intervention

compared to the standard intervention provided in NHS GG&C weight management services.

4.5 Conclusion

In weight loss programmes, the relationship between infrequently collected psychosocial or behavioural factors and intentional weight loss are weak predictors of successful weight loss. Of psychosocial or behavioural factors tested none was a predictor of successful weight loss at 4 years, except bodily pain. Predictors included basic demographics (age and sex) as well as baseline weight and bodily pain, diabetes medications and LDL cholesterol. Yet, the use of this predictive model is moderate. Both LookAHEAD and NHS GG&C findings need to be replicated and expanded on a separate cohort to validate findings externally. This was done in the next chapter.

5 Validation of the predictors of weight loss using Weight loss Referrals for Adults in Primary care (WRAP): data from a randomised controlled trial

5.1 Introduction

Chapters 3 and 4 have reported data suggesting the main candidate predictors of intentional weight loss are: initial weight, initial BMI, triglycerides, LDL, early weight loss, diabetes medications, pain, treatment arm, age, and sex. However, these results require consideration in the context of the literature, as well as external validation.

The importance of baseline body weight and early weight loss in weight management programmes was seen in the majority of studies that tested factors associated with weight loss during interventions and follow-up. In a European, multi-centre randomized trial, Sibutramine Trial of Obesity Reduction and Maintenance (STORM), analysis was done to identify factors associated with greater weight loss at 6 and 24 months (Hansen et al. 2001). At 6 months (Mean weight loss ± Standard Deviation: 11.3 ± 5.5 kg), the only factor associated with greater weight loss was baseline body weight. At 24 months (Mean weight loss ± Standard Deviation: 10.4 ± 9.3 kg), factors associated with greater weight loss were baseline body weight and body weight changes between months 6 and 24. The authors speculated that a greater energy deficit occurs in heavier participants when following a diet with a fixed energy prescription.

The relationship between pre-treatment characteristics & early weight change, and weight loss outcomes at the end of an 8-week intervention (i.e low-calorie diet (LCD)) in adults with overweight and obesity in the European population was tested in the Diet, Obesity and Genes' (DiOGenes) (T. Handjieva-Darlenska et al. 2010b). In a multivariate regression model in DiOGenes, the only factors that were associated with weight loss at the end of the 8-week intervention were initial body weight and early weight loss (week 1 & week 3). These results were similar to what was found in previous chapters (Chapter 3 & Chapter 4). Moreover, in Chapter 4, the prediction of the outcome of successful completion showed that besides the known predictors', initial weight, age, body pain, taking at least 3 diabetes medications and low LDL-cholesterol predictors of successful weight loss.

The relationship between patient characteristics at baseline and weight loss rate during a range of randomised and non-randomised intervention studies was explored in a systematic review (Finkler, Heymsfield, and St-Onge 2012b). This

study created a model based on the study sample and intervention characteristics to determine factors which were related to the rate of weight loss in clinical studies. Consistent factors that were similar to the results found in chapter 4 include participant age, participant age squared and initial body weight. The inconsistent findings of pain scores were seen in Rayan et al study and were explained earlier in chapter 4 (refer to section 4.4) (C. Ryan et al. 2017).

There is a lack of studies testing how diabetes medication and LDL-cholesterol might influence weight loss outcomes. In one study, researchers analysed data from 371 Chinese patients recently diagnosed with Type 2 Diabetes Mellitus (T2DM) (Zhou et al. 2017), to identify factors that influenced weight loss outcomes following 16-weeks of metformin treatment using stepwise linear regression analysis. At baseline, independent variables include age, HbA1c, fasting glucose, lipid measurements, blood pressure, BMI and cumulative dosages of metformin etc. The only variable that was associated with weight loss at the end of the treatment was having a higher weight at the baseline.

In the current study, the Weight loss Referrals for Adults in Primary care (WRAP) dataset was used to externally validate and expand on key findings from the prediction models developed in the earlier chapters for the NHS-GCMWS cohort study and the LookAHEAD Randomised controlled trial. WRAP has the advantage of having data available to broadly validate the findings from both of these previous studies. Validation would provide stronger evidence for using prediction models in clinical settings.

5.1.1 Weight loss Referrals for Adults in Primary care (WRAP) trial:

In the United Kingdom (UK), the most common commercial treatments available to manage the problem of overweight and obesity and the consequences of having excess body weight are the open-group behavioural weight-management programmes (e.g. Weight Watchers (WW)). This programme was similar to chapter 3 (NHS GG&C study).

In WRAP, researchers aimed to identify whether a Commercial Programme for 12 weeks (CP12) led to greater weight loss than the Brief Intervention (BI) (the

control arm) and whether following the Commercial Programme for 52 weeks (CP52) led to greater weight loss) than the CP12.

Secondary aims include changes in risk factors at different timepoints over the trial visits, cost-effectiveness, patient acceptability, and psychosocial influences.

5.1.2 Current study hypothesis

The identified predictor factors from LookAHEAD and NHS-GCWMS are predictive of successful weight loss in the medium-term in WRAP.

5.1.3 Current study aims

1)To validate specific clinical predictive factors that predict successful medium-term weight loss in individuals undertaking behavioural weight management programmes (from NHS-GCWMS cohort):

a. initial BMI,

b. triglycerides

c. early weight change (3 months change in the programme) and

d. diabetes medications

2)To validate behavioural, clinical and sociodemographic predictive factors that predict successful medium-term weight loss in individuals participating in an Intensive Lifestyle Intervention trial (from LookAHEAD cohort):

e. age,

f. initial weight,

g. pain,

h. diabetes medications and

i. LDL cholesterol

5.2 Methods

5.2.1 WRAP protocol

The study protocol was explained in detail elsewhere (Ahern et al. 2014).

5.2.1.1 Design

WRAP was a multicentre, randomised controlled trial (RCT) with a parallel design. The primary hypothesis of WRAP was weight loss at (baseline - 3 months) and (baseline - 24 months) is significantly greater in CP12 and CP52 interventions than in BI. And weight loss at (baseline - 24 months) is significantly greater in CP52 than in CP12.

5.2.1.2 Eligibility Criteria

Inclusion criteria in WRAP, include adults in the UK (age ≥ 18 years), who had a Body Mass Index (BMI) of ≥ 28 kg/m² (i.e. participants who had overweight or obesity) at the time of the recruitment. General Practitioner (GP) was responsible for inviting participants to the study, where they used their clinical judgement of participants eligibility for weight management programmes. If any participants were excluded by the GP, the exclusion reasons should be reported to the study team (e.g. patients who will not be able to co-operate with the study procedures such as those terminally ill, or those having an eating disorder history). Moreover, participants should be willing to take part in the study and willing to follow study procedures.

No further eligibility criteria were applied in the current study.

5.2.1.3 Exclusion Criteria

Any of the following reasons prevents patients from participating in the WRAP study. Mental health or personal problems (e.g. severe mental health problem, a caregiver of a terminal end disease relative, patients with language barriers (spoke a foreign language “other than English” or had Special Communication needs), etc.). Women who were planning to get pregnant or were pregnant, at the recruitment or during the following 2 years. Patients undergoing bariatric surgery (previous/planned). Any participants participating in a monitored weight

loss programme (patients who were on a self-guided diet will not be excluded). Any participants taking weight-loss medicines such as Orlistat were not eligible for exclusion.

5.2.1.4 Recruitment

The recruitment period of the WRAP trial was between October 2012 and February 2014. Three research centres in England were responsible for participant recruitment and follow-up via 23 primary care practices. The coordinating centre of the trial was the Medical Research Council (MRC) Human Nutrition Research in Cambridge. The research centres were: 1) The University of Cambridge (local practices in Cambridgeshire). 2) The University of Liverpool (local practices across Merseyside). 3) The University of Oxford (local practices across England).

Around 12000 eligible individuals were identified for the recruitment of 1200 participants. Participants' eligibility was identified through electronic registers by the primary care provider. The eligible and ineligible participants were identified by the GPs. Invitation letters, offering weight management services and a trial description, were sent to eligible participants. Participants who were interested in taking part in the trial telephone/email study group for further information and preliminary screening via telephone. If participants were willing to participate, agreeable appointment letters were sent to participants with the participants' information sheet. In the first appointment, a baseline assessment was done, and weight and height were taken by the study team to ensure eligibility and enrolment of participants were confirmed. Written informed consent was obtained from all participants before starting randomisation.

5.2.1.5 Randomization

The WRAP trial study team entered and hosted patients' information obtained from the assessments through an online database developed for the trial. After measuring the participants BMI, the database was programmed for automatic randomisation to one of the study groups (BI, CP12, CP52). The trial statistician allocate a 2:5:5 sequence, which was stratified by centre and sex (block size=12). Neither the research team nor the participants know the sequence. After the completion of the enrolment, group allocation was revealed in the database,

which prevent both the researchers and the participants from being blinded to the intervention due to the trial design.

5.2.1.6 Study Interventions

Brief Intervention (BI) control arm

This is the control intervention of the trial. At the baseline visit, researchers provide participants allocated to this group instructions for self-help weight-loss strategies (a booklet from the British Heart Foundation). Those participants attended the baseline and follow-up visits (at 0, 3, 12 and 24 months).

Study Intervention active arm:

1) **Commercial Programme for 12 weeks (CP12):**

   Participants received a free 12 weeks voucher (valid for up to 14 weeks starting from baseline) to attend local Weight Watchers meetings. Meetings were conducted on a weekly basis (1 meeting/week). A list of local meetings was given to participants to choose suitable times and locations.

2) **Commercial Programme for 52 weeks (CP52):**

   Participants received a free 52 weeks voucher to attend local Weight Watchers meetings.

5.2.1.7 Withdrawal and adherence

The option to withdraw (i.e. from the entire trial, not attend/stop attending sessions from the commercial weight loss programme) is available for the participants at any time of the trial. Any data collected from participants who decided to withdraw was retained unless participants asked the research team to discard data.

Participants adherence to Commercial Programme (CP) was measured through their CP meetings attendance. Two methods were used to monitor the attendance: 1) participants report that at assessment appointments. 2) data from weekly meetings at WW.

5.2.2 Validation study using WRAP

An application to access the pre-existing dataset from WRAP was developed. The College Of Medical, Veterinary & Life Sciences Ethics Committee, University of Glasgow, confirmed that no ethical approval was required and full access to the dataset was granted by MRC-Epidemiology Unit on a VPN via the University of Cambridge on 14/06/2021.

5.2.3 Data handling

Data cleaning by range checks and testing for implausible values was done for all intended to test factors (none identified given this is a published RCT). Extra exclusions or predetermined limit values were not applied because as an analysed RCT the data has already been cleaned.

In this study, two variable categories were identified: predictors of weight loss (exposure of interest) and medium-term weight loss (outcome). Each one is described thoroughly below.

5.2.3.1 Predictors

In this study, predictor variables were chosen from the list of variables available in the WRAP trial dataset. Those variables were considered suitable equivalents to predictors identified from the NHS-GCWMS and LookAHEAD datasets (i.e. the final models).

The time window for predictor variables was specified at the baseline visit. This was set to be the first assessment appointment in the WRAP trial.

1) Basic demographic:
    - Age (Continuous, years): the age of the participants at the baseline visit.
    - Sex: two identities were explored, which are male and female. The term gender was originally used in WRAP dataset, but in this thesis, it was replaced with sex as it was labelled as male and female.

2) Variables for validation studies:

- Initial weight (kg): recorded weight at assessment appointment by study staff.
- Initial Body Mass Index (BMI, kg/m^2): calculated BMI at assessment appointment by study staff.
- Triglycerides (mmol/L): Triglycerides at assessment appointment.
- Low-Density Lipoprotein (LDL) cholesterol (mmol/L): calculated LDL Cholesterol at assessment appointment.
- % weight change: 3 months - initial weight: percent of weight change between 3 months & initial weight.
- Medications: a binary variable that showed whether participants were taking medication(s) for diabetes at the assessment appointment.
- Treatment groups: a categorical variable that showed the intervention groups in the WRAP trial. Those groups were Brief Intervention (BI), Commercial Provider 12 weeks (CP12) and Commercial Provider 52 weeks (CP52).
- Pain/discomfort: one dimension of the 3-level version of the EQ-5D (EQ-5D-3L) questionnaire (This questionnaire contains 5 main dimensions) was used to determine the level of pain/discomfort. This was measured at the assessment appointment.

- The derivation of each predictor variable is presented in the tables below (Table 5-1, Table 5-2, Table 5-3).

Table 5-1: Data handling and description of demographic predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	age_bl	Continuous	_	Age of a participant at the first assessment appointment (i.e. baseline visit).	age_bl was originally derived in the WRAP dataset.	Years	Baseline	None	Clinical visit
2	gender	Categorical	0= F 1= M	F refers to female M refers to male	gender was originally derived in the WRAP dataset.	_	Baseline	None	Clinical visit

Table 5-2: Data handling and description of clinical predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	weight_bl	Continuous	_	First weight recorded at the first assessment appointment (i.e. baseline visit).	weight_bl was originally derived in the WRAP dataset.	Kg	Baseline	None	Clinical visit
2	BMI_bl	Continuous	_	Body mass index is a value derived from a person first weight recorded & height at the first assessment appointment (i.e. baseline visit). This was calculated by the study staff.	BMI_bl was originally derived in the WRAP dataset.	Kg/m^2	Baseline	None	Clinical visit

3	trig_bl	Continuous	_	Average of Triglycerides at the first assessment appointment (i.e. baseline visit).	trig_bl was originally derived in the WRAP dataset.	mmol/L	Baseline	n= 425 Replaced using multiple imputations.	Clinical visit
4	ldlchol_bl	Continuous	_		ldlchol_bl was originally derived in the WRAP dataset.	mmol/L	Baseline	n= 432 Replaced using multiple imputations.	
5	weightloss3m	Continuous	_	Weight change between the third month & first assessment appointment.	**To calculate % weight change:** weightloss3m= weight_3m^ – weight_bl replace weightloss3m= weight_bl if weightloss3m is missing ^weight_3m= 3 months weight measured by study clinic visit	%	Baseline	None	Clinical visit
6	diabetesmed_bl	Categorical	0= no 1= yes	A binary variable that showed whether participants were taking medication(s) for diabetes at assessment appointments.	diabetesmed_bl was originally derived in the WRAP dataset.	_	Baseline	n= 396 Replaced using multiple imputations.	Clinical visit

Table 5-3: Data handling and description of other predictor variables.

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Missing values	Data source
1	treatmentgroup	Categorical	1= Brief Intervention (BI) 2= Commercial Provider 12 weeks (CP12) 3= Commercial Provider 52 weeks (CP52)	A categorical variable that showed the intervention groups in the WRAP trial.	treatmentgroup was originally derived from the WRAP dataset.	_	Baseline	None	Clinical visit
2	eq5d_paindiscomfort_bl	Categorical	1= I have no pain or discomfort 2= I have moderate pain or discomfort 3= I have extreme pain or discomfort	A categorical variable to determine the level of pain/discomfort. This was measured at the assessment appointment.	eq5d_paindiscomfort_bl was originally derived in the WRAP dataset.	_	Baseline	n= 40 Replaced using multiple imputations.	Clinical visit

5.2.3.2 Outcomes

The time window for medium-term outcome variables was identified to be 5 years following the first assessment appointment (i.e. baseline).

Weight change: is the amount of weight lost (in percent) at 5 years from baseline weight (i.e. initial weight). This was calculated by subtracting the 5 years weight (depending on available weight) from the first assessment appointment weight (i.e. baseline weight).

Attendance: was also derived as a binary outcome variable. The definition was attendance at 3 months visit versus non-attendance at the 3 months visit.

The medium-term outcome for WRAP:

The outcomes of interest were derived based on different scenarios, similar to chapter 3. The definition for each scenario and the corresponding outcomes are shown below: first based on analyses not considering attendance:

- In scenario (1) the cut-off point for the weight change was set to be 3%. Therefore, two groups were created: 1) Successful completers, those who lost ≥ 3% from the baseline body weight at 5 years. 2) Unsuccessful completers, those who lost < 3% from the baseline body weight at 5 years.

- In scenario (2) the cut-off point for the weight change was set to be 5%. Therefore, two groups were created: 1) Successful completers, those who lost ≥ 5% from the baseline body weight at 5 years. 2) Unsuccessful completers, those who lost < 5% from the baseline body weight at 5 years.

In the next two scenarios, attendance at the 3 month visit was considered. as part of the definition of success.

- In scenario (3) attendance was considered alongside scenario 1. Therefore, two groups were created: 1) Successful completers, those who attended 3 months visit, lost ≥ 5% body weight at 3 months and

lost ≥ 3% from the baseline body weight at 5 years. 2) Non-completers & unsuccessful completers, those who attended & did not attend 3 months visits, lost ≥ 5% body weight at the at 3 months and lost < 3% from the baseline body weight at 5 years.

- In scenario (4) attendance was considered alongside scenario 2. Therefore, two groups were created: 1) Successful completers, those who attended 3 months visit, lost ≥ 5% body weight at 3 months and lost ≥ 5% from the baseline body weight at 5 years. 2) Non-completers & unsuccessful completers, those who attended & did not attend 3 months visits, lost ≥ 5% body weight at 3 months and lost < 5% from the baseline body weight at 5 years.

The medium-term outcome for LookAHEAD validation (section 4.3.4):

The cut-off point for the weight change was set to be 5%. Therefore, two groups were created: 1) Successful completers, those who lost ≥ 5% from the baseline body weight at 5 years. 2) Unsuccessful completers, those who lost < 5% from the baseline body weight at 5 years.

The derivation of each medium-term variable is presented in the table below (Table 5-4).

Table 5-4: Description & derivation of outcome variables (medium-term).

Number	Name	Type	Label	Definition	Derivation	Unit	Times point	Data source
1	weightlcf_5y	Continuous	_	Five years weight, using Last Observation Carried Forward (LOCF).	weightlcf_5y= mvweightstudygpsr_5y^ replace weightlcf_5y= mvweightstudygp_5y^ if weightlcf_5y is missing replace weightlcf_5y= weight_2y^ if weightlcf_5y is missing replace weightlcf_5y= weight_1y^ if weightlcf_5y is missing replace weightlcf_5y= weight_3m^ if weightlcf_5y is missing replace weightlcf_5y= weight_bl^ if weightlcf_5y is missing ^mvweightstudygpsr_5y= 5 years weight reported from study clinic visit if not from GP records if not self-reported by participants ^mvweightstudygp_5y= 5 years weight reported by study clinic visit if not from GP records ^weight_2y= 2 years weight measured by study clinic visit ^weight_1y= 1 year weight measured by study clinic visit ^weight_3m= 3 months weight measured by study clinic visit ^weight_bl= baseline weight measured by study clinic visit	Kg	Medium-term	Clinical visit
2	weightbcf_5y	Continuous	_	Five years weight, using Baseline Observation Carried Forward (BOCF).	weightbcf_5y= mvweightstudygpsr_5y replace weightbcf_5y= mvweightstudygp_5y if weightbcf_5y is missing replace weightbcf_5y= weight_bl if weightbcf_5y is missing replace weightbcf_5y= weight_3m if weightbcf_5y is missing replace weightbcf_5y= weight_1y if weightbcf_5y is missing replace weightbcf_5y= weight_2y if weightbcf_5y is missing	Kg	Medium-term	Clinical visit

3	fiveyrdiffweightbcf	Continuous	_	Amount of weight lost in kilogram between 5 years weight and first weight using BOCF.	Fiveyrdiffweightbcf= weightbcf_5y – weight_bl	Kg	Medium-term	Clinical visit
4	fiveyrdiffweightbcf_pc	Continuous	_	Amount of weight loss in percent between 5 years weight and first weight using BOCF.	fiveyrdiffweightbcf_pc= ((weightbcf_5y - weight_bl)/ weight_bl)*100	%	Medium-term	Clinical visit
5	fiveyr5pcweightlossbcf	Categorical	0= <5% 1= >=5%	A binary variable to distinguish whether the patient achieves 5 percent of weight loss at 5 years using BOCF.	fiveyr5pcweightlossbcf= . replace fiveyr5pcweightlossbcf= 1 if fiveyrdiffweightbcf_pc <=-5.00 & fiveyrdiffweightbcf_pc not missing replace fiveyr5pcweightlossbcf= 0 if fiveyrdiffweightbcf_pc >-5.00 & fiveyrdiffweightbcf_pc not missing	_	Medium-term	Clinical visit
6	fiveyr3pcweightlossbcf	Categorical	0= <3% 1= >=3%	A binary variable to distinguish whether the patient achieves 3 percent of weight loss at 5 years using BOCF.	fiveyr3pcweightlossbcf= . replace fiveyr3pcweightlossbcf = 1 if fiveyrdiffweightbcf_pc <=-3.00 & fiveyrdiffweightbcf_pc not missing replace fiveyr3pcweightlossbcf= 0 if fiveyrdiffweightbcf_pc >-3.00 & fiveyrdiffweightbcf_pc not missing	_	Medium-term	Clinical visit
7	successbcf	Categorical	0= unsuccessful completers_5percent 1= successful completers_5percent	A binary variable to distinguish whether the patient achieves 5 percent of weight loss at 5 years using BOCF.	successbcf = 0 if fiveyr5pcweightlossbcf= 0 replace successbcf= 1 if fiveyr5pcweightlossbcf= 1	_	Medium-term	Clinical visit

8	successthreebcf	Categorical	0= unsuccessful completers_3percent 1= successful completers_3percent	A binary variable to distinguish whether the patient achieves 3 percent of weight loss at 5 years using BOCF.	successthreebcf = 0 if fiveyr3pcweightlossbcf= 0 replace successthreebcf= 1 if fiveyr3pcweightlossbcf= 1	_	Medium-term	Clinical visit
9	fiveyrdiffweight	Continuous	_	Amount of weight lost in kilogram between 5 years weight and first weight using LOCF.	Fiveyrdiffweight= weightlcf_5y – weight_bl	Kg	Medium-term	Clinical visit
10	fiveyrdiffweight_pc	Continuous	_	Amount of weight loss in percent between 5 years weight and first weight using LOCF.	fiveyrdiffweight_pc= ((weightlcf_5y - weight_bl)/ weight_bl)*100	%	Medium-term	Clinical visit
11	fiveyr5pcweightloss	Categorical	0= <5% 1= >=5%	A binary variable to distinguish whether the patient achieves 5 percent of weight loss at 5 years using LOCF.	fiveyr5pcweightloss= . replace fiveyr5pcweightloss= 1 if fiveyrdiffweight_pc <=-5.00 & fiveyrdiffweight_pc not missing replace fiveyr5pcweightloss= 0 if fiveyrdiffweight_pc >-5.00 & fiveyrdiffweight_pc not missing	_	Medium-term	Clinical visit
12	fiveyr3pcweightloss	Categorical	0= <3% 1= >=3%	A binary variable to distinguish whether the patient achieves 3 percent of weight loss at 5 years using LOCF.	fiveyr3pcweightloss= . replace fiveyr3pcweightloss= 1 if fiveyrdiffweight_pc <=-3.00 & fiveyrdiffweight_pc not missing replace fiveyr3pcweightloss= 0 if fiveyrdiffweight_pc >-3.00 & fiveyrdiffweight_pc not missing	_	Medium-term	Clinical visit

13	success	Categorical	0= unsuccessful completers_5percent 1= successful completers_5percent	A binary variable to distinguish whether the patient achieves 5 percent of weight loss at 5 years using LOCF.	success= 0 if fiveyr5pcweightloss= 0 replace success= 1 if fiveyr5pcweightloss= 1	_	Medium-term	Clinical visit
14	successthree	Categorical	0= unsuccessful completers_3percent 1= successful completers_3percent	A binary variable to distinguish whether the patient achieves 3 percent of weight loss at 5 years using LOCF.	successthree= 0 if fiveyr3pcweightloss= 0 replace successthree= 1 if fiveyr3pcweightloss= 1	_	Medium-term	Clinical visit
15	successatt	Categorical	0= unsuccessful completersatt_3percent 1= successful completersatt_3percent	A binary variable to distinguish whether the patient attends 3 months visit, achieves 5 percent weight loss at 3 months, and achieves 3 percent of weight loss at 5 years using LOCF.	successatt= 0 replace successatt= 1 if attended_3m^=1 & weightloss3m <=-5.00 & fiveyr3pcweightloss=1 ^attended_3m= a categorical variable to show whether participant attend 3 months visit or not (0=did not attend, 1= did attend).	_	Medium-term	Clinical visit
15	successattfive	Categorical	0= unsuccessful completersatt_5percent 1= successful completersatt_5percent	A binary variable to distinguish whether the patient attends 3 months visit, achieve 5 percent weight loss at 3 months, and achieve 5 percent of weight loss at 5 years using LOCF.	successattfive= 0 replace successattfive= 1 if attended_3m=1 & weightloss3m <=-5.00 & fiveyr5pcweightloss=1	_	Medium-term	Clinical visit

5.2.4 Power calculation

Assuming a sample size of 1267 participants from the initial screen of the available data and a successful completion rate of 25% (Ahern et al. 2022), an estimation of 90% power was used to detect 10% fewer women being successful than men assuming that 70% (Ahern et al. 2017) of the unsuccessful group are women. Generically, 82% power was also used to detect a binary exposure associated with a successful outcome with an odds ratio of 1.55. For the continuous variable BMI assuming a mean BMI of 35 and a standard deviation of 5.5, 81% power was there to detect if a 1 kg/m^2 increase in BMI was associated with successful weight loss.

5.2.5 Statistical analyses

Binary logistic regression analysis (i.e. multiple regression model) was used to estimate the strength of the association between predictor variables and successful completion. This was done by calculating the measure of association (i.e. odds ratio (OR)) and the statistical significance (i.e. 95% confidence interval (CI) and p-value). A value of $p \leq 0.05$ was considered a statistically significant difference.

External validation models: prediction models that were developed in earlier chapters were tested here for their reproducibility and generalisability. Although generalisability cannot be confirmed after testing only once, using an external cohort that is independent of the original cohorts used for prediction model development substantially increases the probability that the results are generalisable.

The external validation was done by applying the risk factors observed (in original datasets (NHS- GCMWS & LookAHEAD) to an external dataset risk factors (in an independent dataset (i.e. WRAP)) and subjectively comparing the strength of association and discrimination. As part of external validation, both calibration and discrimination should usually be considered when deriving a risk score, but since each dataset was internally weighted, and the definition of early weight change was different, calibration was not assessed here. Discrimination was tested using the area under the curve (AUC).

The overall performance of the model was assumed to be similar to earlier chapters with the further step taken through testing AUC.

Previous studies in this thesis have used available data models to test predictors, but this makes the assumption that missing data do not influence associations. To maximise the value of WRAP as a validation dataset, therefore, used multiple imputations by chained equations (MICE) approach was used to account for missing data in this chapter (Sterne et al. 2009; Brinkgreve and Kumarswamy 2008). In this approach, the handling of missing data is based on creating multiple sets of imputation models (each variable has its own imputation model depending on the variable type). A wide style was declared, and predictor (missing & non-missing) and outcome variables, were registered as imputation variables.

There are three types of missing data: missing completely at random (MCAR); missing at random (MAR); missing not at random (MNAR) (Sterne et al. 2009). MI assumes that the missing data are MAR. In practice, it is difficult to test this assumption formally because the MAR mechanism can be distinguished from the MNAR mechanism only through the missing data that are not observed. Only limited data were missing in WRAP, and therefore MAR was assumed.

Three main steps were involved in MI analysis:

1) imputation step: an exploration of missing data patterns was assessed to check for data with extreme missingness. All variables to be imputed had >50% data availability. Imputation models for different forms of missing variables were then considered (i.e. linear regression model for continuous variables, multinomial (polytomous)

logistic regression model for categorical variables, and logistic regression for binary variables). The code used in STATA was:

mi impute chained (regress) ldlchol_bl trig_bl (mlogit) eq5d_paindiscomfort_bl (logit) diabetesmed_bl = sex age_bl weight_bl treatmentgroup bmi_bl weightloss2m successbcf successthreebcf success successthree successatt successattfive, burnin(100) add(10) reseed(1234) savetrace (file name) augment.

The number of iterations for the burn-in period was set to 100, and the number of imputations was set to 10 (M=10) (Graham, Olchowski, and Gilreath 2007). Assessment of imputed data was performed for continuous and categorical variables that contain missing values. For continuous variables, the convergence of the distribution of the imputed variables across m=10 datasets was investigated to check if imputations were stable across datasets or if any outliers were identified. For categorical variables, comparisons between observed and imputed data were made subjectively.

2) Completed-data analysis (estimation) step: the primary analysis that is intended to be used in this study is binary logistic regression. The 'MI estimate' command was used in SATA (Brinkgreve and Kumarswamy 2008).

3) Pooling step: The results obtained from M completed-data analysis are combined into a single multiple-imputation result via the STATA module.

As was reported in other chapters, there were limited (n=396) missing values for participants weight at 5 years in the WRAP trial. To derive missing weight two methods were used, Last Observation Carried Forward (LOCF) (primary analysis method) and Baseline Observation Carried Forward (BOCF) (sensitivity analysis method).
In LOCF, whenever there was a missing weight measurement, the value was replaced with the last observed value. While for BOCF, whenever

there was a missing weight measurement, the value was replaced with the first observed value.

STATA software version 16.1 was used in the cleaning & analysis of data.

5.3 Results

The baseline characteristics of the whole cohort in WRAP were as follows: the mean age of the participants was 53.2 years (SD= 13.7 years), 67.8% were female (n=859), mean initial weight was 96.2 kg (SD= 17.0 kg) and median initial BMI was 33.3 kg/m^2 (IQR= 30.7,37.0 kg/m^2).

The number of participants included in the analysis was 1267. This includes all participants included in the WRAP trial.

5.4 Validation of successful completion models from NHS- GCMWS

5.4.1 NHS-GCWMS medium-term 3% weight loss model using WRAP (scenario 1)

Predictors tested and retained in the prediction model were initial BMI, triglycerides and the early weight change (3months – initial) (Table 5-5). The model results were broadly consistent with the model found in NHS- GCMWS (Table 3-19).

In WRAP, more early weight loss during 3 months means that the participants were more likely to succeed and achieve 3 % weight loss at 5 years. This was similar to results found in NHS-GCWMS. In addition, a higher baseline BMI means participants were more likely to succeed and achieve 3 % weight loss at 5 years, which was similar to NHS-GCWMS, but weaker. The model in WRAP was different from the NHS-GCWMS model in that triglycerides showed no association with successful weight loss while in NHS-GCWMS it did show an association with successful weight loss, despite the point estimate going in the same direction. Using this model, the AUC-ROC is 0.697 and CI is 0.662,0.733 (Figure 5-1).

Table 5-5: An adjusted model for odds ratios of successful completion in the medium-term (3% weight loss at 5 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.02	1.00-1.04	0.04
Triglycerides, per mmol/L	1.05	0.87-1.27	0.57
% weight change 3months – initial, per %	0.98	0.97-0.98	< 0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **3% weight loss** at 5 years.
Outcome variable: unsuccessful completers (n=780) versus successful completers (n=487).
Number of imputations= 10.
N= 1267.

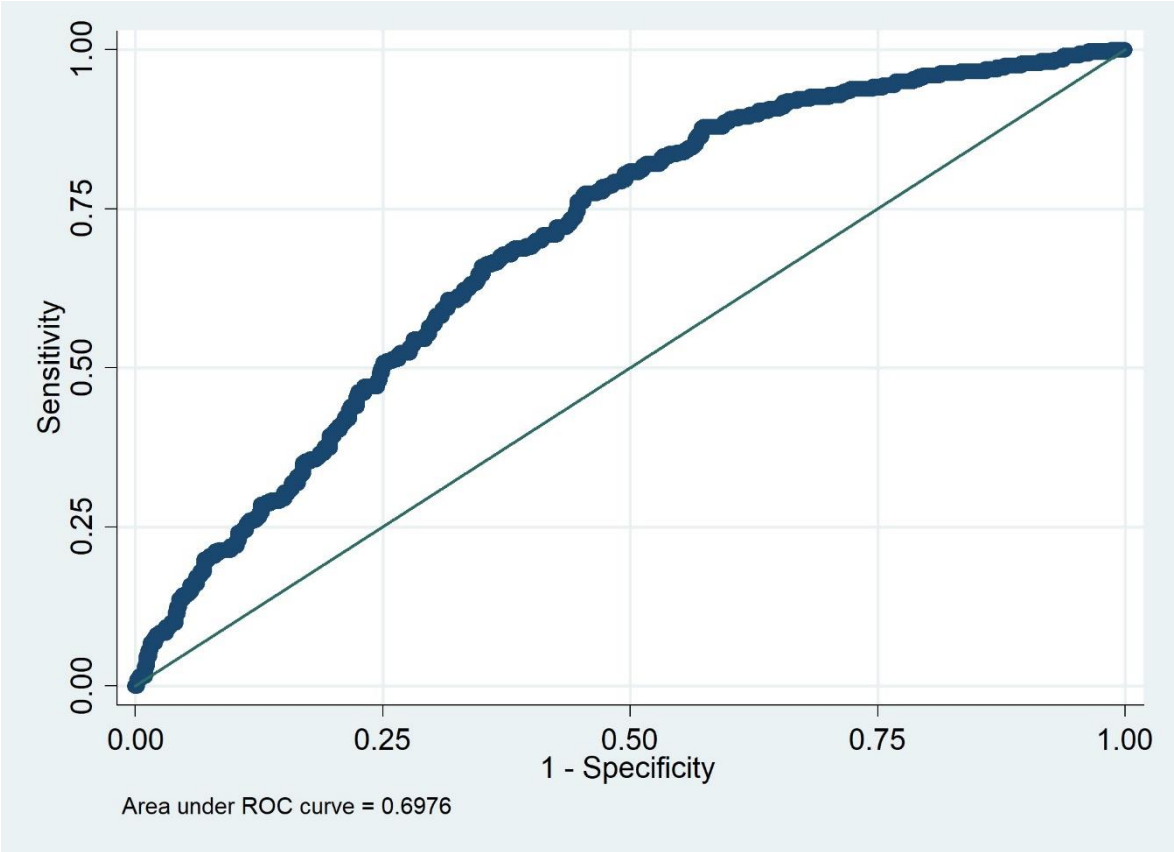

Figure 5-1: ROC curve for successful completion validation from NHS-GCWMS medium-term 3% weight loss.

5.4.2 NHS-GCWMS medium-term 5% weight loss (scenario 2)

Predictors tested and retained in the prediction model were initial BMI, and the early weight change (3months – initial) (Table 5-6). The model results were nearly identical to the model found in NHS-GCMWS (Table 3-23).

In WRAP, more weight loss during 3 months means that the participants were more likely to succeed and achieve 5 % weight loss at 5 years. This was similar to results found in NHS-GCWMS. In addition, a higher baseline BMmeans participants were more likely to succeed and achieve 3 % weight loss at 5 years, which was similar to NHS-GCWMS, but weaker. Using this model, the AUC-ROC is 0.678 and CI is 0.647,0.709 (Figure 5-2).

Table 5-6: An adjusted model for odds ratios of successful completion in the medium-term (5% weight loss at 5 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Initial BMI, per kg/m^2	1.03	1.00-1.05	0.02
% weight change 3months - initial, per %	0.98	0.97-0.98	< 0.001

Abbreviation: BMI, Body Mass Index.
Criteria for success: achieve **5% weight loss** at 5 years.
Outcome variable: unsuccessful completers (n=893) versus successful completers (n=374).
Number of imputations= 10.
N= 1267.

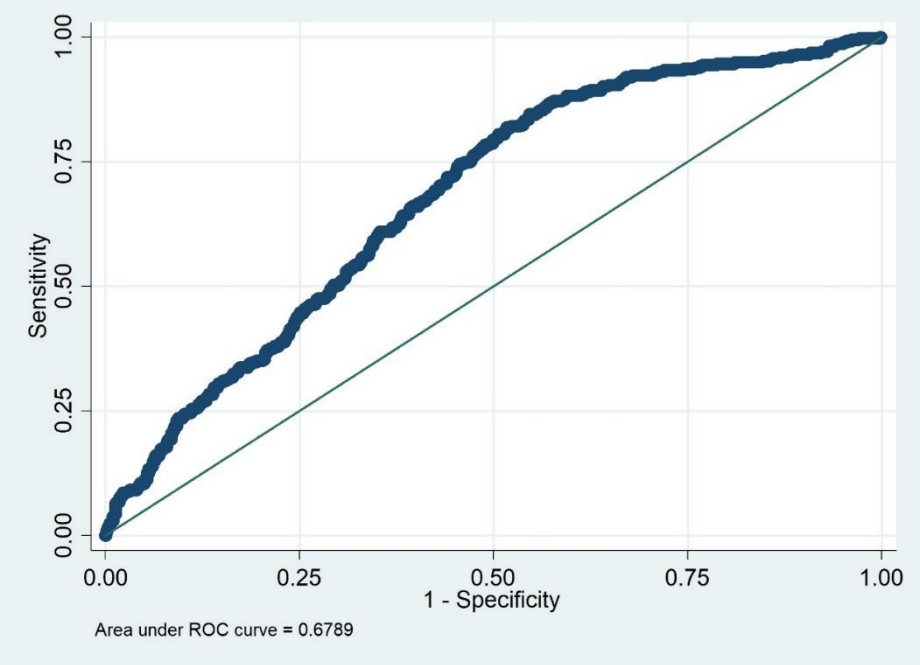

Figure 5-1: ROC curve for successful completion validation from NHS-GCWMS medium-term 5% weight loss.

5.4.3 NHS-GCWMS medium-term 3% weight loss, considering attendance (scenario 3)

Predictors tested and retained in the prediction model were early weight change (3months – initial) and diabetes medications (Table 5-7). The model results were nearly identical to the model found in NHS-GCMWS (Table 3-27).

In WRAP, more weight loss during 3 months means that the participants were more likely to succeed and achieve 3 % weight loss at 5 years. This was similar to results found in NHS-GCWMS.

In contrast, the definitions of diabetes medication variable in WRAP were different from the NHS-GCWMS (categorised into four groups based on the effect of medication on body weight). In WRAP most participants were not on diabetes medication (few were on diabetes medication), while in NHS-GCWMS most participants were on diabetes medication (few were not on diabetes medication). Regardless, the trend in WRAP was being on diabetes medications were more likely to succeed and to achieve 5 % weight loss at 5 years. Although this was not significant due to the low number of participants being on medications. This trend was similar to NHS-GCWMS, specifically the weight-gaining type of medication group. Using this model, the AUC-ROC is 0.930 and CI is 0.914,0.946 (Figure 5-3).

Table 5-7: An adjusted model for odds ratios of successful completion in the medium-term (attend 3 months visit, 5% weight loss at 3 months & 3% weight loss at 5 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change 3months - initial, per %	0.60	0.54-0.63	< 0.001
Diabetes medications			
No	**Reference**		
Yes	1.77	0.90-3.51	0.10

Criteria for success: attend 3 months visit + achieve 5 % weight loss at 3 months + achieve **3% weight loss** at 5 years.
Outcome variable: non-completers & unsuccessful completers (n=1023) versus successful completers (n=244).
Number of imputations= 10.
N= 1267.

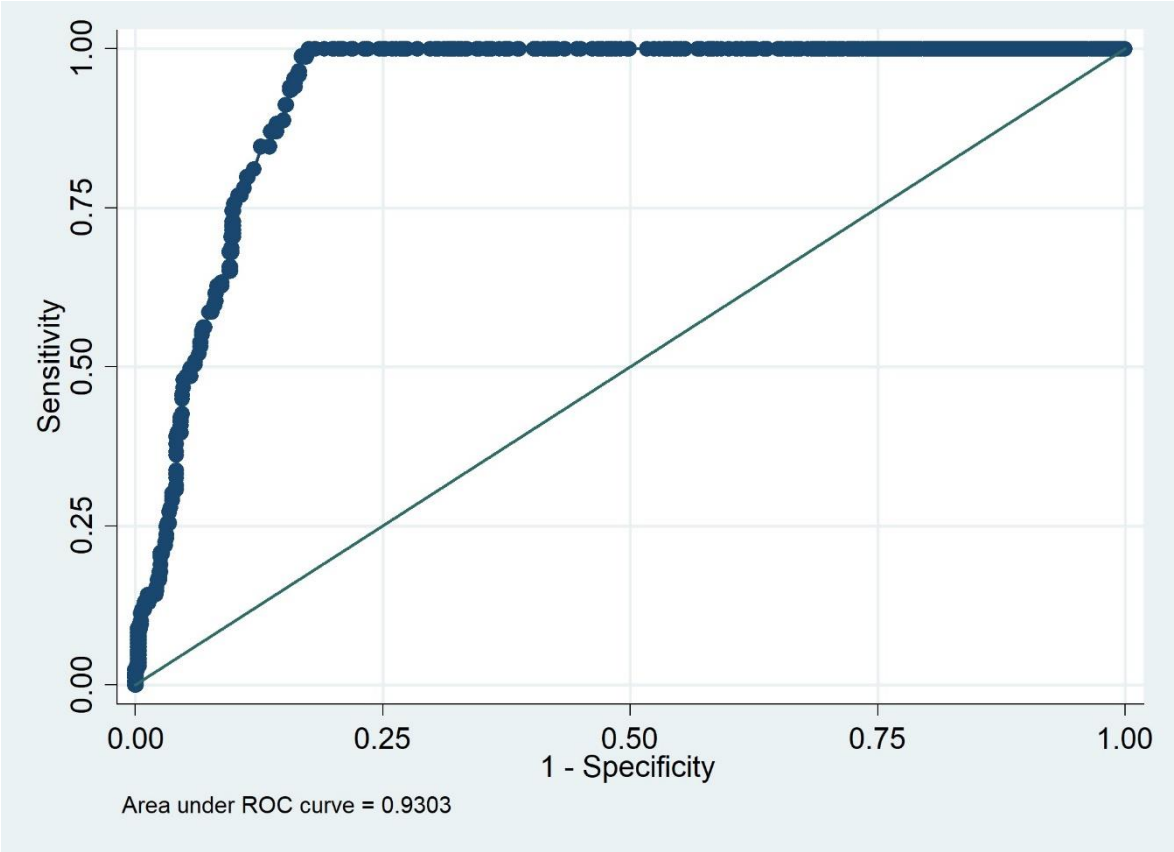

Figure 5-3: ROC curve for successful completion validation from NHS-GCWMS medium-term 3% weight loss, considering attendance.

5.4.4 NHS-GCWMS medium-term 5% weight loss, considering attendance (scenario 4)

Predictors tested and retained in the prediction model were early weight change (3months – initial) and diabetes medications (Table 5-8). The model results were nearly identical to the model found in NHS- GCMWS (Table 3-31).

In WRAP, more weight loss during 3 months means that the participants were more likely to succeed and achieve 5 % weight loss at 5 years. This was similar to results found in NHS-GCWMS. In both models, diabetes medications were not associated with successful weight loss (this was explained in the previous section). Using this model, the AUC-ROC is 0.922 and CI is 0.904,0.939 (Figure 5-4).

Table 5-8: An adjusted model for odds ratios of successful completion in the medium-term (attend 3 months visit, 5% weight loss at 3 months & 5% weight loss at 5 years), 95% confidence intervals and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
% weight change 3months – initial, per %	0.62	0.60-0.66	< 0.001
Diabetes medications			
No	**Reference**		
Yes	1.18	0.52-2.66	0.70

Criteria for success: attend 3 months visit + achieve 5 % weight loss at 3 months + achieve **5% weight loss** at 5 years.
Outcome variable: non-completers & unsuccessful completers (n=1063) versus successful completers(n=204).
Number of imputations= 10.
N= 1267.

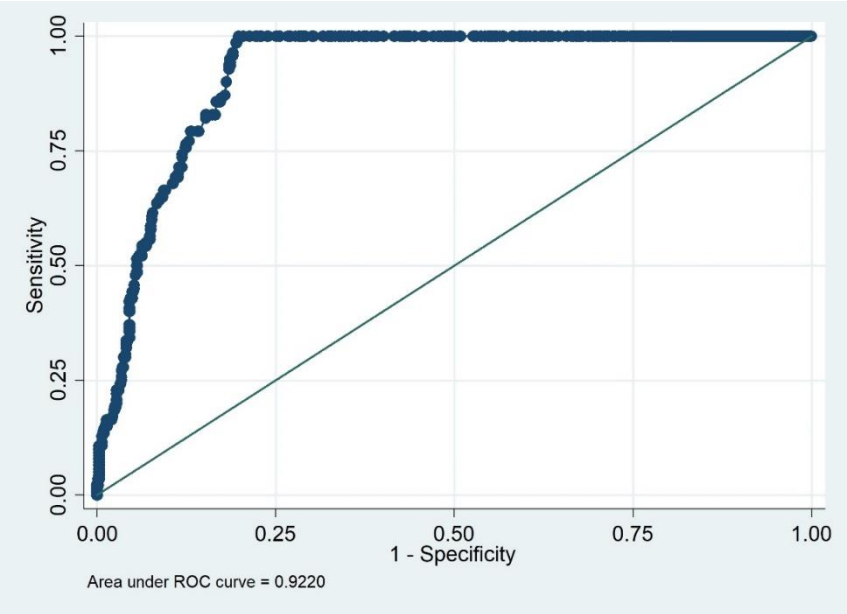

Figure 5-2: ROC curve for successful completion validation from NHS-GCWMS medium-term 5% weight loss, considering attendance.

5.5 Validation of successful completion model from LookAHEAD

Predictors tested and retained in the prediction model were the interaction between sex and treatment arm, age, initial weight, pain/discomfort level, diabetes medications and LDL cholesterol (Table 5-9). The model results were similar to the model found in LookAHEAD in those predictors (interaction between sex and treatment arm, age, initial weight, bodily pain, number of diabetes medications and LDL cholesterol [Table 4-6]).

Specifically, in WRAP, to achieve a 5% weight loss at 5 years, females in the intensive intervention arm of the trial were generally more like to succeed. As this is a different intervention, these ORs are not expected to be identical to LookAHEAD.

In WRAP, model results were nearly identical to the model found in LookAHEAD in age. Older participants were more likely to succeed and achieve a 5% weight loss at 5 years.

In WRAP, pain is a categorical variable and, having extreme pain or discomfort was associated with decreased successful weight loss at 5 years. This was similar to LookAHEAD.

The trend in WRAP for higher initial weight being associated with increase success was similar to LookAHEAD, but it was not formally validated as a predictor of success.

Both models were similar in that higher LDL cholesterol levels decrease successful weight loss. Regardless, this trend was not significant and was not validated in WRAP with the overall trend not reaching formal statistical significance.

Using the model in WRAP, the AUC-ROC is 0.654 and CI is 0.602,0.706 (Figure 5-5).

Table 5-9: An adjusted model with odds ratios, 95% confidence intervals, and p-values for multiple independent variables that predict successful weight loss (5% weight loss at 5 years), identified in LookAHEAD, and validated in WRAP.

Variable	Odds ratio	95% Confidence Interval	P-value
WRAP data (validation model)			
Sex # treatment arm			
Female # BI	**Reference**	0.91-2.65	0.10
Female # CP12	1.56	1.10-3.08	0.03
Female # CP52	1.82	0.34-1.83	0.58
Male # BI	0.80	0.65-2.23	0.55
Male # CP12	1.21	0.88-2.93	0.12
Male # CP52	1.60		
Age, per 5 years	1.10	1.07-1.19	< 0.001
Initial weight, per kg	1.03	0.98-1.07	0.18
Pain/discomfort level			
1	**Reference**		
2	0.84	0.62-1.13	0.25
3	0.42	0.21-0.85	0.01
Diabetes medications			
No	**Reference**		
Yes	0.81	0.50-1.32	0.40
LDL cholesterol, per mmol/L	0.90	0.77-1.05	0.19
LookAHEAD data (from Table 4-6)			
Sex # treatment arm			
Female # Diabetes support & education	**Reference**		
Female # Weight loss intervention	2.30	1.94-2.71	< 0.001
Male # Diabetes support & education	0.70	0.56-0.85	< 0.001
Male # Weight loss intervention	2.15	1.80-2.60	< 0.001
Age, per 5 years	1.11	1.06-1.16	< 0.001
Initial weight, per 5 kg	1.03	1.02-1.06	< 0.001
Bodily pain	0.99	0.98-1.00	0.01
Number of diabetes medications			
1	**Reference**		
0	0.96	0.80-1.18	0.72
2	0.95	0.81-1.10	0.50
≥ 3	0.71	0.60-0.87	< 0.001
LDL cholesterol, per mmol/L	0.90	0.82-0.97	< 0.001

Abbreviation: BI, Brief Intervention; CP12, Commercial Provider 12 weeks; Commercial Provider 52 weeks CP52; LDL, Low-Density Lipoprotein.
Outcome variable (WRAP): unsuccessful completers (n=985) versus successful completers (n=282).
Number of imputations (WRAP)= 10.
N (WRAP)= 1267.
Outcome variable (LookAHEAD): unsuccessful completers versus successful completers.
N (LookAHEAD)= 4667.

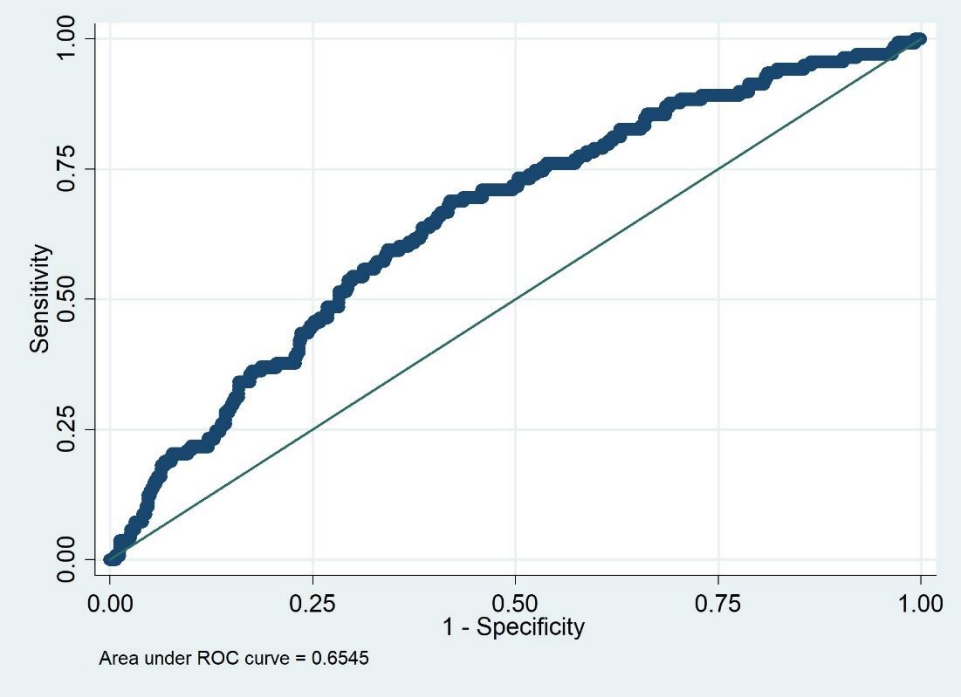

Figure 5-3: ROC curve for successful completion validation of successful completion model from LookAHEAD

When directly comparing the point estimates for initial weight and age in WRAP and LookAHEAD, they are remarkably similar although confidence intervals are wider in WRAP (Figure 5-6).

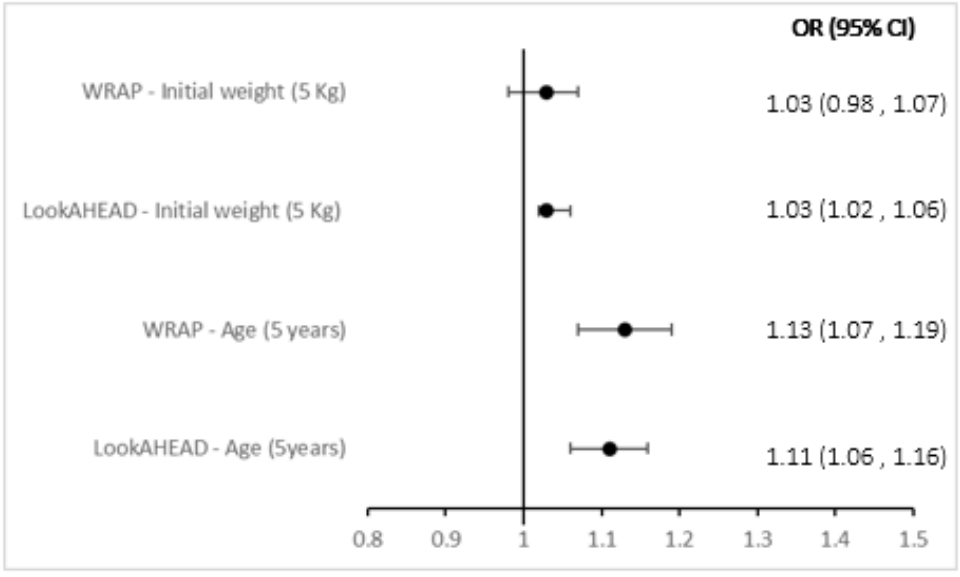

Figure 5-4: A forest plot showing the comparison between the most important variables (age & initial weight) in LookAHEAD and WRAP trials (variables were scaled).

5.6 Discussion

This study is an external validation study using an RCT cohort. This chapter mainly focuses on validating the predictor variables of successful weight loss obtained from previous work done on this thesis, specifically, cohorts from NHS-GCWMS and LookAHEAD. In this chapter, the WRAP dataset was used to externally validate the main predictors from Chapters 3 and 4. In the validation of successful completion models from NHS- GCMWS models were almost identical, while in LookAHEAD, initial weight, diabetes medications and LDL were not validated as a predictor of successful weight loss.

In WRAP the most important variable that was associated with ≥ 5 % weight loss at 5 years in all four scenarios (from NHS-GCWMS) was early weight loss in the programme (3 months – initial). This validated the early weight loss (≈ 4months – initial) predictor variable of successful weight loss of ≥ 5 % weight loss at 3 years found in the NHS-GCWMS chapter. Considering attendance in both models profoundly increases the ROC curve. This is because including completers and non-completers increases the sample size and the difference in weight between non-completers and unsuccessful completers versus successful completers becomes greater.

Early weight loss factor was explored earlier in different studies (JL Unick et al. 2015; Garvin, Hardy, and Xu 2016; Jessica Unick et al. 2015; Postrach et al. 2013). LookAHEAD Research Group were testing the relationship between early weight loss (1 & 2 months) and follow-up weight loss at 4 & 8 years among participants enrolled in the Intensive Lifestyle Intervention (Jessica Unick et al. 2015). Results showed that the odds of achieving at least 5% weight loss at 4 and 8 years were significantly greater among participants losing greater weight in the first and second months of the intervention [1 month "2-4% weight loss" (OR= 1.68, 95% CI: 1.36-2.08), 2 months "3-6% weight loss" (OR= 1.96, 95% CI: 1.55-2.47) and 1 month "2-4% weight loss" (OR= 1.29, 95% CI: 1.04-1.60), 2 months "3-6% weight loss" (OR= 1.23, 95% CI: 0.97-1.55), at 4 and 8 years respectively]. Although study results confirmed what was seen in this chapter, this study was limited to testing associations of successful weight loss. The current study adds to the literature by confirming that there are limited predictors of successful weight loss, but that the best candidates are baseline BMI and early weight loss in the programme. Few

studies have tested early weight loss as a predictor of weight loss success (T. Handjieva-Darlenska et al. 2010a; Teodora Handjieva-Darlenska et al. 2012). A secondary analysis of an RCT study was done to test pre-treatment characteristics and early weight loss as correlates of 10 weeks of weight loss. Results showed that early weight loss can predict 10 weeks of weight loss [early weight loss at 1 week (β= 1.27, p<0.001) and early weight loss at 5 weeks (β= 1.38, p<0.001)]. The results of the study were similar to what was found in this study, regardless, it was lacking validation of early weight loss as a predictor of successful weight loss. The current study advances the results of the previous finding in the literature by validating the weight loss success predictors.

The model in WRAP was seen to be different from the NHS-GCWMS model in that triglycerides showed no significant association with successful weight loss at 5 years while in NHS-GCWMS it did show an association with successful weight loss at 3 years. Although triglyceride was not an important predictor of successful weight loss, a possible explanation is that BMI was much lower in WRAP than in NHS-GCWMS (~33 vs 40). It is known that higher BMI will drive up circulating triglycerides (X. Wang et al. 2021). It may be that lower BMI in WRAP means that triglycerides are not being driven as by those with a very high BMI, therefore modifying the association.

The most important predictor variables to achieve at least 5% weight loss at 4 years and identified in the lookAHEAD chapter were older age and higher initial weight. This was validated here and showed that older participants were more likely to succeed and achieve a 5% weight loss at 5 years. On the other hand, initial weight had a similar trend to LookAHEAD, regardless this was not validated as a predictor of successful weight loss. Several studies were testing age and initial weight variables associated with final weight loss. An RCT testing independent pretreatment factors to achieve 7% weight loss at 6 months showed that being older age (OR= 1.05, p<0.001) and having a higher baseline weight (OR= 1.02, p<0.01) was associated with successful weight loss at the end of the follow-up period (Delahanty et al. 2013a). This trend confirmed what was found in the LookAHEAD and WRAP chapters.

The reason for not validating the main predictors (initial weight, LDL and medications) in WRAP is that WRAP has reduced power compared to the other dataset, which can influence the associations. For the diabetes medications variable, the definitions in both cohorts were different. In LookAHEAD, the number of diabetes medications used by participants were used, while in WRAP whether participants took diabetes medications or not. Despite the differences, similar trends were seen in both models. In WRAP, participants on diabetes medications were more likely to fail to lose 5% of weight at 5 years. Regardless, this was not significant due to the lower numbers of participants being on diabetes medications and the nature of the variable (binary variable).

The pain variable was context-dependent, not generalisable and inconsistent.

5.6.1 Strengths of the study

The follow-up period of the dataset used in this study was long enough to validate both NHS-GCWMS and LookAHEAD cohorts used in this thesis. The broad number of variables tested in the WRAP dataset allows the validation of a different set of predictor variables identified in this thesis. Using an RCT dataset is an advantage for several reasons such as data completeness, high-quality research, a detailed protocol, etc. Regardless, there was missingness in follow-up weight, which was resolved through multiple imputations. Getting almost identical results as found in the NHS-GCWMS chapter is due to the similarities of the intervention used in both cohorts.

5.6.2 Limitations

There were different definitions used for several predictor variables. Thresholds for decision-making (to determine early in the programme who will lose weight to achieve ≥ 5 % weight loss at 5 years) using Sensitivity/Specificity analysis were not possible to be validated in WRAP, due to missing weight data. No validation of very early weight loss in the first 3 sessions.

5.7 Conclusion

The results of this chapter provide strong evidence that baseline weight and early weight loss within the programmes are strong predictors of successful weight loss.

The predictor variables were identified in two separate cohorts (NHS-GCWMS and LookAHEAD) and were validated by an external cohort (WRAP). These results can be advanced and applied in clinical practices.

6 A predictive model for medium-term weight loss in a general population with overweight or obesity – a UK Biobank study

6.1 Introduction

In the earlier chapters, predictor variables were studied that might influence weight loss success in intentional weight loss settings (i.e. clinical studies including RCT and real-world data). However, some people in the general population who are healthy and have overweight or obesity will be engaging in either structured or informal weight-loss interventions, and clinicians and public health decision-makers will not necessarily know who.

A previous systematic review and meta-analysis study explores the prevalence of weight loss and weight maintenance attempts among adults in worldwide epidemiological studies (Santos et al. 2017). Results showed the prevalence of general population adults and ethnic-minority populations who are trying to lose weight were 42% and 44%, respectively. The prevalence of those reporting trying to maintain their weight was 23%. Moreover, geographical, BMI category and sex were important factors in determining the prevalence of weight loss attempts. The prevalence of weight loss attempts was highest among adults in Europe and Central Asia (61.3%), among individuals with overweight or obesity (b= 0.018, $p<0.001$), and among women (b= 0.038, $p<0.001$).

Data from the National Health and Nutrition Examination Survey (2013-2016) was collected to identify weight loss attempts of adults in the United States ((CDC) 2018). Weight-loss attempts were identified in 2 ways: 1) participants were asked to self-report their current weight and if it was at least 10 pounds lower than 1 year ago, participants were asked if their weight loss was intentional or not. Those who reported “yes” to this question were labelled as trying to lose weight. 2) All participants (whether they were identified as intentional or unintentional weight losers of ≥ 10 pounds) were asked a direct question “During the past 12 months, have you tried to lose weight?”. The results showed that 49.1% (approximately one-half) of U.S. adults were trying to lose weight. The percentage of women who are trying to lose weight was higher than men, (56.4%) and (41.7%), respectively. Higher family income and weight status categories increased the percentage of adults trying to lose weight in both men and women, although within each income group and each weight category the percentage of women trying to lose weight was higher than men. In general, the percentages of adults with higher family income, middle family income, and lower family income that were trying to lose

weight were as follows 53.7%, 48.7%, and 42.9%. Moreover, the percentages of the adult in the obesity, overweight and underweight categories who were trying to lose weight were as follows 66.7%, 49%, and 26.5%. The percentage of adults who were trying to lose weight based on their age was lower among older adults (≥60 years) than younger adults (20-39 years) than middle-aged adults (40-59 years), 42.7%, 49.7%, and 52.4%, respectively.

It is important to understand which people are most likely to 'spontaneously' lose weight or actively target weight loss. Identification of predictors of weight loss in the general population may help target weight-loss interventions to those most likely to benefit, even outside of the context of clinical care (chapter 3). For instance, low-intensity interventions might be targeted initially at those most likely to succeed, whereas expensive drug therapy could be targeted at groups that find weight loss more difficult.

There is a lack of studies exploring predictors of weight loss in general population datasets. Most papers that explore predictors of weight loss were clinical and interventional (chapter 2). To our knowledge, this is the first study exploring this area. As was seen in previous chapters using clinical, RCT and real-world data, factors that were identified as predictors of weight loss success were age, sex and initial weight. In this study, the general population cohort (healthy participants) will be used to test the predictivity of these factors to weight loss and whether other factors must be considered.

6.1.1 UK Biobank descriptive information

UK Biobank is a large population-based prospective study that broadly includes middle-aged men and women in the UK, although not nationally representative (Sudlow et al. 2015). This study was conducted with a hypothesis-free design to gain extensive information about the impact of different causes (i.e. genetic and nongenetic factors) that are associated with the disease in both middle and older

ages (UK Biobank 2007; Ollier, Sprosen, and Peakman 2005). The breadth of data is shown in Figure 6-1.

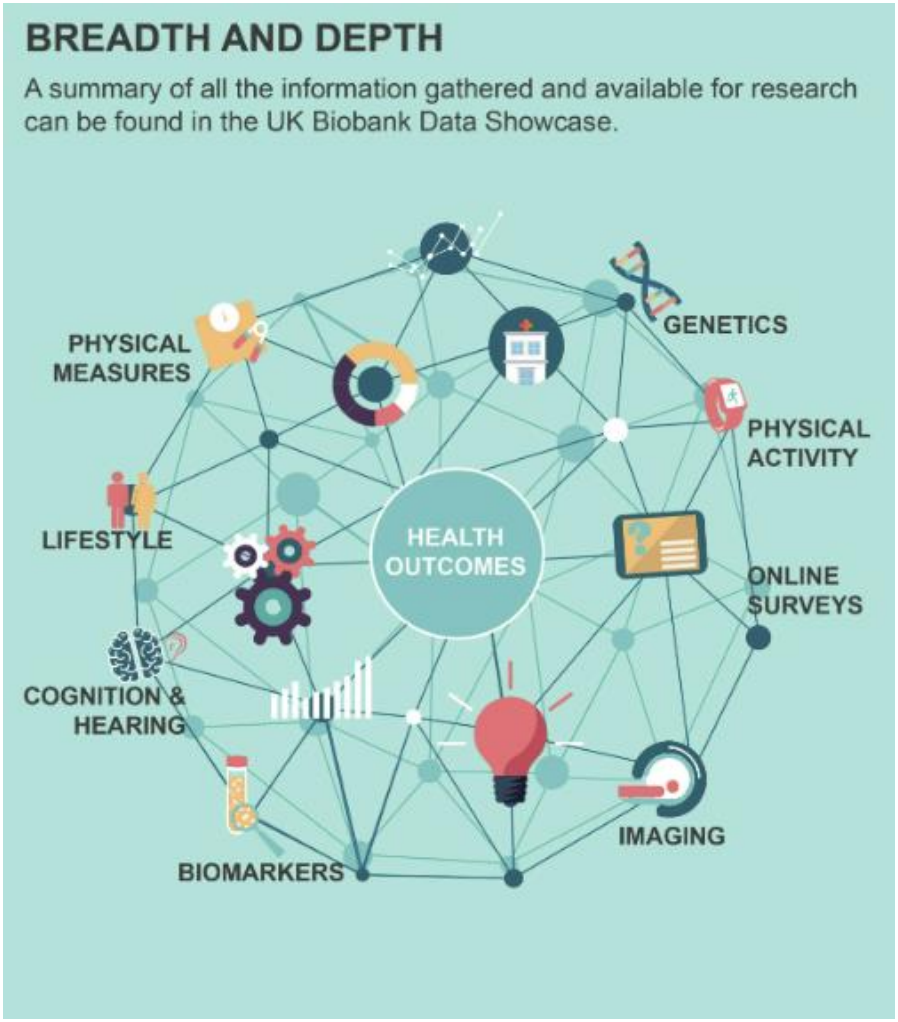

Figure 6-1: Summary of the available information for research in the UK Biobank dataset. Adapted from: https://www.ukbiobank.ac.uk/enable-your-research.

6.1.2 Current study hypothesis

Around 40-50% of adults in the general population report effort to attain weight loss ((CDC) 2018). Therefore, it is hypothesised that substantial (5 %) weight loss is common (>10%) among participants with overweight or obesity in UK Biobank. Sociodemographic, clinical, behavioural, psychological and mental health factors, including specifically baseline weight, are associated with and predict weight loss over 2-5 years among otherwise healthy overweight participants in the large UK Biobank general population study.

6.1.3 Current study aims

In this study, the predictors of medium-term weight loss in healthy overweight participants in a general population were examined using a wide range of exposures available in the UK Biobank study. This includes sociodemographic, clinical, behavioural, psychological and mental health factors.

1. To establish the incidence of 'healthy weight loss' in the absence of known potentially causal comorbidities in UK Biobank over 2-5 years.

2. To identify sociodemographic factors that are associated with successful medium-term weight loss in healthy individuals participating in a general population study.

3. To identify clinical factors that are associated with successful medium-term weight loss in healthy individuals participating in a general population study.

4. To identify behavioural factors that are associated with successful medium-term weight loss in healthy individuals participating in a general population study.

5. To identify psychological and mental health factors that are associated with successful medium-term weight loss in healthy individuals participating in a general population study.

6. To identify sociodemographic, clinical, behavioural, psychological and mental health factors that will predict successful medium-term weight loss in healthy individuals participating in a general population study.

6.2 Methods

The UK Biobank study design and protocol are presented in detail elsewhere (UK Biobank 2007).

6.2.1 UK Biobank protocol

6.2.1.1 Study population

Men and women from the UK general population (n= 502484) were recruited aged 40 to 69.

6.2.1.2 Design

A multicenter prospective cohort study.

6.2.1.3 Ethical approval

The Ethics & Governance Framework (EGF) is assigned by the Medical Research Council, Welcome Trust, and the Department of Health as an independent committee to review, evaluate and give advice for the UK Biobank study (2002-2003).

6.2.1.4 General exclusion/inclusion criteria

Adults in the general population aged 40-69 years. The location of the assessment centres was within 10 miles or takes the participants equivalent time to travel to the centre (Figure 6-2). Accessible transportation for participants either public or private. Assessment centres determination based on identifying groups that were hard to be reached such as minority ethnic groups and socially deprived groups. This was considered to increase the cohort generalisability.

Figure 6-2: UK Biobank assessment centers throughout the UK.

Adapted from https://biobank.ctsu.ox.ac.uk/crystal/exinfo.cgi?src=UKB_centres_map.

6.2.1.5 Testing and piloting

A group of an expert from the UK and internationally were assigned to develop the UK Biobank methods for identifying, inviting, and assessing participants. Following that the feasibility identified methods was tested in two piloting phases between 2005 and 2006. The purpose of this piloting was to test the efficacy of the procedure before starting the actual study recruitment and can be read about here:

6.2.1.6 Recruitment

Potential participants were identified for recruitment based on UK Biobank inclusion criteria (refer to section 6.2.1.4). In the UK, every member of the general population is assigned to a general practitioner, which is organised virtually via the NHS. Therefore, central coordination through the NHS population-based registers was used to identify, invite and recruit eligible participants. This central strategy was used to target the population to take part in the study, thus increasing the rate of participation in the study.

This is the sequence of the recruitment (Figure 6-4)**:**

1. A primary invitation letter with a provisional appointment, participant information leaflet, and a pre-paid postal reply form (for those who choose to confirm their appointment through the mail) was sent by the NHS to the target group via the mail at least 6-8 weeks before the provisional appointment.

2. Potential participants were provided with three response methods to confirm their appointment: a) postal reply. b) Online appointment confirmation. c) Calling the NHS staff to confirm or reschedule the appointment, which requires the NHS to send a confirmation appointment letter and a visit reminder one day before the visit via email, text or postcard. Once the appointment is confirmed, a written confirmation will be sent to participants along with the required information before attending the assessment centre. If participants did not respond within 3 weeks, a re-invitation letter was sent again by the NHS.

3. In case of any appointment cancellation, the assessment centre of the booking system will identify people who have missed the appointment and re-invite them to the study.

A freephone service with the study team is available for each participant to discuss and ask any questions or queries regarding the study.

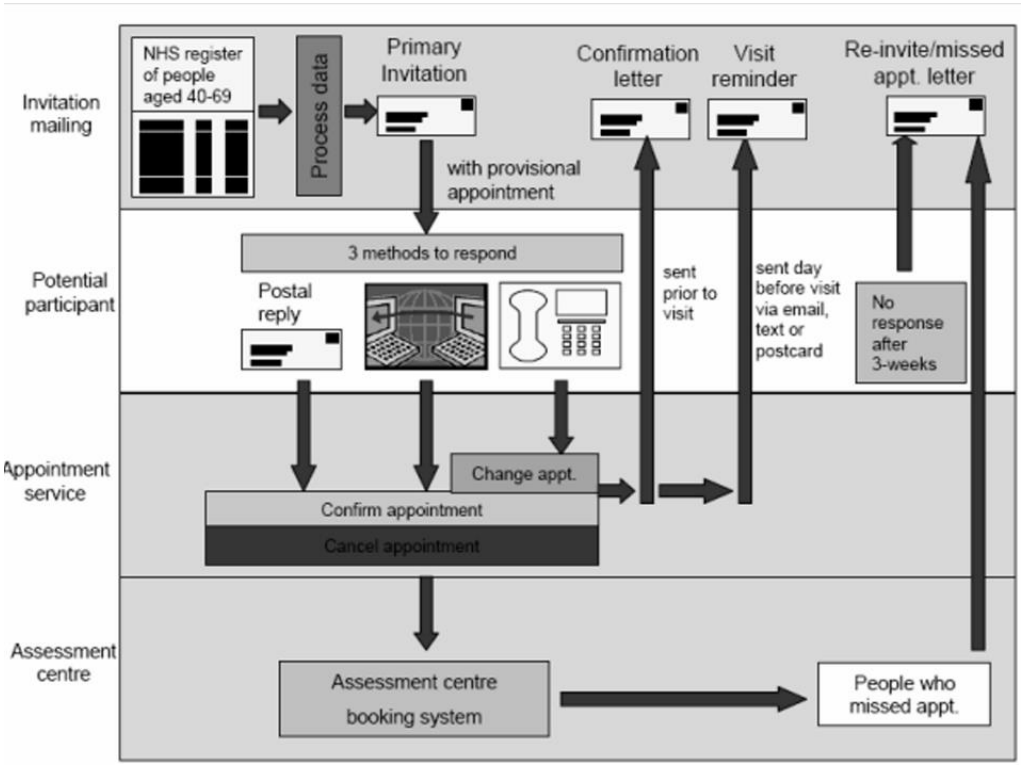

Figure 6-3: Participants' Invitations and recruitments - UK Biobank.
https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0075362.g001

6.2.1.7 Data collection

In the UK Biobank, four time points were identified: 1) Baseline, which is the initial assessment visit (2006-2010) at which participants were recruited and consent is given. 2) First follow-up, which is the first repeat assessment visit (2012-13). At this time point, all measures obtained during the baseline timepoint were repeated. 3) Second follow-up, which is the imaging visit (2014+). 4) Third follow-up, which is the first repeat imaging visit (2019+). For the current study, the first two time points (i.e. baseline and first follow-up) are used.

Baseline assessment:

Twenty-two assessment centres across the UK (i.e. in Scotland, England, and Wales) conducted the baseline assessments, which take an average of 90 minutes to be completed.

Upon agreement of the participants (n= 502484) to take part in the UK Biobank study, participants will attend the assigned assessment centres based on their appointment date and time to collect baseline information, required physical measurements, and biological samples.

The assessment process in the UK Biobank study started early in 2007 and was done in five phases using different stations:

1. **Written consent:** upon arrival and before starting to conduct the study procedures, participants were asked to provide informed consent to take part in the study.

   An existing platform (from a previous clinical trial) was used to develop a computerised record system for the UK Biobank study. This was done to ensure internal consistency, automated checks, easier monitoring, privacy enhancement, and more response to sensitive questions (although prefer not to answer option was available). During the assessment visit at each centre, completed consent forms for each participant were entered immediately into the system.

   Assessment stations were arranged for participants to move through in a series of manners. Stations involved, different measurements, blood/urine

sampling, questionnaires, and interviews. To process over 100 people per day, fourteen UK Biobank staff members were assigned daily. Staff were specifically recruited and trained for the study and including nursing and those with technical experiences.

2. **Touch screen questionnaires:** a self-completed questionnaire was completed by each participant. The majority of the study information was obtained through the touch-screen self-completed questionnaire, which takes about 30 minutes to be completed (if an assistant is required one member of UK Biobank staff was available for each 10-12 participants). (UK Biobank 2021)

3. **Computer-assisted personal interview (CAPI):** a CAPI method was used for any question that requires detailed information. The CAPI method was conducted by a trained nurse and took about 5-10 minutes to be completed. After completing the interview, the blood pressure and pulse were measured twice, readings were connected directly to the computer. The measurements were taken immediately after the interview to ensure that the participants were at rest.

4. **Physical measurements:** standing & sitting height, hip & waist measurement, bio-impedance measurement, hand-grip strength, bone density, and spirometry.

5. **Sample collection of blood, urine and saliva:** a healthcare technician or nurse collected blood samples and urine samples sought. Once samples are collected, they will be immediately transferred to the sample processing area and sample collection box for blood and urine, respectively.

Data and samples collected during each visit and obtained from each station were stored and transferred into a central local server and/or core database at the end of each visit. Before participants go through the stations they were given a Universal Serial Bus (USB) memory to store the information after each station and to act as a participant identifier (since each participant will have one). Those USBs were a temporary storage method used by UK Biobank staff until data were

transferred to the central server. Once transferring data is confirmed, data in the USBs were deleted.

Follow-up:

To obtain detailed information about the participant's medical and other health-related information during follow-up (this includes their past and future information), participants' permission was given during their baseline assessment. This was to allow access to their medical and other health-related records and death and cancer registries. The purpose of this information was to validate and add to what was obtained during the baseline assessment visit. The information included past medical/family history and investigations, medications, cause-specific mortality, and other health events.

The data linkage of participants' information was gained through NHS identifier number, participants' name, date of birth, address, and general practice, which were obtained before inviting potential participants to participate in the study. This reliable mechanism will ensure participants' follow-up and avoid any loss to follow-up.

6.2.2 Current analysis of UK Biobank data

The researcher applied for and was granted UK Biobank approved researcher status on the 7th of January 2021. Consequently, the researcher was granted access to project id 20152 and was able to download the full dataset. https://www.ukbiobank.ac.uk/enable-your-research/apply-for-access

6.2.3 Data handling

Data cleaning of 502484 participants by investigating the datasets for any errors, and edits, applying exclusion criteria, and creating variables based on study requirements was done by two researchers. A large number of variables were investigated and only suitable variables for testing and analysis were presented in this chapter.

In this study, two variables were identified: predictors and medium-term outcomes. Each one is described thoroughly below.

6.2.3.1 Predictors

In this study, predictor variables were chosen based on a literature review done earlier, variables identified in the previous chapter and data availability in UK Biobank.

The time window for predictor variables was identified at the baseline visit. This was set to be the initial assessment visit (2006-2010). The mental health questionnaire variables were completed during an online follow-up assessment between 2016-2017. For the purposes of this study, we assumed the mental health questionnaire responses are representative of the participant's mental health over the whole follow-up period.

- The demographic variables chosen from the UK Biobank study include age, sex, ethnicity, and Townsend deprivation index. The definition of each variable based on this study was:

    - Age (Continuous, years): the age of the participants at the baseline visit. This was derived by calculating the duration between the date of the participant birth and the date of the initial assessment visit.

    - Sex: information obtained from a mixture of self-reported sex and NHS central registry at recruitment. Two identities were explored, which are male and female.

    - Ethnicity: recategorizing the baseline self-reported ethnic groups. A categorical variable that showed the ethnic group of each participant at the baseline visit. Four categories: White (i.e. White, British, Irish, Any other white background), Black (i.e. Caribbean, African, Any other Black background, Black or Black British), South Asian (i.e. Indian, Pakistani, Asian or Asian British, Bangladeshi, Any other Asian background, Chinese) and any other (i.e. White and Black Caribbean, Mixed, White and Black African, White and Asian, Any other mixed background, Other ethnic groups).

    - Townsend deprivation index: this score is a postcode based index that ranks relative socioeconomic deprivation based on census data

and is used clinically in the QRISK CVD score. A score of “0” represents the UK population median, a “negative score” indicates relative affluence, and a “positive score” indicates socio-economic deprivation (Townsend, Phillimore, and Beattie 1988).

- The clinical variables that were chosen from the UK Biobank study and their definitions are described below:

    - Diabetes: a binary variable to identify if the participant had diabetes (type 1 or type 2) at the baseline visit was derived based on the question "Has a doctor ever told you that you have diabetes?". Two categories: yes and no.

    - Initial Height (Continuous, meter): measured by UK Biobank staff at baseline using a Seca 202 device in a standing position (Data-Field 50).

    - Initial weight (Continuous, kg): measured by UK Biobank staff at baseline using a Tanita BC-418 MA body composition analyser (Data-Field 21002).

    - Initial BMI, (Continuous, kg/m^2): during the initial assessment centre visit, each centre calculated BMI by dividing the initial weight by height in metres squared. In case weight or height was not presented, the BMI value was missing.

    - Initial BMI categories: a categorical variable that showed which BMI category each participant fell in at the baseline visit was derived based on initial BMI values. Three categories: pre-obesity or overweight (i.e. BMI≥ 25 and BMI< 30), obesity class I (i.e. BMI≥ 30), and obesity class II (i.e. BMI≥ 35).

    - Weight change: a categorical variable to identify participant weight change at the baseline visit compared to 1 year ago was derived based on the question “Compared with one year ago, has your weight

changed?". Three categories: no-weight about the same, yes-gained weight, yes-lost weight

- Hypertension: participants with a baseline self-reported and nurse interview of cardiovascular diseases were excluded. Therefore, a binary variable to identify if the participant had hypertension at the baseline visit was derived after the exclusion of other diseases. Two categories: yes and no.

- Systolic blood pressure (Continuous, mmHg): mean systolic blood pressure of 3 measurements. Blood pressure was taken by UK Biobank staff up to three times (one of them a few moments apart from the other). This was taken automatically or manually by a trained nurse. This study preferentially used automated measurements, only using manual measurements where automated were not available.

- Diastolic blood pressure (Continuous, mmHg): mean diastolic blood pressure of 3 measurements. Blood pressure was taken by UK Biobank staff up to three times (one of them a few moments apart from the other). This was taken automatically by a trained nurse. This study preferentially used automated measurements, only using manual measurements where automated were not available.

- Seen doctor for nerves, anxiety, tension or depression: a binary variable to identify if the participant had anxiety at the baseline visit was derived based on the question “Have you ever seen a general practitioner (GP) for nerves, anxiety, tension or depression?". Two categories: yes and no.

- Biochemistry variables that were chosen from the UK Biobank study and their definitions are described below:

  UK Biobank adopted a quality-assured protocol for sample handling and storage protocol (Fry et al. 2019). Central (accredited) laboratory received blood and urine samples collected from participants one day after collection via commercial courier. In the central laboratory, samples are

processed and aliquoted to be stored in ultra-low temperature archives. Two separate geographical archives were used to store the aliquoted samples (-80C automated archive and -180C manual liquid nitrogen archive). Low project risk and high-quality methods, which include processes, technology, systems and facilities have been used, followed and implemented in the UK biobank.

- Triglycerides (Continuous, mmol/L): measured by UK Biobank central laboratory after baseline blood sample collection (Fry et al. 2019).

- Plasma glycated haemoglobin (HbA1c) (Continuous, mmol/mol): measured by UK Biobank central laboratory after UK Biobank staff baseline blood sample collection (Tierney et al. 2018).

- The behavioural variables that were chosen from the UK Biobank study and their definitions are described below:

  - Number of days/week walked for more than 10 minutes (Continuous, days): a discrete number of variables to identify how many days per week participants walk for 10 minutes per day at baseline visit. This was derived based on the question "In a typical WEEK, on how many days did you walk for at least 10 minutes at a time? (Include walking that you do at work, travelling to and from work, and for sport or leisure)". In case participants reported numbers <0 or >7, their answers were rejected.

  - Number of days per week doing vigorous activity for more than 10 minutes (Continuous, days): a discrete number variable to identify how many days per week participants do a vigorous type of physical activity for 10 minutes per day at baseline visit. This was derived based on the question "In a typical WEEK, how many days did you do 10 minutes or more of vigorous physical activity? (These are activities that make you sweat or breathe hard such as fast cycling, aerobics and heavy lifting)". In case participants reported numbers <0 or >7, their answers were rejected.

- Usual walking pace: a categorical variable to identify the participant's usual walking pace at the baseline visit. This was derived based on the question "How would you describe your usual walking pace?". Three categories: slow pace (i.e. less than 3 miles per hour), steady average pace (i.e. between 3-4 miles per hour), and brisk pace (i.e. more than 4 miles per hour).

- Frequency of stair climbing in the past 4 weeks: a categorical variable to identify times participants climb stairs per day at the baseline visit. This was derived based on the question "At home, during the last 4 weeks, about how many times a DAY do you climb a flight of stairs? (approx 10 steps)". six categories: none, 1-5 times a day, 6-10 times a day, 11-15 times a day, 16-20 times a day, and more than 20 times a day.

- Basal metabolic rate (Continuous, KiloJoules): the amount of energy (i.e. the number of calories) the body uses to perform the basic life functions. This was obtained at the baseline visit via bioelectric impedance analysis for body composition by Uk Biobank trained staff.

- Time spent watching television (TV) (Continuous, hours): a variable used to identify the time spent by participants watching TV per day at baseline visit. This was derived based on the question "In a typical DAY, how many hours do you spend watching TV? (Put 0 if you do not spend any time doing it)". In case participants reported numbers < 0 or >8 or >24, their answers were rejected.

- Time spent using the computer (Continuous, hours): a variable used to identify the time spent by participants using a computer per day at baseline visit. This was derived based on the question "In a typical DAY, how many hours do you spend using the computer? (Do not include using a computer at work; put 0 if you do not spend any time doing it)". In case participants reported numbers < 0 or >6 or >24, their answers were rejected.

- Time spent driving (Continuous, hours): a variable used to identify the time spent by participants driving per day at baseline visit. This was derived based on the question "In a typical DAY, how many hours do you spend driving?". In case participants reported numbers < 0 or >6 or >24, their answers were rejected.

- Smoking: a categorical variable to identify the participant's smoking status at the baseline visit. Three categories: never, previous, and current.

- Alcohol drinker status: a categorical variable to identify the participant's alcohol drinking status at the baseline visit. Three categories: never, previous, and current.

- The mental health variables that were chosen from the UK Biobank study and their definitions are described below:

  - The job involves heavy manual or physical work: a categorical variable to identify the participant's involvement in heavy work over the whole follow-up period. This was derived based on the question "Does your work involve heavy manual or physical work?". Four categories: Never/rarely, Sometimes, Usually, Always.

  - Weight change during the worst episode of depression: a categorical variable to identify the participant's involvement in heavy work over the whole follow-up period. This was derived based on the question "Did you gain or lose weight without trying, or did you stay about the same weight?". Four categories: Stayed about the same or was on a diet, Gained weight, Lost weight, Both gained and lost some weight during the episode.

  - Psychosis: participants with self-reported mental health problems other than psychosis were excluded. Therefore, a binary variable to identify if the participant had a type of psychosis or psychotic illness over the whole follow-up period was derived after the exclusion of other diseases. Two categories: yes and no.

- Panic attacks: participants with self-reported mental health problems other than panic attacks were excluded. Therefore, a binary variable to identify if the participant had a panic attack over the whole follow-up period was derived after the exclusion of other diseases. Two categories: yes and no.

- Bulimia nervosa: participants with self-reported mental health problems other than bulimia nervosa were excluded. Therefore, a binary variable to identify if the participant had bulimia nervosa over the whole follow-up period was derived after the exclusion of other diseases. Two categories: yes and no.

- Attention-deficit/hyperactivity disorder (ADD_ADHD): participants with self-reported mental health problems other than ADHD were excluded. Therefore, a binary variable to identify if the participant had ADHD over the whole follow-up period was derived after the exclusion of other diseases. Two categories: yes and no.

- Frequency of tiredness/lethargy in the last 2 weeks: a categorical variable to identify the participant's tiredness frequency over the whole follow-up period. This was derived based on the question "Over the last 2 weeks, how often have you been bothered by any of the following problems? [depressive symptoms] Feeling tired or having little energy". Four categories: Not at all, Several days, More than half the days, Nearly every day.

- Guilty feelings: a binary variable to identify if the participants had guilty feelings over the whole follow-up period. This was derived based on the question "Are you often troubled by feelings of guilt?". Two categories: yes and no.

- Miserableness: a binary variable to identify if the participants feel miserable over the whole follow-up period. This was derived based on the question "Do you ever feel 'just miserable' for no reason?". Two categories: yes and no.

- Risk-taking: a binary variable to identify if the participants take risks in life over the whole follow-up period. This was derived based on the question "Would you describe yourself as someone who takes risks?". Two categories: yes and no.

- Sensitivity/hurt feelings: a binary variable to identify if the participants were easily being hurt over the whole follow-up period. This was derived based on the question "Are your feelings easily hurt?". Two categories: yes and no.

- Worrier/anxious feelings: a binary variable to identify if the participants worry over the whole follow-up period. This was derived based on the question "Are you a worrier?". Two categories: yes and no.

- Headaches for 3+ months: a binary variable to identify if the participants had continuous headaches for more than 3 months over the whole follow-up period. This was derived based on the question "Have you had headaches for more than 3 months?". Two categories: yes and no.

- Abdominal pain: participants with a baseline self-reported body pain other than abdominal in the last month were excluded. Therefore, a binary variable to identify if the participant had abdominal body pain that interfered with usual activities over the whole follow-up period was derived after the exclusion of other body part pain. Two categories: yes and no.

- Handling of missing data:

  Demographic, clinical and behavioural: missing values were retained as long as they are less than 250 values. Any variable with ≥250 missing values (except HbA1C and triglycerides) (approx. 1% of those with repeated measurements) was omitted from testing and analysis to achieve a complete case analysis. Any responses with an answer of “don't know” or “prefer not to answer” were set to missing.

Mental health: missing values were retained without any exclusion since few participants participate in the mental health questionnaires. A complete case analysis would substantially reduce power.

6.2.3.2 Outcome

Medium-term:

The time window for medium-term outcome variables was identified to be 4.4 years (IQR= 2-7 years) following baseline (i.e. initial assessment visit (2006-2010)).

Weight change: is the amount of weight lost (in percent) at 4.4 years from baseline weight (i.e. initial weight). This was calculated by subtracting the follow-up weight from the baseline weight.

The cut-off point for the weight change was set to be 5%. Therefore, two groups were created: 1) Weight loss: those who lost ≥ 5% from the baseline body weight at 4.4 years. 2) Weight maintenance/gain, those who lost < 5% from the baseline body weight at 4.4 years.

Any participant with missing values found in the two measures of weight (i.e. the initial weight and the follow-up weight) was excluded from the analysis; this was most of the baseline cohort since only around 20,000 participants attended the second visit.

6.2.3.3 Current study exclusion/inclusion criteria

Any participants with a baseline BMI of less than 25 kg/m^2 were excluded. Given the low degree of missingness (no variable with >250 missing values included), we conducted a complete case analysis in UK Biobank. Any participants who died within 1 year from follow-up weight were excluded. This is because people at the end of life (knowingly or unknowingly) may experience unintentional weight loss, the pathology of which is distinct from intentional weight loss (Iliodromiti et al. 2018).

Severe health conditions that can lead to unintentional weight loss at any time point (including vascular disease and heart conditions, any cancer, etc.) were excluded. Please refer to the flow chart in the result section (Figure 6 6).

6.2.4 Statistical analysis

A test of normality was done using a normal probability plot. Accordingly, a descriptive statistics table for each predictor variable was presented as Mean ± Standard Deviation (SD) (continuous variables & normally distributed data), presented as Median & Interquartile range (IQR) (continuous variables & skewed data), and presented as frequencies (n) and percentages (%) (categorical variables). Then, the test of association between the predictor variables and the outcome of interest was done by formally testing the null hypothesis of no association. This was done through an independent t-test (continuous variables with normally distributed data), a Rank sum test (continuous variables with skewed distribution), and a Chi-square test (categorical variables). A value of $p \leq 0.05$ was considered a nominally statistically significant difference.

Binary logistic regression analysis (a simple and multiple regression model) was used to estimate the strength of the association between predictor variables and weight loss. This was done by calculating the measure of association (i.e. odds ratio (OR)) and the statistical significance (i.e. 95% confidence interval (CI) and p-value). A null/empty model including only the outcome of interest was used where every single predictor variable was added to it at a time to check if it improved the model fit. For continuous predictor variables, these exposures were added to the model using a natural (untransformed scale). The reference group for binary variables was the “zero” category and for categorical variables was the most frequent category. A value of $p \leq 0.05$ was considered a nominally statistically significant difference.

Multiple logistic regression modelling for all the accepted predictor variables from simple logistic regression with a weight loss was conducted. The model fit was optimised using model selection criteria; i.e. Akaike's Information Criteria (AIC) was improved by at least 5 units (Stone 1977). Since there were many predictor variables, this procedure was conducted in sequence to choose the final model: 1) Interactions between 3 main variables were tested (age, sex, and initial weight)

and no interactions were observed. Interactions between the other 3 main variables were tested (age, sex, and initial BMI) and an interaction was observed between sex and BMI. Therefore, two reference models were developed. The first, contained age, sex and initial weight, and the second, contained age, sex and initial BMI, as well as the sex/BMI interaction. Therefore, model development was based on adding predictive variables to these two reference models.

There were missing values in triglycerides and HbA1C variables, therefore, a nested model was tested to determine whether missing values affected the model fit; it did not.

All variables identified as associated with weight loss in Table 6-3 were tested for inclusion into the reference models. The change in AIC was used to check for improvement in model fit (at least 5 units change). The predictor variable that changed the AIC the most was entered into the model preferentially. This was repeated until no predictor changed the AIC. Interactions were then tested between predictor variables within the final models. In the first reference model containing initial weight, an interaction was seen between alcohol drinker status*age, time spent driving*sex, and HbA1c*sex. Testing whether the inclusion of the interaction improved model fit, only the interaction between time spent driving*sex improved model fit via the AIC. In the second reference model containing the initial BMI, an interaction was seen between sex*initial BMI, and time spent driving*sex. Testing whether the inclusion of the interaction improved model fit, none was seen improving model fit via the AIC.

Area Under the Curve – Receiver Operating Characteristics Curve (AUC-ROC) was used to estimate/predict how each predictor variable affects the outcome of interest (i.e. Weight loss).

Mental health work:

This was an exploratory section given the high degree of missingness, A descriptive table was developed after testing all available mental health variables. Only variables that showed a significant prediction of the outcome of interest were included in the table.

STATA-SE software version 15.0 was used in the cleaning & analysis of data.

6.2.5 Power calculation

Assuming a sample size of 8000 participants from the initial screen of the available data and a weight loss rate of 12.5%, an estimation of 84% power was used to detect 5% fewer women experiencing weight loss than men assuming that 55% of the weight maintenance/gain group were women. Generically, 85% power was also used to detect a binary exposure associated with weight loss outcome with an odds ratio of 1.28. For the continuous variable BMI assuming a mean BMI of 29 and a standard deviation of 5, 84% power was there to detect if a 0.5 kg/m^2 increase in BMI was associated with weight loss weight loss.

6.3 Results

6.3.1 Patients Selection

A total of 502484 participants were available in the UK Biobank database. Of 12651 participants with baseline BMI ≥25 and paired measurements at the follow-up were available and a further 3629 participants were excluded due to severe illnesses. Further, eight participants were excluded due to missing repeated measures since participants died within 1 year of the follow-up. In order to get complete data, any participants with missing values in the predictor variables were excluded; therefore 920 participants were omitted. A final of 8094 otherwise healthy participants with complete data was included (Figure 6-6).

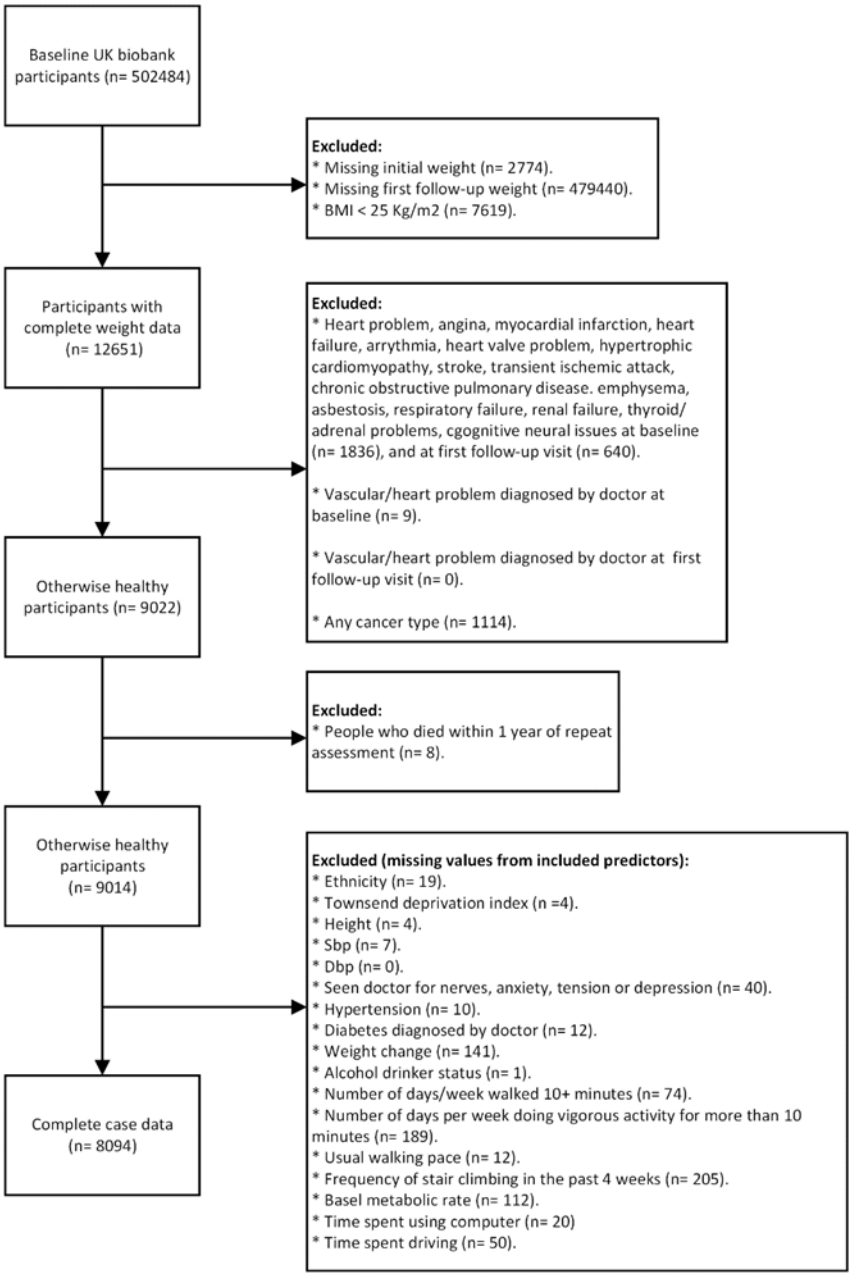

Figure 6-4: Flow chart showing the selected study population.

6.3.2 Descriptive statistics – Complete cohort

Table 6-1 shows the baseline characteristics of the whole cohort. The mean age of the participants was 56.6 years (SD= 7.35 years) and 41.9% were female (n=3393). Participants were mostly from the white ethnic group (98.0%, n=7931). Townsend deprivation index indicates that participants were relatively affluent and the median score was -2.71 (IQR= -3.95, -0.77).

The baseline clinical variables showed that 4.6% of participants were diagnosed with diabetes (n= 371). The median BMI was 28.1 kg/m^2 (IQR= 26.5 – 30.6), most participants fall in overweight category (70.3%, n= 5689), less frequent in obesity class I category (22.7%, n= 1839), and few in obesity class II category (7.0%, n= 566). Based on the weight change variable, 55.1% of the participant reported that the weight change at the baseline visit was about the same when compared to 1 year ago, 29.1% gained weight, and 15.8% lost weight. The median HbA1c was 35.1 mmol/mol (IQR= 32.7 – 37.6). The mean blood pressure was: SBP 139.8 mmHg (SD= 17.3 mmHg) and DBP 83.8 mmHg (SD= 9.4 mmHg). The median triglycerides was 1.66 mmol/L (IQR= 1.18 - 2.33). No anxiety was reported in 73.1% of the participant at the baseline visit.

Participants' smoking status at the baseline visit was as follows: never smoked (57.8%, n= 4677), previous smoker (36.5%, n= 2952), and current smoker (5.7%, n= 465). Participants' alcohol drinking status at the baseline visit was as follows: never drink alcohol (2.3%, n= 187), previous alcohol drinker (2.2%, n= 177), and current alcohol drinker (95.5%, n= 7730).

The psychological variables (i.e. mental health) were not presented in the main result tables, since the mental health variables were over the whole follow-up period and not at baseline. An Exploratory table containing important mental health variables explored in this study is presented in Table 6-8.

Table 6-1: Descriptive statistics for the overall cohort.

Variable	All (n=8094)	
Demographic:		
Age, years	56.6 ± 7.35	(n=8094)
Sex, n (%)		(n=8094)
Female	3393 (41.9%)	
Male	4701 (58.1%)	
Ethnicity, n (%)		(n=8094)
White	7931 (98.0%)	
Black	46 (0.6%)	
South Asian	52 (0.6%)	
Any other	65 (0.8%)	
Townsend deprivation index	-2.71 (-3.95 , -0.77)	(n=8094)
Clinical		
Diabetes, n (%)	371 (4.6%)	(n=8094)
Initial Height, m	170.33 ± 9.24	(n=8094)
Initial weight, kg	84.5 ± 13.3	(n=8094)
Initial BMI, kg/m^2	28.1 (26.5 - 30.6)	(n=8094)
Initial BMI categories, n (%)		(n=8094)
Pre-obesity or overweight	5689 (70.3%)	
Obesity class I	1839 (22.7%)	
Obesity class II	566 (7.0%)	
Weight change, n (%)		(n=8094)
No-weight about the same	4458 (55.1%)	
Yes-gained weight	2357 (29.1%)	
Yes - lost weight	1279 (15.8%)	
Hypertension, n (%)	2179 (26.9%)	(n=8094)
HbA1c, mmol/mol	35.1 (32.7 - 37.6)	(n=7567)
Systolic blood pressure, mmHg	139.8 ± 17.3	(n=8094)
Diastolic blood pressure, mmHg	83.8 ± 9.4	(n=8094)
Triglycerides, mmol/L	1.66 (1.18 - 2.33)	(n=7697)
Seen doctor for nerves, anxiety, tension or depression, n (%)	2179 (26.9%)	(n=8094)
Behavioural:		
Number of days/week walked 10+ minutes, days	6.00 (4.00 - 7.00)	(n=8094)
Number of days per week doing vigorous activity 10+ minutes, days	1.00 (0.00 - 3.00)	(n=8094)
Usual walking pace, n (%)		(n=8094)
Slow pace	365 (4.5%)	
Steady average pace	4459 (55.1%)	
Brisk pace	3270 (40.4%)	
Frequency of stair climbing in the past 4 weeks, n (%)		(n=8094)
None	541 (6.7%)	
1-5 times a day	1485 (18.3%)	
6-10 times a day	3162 (39.1%)	
11-15 times a day	1678 (20.7%)	
16-20 times a day	705 (8.7%)	
More than 20 times a day	523 (6.5%)	
Basal metabolic rate, KiloJoules	7121 ± 1324	(n=8094)
Time spent watching television (TV), hrs	2.00 (2.00 - 3.00)	(n=8094)
Time spent using computer, hrs	1.00 (0.50 - 2.00)	(n=8094)
Time spent driving, hrs	1.00 (0.50 - 1.00)	(n=8094)
Smoking, n (%)		(n=8094)
Never	4677 (57.8%)	
Previous	2952 (36.5%)	

Current	465 (5.7%)	
Alcohol drinker status, n (%)		(n=8094)
Never	187 (2.3%)	
Previous	177 (2.2%)	
Current	7730 (95.5%)	

Abbreviations: BMI, Body Mass Index; HbA1c, glycated haemoglobin. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).

6.3.3 Descriptive statistics – by medium-term outcome status

Over the follow-up (median 4.4 years) 19.7% of the cohort lost 5% of their body weight. Table 6-2 shows the baseline characteristics by weight loss status. The weight loss group were approximately half a year younger than the weight maintenance/gain. The sex variable reveals that the weight loss group are more likely to be female (51.5%).

The weight loss group were 1.4 cm shorter than weight maintenance/gain. The weight loss group were approximately 2 Kg heavier in weight and had around 1 kg/m^2 higher BMI than weight maintenance/gain. Both comparison groups were more likely to be in the overweight category, although weight loss was less likely to be in the overweight category. Both comparison groups were more likely to be in about the same weight at the baseline visit when compared to 1 year ago, although weight loss was less likely to be in the same weight. The weight loss group had slightly higher HbA1c than weight maintenance/gain (0.3 mmol/mol higher). The weight loss group were 1.2 mmHg and 1.3 mmHg higher in SBP and DBP, respectively than weight maintenance/gain. The weight loss group had 6 mmol/L higher triglycerides than weight maintenance/gain. Anxiety was fairly common in the cohort with around a third of participants reporting anxiety overall but anxiety was more common in the weight loss group.

The number of days per week weight loss group walks for 10 minutes per day was less than weight maintenance/gain (1 day less). The number of days per week the weight loss group do vigorous activity for 10 minutes per day was less than weight maintenance/gain. The weight loss group had a lower basal metabolic rate than weight maintenance/gain. Time spent driving every day was around 10 minutes lower in the weight loss group than weight maintenance/gain. Both comparison groups were more likely to be current alcohol drinkers, although the weight loss group are less likely to be alcohol drinkers (94.5%).

Table 6-2: Characteristics of participants, showing the comparison between the weight maintenance/gain versus the weight loss (5% weight loss at 4.4 years).

Variable	Weight maintained/gained (n=6505)	Weight loss (n=1589)	p-value
Demographic:			
Age, years	56.7 ± 7.35	56.2 ± 7.32	0.01
Sex, n (%)			< 0.001
Female	2575 (39.6%)	818 (51.5%)	
Male	3930 (60.4%)	771 (48.5%)	
Ethnicity, n (%)			0.36
White	6373 (98.0%)	1558 (98.0%)	
Black	37 (0.6%)	9 (0.6%)	
South Asian	46 (0.7%)	6 (0.4%)	
Any other	49 (0.8%)	16 (1.0%)	
Townsend deprivation index	-2.72 (-3.96 , -0.78)	-2.67 (-3.88 , -0.64)	0.27
Clinical			
Diabetes, n (%)	290 (4.5%)	81 (5.1%)	0.27
Initial Height, m	170.6 ± 9.25	169.2 ± 9.14	< 0.001
Initial weight, kg	84.1 ± 12.9	86.0 ± 14.7	< 0.001
Initial BMI, kg/m^2	27.9 (26.3 - 30.3)	28.9 (26.9 - 31.8)	< 0.001
Initial BMI categories, n (%)			< 0.001
Pre-obesity or overweight	4725 (72.6%)	964 (60.7%)	
Obesity class I	1404 (21.6%)	435 (27.4%)	
Obesity class II	376 (5.8%)	190 (12.0%)	
Weight change, n (%)			< 0.001
No-weight about the same	3629 (55.8%)	829 (52.2%)	
Yes-gained weight	1785 (27.4%)	572 (36.0%)	
Yes - lost weight	1091 (16.8%)	188 (11.8%)	
Hypertension, n (%)	1745 (26.8%)	434 (27.3%)	0.69
HbA1c, mmol/mol	35.0 (32.7 - 37.5)	35.3 (33.0 - 38.1)	< 0.001
Systolic blood pressure, mmHg	139.6 ± 17.3	140.8 ± 16.9	0.01
Diastolic blood pressure, mmHg	83.6 ± 9.44	84.9 ± 9.42	< 0.001

Triglycerides, mmol/L	1.64 (1.16 - 2.31)	1.70 (1.21 - 2.43)	< 0.001
Seen doctor for nerves, anxiety, tension or depression, n (%)	2006 (30.8%)	540 (34.0%)	0.01
Behavioural:			
Number of days/week walked 10+ minutes, days	6.00 (4.00 - 7.00)	5.00 (4.00 - 7.00)	0.047
Number of days per week doing vigorous activity 10+ minutes, days	1.79 ± 1.82	1.61 ± 1.77	< 0.001
Usual walking pace, n (%)			0.19
Slow pace	281 (4.3%)	84 (5.3%)	
Steady average pace	3578 (55.0%)	881 (55.4%)	
Brisk pace	2646 (40.7%)	624 (39.3%)	
Frequency of stair climbing in the past 4 weeks, n (%)			0.97
None	438 (6.7%)	103 (6.5%)	
1-5 times a day	1183 (18.2%)	302 (19.0%)	
6-10 times a day	2547 (39.2%)	615 (38.7%)	
11-15 times a day	1345 (20.7%)	333 (21.0%)	
16-20 times a day	570 (8.8%)	135 (8.5%)	
More than 20 times a day	422 (6.5%)	101 (6.4%)	
Basal metabolic rate, KiloJoules	7137 ± 1312	7056 ± 1370	0.03
Time spent watching television (TV), hrs	2.00 (2.00 - 3.00)	3.00 (2.00 - 3.00)	0.48
Time spent using computer, hrs	1.00 (0.50 - 2.00)	1.00 (0.50 - 2.00)	0.58
Time spent driving, hrs	1.17 ± 1.23	1.04 ± 1.08	< 0.001
Smoking, n (%)			0.082
Never	3767 (57.9%)	910 (57.3%)	
Previous	2348 (36.1%)	604 (38.0%)	
Current	390 (6.0%)	75 (4.7%)	
Alcohol drinker status, n (%)			< 0.001
Never	153 (2.4%)	34 (2.1%)	

Previous	123 (1.9%)	54 (3.4%)
Current	6229 (95.8%)	1501 (94.5%)

Abbreviations: BMI, Body Mass Index; HbA1c, glycated haemoglobin. Values are mean ± standard deviation, or median (Interquartile Range 'IQR'), or sample size & percentage (n (%)).
Criteria for success: achieve **5% weight loss** at 4.4 years.
Outcome variable: weight maintenance/gain versus weight loss.
For the variables, the number of days per week doing vigorous activity for more than 10 minutes and time spent driving tests of significance across groups were significant using parametric and non-parametric tests. The median (IQR) did not show the direction of increase therefore data were illustrated using mean +/- SD.

6.3.4 Univariable risk factors for weight loss

Next, simple logistic regression was used to identify exposures associated with weight loss (5% weight loss), compared to those who maintain/gain the weight (Table 6-3). All predictor variables were tested but only ones that showed an association with the outcome of interest were reported in the table.

The variables most strongly associated with outcome were baseline BMI or BMI category and sex. In the sex variable, associated odds of weight loss decreased by 38% in the male group (95% CI: 45,31%, p< 0.001) at 4.4 years when compared to the female group. For every kg/ m^2 increase in BMI, the associated odds of weight loss increased by 10% (95% CI: 6,10%, p< 0.001), and there was a similar weak but positive association with initial weight. In the initial BMI categories variable, associated odds of weight loss increased by 52% in the obesity class I group (95% CI: 33,72%, p< 0.001), and being in the obesity class II group (OR: 2.50, 95% CI: 2.05,3.00, p< 0.001) was almost 3 times higher in being successful at losing weight at 4.4 years when compared to the overweight group.

For every year increase in age, the associated odds of weight loss decreased by 1% (95% CI: 2,1%, p=0.01).

For every mmol/mol increase in HbA1c, associated odds of weight loss increased by 2% (95% CI: 1,3%, p< 0.001). For every 10 mmHg increase in SBP, associated odds of weight loss increased by 4% (95% CI: 0,7%, p=0.01). For every mmHg increase in DBP, associated odds of weight loss increased by 1% (95% CI: 1,2%, p< 0.001). For every mmol/L increase in triglycerides, associated odds of weight loss increased by 10% (95% CI: 5,16%, p< 0.001). In the anxiety variable, associated odds of weight loss increased by 15% in the “yes” group (95% CI: 3,30%, p=0.02) at 4.4 years when compared to the “no” group.

For every unit increase in the number of days/week walked for more than 10+ minutes, the associated odds of weight loss decreased by 3% (95% CI: 6,1%, p=0.03). For every unit increase in the number of days/week doing vigorous activity for more than 10 minutes, the associated odds of weight loss decreased by 6% (95% CI: 8,3%, p<0.001). For every 1000 unit increase in basal metabolic rate, the associated odds of weight loss decreased by 5% (95% CI: 9,1%, p=0.03).

For every hour increase in time spent driving, the associated odds of weight loss decreased by 10% (95% CI: 15,6%, p< 0.001). In the alcohol drinker status variable, associated odds of weight loss increased by 82% in the "previous" group (95% CI: 32,152%, p< 0.001) at 4.4 years when compared to the "current" group.

Table 6-3: Unadjusted models for odds ratios of weight loss in the medium-term, 95% confidence intervals, and p-values for each predictor variable (predictor variables that did not show an association with the outcome of interest were omitted from the table). (5% weight loss at 4.4 years).

Variable	N(n)	Odds ratio	95% Confidence Interval	P-value
Demographic:				
Age, per year	8094	0.99	0.98-0.99	0.01
Sex, n (%)				
Female	3393	**Reference**		
Male	4701	0.62	0.55-0.69	< 0.001
Clinical:				
Initial weight, per kg	8094	1.01	1.00-1.01	< 0.001
Initial BMI, per kg/m^2	8094	1.10	1.06-1.10	< 0.001
Initial BMI categories, n (%)				
Pre-obesity or overweight	4725	**Reference**		
Obesity class I	1404	1.52	1.33-1.72	< 0.001
Obesity class II	376	2.50	2.05-3.00	< 0.001
HbA1c, per mmol/mol	7567	1.02	1.01-1.03	< 0.001
Systolic blood pressure, per 10 mmHg	8094	1.04	1.00-1.07	0.01
Diastolic blood pressure, per mmHg	8094	1.01	1.01-1.02	< 0.001
Triglycerides, per mmol/L	7697	1.10	1.05-1.16	< 0.001
Seen doctor for nerves, anxiety, tension or depression, n (%)				
No	5915	**Reference**		
Yes	2179	1.15	1.03-1.30	0.02
Behavioural:				
Number of days/week walked 10+ minutes, per day	8094	0.97	0.94-0.99	0.03
Number of days per week doing vigorous activity 10+ minutes, per day	8094	0.94	0.92-0.97	< 0.001
Basal metabolic rate, per 1000 KiloJoules	8094	0.95	0.91-0.99	0.03
Time spent driving, per hr	8094	0.90	0.85-0.94	< 0.001
Alcohol drinker status, n (%)				
Current	7730	**Reference**		
Never	187	0.92	0.63-1.34	0.70
Previous	177	1.82	1.32-2.52	< 0.001

Abbreviation: N(n), number of risks (number of events); BMI, Body Mass Index.
Outcome variable: weight maintenance/gain versus weight loss.

6.3.5 Multivariable risk factors for weight loss

6.3.5.1 Initial weight as an important factor

In the first reference model, a priori risk factors for the prediction of weight loss were sex, age and initial weight.

The associated odds of wight loss decreased by 50% (95% CI: 58,46%, p< 0.001) at 4.4 years among males. For every Kg increase in initial weight, the associated odds of weight loss increased by 2% (95% CI: 2,3%, p< 0.001).

Table 6-4: An adjusted model with odds ratios, 95% confidence intervals, and p-values for multiple independent variables at the same time (Baseline model).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	0.99	0.99-1.00	0.21
Sex			
Female	**Reference**		
Male	0.50	0.42-0.54	< 0.001
Initial weight, per kg	1.02	1.02-1.03	< 0.001

Outcome variable: weight maintenance/gain versus weight loss.
N= 8094.

All significant variables in Table 6-3 was tested stepwise for inclusion in the model in Table 6-5 and interactions between all significant predictor variables. The model includes sex, age, initial weight, HbA1c, diastolic blood pressure, triglycerides, time spent driving in females, time spent driving in males, and the categorical variable of alcohol drinker status. The importance of sex and initial weight was stronger than in the unadjusted model. There was an interaction seen between time spent driving and sex, such that males who drove more were more likely to lose weight, whereas females who drove were less likely to lose weight. Using this model, the AUC-ROC is 0.622, CI is 0.606, 0.638 (Figure 6-8).

Table 6-5: An adjusted model with odds ratios, 95% confidence intervals, and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	0.99	0.98-1.00	0.02
Sex			
Female	**Reference**		
Male	0.40	0.33-0.48	< 0.001
Initial weight, per kg	1.02	1.01-1.02	< 0.001
HbA1c, per mmol/mol	1.01	1.00-1.02	< 0.001
Diastolic blood pressure, per mmHg	1.01	1.00-1.02	< 0.001
Triglycerides, per mmol/L	1.11	1.05-1.20	< 0.001
Time spent driving in female	0.91	0.86-0.97	< 0.001
Time spent driving in male	1.20	1.05-1.40	< 0.001
Alcohol drinker status, n (%)			
Current	**Reference**		
Never	0.77	0.51-1.18	0.23
Previous	1.71	1.19-2.44	< 0.001

Outcome variable: weight maintenance/gain versus weight loss.
N= 7248.

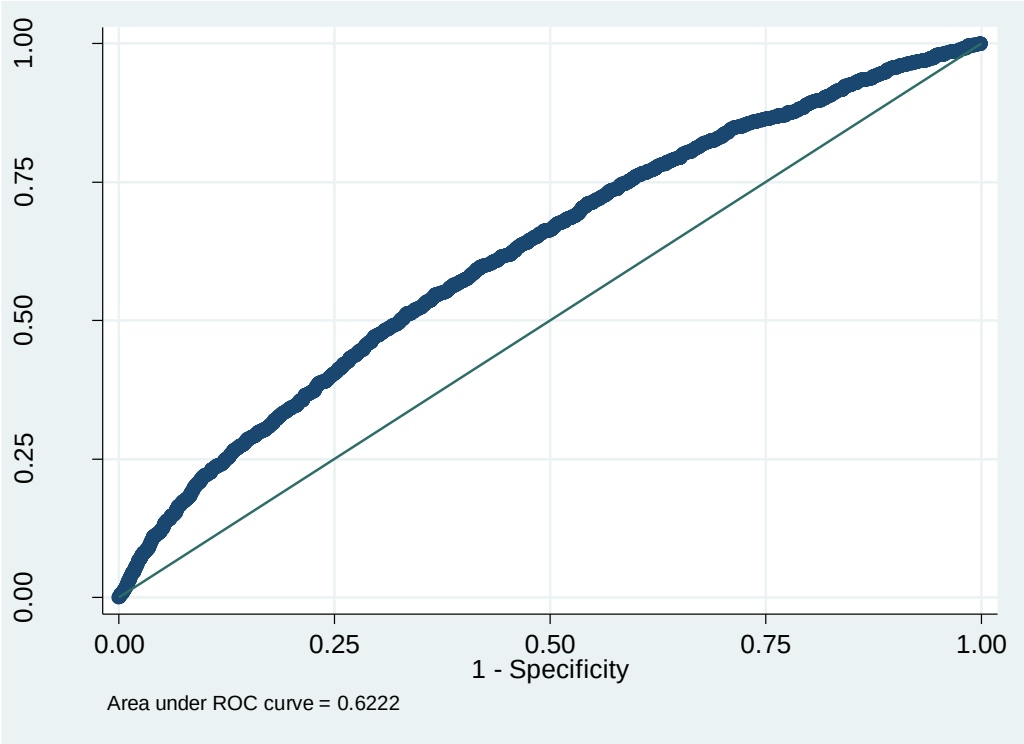

Figure 6-5: ROC curve for successful completion (Model with initial weight).

6.3.5.2 Initial BMI as an important factor

In the second reference model, a priori risk factors for the prediction of weight loss were sex, age and initial BMI.

For every year increase in age, the associated odds of weight loss decreased by 1% (95% CI: 2,1%, p=0.04). The associated odds of weight loss for being male decreased by 36% (95% CI: 43,28%, p< 0.001) at 4.4 years when compared to being female. For every Kg/m^2 increase in initial BMI, the associated odds of weight loss increased by 7% (95% CI: 6,9%, p< 0.001).

Table 6-6: An adjusted model with odds ratios, 95% confidence intervals, and p-values for multiple independent variables at the same time (Baseline model).

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	0.99	0.98-0.99	0.04
Sex			
Female	**Reference**		
Male	0.64	0.57-0.72	< 0.001
Initial BMI, per kg/m^2	1.07	1.06-1.09	< 0.001

Outcome variable: weight maintenance/gain versus weight loss.
N= 8094.

All significant variables in Table 6-3 was tested stepwise for inclusion in the model in Table 6-7 interactions between all significant predictor variables were tested. The model includes sex, age, initial BMI, diastolic blood pressure, triglycerides, and time spent driving. The importance of sex and an initial BMI was slightly better than the unadjusted model. There was no interaction seen between predictor variables. Table 6-7 Using this model, the AUC-ROC is 0.618, CI is 0.602, 0.634 (Figure 6-10).

Table 6-7: An adjusted model with odds ratios, 95% confidence intervals, and p-values for multiple independent variables at the same time.

Variable	Odds ratio	95% Confidence Interval	P-value
Age, per year	0.99	0.98-0.99	0.02
Sex			
Female	**Reference**		
Male	0.61	0.54-0.70	< 0.001
Initial BMI, per kg/m^2	1.06	1.05-1.08	< 0.001
Diastolic blood pressure, per mmHg	1.01	1.00-1.02	< 0.001
Triglycerides, per mmol/L	1.11	1.05-1.18	< 0.001
Time spent driving	0.91	0.86-0.97	< 0.001

Outcome variable: weight maintenance/gain versus weight loss.
N= 7248.

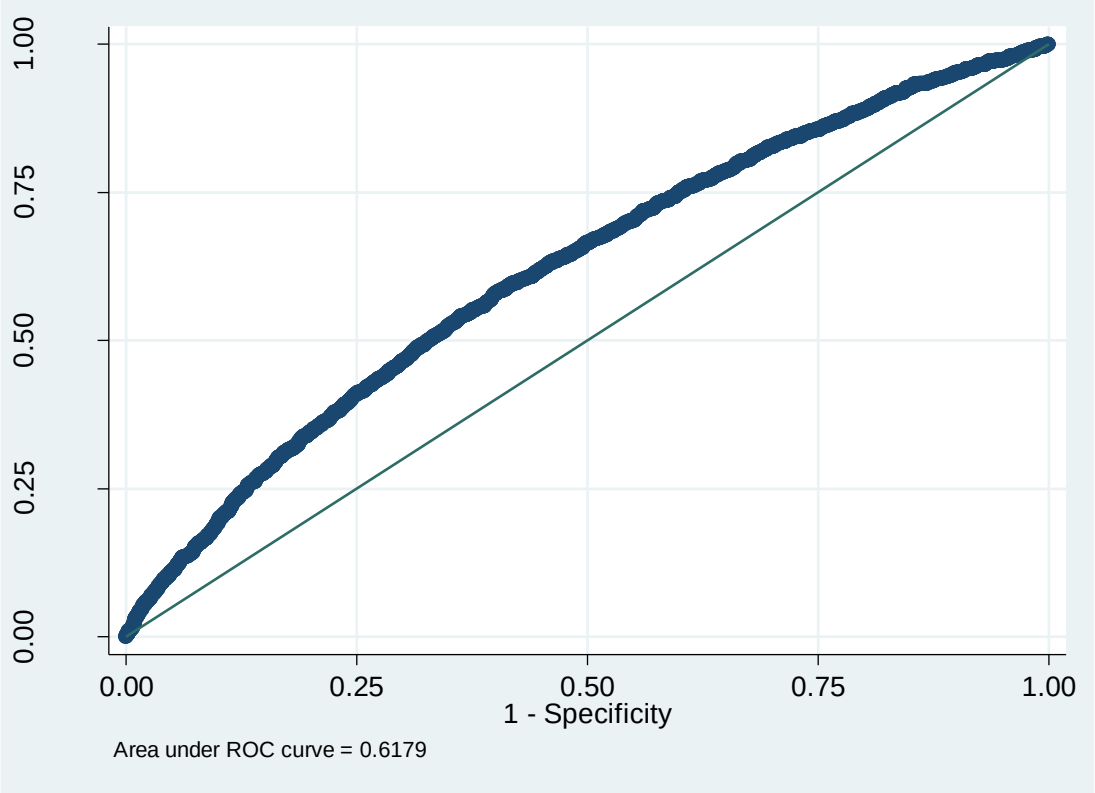

Figure 6-6: ROC curve for successful completion (Model with initial BMI).

6.3.6 Descriptive of mental health exposures by medium-term outcome status

Table 6-8 shows mental health characteristics by weight loss status. Employment in a heavy manual or physical work job was less common in the weight loss group. The weight loss group, perhaps surprisingly, was slightly more likely to report gaining weight during their worst episode of depression than the weight maintenance/gain group. The weight loss group were slightly more likely to report psychosis illnesses, bulimia, or ADHD than the weight maintenance/gain group. Reporting panic attack episodes was less common in the weight loss group. The weight loss group was more likely to have tiredness/lethargy, guilty and miserableness feelings than the weight maintenance/gain. The weight loss group was less likely to take risk in general. The weight loss group was more likely to have sensitivity/hurt anxious feelings than weight maintenance/gain. The weight loss group was more likely to have headaches and abdominal pain than weight maintenance/gain.

Overall, the associations of mental health responses with weight loss were frequently statistically significant, but always modest in strength. As such addition of mental health questions to the prediction model (in the subset with available data for mental health data) did not improve prediction (data not shown).

Table 6-8: Characteristics of participants over the whole follow-up period, showing the comparison between the weight maintenance/gain versus the weight loss (5% weight loss at 4.4 years using mental health variables).

Variable	Weight maintenance/gain (n=6505)	Weight loss (n=1589)	p-value
Mental health:			
Job involves heavy manual or physical work, n (%)			< 0.001
Never/rarely	2845 (69.3%)	736 (74.0%)	
Sometimes	866 (21.1%)	193 (19.4%)	
Usually	229 (5.6%)	42 (4.2%)	
Always	164 (4.0%)	23 (2.3%)	
Weight change during the worst episode of depression, n (%)			0.01
Stayed about the same or was on a diet	838 (43.7%)	198 (38.9%)	
Gained weight	382 (19.9%)	134 (26.3%)	
Lost weight	591 (30.8%)	147 (28.9%)	
Both gained and lost some weight during the episode	108 (5.6%)	30 (5.9%)	
Psychosis, n (%)			0.04
Yes	6 (0.5%)	5 (1.5%)	
No	1253 (99.5%)	323 (98.5%)	
Panic attacks, n (%)			0.03
Yes	215 (17.1%)	40 (12.2%)	
No	1044 (82.9%)	288 (87.8%)	
Bulimia nervosa, n (%)			0.03
Yes	2 (0.2%)	3 (0.9%)	
No	1257 (99.8%)	325 (99.1%)	
ADD_ADHD, n (%)			0.04
Yes	1 (0.1%)	2 (0.6%)	
No	1258 (99.9%)	326 (99.4%)	
Frequency of tiredness/lethargy in last 2 weeks, n (%)			< 0.001
Not at all	3367 (52.6%)	769 (49.2%)	

Several days	2487 (38.9%)	618 (39.6%)	
More than half the days	283 (4.4%)	96 (6.1%)	
Nearly every day	263 (4.1%)	79 (5.1%)	
Guilty feelings, n (%)			< 0.001
Yes	1556 (24.3%)	432 (27.6%)	
No	4848 (75.7%)	1136 (72.4%)	
Miserableness, n (%)			0.04
Yes	2373 (36.9%)	626 (39.7%)	
No	4057 (63.1%)	949 (60.3%)	
Risk-taking, n (%)			< 0.001
Yes	1934 (30.5%)	401 (25.8%)	
No	4411 (69.5%)	1151 (74.2%)	
Sensitivity/hurt feelings, n (%)			0.01
Yes	3081 (48.5%)	810 (52.0%)	
No	3272 (51.5%)	749 (48.0%)	
Worrier / anxious feelings, n (%)			0.03
Yes	3126 (48.9%)	811 (52.0%)	
No	3261 (51.1%)	749 (48.0%)	
Headaches for 3+ months, n (%)			0.01
Yes	483 (41.7%)	156 (49.1%)	
No	675 (58.3%)	162 (50.9%)	
Abdominal pain			0.01
Yes	268 (4.1%)	87 (5.5%)	
No	6237 (95.9%)	1502 (94.5%)	

Values are sample size & percentage (n (%)).
Criteria for success: achieve **5% weight loss** at 4.4 years.
Outcome variable: weight maintenance/gain versus weight loss.

6.4 Discussion

In this chapter, to the best of our knowledge, this is the first data attempted to predict weight loss over the medium term in a general population cohort of healthy people with overweight and obesity. Insights as to who is most likely to lose weight (without a specified, or indeed any, intervention) may allow the targeting of interventions that need it most. It is reported that sex, age, initial BMI, diastolic blood pressure, triglycerides, and time spent driving are predictors of weight loss in the general population. Although, the model strength was moderate with an area under the curve of 0.618.

It is important to be clear that this is not a validation study of predictors of weight loss success among those trying to achieve weight loss (as in previous chapters). Rather, it is a study conducted using a general population cohort of those with overweight (but otherwise healthy) to explore if similar variables predict clinically significant weight loss. Nonetheless, it is interesting that many of the predictor variables we identify are similar to those seen in earlier chapters.

It is common among adults living with overweight or obesity from the general population to have the desire to lose weight, especially women and those with higher BMI. The first observation from this study is that 19.7% of people attain significant weight loss in UK Biobank 'spontaneously'. While in other chapters where participants received an intervention to intentionally lose weight the percentage was 26.5% in GCWMS and 32% in LookAHEAD. This speaks to the fact that weight loss is actually not an unusual phenomena in the general population with overweight or obesity.

An observational study was conducted using a questionnaire sent randomly to the general population (n= 14 126). Men and women participants aged between 30 to 69 years (Molarius, Lindén-Boström, and Karlsson 2020). In this study, individuals with a BMI of ≥25 kg/m^2 were included and divided into 1) those who do not want to lose weight (n =1236), 2) those who want to lose weight but do not believe they need support (n =5484), and 3) those who want to lose weight and believe they need weight loss support (n = 1462). Their findings showed that 69% and 59% of women and men, respectively, reported their desire to lose weight. Older aged

(50-69 years) participants have a higher prevalence than the younger age group (30-49 years). Testing the associations between BMI and the desire to lose weight showed that a higher BMI (≥30 kg/m^2) in reference to normal BMI (18.5 to 24.9 kg/m^2) is the strongest variable among all tested variables (OR: 43.56, 95% CI: 36.45,52.06). Those findings are similar to UK biobank results with the exception of age where in the UK biobank older participants were less likely to lose weight. This study did not report the actual weight loss, but the participants desire to lose weight.

One cross-sectional, non-interventional, descriptive study was conducted to identify the perceptions, attitudes and behaviours of people with obesity and healthcare professionals (Caterson et al. 2019). Findings showed that people living with obesity have the motivation to lose weight. In contrast, health care professionals report a barrier with patients living with obesity due to little interest of patients in weight management.

It is clear from this study and other studies in the literature that a large proportion of people from the general population lost weight and have the desire to lose weight. A large number of people have the desire to lose weight without support. Those groups are highly motivated to lose excess body weight and are willing to adhere to general preventive activities (Caterson et al. 2019; Molarius, Lindén-Boström, and Karlsson 2020). In this chapter, the information on whether participants are engaged in a weight loss programme or not is missing. Therefore, participants maybe are engaged and losing weight because of the weight loss programme.

Secondly, the strongest and most consistent variables for predicting weight loss were (sex, age and initial BMI) which is very similar to variables seen in chapters 3 and 4.

In chapter 3, the short-term models (Table 3-11 & Table 3-12) age was forced into the final model although it was not significant (the direction was similar to UK biobank). The medium-term models (Table 3-18, Table 3-19 & Table 3-22, Table 3-23) showed that initial BMI was a predictor of successful weight loss at 3 years.

Sex was not associated with successful weight loss and this was different from the UK biobank chapter.

In chapter 4, age per 5 years (OR: 1.11, 95% CI: 1.06,1.16, p< 0.001) and initial weight per 5 kg (OR:1.03, 95% CI: 1.02-1.06, p< 0.001) were associated with an increasing successful completion. Whereas being male decrease the chance for successful completion at 4 years when compared to being female (OR: 0.83, 95% CI: 0.72-0.95, p<0.001).

Here, triglycerides were a predictor of weight loss at 4.4 years (OR: 1.11, 95% CI: 1.05,1.18, p<0.001). The trend was similar to chapter 3 where triglycerides were seen as a predictor of successful weight loss at 3 years (OR: 1.12, 95% CI: 1.02,1.23, p<0.001) (Table 3-18 & Table 3-19).

In general, comparing the characteristics of the cohorts, UK biobank participants were 1.2 and 2.3 years younger than NHS GG&C and LookAHEAD, respectively. The percentage of female participants was approximately 20% lower in UK biobank than in NHS GG&C and LookAHEAD. The dominant ethnic group was white participants, although lookAHEAD had the lowest percentage. UK biobank was mostly not diagnosed with T2DM while in NHS GG&C and LookAHEAD, they have diabetes with relatively the same duration.

Having an initial weight within the final model in this study showed that baseline predictor factors associated with people being successful in the general population whether they were undertaking weight loss programmes or not are younger age, being female, higher initial weight, higher HbA1c, higher diastolic blood pressure, higher triglycerides level, less time spent driving in female, more time spent driving in male, and being a previous alcohol drinker.

A stronger model was obtained when the initial BMI was added to the final model. Findings showed that baseline predictor factors associated with people being successful in the general population whether they were undertaking weight loss programmes or not are younger age, being female, higher initial BMI, higher diastolic blood pressure, higher triglycerides level, less time spent driving in both males and females.

The effect of time spent driving was different when added to the weight model and BMI model. In the weight model, time spent driving was influenced by sex, while in the BMI model, sex did not have an influence. One possible explanation for longer time spent driving being associated with reduced odds of weight loss is through sedentary behaviours and occupations making weight loss difficult. The model that contains weight alone is complicated by sex differences in weight, but this effect is simplified in the model containing baseline BMI (Deforche et al. 2015; Mackay et al. 2019).

Little is known about the mental health of people living with overweight or obesity and its association with weight loss in individuals participating in a general population study. In the present study, the associations between mental health responses and weight loss were statistically significant (although modest in strength and did not improve prediction). An observational study was done using the Swedish national registers (n= 3,550,118) to investigate the relationship between ADHD and eating disorders (Yao et al. 2019). There findings showed that individuals with ADHD have a higher risk of anorexia nervosa (OR= 2.68, 95% CI= 2.15, 2.86) and bulimia nervosa (OR= 5.01, 95% CI= 4.63, 5.41) when compared to individuals without ADHD. This may be the reason for individuals with ADHD and bulimia nervosa in this chapter lost more weight.

6.4.1 Strength of the study

Using the dataset from UK Biobank is beneficial in having 1) a very large sample size. 2) Long follow-up period. 3) A different set of predictors in the same cohort. 4) A representative age group. 5) Baseline questionnaire and physical measures that are considered extensive. This allows for a comprehensive investigation of predictor variables.

Using the general population cohort further expands our understanding of predictors of weight loss and makes it encouraging to implement those predictor factors in the general population and give weight loss advice based on these predictors. To help in achieving and sustaining the weight loss required for improving the general health of an individual.

Strict inclusion/exclusion criteria are applied to assure a disease-free cohort without unintentional weight loss. Because it was difficult to know if participants who lost weight were undertaking methods to lose weight or if they were losing weight unconsciously.

6.4.2 Limitation

In this study a somewhat arbitrary cut point of 5% weight loss was used, similar to other chapters; a surprisingly large proportion of people achieved such weight loss. However, no data was available to identify those actively trying to lose weight, or what their chosen intervention is. In this study, weight gaining group was not chosen to be studied (this could be a subject for further study). Exploring mental health variables was limited because of the absence of baseline measures, and the questionnaire was only conducted in a subset of participants after the baseline visit; this may attenuate associations although the direction of attenuation is difficult to predict. UK Biobank is not representative of the general population, and therefore inferences about the UK general population with respect to the prevalence/incidence of weight loss we cannot be made. This is an observational study and any associations cannot be taken as evidence of causality, but are investigated primarily for predictive models.

6.5 Conclusion

In this general population of healthy but overweight middle-aged adults, a fifth of the individuals lost a significant amount of weight ($\geq$ 5%) over 4 years of follow-up. Although no information is known as to why they experienced weight loss and whether the participants engaged in active weight loss, the high proportion achieving weight loss is notable. The relationship between sociodemographic, clinical, behavioural, psychological and mental health factors and weight loss is weak. Out of the factors tested in this chapter, basic demographics (such as age and sex) and initial weight/BMI are the most significant predictors of weight loss. These risk factors were consistent with previous chapters of this thesis, which was done using data from interventional studies.

7 Final discussion

7.1 Chapters summary

This thesis was done to fulfil the aims and objectives presented in sections 1.4 and 1.5. In conclusion, despite the wide range of variables claimed to be important in being associated with successful weight loss, few of the variables (e.g. sociodemographic, clinical, process, behavioural and psychological) was strongly predictive of successful weight loss. The strongest risk factors were baseline BMI (with higher BMI predicting greater success), or early weight loss seen during a weight loss programme. This was true in intervention studies, and in the general population of people with overweight or obesity. A summary of all chapters is presented in Table 7-1.

Table 7-1: Summary of all chapters.

Study name	Sample size	Participants Age	Gender	Diabetes/obesity	Study aim	Timepoints \ Scenario	Predictor of weight loss	Study type & design
NHS GCWMS	1658	57 ± 9	F: 60.0%. M: 40.0%	Have T2DM and living with severe obesity.	To identify sociodemographic, clinical, and process factors that are associated with and will predict successful short and medium-term weight loss in individuals undertaking behavioural weight management programmes.	Short-term (16 wks)	• Greater weight loss between session 3 and session 1.	Real-world data. Longitudinal cohort study.
						Medium-term (3 yrs) - Scenario	1: • Higher initial BMI. • Higher initial triglycerides. • Greater weight loss between session 3 and session 1. • Greater short-term weight loss	
							2: • Higher initial BMI. • Greater weight loss between session 3 and session 1. • Greater short-term weight loss.	
							3: • No drug or mixed type of diabetes drugs. • Greater weight loss between session 3 and session 1. • Greater short-term weight loss.	
							4: • Greater weight loss between session 3 and session 1. • Greater short-term weight loss.	
LookAHEAD	4667	58 ± 6	F: 58.4% M: 41.6%	Have T2DM and living with obesity.	To identify behavioural factors and sociodemographic factors that are associated with and will predict successful medium-term weight loss in individuals undertaking intensive lifestyle intervention programmes.	Medium-term (4 yrs)	• Older age. • Higher initial weight. • Higher body pain. • < 3 of diabetes medications. • Lower LDL cholesterol.	RCT. Longitudinal cohort study.
WRAP	1267	53 ± 13	F: 67.8% M: 32.2%	With or without T2DM. Have overweight or obesity.	• To validate clinical predictive factors that predict successful medium-term weight loss (from NHS-GCWMS cohort). • To validate behavioural, clinical and sociodemographic predictive factors that predict successful medium-term weight loss (from LookAHEAD cohort).	Medium-term (5 yrs)- Scenario	1: • Higher initial BMI. • Greater short-term weight loss.	RCT. Longitudinal cohort study. Validation study.
							2: • Higher initial BMI. • Greater short-term weight loss.	
							3: • Greater short-term weight loss.	
							4: • Greater short-term weight loss.	
						Medium-term (5 yrs) - LookAHEAD	• Older age. • Higher body pain. • No diabetes medications.	
UK Biobank	8094	56 ± 7	F: 41.9%. M: 58.1%	Healthy population. With or without T2DM. Have overweight or obesity.	To identify sociodemographic, clinical, behavioural, psychological and mental health factors that are associated with and will predict successful medium-term weight loss in healthy individuals participating in a general population study.	Medium-term (4.4 yrs)	• Younger age. • Female. • Higher initial weight. • Higher initial Hba1c • Higher DBP. • Higher triglycerides. • Less time spent driving (female). • More time spent driving (male). • Previous alcohol drinker.	General population. Longitudinal cohort study.
							• Younger age. • Female. • Higher initial BMI. • Higher DBP. • Higher triglycerides. • Less time spent driving.	

7.1.1 Chapter 2

The Predictors OF WEight Reduction (POWER) study chapter was the main chapter of this thesis. A literature review was conducted to explore available factors (behavioural and psychological) of successful weight loss. A hypothesis-driven questionnaire (data that are not routinely collected) was built based on this literature review to test baseline factors ability in predicting successful short-term (12 weeks) weight loss in individuals undertaking behavioural weight management programmes (in NHS GG&C region). Unfortunately, this prospective study was not conducted due to COVID-19 but it is ready to implement in the future.

7.1.2 Chapter 3

This prospective study was done to test baseline clinical, sociodemographic and process factors ability to predict successful short (16 weeks) and medium-term (3 years) weight loss in individuals undertaking behavioural weight management programmes (in NHS GG&C region). Previous literature showed a range of predictors of successful weight loss, such as being male (Czeglédi 2017), older age (Delahanty et al. 2013a) and having a high BMI (Latner and Ciao 2014). Regardless, the main finding is that the only predictor variable associated with and predictive of short and medium-term successful weight loss is the early weight loss in the programme. Based on sensitivity and specificity analysis done in this study a threshold of losing at least 0.5% of body weight in the first 3 sessions of the programme is enough to predict successful weight loss of at least 5% of baseline body weight in the short (sensitivity 90.4%, specificity 53.6%, PPV 32.9%, NPV 95.7%) and medium term (sensitivity 89.9%, specificity 49.5%, PPV 19.6%, NPV 97.3%).

7.1.3 Chapter 4

This prospective study was done to compensate for the disruption of chapter 2. Testing of behavioural and psychological factors ability in predicting successful medium-term (4 years) weight loss in individuals undertaking Intensive Lifestyle Intervention, using data from LookAHEAD. Notably, this dataset did not have early weight changes in the programme. The findings showed no associations or

predictive utility of behavioural or psychological factors on medium-term successful weight loss, except for bodily pain (although weak; successful completion decreased when pain decreases). The model includes sex-randomised treatment interaction, basic demographics (age and sex) as well as baseline weight and bodily pain, diabetes medications and LDL cholesterol, with moderate predictive utility (area under the curve of 0.649)

7.1.4 Chapter 5

In this chapter, predictors of successful weight loss identified in Chapter 3 (NHS-GCMWS) and Chapter 4 (LookAHEAD) were externally validated using the RCT cohort from the WRAP dataset. Results from WRAP showed that successful completion models, including early weight loss, were almost identical to the NHS-GCMWS models. This provides strong evidence that early weight loss within the programmes is a strong predictor of successful weight loss and can be applied in clinical settings. In contrast, predictors of successful completion in LookAHEAD were not validated WRAP (discordantly predictive risk factors were initial weight, diabetes medications and LDL).

7.1.5 Chapter 6

To the best of our knowledge, this prospective study was the first to explore and test predictors of weight loss over the medium term in a general population cohort of healthy people with overweight and obesity. In the general population, a fifth of the individuals lost a significant amount of weight (≥5%) spontaneously (i.e. without known specific intervention being implemented). Although interesting, inferences on the reasons for this observation are limited because information on whether individuals lost weight intentionally or unintentionally was missing from the UK biobank dataset. Predictors of weight loss reported in this chapter were sex, age, initial BMI, diastolic blood pressure, triglycerides, and time spent driving are predictors of weight loss in the general population, with moderate predictivity (area under the curve of 0.618).

7.2 Summary of all chapters

As seen from chapter 2, in the literature there was a wide number of important factors reportedly associated with successful weight loss in individuals living with overweight or obesity and undertaking behavioural weight management programmes. Those factors include sociodemographic, clinical, process, behavioural and psychological. Based on our data, most of these factors have moderate predictive utility and they are context dependent (vary from study to study), which makes generalisability difficult. As seen in chapter 4 (data from LookAHEAD) and chapter 5 (data from WRAP) the area under the curve of demographic, behavioural and psychological risk factors are very moderate (AUC-ROC: 0.649 and 0.654, respectively). One of the variables that was repeatedly presented in most of our data was having higher BMI at the baseline level, which predict successful weight loss (reasonably strong association). The only important factor is seen in chapter 3 was early weight loss in an intervention programme. This was also validated in chapter 5 and strongly predicts successful weight loss in the medium-term. Therefore, any clinical programme for weight loss that wants to use precision medicine weight loss to target lifestyle interventions to individual patients probably need a design whereby the service offers the patient the cheapest effective intervention first and then escalates the patient if early weight loss is not observed (Figure 7-1).

7.3 Strength and limitations

The strength of this thesis was, first, the POWER study is a well-designed and hypothesis-driven study with cohort specifications. The questionnaire was thoroughly tested. Implementing this prospective study in the future have several advantages, such as saving time (as preliminary requirements to overcome limitations found in the literature and behavioural weight management programmes were considered), testing a wide range of predictors of successful weight loss in the same study, and minimising loss to follow-up problem faced by each weight management programme.

Second, besides having a comprehensive assessment of clinical sociodemographic and process factors associated with and predictive of weight loss success in

patients attending the behavioural weight management programme. In chapter 3, a novel and a useful criteria to be used in the clinic was found, which is the use of the predictive models thresholds. Moreover, including the non-completers group in our analysis strongly empowered our results to be more relevant to clinical settings where clinicians will be able to identify not only unsuccessful completers but also the non-completers.

Third, the use of an RCT dataset (LookAHEAD) to explore not routinely collected data (behavioural and psychological questionnaire). This allows for more accurate measurements as the RCT are standardised controlled settings.

Fourth, evidence based identified predictors of weight loss success were gained through conducting an external validation, using an RCT dataset (WRAP). This makes the important observations from the real-life NHS GG&C study more generalisable to weight loss interventions in general.

Fifth, to our knowledge, by using a dataset from the UK biobank, this is the first study done to explore predictors of weight loss in the general population. Sixth, long period of follow-up in all chapters allow us to see weight changes over the medium term (3 years or more).

The main limitations of this thesis were that studies were mostly observational (even within the context of RCTs) and any associations cannot be taken as evidence of causality but are investigated primarily for predictive models which are not predicated on causality. Also, a degree of missing weight data (either at the baseline or follow-up) was seen in the used datasets, which was due to loss to follow-up and errors in the reporting; this was dealt with by approaches such as observation carried forward, which may underestimate weight loss and bias results. Generally, multiple testing was not considered in the context of multiple exposures, due to the exploratory nature of the work, and the extent of generalisability of studies conducted in this thesis is generally limited. However, both of these potential issues were overcamed to some extent through external validation. Validating Sensitivity/Specificity or very early weight loss in the first 3 sessions highlighted in chapter 3 was not possible in WRAP.

7.4 Future perspectives and applications

First, although this thesis reports that behavioural and psychological factors in the LookAHEAD chapter were not important predictors, conducting the POWER study in the post-COVID-19 era is highly recommend. The reasons for that are 1) the questionnaire built in this thesis was systematic and purpose designed (not as in LookAHEAD). 2) POWER study can give information on short-term successful weight loss.

Second, it would be important to implement the findings of this thesis in clinical practices to test its efficiency and cost-effectiveness. Allow it to become standard in the treatment of obesity. Clinicians can use the early weight loss predictor to determine early in the programme who will be successful in losing weight in the short and medium terms. They can use a threshold of 0.5% weight loss for both short (sensitivity 90.4%, specificity 53.6%, PPV 32.9%, NPV 95.7%) and medium term (sensitivity 89.9%, specificity 49.5%, PPV 19.6%, NPV 97.3%). By using this threshold the sensitivity and NPV are very strong, and clinicians will be able to identify patients who are not losing weight. At the same time, those patients will be allowed to continue treatment and will be offered alternative interventions (e.g. Counterweight, pharmacological options, bariatric surgery etc.) before the patients disengage from treatment (accelerate depend on settings). This is a cost-effective criterion as this threshold identified a relatively small number of patients. Also, an RCT design study can be conducted to compare the proposed treatment plan after implementation to the standard care to test the efficiency of this intervention (Figure 7-1).

Third, one of the things the UK Biobank data highlights is that a lot of otherwise healthy people with overweight or obesity and manage to lose weight successfully over the medium-term. It would be useful to design a study using the general population to identify the question of why are they losing weight. Weight loss might be attributed to deliberate self-directed weight loss interventions or other reasons such as family bereavement (Mercan, Barlin, and Cebeci 2016), divorce, food poverty (The Food Foundation 2022), or change in job (Hughes and Kumari 2017). As such not all weight loss might reflect advantageous personal circumstances. This data would help us in knowing how important clinical

intervention is as opposed to self-directed weight loss interventions and other circumstances. Difficulties in design such a study might include sample size and long term follow-up to identify changing intentions with respect to weight loss and well as weight measurements. These could be overcome with modern digital solutions.

7.5 Final conclusion

It is recommend that clinicians use the 0.5% threshold criteria of weight loss within 4 weeks of behavioural weight management programmes. This can help people living with overweight and/or to lose clinically significant weight loss of ≥ 5% at the follow-up, which will improve their health status.

After calculating the amount of weight loss between the baseline session and the third, the clinicians can move patients to alternative treatments and more support strategies while still in the programme (e.g. slimming world, Counterweight/DiRECT, GLP-1 or GLP-1/GIP, bariatric surgery.) if they can not achieve a weight loss of 0.5% or more. On the other hand, if patients successfully lost weight in the short and longer term, monitoring the weight and offering re-entry as a rescue intervention if they start to gain weight again (Figure 7-1). In the longer term, an approach such as this needs to be subjected to an RCT (usual care vs. newly developed approach) to compare the effectiveness of the approach.

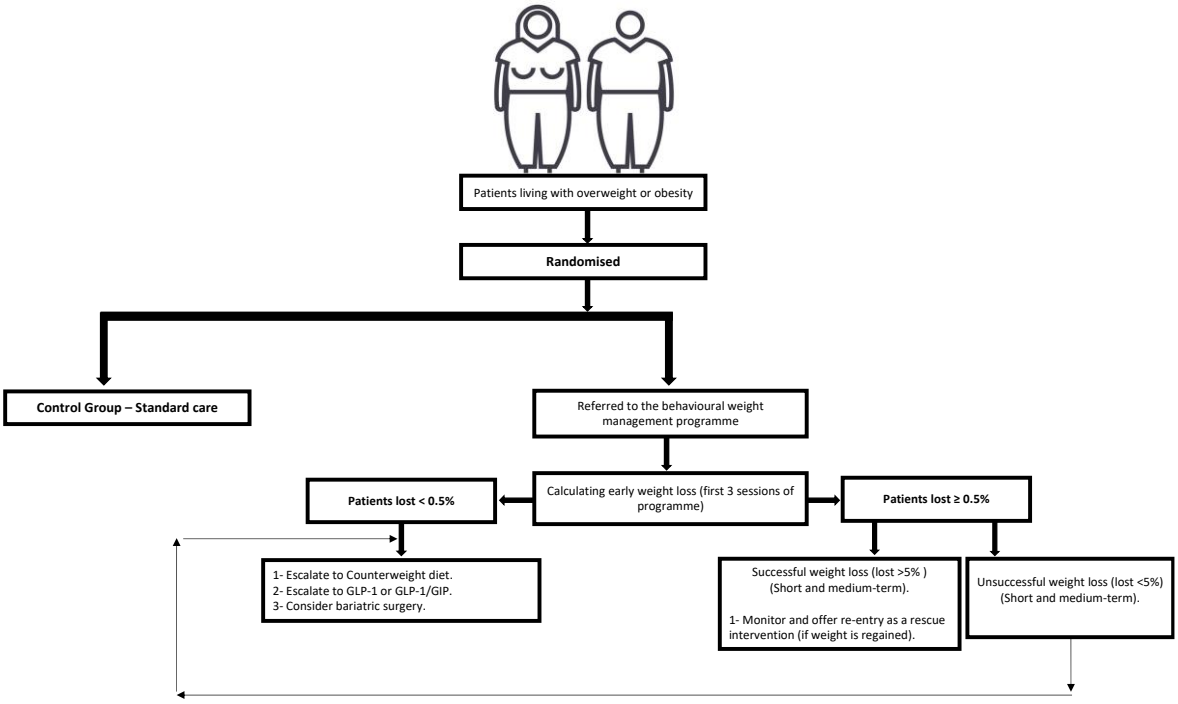

Figure 7-1: New concept for a trial to improve weight loss intervention in clinical practice using an early weight loss threshold.

Appendices

Appendix 1: POWER study Participants information sheet – Consent form – Questionnaire

PARTICIPANT INFORMATION SHEET

Study title: Predictor **O**f **WE**ight **R**eduction **(POWER)**

We are a group of researchers at the University of Glasgow conducting a research study and would like to invite you to take part in. Before you decide it is important for you to understand why the research is being done and what it will involve.

What is the purpose of the study?
In this study we are trying to understand how a person's background, lifestyle, weight history, motivation to lose weight and social support (that are known before starting at Weight Watchers) can help us to predict who will have successful weight loss. This knowledge at the start of the program, will help weight management staff and researchers to know which treatment is more suitable for each client to allow him/her to attain their weight loss goals. So, we are hoping that in future this information will help us in improving the weight management services.

Why have I been invited to take part?
You are about to start attending a weight management programme.

Do I have to take part?
Your participation in this questionnaire is completely voluntary and you are free to take the decision whether you want to participate or not. You can withdraw out of the study at any point of time without giving a reason. Whatever your decision will be, it will not affect your participation or continuation in the weight management program and the standard of care you receive.

What will happen if I take part?
This study has two parts – you can opt to do part 1 alone or parts 1 &2:

Part 1. Questionnaire:

- This should be completed before you reach the end of the first week of the programme and ideally before you attend your first meeting.
- It can be completed online on a secure website (https://webropol.com/s/powerstudy2020) or on paper (upon request).
- This questionnaire asks you about your weight loss history, motivation, attitudes and the support from family and friends that you receive before you begin the Weight Watchers programme.
- You will receive a £10 amazon voucher for completing this.

Part 2. An interview:

- This would be 3-5 weeks after starting your Weight Watchers programme.

- The interviews will take between 60-90 minutes. If you opt in to the interview, additional information will be sent to you separately.
- The interview can be over the phone or face to face in our city centre department (200 Renfield Street, Glasgow). Travel expenses will be reimbursed.
- The interview will ask you questions about the program, social life and personal factors associated with your weight loss journey.
- You will receive another £10 amazon voucher for taking part in this.

You are about to start the questionnaire.

Before starting the questionnaire:

- you will be asked to provide the date you start at Weight Watchers, the date you start completing the questionnaire, your email or home address (in order to receive the voucher), and to provide NHS identifiable number (Weight Watchers ID). *Instructions will be given in the required section.* We will need your Weight Watchers ID number to allow us from following up your attendance and weight change during your weight management program. This will be done by linking your questionnaire to your weight management record (NHS record) through NHS SafeHaven. This will be fully anonymised and completed on secure NHS computers.

- you will be asked to fill a consent form to indicate your consent to your participation in the questionnaire.

Starting the questionnaire:

- we will ask you questions about your age, gender, marital status, ethnicity, education, employment, weight, attitude and social life. We expect that the questionnaire will take around (15-20 min) to complete.

End of questionnaire:

- once you completed the questionnaire, you will receive a £10 amazon voucher that will be sent to you by email/post.

What are the possible benefits of taking part?

Taking part in this study will not have direct benefits to you. However, we hope the information we get from this questionnaire will help us in finding the factors that can allow us to know who will be able to lose weight before starting the weight management program. This may result in future improvement of treatment and medical care. Also, as an appreciation of the time you spend completing the questionnaire, you will receive a £10 amazon voucher.

What are the possible disadvantages and risks of taking part?

There are no known risks or disadvantages from taking part in this study.

What if there is a problem?

If you have any concerns regarding the study, any questions about your rights as a participant in this research project, or if you have a question later that you didn't think of before you can contact us (Please find the details at the end of the document).

What happens when the study is finished?
We will analyse the results of this study. The results will be submitted for a Ph.D. exam, published in medical journals, and presented in scientific presentations and meetings. We will make sure that your information is kept fully anonymous and that you will not be identifiable in any way.
Once we have all the questionnaires and the Weight Watchers ID numbers for each participant, we will download all the results to the NHS SafeHaven computer. They will link the questionnaires to weight management records (NHS record) by Weight Watchers ID number. We will then analyse the data on the NHS computer, and they will store it in their computer securely for 10 years after the study has finished. At the end of the study, if you wish to know the summary of results, we will send it to you via email or post.

Who is organising and funding the research?
This research is organised by the University of Glasgow as a part of a Ph.D. project.

Will my participation in this study be kept confidential?
NHS Greater Glasgow and Clyde (NHS GG&C) is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. NHS GG&C will keep identifiable information about you for 10 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information as a research team (contact details next page).

Your data will be used as follows:
1- The results of this study (questionnaire data) will be transferred securely to the NHS.
2- They will link your questionnaire results to the weekly results of your attendance at the weight management service held by NHS GG&C (NHS weight management record) by using your Weight Watchers ID number and then they will remove any information that would make you identifiable.
3- The NHS allows us to access the anonymous data to do the analysis using their secure computer.
4- The data collected from you during the study, may be looked at by individuals from University of Glasgow, from regulatory authorities or from the NHS GG&C Health Board, where it is relevant to you taking part in this research. This information will be used to support other research in the future and may be shared anonymously with other researchers. Individual results will not be shared with the teams that work in weight management.

Who has reviewed the study?
This study has been reviewed by Yorkshire and the Humber – Sheffield Research Ethics Committee.

If you have any further questions about the study, please contact:

Ph.D. Research Student:
Lulwa Alabdullah
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126 University Place
G12 8TA
E-mail: cams-ins-powerstudy-project@glasgow.ac.uk
Phone Number:

Supervisor:
Dr. Jennifer Logue
University of Glasgow
BHF Glasgow Cardiovascular Research Center
University Avenue
Glasgow
G12 8TA
E-mail: Jennifer.logue@glasgow.ac.uk
Phone Number:

If you would like to discuss your potential participation in the study with someone independent, please contact:
Dr. Lyn Ferguson
University of Glasgow
BHF Glasgow Cardiovascular Research Center (GCRC)
126 University Place
G12 8TA
E-mail: Lyn.Ferguson@glasgow.ac.uk

Thank you for taking the time to read this information sheet and considering this study

Participants Details

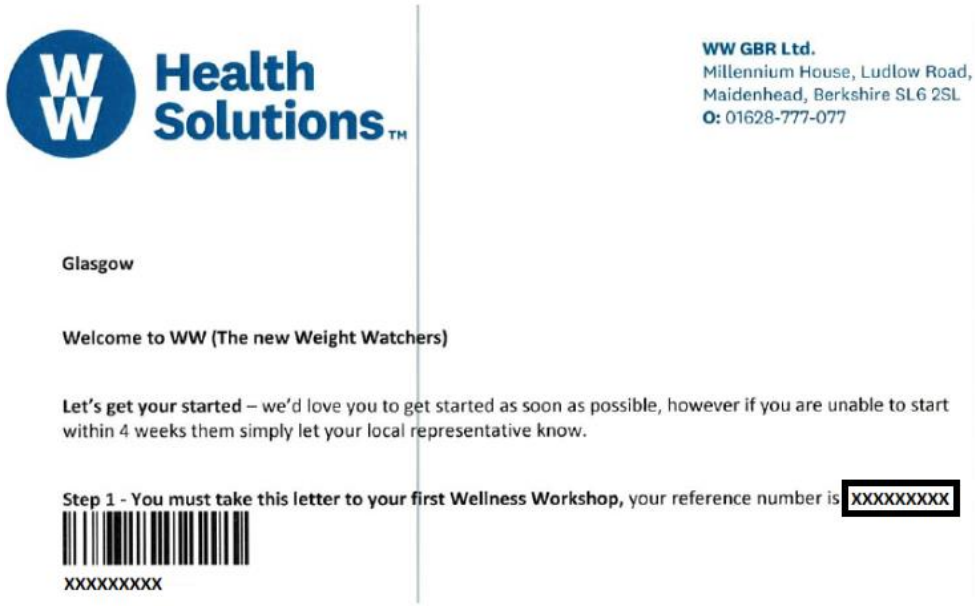
1. **Date starting Weight Watchers**: .....
2. **Date starting the questionnaire**: .....
3. **To receive the voucher, please leave your**:

   E-mail address ……

   Or

   Home address …….
4. **Please provide your Weight Watchers ID number**: ……..

You will find Weight Watchers ID number in NHS appointment letter that you receive before starting at Weight Watchers (please see the example below).



WW Health Solutions™

WW GBR Ltd.
Millennium House, Ludlow Road,
Maidenhead, Berkshire SL6 2SL
O: 01628-777-077

Glasgow

Welcome to WW (The new Weight Watchers)

Let's get your started – we'd love you to get started as soon as possible, however if you are unable to start within 4 weeks them simply let your local representative know.

Step 1 - You must take this letter to your first Wellness Workshop, your reference number is XXXXXXXXX

XXXXXXXXX

CONSENT FORM

Instructions:

As part of the POWER study, the researcher requests your consent for participation in this questionnaire about predictors of weight reduction. This consent form asks you to allow the researcher to use your answers you give in this questionnaire and your weight record provided by the NHS to analyse the data and enhance understanding of the topic. Please tick/ initial boxes to indicate your consent to your participation in this study and to the following statements:

	Yes	No
• I have had the opportunity to read the information sheet **(Version V1.01, 25/11/2019)**, consider the information ask questions and have had these answered satisfactorily.	☐	☐
• I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐	☐
• I understand that relevant sections of my data collected during the study, may be looked at by individuals from University of Glasgow, from regulatory authorities or from the NHS Greater Glasgow and Clyde Health Board, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐	☐
• I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐	☐
• I understand that the answers I give to this study will be linked to the weekly results of my attendance at the weight management service held by NHS Greater Glasgow and Clyde, and that this will only be done on secure NHS computers. I understand that my individual results will not be shared with the teams that work in weight management.	☐	☐
• I agree to complete the questionnaire.	☐	☐

Dear participant

You are planning to start or have recently started a weight management programme. Thank you very much for agreeing to complete this questionnaire. This questionnaire takes around (15-20min) to be completed.
You will be asked about your background, weight and previous attempts at weight loss, reasons and motivation to lose weight, lifestyle, eating habits, attitudes toward physical activities, and if you are receiving support from family and friends before starting the weight management programme. Your answers will help us to understand how we can better predict weight loss success for people taking part in weight management programs and will help us develop better in treatments in future. Your answers to these questions will be linked to your weight that is recorded each week during the weight management programme. This will be done by the NHS on NHS computers and any information that would identify who you were will be removed.
Your answers to this questionnaire are confidential, will be saved on a secure computer server and will not be reported back to your weight loss team or your GP.
Please answer all the questions as honestly as possible. There are no good or bad answers.

THANK YOU VERY MUCH FOR YOUR HELP

Contents

About you: The first set of questions will ask about who you are and what you do.

Directions:

1. **Blank(s) should be filled with the correct answer. Answers may be more than one word or may contain numbers.**
2. **Boxes should be ticked appropriately. Please select only one answer per question, unless otherwise specified. Answer all relevant questions. Do not leave blank boxes where an answer is expected.**

Demographic

1-What is your current age?_____

2- To which gender identity do you most identify?

☐ Female

☐ Male

☐ Transgender Female

☐ Transgender Male

☐ Gender Variant / Non-Conforming

☐ Other, please specify_____

☐ Prefer not to say

3- What is your marital status?

☐ Married / Civil Partnership

☐ Living with partner

☐ Single

☐ Married / Civil Partnership - separated

☐ Divorced / dissolved Civil Partnership

☐ Widowed / surviving Civil Partner

☐ Other, please specify_____

4- What is your ethnic group?

☐ White

☐ Mixed

☐ Asian, Asian Scottish or Asian British

☐ African Caribbean or Black

☐ Arab

☐ Other, please specify_____

5- Did you do any further training after you left school?

☐ No

☐ Formal qualifications through training at work

☐ Degree from college or university

☐ Higher-level study (Postgraduate qualification)

☐ Other, please specify_____

6- Please select a category that best describes your current employment status?

☐ Working full time (30hrs or more per week)

☐ Working part time (less than 30hrs or more per week)

☐ Unable to work (illness and disability) / unable to work (other reason)

☐ Student

☐ Unemployed and looking for work

☐ Carer for children or relative

☐ At home and not looking for paid employment

☐ Other, please specify_____

7- Has a doctor ever told you that you have diabetes?

☐ Yes

☐ No

7a- If yes, What type of diabetes?

☐ Type 1 diabetes

☐ Type 2 diabetes

Weight related: This set of questions will ask about your weight, weight loss history and expectations.

Directions:

1. **Blank(s) should be filled with the correct answer. Answers may be more than one word or may contain numbers.**
2. **Boxes should be ticked appropriately. Please select only one answer per question, unless otherwise specified. Answer all relevant questions. Do not leave blank boxes where an answer is expected.**

Weight today

1. What would you like to record your weight in? ☐ kgs ☐ stone ☐ lbs
2. What is your weight today in Kgs / stones / lbs?_____

Weight Loss History

1. How many times in the past have you lost 10 lbs / 4.5 kgs / 0.7 stone or more?

☐ Never

☐ 1-2

☐ 3-5

☐ 6-10

☐ More than 10

2. If you have tried to lose weight before, how much did you lose in your most successful attempts?

☐	0-5 lbs	≈	0-2.3 kg	≈	0-0.36 stone
☐	6-10 lbs	≈	2.7-4.5 kg	≈	0.4-0.7 stone
☐	11-15 lbs	≈	5-6.8 kg	≈	0.8-1 stone
☐	16-20 lbs	≈	7.2-9 kg	≈	1.1-1.4 stone
☐	21-30 lbs	≈	9.5-13.6 kg	≈	1.5-2.1 stone
☐	31-40 lbs	≈	14-18.1 kg	≈	2.2-2.9 stone
☐	41-50 lbs	≈	18.6-22.7 kg	≈	2.9-3.6 stone
☐	More than 50 lbs	≈	22.7 kg	≈	3.6 stone

☐ Never tried to lose weight before

3. How many times in the past have you sought assistance to lose weight (e.g., commercial diet program, NHS, or help from a dietitian)?

☐ Never

☐ 1-2

☐ 3-5

☐ 6-10

☐ More than 10

4. How many times in the past have you tried to lose weight without assistance?

☐ Never

☐ 1-2

☐ 3-5

☐ 6-10

☐ More than 10

5. How many times in the past have you tried to lose weight by doing more exercise (e.g., walking, running, biking)?

☐ Never

☐ 1-2

☐ 3-5

☐ 6-10

☐ More than 10

6. Have you ever used any of the following to try and lose weight? ***(Tick all that you have tried)***

☐ Prescription drugs (prescribed by your doctor)

☐ Over the counter drugs (that is, not requiring a prescription)

☐ Dietary or herbal supplements (such as Herbalife)

☐ Meal replacements (such as slim fast, CAMBRIDGE or other liquid or powdered meals)

☐ Have not used these methods

7. The first part of the NHS Weight Watchers program is 12 weeks. Realistically, how much weight do you estimate you will lose in that program?
_____ lbs / kgs / stone

8. What weight do you think it would be best for you to be?
_____ lbs / kgs / stone

Weight loss expectations

Please write a numerical weight (lbs / kgs / stone) for each of the following four items:

1. **Dream weight** (a weight you would choose in cases where you could weigh whatever you wished): _____

2. **Happy weight** (although not ideal, a weight you would be happy to achieve): _____

3. **Acceptable weight** (a weight you would not be particularly happy with, but could accept, because it would be less than your current weight): _____

4. **Disappointing weight** (a weight that, although less than your current weight, would not be viewed as successful and would cause you to feel disappointment if where this were your final weight after the program): _____

Behaviour related: In this section we will ask you about your behaviours (motivation, weight goal, self-efficacy, sleep, and eating behavior).

Direction:

1. **Please choose a number from 1-7 that best represents your own belief or feelings about each statement and write it next to each statement.**

Motivation

The items on this questionnaire are broken into four groups. Please read the statement at the beginning of each group and then consider the reasons that follow it in terms of how true that reason is for you. The scale is:

1	2	3	4	5	6	7
Not at all true	→		Somewhat true	→		Very true

A. I decided to enter this weight-loss program because:

Rate (1-7)

1. I won't like myself very much until I lose weight ☐
2. People will like me better when I'm thin ☐
3. It feels important to me personally to be thinner ☐
4. I really want to make some changes in my life ☐

B. If I remain in treatment it will probably be because:

5. I'll feel like a failure if I don't ☐
6. People will think I'm a weak person if I don't ☐
7. I'll feel very bad about myself if I don't ☐
8. Others will be angry at me if I don't ☐
9. I feel like it's the best way to help myself ☐

C. I plan to lose weight because:

10. I'll be ashamed of myself if I don't ☐
11. I'll hate myself if I can't get my weight under control ☐
12. My friends/family don't like the way I look ☐
13. Being overweight makes it hard to do many things ☐

D. I have agreed to follow the procedures of the program because:

14. I am worried that I will get in trouble with the weight management staff if I don't follow all the guidelines ☐

15. I'll feel guilty if I don't comply with all the procedures ☐

16. I want others to see that I am really trying to lose weight ☐

17. I believe they will help me solve my problem ☐

18. It's important to me that my efforts succeed ☐

Weight goal

1. Weight Goal: Indicate your target weight (in lbs / kgs / stone) for the present weight loss attempt_____

2. Goal Striving:

Direction:

1. **Please choose a number from 1-9 that best represents your own belief or feelings about each statement and write it next to each statement.**

1	2	3	4	5	6	7	8	9
Not at all for this reason	→							Completely because of this reason

Rate (1-9)

a. I want to lose weight because others expect me to. ☐
b. I want to lose weight because I would feel ashamed or guilty if I didn't. ☐
c. I want to lose weight because I personally feel a healthy weight is important. ☐
d. I want to lose weight because watching my progress will keep me happy motivated. ☐

3. Goal Commitment:

Direction:

1. **Please circle the answer that best represents your own belief about each statement.**

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
a. It's hard to take my weight goal seriously	-2	-1	0	1	2
b. I don't care If I achieve my weight goal or not	-2	-1	0	1	2
c. I am strongly committed to pursue my weight goal	-2	-1	0	1	2
d. It wouldn't take much to make me abandon my weight goal	-2	-1	0	1	2
e. I think this is a good weight goal to aim for	-2	-1	0	1	2

Self-efficacy (How confident you are in achieving your weight target)
Direction:

1. **Please circle the answer that best represents your own belief about each statement.**

a. Do you think you will succeed in achieving your target weight	Definitely no						Definitely yes
	-3	-2	-1	0	1	2	3

b. Do you think it is difficult or easy to attain your target weight	Very difficult						Very easy
	-3	-2	-1	0	1	2	3

c. Do you feel confident that you will attain your target weight	Not at all confident						Very confident
	-3	-2	-1	0	1	2	3

Self-efficacy (How strong you believe in achieving your weight target)
Direction:

1. **Please choose a number from 1-9 that best represents your own belief or feelings about each statement and write it next to each statement.**

1	2	3	4	5	6	7	8	9
Not at all able/capable	→							Very much able/capable

Rate (1-9)
a. To what degree do you feel you possess the ability to realise your goal? ☐
b. To what extent do you feel you have the capabilities necessary to attain your goal? ☐

Sleep

Direction:

1. **The following questions relate to your usual sleep habits during the past *month only*. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.**

1. During the past month, when have you usually gone to bed at night?
USUAL BEDTIME _____
2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?
NUMBER OF MINUTES _____
3. During the past month, when have you usually gotten up in the morning?
USUAL GETTING UP TIME _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)
HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, tick the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes.				
b. Wake up in the middle of the night or early morning.				
c. Have to get up to use the bathroom.				
d. Cannot breathe comfortably.				
e. Cough or snore loudly.				
f. Feel too cold.				
g. Feel too hot.				
h. Had bad dreams.				
i. Have pain.				

j. Is there any other reason you have had trouble sleeping?	Yes		No	
1. If yes, please describe				
2. How often during the past month have you had trouble sleeping because of this?	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				

8. During the past month, how would you rate your sleep quality overall?

☐ Very good

☐ Fairly good

☐ Fairly bad

☐ Very bad

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

☐ No problem at all

☐ Only a very slight problem

☐ Somewhat of a problem

☐ A very big problem

10. Do you have a partner or roommate?

☐ No partner or roommate

☐ Partner/roommate in other room

☐ Partner in same room, but not same bed

☐ Partner in same bed

If you have a roommate or partner, ask him/her how often in the past month you have had...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Loud snoring.				
b. Long pauses between breaths while asleep.				
c. Legs twitching or jerking while you sleep.				
d. Episodes of disorientation or confusion during sleep.				
e. Other restlessness while you sleep: please describe.				

Eating behavior

Direction:

1. **Please circle the answer that best represents your own belief about each statement.**

	Definitely true	Mostly true	Mostly false	Definitely false
1. I deliberately take small helpings to control my weight.	4	3	2	1
2. I consciously hold back at meals to keep from gaining weight.	4	3	2	1
3. I don't eat some foods because they make me fat.	4	3	2	1
4. I start to eat when I feel anxious.	4	3	2	1
5. When I feel sad, I often eat too much.	4	3	2	1
6. When I feel tense or "wound up," I often feel a need to eat.	4	3	2	1
7. When I feel lonely, I console myself by eating.	4	3	2	1
8. If I feel nervous, I try to calm down by eating.	4	3	2	1
9. When I feel downhearted and depressed, I want to eat.	4	3	2	1
10. When I smell a sizzling steak or a juicy piece of meat, I find it very difficult to keep from eating, even if I've just finished a meal.	4	3	2	1
11. Sometimes when I start eating, I just can't seem to stop.	4	3	2	1
12. Being with someone who is eating often makes me want also to eat.	4	3	2	1
13. When I see something that looks very delicious, I often get so hungry that I have to eat right away.	4	3	2	1
14. I often get so hungry that my stomach seems like a bottomless pit.	4	3	2	1
15. I'm always so hungry that it's hard for me to stop eating before I finish the food on my plate.	4	3	2	1
16. I'm always hungry enough to eat at any time.	4	3	2	1

	Almost never	Seldom	Moderately likely	Almost always
17. How often do you avoid “stocking up” on tempting foods?	1	2	3	4

	Unlikely	Slightly likely	Moderately likely	Very likely
18. How likely are you to make an effort to eat less than you want?	1	2	3	4

	Never	Rarely	Sometimes	At least once a week
19. Do you go on eating binges though you’re not hungry?	1	2	3	4

	Only at mealtimes	Sometimes between meals	Often between meals	Almost always
20. How often do you feel hungry?	1	2	3	4

On a scale of 1 to 8, what number would you give yourself:

1	2	3	4	5	6	7	8
No restraint in eating							Total restraint in eating

Rate (1-8) ☐

21. To what degree you feel yourself restrained from food?

(**Note:** Food restraint means how tightly food intake is controlled by someone to manage weight)

Social network: Who we spend time with can influence our likelihood of making healthy lifestyle decisions and being able to change our behaviours. The following questions aim to look at how many people in your life could affect your weight loss journey.

Direction:

1. **For each question, consider the average over the last 2-3 months and provide only whole numbers answer.**

Question 1 In a typical week, how many people do you talk to (more than saying "hello") and/or spend time with? (E.g. discuss matters with, eat meals with, attend clubs or activities with, contact via social media, or live with)	
Question 2 Of these, how many do you think have a healthy lifestyle? (E.g. low-fat diet, eat a lot of fruit and vegetables, exercise 2-3 times per week)	
Question 3 From time to time, most people discuss important matters with other people. Looking back over the last 2-3 months, how many people, from Q1, have you discussed your weight and weight loss goals with? (E.g. confiding in, asking for advice, discussing exercise or recipes)	
Question 4 How many mentioned in Q1 do you attend any health or fitness activities with? (E.g. fitness or cooking classes, walking, weight watchers, gym)	
Sometimes when we are trying to eat more healthier or be more active, we avoid people we would typically spend time with. This may be because we feel they are a bad influence (encourage unhealthy choices such as a takeaway) or are unsupportive of our healthier choices.	
Question 5 Of those mentioned in question 1, how many people have you tried to avoid or spend less time with in the last 2-3 months to try and be more active or eat healthier?	

- **We are also conducting interviews with people to learn more about their weight loss journey while they are in Weight Watchers. This would take place in 3-5 weeks' time from now. If you would like to take part in an interview, please select the box below and leave your contact information (i.e. telephone number or email). Interviews will take place over the phone or face-to-face in our department (whichever is more convenient for you). Your travel expenses will be reimbursed, and you will receive another £10 voucher for taking part in the interviews.**

  □ Yes

  □ No

- **If yes, please leave your contact details below:**

  E-mail:……

  Or

  Phone number:……..

- **Please leave your postal address below to send you the participant information sheet and the consent form:**

  Address: ……

  ……

  ……

  ……

- **If you have a preferable time to be contacted to arrange the interview, please enter this below:**

  Time: ……

Debrief

Thank you for taking the time to complete this questionnaire

What was the study about?

In this study, we want to investigate and find a way to tell from the beginning of weight loss programme who is more likely to have lost weight at the end of the program.

People are different from each other in a variety of ways. They are different in their age, gender, weight, ethnicity, etc. Also, their attitude, habits, acts, and feelings might differ with themselves and with others. This means that some people lose more weight than others in a weight loss programme. We are interested in understanding what parts of all this information is the most important to know before individuals start the weight loss program. Knowing this would mean that programmes can provide more support strategies and alternative programmes for people who are not finding the current weight management programme useful for them. The questionnaires you have completed will allow us to investigate this issue and improve services.

We are very appreciative of the time you have taken to complete this questionnaire. We truly value the information you have provided.

If you wish to be sent a summary of the results of the questionnaire for the study (not your individual results) then please leave your:

Email address: _____

Or

Home address: _____

If you require any further information, please do not hesitate to ask the researchers.

Ph.D. Research Student:

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Phone Number:

Supervisor:

Dr Jennifer Logue

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Phone Number:

If you have questions regarding your weight loss aims, please speak to the group leader of your weight management program.

Appendix 2: POWER study Leaflet

University of Glasgow

Can you help in the

POWER Study ?

NHS Greater Glasgow and Clyde

What is the study?
We are a group of researchers from the University of Glasgow. Our research is exploring what helps and hinders weight loss success in people attending weight watchers. We want to understand what helps and prevents people from achieving their goals. This will allow us to develop ideas on how to improve such programmes.

What does the study involve?
This study is completely voluntary and consists of 2 parts, you can do one or both

Questionnaire (20 minutes)
You will be asked questions about your weight loss history, motivation, and support before you begin Weight Watchers

Interview (60-90 minutes)
You can chat with one of our researchers about your experience in Weight Watchers and what has affected your weight loss journey

What are the benefits?
There are no direct benefits to you, but you will receive a £10 amazon voucher for completing the questionnaire and a further £10 amazon voucher for completing the interview

To take part,
please follow this URL:

https://webropol.com/s/powerstudy2020

Any questions?

Contact us:
cams-ins-powerstudy-project@glasgow.ac.uk

Appendix 3: Methods used to conduct the review in POWER study

Research Aims/Questions:

i. To describe the weight loss trajectories of individuals undertaking behavioural weight management programmes.
ii. To identify predictors of short-term successful weight loss (~3m) including patient factors (clinical, demographic, behavioural) and process factors (attendance, completion, early weight loss, repeat attempts).
iii. To identify predictors of longer-term successful weight loss (>2 years) including patient factors (clinical, demographic, behavioural) and process factors (attendance, completion, early weight loss, repeat attempts).

PICO:

P: Population/Patient → *Adult Patients with obesity &T2DM.*

I: Intervention → *Behavioural weight management programmes.*

C: Comparison → *Predictors of successful weight loss.*

O: Outcome → *weight loss (any duration).*

Phase I: Initial proposal for keywords for each element.

Concept 1 *Adult Patients with obesity &T2DM*	Concept 2 *Behavioural weight management programmes*	Concept 3 *Predictors of successful weight loss*	Concept 4 *weight loss (any duration)*
Keywords: -Obese patients. -Overweight patients. -Diabetic patients. -Obese patients with type 2 diabetes mellitus (T2DM). -Insulin resistance patients. -Adults participants.	**Keywords:** -Multicomponent lifestyle intervention. -Behaviour change treatments (BCTs). -Lifelong program. -Comprehensive lifestyle intervention. -Weight loss management program. -Weight control therapy. -Behavioural therapy. -Cognitive Behavioural Therapy (BCT). -Obesity Management Program.	**Keywords:** -Pre-treatment predictors. -Baseline predictors. -Treatment predictors. -Behavioural predictors. -Psychological predictors. -Psychosocial predictors. -predictors of weight loss.	**Keywords:** -Weight loss outcome. -Weight loss in kilogram (kg). -Percentage of weight loss. -Long-term weight loss. -Weight control. -Cut-off value

Phase II: Secondary proposal for keywords for each element (after consultation with supervisors).

Concept 1 *Adult Patients with obesity &T2DM*	Concept 2 *Behavioural weight management programmes*	Concept 3 *Predictors of successful weight loss*	Concept 4 *weight loss (any duration)*
Keywords: -Obes* -Diabet* -Overweight. -Impaired fasting glucose. -Impaired glucose tolerance.	**Keywords:** -Multicomponent. -lifestyle. -Obesity management. -Obesity treatment. -Weight loss. -Weight management. -Behavio*	**Keywords:** -Predict* -Factor* -Explan* -Associat* -Correlat* -Estimat* -Mediat* -Determin* -Biomarker. -Characteristic*	**Keywords:** -Weight* -Body mass -Success* -Reduction. -Fat. -Adipos* -BMI. -Target*

Phase III: Final list of keywords for each element to be used in the search.

Concept 1 *Adult Patients with obesity &T2DM*	Concept 2 *Behavioural weight management programmes*	Concept 3 *Predictors of successful weight loss*	Concept 4 *weight loss (any duration)*
Keywords: -Obes* OR -Overweight.	**Keywords:** -Multicomponent. OR -Multi-component OR -lifestyle. OR -Obesity management. OR -Obesity treatment. OR -Weight loss. OR -Weight management.	**Keywords:** -Predict* OR -Explan* OR -Associat* OR -Correlat* OR -Estimat* OR -Mediat* OR -Determin* OR -Biomarker. OR -Characteristic*	**Keywords:** -Weight* OR -Body mass OR -Success* OR -Reduction. OR -Fat. OR -Adipos* OR -BMI. OR -Target*

AND AND AND

Criteria used to conduct the search: (a) keywords excluded from the search from the Population/Patient element. (b) Dates identified for the review. (c) Additional identification for the search.

(a)
NOT:
-Pregn*
OR
-Child*
OR
-Adolescent*
OR
-Infant

(b)
Medline 1996 - week 3 2019
Embase 1996 – week 3 2019
OvidMedline Epubahead of print in process other non-indexed citations daily 2014 to jan 21th 2019

(c)
Limit to:
-(2008 – week 3, 2019)
-Human (s).
-English.
-Deduplicate.

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