The use of the Mediterranean diet and intermittent fasting in the management of obesity in the UK

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Abstract

Obesity is a global public health issue, with approximately 30% of the world's population (equating to over 2.1 billion people) classified as overweight or obese, and 5% of worldwide deaths attributed to this disease in 2014. Because of the significance of obesity and its related comorbidities such as type 2 diabetes and cardiovascular disease alongside its economic impact, there is a clear need for a novel method to prevent and treat obesity alongside controlling weight regain in the long term. This thesis therefore aimed to investigate the use of the Mediterranean diet and intermittent fasting in combination (originally studied together during the Seven Countries Study) for health promotion by considering these patterns' effectiveness, alongside their acceptability and feasibility to the UK public.

As shown in Figure 1 this thesis followed a series of logical phases, beginning with an evidence generation and understanding phase which suggested that there was a gap in the literature around these dietary patterns and a requirement to consolidate the literature. The second phase therefore aimed to investigate the impact of adherence to a Mediterranean diet and intermittent fasting on outcomes such as body weight and blood lipids by conducting systematic reviews and meta-analyses in order to reflect current understanding. Results suggested that both studied diets were moderately beneficial, for example results of 27 studies suggested that consumption of the Mediterranean diet was associated with improvements to total cholesterol levels, systolic blood pressure and BMI (all $p>0.05$), and adherence to intermittent fasting was linked to significant decreases in BMI and body fat percentage (both $p<0.05$).

Therefore to ensure that these eating plans were acceptable to the public, further work in phase 3 involved gathering data to investigate the use of these plans by the public. Findings of a survey of 551 respondents suggested that the UK public are not currently eating a Mediterranean diet and have not readily utilised fasting regimes in their weight loss attempts, although many reported a readiness to attempt weight loss and an acceptance of Mediterranean-style foods. A further investigation suggested that the 45 healthcare professionals who responded to an online survey did not readily recommend a Mediterranean diet or a fasting regime to their patients or use these in their own eating patterns, however respondents did report a knowledge of the benefits of these novel plans, and highlighted potential barriers to their own healthy eating and the recommendation of the Mediterranean diet to their patients. These findings were reflected in a systematic review of 17 studies.

During phase 4, all previously gathered information was used to inform a pilot study investigating the use of a lifestyle intervention involving promotion of either the Mediterranean diet or Eatwell Guide in combination with intermittent fasting. Results suggested that the public found this trial both acceptable and feasible under 'real-life' conditions, with a small proportion of drop-outs and generally positive feedback. Advantageous changes were noted with regards to adherence to

dietary guidelines, and food diaries reflected beneficial modifications to eating habits for example increased vegetable and decreased soft drink consumption. Findings also suggested a beneficial impact of both study groups on body composition; with significant weight loss observed alongside significant reductions to blood pressure (both $p<0.05$) and positive changes to blood lipids, however no changes were reported with regards to physical activity levels. Results of this thesis suggest that further research into novel ways of preventing and treating obesity are required, with potential work investigating the use of various forms of intermittent fasting in combination with an eating plan known to be beneficial, such as the Mediterranean diet. This work may be of interest to policy makers or researchers who may find benefit in utilising these studies as a grounding for future investigations.

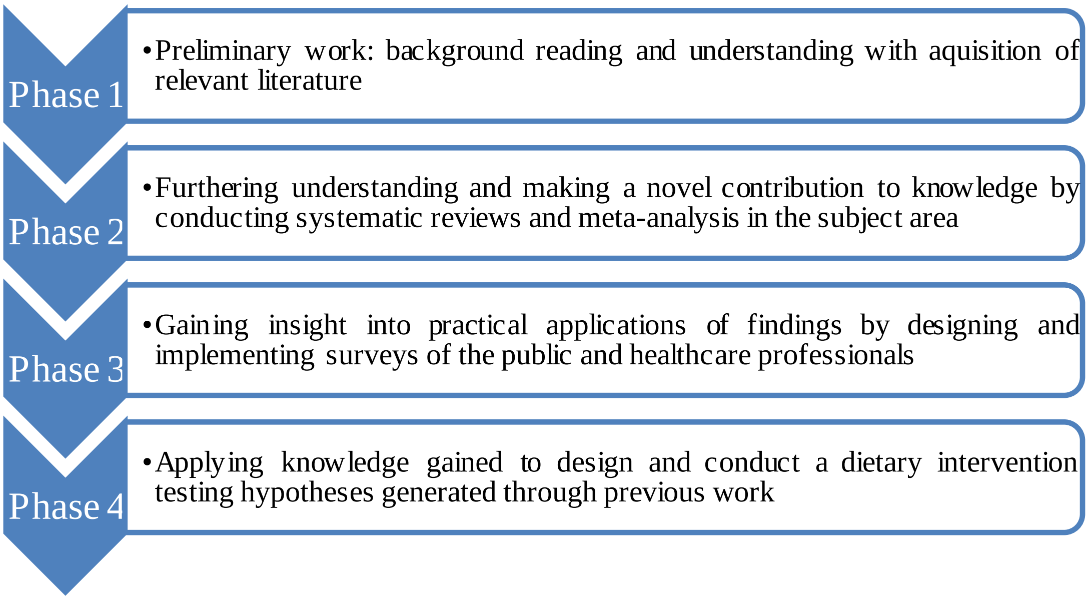

Figure 1: Flow diagram showing phases of thesis

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List of abbreviations

AGE	Advanced glycation end-products
ADF	Alternate-day fasting
BCT	Behaviour change technique
BMI	Body mass index
BMR	Basal metabolic rate
CVD	Cardiovascular disease
CHERRIES	CHEcklist for Reporting Results of Internet E-Surveys
CCR	Continuous caloric restriction
CHD	Coronary heart disease
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
EDTA	Ethylenediaminetetraacetic acid
EG	Eatwell Guide
ENCAT	Evaluations of Nutritional Status in Catalonia
EPIC	European Prospective Investigation Into Cancer and Nutrition
FEV1	Forced expiratory volume
FFQ	Food frequency questionnaire
FTO	Fat Mass and Obesity-Associated gene
FVC	Forced vital capacity
GDP	Gross domestic product
GORD	Gastro-oesophageal reflux disease
HbA1c	Glycated haemoglobin
HDL	High-density lipoprotein
HIIT	High-intensity interval training
HR	Hazard ratio
HSE	Health Survey for England
IER	Intermittent energy restriction
IF	Intermittent fasting
IL-6	Interleukin-6
INN-CA	Nationwide Nutritional Survey of Food Behaviour of the Italian population
IPAQ	International Physical Activity Questionnaire
PROSPERO	International Prospective Register of Systematic Reviews
LDL	Low-density lipoprotein
MAI	Mediterranean adequacy index
MD	Mediterranean diet
MHO	Metabolically healthy obesity
NAFLD	Non-alcoholic fatty liver disease
NDNS	National Diet and Nutrition Survey
NHANES	National Health and Nutrition Examination Survey
NICE	National Institute for Health and Care Excellence
NOO	National Obesity Observatory
NSP	Non-starch polysaccharide
PBHE	Perceived barrier to healthy eating
PP	Per protocol
PREDIMED	Prevención con Dieta Mediterránea

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RAGE	Receptor for advanced glycation end-products
RCT	Randomised controlled trial
RR	Relative risk/risk ratio
SACN	Scientific Advisory Committee on Nutrition
SD	Standard deviation
SE	Standard error
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SBP	Systolic blood pressure
TRF	Time-restricted feeding
TNFα	Tumour necrosis factor alpha
T2DM	Type 2 diabetes mellitus
VLCD	Very low calorie diet
WC	Waist circumference
WHO	World Health Organisation

Preface

Conference presentations arising from this thesis:

The scope, efficacy and effectiveness of Mediterranean diet interventions outside Mediterranean countries: A systematic review and meta-analysis of intervention studies. By L. Francis, J. Young and J. Lara, *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Oral presentation at the Nutrition Society Student Conference, September 2016, Chester, UK**

The impact of intermittent fasting on body composition and cardiovascular biomarkers: a systematic review and meta-analysis. By L. Francis, J. Young and J. Lara. *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* (**Student competition prize winner**) **Poster presentation at the Nutrition Society Spring Meeting, March 2017, Stirling, UK: Proceedings of the Nutrition Society 76 (OCE2)**

The scope, efficacy and effectiveness of Mediterranean diet interventions outside Mediterranean countries: An updated systematic review and meta-analysis of intervention studies. By L. Francis, J. Young and J. Lara, *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Poster presentation at the Nutrition Society Spring Meeting, March 2017, Stirling, UK: Proceedings of the Nutrition Society 76 (OCE2)**

Investigating the opinions of healthcare professionals on the Mediterranean diet and their current levels of adherence to this diet. By L. Francis, J. Young, and J. Lara, *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST* **Poster presentation at the Health and Life Sciences PGR Conference, June 2017, Newcastle, UK**

Investigating the dietary habits of metabolically healthy obese individuals: a systematic review and meta-analysis. By L. Francis, J. Young, and J. Lara, *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST* **Poster presentation at The Nutrition Society Student Conference, September 2017, Reading, UK**

Association of perceived barriers to healthy eating, adherence to the Mediterranean diet and health behaviours with current health status among young adults in the UK. By L. Francis, J. Young, and J. Lara, *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST* **Poster presentation at The Nutrition Society Student Conference, September 2017, Reading, UK**

Weight loss behaviours and their association with diet and perceived barriers to healthy eating among young adults in North East England. By L. Francis, J. Young and J. Lara. *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Poster presentation at the Nutrition Society Summer Conference, July 2018, Leeds, UK: Proceedings of the Nutrition Society 77 (OCE4)**

Adherence to and acceptability of the Mediterranean diet amongst young adults in the North East of England. By L. Francis, J. Young and J. Lara. *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Oral presentation at the Nutrition Society Summer Conference, July 2018, Leeds, UK: Proceedings of the Nutrition Society 77 (OCE4)**

The Mediterranean diet and intermittent fasting for weight loss: study protocol for a randomised controlled trial. By L. Francis, J. Young and J. Lara. *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Lightening presentation at The Nutrition Society Nutrition Futures Conference, September 2018, Newcastle, UK**

The impact of intermittent fasting on body composition and cardiovascular biomarkers: an updated systematic review and meta-analysis. By L. Francis, J. Young and J. Lara. *Department of Applied Sciences, Faculty of Health and Life Sciences, University of Northumbria at Newcastle, NE1 8ST, UK* **Poster at the North East Postgraduate Conference, November 2018, Newcastle, UK**

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I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas and contributions from the work of others.

Ethical clearance for the research presented in this thesis has been approved. Approval has been sought and granted by the Faculty Ethics Committee on 7th August 2017.

I declare that the Word Count of this Thesis is 37, 843 words.

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Signature:

1. General Introduction

It is well documented that there is currently a global obesity pandemic and that this condition has been identified as a causal factor in many illnesses leading to premature morbidity and mortality. This chapter aims to explore the causes and effects alongside novel options for potential prevention and treatment of obesity.

1.1. Obesity

1.1.1. Definition and incidence of obesity

Overweight and obesity are defined by the World Health Organisation (WHO) as 'abnormal or excessive fat accumulation that may impair health' (2006). First described in the 19^{th} century by Flemish statistician Adolphe Quetelet before being later refined and renamed by Ancel Keys during the Seven Countries Study, Body Mass Index (BMI; previously the Quetelet Index) is one of the most commonly used anthropometrical characterisation tools. Calculated as weight in kilograms divided by height in metres squared, a BMI of 25-29.9kg/m^2 classifies an adult individual as overweight, 30-39.9kg/m^2 as obese and a BMI of above 40kg/m^2 as severely obese (Blackburn and Jacobs, 2014, Keys *et al.*, 1972). National Institute for Health and Care Excellence (NICE) guidelines (Clinical Guideline 189) recommend employing alternative BMI thresholds when dealing with black African, African-Caribbean and Asian ethnic groups because these populations have differing amounts of body fat compared to Caucasians which alters mortality risk (NICE, 2014a). Although BMI is a simple, cost-effective, easily employed method to establish disease risk with classification cut-off points based on well-researched links between adiposity and premature mortality (Aune *et al.*, 2016), this method is sometimes criticised as it does not distinguish between lean and fat mass, provides no information about body fat distribution, and can be inaccurate when employed on individuals with particularly high (e.g. athletes) or low (e.g. the elderly) muscle mass (Adab *et al.*, 2018).

Obesity remains a public health issue globally, with approximately 30% of the world's population (over 2.1 billion people) classified as overweight or obese and 5% of worldwide deaths attributed to this disease in 2014 (Dobbs *et al.*, 2014). The 2017 Health Survey for England (HSE) showed that prevalence of obesity rose steeply from around 15% in 1993 to 20% in 2000, with rates of increase slowing thereafter to 25% in 2014 but rising to approximately 29% in 2017 as shown in Figure 2 (NHS, 2017). Should this trajectory continue, it is estimated that approximately half of the world's population will be classified as overweight or obese by 2030, with projections suggesting that the cost to the NHS could rise to between £10 billion and £12 billion in 2030 (Dobbs *et al.*, 2014).

Certain subgroups of society have a higher likelihood of obesity. For example, Figure 3 uses data from the HSE and shows that incidence of obesity varied by region, with the North East showing one of the highest rates in England, at 26% of the adult population, alongside morbid obesity at 4% and the one of the lowest proportions of healthy weight adults at 32% (NHS, 2017). An NHS report into obesity, physical activity and diet shows that obesity was more prevalent in men aged 45-64 (36% falling into the obese category) and women aged 45-54 (37%) and that obesity prevalence decreases with educational attainment; 30% of men and 33% of women without qualifications were classified as obese compared to 21% of men and 17% of women with a degree or equivalent. This report also suggested that obesity was most prevalent in black African females (38%) and least prevalent amongst Bangladeshi and Chinese males (6%) (NHS, 2019b). A study across eleven developed countries also suggested that obesity is negatively associated with socioeconomic status, with men in the lowest studied socioeconomic group twice as likely to be obese than those in the highest group (Devaux and Sassi, 2011).

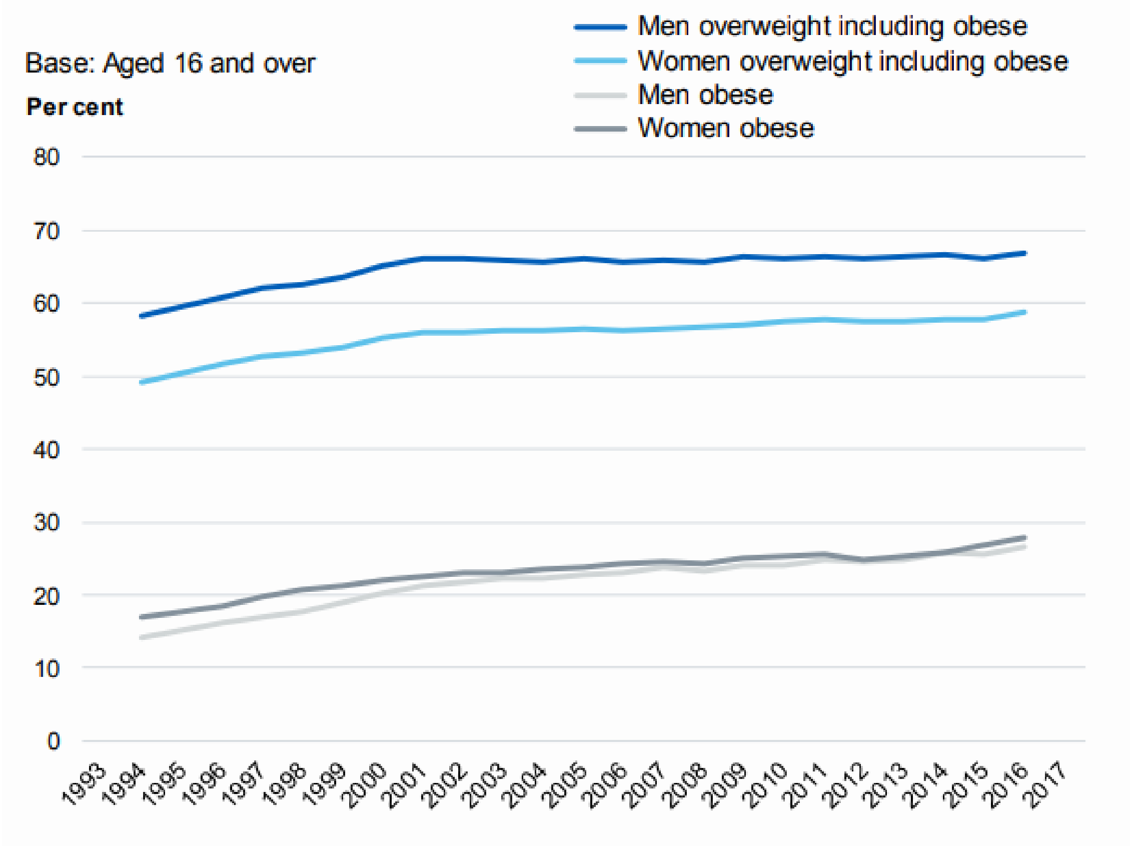

Figure 2: Adult overweight and obesity prevalence from 1993-2017 by sex (NHS, 2017). Contains public sector information licensed under the Open Government Licence v1.0

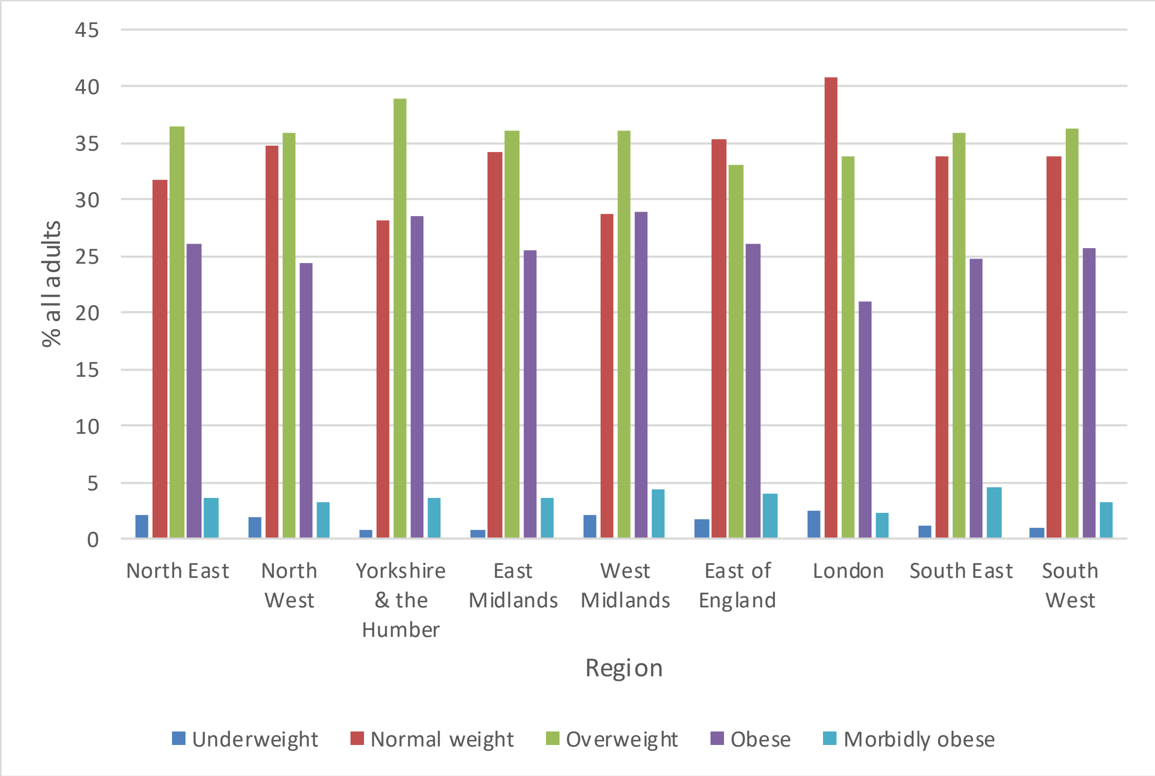

Figure 3: Health Survey for England data showing percentages of adults in the underweight, normal weight, overweight, obese and morbidly obese categories in each region of the UK (NHS, 2017). Contains public sector information licensed under the Open Government Licence v1.0

1.1.2. Aetiology of obesity

Although the basis of obesity can seem simple - energy intake exceeding energy expenditure leading to positive energy balance - the factors leading to this are multifaceted and interlinked with complex interplay between variables (Butland *et al.*, 2007). Risk factors for obesity are often split into two categories: modifiable and non-modifiable. A significant non-modifiable factor can be genetic make-up, for example a polymorphic variation (rs9939609) of the Fat Mass and Obesity-Associated (*FTO*) gene has been associated with increased daily protein and total energy intake (Speakman *et al.*, 2008) which may be due to the link identified via a study of 103 individuals between rs9939609 and decreased postprandial satiety leading to hyperphagia (den Hoed *et al.*, 2009). Similarly, obesity can be caused by several endocrine disorders such as polycystic ovarian syndrome or, more rarely, Cushing's syndrome via various mechanisms such as increased adipocyte differentiation caused by interactions between thyroid and growth hormones (Weaver, 2008). Amongst modifiable risk factors are behavioural aspects, for example a low level of physical activity (approximately 42% of men and 42% of women in the UK are deemed 'not active enough for good health' by the NHS (PHE, 2018b)) due in part to the general shift in the population from manual work to more sedentary jobs alongside an increase in working hours and a growth in car ownership (Butland *et al.*, 2007). The current environment is often referred to as obesogenic; defined as the 'sum of the influences that the surroundings, opportunities or conditions of life have on promoting obesity in individuals and populations' (Bell and Esses, 2002) which means that the environment is set up in such a way that gives the individual little control over their food consumption and eating habits. For example, studies mainly carried out in the USA have shown that portion sizes, particularly of foods of high energy density such as fast foods, have increased significantly since the 1970's and that vendors have done little to alter this although health authorities have called for reductions to portion sizes of many fast food items (Young and Nestle, 2007). This is significant because literature shows that generally the larger the portion served, the more food consumed as demonstrated by a meta-analysis showing that a doubling of portion sizes leads on average to a 35% increase in energy consumption (Zlatevska *et al.*, 2014).

1.1.3. Health impact of obesity

Obesity has a major deleterious impact on many aspects of general health and has been deemed a 'low-grade chronic inflammatory condition' implicated in the development of musculoskeletal diseases such as rheumatic and psoriatic arthritis (Nikiphorou and Fragoulis, 2018). Gastro-oesophageal reflux disease (GORD) is the most commonly-reported disorder of the upper digestive tract, with symptoms including heartburn and acid reflux. After 20 years of follow-up, participants in a population study with a BMI in the highest quintile had almost twice the incidence of hospitalisation due to GORD compared to lower BMI groups (Ruhl and Everhart, 1999). Obesity has also been associated with increased prevalence of multiple cancers, with GORD shown to be a risk factor for oesophageal cancers. A study involving a large dataset from twelve epidemiological studies showed that when compared with individuals with a BMI <25kg/m^2, the increase in risk of oesophageal adenocarcinoma in people with a BMI of 25-29.9kg/m^2 was 1.54 (95% CI 1.26-1.88) and increased to two-fold in those with a BMI 30-

34.9kg/m^2 (OR 2.39, 95% CI 1.86–3.06) (Hoyo *et al.*, 2012). Similarly, the Million Women Study (Reeves *et al.*, 2007) encompassing 1.2 million participants in the UK and involving a mean follow-up of 5.4 years demonstrated a 30% higher risk of postmenopausal breast cancer in individuals with obesity (RR 1.29, 95% CI 1.22-1.36).

Particularly significant to this thesis, obesity has a major impact on the cardiovascular system. A 2016 study involving 13,730 participants with a mean follow-up time of 23 years suggested that severe obesity was associated with a four-fold increase in risk of heart failure alongside a two-fold increase in CHD and stroke incidence (Ndumele *et al.*, 2016). Obese and overweight individuals may have normal low-density lipoprotein (LDL) cholesterol levels, however they tend to have an increased proportion of small, dense LDL particles which are more easily oxidised and therefore more atherogenic than the larger, more buoyant LDL particles seen in non-obese people meaning that obese individuals are at higher risk of atherosclerosis, which is a major predictor of CVD. Excess body weight also leads to increased risk of hypertension which is itself a risk factor for CVD, particularly heart failure and stroke (Lavie *et al.*, 2018) with the Framingham Heart Study suggesting that over 30% of hypertension incidence in male and more than 60% in female participants could be attributed to having a BMI of above 25kg/m^2 (Wilson *et al.*, 2002).

1.1.4. Current dietary methods of obesity management

Due to the scale of the epidemic, various dietary methods have been tested in the treatment and prevention of obesity and overweight, however although literature suggests success in the short term, many individuals regain between 30 and 70% of the weight lost. As shown in Figure 4 taken from a meta-study of clinical trials, use of a very low calorie diet (VLCD) is associated with the most rapid weight loss and regain, and a combination of diet and exercise shows lower levels of regain (Dobbs *et al.*, 2014). The NHS promote contacting a GP for weight loss advice, and NICE Guideline 7 (NICE, 2015b) recommends consulting the NHS website which advocates reducing caloric intake by approximately 600kcal per day (continuous caloric restriction; CER) alongside consuming a diet high in fruits, vegetables; wholegrain versions of starchy carbohydrate sources; some dairy foods; some non-dairy protein sources; and small amounts of high-fat or high-sugar foods. NHS advice warns against ‘fad diets’ such as zero calorie fasting or cutting out whole food groups and states that VLCD should only be undertaken under the supervision of a properly-trained healthcare professional, with exercise promoted in conjunction with a healthy diet to aid weight loss. The NHS website also provides information about the use of Orlistat which is only prescribed to individuals with a BMI over 30kg/m^2 or those with a BMI over 28kg/m^2 in conjunction with weight-related conditions (NHS, 2016b) and as Figure 4 shows, weight regain after loss via medications is common.

Due to a relative lack of success in the use of traditional dietary methods of obesity treatment, research has been carried out into more novel approaches such as the employment of the Mediterranean diet (MD) and Intermittent Fasting (IF) to improve health and as weight loss mechanisms.

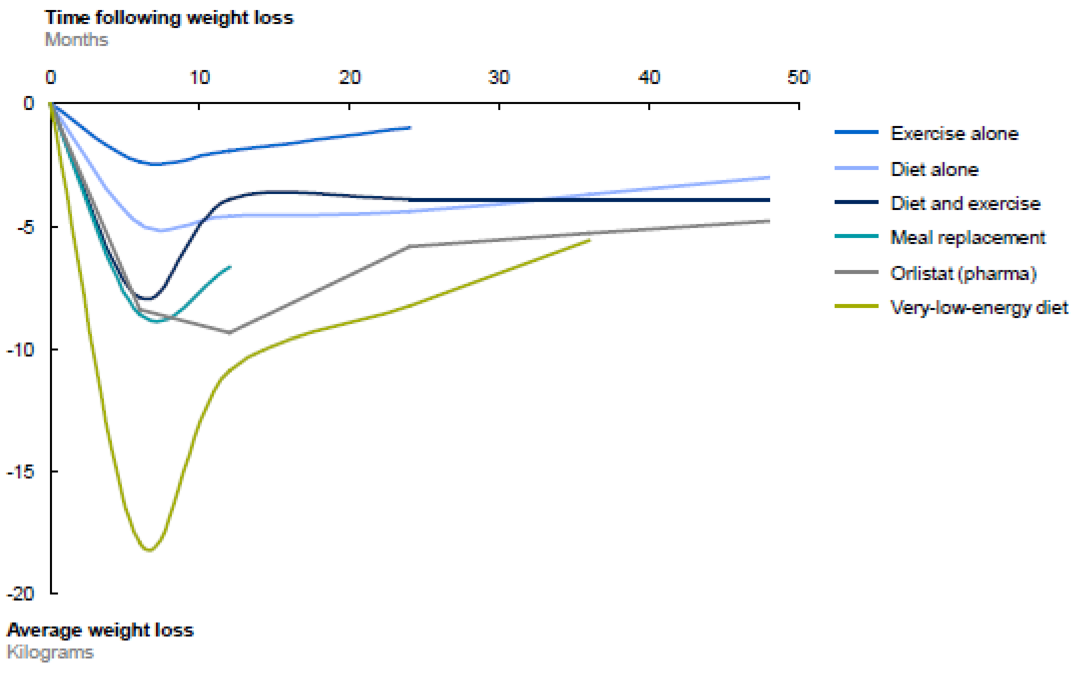

Figure 4: Graph showing average weight loss/regain 10, 20, 30, 40 and 50 months after initial weight loss using various methods (Dobbs et al., 2014)

1.2. The Mediterranean Diet

1.2.1. Mediterranean diet guidelines and implementation in research

While most overviews of the MD are similar in their promotion of unprocessed foods and emphasis on wholesome meals, there are various definitions of the MD originating from diverse parts of the Mediterranean's geographical area as well as from differing research studies. The traditional MD is defined by the authors of the Prevención con Dieta Mediterránea (PREDIMED) study as 'a high intake of olive oil, fruits, nuts, vegetables, and cereals; a moderate intake of fish and poultry; a low intake of dairy products, red meat, processed meats, and sweets; and wine in moderation, consumed with meals' (Estruch *et al.*, 2013) as shown in Figure 5 (copyright permission granted, see Appendix A1). Similarly, the Lyon Diet Heart Study recommended a diet with 'more bread, more root vegetables and green vegetables, more fish, less beef, lamb and pork replaced with poultry, no day without fruit, and butter and cream replaced with margarine high in *a*-linolenic acid' (Kris-Etherton *et al.*, 2001). Martínez-González *et al.* (2004) note that 'the very definition of the Mediterranean diet is not a minor issue' and Table 1 taken from a paper by Davis *et al.* (2015) highlights the differences in MD recommendations given by three prominent sources: Oldway's Preservation and Trust (2009), the Mediterranean Diet Foundation (Bach-Faig *et al.*, 2011), and the Greek Dietary Guidelines as defined by the Ministry and Health and Welfare (1999). Notably, recommendations differ with regards to fish and seafood, poultry, nuts, legumes, fruits and vegetables. This lack of a standard definition causes difficulty in study comparison, and means that conclusions cannot often be generalised. Uncertainty has also arisen around the reliability of indexes of adherence to the MD, with a 2011 study suggesting that levels of adherence of a cohort comprised of 324 healthy students varied dramatically depending which index was employed. It is thought that this is due to the variations in the dietary components included in the creation of the index, alongside the weight given to each and the score used (Milà-Villarroel *et al.*, 2011).

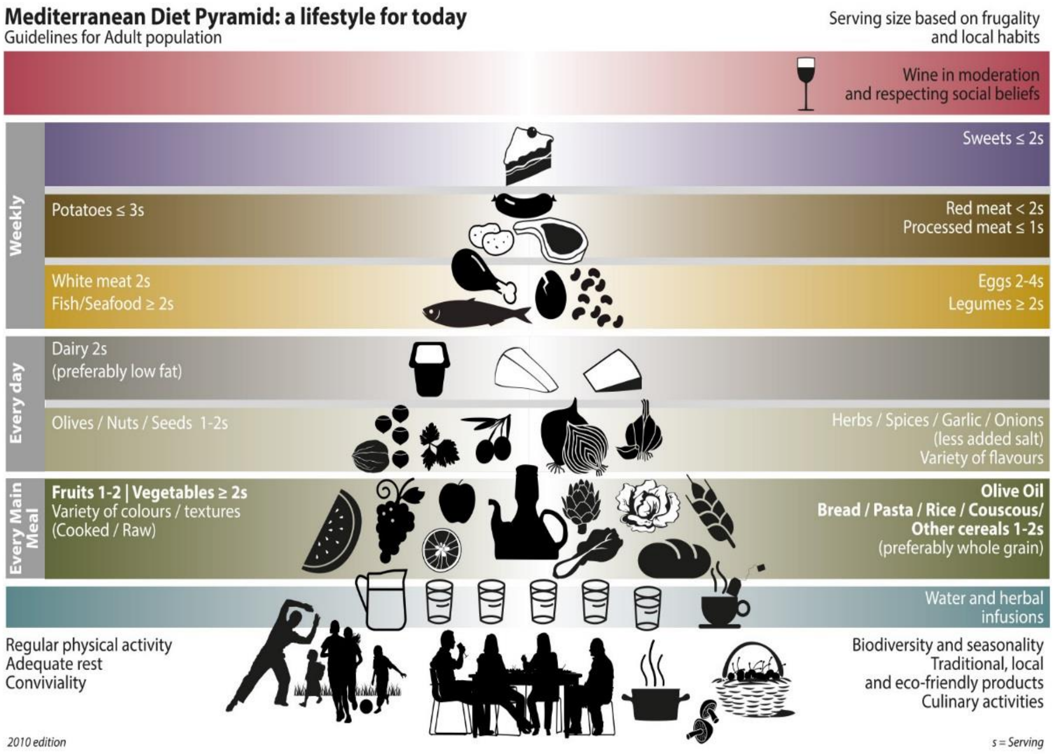

Figure 5: The Mediterranean Diet Foundation Pyramid (Bach-Faig, 2011) (copyright permission granted)

Table 1: Differences in MD recommendations between Oldway's, MD Foundation and Greek Dietary Guidelines (Davis et al., 2015)

Foods	**Oldway's Preservation and Trust (2009)**	**Mediterranean Diet Foundation (2011)**	**Greek Dietary Guidelines (1999)**
Olive oil	Every meal	Every meal	Main added lipid
Vegetables	Every meal	≥2 serves every meal	6 serves daily
Fruits	Every meal	1-2 serves every meal	3 serves daily
Breads and cereals	Every meal	1-2 serves every meal	8 serves daily
Legumes	Every meal	≥2 serves weekly	3-1 serves weekly
Nuts	Every meal	1-2 serves daily	3-4 serves weekly
Fish/seafood	Often, at least two times per week	≥2 serves weekly	5-6 serves weekly
Eggs	Moderate portions, daily to weekly	2-1 serves weekly	3 serves weekly
Poultry	Moderate portions, daily to weekly	2 serves weekly	4 serves weekly
Dairy foods	Moderate portions, daily to weekly	2 serves daily	2 serves daily
Red meat	Less often	<2 serves per week	4 serves monthly
Sweets	Less often	<2 serves per week	3 serves weekly
Red wine	In moderation	In moderation and respecting social beliefs	Daily in moderation

1.2.2. Seminal research and further intervention trials into the Mediterranean diet

The MD was first described in the late 1950s by American physiologist Ancel Keys during the now-famous Seven Countries Study. This research involved 12,763 middle-aged men from sixteen cohorts in America, Finland, the Netherlands, Italy, Yugoslavia (now Croatia and Serbia), Greece and Japan (Keys *et al.*, 1986). The purpose of the study was to investigate associations between various risk factors and coronary heart disease (CHD) and assess differences based on diets of cohorts around the world (Verschuren *et al.*, 1995). With similar findings to the five-year follow-up, a 25-year follow-up study concluded that total serum cholesterol levels were associated with death from CHD, with cohorts in the Mediterranean (Southern Europe) demonstrating mean total cholesterol levels of 5.15mmol/L and age-standardised CHD mortality rates of 4.7%, compared to Northern European cohorts with total cholesterol levels of 6.55mmol/L and CHD mortality rates of 20.3% (Verschuren *et al.*, 1995). Further studies have investigated the impact of fibre, antioxidants, *trans* fats and many other substances on risk of CHD, and findings from the Seven Countries Study have informed many peer-reviewed journal articles and contributed much knowledge to the fields of nutritional science and public health, however it is important to note that the Seven Countries Study does have limitations, such as the inclusion of solely men of approximately the same age disallowing generalisation to the whole population.

Since the Seven Countries Study, there have been various intervention studies carried out investigating various aspects of the MD. For example, the Lyon Diet Heart Study is a significant intervention study carried out in France involving 423 participants with histories of myocardial infarction adhering to either a MD or a prudent Western-style diet, and showed that rates of cardiac death and nonfatal infarction after 46 months of intervention was 1.24 per 100 participants per year in the experimental group, compared to 4.07 in the control group. This study highlighted the protective effects of the MD and demonstrated that participants were able to closely adhere to the MD pattern for long periods of time, suggesting that the MD regime is both acceptable and palatable to participants (de Lorgeril *et al.*, 1999). Issues with this study have been raised, for example that the fat source utilised was linolenic acid from canola-based margarine which is not widely consumed; and that with 14 end-points in one intervention group and 44 in another, the small sample size limits generalisation and restricts use as a foundation for public health guidelines (Arós and Estruch, 2013).

Consumption of a MD has been linked to increased health span and reduced morbidity, with the well-known PREDIMED study involving 7447 Spanish participants at high risk of cardiovascular disease showing that adherence to the MD supplemented with either nuts or olive oil was associated with an absolute risk reduction of around three cardiovascular events per 1000 person-years with a relative risk reduction of 30% (Estruch *et al.*, 2013). This study was subsequently retracted and republished as authors became aware of protocol deviations such as incorrect randomisation, leading to the omission of 1588 participants. This caused minor changes to study results, with 96 primary end-point events reported in the group assigned to a MD with extra-virgin olive oil (3.8%), 83 in the group assigned to a MD with nuts (3.4%), and 109 in the control group (4.4%) (Estruch *et al.*, 2018). Some controversy remains around this study, for example that participants in the control group did not manage to achieve the low-fat diet prescribed; only reducing their total fat intake from 40% of caloric intake to around 37% thus missing the target of 30% (Jebb, 2016). The PREDIMED research team counter that reducing fat consumption was difficult amongst this cohort of Mediterranean participants because olive oil is used abundantly both during cooking and at the table, and that poor palatability of a low-fat diet reduces compliance levels (Guasch-Ferre *et al.*, 2017). Similarly, it has been noted that participants in the control group originally received a less intense intervention than those randomised to experimental groups, with control participants only given a yearly leaflet describing the low-fat diet compared to the quarterly meetings with a dietician attended by the other intervention arms (McConway, 2016). Guasch-Ferre *et al.* (2017) state that the intervention intensity was altered before recruitment was complete and that final results did not change when the differing intensities were taken into account during analysis.

1.2.3. Systematic reviews and meta-analyses investigating the Mediterranean diet

Various analyses have highlighted the protective properties of a MD, including associations with reduced cognitive impairment. A meta-analysis of 22 studies showed that higher levels of MD adherence was consistently associated with a lower risk of stroke (RR= 0.71), depression (RR= 0.68) and cognitive impairment (RR= 0.60) (Psaltopoulou *et al.*, 2013). Results of a meta-analysis including nine cohort studies published between 2002 and 2016 involving 34,168 participants with a mean age of 45 years suggested that the highest analysed MD adherence score was inversely associated with the incident risk of cognitive disorders such as dementia (RR= 0.79, I^2= 22%, p=0.22) but a medium adherence score showed no significant association (RR= 0.98, I^2= 34%, p=0.12). Dose-response analysis indicated a trend of a linear relationship between the MD and the incident risk of cognitive disorders (Wu and Sun, 2017).

Studies also suggest an association with reduced premature mortality, for example a 2014 systematic review and meta-analysis involving 4,172,412 participants across 35 cohort prospective studies showed that analysis using a random-effects model suggested there was significant association between a two-point increase in adherence to the MD and reduced risk of mortality from all causes ($p<0.00001$) with low statistical heterogeneity between studies (I^2= 47%) (Sofi *et al.*, 2014). Similarly, a meta-analysis of 56 observational studies with a total population of 1,784,404 participants suggested that the highest MD adherence score studied was significantly associated with a lower risk of all-cause cancer mortality (risk ratio (RR)= 0.87, I^2= 84%), colorectal cancer (RR= 0.83, I^2= 56%), breast cancer (RR= 0.93, I^2= 15%), gastric cancer (RR= 0.73, I^2= 66%), prostate cancer (RR= 0.96, I^2= 0%) and liver cancer (RR= 0.58, I^2= 0%). There were non-significant associations between the highest level of MD adherence and risk of cancer mortality (RR= 1.01) and cancer recurrence (RR= 0.61) in cancer survivors (Schwingshackl and Hoffmann, 2015). A meta-analysis of eleven papers including both prospective studies and RCTs involving 888,257 participants suggested that individuals with the highest MD adherence level had the lowest incidence of CVD (RR= 0.76), coronary heart disease (CHD) (RR= 0.72), myocardial infarction (RR= 0.67) and stroke (RR= 0.76) compared to the least adherent. Pooled analysis of dietary impact suggested that olive oil, vegetables, fruits and legumes had the most significant protective effects (Grosso *et al.*, 2017).

1.2.4. Trends in adherence

Despite the wealth of literature showing the multiple health benefits of a MD, literature suggests that adherence to the MD in Mediterranean countries is decreasing. In order to give an idea of a region's MD adherence, the Mediterranean Adequacy Index (MAI) was devised and is calculated by dividing the energy provided by the total sum of Mediterranean food groups by the energy from non-Mediterranean food groups. Foods considered Mediterranean are olive oil, olives, fruits, vegetables, herbs, spices, nuts, fish and seafood, wine and legumes. Non-Mediterranean foods include sources of fat other than olive oil, sugar, sweeteners, alcohol except wine, and meat and offal, amongst others (Alberti-Fidanza *et al.*, 1999). As displayed in Figure 6 (copyright permission granted, see Appendix A2), worldwide MAI calculated from 169 countries in 1961-

1965 was 2.86 but dropped to an average score of 2.03 from 2000-2003, and while Mediterranean countries showed the highest MAI during both 1961-1965 and 2000-2003, the decrease in MAI was more significant in Mediterranean countries (average decrease of 1.45 points SD 0.99) compared to non-Mediterranean countries (average decrease of 0.41 points SD 0.76). Northern Europe was the only region to demonstrate an increase in MAI, however this was not statistically significant. During the first time period (1961-1965) fifteen countries had average MAI values above 3.00, with three of these having MAI values over 5.00, however by the second studied time period (2000-2003) no country had a MAI over 5.00, only Egypt had a value above 4.00 and just three had a value over 3.00 (da Silva *et al.*, 2009). More specifically, research utilising Spanish Household Consumption Surveys has shown that MAI and therefore MD adherence in Spain dropped significantly between 1987 and 2005 (p=0.001), indicating that the energy contribution of Mediterranean and non-Mediterranean foods has been progressively equalising over the decades. Researchers suggest that this steady Westernisation of the Spanish diet may have been caused by increasing wages, technical improvements in food manufacture and the increased proportion of women in work (Bach-Faig *et al.*, 2010).

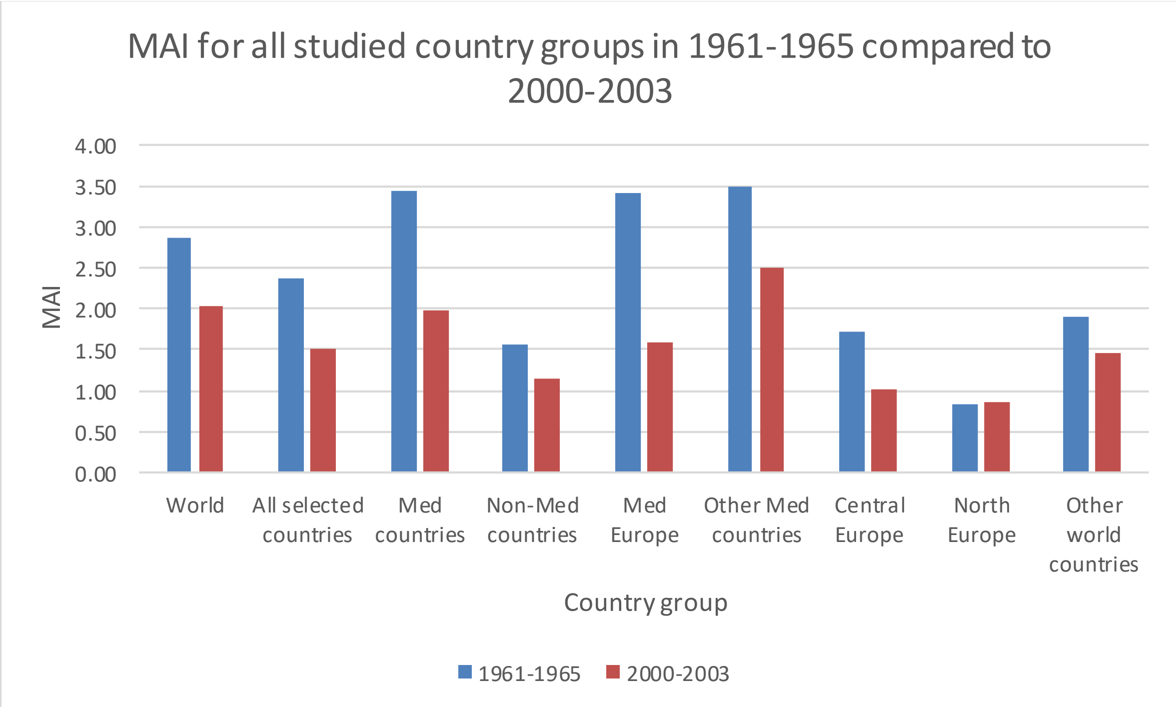

Figure 6: Mediterranean Adequacy Index of all studied country groups in 1961-1965 compared to 2000-2003 using data taken from da Silva et al. (2009). Copyright permission granted

1.3. Intermittent fasting

1.3.1. History and types of fasting

Intermittent energy restriction (IER) regimes in differing formats have long been used by religious groups; of particular interest in this thesis are the many participants in the Cretan cohort of the Seven Countries Study who adhered to strict fasting procedures set out by the Greek Orthodox Church (Keys *et al.*, 1986). This involved abstaining from animal products, dairy and olive oil during three major periods (Christmas, Lent and the Assumption), totalling around 200 days each year (Sarri *et al.*, 2004) and has been shown to increase fibre and iron consumption while decreasing total energy, total fat and cholesterol intake (Papadaki *et al.*, 2011). The most commonly studied form of IER is intermittent fasting (IF) which involves regular periods of restricted energy intake (often as low as 500kcal per day) followed by periods of unrestricted intake (Davis *et al.*, 2016).

1.3.2. Systematic reviews and meta-analyses

There have been a small number of systematic review and meta-analyses carried out in order to investigate the impact of IF on a number of outcomes. A 2015 systematic review showed that 37 of the 40 included studies reported weight loss, with an average of 3-5kg lost after ten weeks of IF. Authors suggest that weight loss was not reported by the remaining three studies as these involved only lean participants and two of these involved just two weeks of IF regime which may have been insufficient to see any significant results. Similarly, ten of the thirteen included studies reporting on BMI showed a decrease following a period of IF, with the two studies involving lean participants showing no change to BMI. Twelve of the thirteen studies recording waist circumference showed a decrease in this measurement following IF, alongside all three of the studies reporting hip circumference noting a decrease. Nine of the twelve studies comparing the effectiveness of IF and CER reported no difference with respect to weight loss, one noted greater weight loss in the CER group, and two others reported higher weight loss in the IF intervention arm. IF and CER were shown in all seven studies reporting on these outcomes to be equal with regards to reduction in BMI, waist circumference and hip circumference (Seimon *et al.*, 2015). Similarly, a recent meta-analysis of five studies lasting a minimum of twelve weeks involving

376 overweight and obese participants intermittently consuming a significantly lower number of calories interspersed amongst periods of less restricted food intake suggested that IF is as effective for weight loss as CER ($p=0.15$) over short periods with an average weight loss of >5kg, but authors state that there is currently insufficient evidence on the sustainability of this eating pattern and weight loss (Harris *et al.*, 2018). Similar results were shown by a 2018 systematic review and meta-analysis including 630 participants at enrolment across eleven RCTs lasting at least four weeks and involving a maximum caloric intake of 500kcal for women and 660kcal for men on fast days. All included studies reported weight loss in the IER arms from 5.2% to 12.9% of starting weights compared to 4.3% to 12.1% of initial weights in the CER arms ($p=0.27$). No difference between arms was suggested with regards to change in fat mass ($p=0.58$) measured using various techniques, waist circumference ($p=0.83$), blood glucose levels ($p=0.51$) or HbA1c ($p=0.62$). However fasting insulin levels were shown to be significantly reduced in IER study arms compared to CER ($p=0.009$), with subgroup analysis suggesting that '5:2' fasting regimes were associated with the greatest insulin reductions. Most included studies suggested no hyperphagia on non-fasting days but that participants on IER regimes reported increased hunger compared to those undertaking CER which may explain the higher levels of attrition in IER arms and the lower proportion of participants planning to continue following an IER regime post-intervention (Cioffi *et al.*, 2018). Importantly, a 2016 meta-analysis of six trials lasting at least six months demonstrated that there were few long-term studies with large sample sizes and that there was no statistical difference in weight loss between IER and CER regimes ($p=0.458$) (Headland *et al.*, 2016).

1.3.3. Adverse side effects and controversy

Literature suggests that reported deleterious side-effects of IF patterns are minor, with a 2018 study of older, male war veterans in Australia demonstrating that during the first two weeks of the trial, half of the participants adhering to a '5:2' regime reported hunger, falling to 18.2% at six months; with small amounts (18.2%) of participants reporting headaches (Conley *et al.*, 2018). Headland *et al.* (2016) demonstrated that none of the eight studies included in their meta-analysis reported any serious adverse impact of IF, and Harvie *et al.* (2011) showed that 4.8% of participants in the IF group reported a lack of energy, constipation, feelings of coldness and headaches, 15% complained of hunger, and 15% described a worsened temper, preoccupation with food and difficulty concentrating. Eleven percent of participants undertaking an IF regime reported dizziness, 20% mild headache, 6% mild nausea and 2% temporary sleep disruption compared to 3% of the CER intervention arm reporting dizziness, 5% mild headache and 2% mild nausea during a six month trial (Sundfor *et al.*, 2018). There are few reports of hyperphagia, with a 2016 study showing a transient increase in subjective appetite levels and an increase in energy intake of around 2% following one day consuming 25% of normal caloric needs (2016) and a 2010 study demonstrating a significantly lower energy consumption the day following a day consuming no calories compared to the day after *ad libitum* feeding ($p<0.05$) (Levitsky and DeRosimo, 2010). Similarly, it was shown that energy intake on an *ad libitum* feeding day increased by only 20% above control values in lean men and women following a day consuming no energy (Johnstone *et al.*, 2002).

A recent unpublished poster (Bonassa and Carpinelli, 2018) presented at the European Society of Endocrinology annual meeting was widely reported by the media for suggesting that IF may 'damage the pancreas and affect insulin function in normal healthy individuals' thus leading to increased risk of T2DM. The abstract reports decreased body weight and food intake, with increases in stomach size, adipose tissue, plasma insulin levels, pancreatic secretion of insulin and glucose metabolism, alongside a decrease in muscle tissue. However, it is important to note that this study was carried out using thirty-day-old female Wistar rats fasted for one day which is equivalent to approximately three to four weeks of fasting in humans, therefore this study cannot be cited as applicable to the two day per week IF carried out by humans (Guess, 2018). Similarly, this study showed an increase in markers of insulin resistance which does not mean that the rat had actually become diabetic, as reported (Cork, 2018).

1.4. Points covered in Chapter 1

i) Incidence, aetiology and significance of obesity

ii) Overview of the MD and IF including details of interventions and observational studies alongside systematic reviews and meta-analyses highlighting beneficial outcomes associated with both dietary patterns

1.5. Research questions to be answered in Chapter 2

i) How acceptable is this dietary pattern to the non-Mediterranean general public?

ii) What impact does consumption of the MD have on cardiovascular biomarkers and body composition?

2. The acceptability and impact on body composition and cardiovascular biomarkers of Mediterranean dietary interventions in non-Mediterranean countries: a systematic review and meta-analysis

This chapter outlines a systematic review and meta-analysis run to investigate the use of the Mediterranean diet in non-Mediterranean countries such as the UK to better understand the dietary pattern outside of environmental factors such as weather and culture.

2.1. Introduction

As described in Section 1.2, the MD has been shown to be a particularly healthy dietary pattern with regards to prevention of cardiovascular disease and other major causes of mortality. To date, the strongest epidemiological and clinical evidence on the health benefits of the MD originates from Greece, Italy, France and Spain. It is possible that Mediterranean dwellers might also benefit from exposure to other health-related factors such as lifestyle, e.g. more likely to be physically active (Bach-Faig *et al.*, 2011), socialization, e.g. conviviality and greater likelihood to be socially engaged and stress-free (Bach-Faig *et al.*, 2011, Ficca *et al.*, 2010), and environment, e.g. warm and sunny climates (van der Rhee *et al.*, 2013). Such factors could potentially reduce the health benefits of implementing a MD among non-Mediterranean populations.

However, recent epidemiological evidence indicates that the beneficial effects of a MD are, at least to some extent, independent from these other factors and therefore not exclusive to people living in Mediterranean countries. Studies such as the European Prospective Investigation into Cancer and Nutrition (EPIC) (Trichopoulou, 2005, Couto *et al.*, 2011, Hoevenaar-Blom *et al.*, 2012), the Healthy Ageing Longitudinal Study in Europe (HALE project) (Knoops *et al.*, 2004), the Monitoring Trends and Determinants of Cardiovascular Disease study (MONICA) (Tognon *et al.*, 2014), the Melbourne Collaborative Cohort Study (Hodge *et al.*, 2011), or the Northern Manhattan Study (Gardener *et al.*, 2011), substantiate the fact that health benefits can be achieved by adopting these dietary patterns in other latitudes independently of other factors lifestyle and environmental factors as well as ethnic origin.

Some evidence shows that, outside Mediterranean countries, the MD is becoming an effective and acceptable model of healthy eating and interventions have been successfully implemented among healthy Canadian (Goulet *et al.*, 2003) and Scottish women (Papadaki and Scott, 2005), as well as among patients with coronary heart disease in Northern Ireland (Logan *et al.*, 2010). From a public health perspective, a critical analysis of the evidence on the level of success of MD interventions outside the Mediterranean should be particularly useful to those interested in health promotion among non-Mediterranean populations (Mathers, 2015).

2.1.1. Aims

This systematic review and meta-analysis aims to synthesise the evidence from MD interventions among adult subjects in non-Mediterranean populations, particularly focusing on efficacy and effectiveness measured by assessing the impact of interventions on body composition and cardiovascular biomarkers.

2.2. Methods

2.2.1. Search strategy

The protocol has been registered with PROSPERO, the International Prospective Register of Systematic Reviews (Registration number CRD42014015560). This systematic review was conducted in adherence to Cochrane (Higgins and Green, 2008) and the Centre for Reviews and Dissemination (University of York, 2009) guidelines and is reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher *et al.*, 2010), see Appendix B3 for PRISMA checklist.

In June 2019 Medline, Embase and Scopus were searched systematically from inception. Reference lists of identified publications and previously published related systematic reviews were hand-searched to identify other studies potentially eligible for inclusion.

The search strategy included the following search string: “Mediterranean” OR “Cretan” AND “diet” OR “dietary pattern” with filters to exclude papers in languages other than English, animal studies, or any papers which were not clinical trials, for example reviews (Higgins and Green, 2008). Quality of included studies was assessed using the Cochrane risk of bias tool.

2.2.2. Study selection criteria

Searches were tailored to identify interventions specifically declaring the use of the MD in their intervention arm, and carried outside the main Mediterranean countries associated with evidence on the benefits of the MD such as Cyprus, France, Gibraltar, Greece, Italy, and Spain. Studies originating from countries in the Mediterranean basin but not strongly associated with what is known as a traditional Mediterranean diet such as Albania, Algeria, Bosnia and Herzegovina, Croatia, Egypt, Israel, Lebanon, Libya, Malta, Monaco, Montenegro, Morocco, Slovenia, Syria, Tunisia, and Turkey were excluded from this review.

Both randomised and non-randomised intervention studies were sought. Only publications with an English language abstract were included. Studies on non-institutionalised adult subjects ≥18 years of age adults with or without health risk factors (such as overweight, abdominal obesity, raised blood pressure, abnormal lipid levels and metabolic syndrome) were included.

Studies investigating lifestyle interventions including other components, such as physical activity, were included only if the effects of the nutrition/dietary intervention were reported independently for analysis. Only interventions with a follow-up of one month or longer were included.

2.2.3. Outcome measures

Primary outcome measures included effect of intervention on markers of health (e.g. blood-borne biomarkers such as total cholesterol), body weight or body composition. Secondary outcomes included measures of acceptability of this dietary pattern. Interventions were considered efficacy trials if there was a high degree of assurance of delivery of the ‘treatment/Mediterranean diet’, generally under carefully controlled research conditions (e.g. provision of a specific or fortified complementary food with frequent follow-up to assess adherence). On the other hand, evaluations of interventions carried out in a programme setting, generally with less ability to control delivery of and adherence to 'treatment', were considered effectiveness studies.

2.2.4. Data extraction

Two reviewers (LF and JL) independently assessed publications for eligibility. The decision to include studies was hierarchical and made initially on the basis of the study title and abstract; when a study could not be excluded with certainty at this stage, the full-text was obtained for evaluation. Discrepancies between reviewers were resolved through discussion with a third reviewer and a consensus approach was used.

Two reviewers extracted data, one independently and the second confirming or completing information required. Extracted information included: study design (country of origin, follow-up length, methods of analysis, completion rates); participants' characteristics (population and setting, inclusion/exclusion criteria, baseline characteristics); description of measurement methods; dietary and health-related outcome measures; and information to assess the risk of bias. Study quality was assessed using the Cochrane risk of bias tool (Higgins *et al.*, 2008).

2.2.5. Data synthesis and statistical analysis

Results from the individual studies were pooled and meta-analysed using Review Manager software (RevMan Version 5.1 for Windows Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2015). Where available, results from multivariate models with the most complete adjustment for potential confounders reported in original studies were used. Pooled results were reported as weighed mean differences with 95% CIs and with two-sided p values. Random effects models were used. When studies reported multiple dietary intervention arms studies the method suggested by Higgins *et al.* (2008) was employed, in which excessive weightings from 'double counts' originating from the 'shared' group (i.e. the control group) were controlled by splitting the sample size of the shared group into approximately equal smaller groups for the comparisons, with means and standard deviations left unchanged.

Statistical heterogeneity was evaluated using the I^2 statistic; the 95% CI for I^2 were calculated using Higgins *et al.*'s (2008) method. Where I^2 was >50%, the degree of heterogeneity was considered high. Meta-regression analyses were performed to assess the effect of sample size and length of follow-up as continuous variables.

2.3. Results

The searches yielded 3051 publications after removal of duplicates, and after screening 48 papers were included in the qualitative synthesis and 27 of these in the meta-analysis. Results of the screening process are described in Figure 7.

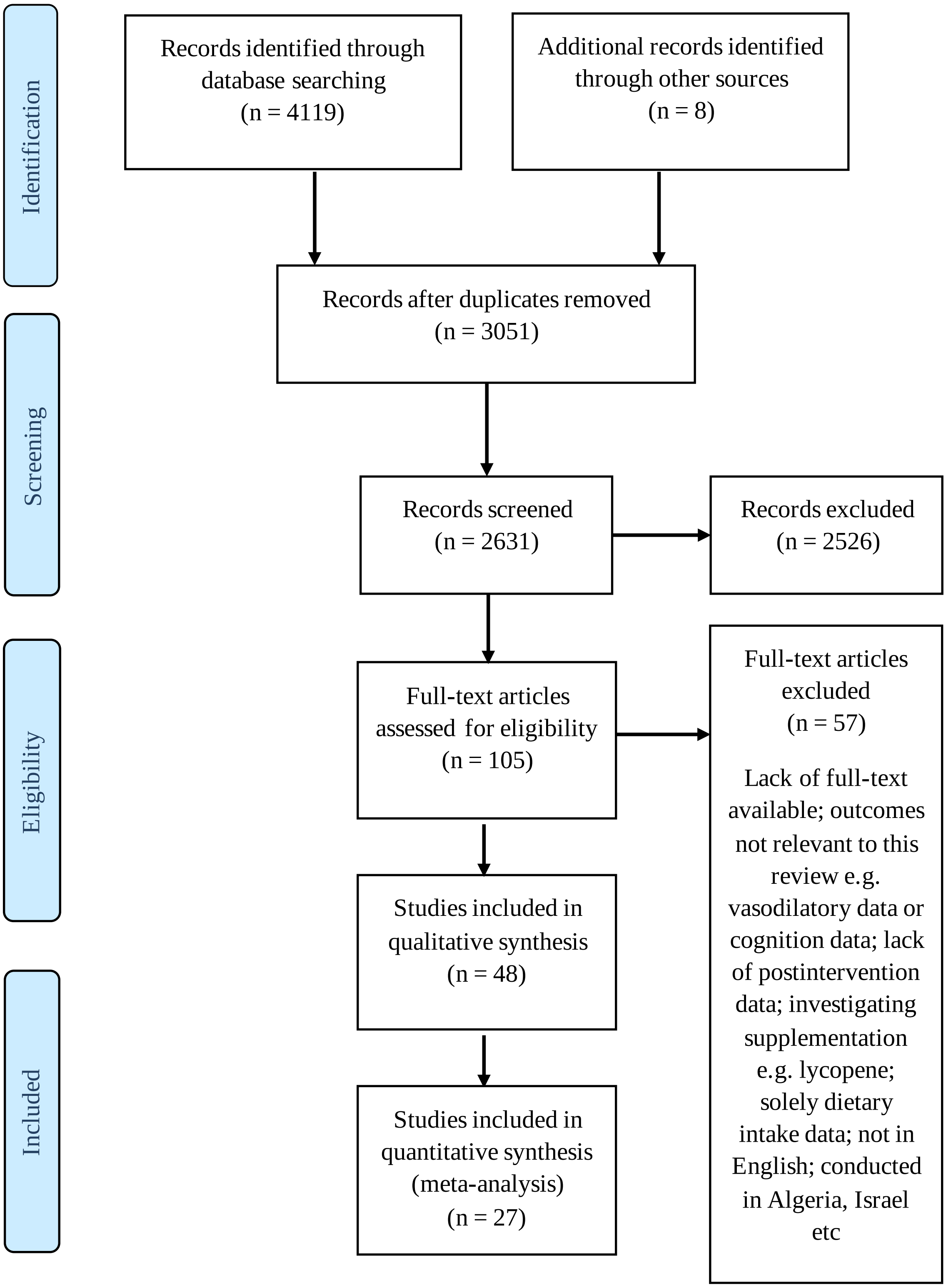

Figure 7: PRISMA flow diagram showing results of screening process

2.3.1. Study characteristics

Twenty-five studies included in this meta-analysis used a RCT design, one of which was the protocol of a pilot RCT in pregnant women; and two studies reported a non-randomised study design. The pooled study populations in these studies included 3185 participants with a mean sample size of 122 subjects per study. Eight studies recruited women only and four studies men only. The mean age of participants in these studies ranged from 18 to 77 years. On average participants were followed-up for 10.0 months (range 2 weeks to 4.3 years). Details of studies included in this meta-analysis are found in Table 2.

Table 2: Studies included in Chapter 2 systematic review and meta-analysis

Author, year	Country	Study type	Mean study length (weeks)	Participant number	Number female	Age	Health status	Outcomes reported
Ambring, 2004+2006	Sweden	CO-RCT	4	22	10	43±1	Healthy	FPI, FPG, BMI, TC, LDL, HDL, TG
Austel, 2015	Germany	RCT	52	212	174	25-70	Overweight/obese	Body weight change, BMI, WC
Bihuniak, 2016	USA	CO-RCT	24	16	16	77±6.8	Healthy; postmenopausal	TG, TC, HDL, LDL
Brehm, 2009	USA	RCT	52	124	78	56.5	T2DM	Body weight, body fat %, SBP, DBP, TC, TG, LDL, HDL, FPG, FPI
Djuric, 2009	USA	RCT	26	69	69	44	Healthy	FPI, FPG, TC, LDL, HDL, TG
Due, 2015	Denmark	RCT	78	131	76	28±5	Healthy	BMI, FPG, HDL-LDL ratio, TC, LDL, body weight change, HDL
Itsiopoulos, 2005	Australia	CO-RCT	24	27	11	59	T2DM	BMI, FPG, FPI, TC, LDL, HDL, TG, SBP, DBP
Jones, 2011 Lipidol	USA	RCT	12	89	89	44±11	Met S	FPG, SBP, LDL, body weight change, HDL, WC, DBP, TG
Lee, 2015	Australia	RCT	1	24	24	26±5	Healthy	SBP, DBP
Michalsen, 2006	Germany	RCT	52	101	23	59±9	CAD	BMI, TC, LDL, HDL, TG, FPI

Author, year	Country	Study type	Mean study length (weeks)	Participant number	Number female	Age	Health status	Outcomes reported
Papadaki, 2008	UK	RCT	36	72	72	25-55	Healthy	Total-C:HDL-C ratio, TC, LDL, HDL, TG
Parcina, 2015	Germany	RCT	2	39	0	30±6	Healthy	BMI, TC, LDL, body weight change, HDL, TG
Richard, 2011	USA	NRT	10	26	0	18-65	Met-S	Body weight change, WC, HDL
Richard, 2012	Canada	CO-RCT	5	19	0	18-65	Met-S	Weight change, BMI, WC, TC, LDL, HDL
Richard, 2013	Canada	CO-NRT	5	52	52	25-62	Met S	Body weight change, HDL-C, WC
Ryan, 2013	Australia	CO-NRT	6	12	6	55±14	NAFLD	FPI, FPG, BMI, SBP, body weight change, WC, DBP
Sexton, 2013	New Zealand	RCT	12	38	18	38±4	Asthma	TC, LDL, HDL, TG
Singh, 2002	India	RCT	104	1000	103	48.5	Hypercholesterolaemia	Weight change, BMI, SBP, DBP, LDL, HDL, TG
Skoldstam, 2002	Sweden	RCT	12	51	41	59	Arthritis	TC, body weight change, TG

Table 2 cont.

Author, year	Country	Study type	Mean study length (weeks)	Participant number	Number female	Age	Health status	Outcomes reported
Stendell-Hollis, 2013	USA	RCT	17	138	138	30±5	Healthy, postpartum	Body weight, BMI, WC, waist:hip, body fat %,
Thomazella, 2011	Brazil	NRT	13	40	0	55±5	≥1 coronary event	Body weight, BMI, WC, waist:hip, SBP, DBP, TC, LDL, HDL, TG, FPG
Timar, 2007	Romania	RCT	52	223	118	45-65	T2DM, overweight	BMI, LDL, TG, SBP, DBP
Toobert, 2003	USA	RCT	226	279	279	58±11	T2DM	BMI, SBP, TC, LDL, waist:hip ratio, HDL, DBP, TG
Toobert, 2011 TBM	USA	RCT	104	280	280	56	T2DM	BMI
Tuttle, 2008	USA	RCT	104	101	26	58±10	MI	HDL, TG, LDL, SBP, DBP, BMI, FPG, FPI

FPI: fasting plasma insulin
FPG: fasting plasma glucose
BMI: body mass index
TC: total cholesterol
LDL: low density lipoprotein
HDL: high density lipoprotein
TG: triglycerides
WC: waist circumference
SBP: systolic blood pressure
DBP: diastolic blood pressure

Table 2 cont.

2.3.2. Scope and origin of studies

Some studies looked at healthy patients (n=9) and others focused on clinical samples of subjects with a range of diagnoses such as cardiovascular diseases (n=4), type 2 diabetes mellitus (n=5), rheumatoid arthritis (n=1) or other diagnoses such as metabolic syndrome and asthma (n=8).

These studies originated from eleven countries around the world. Nine studies were conducted in Europe (Sweden n=2, Germany n=3, UK n=1, Romania n=1, and Denmark n=1), eleven in North America (Canada n=2 and USA n=9), one in South America (Brazil n=1), one in Asia (India n=1) and six in Oceania (Australia n=5 and New Zealand n=1). Israel and Algeria were the only countries located in the Mediterranean basin in which MD studies were identified, and these were excluded from meta-analysis.

2.3.3. Acceptability of Mediterranean diet interventions

Studies reported high completion rates, ranging from 72% to 95%, and MD interventions were generally well received, with informal feedback showing that participants felt ‘heartened by their weight loss’, saw ‘improvements in overall energy and well-being’, and that the majority continued on the MD diet plan post-intervention (Erdrich *et al.*, 2015). Another intervention found that uptake of a MD dietary pattern was an ‘enjoyable and pleasurable experience’, generating a sense of ‘fulfilment’ at meal times with participants stating they thought they had ‘widened their food horizon’ and introduced ‘a better quality of food into their normal eating habits’ (Middleton *et al.*, 2015). Ambring *et al.* (2006) reported that ‘compliance with the diets was excellent’ and that all participants adhered to the pattern well, as assessed by 24-h recalls and the return of any uneaten foods. A number of barriers to this eating pattern were also highlighted by this study, with participants reporting that adherence to the MD required substantial changes in shopping and eating habits compared to their normal diets, and that time pressures due to work and other commitments could make it difficult to spent the required time making meals from scratch. Some participants indicated that it was not always possible to find the necessary ingredients, and that some foods were more expensive than products habitually purchased. Another study reported that participants adhered well to the diet, with a mean compliance level of 98% based on food checklists (Richard *et al.*, 2013). Djuric *et al.* (2012) found that 'satisfaction with study participation was high' and that participants did not find the diet too 'burdensome'.

2.3.4. Effectiveness and efficacy of Mediterranean diet interventions

Eight studies were deemed to be evaluating efficacy of MD interventions with the remainder assessing effectiveness, as shown in Table 3. In order to assess efficacy, researchers employed many techniques such as supplying all or most of the required foods, providing detailed meal plans and recipes, or organising intensive group or individual counselling sessions with nutritionists or dietitians. Studies investigating effectiveness involved the supply of recipes and dietary inspiration for participants to use under free-living conditions, alongside less frequent meetings with study staff.

Table 3: Effectiveness and efficacy decision table for MD systematic review

Author, date	Effectiveness/efficacy	Notes
Ambring, 2004+2006	Efficacy	Food equal to 60% of daily caloric requirement given.
Austel, 2015	Efficacy	Participants received weekly instructions during the first 6 weeks of intervention, these consisted of an informational letter, seven daily diet/ cooking plans, a shopping list and a supply manifest for that week. Every daily diet plan included recipes for breakfast, lunch, dinner and two portion-controlled sweet snacks with cooking instructions and exact food quantities for all meals.
Bihuniak, 2016	Efficacy	Participants provided with EVOO, walnuts and fish, and personalised nutritional counselling, sample Mediterranean meal plans, cooking recipes, and a book discussing the details and origins of the diet.
Brehm, 2009	Effectiveness	Individualised diet plan. Participants met with a dietitian weekly during months 1 and 2, biweekly during months 3 and 4, and monthly during months 5 through 12 for either individual counselling or a group session (alternating every other visit).
Djuric, 2009	Effectiveness	Dietary counselling.
Due, 2015	Effectiveness	Prescribed percentages of fat for each intervention arm.
Itsiopoulos, 2005	Efficacy	All food provided – in excess of energy requirements so participants could eat *ad libitum*.
Jones, 2011	Effectiveness	Instructional DVD viewed and detailed dietary booklets were distributed summarizing dietary guidelines, lists of suitable foods, suggested serving sizes, and recipes.
Lee, 2015	Effectiveness	Provided with an eating plan.
Michalsen, 2006	Effectiveness	Intensive instruction and education.

Author, date	Effectiveness/efficacy	Notes
Papadaki, 2008	Effectiveness	Tailored feedback letters based on food frequency questionnaires.
Parcina, 2015	Efficacy	All food provided and eaten in the research centre.
Richard, 2011	Effectiveness	All food provided for first 5 weeks, then 20 weeks free-living conditions with dietary advice, then another 5 weeks with all food provided.
Richard, 2012+2013	Efficacy	Participants' diet was first standardized to a control diet reflecting current averages in macronutrient intake in North American men, with all foods and beverages provided under isoenergetic conditions for 5 weeks. Participants were then fed an isoenergetic MedDiet over a subsequent period of 5 weeks to maintain their weight.
Ryan, 2013	Effectiveness	Recipes and two-weekly meal plans given, two-weekly appointments with study dietician who checked food diaries.
Sexton, 2013	Effectiveness	High-intervention group: encouraged to adopt MD, received intensive initial advice and 41-h consultation sessions with a dietitian. Low-intervention group: received less intensive advice and spent 2h with a dietitian. Control group: offered one session with a dietitian, recipes, and free food at the end of the trial. Both intervention groups were provided with written advice, olive oil, and vouchers for the purchase of appropriate foods.
Singh, 2002	Effectiveness	Dietary advice.
Skoldstam, 2002	Efficacy	Margarine provided. MD from the hospital canteen was served for the first three weeks. During these weeks each group of MD patients had six lessons from a dietician about Mediterranean food and cooking. After this

		the same dietician was available weekly for telephone consultation. Written instructions and recipes to facilitate the preparation of meals at home.
Stendell-Hollis, 2013	Effectiveness	One-on-one dietary counselling with registered dietitian. 28g/d walnuts provided.
Thomazella, 2011	Effectiveness	Advice about daily food plans, including portion size models, desired food intake frequency, and specific recipes given. Individual food plans were tailored to nutritional assessments including BMI, energy needs by the Harris-Benedict equation, and daily and cultural habits.
Timar, 2007	Effectiveness	Dietary advice.
Toobert, 2003+2011	Effectiveness	3-day non-residential retreat followed by weekly meetings lasting 6 months and consisting of 1h each of physical activity, stress management, group Mediterranean potluck dinner, and support groups. Dietary advice given.
Tuttle, 2008	Effectiveness	Two individual dietary counselling sessions from study dietitians within the first month, followed by additional individual sessions at months 3, 6, 12, 18, and 24. Participants attended 6 different group sessions focused on behavioural modification and practical aspects of their assigned diets, including recipes, grocery shopping, and dining out. After completing 6 classes, participants were invited but not required to continue attending group sessions.
Davis, 2016+2017	Efficacy	45-min consultation with a trained dietitian to receive dietary instructions. Resources provided: recipe book, guidelines for eating out, serving sizes, and the recommended number of servings. Foods provided: olive oil, nuts, legumes, tuna, and Greek yogurt.

Table 3 cont.

2.3.5. Meta-analysis

Table 4 shows that there were no significant changes to any outcome, but that consumption of the MD is associated with trends for decreased TC, LDL, TG, FPI, SBP, DBP, WC, weight and BMI alongside increases in HDL and FPG when compared to a control group. There were high levels of heterogeneity amongst most of the studies reporting on each outcome, with the exception of FPI (0%), DBP (40%) and WC (45%). See Appendix B4 for an example forest plot showing meta-analysis results.

Table 4: Number of included studies, mean difference, 95% CI, p value and heterogeneity levels for each reported outcome

Outcome	Included studies reporting outcome	Mean difference	95% CI (lower, upper)	P value	Heterogeneity (%)
TC	19	-0.18mmol/L	-0.37, 0.01	0.06	74
LDL	21	-0.03mmol/L	-0.25, 0.18	0.50	92
HDL	17	0.01mmol/L	-0.03, 0.04	0.64	53
TG	19	-0.06mmol/L	-0.21, 0.09	0.43	92
FPI	8	-0.11mmol/L	-0.30, 0.07	0.22	0
FPG	13	0.06mmol/L	-0.11, 0.22	0.50	78
SBP	13	-2.03mmHg	-4.68, 0.63	0.13	81
DBP	11	-1.34mmHg	-2.28, -0.41	0.08	40
WC	8	-0.10cm	-2.34, 2.14	0.93	45
Weight	14	-0.63kg	-2.02, 3.29	0.64	83
BMI	19	-0.03kg/m^2	-0.86, 0.79	0.93	90

*Significant p values are shown in bold with an asterisk

2.4. Discussion

2.4.1. Statement of principle findings

This systematic review and meta-analysis showed that there is a growing body of literature investigating the use of the MD in non-Mediterranean countries, with results suggesting that the

MD is deemed an acceptable dietary pattern and associations shown with between adherence to the MD and beneficial changes to TC, LDL, HDL, TG, FPI, FFG, SBP, DBP, WC, weight and BMI.

2.4.2. Comparison to other literature

Dietary interventions based on the MD as a model of healthy eating outside Mediterranean countries are not uncommon and the number of included studies in the present systematic review reveals a growing interest in the adoption of the Mediterranean dietary pattern in health prevention and disease management in non-Mediterranean countries. A number of trials included in this study support the efficacy of the MD in modifying a number of health risk factors among healthy subjects and patients with different health problems, thus confirming that the health benefits of the MD are certainly applicable to populations in other latitudes outside the Mediterranean. Although no results were statistically significant, adherence to the MD is associated here with trends for beneficial alterations to outcomes related to body composition and biomarkers of cardiovascular disease, which is concurrent with a recent systematic meta-review including nine systematic reviews and 24 meta-analyses suggesting an inverse association between higher adherence to a MD and both body weight and BMI, with one meta-analysis showing a mean weight loss of 1.75kg and another suggesting that participants adhering to a MD lost on average 0.29kg more than those on the control diet. All included studies showed a positive effect of the MD on CVD biomarkers and blood pressure (Martinez-Lacoba *et al.*, 2018). The results of the present systematic review and meta-analysis therefore have important public health implications. The development of effective lifestyle interventions are of significant value to policy makers and national health systems. Lifestyle strategies involving the MD are likely to be highly cost-effective, however further research is required to investigate the most efficient method of implementation. Results of this study are later used to inform a clinical trial investigating the impact on body composition and biomarkers of cardiovascular disease alongside feasibility and acceptability of the MD when employed in the UK (Chapters 6-9).

2.4.3. Strengths and weaknesses

The strengths of this study include the rigorous methodology in the systematic review of the literature, adherence to Cochrane guidelines and use of PRISMA flow diagram and checklist, overall good quality of the included studies (including low attrition rates) providing confidence in the robustness of the findings, and the consistency of findings showing positive effect of MD interventions on a number of clinical outcomes across the diversity of RCTs. Three mainstream databases (Scopus, PubMed and Embase) relevant to the research area were searched from inception, and specific search terms were utilised to ensure inclusion of all relevant references. Some limitations surrounding these findings must be acknowledged; among these are the high levels of heterogeneity between studies, meaning that findings and conclusions should be treated with caution. Subgroup analysis to explore potential sources of heterogeneity was not possible due to time constraints alongside small participant numbers and overall small number of studies, however these may have identified sex, ethnicity, type of intervention, or geographic origin of studies as possible causes of high heterogeneity levels, as assessed by I^2 tests. A potential limitation is that most studies involved Caucasians, allowing little assessment of MD interventions amongst non-Caucasians. Also of note is that only studies published in English were screened for inclusion, due to lack of access to accurate translation capabilities. Other limitations are related to the use of dietary assessment tools such as food-frequency questionnaires and other self-reported questionnaires which are prone to misreporting therefore the well-recognised limitations of all such methods would be of importance. Another issue with the studies included in this analysis is that participant blinding is impossible during dietary interventions, potentially leading to a higher risk of bias and not reflecting the true intervention effect size.

2.4.4. Conclusions

Although results should be interpreted with caution, this systematic review and meta-analysis add to the emerging body of research suggesting that consumption of a MD has beneficial effects on blood biomarkers such as total cholesterol levels and triglyceride levels, alongside anthropometric measures for example waist circumference and BMI. Also of note is the acceptance of the diet by participants demonstrated by high completion rates, signifying high palatability.

2.5. Points covered in Chapter 3

i) Meta-analysis looking at the use of the MD outside Mediterranean countries, conducted according to appropriate guidelines, involving a thorough search of major search engines, and resulting in 27 included studies suggesting there is interest in this pattern

ii) Results tentatively suggest that the MD is associated with non-significant improvements in important measures of health such as total cholesterol levels and systolic blood pressure

2.6. Research questions to be answered in Chapter 3

i) How adherent are the general public in England to the MD, how much do they know about this dietary pattern, and how acceptable do they find the dietary guidelines?

ii) Which methods do individuals utilise in weight loss attempts, how many attempts do they make, and how successful are they?

iii) What are the most commonly reported perceived barriers to healthy eating?

iv) Are there links between these variables?

3. An online survey investigating barriers to healthy eating and the acceptability of and adherence to the Mediterranean diet in the North East of England

This chapter utilises an anonymous online survey to address the use and public opinion of the Mediterranean dietary pattern in the UK to assess acceptability of this way of eating, alongside investigating the public's perceived barriers to healthy eating.

3.1. Introduction

3.1.1. The Mediterranean diet

As discussed in Section 1.2, the MD has been shown to be a beneficial dietary pattern in both Mediterranean and non-Mediterranean countries, with multiple health benefits including increased longevity and reduced incidence of cardiovascular disease and stroke (Estruch *et al.*, 2013, de Lorgeril *et al.*, 1999). Although the majority of research on the MD has been carried out in Mediterranean countries, literature has also suggested that this dietary pattern is deemed acceptable and palatable by the UK public, as described in section 2.3.3.

3.1.2. UK dietary habits

The average UK diet is not currently meeting government dietary recommendations, as laid out in the Eatwell Guide (Figure 12). Results of the most recent National Diet and Nutrition Survey (NDNS) 2015-2016 showed that UK adults aged 19-64 years ate on average 4.2 portions of fruit and vegetables per day, with adults aged over 65 consuming 3.9 portions per day. In the 19-64 years age bracket, 29% of men and 32% of women; alongside 31% of men and 32% of women aged over 65 met the 5-A-Day fruit and vegetable guidelines. Mean oily fish intake for adults was 54-87g/week, with the vast majority of participants missing the 140g/week (one portion/week) target. Positively, mean intakes of red meat by women met the current guideline of not consuming more than 70g/day, with women aged 19-64 consuming around 47g/day and those aged over 65 eating around 49g/day. This is in contrast with the average male intake of red meat, with men aged 19-64 eating 77g/day and those over 65 consuming 70g/day. Mean intake of non-starch polysaccharides (NSP) was below the 30g/day recommendation at 19g/day for adults aged 19-64, and 18.4g/day for those aged over 65. Participants met recommendations relating to total fat intake, with all surveyed groups consuming no more than 35% of food energy as fat, however average saturated fat intake was above the 11% of food energy recommendation, at 11.9% for participants aged 19-64 and 12.5% for those aged over 65 (PHE, 2018a).

3.1.3. Perceived barriers to healthy eating

There are various factors that dictate an individual's eating pattern, with a pan-European study suggesting that the most common perceived barriers to healthy eating (PBHE) amongst the EU cohort were 'irregular working hours' (24%), 'giving up liked foods' (23%) and 'willpower' (18%), with 'giving up liked foods' (33%) ranked the most important amongst UK respondents, and no significant impact accredited to gender, educational level or employment status. Only 7% of participants reported that a lack of knowledge about healthy foods was a PBHE, with 'lengthy preparation time' (8%), 'lack of cooking skills' (7%) and 'limited storage facilities' (2%) also not seen as particularly significant (Kearney and McElhone, 1999). In a study of 50 individuals, three days of meals which met government dietary recommendations were provided for consumption at home and participants were asked to use this experience to identify PBHE. The PBHE reported tended to be more commonly associated with societal issues such as the need for convenience due to working hours, habits surrounding portion sizes (such as being taught as a child to 'clear your plate' and concerns around being hungry later) and importance of value for money, with a lack of cooking skills or nutritional knowledge reported less frequently (Macdiarmid *et al.*, 2013). A 2017 study of 8319 Scottish adults showed that a 'lack of willpower' was the most commonly reported PBHE, with a significantly higher proportion of women than men reporting 'lack of willpower' and 'lack of support from others' as PBHE ($p<0.001$). A significantly higher proportion of men reported that 'not liking healthy foods' or 'healthy foods are too boring' ($p<0.001$) and 'lack of cooking skills' ($p<0.002$) as PBHE in comparison to women. This analysis also suggested that men are 2.56% and women are 3.00% less likely to meet the government recommendation of consumption of 400g of fruit and vegetables per day if they reported 'lack of willpower' as a PBHE, compared to those who did not report this PBHE (McMorrow *et al.*, 2017). Similarly, a cross-sectional online survey of 206 adults of retirement age showed that the higher the number of reported PBHE, the higher the BMI tended to be ($p<0.001$), and the higher the number of PBHE, the lower the Mediterranean dietary adherence score ($p=0.001$) (Lara *et al.*, 2014b), suggesting that PBHE have significant impact on dietary choices and overall health.

3.1.4. Aims

This study aims to assess the acceptability of the MD pattern, alongside current adherence to this diet amongst the UK population. This study will also investigate participants' perceived barriers to healthy eating and the links between these factors with dietary patterns.

3.2. Methods

3.2.1. Ethics

Ethical clearance was granted by the Northumbria University Health and Life Science Ethics Committee (Appendix C5). Participants provided consent online before beginning the survey.

3.2.2. Study design

This is an observational, cross-sectional online survey of dietary habits, MD adherence and barriers to healthy eating. The study is reported according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement (von Elm *et al.*, 2014) and CHERRIES (The Checklist for Reporting Results of Internet E-Surveys) statement (Eysenbach, 2004).

3.2.3. Questionnaire design

Bristol Online Survey software (Jisc, UK; subsequently renamed Online Surveys) was utilised to create the online questionnaire (shown in full in Appendix C6), as this assured anonymity. Participants were emailed links to the online survey; the first page of which contained the study information sheet, leading on to an informed consent form. If the participant consented to take part in the study, they advanced to the first section of the questionnaire. If they did not consent, they were routed to a page thanking them for their time and explaining that they would not be able to complete the questionnaire. The first section of the questionnaire included background information questions, such as weight, educational status, and marital status. The second section included questions about previous weight loss attempts, such as the methods used and any weight lost. The third segment was made up of an altered version of the PREDIMED 14-item MD adherence screener (Estruch *et al.*, 2013). Participants were then asked about their understanding of the MD, and asked questions to investigate feasibility of consumption of certain elements of the MD in their everyday lives. The final section asked participants about their perceived barriers to healthy eating, using a list from a previously published paper (Kearney and McElhone, 1999). All questions were mandatory and included a non-response option to avoid missing answers.

3.2.4. Recruitment

Participants were recruited via explanatory emails containing links to the online survey utilising the snowball effect. Participation was voluntary, respondents answered questions anonymously, and there was no reward for participation. This was a voluntary, 'open survey' whereby no password was applied therefore was available to all potential participants. This questionnaire was launched on 9th August 2017 and closed on 18th February 2018.

3.2.5. Inclusion criteria

Participants were healthy, above 18 years of age, and a UK resident with a good standard of English due to a lack of reliable translational facilities.

3.2.6. Pilot testing

The online questionnaire was pilot tested amongst a group of ten individuals fitting the inclusion criteria. Participants were asked to complete a feedback survey about the questionnaire, particularly investigating the ease of understanding of questions, relevance of questions, and length of time taken to complete the survey. This feedback was analysed and used to make alterations to question wording and answer options in order to improve clarity.

3.2.7. Study outcomes

Outcomes of interest included participant demographics, measures of understanding and acceptability of the MD, levels of dietary adherence, and reported barriers to participants' healthy eating.

3.2.8. Statistical analysis

IBM's SPSS v26 for Windows was used to compare continuous variables using independent t-tests, with nominal and ordinal variables compared using Chi-squared tests. Natural groupings of participants' characteristics were identified using two-step cluster analysis. The first step involved creation of pre-clusters by use of an algorithm known as the cluster feature tree. The second step involved the merging of pre-clusters using agglomerative hierarchical clustering. Cluster membership and the most feasible number of separate clusters were determined using model fit indices such as log-likelihood distance measure and Schwarz's Bayesian information criterion. Pearson correlation analysis was utilised to investigate associations between variables, and binary logistical regression was performed to further understand links between variables, with adjustment for covariates using the Enter method.

3.3. Results

3.3.1. Demographics

Overall, 566 respondents completed the informed consent page, with 554 complete questionnaires received and three participants excluded as they were not UK residents, leaving 551 completed surveys (incomplete questionnaires i.e. those not reaching the final page were not analysed). Table 5 shows that the majority of participants were female, with a mean weight of 71.89kg ± 34.38 (81.31kg ± 14.47 for men and 70.48kg ± 36.24 for women), and a mean BMI of 25.67kg/m^2 ± 11.47 (25.19kg/m^2 ± 5.00 for men and 25.74kg/m^2 ± 12.15 for women). 5.08% of participants (5.65% of men and 5.22% of women) had a BMI in the underweight category, 51.36% (43.06% of men and 52.82% of women) had a BMI falling into the healthy range (BMI 18.5-24.9kg/m^2), 25.59% (40.28% of men and 23.38% of women) were overweight, with 17.60% (11.11% of men and 18.58% of women) obese. Mean age was 28.2 years ± 44.44; 92.92% were Caucasian and 91.65% lived in the North East of England. Participants were mainly single (70.78%) and were full-time students (62.25%) with University level education (66.06%). 74.59% of participants had never smoked, and 77.13% drank some amount of alcohol. Rates of cardiovascular disease (1.45%), hypertension (0.91%), type 2 diabetes (0.18%) and high cholesterol (2.00%) were low, and 5.63% of participants stated they were following a special diet due to a health condition (for example Crohn's Disease, Ulcerative Colitis, Irritable Bowel Syndrome, alongside various food intolerances and allergies). The majority (59.71%) of participants claimed to weigh themselves weekly or monthly, and 62.43% stated that they were currently trying to lose weight.

Table 5: Demographics of 551 participants

	All samples (n= 551)	**Men (n= 72)**	**Women (n= 479)**
	Mean ± SD		
Weight (kg)	71.89 ± 34.38	81.31 ± 14.47	70.48 ± 36.24
Height (m)	1.78 ± 2.45	1.83 ± 0.41	1.78 ± 2.62
BMI (kg/m²)	25.67 ± 11.47	25.19 ± 5.00	25.74 ± 12.15
Age (years)	28.25 ± 44.44	31.86 ± 14.45	27.71 ± 10.83
	N (%)		
BMI status (kg/m²)			
Underweight (<18.5)	28 (5.08)	4 (5.65)	25 (5.22)
Healthy weight (18.5-24.9)	283 (51.36)	31 (43.06)	253 (52.82)
Overweight (25.0-29.9)	141 (25.59)	29 (40.28)	112 (23.38)
Obese (>30)	97 (17.60)	8 (11.11)	89 (18.58)
Age groups (years)			
18-30	385 (69.87)	45 (62.50)	340 (70.98)
31-40	84 (15.25)	10 (13.89)	74 (15.45)
41-50	45 (8.17)	8 (11.11)	37 (7.72)
51-60	28 (5.08)	6 (8.33)	22 (4.59)
>60	9 (1.63)	3 (4.17)	6 (1.25)
Ethnicity			
Caucasian	512 (92.92)	69 (95.83)	443 (92.48)
Black	5 (0.91)	0 (0)	5 (1.04)
South Asian	20 (3.63)	0 (0)	20 (4.18)
East Asian	8 (1.45)	2 (2.78)	6 (1.25)

	All samples (n= 551)	Men (n= 72)	Women (n= 479)
Other	6 (1.09)	1 (1.39)	5 (1.04)
Place of residence			
North East England	505 (91.65)	67 (93.06)	438 (91.44)
Other	46 (8.35)	5 (6.94)	41 (8.56)
Relationship status			
Single	390 (70.78)	46 (63.89)	344 (71.82)
Married	104 (18.87)	18 (25.00)	86 (17.95)
Divorced/Separated/Widowed	29 (5.26)	4 (5.56)	25 (5.22)
Prefer not to say	5 (0.91)	1 (1.39)	4 (0.84)
Other	23 (4.17)	3 (4.17)	20 (4.18)
Employment status			
Unemployed	19 (3.45)	0 (0)	19 (3.97)
Working part-time	95 (17.24)	19 (26.39)	76 (15.87)
Working full-time	68 (12.34)	6 (8.33)	62 (12.94)
Carer/housewife/househusband	1 (0.18)	0 (0)	1 (0.21)
Retired	5 (0.91)	2 (2.78)	3 (0.63)
Full-time student	343 (62.25)	44 (61.11)	299 (62.42)
Part-time student	14 (2.54)	1 (1.39)	13 (2.71)
Other	6 (1.09)	0 (0)	6 (1.25)
Education			
None	3 (0.54)	1 (1.39)	2 (0.42)
Secondary school	174 (31.58)	14 (19.44)	160 (33.40)
University	364 (66.06)	53 (73.61)	311 (64.93)
Prefer not to say	4 (0.73)	2 (2.78)	2 (0.42)
Other	6 (1.09)	2 (2.78)	4 (0.84)
Smoking			
Never smoker	411 (74.59)	50 (69.44)	361 (75.37)

	All samples (n= 551)	Men (n= 72)	Women (n= 479)
Ex-smoker	86 (15.61)	13 (18.06)	73 (15.24)
Current smoker	54 (9.80)	9 (12.50)	45 (9.39)
Alcohol			
Drinks alcohol	425 (77.13)	61 (84.72)	364 (75.99)
Does not drink alcohol	126 (22.87)	11 (15.28)	115 (24.01)
Health conditions			
Cardiovascular disease	8 (1.45)	5 (6.94)	3 (0.63)
Hypertension	5 (0.91)	4 (5.56)	1 (0.21)
Type 2 diabetes	1 (0.18)	1 (1.39)	0 (0)
High cholesterol	11 (2.00)	7 (9.72)	4 (0.84)
Following a health condition-specific diet	31 (5.63)	4 (5.56)	27 (5.64)
Weighing			
Never/Yearly	120 (21.78)	18 (25.00)	102 (21.29)
Daily	43 (7.80)	7 (9.72)	36 (7.52)
Weekly/Monthly	329 (59.71)	40 (55.56)	289 (60.33)
Other	59 (10.71)	7 (9.72)	52 (10.86)
Weight status			
Trying to lose weight	344 (62.43)	32 (44.44)	312 (65.14)
Trying to gain weight	21 (3.81)	9 (12.50)	12 (2.51)
Not trying to change weight	186 (33.76)	31 (43.06)	155 (32.36)

*Significant p values are shown in bold with an asterisk

Table 5 cont.

3.3.2. Past weight loss attempts

As shown in Table 6, 79.47% of all participants reported making an attempt to lose weight in the past, with significant differences between men and women (70.83% and 81.00%; p= 0.046). 28.86% of participants utilised diet plans with group meetings in past weight loss attempts, 30.76% used diet plans without group meetings, 48.46% involved exercise plans in their regime, 21.05% used meal replacements, 14.52% used medicinal aids, 24.50% fasted, and 0.18% underwent surgery. There were statistically significant differences between men and women in terms of use of diet plans with and without group meetings, exercise plans, medicines, and fasting (p=0.000; 0.005; 0.001; 0.020; 0.005). Overall, participants who stated they had tried to lose weight in the past (n= 439) made on average five (SD 12.57) attempts, with participants reporting that on average two (SD 2.69) of these attempts were successful.

Table 6: Number of past weight loss attempts, number of successful weight loss attempts and the weight loss methods used by participants

	All samples (n= 551)	**Men (n= 72)**	**Women (n= 479)**	**P value**
	N (%)			
Have made an attempt to lose weight in past	439 (79.67)	51 (70.83)	388 (81.00)	**0.046***
Weight loss methods				
Diet plans with group meetings	159 (28.86)	8 (11.11)	151 (31.52)	**0.000***
Diet plans w/o group meetings	169 (30.76)	12 (16.67)	157 (32.78)	**0.005***
Exercise plans				
Meal replacements	267 (48.46)	22 (30.56)	245 (51.15)	**0.001***
Medicines	116 (21.05)	10 (13.89)	106 (22.13)	0.108
Fasting	80 (14.52)	4 (5.56)	76 (15.87)	**0.020***
Surgery	135 (24.50)	8 (11.11)	127 (26.51)	**0.005***
	1 (0.18)	0 (0)	1 (0.21)	0.698
	All samples (n= 384)	**Men (n= 57)**	**Women (n= 327)**	
	Mean ± SD			
Weight loss attempts	4.69 ± 12.57	3.99 ± 6.49	4.79 ± 13.25	0.612

Successful weight loss attempts	2.30 ± 2.69	2.18 ± 1.90	2.34 ± 2.81	0.677

*Significant p values are shown in bold with an asterisk

3.3.3. Understanding and acceptability of the Mediterranean diet

Table 7 shows the level of MD knowledge of participants, with the majority (43.00%) of volunteers stating they 'know a little bit about the MD' and only 10.53% selecting the 'I fully understand the concept of the MD' category. Most participants (45.37%) selected Mediterranean as their favourite cuisine, followed by 27.40% choosing Asian. Table 8 shows that acceptance of the MD was generally high in this population of participants, with 90.93% stating they thought a guideline of more than three portions of vegetables per day was acceptable, and the lowest percentage of participants (20.87%) saying that more than four tablespoons of olive oil per day was an acceptable guideline. Mean MD acceptability score was 9.19 points overall, 9.16 for women and 9.40 for men. There were no statistically significant differences between genders, except where the nut consumption guideline was concerned (p=0.046).

Table 7: Knowledge of the MD and preferred cuisines when dining out

	All samples (n= 551)	Men (n= 72)	Women (n= 479)	P value
	N (%)			
MD knowledge				0.066
I've never heard of the MD	182 (33.03)	19 (26.39)	163 (34.03)	
I know a little bit about the MD	237 (43.00)	31 (43.06)	206 (43.01)	
I know quite a bit about the MD	73 (13.25)	12 (16.67)	61 (12.73)	
I fully understand the concept of the MD	58 (10.53)	9 (12.50)	49 (10.23)	
Other	1 (0.18)	1 (1.39)	0 (0)	
Preferred cuisine				0.367
Asian	151 (27.40)	19 (26.39)	132 (27.56)	
Mediterranean	250 (45.37)	28 (38.89)	222 (46.35)	
British or American	80 (14.52)	15 (20.83)	65 (13.57)	
Other	70 (12.70)	10 (13.89)	60 (12.53)	

Table 8: Percentages of participants stating that each MD guideline would be acceptable and overall mean MD acceptance score

MD guideline	**All samples (n= 551)**	**Men (n= 72)**	**Women (n= 479)**	**P value**
	N (%)			
Use olive oil as main fat for cooking	357 (64.79)	49 (68.06)	308 (64.30)	0.280
≥4 tbsp of olive oil per day	115 (20.87)	21 (29.17)	94 (19.62)	0.087
≥3 portions of vegetables per day	501 (90.93)	68 (94.44)	433 (90.40)	0.361
≥2 portions of fruit per day	438 (79.49)	55 (76.39)	383 (79.96)	0.615
<1 portions of red meat, hamburger or meat products per week	374 (67.88)	46 (63.89)	328 (68.48)	0.670
<1 portion of butter, margarine or cream per day	401 (72.78)	47 (65.28)	354 (73.90)	0.110
<1 glass of sweet or carbonated beverages per day	416 (75.50)	54 (75.00)	362 (75.57)	0.866
≥7 glasses of wine per week	169 (30.67)	19 (26.39)	150 (31.32)	0.539
≥3 portions of legumes or pulses per week	348 (63.16)	46 (63.89)	302 (63.05)	0.346
≥3 portions of fish or shellfish per week	320 (58.08)	49 (68.06)	271 (56.58)	0.184
<3 portions of sweets or pastries per week	439 (79.67)	58 (80.56)	381 (79.54)	0.802
≥3 servings of nuts per week	314 (56.99)	46 (63.89)	268 (55.95)	**0.046***
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	421 (76.41)	58 (80.56)	363 (75.78)	0.179
Use of a tomato-based sauce in cooking ≥2 times per week	450 (81.67)	61 (84.72)	389 (81.21)	**0.012***
MD acceptance score (mean ± SD)	9.19 ± 2.61	9.40 ± 2.52	9.16 ± 2.63	0.456

*Significant p values are shown in bold with an asterisk

3.3.4. Mediterranean diet adherence

Table 9 outlines MD adherence levels, with the lowest percentage of participants consuming more than four tablespoons of olive oil per day (3.81%) followed by 4.54% drinking seven or more glasses of wine per week, 14.88% eating more than three servings of nuts per week, 15.61% eating more than three portions of fish or shellfish per week, 22.50% eating less than one portion of red meat per week, 23.41% eating more than three portions of legumes per week, 27.22% eating more than two portions of fruit per day, 30.31% drinking less than one glass of sweet or carbonated beverages per day, 40.83% eating less than three portions of sweets or pastries per week, 61.71% using olive oil as the main fat in cooking, 76.23% eating more than three portions of vegetables per day, 84.03% preferentially consuming white meat over red meat, and 87.84% using a tomato-based cooking sauce two or more times per week. Statistically significant differences were only seen between genders in the consumption of red meat, with 8.33% of men eating less than one portion of red meat per week, compared to 24.6% of women ($p=0.002$). Mean adherence score out of a maximum of 14 points was 5.24 ± 2.09 overall, with no difference between men (5.31 ± 1.92) and women (5.23 ± 2.11); $p= 0.780$.

Table 9: Percentages of participants gaining 1 point for adherence to specific food guidelines and mean MD adherence score

MD adherence criteria	All samples (n= 551)	Men (n= 72)	Women (n= 479)	P value
	N (%)			
Use olive oil as main fat for cooking	340 (61.71)	52 (72.22)	288 (60.13)	**0.049***
≥4 tbsp of olive oil per day	21 (3.81)	5 (6.94)	16 (3.34)	0.136
≥3 portions of vegetables per day	420 (76.23)	59 (81.94)	361 (75.37)	0.221
≥2 portions of fruit per day	150 (27.22)	20 (27.78)	130 (27.14)	0.910
<1 portions of red meat, hamburger or meat products per week	124 (22.50)	6 (8.33)	118 (24.63)	**0.002***
<1 portion of butter, margarine or cream per day	172 (31.22)	23 (31.94)	149 (31.11)	0.886
<1 glass of sweet or carbonated beverages per day	167 (30.31)	20 (27.78)	147 (30.69)	0.616
≥7 glasses of wine per week	25 (4.54)	5 (6.94)	20 (4.18)	0.293
≥3 portions of legumes or pulses per week	129 (23.41)	15 (20.83)	114 (23.80)	0.579
≥3 portions of fish or shellfish per week	86 (15.61)	15 (20.83)	71 (14.82)	0.190
<3 portions of sweets or pastries per week	225 (40.83)	34 (47.22)	191 (39.87)	0.237
≥3 servings of nuts per week	82 (14.88)	10 (13.89)	72 (15.03)	0.800
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	463 (84.03)	62 (86.11)	401 (83.72)	0.605
Use of a tomato-based sauce in cooking ≥2 times per week	484 (87.84)	62 (86.11)	422 (88.10)	0.630
	Mean ± SD			
MD adherence score	5.24 ± 2.09	5.31 ± 1.92	5.23 ± 2.11	0.780

*Significant p values are shown in bold with an asterisk

3.3.5. Barriers to healthy eating

As shown in Table 10, 48.46% of participants think their current diet is healthy, with no significant difference between genders (56.94% of men, 47.18% of women; p=0.404). The most commonly reported barriers to healthy eating were ‘lack of willpower’ (36.66%), ‘busy lifestyle’ (33.21%) and ‘giving up foods that I like’ (31.76%). Lowest reported barriers were ‘feeling conspicuous amongst others’ (4.54%), ‘I don’t want to change my eating habits’ (7.99%) and ‘limited cooking facilities’ (8.71%). Statistical differences were only seen between genders in relation to the barriers ‘irregular working hours’, ‘lack of willpower’, ‘limited cooking skills’, and ‘taste preferences of family and friends’ (p=0.018, 0.028, 0.025, and 0.004).

Table 10: Percentages of participants believing their current diet is healthy, and percentages of participants affected by each potential barrier to healthy eating

	All samples (n= 551)	Men (n= 72)	Women (n= 479)	P value
	N (%)			
Believe current diet is healthy	267 (48.46)	41 (56.94)	226 (47.18)	0.404
Barriers to healthy eating				
Irregular working hours	139 (25.23)	10 (13.89)	129 (26.93)	**0.018***
Busy lifestyle	183 (33.21)	18 (25.00)	165 (34.45)	0.113
Giving up foods that I like	175 (31.76)	21 (29.17)	154 (32.15)	0.612
Lack of willpower	202 (36.66)	18 (25.00)	184 (38.41)	**0.028***
I don't want to change my eating habits	44 (7.99)	8 (11.11)	36 (7.52)	0.294
Limited cooking skills	78 (14.16)	4 (5.56)	74 (15.45)	**0.025***
Healthy food is more perishable	106 (19.24)	11 (15.28)	95 (19.83)	0.361
Lengthy preparation time of healthy food	157 (28.49)	15 (20.83)	142 (29.65)	0.122
Limited storage facilities	71 (12.89)	6 (8.33)	65 (13.57)	0.216
Limited cooking facilities	48 (8.71)	4 (5.56)	44 (9.19)	0.308
Increased price of healthy foods	150 (27.22)	14 (19.44)	136 (28.39)	0.112
Unappealing healthy foods	98 (17.79)	10 (13.89)	88 (18.37)	0.354
Strange or unusual healthy foods	58 (10.53)	6 (8.33)	52 (10.86)	0.515
Feeling conspicuous amongst others	25 (4.54)	1 (1.39)	24 (5.01)	0.169
Taste preferences of family and friends	86 (15.61)	3 (4.17)	83 (17.33)	**0.004***
Not knowing enough about healthy eating	64 (11.62)	8 (11.11)	56 (11.69)	0.886
Experts keep changing their minds about healthy foods	59 (10.71)	7 (9.72)	52 (10.86)	0.772
Limited healthy choice when I eat out	114 (20.69)	9 (12.50)	105 (21.92)	0.066
Healthy options not available at work	91 (16.52)	10 (13.89)	81 (16.91)	0.520
Not enough healthy food to satisfy hunger	116 (21.05)	11 (15.28)	105 (21.92)	0.197

*Significant p values are shown in bold with an asterisk

3.3.6. Cluster analysis

Two-step cluster analysis produced four discrete clusters of participants based on their results from the section of the questionnaire about perceived barriers to healthy eating (PBHE). Figure 8 shows that the presence or absence of the PBHE ‘lack of willpower’ was the defining characteristic creating the clusters. Clusters 1 (n=307) and 2 (n=48) were classified by an absence of the PBHE ‘lack of willpower’ (100% and 52.1% consecutively), while clusters 3 (n=135) and 4 (n=60) were classified by a presence of the PBHE ‘lack of willpower’ (88.1% and 100% consecutively). Individuals in clusters 1 and 2 reported that giving up foods they like was not a PBHE (99.4% and 75%) however participants in clusters 3 and 4 stated that this was a PBHE (75.6% and 98.3%). Participants in cluster 1 stated that a busy lifestyle was not a PBHE (100%) compared to clusters 2, 3 and 4 who identified busy lifestyles as a PBHE (81.2%; 74.1% and 73.3%).

Input (Predictor) Importance
1.0 0.8 0.6 0.4 0.2 0.0

Cluster	1	3	4	2
Label				
Description				
Size	55.9% (308)	24.5% (135)	10.9% (60)	8.7% (48)
Inputs	Willpower No (100.0%)	Willpower Yes (88.1%)	Willpower Yes (100.0%)	Willpower No (52.1%)
	Givingup No (99.4%)	Givingup Yes (75.6%)	Givingup Yes (98.3%)	Givingup No (75.0%)
	Busylifestyle No (100.0%)	Busylifestyle Yes (74.1%)	Busylifestyle Yes (73.3%)	Busylifestyle Yes (81.2%)
	Preptime No (100.0%)	Preptime Yes (82.2%)	Preptime No (61.7%)	Preptime No (52.1%)
	Price No (100.0%)	Price Yes (82.2%)	Price No (65.0%)	Price No (62.5%)
	Perishable No (100.0%)	Perishable Yes (66.7%)	Perishable No (93.3%)	Perishable No (75.0%)
	Satisfaction No (100.0%)	Satisfaction Yes (63.0%)	Satisfaction No (58.3%)	Satisfaction No (87.5%)
	Workinghours No (100.0%)	Workinghours Yes (55.6%)	Workinghours Yes (55.0%)	Workinghours Yes (64.6%)
	Unappealing No (100.0%)	Unappealing Yes (57.0%)	Unappealing No (85.0%)	Unappealing No (75.0%)
	Diningout No (100.0%)	Diningout Yes (57.0%)	Diningout No (55.0%)	Diningout No (79.2%)
	Taste No (99.7%)	Taste No (50.4%)	Taste No (83.3%)	Taste No (83.3%)
	Cookingskills No (100.0%)	Cookingskills No (57.0%)	Cookingskills No (95.0%)	Cookingskills No (64.6%)
	Workfood No (100.0%)	Workfood No (56.3%)	Workfood No (58.3%)	Workfood No (85.4%)
	Storagefacil No (100.0%)	Storagefacil No (57.8%)	Storagefacil No (91.7%)	Storagefacil No (81.2%)
	Knowledge No (100.0%)	Knowledge No (60.0%)	Knowledge No (95.0%)	Knowledge No (85.4%)
	Experts No (100.0%)	Experts No (62.2%)	Experts No (93.3%)	Experts No (91.7%)
	Strangefoods No (100.0%)	Strangefoods No (65.2%)	Strangefoods No (90.0%)	Strangefoods No (89.6%)
	Cookingfacil No (100.0%)	Cookingfacil No (71.1%)	Cookingfacil No (98.3%)	Cookingfacil No (83.3%)
	Habits No (100.0%)	Habits No (83.7%)	Habits No (80.0%)	Habits No (79.2%)
	Conspicuous No (100.0%)	Conspicuous No (87.4%)	Conspicuous No (88.3%)	Conspicuous No (97.9%)

Figure 8: Predictor importance for two-step cluster analysis

Table 11 shows that participants in cluster 1 were on average oldest (mean age 29.90 years), lightest (mean BMI 24.73kg/m^2), had the highest MD adherence score (6.08 points), the lowest number of PBHE (0.01) and the highest MD acceptability level (9.44 points). There were significant statistical differences between clusters for age, MD adherence score, PBHE and MD acceptability (p=0.000; 0.000; 0.000 and 0.017). There was no significant difference in gender, education status, place of residence, alcohol status or use of some weight loss methods (diets without group meetings, fasting and surgery) between clusters. There was significant difference in ethnicity between clusters, with cluster 4 showing the largest proportion of Caucasian participants (96.7%) and smallest fraction of other ethnicities (1.7% South Asian and 1.7% other).

Table 12 shows that there were significant differences in marital status, with the highest number of single participants in cluster 2 (83.33%) and highest numbers of married participants in cluster 1 (22.48%); p=0.034. Levels of unemployment were highest in cluster 3 (5.19%), full-time work in cluster 2 (18.75%) and full-time student status in cluster 3 (77.04%); p=0.005. Current smoker status was highest in cluster 3 (15.56%); p=0.027. Participants in cluster 1 were more likely to have a BMI in the healthy range (60.26%), while those in cluster 2 were more likely to be overweight (31.25%) and cluster 3 had highest rates of obesity (30.37%); p=0.000. Participants in cluster 1 ate out least (74.92% ate out between 0 and 5 times per month) and those in cluster 3 had the highest rates (3.70% ate out 20 or more times per month); p=0.000. Participants in cluster 3 were most likely to prefer Mediterranean cuisine (49.63%); p=0.052. MD knowledge was highest in cluster 1 (15.61% stating they fully understand the MD) compared to cluster 2 where it was lowest (54.17% stated they had never heard of the MD); p=0.000. 86.79% of participants in cluster 1 rated their diet as healthy compared to 0% in clusters 2, 3 and 4; p=0.000.

Table 11: Age, BMI, MD adherence score, number of PBHE and MD acceptability score by cluster

Variable	Cluster 1 (n=307) Mean ± SD	Cluster 2 (n=48) Mean ± SD	Cluster 3 (n=135) Mean ± SD	Cluster 4 (n=60) Mean ± SD	P value
Age	29.90 ± 12.16	26.19 ± 11.10	24.62 ± 8.26	29.63 ± 12.18	**0.000***
BMI	24.73 ± 13.90	25.45 ± 5.54	27.36 ± 8.21	26.85 ± 5.57	0.131
MD score	6.08 ± 1.15	4.13 ± 2.00	3.94 ± 1.54	4.75 ± 1.96	**0.000***
Number PBHE	0.01 ± 0.098	5.46 ± 1.83	10.50 ± 2.12	6.35 ± 1.87	**0.000***
MD acceptability	9.44 ± 2.58	8.94 ± 2.68	8.61 ± 2.53	9.38 ± 2.73	**0.017***

*Significant p values are shown in bold with an asterisk

Table 12: Gender, ethnicity, residence, marital status, employment status, education status, smoking status, alcohol status, BMI category, weight loss methods, meals out per month, MD knowledge, and perceived health status of diet by cluster

Variable	Cluster 1 (n=307) N (%)	Cluster 2 (n=48) N (%)	Cluster 3 (n=135) N (%)	Cluster 4 (n=60) N (%)	P value
Gender					0.522
Female	263 (85.67)	41 (85.42)	122 (90.37)	53 (88.33)	
Male	45 (14.66)	7 (14.58)	13 (9.63)	7 (11.67)	
Ethnicity					**0.039***
Caucasian	289 (94.14)	44 (91.67)	121 (89.63)	58 (96.67)	
Black	5 (1.63)	0 (0)	0 (0)	0 (0)	
East Asian	5 (1.63)	1 (2.08)	2 (1.48)	0 (0)	
South Asian	5 (1.63)	2 (4.17)	12 (8.89)	1 (1.67)	
Other	4 (1.30)	1 (2.08)	0 (0)	1 (1.67)	
Residence					**0.002***
North East England	270 (87.95)	46 (95.83)	131 (97.04)	58 (96.67)	
Other	38 (12.38)	2 (4.17)	4 (2.96)	2 (3.33)	
Marital status					**0.034***

Variable	Cluster 1 (n=307) N (%)	Cluster 2 (n=48) N (%)	Cluster 3 (n=135) N (%)	Cluster 4 (n=60) N (%)	P value
Single	205 (66.78)	40 (83.33)	107 (79.26)	38 (63.33)	
Married	69 (22.48)	4 (8.33)	20 (14.81)	11 (18.33)	
Divorced/widowed /separated	17 (5.54)	3 (6.25)	3 (2.22)	6 (10.00)	
Prefer not to say	4 (1.30)	1 (2.08)	0 (0)	0 (0)	
Other	13 (4.23)	0 (0)	5 (3.70)	5 (8.33)	
Employment status					**0.005***
Unemployed	9 (2.93)	0 (0)	7 (5.19)	3 (5.00)	
Working part-time	64 (20.85)	5 (10.42)	10 (7.41)	16 (26.67)	
Working full-time	41 (13.36)	9 (18.75)	11 (8.15)	7 (11.67)	
Carer/housewife	1 (0.33)	0 (0)	0 (0)	0 (0)	
Retired	4 (1.30)	0 (0)	1 (0.74)	0 (0)	
Full-time student	174 (56.68)	33 (68.75)	104 (77.04)	32 (53.33)	
Part-time student	12 (3.91)	0 (0)	2 (1.48)	0 (0)	
Other	3 (0.98)	1 (2.08)	0 (0)	2 (3.33)	
Education status					0.127
None	2 (0.65)	0 (0)	1 (0.74)	0 (0)	
Secondary school	81 (26.38)	21 (43.75)	56 (41.48)	16 (26.67)	
University	219 (71.34)	27 (56.25)	75 (55.56)	43 (71.67)	
Prefer not to say	2 (0.65)	0 (0)	2 (1.48)	0 (0)	
Other	4 (1.30)	0 (0)	1 (0.74)	1 (1.67)	
Smoking status					**0.027***
Never smoker	242 (78.83)	30 (62.50)	97 (71.85)	42 (70.00)	
Ex-smoker	46 (14.98)	11 (22.92)	17 (12.59)	12 (20.00)	
Current smoker	20 (6.51)	7 (14.58)	21 (15.56)	6 (10.00)	

Variable	Cluster 1 (n=307) N (%)	Cluster 2 (n=48) N (%)	Cluster 3 (n=135) N (%)	Cluster 4 (n=60) N (%)	P value
Alcohol status					0.833
No	72 (23.45)	12 (25.00)	31 (22.96)	11 (18.33)	
Yes	236 (76.87)	36 (75.00)	104 (77.04)	49 (81.67)	
BMI category					**0.000***
Underweight	19 (6.19)	4 (8.33)	6 (4.44)	0 (0)	
Healthy	185 (60.26)	19 (39.59)	51 (37.78)	29 (48.33)	
Overweight	71 (23.13)	15 (31.25)	37 (27.41)	18 (30.00)	
Obese	33 (10.75)	10 (20.83)	41 (30.37)	13 (21.67)	
Eating out per month					**0.000***
0-5	230 (74.92)	30 (62.50)	84 (62.22)	32 (53.33)	
6-10	63 (20.52)	9 (18.75)	30 (22.22)	21 (35.00)	
11-15	4 (1.30)	5 (10.42)	5 (3.70)	6 (10.00)	
16-20	9 (2.93)	4 (8.33)	11 (8.15)	0 (0)	
20+	2 (0.65)	0 (0)	5 (3.70)	1 (1.67)	
Cuisine					0.052
Asian	88 (28.66)	11 (22.92)	35 (23.93)	17 (28.33)	
Mediterranean	136 (44.3)	23 (47.92)	67 (49.63)	24 (40.00)	
British or American	34 (11.07)	9 (18.75)	26 (19.26)	11 (18.33)	
Other	50 (16.29)	5 (10.42)	7 (5.19)	8 (13.33)	
MD knowledge					**0.000***
Never heard of MD	65 (21.17)	26 (54.17)	70 (51.85)	21 (35.00)	
Know little bit	138 (44.95)	18 (37.50)	50 (37.04)	31 (51.67)	
Know quite a bit	56 (18.24)	3 (6.25)	10 (7.41)	4 (6.67)	
Fully understand	48 (15.64)	1 (2.08)	5 (3.70)	4 (6.67)	

Variable	Cluster 1 (n=307) N (%)	Cluster 2 (n=48) N (%)	Cluster 3 (n=135) N (%)	Cluster 4 (n=60) N (%)	P value
Healthy diet					**0.000***
No	3 (0.98)	48 (100)	135 (100)	60 (100)	
Yes	267 (86.97)	0 (0)	0 (0)	0 (0)	

*Significant p values are shown in bold with an asterisk

Table 12 cont.

3.3.7. Correlation between study outcomes

Table 13 contains results of Pearson correlation analysis, where age was shown to be non-significantly positively associated with BMI (p=0.141); significantly positively associated with MD adherence score (p=0.000) and MD acceptability (p=0.000); alongside being significantly negatively associated with number of PBHE (p=0.000). BMI was shown to be significantly negatively associated with MD adherence score (p=0.041); significantly positively associated with PBHE (p=0.023), and non-significantly positively associated with MD acceptability (p=0.002). MD adherence score was negatively associated with PBHE (p=0.000) and positively associated with MD acceptability (p=0.000). PBHE were significantly negatively associated with MD acceptability (p=0.000).

	BMI (kg/m^2)	MD score	Number PBHE	Weight loss attempts	Successful weight losses	MD acceptability
Age	P = 0.141 R = 0.063	P = 0.000 R = 0.179	P = 0.000 R = -0.192	P = 0.581 R = -0.028	P = 0.504 R = 0.034	P = **0.000*** R = 0.221
BMI (kg/m^2)		P = 0.041 R = -0.087	P = 0.023 R = 0.097	P = 0.794 R = -0.013	P = 0.683 R = -0.021	P = 0.959 R = 0.002
MD score			P = 0.000 R = -0.463	P = 0.306 R = -0.052	P = 0.358 R = -0.047	P = **0.000*** R = 0.256
Number PBHE				P = 0.084 R = 0.088	P = 0.476 R = 0.036	P = **0.000*** R = -0.150
Weight loss attempts					P = 0.000 R = 0.248	P = 0.532 R = -0.032
Successful weight losses						P = 0.686 R = -0.021

Table 13: Pearson correlation analysis of age, BMI, MD adherence score, number of PBHE and MD acceptability score

*Significant p values are shown in bold with an asterisk

3.3.8. Association between PBHE and MD adherence

Table 14 shows binary logistical regression results investigating associations between adherence to the MD guidelines and the most commonly reported PBHE (shown in Section 3.3.5) adjusted for age, sex and BMI and suggests little difference to unadjusted values (shown in Appendix C7) with participants reporting irregular working hours as a PBHE around 65% less likely to meet the MD guideline concerning wine consumption and 19% less likely to meet the nuts requirement. Reporting this PBHE was significantly associated with higher likelihood of meeting guidelines concerning white meat and vegetables (p=0.000; 0.017) however after adjusting for co-variables, statistical significance was lost concerning the likelihood of having a MD adherence score above the median value (p=0.455). Reporting irregular working hours was associated with insignificantly increased likelihood of adhering to guidelines concerning fruit, legumes and fish; alongside trends for increased likelihood of meeting recommendations to consume four or more tablespoons of olive oil per day and reduce butter intake, alongside increased likelihood of a MD adherence score above the median value. Reporting ‘busy lifestyle’ as a PBHE was associated with increased likelihood of meeting soft drink, vegetable and legume guidelines alongside overall MD adherence score (52%; 65%; 77%; 55%) with statistically significant results for vegetables, legumes and overall MD score (p=0.001; 0.000; 0.015). Reporting a busy lifestyle was also associated with twice the likelihood of meeting guidelines concerning sofrito. Statistically significant results were observed between reporting of the PBHE relating to not wanting to give up enjoyed foods and both the sweets and nuts guidelines (p=0.028; 0.040). Reporting of this PBHE was also associated reductions in likelihood of meeting vegetable, soft drink, sweets and nuts guidelines (40%; 43%; 50%; 67%). Significant results remained for vegetable and fruit guidelines (56%; 59% reductions in likelihood of meeting targets; p=0.037; 0.026). Time-poor participants were 50% less likely to meet legume consumption guidelines and 37% less likely to have a MD adherence score over the median value. Significant association was shown between this PBHE and consumption of sofrito (81%; p=0.002). Respondents reporting that the cost of healthy foods was a PBHE were 44% less likely to consume the recommended amount of wine, 20% less likely to have a MD adherence score above the median value and significance remained with participants 55% less likely to meet soft drinks guidelines (p=0.028).

Table 14: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between the top six most commonly reported perceived barriers to healthy eating (PBHE) and adherence adjusted for age, sex and BMI

PBHE	Adherence to MD guideline OR (95% CI); p value			
	Olive oil[1]	Volume olive oil[2]	White meat[3]	Vegetables[4]
Irregular working hours	0.981 (0.563-1.710); 0.946	1.505 (0.141-7.822); 0.962	2.887 (1.365-6.106); **0.006***	2.077 (1.142-3.779); **0.017***
Busy lifestyle	0.790 (0.450-1.387); 0.412	0.913 (0.130-6.421); 0.928	0.614 (0.294-1.281); 0.193	0.350 (0.189-0.647); **0.001***
Giving up foods that I like	1.066 (0.600-1.893); 0.828	0.269 (0.042-1.741); 0.168	0.889 (0.410-1.927); 0.766	0.602 (0.326-1.111); 0.104
Lack of willpower	0.760 (0.382-0.510); 0.433	0.427 (0.057-3.180); 0.406	0.657 (0.260-1.660); 0.374	0.449 (0.211-0.953); **0.037***
Lengthy preparation time of healthy foods	0.594 (0.336-1.050); 0.073	2.994 (0.387-23.132); 0.293	0.528 (0.245-1.138); 0.103	0.681 (0.371-1.247); 0.213
Increased price of healthy foods	0.912 (0.537-1.549); 0.734	0.732 (0.115-4.643); 0.740	1.524 (0.747-3.110); 0.247	1.195 (0.679-2.105); 0.537
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
Irregular working hours	1.128 (0.570-2.232); 0.730	1.244 (0.634-2.362); 0.547	0.904 (0.444-1.838); 0.780	0.970 (0.457-2.060); 0.936
Busy lifestyle	1.264 (0.635-2.516); 0.505	0.557 (0.293-1.061); 0.075	0.775 (0.388-1.547); 0.470	0.485 (0.234-1.004); 0.051
Giving up foods that I like	0.878 (0.452-1.704); 0.701	0.715 (0.376-1.360); 0.307	0.871 (0.424-1.790); 0.708	0.573 (0.274-1.198); 0.139

Lack of willpower	0.415 (0.192-0.899); **0.026***	0.829 (0.384-1.791); 0.633	1.179 (0.514-2.704); 0.698	1.436 (0.586-3.522); 0.429
Lengthy preparation time of healthy foods	0.814 (0.410-1.615); 0.555	0.678 (0.349-1.314); 0.249	0.774 (0.376-1.593); 0.486	0.990 (0.468-2.094); 0.979
Increased price of healthy foods	1.031 (0.543-1.957); 0.925	1.304 (0.701-2.424); 0.402	1.529 (0.765-3.055); 0.229	0.458 (0.228-0.918); **0.028***
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes**[10]	**Fish**[11]	**Sweets**[12]
Irregular working hours	0.358 (0.080-1.600); 0.179	1.561 (0.671-3.627); 0.301	1.972 (0.772-5.040); 0.156	0.933 (0.496-1.754); 0.829
Busy lifestyle	1.072 (0.226-5.097); 0.930	0.234 (0.105-0.519); **0.000***	0.977 (0.772-5.040); 0.156	0.779 (0.416-1.457); 0.434
Giving up foods that I like	0.651(0.147-2.891); 0.573	1.708 (0.717-4.071); 0.227	0.820 (0.355-1.893); 0.642	0.504 (0.273-0.929); **0.028***
Lack of willpower	5.023 (0.681-37.032); 0.113	0.726 (0.277-1.907); 0.516	0.656 (0.244-1.760); 0.402	0.692 (0.336-1.428); 0.319
Lengthy preparation time of healthy foods	1.289 (0.303-5.477); 0.731	0.502 (0.217-1.163); 0.108	0.894 (0.367-2.180); 0.806	0.907 (0.479-1.717); 0.764
Increased price of healthy foods	0.566 (0.136-2.363); 0.435	0.945 (0.436-2.048); 0.886	0.619 (0.270-1.422); 0.258	1.061 (0.585-1.923); 0.845
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Nuts[13]	**Sofrito**[14]	**Overall adherence**[15]	
Irregular working hours	0.812 (0.273-2.414); 0.708	0.983 (0.418-2.307); 0.968	1.287 (0.663-2.499); 0.455	

Busy lifestyle	0.534 (0.185-1.541); 0.246	2.151 (0.936-4.945); 0.071	0.456 (0.242-0.861); **0.015***	
Giving up foods that I like	0.338 (0.120-0.950); **0.040***	1.341 (0.570-3.154); 0.502	0.643 (0.340-1.218); 0.175	
Lack of willpower	2.307 (0.641-8.303); 0.201	0.822 (0.282-2.395); 0.720	0.685 (0.326-1.439); 0.318	
Lengthy preparation time of healthy foods	0.483 (0.165-1.410); 0.183	0.190 (0.068-0.531); **0.002***	0.636 (0.331-1.219); 0.173	
Increased price of healthy foods	0.755 (0.277-2.059); 0.583	1.808 (0.811-4.030); 0.148	0.800 (0.436-1.464); 0.469	

Definitions of adherence to guideline: use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14]; Odds ratios for MD adherence[15] refer to values above the median value of 5.
P values shown in bold and with an asterisk were statistically significant (<0.05).

Table 14 cont.

3.3.9. Association between BMI and MD adherence

Table 15 shows results of binary logistic regression comparing adherence to various MD adherence guidelines based on BMI category adjusted for age and sex (see Appendix C8 for unadjusted results). Respondents with self-reported BMI categories in the underweight category (below 18.5kg/m^2) were excluded as this group was small therefore overweight and obese categories were compared to the healthy weight group. Overweight participants were shown to be 51% less likely to adhere to soft drink guidelines and 47% less likely to report a MD adherence score above the median value (p=0.007; 0.009) than respondents in the healthy weight BMI category. Participants in the overweight category were shown to be less likely to consume olive oil as their main fat source, preferentially consume white meat, consume the required amounts of butter, red meat, soft drinks, or eat enough vegetables, fruit, legume, fish or nuts. Overweight participants were more likely to adhere to guidelines concerning the volume of olive oil, wine, sweets and sofrito consumed. Similarly, those in the obese category were less likely to consume olive oil as the main fat source, eat sufficiently little butter, red meat and soft drinks, eat enough fruit, legumes, fish or sofrito, alongside being less likely to have a MD score above the median value. Obese participants were more likely than those in the healthy weight category to consume sufficient olive oil, preferentially eat white meat over red, consume enough vegetables, wine and nuts, and meet guidelines about sweets.

Table 15: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between BMI 25.00-29.99kg/m^2 and >=30 kg/m^2 in comparison to BMI 18.50-24.99kg/m^2 and adherence to the MD guidelines adjusted for age and sex

BMI (kg/m^2)	Adherence to MD guideline OR (95% CI); p value			
	Olive oil[1]	**Volume olive oil[2]**	**White meat[3]**	**Vegetables[4]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.656 (0.402-1.071); 0.092	2.336 (0.514-10.606); 0.272	0.790 (0.421-1.480); 0.461	0.958 (0.557-1.648); 0.877
>=30	0.829 (0.475-1.447); 0.510	2.079 (0.404-10.683); 0.381	1.542 (0.716-3.318); 0.268	1.103 (0.592-2.054); 0.757
BMI (kg/m^2)	**Adherence to MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.828 (0.497-1.378); 0.467	0.830 (0.508-1.357); 0.458	0.703 (0.410-1.204); 0.199	0.499 (0.302-0.824); **0.007***
>=30	0.961 (0.543-1.699); 0.890	0.885 (0.509-1.540); 0.665	0.770 (0.419-1.416); 0.401	0.701 (0.403-1.222); 0.211
BMI (kg/m^2)	**Adherence to MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	5.160 (0.645-41.471); 0.123	0.651 (0.383-1.108); 0.114	0.919 (0.490-1.725); 0.792	1.105 (0.679-1.798); 0.687
>=30	4.468 (0.520-38.370); 0.172	0.839 (0.464-1.517); 0.561	0.743 (0.359-1.538); 0.423	1.627 (0.948-2.794); 0.077

BMI (kg/m²)	Adherence to MD guideline OR (95% CI); p value			
	Nuts[13]	**Sofrito[14]**	**Overall adherence[15]**	
18.50-24.99	Reference	Reference	Reference	
25.00-29.99	0.648 (0.338-1.241); 0.191	1.360 (0.659-2.805); 0.406	0.534 (0.334-0.854); **0.009***	
>=30	1.076 (0.539-2.148); 0.834	0.752 (0.353-1.603); 0.460	0.694(0.410-1.175); 0.174	

Definitions of adherence to guideline: use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14]; Odds ratios for MD adherence[15] refer to values above the median value of 5.
P values shown in bold and with an asterisk were statistically significant (<0.05).

3.3.10. Association between BMI and MD acceptability

Table 15 shows results of binary logistic regression investigating association between BMI categories and acceptance of various MD adherence guidelines adjusted for age and sex, with unadjusted values in Appendix C9. No statistically significant results were observed, however participants with self-reported BMI in the overweight category were less likely to report acceptance of guidelines concerning nuts, wine, legumes, sweets, olive oil and vegetables than their healthy weight counterparts, alongside being slightly less likely to report a MD acceptance score above the median value. Those in the obese category were less likely to report acceptance of guidelines concerning nuts, wine, legumes, olive oil, vegetables and preferential consumption of white meat than those in the healthy weight BMI category.

Table 16: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating associations between BMI 25.00-29.99kg/m^2 and >=30 kg/m^2 in comparison to BMI 18.50-24.99kg/m^2 and acceptance of the MD guidelines adjusted for age and sex

BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			
	Olive oil[1]	**Volume olive oil[2]**	**White meat[3]**	**Vegetables[4]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.685 (0.415-1.132); 0.140	0.777 (0.446-1.354); 0.373	1.231 (0.720-2.104); 0.448	0.605 (0.242-1.501); 0.282
>=30	0.759 (0.430-1.304); 0.342	0.849 (0.456-1.583); 0.607	0.987 (0.544-1.791); 0.966	0.593 (0.218-1.607); 0.304
BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	1.010 (0.570-1.788); 0.973	1.051 (0.626-1.764); 0.852	1.189 (0.731-1.935); 0.484	1.129 (0.672-1.896); 0.648
>=30	1.278 (0.660-2.475); 0.466	1.048 (0.583-1.883); 0.875	1.403 (0.801-2.460); 0.237	1.411 (0.772-2.580); 0.263
BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.791 (0.480-1.303); 0.357	0.604 (0.365-1.001); 0.051	1.029 (0.641-1.651); 0.906	0.859 (0.483-1.528); 0.605
>=30	0.596 (0.335-1.062); 0.079	0.576 (0.329-1.010); 0.054	1.075 (0.629-1.837); 0.793	1.047 (0.540-2.028); 0.892

BMI (kg/m^2)	Acceptance of MD guideline OR (95% CI); p value			
	Nuts[13]	**Sofrito[14]**	**Overall acceptance[15]**	
18.50-24.99	Reference	Reference	Reference	
25.00-29.99	0.709 (0.441-1.139); 0.155	1.035 (0.578-1.854); 0.908	0.933 (0.579-1.502); 0.775	
>=30	0.921 (0.538-1.577); 0.763	1.300 (0.658-2.567); 0.450	1.131 (0.657-1.946); 0.656	

Definitions of MD guidelines: use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14]; Odds ratios for overall acceptance[15] refer to values above the median value of 9.
P values shown in bold and with an asterisk were statistically significant (<0.05).

3.3.11. Association between PBHE and MD acceptability

Table 17 shows results of binary logistic regression investigating association between the six most commonly reported PBHE and acceptance of each MD guideline adjusted for BMI, sex and age (unadjusted results are shown in Appendix C10). Significantly, participants reporting that time was a PBHE were less likely to find the guidelines advocating olive oil as the main dietary fat source, preferential consumption of white meat and rare consumption of red meat acceptable (p=0.010; 0.008; 0.001) than those not reporting this barrier. Those reporting that cost was an issue were more likely to report that guidelines around consuming olive oil as the main fat source and preferentially consuming white meat were acceptable (p=0.043; 0.022) but 45% less likely to report that legume recommendations were acceptable (p=0.029) than individuals without this PBHE. Respondents reporting that giving up liked foods was a PBHE were 1.8 times more likely to report that legume guidelines were acceptable and twice as likely to report sofrito guidelines were acceptable (p=0.041). Those reporting a lack of willpower were 76% less likely to report that sofrito guidelines were acceptable than those not struggling with willpower (p=0.007). Individuals reporting that they were unwilling to give up favourite foods, had a lack of willpower or were time-poor were less likely to record a MD acceptance score above the median value of nine points out of fourteen. Overall, participants reporting that they were lacked time were less likely to report that all surveyed MD guidelines except sofrito were acceptable (ranging from 8% less likely to think that butter guidelines were acceptable to 69% less likely to report rare consumption of red meat was acceptable). Those reporting irregular working hours as a PBHE were less likely to deem six of the 14 guidelines acceptable; those with busy lifestyles, lacking willpower and those with cost issues were less likely to report seven guidelines as acceptable; and participants reporting that they do not want to give up liked foods were less likely to accept six guidelines.

Table 17: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between the top six most commonly reported perceived barriers to healthy eating (PBHE) and acceptance of MD guidelines adjusted for age, sex and BMI

PBHE	Acceptance of MD guideline OR (95% CI); p value			
	Olive oil[1]	**Volume olive oil[2]**	**White meat[3]**	**Vegetables[4]**
Irregular working hours	0.719 (0.407-1.272); 0.258	0.908 (0.454-1.819); 0.786	1.733 (0.872-3.445); 0.117	0.926 (0.357-2.401); 0.875
Busy lifestyle	1.101 (0.618-1.964); 0.743	0.961 (0.470-1.964); 0.912	0.671 (0.341-1.321); 0.248	0.564 (0.212-1.498); 0.250
Giving up foods that I like	0.609 (0.340-1.088); 0.094	0.760 (0.379-1.522); 0.438	1.208 (0.608-2.402); 0.590	1.049 (0.412-2.666); 0.921
Lack of willpower	1.184 (0.586-2.392); 0.637	2.196 (0.904-5.334); 0.082	1.248(0.553-2.816); 0.593	1.826 (0.626-5.321); 0.270
Lengthy preparation time of healthy foods	0.457 (0.251-0.831); **0.010***	0.637 (0.319-1.272); 0.201	0.635 (0.174-0.764); **0.008***	0.589 (0.218-1.590); 0.296
Increased price of healthy foods	1.767 (1.017-3.068); **0.043***	0.820 (0.427-1.574); 0.551	2.145 (1.115-4.124); **0.022***	1.401 (0.575-3.413); 0.458
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
Irregular working hours	1.262 (0.663-2.404); 0.479	0.932 (0.512-1.693); 0.816	1.624 (0.872-3.027); 0.127	1.522 (0.812-2.852); 0.190
Busy lifestyle	0.730 (0.376-1.419); 0.353	0.755 (0.408-1.396); 0.370	1.702 (0.930-3.115); 0.085	0.723 (0.384-1.362); 0.316
Giving up foods that I like	0.715 (0.364-1.403); 0.329	1.046 (0.573-1.907); 0.885	1.447 (0.769-2.721); 0.252	0.946 (0.498-1.798); 0.866
Lack of willpower	1.072 (0.482-2.387); 0.865	0.834 (0.397-1.748); 0.630	0.648 (0.298-1.406); 0.272	1.296 (0.605-2.775); 0.504

Lengthy preparation time of healthy foods	0.860 (0.443-1.672); 0.657	0.920 (0.499-1.695); 0.788	0.314 (0.158-0.623); **0.001***	0.686 (0.356-1.321); 0.259
Increased price of healthy foods	0.997 (0.537-1.849); 0.992	0.920 (0.499-1.695); 0.788	1.524 (0.841-2.762); 0.165	0.986 (0.539-1.803); 0.964
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
Irregular working hours	1.074 (0.586-1.970); 0.818	0.952 (0.542-1.673); 0.865	1.493 (0.855-2.607); 0.159	0.851 (0.435-1.663); 0.636
Busy lifestyle	1.421 (0.756-2.669); 0.275	1.366 (0.765-2.440); 0.291	1.133 (0.647-1.984); 0.662	0.851 (0.436-1.661); 0.636
Giving up foods that I like	1.048 (0.567-1.936); 0.881	1.855 (1.025-3.357); **0.041***	0.794 (0.449-1.405); 0.428	0.796 (0.405-1.561); 0.506
Lack of willpower	0.882 (0.420-1.852); 0.741	0.491 (0.240-1.002); 0.051	0.796 (0.398-1.592); 0.519	1.696 (0.768-3.748); 0.192
Lengthy preparation time of healthy foods	0.891 (0.481-1.652); 0.715	0.707 (0.396-1.264); 0.242	0.825 (0.480-1.511); 0.583	0.542 (0.268-1.099); 0.089
Increased price of healthy foods	0.732 (0.414-1.296); 0.285	0.550 (0.322-0.941); **0.029***	1.157 (0.681-1.966); 0.590	1.051 (0.557-1.983); 0.877
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Nuts[13]	**Sofrito[14]**	**Overall acceptance[15]**	
Irregular working hours	1.720 (0.981-3.017); 0.058	1.499 (0.708-3.174); 0.291	1.047 (0.601-1.821); 0.872	
Busy lifestyle	1.063 (0.605-1.867); 0.832	1.734 (0.818-3.677); 0.151	1.125 (0.643-1.968); 0.872	
Giving up foods that I like	1.172 (0.661-2.079); 0.588	2.180 (1.018-4.668); **0.045***	0.775 (0.440-1.364); 0.377	

Lack of willpower	0.595 (0.297-1.193); 0.143	0.246 (0.089-0.678); **0.007***	0.950 (0.480-1.881); 0.883	
Lengthy preparation time of healthy foods	0.875 (0.494-1.549); 0.646	1.315 (0.618-2.798); 0.478	0.715 (0.404-1.266); 0.250	
Increased price of healthy foods	0.750 (0.442-1.271); 0.285	1.235 (0.606-2.516); 0.561	1.081 (0.639-1.831); 0.771	

Definitions of adherence to guideline: use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14]; Odds ratios for overall acceptance[15] refer to values above the median value of 9.
P values shown in bold and with an asterisk were statistically significant (<0.05). Results are adjusted for age, sex and BMI

Table 17 cont.

3.4. Discussion

3.4.1. Statement of principle findings

Results of this online survey involving 551 mainly young (mean age 28.20 years), Caucasian (92.92%) females (86.93%) living in the North East of England (91.65%) demonstrated a mean BMI of 25.67kg/m^2, with 25.59% of participants classified as overweight and 79.47% of all participants reported making an attempt to lose weight in the past, and the most commonly utilised method of weight loss involved exercise plans (48.46%). The majority (43.00%) of participants reported that they 'know a little bit about the MD' and only 10.53% selected the 'I fully understand the concept of the MD' category. The MD was shown to be acceptable by this population, with a mean acceptance score of 9.19 point of a possible 14, compared to a low mean adherence score of 5.24 points out of 14, and the most commonly reported barrier to healthy eating was 'lack of willpower' (36.66%). Associations were observed between age, BMI, MD adherence, MD acceptability and number of PBHE.

3.4.2. Comparison with other literature

The 2014 Health Survey for England showed that an estimated 24% of men and 27% of women were obese, alongside 41% of men and 31% of women classified as overweight with a mean BMI of 27.2kg/m^2 (NHS, 2014b) both of which are higher than values found in this study; potentially because participants were young and well-educated. The high percentage of participants (79.47%) who stated that they had attempted to lose weight in the past is in line with a South African study conducted in a University population, in which 64.8% of participants had made weight loss attempts in the past year (Senekal *et al.*, 2016).

Results of this study suggest that adherence levels to the MD were generally low, with lowest adherence to guidelines based around olive oil, wine and nuts and highest to those about sofrito, white meat and vegetables. Similarly, a study involving 206 individuals of retirement age showed that MD adherence was low (5.6 ± 2), with participants adhering best to guidelines around preferential consumption of white meat over red, vegetable intake and carbonated beverage consumption, and adhering least to recommendations concerning nuts, olive oil, red meat and wine (Lara *et al.*, 2014b). Decreased likelihood of high adherence was seen in overweight and obese participants compared to those of a healthy weight, and also amongst participants reporting multiple of the studied PBHE. This is supported by a 2004 study involving 3162 Spanish participants who completed FFQ used to calculate an MD adherence score which suggested that individuals with the highest MD adherence score were least likely to be obese (Schroder *et al.*, 2004).

As suggested by this study, UK adults seem to consider the MD a palatable dietary pattern, with participants deeming most of the studied MD guidelines acceptable and also choosing Mediterranean as their preferred cuisine. Sub-group analysis showed that participants reporting that they were not willing to give up their favourite foods, lacked willpower or lacked time were less likely than those without these barriers to report a MD acceptance score above the median value. Similarly, respondents in the overweight and obese BMI categories were less likely than their healthy weight counterparts to report an acceptance level above the median value. This analysis may highlight specific groups of the population who require further intervention to make this dietary pattern more palatable. A 2015 study of 23 older adults in the UK showed that adopting a MD for three weeks was deemed highly acceptable by participants (Lara *et al.*, 2015), and a small-scale study showing that participants thought embracing the MD was a positive experience, with the diet introducing a better quality of food to their eating, and 'broadening their food horizon'. This study did suggest that there were also negative connotations, with participants finding that Mediterranean meals took longer to prepare, could be more expensive, and certain ingredients proved difficult to find in supermarkets (Middleton *et al.*, 2015) which may be potential causes of low acceptability ratings amongst those with multiple PBHE, higher BMIs and with history of weight loss attempts.

A cross-sectional study involving 14,331 adults across multiple European countries showed that 33% of UK respondents thought that 'giving up foods' was their main barrier to healthy eating, with 27% selecting 'willpower', and 25% choosing 'irregular working hours' (Kearney and McElhone, 1999), echoing the results of this survey and suggesting that future interventions targeting a change in mentality may improve healthy eating habits as participants not selecting willpower as a PBHE tended to be leaner, more adherent to the MD and find MD guidelines more acceptable than those with issues around willpower. Results of this public survey suggested that those reporting that they had a busy lifestyle, resisted giving up favourite foods, lacked willpower or time, or were concerned about cost of healthy foods were less likely to have high adherence to the MD, which is in agreement with a 2018 pan-European study of 5900 participants suggesting that those perceiving any barrier to their healthy eating were less likely to report higher consumption of foods deemed healthy; with a lack of willpower, time constraints and taste preferences the most significant contributors (Pinho *et al.*, 2018). Overweight and obese respondents to this survey were more likely than their healthy weight counterparts to report that the cost of healthy foods was a barrier to their healthy eating. This may be linked to the often low price of foods high in fat and sugar, and suggests that efforts should be made to better educate those in these BMI categories about cheaper sources of nutritious foods and highlights that there are specific PBHE to be tackled when designing healthy eating plans. Further research into the use of the MD as a healthy eating pattern and weight loss aid is thus warranted as studies have shown that small changes towards a more Mediterranean eating pattern are strongly linked to reduced mortality rates (Estruch *et al.*, 2013) and that closer adherence to this diet is linked with lower levels of obesity (Schroder *et al.*, 2004).

3.4.3. Strengths and limitations

Strengths of this study include the large sample size and the correlation of results with previous literature. There are various limitations to this work, not least that self-reported data is well-known to be susceptible to recall problems and biases such as social desirability, which was minimised by use of an anonymous survey (Althubaiti, 2016). Importantly, significantly fewer men partook in this survey therefore conclusions regarding gender difference may not be accurate, and further work into male eating patterns is required. Another limitation is that this study population was mainly made up of young students, meaning that conclusions cannot accurately be generalised as students have been shown to have a relatively poor diet which may not be in line with that of the general population (Tanton *et al.*, 2015). No checks (for example IP address recording) to ensure that the same individual did not complete multiple surveys were in place, and no record was kept of the number of visitors to the questionnaire page therefore no conclusions could be made about the number of people deciding not to partake.

3.5. Conclusions

In conclusion, this online survey was well-received and demonstrated that much of the UK population remains overweight or obese, suggesting that there is scope for novel dietary interventions promoting weight loss and a healthier lifestyle. Although current MD adherence in this study population was low, MD guidelines were deemed acceptable suggesting that future MD-based interventions aiming to tackle the highlighted PBHE may be successful, and further research into this is warranted.

3.6. Points covered in Chapter 3

i) Perceived barriers to healthy eating significantly impact dietary patterns – this online survey received 551 responses and demonstrated that the UK public do not readily utilise a MD however rate the guidelines for this diet acceptable.

ii) As hypothesised, the most commonly reported perceived barrier to healthy eating was 'lack of willpower', with distinct clusters of participants giving an idea of groups to be targeted during dietary interventions

3.7. Research questions to be answered in Chapter 4

i) How does intermittent fasting impact cardiovascular biomarkers?

ii) How does intermittent fasting impact body composition?

4. The impact of intermittent fasting on body composition and cardiovascular biomarkers: a systematic review and meta-analysis

This chapter involves a systematic review and meta-analysis investigating the relationship between intermittent fasting regimes lasting longer than twelve weeks with anthropometrical measures such as body weight alongside biomarkers of cardiovascular disease such as serum triglyceride and cholesterol levels.

4.1. Introduction

Results of the Health Survey for England 2015 showed that 62.9% of adults (67.8% of men and 58.7% of women) were overweight or obese (PHE, 2015b), with incidence and causes of obesity discussed in sections 1.1.1 and 1.1.2. Severe obesity has been shown to have links with reduced employment prospects, decreased educational achievement and lower socioeconomic status, (PHE, 2015a). The health implications of obesity such as increased risk of CVD and type two diabetes are covered in section 1.1.3. Loss of 5-10% of body weight has been linked to improvements in blood pressure, HDL cholesterol, and glycaemia, with greater weight losses shown to significantly affect CVD risk markers (Wing *et al.*, 2011), therefore there is a rightfully large body of literature examining potential methods of prevention and treatment of obesity and overweight. Current methods employed to combat obesity are discussed in section 1.1.4, with CER the main method of weight loss via dietary methods which involves a daily decreased calorie intake over a long period of time. Compliance to this regime has been shown to be poor (Dansinger *et al.*, 2005) therefore there has been research carried out into alternative ways to use diet for weight loss such as various fasting regimes, as discussed in section 1.3, with fasting shown to be often more palatable, and therefore effective, than CER (Harvey *et al.*, 2018). It has, however, been highlighted by a 2018 systematic review amongst other papers that although short-term IF has shown positive outcomes, there is currently insufficient research into the long-term safety and effectiveness of this way of eating (Ganesan *et al.*, 2018).

4.1.1. Aims

The aim of this systematic review and meta-analysis was to collate appropriate literature in order to determine the impact of IF on body composition including weight and blood-borne biomarkers of CVD such as serum cholesterol levels.

4.2. Methods

4.2.1. Study selection

The protocol was registered with PROSPERO, the International Prospective Register of Systematic Reviews (Registration number: CRD42017055434). This systematic review was conducted in adherence to Cochrane (Higgins and Green, 2008) and the University of York Centre for Reviews and Dissemination (2009) guidelines and is reported according to PRISMA guidelines (see Appendix D11 for PRISMA checklist) (Moher *et al.*, 2010).

In December 2016 Medline, Web of Science and Scopus were searched systematically from inception. Reference lists of identified publications and previously published related systematic reviews were hand-searched to identify other studies potentially eligible for inclusion.

Search terms used were: "intermittent fast*" OR "intermittent calor* restriction" OR "intermittent energy restriction" OR "intermittent diet* restriction" OR "alternate day fast*" OR "alternate day calor* restriction" OR "alternate day diet* restriction" OR "periodic fast*" OR "5:2 diet", with filters to exclude papers in languages other than English, animal studies, or any papers which were not clinical trials, for example reviews.

Both randomised and non-randomised intervention studies were sought. Inclusion criteria permitted papers reporting human clinical trials/interventions; involving free-living participants over 18 years of age; with a focus on intermittent fasting and reporting on primary outcomes such as body weight, BMI or fat mass, and secondary outcomes such as blood borne biomarkers. Exclusion criteria included conference papers, reviews, case studies, abstracts, letters, comments or dissertations; animal studies; papers not in English; papers including participants: with cancer or Crohn's disease, with any illness affecting food intake, with history of bariatric surgery (e.g. gastric sleeve), with history of eating disorders, participants currently taking weight loss or gain medications, under 18 years of age, pregnant or breast feeding, or having recently fasted; interventions lasting less than 3 months (12 weeks); papers reporting on Ramadan fasting (however papers reporting Sunnah fasting are included); papers reporting on the impact of exercise; and papers without control groups were included in the systematic review but not meta-analysis.

4.2.2. Outcome measures

The primary outcome measures of this study were body composition measurements: waist circumference, body weight, BMI and body fat percentage alongside blood pressure. Secondary outcome measures were all blood-borne biomarkers of CVD: total cholesterol, LDL, HDL and triglyceride levels.

4.2.3. Data extraction

Data extraction methodology has been previously described in section 2.2.4.

Two reviewers extracted data, one independently and the second confirming or completing information required. Extracted information included: study design (follow-up length, completion rates); participants' characteristics (population and setting, inclusion/exclusion criteria, baseline characteristics); description of measurement methods; health-related outcome measures (e.g. body weight, cholesterol levels); and information to assess the risk of bias.

4.2.4. Data synthesis and statistical analysis

Data synthesis and statistical analysis has been previously described in section 2.2.5.

4.3. Results

4.3.1. Study characteristics

As shown in Figure 9, searches yielded 516 results with 366 after removal of duplicates. 130 papers were screened for eligibility, with 15 included in the systematic review and nine in the meta-analysis. Of the studies included in the systematic review, six originated in North America (USA n = 5, Canada n = 1), two in Australia, four in Europe (UK n = 2, Denmark n = 1 and Sweden n = 1) and three in Asia (Malaysia n = 3). 746 participants in total completed the interventions, with an average of 50 participants per study and a mean completion rate of 77.4%. Interventions lasted an average of 57 weeks and all reported on overweight or obese individuals with an average age of 51 years. Interventions reported on weight loss, BMI, waist circumference, total cholesterol, LDL, HDL, triglycerides, SBP, DBP, body fat percentage, serum glucose and serum insulin, as shown in Table 18. The complexity of diet methodologies involved in this meta-analysis means that results should be interpreted with caution.

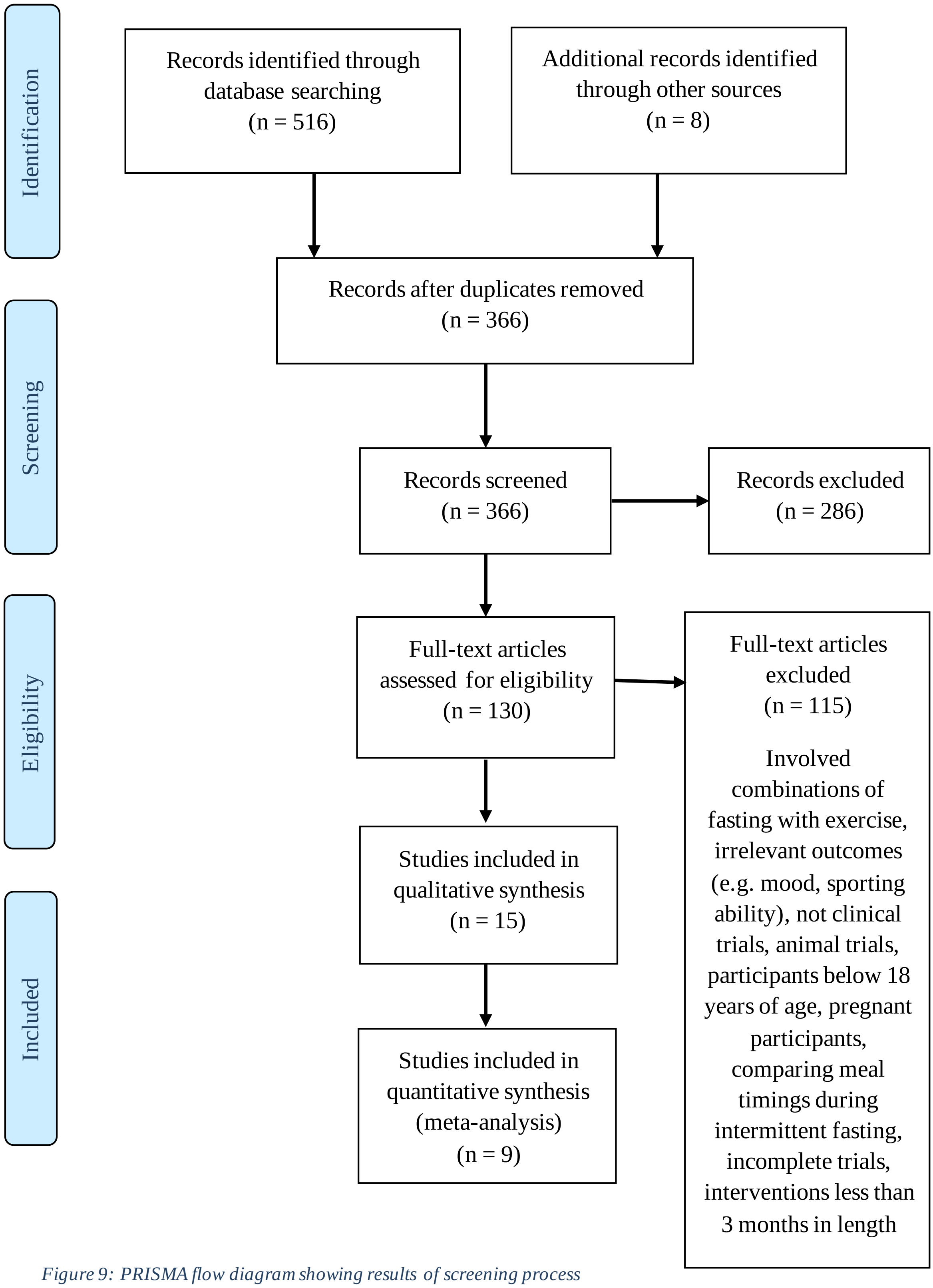

Figure 9: PRISMA flow diagram showing results of screening process

Table 18: Studies included in Chapter 4 systematic review and meta-analysis

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete-rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
Arciero, 2016	USA	Protein-pacing caloric reduction diet of shakes and meal-replacement bars with 1 fast day per week	National Cholesterol Education Program Therapeutic Lifestyle Changes diet	Weekly meetings; provision of foods	43	55.8	Sedentary, overweight or obese, 30–65 years old	19	48±9	52
Arguin, 2012	Canada	Intermittent diet	Continuous caloric reduction	Both groups followed same diet for first 5 weeks	E: 12 C: 10	100.0	Sedentary, obese, postmenopausal, non-smokers	22	E: 60.8±5.5 C: 61.0±7.3	52
Ash, 2003	Australia	IER, pre-portioned meals (PPM) and self-selected meals (SSM). All diets isocaloric, averaging 1400– 1700 kcal/day	None	Visit to dietitian fortnightly; telephone contact with dietitian on alternate weeks	51	52.9	T2DM, BMI 25-40 kg/m²	0	54	12

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete -rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
Belza, 2009	Denmark	Intermittent caloric restriction	None	8-week low energy diet (LED) then 4-week weight maintenance program, then additional 4-week LED then 4-week weight maintenance diet	41	80.5	Obese	17	43.0±10.5	20
Bhutani, 2013	USA	Alternate day fasting	Usual diet	4-week controlled then 8-week self-selected feeding period. During weeks 1-4 participants consumed 25% of their needs on the ‘‘fast day’’ and *ad libitum* on each ‘‘feed day’’	83	77.1	Aged 25-65 years; BMI between 30 and 39.9 kg/m²	39	E: 42±2 C: 49±2	12

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete-rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
Harvie, 2010	UK	IER of 25% restriction delivered as a VLCD for 2 days/week, no restriction on the other 5 days/week	CER of 25% restriction below estimated requirements for 7 days per week	NA	107	83.2	BMI 24-40	107	E: 40.1±4.1 C: 40.0±3.9	26 weeks
Harvie, 2013	UK	IECR: 70% energy restriction then euenergetic MD for 5 days. IECR + PF: same as IECR but with unlimited lean meat, fish, eggs, tofu, MUFA and PUFA	Daily energy-restricted Mediterranean-type diet	NA	115	76.5	BMI 24-45, increased risk of breast cancer, but no personal history of the disease	115	IECR: 45.6± 8.3 IECR + PF: 48.6 ±7.3 DER: 47.9±7.7	17

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete-rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
Hussin, 2013	Malaysia	Reduction of 300 to 500 kcal/day from participants' baseline energy intake combined with two days of Muslim Sunnah fasting/week	Maintain current lifestyle	NA	32	96.9	BMI 23-29.9, male, healthy, age 50-70	0	59.7±6.3	13
Keogh, 2014	Australia	1 week normal diet followed by 1 week energy restriction (5500kJ)	CER (5500kJ)	'Total Wellbeing Diet' portion and recipe system Both groups attended research centre every 2 weeks for 8 weeks, then follow-up visit at 52 weeks	75	48.0	Overweight or obese, healthy or T2DM managed by diet	75	C: 60.8±12.5 E: 59.5±8.7	52
Lantz, 2003	Sweden	Intermittent group repeated VLCD for 2 weeks every third month. On-demand group used VLCD when	None	All participants underwent a 16 week VLCD period, then a 3-week refeeding phase, in which ordinary food	334	35.0	>30 kg/m²	248 of 334	Intermittent: 41.9±10.6. On-demand: 41.4±11.3	104

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete-rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
		body weight passed an individualised, predetermined cut-off level		was gradually introduced						
Teng, 2011	Malaysia	FCR regime = reduction of 300 to 500 kcal/day from habitual energy intake combined with two days of Muslim Sunnah fasting/week	Maintain current lifestyle	NA	28	89.3	Healthy, BMI 23.0 to 29.9 kg/m²	0	58.8±5.1	12
Teng, 2013	Malaysia	FCR regime = reduction of 300 to 500 kcal/day from habitual energy intake combined with two days of Muslim Sunnah fasting/week	Maintain current lifestyle	NA	56	100.0	Healthy, BMI 23.0 to 29.9 kg/m131	0	C: 59.1±6.2 E: 59.6±5.4	12

Author, year	Country	Experimental group	Control group	Regime	Participa-nt number	% complete-rs	Participant characteristics	Number female	Mean age±SD	Length (weeks)
Varady, 2013	USA	ADF = 25% of baseline energy needs on the fast day then *ad libitum* on each alternating feed day	Maintain current lifestyle	NA	32	93.8	BMI 20–29.9 kg/m², aged 35-65 years; pre- or post-menopausal	22	E: 47±3 C: 48±2	12
Williams, 1998	USA	1-day followed a VLCD for 5 consecutive days during week 2 then 1 day a week for 15 weeks. 5-day followed a VLCD for 5 consecutive days during weeks 2, 7, 12, and 17	Standard behavioural therapy: 1,500-1,800 kcal/day	Weekly group meetings; all food for VLCD provided	54	87.0	More than 20% over ideal body weight, T2DM, 30-70 years of age	31	SBT: 54.1 ±7.0 1-day: 51.4 ±7.9 5-day: 50.3 ±8.6	20
Wing, 1994	USA	400 to 500 kcal /day for weeks 1 to 12 and 24 to 36	LCD: 1,000 to 1,200 kcal/day	Weekly group meetings	93	84.9	More than 30% above ideal body weight, T2DM, aged 30-70	60	LCD: 51.3±8.7 VLCD: 52.3 52.3±10.7	552

Table 18 cont.

4.3.2. Systematic review

Of the studies included in this systematic review but not in the meta-analysis, mean weight losses in experimental groups were 6.47±4.6kg; $p<0.001$ (Ash *et al.*, 2003), 15±15.3kg; $p<0.05$ (Belza *et al.*, 2009), 2.1±3.8kg (Keogh *et al.*, 2014), 5.2±0.9kg (Varady *et al.*, 2013), 7.2±8.0kg (Wing *et al.*, 1994), 7.0kg; $p<0.001$ for a group using continuous IF and 9.1kg; $p<0.001$ for IF used only when body weight reached a predetermined limit (Lantz *et al.*, 2003), 10.4±5.4kg; $p=0.04$ for a group following a VLCD for 1 day per week every week and 9.6±5.7kg; $p=0.04$ for 5 consecutive days every 5 weeks (Williams *et al.*, 1998). Belza *et al.* (2009) reported a significant mean BMI change of -4.8±3.5kg/m^2. Mean waist circumference decreased in three studies, by 8.1±4.6cm; p=<0.001 (Ash *et al.*, 2003), 13±11cm; p=<0.05 (Belza *et al.*, 2009) and 2.9±4.1cm (Keogh *et al.*, 2014), with Ash *et al.* demonstrating a mean body fat decrease of 1.9±1.5%; $p<0.001$ (Ash *et al.*, 2003). One study found that mean total cholesterol decreased significantly by 0.5±0.2mmol/L (Belza *et al.*, 2009) however two studies found that total cholesterol levels at the end of the experiment did not differ significantly from those at baseline (Ash *et al.*, 2003, Varady *et al.*, 2013) and one similarly found significant short term decreases however levels at follow-up were not significantly different from those at baseline (Lantz *et al.*, 2003). Three studies included in the systematic review showed no significant difference in LDL levels after intervention (Ash *et al.*, 2003, Lantz *et al.*, 2003, Varady *et al.*, 2013); however Belza *et al.* (2009) showed a statistically significant decrease of 0.4±0.2mmol/L. Ash *et al.* (2003) reported no significant change in HDL levels after intervention however at a follow-up at 18 months HDL levels had significantly increased by 0.15±0.18mmol/l, and Lantz *et al.* (2003) reported significant increases in HDL levels of 0.2mmol/L, however Belza *et al.* (2009) found a non-significant increase of 0.1±0.1mmol/L and Varady *et al.* (2013) reported no change. Varady *et al.* (2013) stated that decreases in triglyceride levels were significant while two studies showed significant decreases of 0.3±0.6mmol/L and 0.5±0.1mmol/L respectively in triglyceride levels after intervention (Ash *et al.*, 2003, Belza *et al.*, 2009). Belza *et al.* (2009) showed a significant decrease in SBP levels of 5±12mmHg compared to Varady *et al.* (2013) who reported a non-significant decrease, with Belza *et al.* (2009) also reporting a significant decrease in DBP levels of 4±7.5mmHg. Belza *et al.* (2009) also reported a non-significant decrease in serum glucose levels of 0.1±0.1mmol/L which is in agreement with Bhutani *et al.* (2013) also reporting non-significant decreases. Two studies reported significant decreases in serum insulin levels of 22.9pmol/L and 4.9mUL^{-1} respectively (Belza *et al.*, 2009, Lantz *et al.*, 2003), in comparison to Bhutani *et al.* (2013) reporting no change.

4.3.3. Meta-analysis

See Appendix B4 for an example forest plot showing meta-analysis results. **Error! Reference source not found.** shows that IF was associated with significantly decreased BMI (p=0.05) and body fat percentage (p=0.02) alongside trends for reduced TG, FPI, SBP, DBP, WC and weight in experimental groups compared to control groups. All included studies had low heterogeneity.

Table 19: Number of included studies, mean difference, 95% CI, p value and heterogeneity levels for each reported outcome

Outcome	Included studies reporting outcome	Mean difference	95% CI (lower, upper)	P value	Heterogeneity (%)
TC	7	0.07mmol/L	-0.10, 0.24	0.40	0
LDL	7	0.08mmol/L	-0.07, 0.23	0.27	0
HDL	7	0.03mmol/L	-0.01, 0.08	0.16	0
TG	7	-0.11mmol/L	-0.22, 0.01	0.08	13
FPI	4	-0.17mmol/L	-0.39, 0.06	0.14	0
FPG	5	0.04mmol/L	-0.16, 0.08	0.51	0
SBP	4	-0.46mmHg	-3.89, 2.97	0.79	0
DBP	4	-1.68mmHg	-5.25, 1.90	0.36	48
WC	4	-2.93cm	-2.93, 0.15	0.06	0
Weight	7	-1.80kg	-4.53, 0.92	0.19	46
BMI	4	-0.74kg/m^2	-1.47, -0.01	**0.05***	0
Body fat	5	-1.14%	-2.12, -0.17	**0.02***	0

*Significant p values are shown in bold with an asterisk

4.4. Discussion

4.4.1. Statement of principal findings

Results of this work involving 15 studies in the systematic review and nine in the meta-analysis suggest that IF is associated with statistically significant decreases in BMI and body fat percentage, non-significant decreases in body weight, waist circumference, total cholesterol, triglycerides, SBP, DBP, serum glucose and serum insulin levels alongside non-significant increases in HDL and LDL.

4.4.2. Comparison with other literature

These findings support literature suggesting that adherence to IF regimes can be effective in short-term improvement of anthropometrical measures such as body weight (Ganesan *et al.*, 2018). Seimon *et al.* (2015) reported that in a meta-analysis involving 40 studies, all but three of the included papers (which involved only lean participants not looking to lose weight) showed a reduction in body weight with no reports of weight gain after adherence to an IF regime, with this paper also showing reductions in BMI, waist circumference and hip circumference and concluding that IF is comparable to CER as a weight loss regime. A 2019 study demonstrated a larger proportion of participants adhering to an IF regime (500-600kcal per day for two days per week with their usual diet for the remaining five days) losing more than 5% of their baseline body weight compared to those on a CER plan (1200-1500kcal per day for seven days per week) (Carter *et al.*, 2019). Similarly, a meta-analysis involving six interventions of at least six months in length with an average drop-out rate of 31% (similar in IF and CER groups) found that there was no significant difference in weight loss between intervention groups (p=0.458) with authors therefore concluding that IF is as effective as CER for weight management (Headland *et al.*, 2016). It is hypothesised that this may be due to the reduced burden of caloric restriction in IF in combination with a similar weekly caloric intake as CER, making IF a more palatable way to lose weight in the longer-term and leading to increased adherence (Carter *et al.*, 2019).

This work highlights the small amount of robust, long-term research behind the fasting diets gaining media attention recently, with just 15 included in the systematic review and nine in the meta-analysis. Although fasting has long been used by many religious groups and health-conscious individuals, there are few large scale, long-term studies which evaluate the safety and effectiveness of IF used in the ways which have recently become popular with the public (Seimon *et al.*, 2015). Importantly, the majority of research into IF has been carried out in overweight or obese but healthy participants, demonstrating a gap in knowledge concerning the use of these diet plans in people who may benefit greatly from weight loss and other proven outcomes, such as those with diabetes or CVD (Headland *et al.*, 2016).

4.4.3. Strengths and weaknesses of the study

Strengths of this study include low levels of heterogeneity of included studies, consistency of findings and rigorous methodology used including adherence to Cochrane guidelines and use of PRISMA flow diagram and checklist. Three mainstream databases (Scopus, Medline and Web of Science) relevant to the research area were searched from inception, and specific search terms were utilised to ensure inclusion of all relevant references. Limitations comprise the small number of included studies, and the small participant numbers involved. Also of note is that only studies published in English were screened for inclusion, due to lack of access to accurate translation capabilities.

4.4.4. Conclusions

In conclusion, this systematic review and meta-analysis suggests that IF regimes may be of use for weight loss and improvement of overall health, particularly for overweight and obese patients who may not comply well with traditional CER strategies, however further larger scale research is needed into the effectiveness, viability and safety of long-term use of such a diet plan.

4.1. Points covered in Chapter 4

i) Systematic review and meta-analysis of 15 studies investigating the impact of IF on markers of health, highlighting the paucity of high-quality research in this area and suggesting that further work is required

ii) Results suggest a moderately beneficial effect of IF, with significant decreases in BMI and body fat percentage reported

iii) Research into the acceptability and feasibility of this pattern would be beneficial before implementing in the public

4.2. Research questions to be answered in Chapter 5

i) Are intermittent fasting and the Mediterranean diet employed in weight loss strategies by healthcare practitioners?

ii) How much literature is available about the diets of healthcare practitioners?

iii) How acceptable is the Mediterranean diet to healthcare professionals and what are their opinions on its acceptability to patients?

iv) How healthy are healthcare professionals' diets and what are the specific dietary challenges in this group compared to the general public?

5. Healthcare professionals and the Mediterranean diet: a systematic review and online survey

This chapter utilises a systematic review in conjunction with an online survey to investigate the dietary habits and perceived barriers to healthy eating of healthcare professionals, alongside their opinions of patients' eating patterns, specifically exploring the use and acceptability of the Mediterranean diet in healthcare practitioners' own lives and implications for patients.

5.1. Introduction

5.1.1. Importance of healthcare professionals

Reducing unhealthy lifestyle features such as smoking, malnutrition and alcohol overuse shown to be risk factors for non-communicable diseases such as cardiovascular disease, obesity and cancers is currently a global goal for the WHO (2008). Healthcare professionals (HP) have been highlighted as significant tools in health promotion, specifically nutritional engagement, with the NHS aiming to increase the health of its staff via the Five Year Forward View which involves decreasing access to unhealthy foods on NHS premises and providing healthier options for night-shift workers alongside requiring staff to act as 'health ambassadors' (NHS, 2014a). The impact on the public of HP such as dietitians, nutritionists, doctors and nurses should not be underestimated as these individuals are often responsible for providing nutritional guidance, with the NHS website heavily promoting contacting a GP for advice about healthy eating or weight loss methods (NHS, 2016a). A recent Australian study suggested that approximately 60% of allied healthcare professionals (dietitians, exercise physiologists, nurses, occupational therapists, physiotherapists and psychologists) believe that providing dietary and physical activity advice to patients is within their scope of practice and would be willing to give such guidance, but that there is a lack of weight management education in HP (Snodgrass *et al.*, 2016).

5.1.2. Impact of healthcare professionals' lifestyle on patients

Alongside the direct impact of HP on patients, for example provision of nutritional guidance and support, it is thought that HP's own lifestyle factors may play a role in their ability to increase their patients' adherence to a healthy diet (Cummings, 2016), with a 2008 study suggesting that patients were less likely to feel confident about dietary advice given by an overweight nurse compared to a nurse of a healthy weight (Hicks *et al.*, 2008). Similarly, a 2015 study showed that 77% of surveyed nurses thought that their patients would pay more attention to advice from HP who appeared to follow the advice themselves, and 48% stated difficulties in recommending healthy lifestyle advice that they did not adhere to (Blake and Patterson, 2015). A study involving interviews with overweight and obese nurses suggested that while some nurses worry that patients will not respond to nutritional advice from an overweight HP, some utilised their weight as a way to build rapport with patients by drawing on their own personal experience of dieting and weight loss, and reported finding it easier to bring up a patient's weight without offence (Aranda and McGreevy, 2014). In a 2017 systematic review three of the five relevant included studies suggested that nurses who were more active tended to recommend physical activity to patients more frequently, however two studies reported no association between personal physical activity levels and promotion of this to patients. This study also suggested that nurses' probability of undertaking health promotion with patients increased with self-efficacy, and that nurses reporting unhealthy lifestyle factors reported lower levels of positive attitudes about health promotion techniques. Authors suggest that common barriers to nurses' abilities to deliver health promotion included lack of training, experience and specific resource availability (Kelly *et al.*, 2017). This suggests that HP's own lifestyle factors play an important role in bettering patients' adherence to a healthy diet, and that more can be done to aid HP in increasing the healthiness of their own lives in order to better help their patients.

5.1.3. Aims

Knowledge is lacking about whether or not HP would accept the use of the MD in practice and HP's perceptions of the factors influencing their patients' healthy eating, with NICE stating that research into weight loss should investigate PBHE as this would be significant in designing successful dietary interventions (NICE, 2015a). Therefore this work aims to research current dietary advice, acceptability of a novel dietary pattern and HP's ideas of their patients' PBHE alongside their own eating habits via a systematic review of literature complemented by an online survey sent to HP. Results will inform future dietary interventions investigating the feasibility and acceptability of the MD as a novel dietary pattern for weight loss and improvement of cardiovascular biomarkers.

5.2. Methods

5.2.1. Systematic review

5.2.1.1. Study selection

This systematic review was conducted in adherence to Cochrane (Higgins and Green, 2008) and the University of York Centre for Reviews and Dissemination (2009) guidelines and is reported according to PRISMA guidelines (see Appendix E12 for PRISMA checklist) (Moher *et al.*, 2010). Medline, Web of Science and Scopus were searched systematically from inception to January 2019. All reference lists of included literature returned from these searches were hand-searched to identify additional studies to be screened for inclusion. The search string used was: TOPIC: (('healthcare professional' OR 'doctor' OR 'nurse' OR 'dietitian' OR 'nutritionist' OR 'physiotherapist' OR 'psychologist')) AND TOPIC: ('mediterranean diet' OR 'healthy diet') AND TOPIC: ('adherence' OR 'barriers').

5.2.1.2. Outcome measures

Included studies were randomised controlled trials or observational studies but not reviews, written in English, involved healthcare professionals, and reported on outcomes relating to their opinions on the MD, their use of the MD with patients, their own adherence to the MD, and the barriers to their and their patients' healthy eating. Included study types and outcome measures were different between studies, therefore study results could not be compared via meta-analysis.

5.2.1.3. Data extraction

Data extraction methods have been previously described in section 2.2.4.

Two reviewers extracted data, one independently and the second confirming or completing information required. Extracted information included HP's use of the MD with patients and their opinion of this dietary pattern, their own adherence to the MD and their perceived barriers to healthy eating.

5.2.2. Online questionnaire

5.2.2.1. Questionnaire design

Bristol Online Survey software (Jisc, UK; subsequently renamed Online Surveys) was utilised to create the online questionnaire (shown in full in Appendix E13) as this assured anonymity and aided in data collection. The first page of the survey contained the study information sheet and lead on to an informed consent form. If the participant consented to take part in the study, they advanced to the first section of the questionnaire. If they did not consent, they were routed to a page thanking them for their time and explaining that they would not be able to complete the questionnaire. Participants could save their survey and complete it at another time, and were able to withdraw from the study before submitting their completed survey without their answers being recorded. The first section of the questionnaire included background information questions such as job title, years in practice and main area of work. The second section of the questionnaire contained questions designed to elicit information concerning current healthy eating advice given to patients and its effectiveness. The third section was made up of questions designed to investigate the opinions of HP on the achievability of important aspects of the MD (such as high intakes of olive oil and low intakes of refined sugar). Participants were asked about their own and their patients' perceived barriers to healthy eating (PBHE) using a previously published list of barriers taken from a pan-European study (Kearney and McElhone, 1999). The final section comprised a slightly altered version of the PREDIMED 14-item MD adherence list (Estruch *et al.*, 2018) aimed at investigating the MD adherence of healthcare professionals, shown in Appendix E13. Participants were asked to submit their survey once completed, and were then directed to a debrief sheet.

5.2.2.2. Recruitment

Participants were recruited by advertisement of the survey on the 13th November 2018 on an NHS staff weekly newsletter circulated around the Newcastle-upon-Tyne Hospitals Trust, reaching approximately 30,000 email addresses; alongside advertisement on Sunderland Royal Hospital's staff newsletter and emails circulated by Heads of Departments from the 22nd March until 12th May 2019. Participation was voluntary, respondents answered questions anonymously, and there was no reward for participation. As this was an exploratory survey, sample size calculations were not carried out *a priori*.

5.2.2.3. Inclusion and exclusion criteria

Participants were healthcare professionals such as dietitians, nutritionists, nurses and doctors currently working in their field. The only individuals excluded from this work were who were retired, or no longer working in healthcare for any other reason.

5.2.2.4. Ethical approval

Ethical clearance was granted by the Northumbria University Health and Life Science Ethics Committee (see Appendix E14), alongside Health Research Authority ethical approval (see Appendix E15) and Confirmation of Capacity from the Newcastle Trust Hospitals (see Appendix E16) and Sunderland Royal Hospital (see Appendix E17).

5.2.2.5. Statistical analysis

IBM's SPSS v26 for Windows was used to compare continuous variables using independent t-tests, with nominal and ordinal variables compared using Chi-squared tests or Binomial tests where Chi-squared was not possible.

5.3. Results

5.3.1. Systematic review

5.3.1.1. Study characteristics

As shown in Figure 10, the systematic review search yielded 937 records after searching the mentioned databases and removing duplicates. 68 full-texts were screened, with 17 papers reporting 16 studies included in the final qualitative synthesis. As shown in Table 20, eleven studies reported cross-sectional surveys, two involved focus groups, two reported semi- or unstructured interviews, and one was a prospective cohort study. Five studies originated in the

USA, five in the UK, and one in Australia, Italy, Egypt, South Africa and Spain. The total number of participants involved was 58865 with an average of 3679 participants per study. Six studies involved exclusively nurses, six included only doctors, and four involved multiple HP categories. One study briefly mentioned the opinions of HP on the MD, one looked at the use of the MD in practice, nine gave some information relating to the HP's own eating habits while two reported MD adherence score specifically, and nine reported on barriers to healthy eating.

PRISMA 2009 Flow Diagram

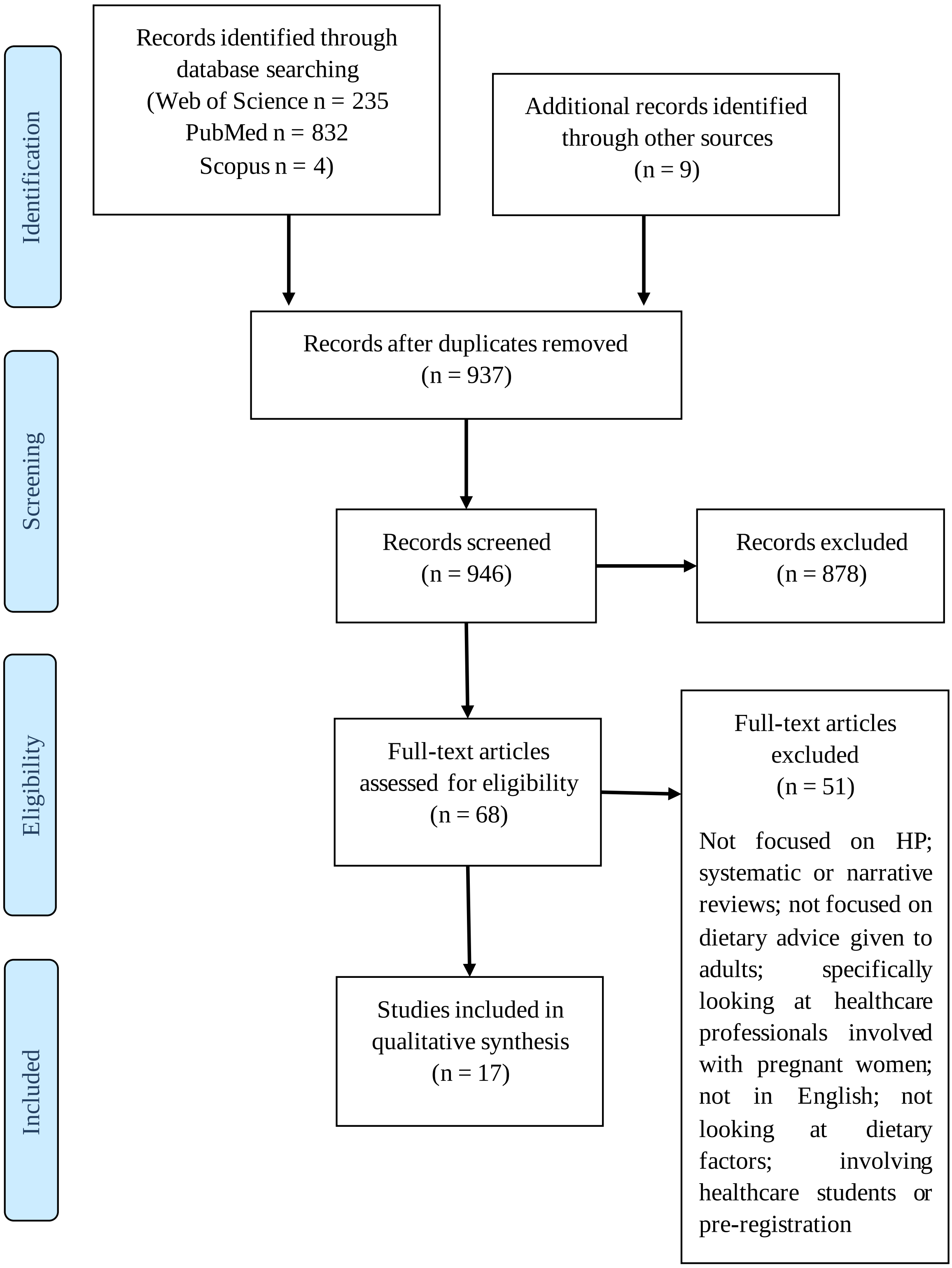

Figure 10: PRISMA flow diagram showing results of screening process

Table 20: Studies included in Chapter 5 systematic review

Author, year	Title	Country	Study type	Sample size	HP included	Opinions of MD?	Use of MD?	Own MD adherence?	Barriers to healthy eating?
Albert, 2014	Factors Related to Healthy Diet and Physical Activity in Hospital-Based Clinical Nurses	USA	Cross-sectional survey	278	Nurses	×	×	Some dietary info	Some
Blake, 2012	Health in the NHS: lifestyle behaviours of hospital employees	UK	Cross-sectional survey	1452	All in hospital	×	×	Some dietary info	×
Borgan, 2015	The lifestyle habits and wellbeing of physicians in Bahrain: a cross-sectional study	Bahrain	Cross-sectional survey	152	Doctors	×	×	Some dietary info	×
Faugier, 2001	Barriers to healthy eating in the nursing profession: part 2	UK	Unstructured interviews	24	Nurses	×	×	×	✓
Hakim, 2016	Dietary behaviour and its relation with lifestyle, rotating work shifts and job satifsaction among nurses of Ain Shams university hospitals	Egypt	Cross-sectional survey	400	Nurses	×	×	Some dietary info	Not directly studied
Frank, 2002	Personal and professional nutrition-related practices of US female physicians	USA	Cross-sectional survey	4501	Female physicians	×	×	Some dietary info	×

Author, year	Title	Country	Study type	Sample size	HP included	Opinions of MD?	Use of MD?	Own MD adherence?	Barriers to healthy eating?
Howe, 2010	Patient-related diet and exercise counseling: do providers' own lifestyle habits matter?	USA	Cross-sectional survey	183	Physicians	✗	✗	Some dietary info	✗
Kenfield, 2014	Mediterranean diet and prostate cancer risk and mortality in the health professionals follow-up study	USA	Prospective cohort study follow-up	47867	Male healthcare professionals	✗	✗	✓	✗
Kosteva, 2012	Physician variation in perceived barriers to personal health	USA	Cross-sectional survey	183	Physicians	✗	✗	Some dietary info	✓
Mittal, 2017	A cross-sectional survey of cardiovascular health and lifestyle habits of hospital staff in the UK: do we look after ourselves?	UK	Cross-sectional survey	1158	Clinical and non-clinical hospital staff	✗	✗	Some dietary info	✓
Phiri, 2014	Nurses' lifestyle behaviours, health priorities and barriers to living a healthy lifestyle: a qualitative decsriptive study	South Africa	Focus groups and key informant interviews	103	Management and nurses	✗	✗	✗	Some

Author, year	Title	Country	Study type	Sample size	HP included	Opinions of MD?	Use of MD?	Own MD adherence?	Barriers to healthy eating?
Power, 2017	Understanding perceived determinants of nurses' eating and physical activity behaviour: a theory-informed qualitative interview study	UK	Semi-structured interviews	16	Nurses	×	×	×	✓
Sentenach-Carbo, 2017	Adherence of Spanish primary physicians and clinical practise to the Mediterranean diet	Spain	Cross-sectional survey	422	Physicians	×	✓	✓	×
Temporelli, 2013	Cardiovascular risk profile and lifestyle abits in a cohort of Italian cardiologists (from the SOCRATES survey)	Italy	Cross-sectional survey	1770	Cardiologists	×	×	Some dietary info	×
Torquati, 2016	Diet and physical activity behaviour in nurses: a qualitative study	Australia	Focus groups	17	Nurses	×	×	Some dietary info	✓
Winston, 2008	Barriers to healthy eating by National Health Service (NHS) hospital doctors in the hospital setting: results of a cross-sectional survey	UK	Cross-sectional survey	328	Doctors	×	×	Some dietary info	✓
Zapka, 2009	Lifestyle behaviours and weight among hospital-based nurses	USA	Cross-sectional survey	194	Nurses	×	×	Some dietary info	×

Table 20 cont.

5.3.1.2. Healthcare professionals' opinions of the Mediterranean diet

Only one study reported on the opinions of HP on the MD, with 46% of surveyed doctors answering that they believed implementation of the MD could have a beneficial impact on the eating habits and lifestyle of patients (Sentenach-Carbo *et al.*, 2018).

5.3.1.3. Use of the Mediterranean diet

Although studies reported on the provision of general nutritional information to patients, only one touched on the use or prescription of the MD to patients. Sentenach-Carbo *et al.* (2018) reported that 70% and 77% of the surveyed doctors thought themselves and their team respectively were highly knowledgeable about the MD's benefits and the scientific evidence accumulated around the pattern but encountered difficulties in prescribing the MD to patients due to a lack of time to properly explain the dietary pattern and its advantages (reported by 29% of respondents), difficulty motivating patients to change their eating habits (29%), a lack of interest from patients (14%), inadequate materials and resources (9%), and a lack of specific training (19%).

5.3.1.4. Healthcare professionals' eating habits and adherence to the Mediterranean diet

Kenfield *et al.* (2014) showed that 37% of male HP followed during a large cohort study focussing on prostate cancer risk had low, 34% moderate and 29% high adherence to the MD when calculated using Trichopoulou's Traditional MD Score (Trichopoulou *et al.*, 2003). This paper also showed that median levels of specific components of the MD reported in 2006 were 3.2 servings/day of vegetables, 2.8 servings/day of fruit, 0.4 servings/day of legumes, 2.7 servings/day of cereals, 0.3 servings/day of fish and seafood, 6.9g/day of alcohol, 0.9 servings/day of red and processed meat, and 1.9 servings/day of dairy products (Kenfield *et al.*, 2014).

Sentenach-Carbo *et al.* (2018) report that 3% of Spanish doctors had a high level of adherence to the MD, 52% had medium level adherence, 33% a low level and 12% a very low level according to the validated 14-item PREDIMED tool (Estruch *et al.*, 2013) and a similar study also conducted in the Mediterranean suggested that 83.5% of Italian cardiologists self-reported following a MD (Temporelli *et al.*, 2013). The Spanish paper also gives information about adherence to individual factors of the PREDIMED tool, with 98.10% of participants reporting that they used olive oil used as their main culinary fat, 24.88% reported consuming ≥4 tbsp olive oil/day, 55.21% eat ≥2 portions of vegetables/day, 30.09% eat ≥3 portions of fruit/day, 83.65% eat <1 portion of red or processed meat/day, 97.39% eat <1 portion butter/day, 90.28% consume <1 soft drink/day, 5.21% drink ≥7 glasses of wine/week, 31.99% consume ≥3 portions of legumes/week, 54.03% eat ≥3 portions of fish or seafood/week, 75.59% consume <2 portions of sweets/week, 27.49% report eating ≥3 portions of tree nuts/week, 80.09% eat more poultry than red meat, and 34.60% eat a meal containing sofrito ≥2 times/week (Sentenach-Carbo *et al.*, 2018).

A 2014 cross-sectional study of nurses used the Survey of Dietary and Exercise Habits (Silliman *et al.*, 2004) to assess healthiness of eating habits, with 66.3% of participants deemed to have a 'moderately healthy diet', 16.7% a 'mostly healthy diet' and 17% an 'unhealthy diet'. This study also reported that the majority of respondents eat fruit 2-3 times/day (39.7%), eat vegetables 2-3 times/day (41.2%), eat lean meats 2-4 times/week (52.9%), eat processed meats once per week or less (58.7%), consume only skimmed milk products rather than full-fat equivalents (52.9%), drink sugary beverages occasionally (39.6%), and consume 0-7 alcoholic drinks/week (88.8%) (Albert *et al.*, 2014).

However a similar cross-sectional survey found that 'poor health behaviours are still prevalent amongst NHS employees' with 56.5% of respondents reporting not consuming five portions of fruit and vegetables/day, 30.4% and 7.0% reporting eating foods high in both fat and sugar once/day and 2-3 times/day respectively, and 22% drinking the recommended eight glasses of water/day (Blake *et al.*, 2012).

Another study carried out in the NHS suggested relatively low compliance with dietary guidelines amongst both clinical and non-clinical hospital staff, with 16.8% of respondents meeting five-a-day fruit and vegetable targets, 47.4% eating oily fish more than once per week, 11.1% consuming less than 85g of fat/day, 16.0% reporting less than 60g/day non-milk extrinsic sugars (NMES) and 18% recording alcohol levels above the guideline limit (Mittal *et al.*, 2018).

In a study finding more positive results, 77% of NHS doctors surveyed classed themselves as healthy eaters, with 54.9% reported consuming more than two but less than five portions of fruits and vegetables per day, 70.8% eating breakfast every day and 48.8% eating takeaway meals once per month or less (Winston *et al.*, 2008).

A study conducted in Bahrain found results comparable to those shown in the NHS, with 28.9% of surveys doctors reporting consumption of fast food once/week, 15.8% twice/week and 2% on most days of the week, alongside 44% consuming at least one soft drink daily and 86.2% drinking at least one caffeinated beverage daily, leading authors to conclude that HP engage in 'unfavourable lifestyle habits' (Borgan *et al.*, 2015).

Similarly, authors of a cross-sectional survey carried out in the USA suggested that HP do not currently meet dietary recommendations, with junior doctors and consultants eating fast food 1.2±1.4 and 0.8±1.1 times/week respectively; 1.7±1.0 and 2.2±1.2 portions of fruit/day respectively; 2.1±1.0 and 2.6±1.3 portions of vegetables/day respectively (Howe *et al.*, 2010, Kosteva *et al.*, 2012).

Using a non-validated scored dietary questionnaire, Hakim *et al.* (2016) suggest that 8.8% of the 400 surveyed nurses who work rotating shift patterns gained a dietary score that placed them in the 'unhealthy diet' category, 89.0% had a 'semi-healthy diet' and 2.2% were deemed to have a 'healthy diet', with the majority of participants eating red meat ≥4 times/week (61.3%), chicken or fish 2-3 times/week (48.8%), rarely removing the skin from chicken (42.7%), eating eggs 2-3 times/week (43.5%), consuming lentils or beans ≥4 times/week (52.8%), eating dairy products 2-3 times/week (46.2%), consuming 2-3 portions of fruit or vegetables/week (41.5%), using plant oil as their main source of fat in cooking (58.8%), eating breakfast once or never/week (48.8%), and rarely eating fast food (43.3%).

Low fruit and vegetable consumption was commonly reported amongst included studies, with an American cross-sectional study of female doctors showing that average fruit and vegetable intake was 3.5±0.0 portions/day (compared to 4.0 found in a 2009 American study of nurses (Zapka *et* *al.*)), alongside an average number of alcoholic beverages amongst those not abstaining from alcohol (72.4% of respondents) of 1.3±0.1/week (Frank *et al.*, 2002).

5.3.1.5. Healthcare professionals' perceived barriers to healthy eating

Albert *et al.* (2014) suggest that surveyed nurses had, in general, few PBHE and that those more likely to have a healthier diet reported fewer PBHE. However issues around limited availability of healthy foods or meals while at work was frequently reported (Faugier *et al.*, 2001, Mittal *et al.*, 2018, Phiri *et al.*, 2014, Torquati *et al.*, 2016, Winston *et al.*, 2008) alongside inadequate food storage and cooking facilities in the workplace (Faugier *et al.*, 2001, Kosteva *et al.*, 2012), the inability of doctors and nurses to take proper breaks in order to eat (Faugier *et al.*, 2001, Power *et al.*, 2017, Torquati *et al.*, 2016, Winston *et al.*, 2008) and long or irregular working hours making home cooking difficult and causing cravings for unhealthy foods (Hakim *et al.*, 2016, Mittal *et al.*, 2018, Torquati *et al.*, 2016, Power *et al.*, 2017).

5.3.2. Online questionnaire

5.3.2.1. Demographics

Table 21 shows that 45 complete responses were received from 42 females and three males (93.33% female) with a mean age of 41.53 years, 91.11% Caucasian and 97.78% working in the North East of England (one participant reported working in the South East). 55.56% of respondents were nurses or healthcare assistants with 22.22% dietitians or dietetic assistants and 4.44% doctors. The remaining 17.78% included both clinical (physiotherapists, podiatrists and clinical psychologists) and non-clinical staff (medical secretaries). The majority (73.33%) of participants stated that they worked in a hospital and the mean time employed in their field of work was 15.80 years.

Table 21: Demographic information for 45 survey respondents

	All responses (n= 45)
Age (years) mean ± SD	41.53 ± 11.29
Employment time (years) mean ± SD	15.80 ± 12.83
Ethnicity n (%)	
Caucasian	41 (91.11)
Asian	2 (4.44)
Mixed	2 (4.44)
Geographical place of work n (%)	
North East England	44 (97.78)
Other	1 (2.22)
Job title n (%)	
Nurse/Healthcare Assistant	25 (55.56)
Dietitian/Dietetics Assistant	10 (22.22)
Doctor	2 (4.44)
Other	8 (17.78)
Location of work n (%)	
Hospital	33 (73.33)
Community	5 (11.11)
Both	7 (15.56)

5.3.2.2. Current healthy eating advice

Of the 45 responses received, five belonged to participants whose reported job roles do not commonly entail direct provision of nutritional advice to patients (medical secretaries, diabetic food screeners, podiatrists and podiatry technicians) and were therefore excluded from sections of analysis pertaining to patients (current healthy eating advice provided, thoughts on MD acceptability and PBHE) however data concerning their own dietary habits and PBHE were included in analysis. Table 22 shows that the largest percentage of survey respondents (52.50%) reported use of the EG when helping patients improve their eating habits, with IF the least commonly employed (7.50%). Analysis also showed that 42.20% of respondents reported 0-25% success rate in improving patients' eating habits, 26.70% reported 26-50% success and 20.00% reported above 51% success rates.

Table 22: Survey respondents reporting recommendation of various methods of dietary advice to patients

Technique	**Respondents reporting use n (%) (total n= 40)**
Eatwell Guide	21 (52.50)
Mediterranean diet	20 (50.00)
Behaviour change techniques	13 (32.50)
Commercial programs	7 (17.50)
Surgery	7 (17.50)
Meal replacements	4 (10.00)
Intermittent fasting	3 (7.50)

5.3.2.3. Mediterranean diet acceptability

Table 23 displays HP survey respondents (n= 40) reporting on whether or not they believe each MD guideline would be acceptable to their patients. Nine of the fourteen guidelines were deemed acceptable for patients by HP, with rates of 'I don't know' responses high for each guideline at between 22.50% and 45.00%. Sixty-five percent of HP reported that their patients would find a recommendation of at least three portions of vegetables per day acceptable, compared to 20.00% stating that the legumes guideline would be acceptable.

Table 23: HP opinions of patient acceptance of MD guidelines

MD guideline	Acceptability (n= 40) n (%)
Use olive oil as main fat for cooking	19 (47.50)
≥4 tbsp of olive oil per day	9 (22.50)
≥3 portions of vegetables per day	26 (65.00)
≥2 portions of fruit per day	20 (50.00)
<1 portions of red meat, hamburger or meat products per week	19 (47.50)
<1 portion of butter, margarine or cream per day	15 (37.50)
<1 glass of sweet or carbonated beverages per day	19 (47.50)
≥7 glasses of wine per week	14 (35.00)
≥3 portions of legumes or pulses per week	8 (20.00)
≥3 portions of fish or shellfish per week	11 (27.50)
<3 portions of sweets or pastries per week	14 (35.00)
≥3 servings of nuts per week	12 (30.00)
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	24 (60.00)
Use of a tomato-based sauce in cooking ≥2 times per week	21 (52.50)
MD acceptability score (mean ± SD)	5.77 ± 4.22

5.3.2.4. Perceived barriers to healthy eating

Table 24 shows data from the 37 HP respondents stating that they thought improvement of their own diet was possible i.e. that their current diet was not as healthy as it could potentially be. Amongst these participants, the most commonly reported PBHE were busy lifestyle (62.16%), not wanting to give up liked foods (62.16%) and a lack of willpower (56.76%). HP reported that their patients' PBHE were a lack of willpower (95.00%), not wanting to give up liked foods (87.50%) and not knowing enough about healthy eating (82.50%). A statistically significant difference was observed between the numbers of HP stating that healthy food being more perishable was a PBHE for their patients (35.00%) but less so for themselves (13.51%) ($p=0.015$).

Due to zero counts present in data concerning 'feeling conspicuous amongst others' and 'limited cooking facilities' Chi² tests were not applicable, therefore these data were compared using Binomial tests. Both outcomes showed significant difference between HP and patients (p=0.000). HP also reported significantly fewer PBHE than they observed in their patients (4.76 vs 12.25; p=0.000).

Table 24: Respondents believing each factor was a PBHE for their patients or themselves

PBHE	Patients n (%) n= 40	Healthcare professionals n (%) n= 37	P value
Irregular working hours	31 (77.50)	17 (45.95)	0.306
Busy lifestyle	30 (75.00)	23 (62.16)	0.423
Giving up foods that I like	35 (87.50)	23 (62.16)	0.105
Lack of willpower	38 (95.00)	21 (56.76)	0.204
I don't want to change my eating habits	25 (62.50)	1 (2.70)	0.168
Limited cooking skills	32 (80.00)	4 (10.81)	0.742
Healthy food is more perishable	14 (35.00)	5 (13.51)	**0.015***
Lengthy preparation time of healthy food	30 (75.00)	14 (37.84)	0.749
Limited storage facilities	10 (25.00)	1 (2.70)	0.594
Limited cooking facilities	12 (30.00)	0 (0)	**0.000***[a]
Increased price of healthy foods	29 (72.50)	6 (16.22)	0.532
Unappealing healthy foods	22 (55.00)	3 (8.11)	0.647
Strange or unusual healthy foods	22 (55.00)	3 (8.11)	0.647
Feeling conspicuous amongst others	11 (27.50)	0 (0)	**0.000***[a]
Taste preferences of family and friends	32 (80.00)	12 (32.43)	0.809
Not knowing enough about healthy eating	33 (82.50)	2 (5.41)	0.183
Experts keep changing their minds about healthy foods	25 (62.50)	8 (21.62)	0.398
Limited healthy choice when I eat out	18 (45.00)	12 (32.43)	0.286
Healthy options not available at work	22 (55.00)	16 (43.24)	0.199
Not enough healthy food to satisfy hunger	19 (47.50)	5 (13.51)	0.677
Number PBHE (mean ± SD)	12.25 ± 5.06	4.76 ± 2.89	**0.000***

*Significant p values are shown in bold with an asterisk
[a]Calculated using binomial tests

5.3.2.5. Dietary intake and Mediterranean diet adherence

Table 25 displays mean intakes of each foodstuff outlined in the PREDIMED 14-item adherence screener (Estruch *et al.*, 2013) reported by HP. This suggests that the mean intakes of olive oil, wine, legumes, nuts and fish were inadequate, while mean intakes of butter and sweetened beverages were too high to fulfil MD recommendations.

Table 26 shows levels of adherence to MD guidelines (outlined by Estruch *et al.* (2018)) of HP, with highest levels of adherence observed for preferential consumption of white meat over red (91.11%), eating three or more portions of vegetables per day (86.67%) and use of sofrito twice or more per week (82.22%). Lowest adherence concerned consumption of four or more tablespoons of olive oil per day (4.44%) and drinking seven or more small glasses of wine per week (20.00%), alongside eating three or more portions of fish or shellfish per week (17.78%). Mean MD adherence score was relatively low at 5.82 of a possible fourteen.

Table 25: Mean intakes of each studied foodstuff by healthcare professionals

Food item/group	Mean intake ± SD
Olive oil (tbsp/day)	1.13 ± 1.18
Vegetables (portions/per day)[1]	3.08 ± 1.53
Fruit (portions/day)[2]	2.35 ± 1.53
Red meat (portions/week)[3]	1.73 ± 1.21
Butter, margarine or cream (portions/day)[4]	1.20 ± 1.00
Sweet or carbonated beverages (portions/day)[5]	1.75 ± 2.21
Wine (glasses/week)[6]	2.33 ± 2.82
Legumes or pulses (portions/week)[7]	2.00 ± 1.67
Fish or shellfish (portions/week)[8]	1.42 ± 1.18
Sweets or pastries (portions/week)	2.40 ± 1.95
Unsalted nuts (portions/week)[9]	1.42 ± 1.79
Sofrito (portions/week)[10]	3.62 ± 1.96

[1] 1 portion = 80g
[2] 1 portion = 80g
[3] 1 portion = 70g
[4] 1 portion = 10g
[5] 1 portion = 150ml
[6] 1 glass = 125ml
[7] 1 portion = 5 heaped tablespoons cooked
[8] 1 portion = 140g
[9] 1 portion = 40g
[10] 1 portion = a meal containing vegetables, pasta, rice, or other dishes seasoned with sauces made with tomato and onion, leek or garlic, and olive oil

Table 26: Adherence of healthcare professionals to each MD guideline

MD adherence criteria	**Adherence (n= 45) n (%)**
Use olive oil as main fat for cooking	30 (66.67)
≥4 tbsp of olive oil per day	2 (4.44)
≥3 portions of vegetables per day	39 (86.67)
≥2 portions of fruit per day	19 (42.22)
<1 portions of red meat, hamburger or meat products per week	21 (46.67)
<1 portion of butter, margarine or cream per day	9 (20.00)
<1 glass of sweet or carbonated beverages per day	21 (46.67)
≥7 glasses of wine per week	9 (20.00)
≥3 portions of legumes or pulses per week	13 (28.89)
≥3 portions of fish or shellfish per week	8 (17.78)
<3 portions of sweets or pastries per week	18 (40.00)
≥3 servings of nuts per week	9 (20.00)
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	41 (91.11)
Use of a tomato-based sauce in cooking ≥2 times per week	37 (82.22)
MD adherence score (mean ± SD)	5.82 ± 2.14

5.4. Discussion

5.4.1. Statement of principle findings

This systematic review involved 16 studies and suggested that there is relatively little literature investigating MD knowledge and understanding of HP alongside their views on novel dietary patterns. Results of nine included studies showed that HP's eating habits could be improved for example low levels of vegetable intake were described, with work-related PBHE such as the limited availability of healthy foods and inability to take proper breaks frequently reported. This was reflected in the online survey, which showed that a busy lifestyle was one of the most common PBHE (reported by 62.20% of participants) and that HP had low levels of MD adherence, at 5.82 of a possible fourteen.

5.4.2. Comparison with other literature

There is currently a small volume of research into the use of the MD by HP in practice as shown by the relatively low number of studies included in this systematic review, however results of this online survey showed that high numbers of HP employ the MD with their patients with results of this systematic review suggesting that although opinions of the MD as a healthy eating tool are positive, HP can struggle to implement this dietary plan with their patients due mainly to a lack of time to properly explain the regime and lack of motivation from patients. Importantly, HP rated the MD guidelines less acceptable to their patients than respondents to a public survey (see Chapter iv)) viewed guidelines for themselves, therefore HP have a potentially negative view of the types of diet their patients would find acceptable which could be a barrier to the employment of the MD in clinical practice. The MD has been described as an acceptable and palatable dietary pattern, with a 2015 study involving an eight-week MD intervention amongst middle-aged individuals in the East of England suggesting that undertaking the MD was a 'pleasurable and enjoyable experience' (Middleton *et al.*, 2015). When compared to data collected from the public via online questionnaire in Chapter iv), HP believed that statistically fewer MD guidelines would be acceptable to their patients than the public deemed acceptable for themselves (5.77 vs 9.19). Highest levels of adherence amongst both HP and the public were observed for preferential consumption of white meat over red (91.1%; 84.0%), eating three or more portions of vegetables per day (86.7%; 76.2%) and use of sofrito twice or more per week (82.2%; 87.8%). Lowest adherence amongst both HP and the public concerned consumption of four or more tablespoons of olive oil per day (4.4%; 3.8%) and drinking seven or more small glasses of wine per week (20.0%; 4.5%), alongside eating three or more portions of fish or shellfish per week for HP (17.8%) and consuming three or more portions of nuts per week amongst the public (14.9%). Mean MD adherence score was 5.82 of a possible fourteen for HP and 5.24 amongst the public, showing insignificant difference between these groups.

HP responding to this survey reported generally low levels of success in improving patients' dietary habits and high levels of HP selected the 'I don't know' option when asked about acceptability of MD guidelines which may suggest a lack of knowledge around nutrition and behaviour change techniques. A recent Australian survey of HP including dietitians, physical therapists and psychologists showed that around 60% of participants believed that it was within their scope of practice to offer dietary and exercise advice to patients however, excluding dietitians, few HP reported having received any training in weight management. HP were more likely to report provision of diet and physical activity advice when they believed it was within their scope of practice and when they had received education or training about weight management, meaning that efforts should be made to further train HP in the provision of dietary advice to patients and to ensure dietary advice forms part of each patient contact with a HP (Snodgrass *et al.*, 2016).

Both this systematic review and online questionnaire suggest that HP report few PBHE but that a common theme was the workplace, with participants reporting that a lack of cooking facilities and long or irregular working hours interfered with attempts to eat healthily; alongside a lack of willpower. A recent study suggested that increasing support from management could increase staff wellbeing, however just 34% of surveyed managers were aware of the NHS health and wellbeing policy (Mittal *et al.*, 2018). HP reported that their patients' PBHE included a lack of willpower and not wanting to give up liked foods, which is in accordance with a pan-European study investigating PBHE amongst 14,331 participants (Kearney and McElhone, 1999). However, in this online questionnaire 82.5% of HP reported that a lack of nutritional knowledge was a PBHE for their patients, in comparison to just 7% of participants in Kearney and McElhone's study. This could suggest a lack of appreciation by HP of how much about nutrition their patients really understand, or that the cross-sections of individuals involved in these two studies differed with regards to dietary knowledge.

Few papers included in this systematic review reported on HP's adherence to the MD, however results of both the review and questionnaire suggest low adherence to this dietary pattern amongst HP in both the UK and Mediterranean. 70% of Spanish doctors surveyed by Sentenach-Carbo *et al.* (2018) stated that they thought themselves aware of the health benefits associated with the MD, however just 3% were deemed to have high levels of adherence to this diet. Higher percentages of participants in this Spanish study used the recommended amount of olive oil, ate sufficiently low levels of red meat, butter, sweets and soft drinks, alongside adequate consumption of legumes, fish and nuts than HP in this survey conducted in England. The relatively low levels of consumption of fish, nuts and olive oil observed in this online survey are reflected in previous studies conducted within the NHS and amongst HP in other countries (Kenfield *et al.*, 2014, Blake *et al.*, 2012) and highlight specific areas of dietary improvement. It is important to increase adherence to a healthy diet plan amongst HP, as it has been shown that HP engaging in healthy lifestyle factors are more likely to counsel their patients about these factors, for example doctors reporting higher fruit and vegetable consumption were more likely to discuss nutrition with patients, meaning that improving the health of HP could have a positive impact on patients (Frank *et al.*, 2010).

5.4.3. Strengths and limitations

Strengths of this study include the rigorous methodology used during the systematic review. Three mainstream databases relevant to the research area were searched from inception, specific search terms were utilised to ensure inclusion of all relevant literature, and the review was reported according to the appropriate guidelines. Use of a validated method of assessing dietary adherence and previously-published list of PBHE in the online questionnaire (the PREDIMED MD screener and list of PBHE from Kearney & McElhone) ensures reproducibility and allows between-study comparison.

This work also has various limitations, for example in order to conduct more in-depth statistical analysis, this online survey could have collected data on BMI and HP's own MD acceptability. With this information, similar analysis to that in Chapter iv) could have been conducted, for example Pearson correlation analysis comparing BMI with MD adherence, MD acceptability and PBHE. A low response rate is commonly found in online or postal surveys, which may introduce a sampling error and selection bias caused by individuals with less healthy lifestyles declining to partake in the study (Mittal *et al.*, 2018). Low numbers of male respondents (consistent with the NHS workforce) disallowed gender-based subgroup analysis, and low numbers of respondents from different job roles meant differences between clinical and non-clinical, or between job roles could not be investigated. Future work should attempt to target male HP in order to gain an insight into any gender differences in responses, and also higher sample numbers from different job roles would allow better understanding of the impact of employment field on the outcomes studied here. It is also important to mention that when using self-reported data, there is always potential for bias or inaccurate responses.

5.5. Conclusions

Overall there is limited scientific evidence and research into the use of the MD by HP in practice, HP's opinions of their patients' eating habits, and the dietary habits and PBHE of HP, as shown by the relatively small number of studies included in this systematic review. However this work adds to a body of evidence suggesting that although general adherence to the MD in the UK is relatively low, further research into potential methods to increase levels of adherence of HP is necessary as the MD has been shown to be a healthy way to eat, is seen as an acceptable dietary pattern, and reported PBHE are not insurmountable. Importantly, this gathered information could be used to inform future work into dietary interventions aiming to improve eating habits by overcoming PBHE and increase MD acceptability.

5.1. Points covered in Chapter 5

i) Intermittent fasting and the Mediterranean diet are not readily employed by healthcare practitioners in their own lives or when aiding patients with weight loss strategies, however these are perceived as acceptable patterns

ii) Healthcare professionals' eating patterns could be improved, with a body of literature showing that unhealthy practices were commonplace, with trends for PBHE related to this profession

5.2. Research questions to be answered in Chapter 6

i) How should the acceptability and feasibility of a combination of the MD and IF be investigated?

ii) How should dietary changes associated with adherence to this intervention be measured?

iii) How should physical activity and physical capability be measured?

iv) How should body composition be assessed?

v) How should blood-borne biomarkers of CVD be investigated?

6. Combining the Mediterranean diet and intermittent fasting to improve health of overweight and obese adults: pilot study protocol

This chapter outlines methodologies applied during a randomised dietary intervention study investigating the impact of a combination of the Mediterranean diet or Eatwell Guide and intermittent fasting amongst an overweight and obese sample population in the UK.

6.1. Introduction

6.1.1. Evidence for this trial design

It is well documented that novel solutions are required in the management of the current obesity epidemic. Importantly, so-called 'crash diets' or other short-term fixes cannot adequately solve the obesity problem therefore eating patterns acceptable and effective in the long term and which offer the required macro- and micronutrient constituents should be investigated. In order to inform the protocol for this study, multiple systematic reviews, meta-analyses and surveys were undertaken. Results of this work suggest that the MD is an effective dietary pattern in the management and prevention of obesity and associated health problems (as detailed in section 1.2) alongside being palatable and well-accepted in non-Mediterranean countries (section 2.3.3). The public survey discussed in Chapter iv) showed that although adherence to the MD in a UK sample was generally low, it was deemed an acceptable eating pattern by the majority of respondents. Amongst the original cohort of the Seven Countries Study, a large proportion practiced religious fasting (impacting to some degree around 200 days per year) and it is thought that this may have had an effect on the overall health of study participants (Keys *et al.*, 1986). Small-scale studies have demonstrated that IF is a suitable method of caloric restriction as it is generally effective and well-accepted (Chapter 4), however further work involving longer-term interventions is required into the impact of IF on body composition and cardiovascular biomarkers. Chapter 5 suggested that both the MD and IF were utilised equally by HP in weight management, however these dietary patterns were shown to be acceptable to both HP and their patients suggesting that there is scope to investigate both patterns in a randomised intervention. Although there is a wealth of literature concerning the MD and to a lesser extent IF, little research has been carried out into the 'real-world' connotations (i.e. efficacy) of these dietary patterns, and these diets have not been thoroughly tested in combination. Therefore previous work supports the notion that a combination of the MD and IF warrants further research in the form of a randomised dietary intervention.

6.1.2. Intervention development

In order to design an effective trial protocol, the techniques employed in successful dietary interventions should be studied. Research has shown that impactful dietary interventions commonly utilise targeted behaviour change techniques (BCT), with a study resulting in increased consumption of fruit and vegetables involving the use of BCTs such as barrier identification, planning social support, goal setting and the use of follow-up prompts (Lara *et al.*, 2014a). Use of the Internet in dietary interventions has also been shown to be effective, with a meta-analysis of 30 studies showing that 93% of included literature involving web-based dietary interventions resulted in positive health outcomes for participants, such as advantageous changes to nutritional knowledge, behaviour and attitude towards food (Maon *et al.*, 2012). Similarly, a systematic review and meta-analysis demonstrated that the effectiveness of Internet-based interventions is associated with increased use of BCT, with authors concluding that there is scope for investment in theory-based interventions involving multiple BCT and different modes of delivery (Webb *et al.*, 2010). NICE suggests that research into obesity should focus on 'lifestyle weight management programs', in particular if short-term interventions can be created to provide individuals with the knowledge and skills required for long-term weight loss and maintenance, and the impact of lifestyle programs on alterations of dietary habits, physical activity and health conditions (NICE, 2014b). NICE also suggest the use of 'new technologies' in dietary interventions (NICE, 2014b), of which social media and websites could be valuable ways to supply participants with information. Therefore it was decided that this trial would make use of BCT and be Internet-based in order to test a low-contact, low-cost dietary intervention under 'real-world' conditions to investigate effectiveness as previous literature has considered efficacy.

6.1.3. Aims

This chapter aims to detail all methodology utilised during this trial investigating the acceptability and feasibility alongside impact on diet, body composition, physical capability and physical activity of a lifestyle intervention involving a combination of the EG or MD and IF.

6.2. Methods

6.2.1. Study design

This is a randomised controlled two-arm pilot intervention trial was approved by the Northumbria University Health and Life Science Ethics Committee (see Appendix F18). Recruitment involved circulating mass emails around staff and students of Northumbria University and displaying posters around the campus and local area. As displayed in Figure 11, participants were asked to complete an online screening questionnaire and, where eligible, were required to provide written informed consent. Participants were then randomised (1:1) to the experimental group (MD) or control group (Eatwell Guide (EG)), both of which involved intermittent fasting (IF). Participants completed an online background information form, dietary adherence questionnaire and a physical activity questionnaire. During testing visits, physical capability tests and anthropometrical tests were carried out alongside collection of a venous blood sample. Participants in both intervention arms had access to specially designed webpages tailored to each intervention group which contained all relevant dietary information in the form of videos of researchers giving lectures alongside text and diagrams, example weekly meal plans, recipes and shopping lists. Participants could also utilise intervention-specific social media accounts which were updated periodically with further information and recipe inspiration. After eight weeks of intervention, measurements (all described online questionnaires excluding those for screening and background information, and physical tests during the testing visit) were repeated and participants completed an additional online questionnaire aiming to collect feedback about the trial.

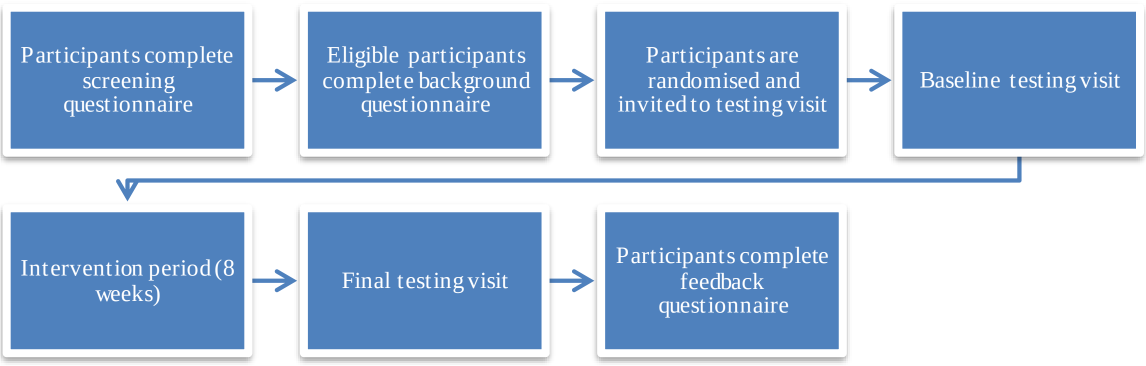

Figure 11: Study schematic

6.2.2. Participants

Participants were healthy (no pre-existing medical conditions) adults (aged 18-70 years) with a BMI in the overweight or obese categories (25.0-39.9kg/m^2). Exclusion criteria were: cardiovascular problems/documented history of CVD including angina, myocardial infarction, coronary revascularization procedures, stroke (ischemic or haemorrhagic, including transient ischemic attacks), symptomatic peripheral artery disease that required surgery or was diagnosed with vascular imaging techniques, ventricular arrhythmia, uncontrolled atrial fibrillation, congestive heart failure, hypertrophic myocardiopathy or aortic aneurism; active malignant cancer or history of malignancy within the last five years (except non-melanoma skin cancer), issues affecting food intake e.g. dysphagia, severe allergies, food neophobia, strong dislike of foods in diet plan or religious issues; lack of motivation to change diet/lifestyle; lack of motivation to fast, or medical reason disallowing very low calorie intake; type 1 or 2 diabetes; pregnancy, plans to become pregnant, or breastfeeding; current adherence to other weight loss or exercise program; illiteracy or inability/unwillingness to give written informed consent or communicate with study staff; institutionalisation; history of surgical procedures for weight loss or intention to undergo bariatric surgery in the next 12 months; obesity of known endocrine origin e.g. hypothyroidism or polycystic ovarian syndrome; serious psychiatric disorders including schizophrenia, bipolar disorder, eating disorders, or depression with hospitalisation within the last six months; alcohol abuse or addiction (or total daily alcohol intake >50 g) or drug abuse within the past six months; current use of weight loss medication; or any other condition that may interfere with adherence to the study protocol.

6.2.3. Recruitment and randomisation

Participants were recruited from 15th January until 31st March 2019 using mass emails to students and staff at Northumbria University; posters and leaflets displayed around the University campus (Students' Union, library and various places in other University buildings) and local area (e.g. leaflets left with permission in the Grainger Market's Weigh House - a popular place to have body weight measured accurately and where slimming groups advertise); use of the Northumbria University Brain, Performance and Nutrition Research Centre's volunteer database; and targeted advertising (e.g. posts in gym social media groups and talks in University lectures) to utilise the snowball effect. Recruitment posters and emails contained information about the trial and a link to an online screening questionnaire (created using www.onlinesurveys.com). Participants were routed through a series of questions designed to assess eligibility. Where participants were not eligible for the study, they were thanked for their time and notified that they would be unable to take part via an on-screen message. Those who were eligible where instructed to leave a telephone number or email address, were contacted and asked to complete a background information questionnaire. Self-reported BMI from this questionnaire was used during randomisation where an online randomisation tool (www.randomization.com) was employed to create two lists of 'MD' and 'EG' in random orders. Participants were assigned to an intervention group stratified by BMI to ensure equal numbers of overweight and obese BMI categories in each intervention group. As this was a dietary intervention, it was not possible to blind researchers and participants to the intervention group however the randomisation and recruitment were carried out by separate people. Participants were assigned participant numbers created using a random number generator (www.randomization.com) and asked to use only this number on all questionnaires and forms to ensure anonymity. No sample size was calculated as this was a pilot study, and results such as number of drop-outs were analysed to assess acceptability and feasibility of this trial.

6.2.4. Interventions

6.2.4.1. Intermittent fasting

A review of literature was carried out involving all papers researching intermittent fasting published from 2000-2018, as shown in Appendix F19. This was used to decide upon the fasting regime utilised in this dietary intervention. Both intervention groups were asked to adhere to an IF regime involving consumption of 500kcal per day for women and 625kcal per day for men, resulting in 75% daily caloric restriction. Participants were advised to remain adherent to their study diet throughout fasting days where possible within the small calorie limit. Participants were given the choice of which two days to fast, as long as fasting days were not consecutive. As this was a feasibility study, participants were allowed to choose how to allocate calories to meals on fasting days. Example meal plans were provided to be used as inspiration for days involving: three meals of around 160kcal each; two meals of around 250kcal each; or two meals of around 100kcal with a 300kcal meal, so that individuals could select a pattern that suited them. Men were recommended to consume 625kcal per day, therefore meal plans reflected this by suggesting larger portion sizes or snacks. Participants were encouraged to stay well hydrated, and were allowed to consume sugar-free drinks such as tea or coffee.

6.2.4.2. Experimental arm: the Mediterranean diet

Participants randomised to the MD were advised to follow a traditional MD based on the Mediterranean Diet Foundation Pyramid (shown in Figure 5) with selection of this diet based on a literature search shown in Appendix F20. This dietary pattern involved basing meals around fruits, vegetables and grains, replacing red meats with white meats such as poultry, using olive oil as the main fat source, reducing reliance on processed foods, consuming legumes and pulses, eating sweets infrequently, and optional consumption of a small glass of red wine with evening meals. Participants not consuming alcohol were suggested to drink a small glass of grape juice in order to benefit from some of the antioxidants found in wine. Participants were asked to adhere to the UK government's calorie guidelines of 2000kcal per day for women and 2500kcal for men on non-fasting days.

6.2.4.3. Control arm: the Eatwell Guide

Participants randomised to the EG were instructed to follow the UK Government's Eatwell Guide, shown in Figure 12 which involves basing meals on starchy carbohydrates, eating at least five portions of fruits and vegetables per day, consumption of some dairy products, pulses, fish and other protein sources, and the selection of small amounts of unsaturated oils and spreads. This diet was chosen as government dietary guidelines are commonly employed as control diets in many dietary intervention trials, as show in Appendix F20. Participants were also asked to adhere to the UK government's calorie guidelines of 2000kcal per day for women and 2500kcal for men on non-fasting days.

Figure 12: The Eatwell Guide (PHE, 2016). Contains public sector information licensed under the Open Government Licence v1.0

6.2.5. Participant support

6.2.5.1. Webpages

This intervention was designed to be low-intensity and low-contact, therefore all information required for the trial was given via the Internet to remove the need for participants to make multiple visits the University in person. Separate user-friendly information webpages were created for each intervention arm using Wix software (www.wix.com) (MD arm: https://louisefrancis.wixsite.com/website and EG arm: https://louisefrancis.wixsite.com/website-5 with example screenshots shown in Appendix F21 and Appendix F22). Webpages included a screen recording on the home page giving an explanation of how webpages should be used and what information could be accessed. Much background information about each dietary pattern and IF was uploaded, for example rationale behind dietary guidelines and copies of the MD pyramid or EG graphic. Various topics were covered, including information about the various food groups, tips on how to make healthy packed lunches, and a page about increasing physical activity levels which contained hyperlinks to videos such as at-home yoga tutorials or high-intensity interval training (HIIT) sessions on YouTube (www.YouTube.com). The majority of recipes were taken from a popular recipe-hosting website (www.bbcgoodfood.com, copyright permission granted) or a MD website (www.oldwayspt.org, copyright permission granted) and re-formatted to ensure ease of understanding (for example by standardising units across recipes or substituting particularly unusual ingredients). Included recipes were relatively quick to make, showed the amount of time needed to complete a full meal, did not include expensive or unusual ingredients, stated how many portions were made, had easily scalable portion numbers so participants could include their families, and adhered to each of the intervention's dietary protocols. Recipe ideas for fasting days also included approximate calorie counts. Videos were created of researchers preparing a selection of example recipes to add interest. Example weekly meal plans including fasting days were outlined, involving hyperlinks to some recipes given on the site to facilitate ease of use. Further information on the mentioned topics was given in the form of videos, involving voiceovers of PowerPoint slides. Participants were encouraged to keep in contact with the research team via email, a form on the website, or the website's online chat facility.

6.2.5.2. Social media

Periodic uploads were made to two separate social media accounts (@mediterranean_research and @eatwell_research, using www.instagram.com) including recipes, exercise examples and fasting meal ideas, with examples shown in Appendix F23 and Appendix F24.

6.2.6. Nutritional analysis

Participants were supplied with food diary templates and were given instructions on how to keep detailed three-day food diaries of everything eaten and drunk with cooking methods and portion sizes on two weekdays and one weekend day for the baseline diary, and one non-fasting weekday, one non-fasting weekend day, and one fasting day (weekday or weekend day) for the post-intervention diary. Participants were encouraged to carry their diary with them and to add entries as they occurred to minimise recollection errors.

Nutritional analysis of food diaries was carried out using Nutritics software (www.nutritics.com; Dublin, Ireland) with three-day food diaries input into software by the same researcher to ensure continuity. Where detail in food diaries was lacking or seemed unfeasible, participants were contacted and asked for clarification. Intakes of macronutrients such as protein and carbohydrate were analysed however micronutrient analysis was minimal and focused on micronutrients shown to be lacking in the average UK diet and in various Mediterranean countries alongside those with known links to CVD because only three days of food diaries (with only one fasting day) were collected which would not provide sufficient data for reliable analysis of micronutrient intakes. Data from food diaries was used to compare basal metabolic rate (BMR) calculated using the Harris-Benedict equations (Harris and Benedict, 1918) with baseline energy intakes to gain understanding of over- and underreporting in food diaries. Cut-off points for classification of reporting were based on those utilised by Johansson *et al.* (1998) with an energy intake:BMR ratio of ≤1.14-1.34 classed as underreporting, 1.35-2.39 as in the normal range, and ≥2.40 as over-reporting.

The PREDIMED 14-item screener (Martínez-González *et al.*, 2012) was slightly modified to reflect use in a British population and was used to assess adherence to the experimental diet at baseline and at the end of the trial. A similar EG adherence screener was created in which one point was allocated for each Eatwell guideline fulfilled (resulting in a score out of a possible twelve points) to allow comparison to the PREDIMED screener. This gave a rudimentary method of assessing dietary adherence and was pilot tested on a convenience sample but has not been employed on a large population.

6.2.7. Anthropometry and body composition

Participants underwent body fat percentage measurement while supine using the same body composition analyser (BodyStat 1500, Isle of Man, UK) for each measurement with electrodes attached via ECG pads in the tetrapolar arrangement on the right hand (red electrode attached just behind the metacarpals and black on the styloid process of the ulna i.e. just before the wrist) and right foot (red electrode attached just behind the metatarsals and black on the styloid process of the fibula i.e. just before the ankle). Height was measured to the nearest centimetre using a portable stadiometer without shoes. Weight measured wearing light clothing without shoes using portable bathroom-style scales to the nearest kilogram after removal of any personal items which may impact weight (e.g. phone or wallet). Waist circumference was measured at the approximate midpoint between the lowest rib and the top of the iliac crest; and hip circumference measured around the widest point of the buttocks using a flexible tape measure. Blood pressure was measured in triplicate using a non-invasive digital automatic blood pressure monitor (Carescape™ V100, GE Healthcare, UK) with the cuff placed on the right arm as the participant was seated with feet flat on the floor after resting alone in a quiet examination room for five minutes.

6.2.8. Physical activity

Participants completed the short form version of the International Physical Activity Questionnaire (IPAQ) (Craig *et al.*, 2003) at baseline and post-intervention. Sitting time data is frequently incorrectly reported on a weekly basis rather than daily, therefore data that seemed unlikely was divided by seven to give a daily sitting time in minutes, and calculations to assess IPAQ categories were carried out using an Excel template and given in metabolic equivalents (MET-mins) (Cheng, 2016). Participants wore a pedometer (Walking Style One 2.1, Omron, Kyoto, Japan) and accelerometer (wGT3X-BT ActiGraph Inc, Florida, USA) for three days at baseline and again at the end of intervention. Participants were allowed to keep pedometers as these devices have been shown to increase daily step count (Bravata *et al.*, 2007) and were encouraged to increase their exercise levels by walking alongside other physical activity such as yoga and swimming. Pedometers and accelerometers were both worn at the waist on the right-hand side as recent literature suggests that devices measure step count more accurately and consistently when worn at this location in comparison to the dominant or non-dominant wrist under both free-living and research conditions (Gaz *et al.*, 2018, Tudor-Locke *et al.*, 2015). ActiGraph wGT3X-BT accelerometers were utilised as it has been shown that these tri-axial models more accurately measure energy expenditure than uni-axial versions (Hendelman *et al.*, 2000) thus giving a more reliable vector magnitude, and high inter-device reliability has been demonstrated (Brage *et al.*, 2003). Wear time validation was carried out using the Choi (2011) algorithm as it is thought that algorithms using 90 minutes of continuous zeroes as a cut-off for non-wear time report participants' sedentary and non-wear time more accurately than those employing 60 minutes as the cut-off, such as the Troiano algorithm, which may over-estimate sedentary behaviour and wear time by up to 30 minutes per day (Chudyk *et al.*, 2017).

6.2.9. Physical capability

Physical capability was investigated via a grip strength test assessed using a handheld dynamometer (JAMAR, Huthwaite, UK) with the participant sitting in a chair with both feet flat on the floor, holding the dynamometer with their arm resting on the arm of the chair. Participants were instructed to squeeze the dynamometer as hard as they could without injury and to release straightaway, with three measurements taken with each the dominant and non-dominant arm. Forced Expiratory Volume (FEV1) alongside Forced Vital Capacity (FVC) were measured with a spirometer (CareFusion, Basingstoke, UK) fitted with a disposable mouthpiece. Participants sat in a chair with their feet flat on the floor and were instructed to take a deep breath, form a secure seal around the spirometry tube with their mouth, and exhale quickly. Three measurements were taken, with the participant instructed to rest and take deep breaths between readings to ensure they did not become light-headed. All participants were asked to complete a practice measurement of each test so that proper technique was ensured.

6.2.10. Blood collection and analysis

Blood samples were obtained by venepuncture in the cubital fossa of the forearm after a 12 hour fast (no food or caffeinated drinks but water was permitted) using a BD Safety-Lok blood collection kit and purple-capped (EDTA) tubes.

Samples were centrifuged immediately after collection at 2000rpm at 4°C for 10 minutes before serum (buffy coats) was pipetted into labelled 1ml Eppendorf tubes and stored at -80°C until analysis at the Royal Victoria Infirmary's Department of Blood Sciences, Newcastle. Samples were analysed for total cholesterol, triglycerides and HDL via enzymatic colorimetric tests using the Roche Cobas 8000 analytical line with the c702 chemistry module using CHOL2, TRIGL and HDLC4 kit inserts (Cobas Roche Diagnostics, Indianapolis, USA). LDL values were calculated from total cholesterol and HDL results. Samples were analysed in a single batch to reduce any inter-batch variability.

6.2.11. Participant feedback

Participants were required to complete an online questionnaire after completion of the trial in order to gain insight into their opinions of various facets of the study. Questionnaires were tailored to individual study diets and questions were asked about the research website, social media account, researcher, fasting regime and relevant study diet. Informal, unstructured qualitative feedback was also collected during testing visits whereby participants were free to give feedback on any aspects of the trial they deemed pertinent. This feedback was analysed in order to assess acceptability and feasibility.

6.2.12. Statistical analysis

IBM's SPSS v26 for Windows was used to test for normal distribution (Kolmogorov-Smirnov test) and compare continuous variables using paired or independent t-tests, with nominal and ordinal variables compared using McNemar's test, Chi-squared tests or Binomial tests where Chi-squared was not possible. Fisher's Exact Test was used in place of Chi^2 where sample sizes were small. General linear model (GLM) repeated measures was utilised to compare groups of paired variables, for example pre- and post-intervention weight in each intervention group. GLM univariate analysis was employed in the comparison of non-related variables, for example to compare the difference in pre-intervention BMI between study groups. Partial correlation was utilised to analyse association between variables such as total cholesterol and weight loss. Due to small sample sizes, values were adjusted only for age, sex and baseline values where appropriate to avoid over-adjustment for multiple covariates. Separate per protocol (PP) and intention-to-treat (ITT) via last observation carried forward (LOCF) analyses were carried out to ensure no under- or overestimation of treatment effect, as ITT preserves the original randomisation and avoids bias due to drop-outs, but PP analysis aims to identify the treatment effect under optimal conditions and excludes those with protocol deviations.

6.3. Results

Demographic results alongside acceptability and feasibility data are reported in Chapter 7 alongside results concerning diet, physical activity and physical capability; and all results regarding blood analysis (including blood pressure) and body composition.

6.4. Points covered in Chapter 6

i) Details of study rationale and literature gaps

ii) Full pilot study protocol, including study schematic

6.5. Research questions to be answered in Chapter 7

i) What were the characteristics of the participants taking part in this trial?

ii) How acceptable and feasible is this dietary intervention?

iii) What dietary, physical activity, and physical capability changes were associated with this trial?

iv) What impact did this trial have on body composition and cardiovascular biomarkers?

v) What changes could be made if this trial was carried out again, and what future work is required?

7. A pilot study investigating the impact of the Mediterranean diet and intermittent fasting in a population of healthy, overweight and obese adults

This chapter includes demographic results of study participants and details the acceptability of a combination of intermittent fasting and the Mediterranean diet or Eatwell Guide alongside its impact on body composition, physical activity, physical capability and biomarkers of cardiovascular disease.

7.1. Introduction

7.1.1. Acceptability and feasibility of the Mediterranean diet and intermittent fasting

Chapters 2 and iv) alongside section 5.3.2.3 show that the MD is rated as both acceptable and feasible amongst the UK public, with section 1.3 highlighting that there are few studies investigating the acceptability of IF, but that most portray this eating pattern favourably. Further work is therefore required to investigate the acceptability and feasibility of these dietary patterns in combination as part of a lifestyle intervention.

7.1.2. Acceptability and feasibility of Internet-based interventions

With the rise of Internet use in recent years, research has focussed on novel methods of dissemination of health and dietary information, for example using websites, social media and messaging to mobile phones. Research has shown that these types of interventions are often impactful alongside being cost-effective and useful for individuals living a distance from places where face-to-face meetings such as Weight Watchers are held (Waterlander *et al.*, 2014). A 2014 study utilising an interactive website and daily text messages promoting healthy eating behaviours suggested that an Internet-based intervention was deemed both acceptable and feasible to participants, with 81% of completers using the study website at least once in the 16-week intervention period (Ni Mhurchu *et al.*, 2014). Similarly, a MD Internet-based intervention showed that participants visited the study webpages on average 15.5 times over the six month trial period, with those in the intervention group receiving access to the specialised website more likely to be 'highly satisfied' with the nutrition education materials received than those given standard informational brochures (Papadaki and Scott, 2005). A review of interventions across multiple research areas suggested that the Internet may provide a solution to many of the problems associated with face-to-face interventions, with studies utilising the Internet shown to be relatively cheap, effective across multiple stages of intervention including prevention and maintenance, and accompanied by reports of high participant satisfaction and low attrition rates (Baulch *et al.*, 2012).

7.1.3. Relationship between diet and health factors

Recent NDNS data detailed in section 3.1.2 shows that the current UK diet is inadequate in some areas of food intake such as fruits, vegetables and oily fish (PHE, 2018a), suggesting that current public adherence to the EG is low and section 3.3.3 demonstrating the lack of MD adherence. This can translate to macronutrient intakes, with NDNS data in Figure 13 suggesting insufficient average fibre intake at 19g compared to the recommended 30g per day (PHE, 2016a), increased protein intake (87.4g for men and 66.6g for women compared to the prescribed 55.5g and 45.0g respectively), insufficient carbohydrate consumption (249g/199g compared to the recommended 333g/267g), and heightened free sugar intake (64.3g/50g compared to 33g/27g). Sufficient intake of dietary fibre (often linked to appropriate carbohydrate consumption) has been associated with positive effects on multiple health conditions, for example short chain fatty acids are produced during bacterial fermentation of soluble fibre and resistant starch molecules which can reduce blood cholesterol levels and therefore impact CVD risk (Slavin *et al.*, 1999). A 2013 meta-analysis of 22 studies showed that a 9% lower risk of CVD and CHD was associated with each additional 7g of fibre consumed per day, achievable by eating a portion of wholegrains alongside one of pulses (Threapleton *et al.*, 2013). With low energy density, some fibres have been shown to have a satiating effect and epidemiological studies have linked higher fibre intake with lower weight. This study also suggested that dietary fibres can attenuate absorption of other nutrients, with a body of research proposing that fibres can impede digestion of fats and therefore decrease caloric consumption (Hervik and Svihus, 2019). Heightened protein intake has been associated with weight gain due to increased caloric intake, and a 2013 review of 32 studies also suggested that protein intake above the recommended level was linked to disruption of calcium homeostasis alongside renal disorders such as kidney stones (Delimaris, 2013). Both epidemiological and interventional studies have suggested that increased consumption of free sugars is linked with heightened risk of obesity, type 2 diabetes, CVD, hypertension and dyslipidaemia, with analysis of the US National Health and Nutrition Examination Survey showing that individuals consuming between 17% and 21% of energy intake from free sugars had a 38% higher risk of mortality from CVD than those consuming 8% of calories from sugars (Yang *et al.*, 2014).

Alongside macronutrient issues, several important micronutrients are lacking in the average UK diet, most worryingly those implicated in various forms of CVD. NDNS data suggests that although percentages of adults with a mean intake of Vitamin A, Vitamin B2 and Vitamin B12 below the lower reference nutrient intake (LRNI) were low (at 13%, 10% and 5% respectively) mean intakes of Vitamin D from food sources were commonly inadequate, at 31% of the reference nutrient intake (RNI) for men, 25% for women and 28% overall for adults aged 19-64 in the UK (no LRNI has been set for Vitamin D). NDNS data also shows that the highest percentages of minerals below the LRNI were seen in selenium (25% of men, 47% of women and 36% of all adults), potassium (11%; 23%; 17%) and iron (2%; 27% and 15%) (PHE, 2018a), with mean daily salt intake for adults aged 19 to 64 estimated at 8g (136.8mmol of sodium) which is 33% higher than the Scientific Advisory Committee on Nutrition (SACN) recommended maximum intake of 6g (PHE, 2018a).

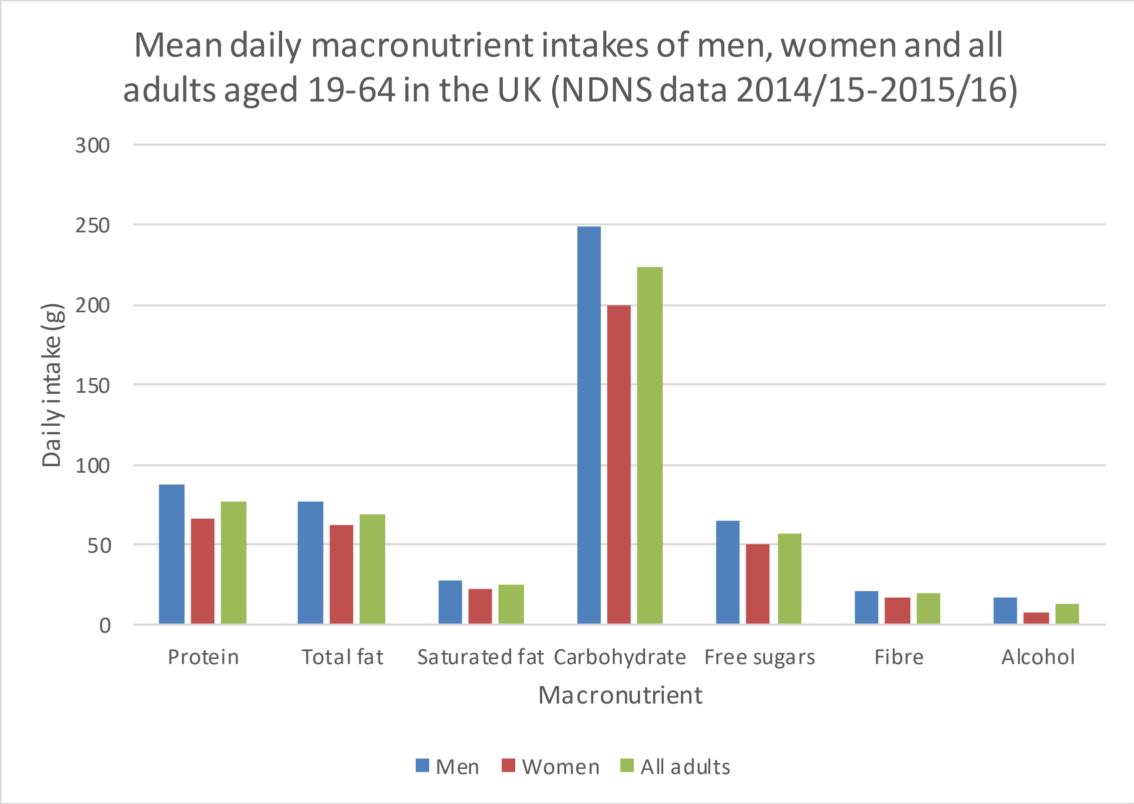

Figure 13: Mean daily macronutrient intakes of men, women and all adults aged 19-64 in the UK (NDNS data 2014/15-2015/16) Contains public sector information licensed under the Open Government Licence v1.0

7.1.4. Physical activity

The link between physical activity and CVD was first reported in 1958 when researchers noted a difference in coronary heart disease incidence between the sedentary drivers and more active conductors on London buses (Morris and Crawford, 1958). Since this first study, it has been well-reported that physical inactivity is a major issue, with the 2004 INTERHEART Study citing it alongside factors such as hypertension and type 2 diabetes as one of the nine most significant contributors to heart disease and mortality worldwide (Yusuf *et al.*, 2004), and substantial evidence from observational studies suggesting an inverse dose-response association between physical activity and risk of CVD (Shiroma and Lee, 2010). Cross-sectional studies have shown that lower prevalence of obesity is associated with higher levels of physical activity, with individuals with a high BMI and high physical activity levels shown to be at greater risk for CVD than those with a healthy BMI engaging in little physical activity (Fogelholm, 2010). UK guidelines recommend that adults partake in at least 150 minutes of moderate activity or 75 minutes of vigorous activity per week or an equivalent combination of both, in bouts of 10 minutes or more, however 66% of men and 58% of women aged 19 years or over meet these recommendations while 21% of men and 25% of women were classed as inactive (NHS, 2018). Although current adherence to physical activity guidelines in the UK is relatively low, a prospective cohort study of 416,175 participants demonstrated that when compared to inactive participants, those exercising on average for 92 minutes/week had a 14% reduced risk of all-cause mortality alongside an increased life expectancy of three years (Wen *et al.*, 2011). This suggests that even a small increase in physical activity levels has beneficial impact on health. Common methods of physical activity measurement involve utilising the validated IPAQ alongside accelerometers, discussed in section 6.2.8.

7.1.5. Physical capability

There are various valid measures of physical capability such as sit-to-stand tests, walking tests, spirometry and tests of grip strength. Grip strength is a well-researched predictor of many chronic diseases alongside mortality and is therefore utilised as a marker of health, with a study across twelve countries showing that the grip strength of participants who were obese at baseline declined faster over the median follow-up of 9.42 years than that of non-obese individuals. Higher levels of baseline physical activity were also associated with stronger grip strength at follow-up, with researchers concluding that a combination of obesity and physical inactivity may be a significant factor in the decline of grip strength (Wang *et al.*, 2019). A large study of UK Biobank data from 502, 293 participants showed that a 5kg lower grip strength was associated with a higher hazard ratio for all-cause mortality alongside incidence of CVD and deaths occurring from this disease (Celis-Morales *et al.*, 2018). Lung function is often tested via spirometry which is thought to be a reliable measure of Forced Expiratory Volume (FEV1) and Forced Vital Capacity (FVC); measures which have been shown to be inversely correlated with CVD and other morbidities, with a study of 4019 participants showing that every 5% decrease in FEV1 and FVC was associated with a 0.47% increase in CVD risk over ten years (Wang *et al.*, 2018). A study involving 5115 participants showed strong association between lung function and BMI, with both FEV1 and FVC showing marked decrease in those with higher baseline BMI values and those gaining the most weight over the ten year study period (Thyagarajan *et al.*, 2008). In a study of 3391 British adults, it was shown that weight loss was associated with increased FEV1 values, with the effect almost twice as large in males compared to females, potentially because the android pattern of adiposity involves increased fat deposition around the abdomen and therefore impedes breathing (Carey *et al.*, 1999). Similarly, a 2009 study demonstrated that a 1cm increase in waist circumference was associated with a decrease in FEV1 of 4ml in women and 17ml in men, and a 1kg/m^2 increase in BMI was associated with a reduction in FVC of 266ml in men and 88ml in women (Steele *et al.*, 2009). Physical activity has been shown to impact measures of lung function, with a recent study of 341 healthy participants demonstrating that the most active individuals, measured using accelerometers, had higher FEV1 and FVC results than those partaking in less physical activity (Luzak *et al.*, 2017).

7.1.6. Anthropometry and body composition

As described in Section 1.1, obesity remains a major health issue concerning the NHS in the UK and for healthcare providers worldwide, with a 2017 systematic review and meta-analysis of 34 studies and 30,206 participants showing that weight reduction in obese adults was associated with a 18% reduction in relative risk of premature morbidity (Ma *et al.*, 2017). Similarly, losing 5% of body weight has been associated with clinically significant improvements to SBP, blood glucose, triglycerides and markers of insulin resistance (Wing *et al.*, 2011). BMI is often used as the main form of weight classification and therefore level of disease risk, with potential criticisms detailed in section 1.1.1. Alongside BMI there are other useful predictors of CVD and mortality such as waist circumference and waist-to-hip ratio (WHR). A systematic review and meta-analysis of 15 studies involving 258,114 participants showed that a 1cm increase in waist circumference and 0.01 increase in WHR were associated with 2% and 5% increased risk of CVD. It is thought that measures of abdominal obesity like waist circumference and WHR may be more strongly associated with incident CVD and mortality than BMI because these factors take into account visceral adipose tissue which is linked with insulin resistance, hypertension and dyslipidaemia. Adjusting findings for various confounders showed that abdominal obesity is an independent CVD risk factor over and above other correlates such as smoking and high blood cholesterol levels, and lead authors to recommend the inclusion of waist circumference and WHR in CVD risk assessments (de Koning *et al.*, 2007). Sections 1.2.2 and 1.2.3 include information about research into the impact of adherence to a MD on body composition such as weight and WHR, while section 1.3.2 details literature which deals with the effects of IF on these outcomes.

7.1.7. Cardiovascular biomarkers

According to the Global Disease Burden Study (Vos *et al*., 2015), CVD is one of the leading contributors to the burden of disease in multiple countries worldwide and although age-standardised mortality from CVD has declined by 70% over the last 30 years (Bhatnagar *et al.*, 2016), this disease remains the second most common cause of death in the UK, accounting for over a quarter of deaths (BHF, 2018). First researched during the Framingham Heart Study, the most significant risk factors for CVD are said to be hypertension, high LDL/low HDL cholesterol levels, smoking, type 2 diabetes, physical inactivity and obesity (Donnell and Elosua, 2008). Total blood cholesterol levels are deemed high when measured above 5mmol/L, with a meta-analysis including over one million people showing that every 1mmol/L increase in total cholesterol level increased the risk of CHD by 20% in women and 24% in men (Peters *et al.*, 2016). Similarly, a clear inverse relationship has been shown between HDL and risk of CVD, with each 1mg/dl (0.02586mmol/L) increase in HDL reducing the CVD risk by 3% in females and 2% in males (Gordon *et al.*, 1989). A combination of low HDL and high TG levels has been termed 'atherogenic dyslipidemia' and used as a marker for atherosclerosis risk, with a study of 3216 healthy American Indians showing that those with this marker had a 1.32-fold greater hazard ratio of heart disease than those with normal HDL and TG levels, with heightened risk in diabetic participants (Lee *et al.*, 2017). There has recently been some controversy concerning the links between LDL and CVD, with some researchers (including some involved in the previously-mentioned Lyon Diet Heart study) suggesting that individuals with low LDL levels become just as atherosclerotic as those with higher levels and that therefore LDL is not implicated in CVD risk (Ravnskov *et al.*, 2018). However, a consensus statement from the European Atherosclerosis Society Consensus Panel which involved meta-analysis of 200 prospective cohort studies and randomised controlled trials involving two million participants demonstrated a consistent dosedependent association between increased blood LDL levels and incidence of atherosclerosis (Ference *et al.*, 2017). Shown to be more likely in overweight or obese individuals and those consuming high levels of salt alongside small amounts of fruits, vegetables and nuts; hypertension is classified as a SBP over 140mmHg and DBP over 90mmHg (NHS, 2019a) with high SBP thought to be the leading cause of CVD deaths globally (Jagannathan *et al.*, 2019). Alongside hypertension, associations between blood lipid levels and weight have also been demonstrated, with a 2019 study of 102 older adults undertaking a 12 week programme involving dietary changes and exercise demonstrating that significant weight loss was associated with positive impact on total cholesterol, TG and SBP, together with reduction in use of antihypertensive medications (Haywood *et al.*, 2019). Sections 2.3 and 4.3 show results of meta-analyses involving studies showing impact of the MD and IF on blood-borne biomarkers of CVD alongside blood pressure, with both dietary patterns showing favourable outcomes.

7.1.8. Aims

This pilot study aims to investigate:

- The acceptability and feasibility of a lifestyle intervention involving a combination of the MD or EG and IF in a population of overweight and obese adults in the UK by assessing recruitment and retention alongside analysing participants' feedback in both qualitative and quantitative forms.
- The impact of this intervention on diet, physical activity and physical capability amongst a healthy but overweight or obese sample population. Dietary patterns will be investigated by analysing food diaries to assess overall energy consumption and macro- and micronutrient intakes alongside utilising online questionnaires to investigate dietary adherence scores, with physical activity assessed via use of accelerometers and a validated physical activity questionnaire, and physical capability by measurement of lung function and grip strength.
- The impact of this intervention on blood-borne cardiovascular biomarkers such as serum cholesterol levels and blood pressure alongside anthropometry and body composition measures, for example body fat percentage and blood pressure.

7.2. Methods

Methodology for this trial is laid out in Chapter 6.

7.3. Results

7.3.1. Participant flow diagram

The CONSORT participant flow diagram is laid out in Figure 14 and shows that of the 75 randomised participants there were twenty participants in each study group beginning the intervention, with eleven participants in the EG study group and twelve in the MD completing the pilot study as per protocol (55% and 60% completion rates respectively). The majority of participants not completing the intervention were lost to not replying to emails to arrange testing visits, family commitments and ill health unrelated to the study.

CONSORT
TRANSPARENT REPORTING of TRIALS

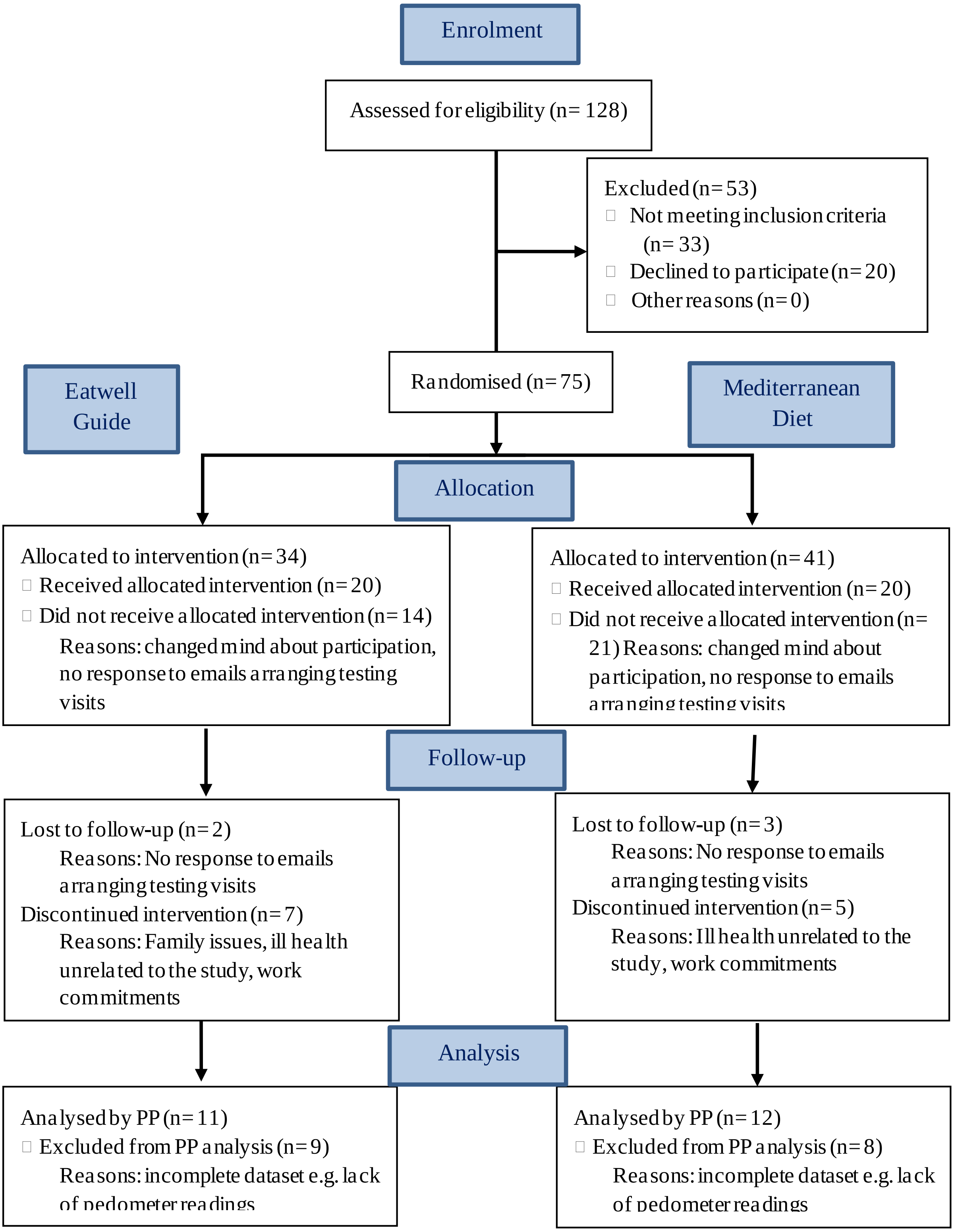

Figure 14: CONSORT participant flow diagram

7.3.2. Demographic information

Table 27 shows that of the 40 participants who were randomised and began the trial, mean age was 34.25 years, 82.50% were female, 95.00% were Caucasian, 55.00% were students, 77.50% had a University-level education, 5.00% smoked and 10.00% reported being vegetarian or vegan. Twenty-three participants completed the trial per protocol, with reasons for non-completion including unrelated health issues, inability to attend testing visits, and negative impact of fasting regime. Mean age of study completers was 37.57 years, 73.91% were female, 95.65% were Caucasian, 43.48% were students, 73.91% had a University-level education, 4.35% smoked and 4.35% reported being vegetarian or vegan. No statistically significant differences were observed between completers and non-completers, however non-completers were non-significantly younger (p=0.078) and heavier (p=0.613) with higher proportions of students (p=0.198) and lower proportions of University education (p=0.527) than study completers.

Table 28 shows that for all randomised participants and for study completers the most commonly reported reason for study participation was to lose weight and become healthier (57.50%; 54.50%) with wanting to help the researcher or learn about IF reported least (2.50% all participants and 4.35% completers). No significant differences were observed between completers and non-completers.

Of completers and non-completers, 88.20% and 91.30% reported having previously made a weight loss attempt. Table 29 shows that the most commonly reported method of previous weight loss attempt amongst the 40 randomised participants was diet plans involving group meetings (55.56%) with meal replacements used least frequently (5.56%), however study completers reported utilising exercise plans (52.38%) most commonly and meal replacements least frequently (9.52%). Non-completers were significantly more likely than completers to report use of diet plans that did not involve group meetings (p=0.032).

Table 27: Demographic information for all randomised participants, study completers and non-completers

	All participants (n= 40)	**Completers (n= 23)**	**Non-completers (n= 17)**
Gender (n % female)	33 (82.50)	17 (73.91)	16 (94.12)
Age (mean ± SD)	34.25 ± 13.85	37.57 ± 15.04	29.76 ± 10.94
Ethnicity			
Caucasian	38 (95.00)	22 (95.65)	16 (94.12)
Other	2 (5.00)	1 (4.35)	1 (5.88)
BMI (mean ± SD)	29.10 ± 3.47	28.85 ± 3.43	29.42 ± 3.59
Employment			
Student	22 (55.00)	10 (43.48)	12 (70.59)
Working full/part time	17 (42.50)	12 (52.17)	5 (29.41)
Housewife/husband/carer	1 (2.50)	1 (4.35)	0 (0)
Education			
University	31 (77.50)	17 (73.91)	14 (82.35)
Non-university	9 (22.50)	6 (26.09)	3 (17.65)
Tobacco smoking (n %)	2 (5.00)	1 (4.35)	1 (5.88)
Vegetarian/vegan (n %)	4 (10.00)	1 (4.35)	3 (17.65)

Table 28: Reasons for study participation of all randomised participants, study completers and non-completers

Reason for participation n (%)	All participants (n= 40)	Completers (n= 23)	Non-completers (n= 17)
To lose weight and be healthier	23 (57.50)	12 (54.17)	11 (64.71)
To lose weight and look better	7 (17.50)	4 (17.39)	3 (17.65)
Out of interest in the project	5 (12.50)	1 (4.35)	4 (23.53)
To be healthier regardless of weight loss	3 (7.50)	3 (13.04)	0 (0)
To help the researcher	1 (2.50)	1 (4.35)	0 (0)
To learn about intermittent fasting	1 (2.50)	1 (4.35)	0 (0)

Table 29: Use of weight loss techniques amongst participants reporting previous weight loss attempts

Weight loss technique n (%)	All participants (n= 36)	Completers (n= 21)	Non-completers (n= 15)
Group meetings	20 (55.56)	10 (47.62)	10 (66.67)
Exercise plans	15 (41.67)	11 (52.38)	4 (26.67)
Other diet plans	10 (27.78)	3 (14.29)	7 (46.67)
Medicinal aids	5 (13.89)	3 (14.29)	2 (13.33)
Fasting	5 (13.89)	4 (19.05)	1 (6.67)
Meal replacements	2 (5.56)	2 (9.52)	0 (0)

7.3.3. Post-intervention study feedback

7.3.3.1. Study diets and fasting

Results of an online survey showed that of the 11 completers in the EG group, 90.10% stated that they enjoyed adhering to the EG, with one participant reporting that they did not like the foods involved in the diet plan. One participant reported side effects (cravings for certain foods) and one reported that continuing to follow the EG would be unfeasible. Table 30 shows high numbers of participants reporting an intent to continue adhering to the EG guidelines after the intervention, with lowest levels of participants stating that they would attempt to eat two or more portions of fish per week (63.64%). On average, participants reported that they would attempt to adhere to 10.54 of the 12 EG guidelines. Similarly, of the 12 completers in the MD group, 100% stated that they enjoyed adhering to the MD and that future adherence would be feasible.

Table 31 shows that levels of intent to continue adhering to a MD were high, with lowest percentages of participants answering that that they would try to drink seven glasses of wine per week (8.33%) and consume four or more tablespoons of olive oil per day (33.33%). On average, participants reported that they would continue following 11.12 of the 14 MD guidelines.

In the EG, 63.60% and 75.00% of MD participants deemed this IF regime acceptable, with the majority of these in each study group intending to continue with some form of fasting plan. The most common reasons amongst those reporting that fasting was not an acceptable eating plan were a lack of willpower and negative side effects.

In the EG, six participants reported that foods involved in the study diet cost the same as their usual diet, with three reporting that the study foods were cheaper and two saying they were more expensive. In the MD, ten said the study diet cost the same, with two reporting an increase in food costs. Overall, 90.90% of EG and 91.60% of MD completers reporting getting what they wanted out of the study.

Table 30: Participants reporting intent to adhere to EG guidelines post-intervention

Eatwell Guide guideline	Participants reporting future adherence (n= 11) n (%)
≥5 portions of fruits and vegetables per day	11 (100.00)
Base meals around starchy carbohydrates	9 (81.82)
Choose wholegrain versions	10 (90.91)
Dairy each day	10 (90.91)
Choose lower fat and sugar options	11 (100.00)
Protein sources each day	10 (90.91)
≥2 portions of fish (1 oily) per week	7 (63.64)
<70g red or processed meat per day	10 (90.91)
Choose unsaturated fat sources	10 (90.91)
Small amounts of oils and spreads	10 (90.91)
6-8 cups of water per day	10 (90.91)
<14 units of alcohol per week	8 (72.73)

Table 31: Participants reporting intent to adhere to MD guidelines post-intervention

Mediterranean diet guideline	Participants reporting future adherence (n= 12) n (%)
Use olive oil as main fat for cooking	12 (100.00)
≥4 tbsp of olive oil per day	4 (33.33)
≥3 portions of vegetables per day	12 (100.00)
≥2 portions of fruit per day	12 (100.00)
<1 portions of red meat, hamburger or meat products per week	10 (83.33)
<1 portion of butter, margarine or cream per day	9 (75.00)
<1 glass of sweet or carbonated beverages per day	11 (91.67)
≥7 glasses of wine per week	1 (8.33)
≥3 portions of legumes or pulses per week	10 (83.33)
≥3 portions of fish or shellfish per week	9 (75.00)
<3 portions of sweets or pastries per week	9 (75.00)
≥3 servings of nuts per week	12 (100.00)
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	10 (83.33)
Use of a tomato-based sauce in cooking ≥2 times per week	10 (83.33)

7.3.3.2. Participant support and information sources

High percentages (72.70% in the EG and 100.00% in the MD groups) of participants visited the respective study webpages, with the majority of participants reporting that they visited the webpage once or twice per week. Table 32 shows that participants rated most webpage sections highly for their usefulness, with the segment concerning exercise rated lowest in both study groups (5.50 in the EG and 5.63 in the MD; where 1 is useless and 10 is incredibly useful) with general dietary information rated highest in the EG group (8.00) and non-fasting day recipes rated most useful by the MD participants (7.90). Participants reported that the webpage content was useful however although the webpages were attractive, they could be made more user-friendly. Just 27.30% of EG study completers and 58.30% of those in the MD group reported utilising the social media page, with participants stating that they did not use social media or did not think the social media page would be useful during the trial. Of those reporting use of the social media offering, the majority deemed it ‘a little bit useful’ or ‘very useful’.

The researcher was regarded highly, with the majority of study participants giving the highest possible score of ten for each when asked how helpful, empathetic, personable, approachable, professional and supportive the researcher was.

Table 32: Mean scores of usefulness for each of the webpage sections by study group

Webpage section	Mean score out of 10	
	EG	MD
Non-fasting day recipes	6.88	7.90
Fasting day recipes	7.88	7.70
Weekly meal plans	7.25	7.22
Motivation techniques	6.88	7.00
General dietary information	8.00	7.09
Exercise tips	5.50	5.63
Fasting information	7.75	7.00
Eating out tips	7.13	6.13
Recipe videos	5.88	6.00

7.3.3.3. Qualitative feedback

In addition to the post-intervention feedback questionnaire, informal qualitative feedback was gathered through conversations with participants. Commonly, when asked how the study had progressed for them, participants spoke first about their experience of IF, while the EG and MD were only discussed when prompted. Many participants stated that family and friends were an important factor during fasting, with multiple participants explaining that on fasting days, time constraints meant that cooking separately at home for themselves and for others not taking part in the study was difficult. Importantly, participants also highlighted that following a fasting plan often lead to isolated meals due to different meal timings and composition amongst the household. With part of this study taking place over Easter, some participants reported difficulty adhering to the diet plan because of celebration meals and wanting to partake in seasonal treats. There was also concern amongst a small number of individuals that their children would be influenced by their eating pattern, which lead to parents not eating with their children. Positively, participants reported "*feeling more energetic and healthy*" and "*being more mindful*", with "*food choices and especially portion sizes…influenced by an appreciation of what I could eat on fast days*". Similarly, some reported dietary improvements such as increasing vegetable and fish consumption and eating less red meat. Many participants reported planning to continue with the study diet exactly and others decided to make small changes, such as slightly increasing caloric intake on fasting days. Many reported that routine was important, with one participant stating that "*after a little while the fasting and new eating plan doesn't really feel like a 'diet' – it just becomes the way you eat once you're in the routine*". In terms of trial design, some individuals reported that a mid-point check-in would have increased motivation, however this was not shared amongst all participants. Overall, qualitative feedback was positive amongst those completing the trial.

7.3.4. Dietary adherence: Eatwell Guide

As shown by Table 33, mean adherence to the EG at baseline amongst the 20 participants randomised to this intervention group was relatively high at 8.55 points out of a possible 12, with the highest proportion of participants reporting that they consume a protein source each day (100.00%) and the lowest reporting consumption of two portions of fish per week (25.00%). After Intention-To-Treat (ITT) analysis, post-intervention data showed that the highest adherence remained at 100.00% of participants consuming daily protein and the lowest proportion remained concerning fish consumption, however this was increased to 40.00%. No statistically significant differences were observed in adherence to each guideline, however non-significant increases in the percentages of participants consuming adequate fruits and vegetables, wholegrains, dairy, fish, unsaturated fats and fluids alongside eating less red meat were noted. A statistically significant difference between mean EG adherence score before and after the intervention was observed (p=0.034).

As detailed in Table 34, per-protocol (PP) analysis of the 11 participants completing the study according to protocol showed that baseline EG adherence was relatively high, with significant difference shown in comparison to post-intervention adherence levels (p=0.029). 100.00% of participants reported consuming a protein source every day, however just 36.36% reported eating two portions of fish each week. No significant differences were observed between baseline and post-intervention adherence to each guideline, however non-significant increases were noted in consumption of fruits, vegetables, starchy carbohydrates, wholegrains, dairy, fish, unsaturated fats and fluids alongside decreased intake of red or processed meats.

Table 33: Dietary adherence pre- and post-intervention in the EG group (ITT; n= 20)

Eatwell Guide adherence n (%)	Baseline	Final	P value
≥5 portions of fruits and vegetables per day	8 (40.00)	13 (65.00)	0.063
Base meals around starchy carbohydrates	14 (70.00)	13 (65.00)	1.000
Choose wholegrain versions	16 (80.00)	18 (90.00)	0.500
Dairy each day	18 (90.00)	19 (95.00)	1.000
Choose lower fat and sugar options	16 (80.00)	16 (80.00)	1.000
Protein sources each day	20 (100.00)	20 (100.00)	1.000
≥2 portions of fish (1 oily) per week	5 (25.00)	8 (40.00)	0.375
<70g red or processed meat per day	17 (85.00)	18 (90.00)	1.000
Choose unsaturated fat sources	10 (50.00)	14 (70.00)	0.125
Small amounts of oils and spreads	17 (85.00)	16 (80.00)	1.000
6-8 cups of water per day	16 (80.00)	19 (95.00)	0.250
<14 units of alcohol per week	14 (70.00)	14 (70.00)	1.000
EG adherence score (mean ± SD)	8.55 ± 1.96	9.40 ± 2.28	**0.034***

*Significant p values are shown in bold with an asterisk

Table 34: Dietary adherence pre- and post-intervention in the EG group (PP; n= 11)

Eatwell Guide adherence n (%)	**Baseline**	**Final**	**P value**
≥5 portions of fruits and vegetables per day	4 (36.36)	8 (72.73)	0.236
Base meals around starchy carbohydrates	9 (81.82)	8 (72.73)	0.491
Choose wholegrain versions	9 (81.82)	11 (100.00)	1.000
Dairy each day	10 (90.91)	11 (100.00)	1.000
Choose lower fat and sugar options	10 (90.91)	11 (100.00)	1.000
Protein sources each day	11 (100.00)	11 (100.00)	1.000
≥2 portions of fish (1 oily) per week	4 (36.36)	7 (63.64)	0.375
<70g red or processed meat per day	10 (90.91)	10 (90.91)	1.000
Choose unsaturated fat sources	5 (45.45)	9 (81.82)	0.125
Small amounts of oils and spreads	10 (90.91)	10 (90.91)	1.000
6-8 cups of water per day	8 (72.73)	11 (100.00)	1.000
<14 units of alcohol per week	8 (72.73)	8 (72.73)	1.000
EG adherence score (mean ± SD)	8.91 ± 1.30	10.45 ± 1.37	**0.029***

*Significant p values are shown in bold with an asterisk

7.3.5. Dietary adherence: Mediterranean diet

Table 35 shows that MD adherence of all randomised participants was relatively low at baseline (4.40 points of a possible 14) increasing significantly to 6.40 after eight weeks of intervention (p=0.000). At both baseline and after intervention, the highest proportion of participants reported adherence to the MD guideline recommending preferential consumption of white meat over red (95.00%), and the lowest proportion reported consuming sufficient olive oil and wine (0% for both outcomes). A significant increase in participants consuming three or less portions of sweets or pastries per week was observed (p=0.008), alongside non-significant increases in consumption of olive oil, vegetables, fruit, legumes, fish, nuts and sofrito and decreased consumption of butter, red meat and soft drinks.

Table 36 shows that MD adherence at baseline was relatively low (4.58 of a possible 14 points), with PP analysis suggesting a significant difference in adherence level between baseline and post-intervention (p=0.000). At baseline, 91.67% of completers reported preferential consumption of white meat over red, however 0% of participants reported consuming sufficient olive oil or wine. No significant differences were observed in adherence to each guideline pre- and post-intervention, however non-significant increases in olive oil, vegetables, fruit, legumes, fish, nuts and sofrito were noted, alongside decreases in consumption of red meat, butter and soft drinks.

Table 35: Dietary adherence pre- and post-intervention in the MD group (ITT; n= 20)

Mediterranean diet adherence n (%)	Baseline	Final	P value
Use olive oil as main fat for cooking	14 (70.00)	18 (90.00)	0.125
≥4 tbsp of olive oil per day	0 (0)	0 (0)	1.000
≥3 portions of vegetables per day	13 (65.00)	16 (80.00)	0.250
≥2 portions of fruit per day	10 (50.00)	11 (55.00)	1.000
<1 portions of red meat, hamburger or meat products per week	4 (20.00)	6 (30.00)	0.500
<1 portion of butter, margarine or cream per day	3 (15.00)	6 (30.00)	0.375
<1 glass of sweet or carbonated beverages per day	5 (25.00)	8 (40.00)	0.250
≥7 glasses of wine per week	0 (0)	0 (0)	1.000
≥3 portions of legumes or pulses per week	9 (45.00)	10 (50.00)	1.000
≥3 portions of fish or shellfish per week	2 (10.00)	3 (15.00)	1.000
<3 portions of sweets or pastries per week	3 (15.00)	11 (55.00)	**0.008***
≥3 servings of nuts per week	2 (10.00)	5 (25.00)	0.375
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	19 (95.00)	19 (95.00)	1.000
Use of a tomato-based sauce in cooking ≥2 times per week	16 (80.00)	19 (95.00)	0.250
MD adherence score (mean ± SD)	4.40 ± 2.09	6.40 ± 2.52	**0.000***

*Significant p values are shown in bold with an asterisk

Table 36: Dietary adherence pre- and post-intervention in the MD group (PP; n= 12)

Mediterranean diet adherence n (%)	Baseline	Final	P value
Use olive oil as main fat for cooking	9 (75.00)	12 (100.00)	1.000
≥4 tbsp of olive oil per day	0 (0)	0 (0)	1.000
≥3 portions of vegetables per day	9 (75.00)	12 (100.00)	1.000
≥2 portions of fruit per day	7 (58.33)	8 (66.67)	1.000
<1 portions of red meat, hamburger or meat products per week	1 (8.33)	3 (25.00)	1.000
<1 portion of butter, margarine or cream per day	2 (16.67)	5 (41.67)	0.375
<1 glass of sweet or carbonated beverages per day	4 (33.33)	7 (58.33)	0.081
≥7 glasses of wine per week	0 (0)	0 (0)	1.000
≥3 portions of legumes or pulses per week	5 (41.67)	6 (50.00)	1.000
≥3 portions of fish or shellfish per week	2 (16.67)	3 (25.00)	1.000
<3 portions of sweets or pastries per week	2 (16.67)	10 (83.33)	0.008
≥3 servings of nuts per week	2 (16.67)	5 (41.67)	0.375
Preferential consumption of chicken or turkey instead of veal, hamburger or sausage	11 (91.67)	11 (91.67)	1.000
Use of a tomato-based sauce in cooking ≥2 times per week	9 (75.00)	12 (100.00)	1.000
MD adherence score (mean ± SD)	4.58 ± 2.28	7.83 ± 1.64	**0.000***

*Significant p values are shown in bold with an asterisk

7.3.6. Macronutrient intakes

Baseline energy intake (derived from food diaries) to BMR ratio suggests that 30 of the 40 randomised participants underreported energy intake in their first food diary. This means that minimal analysis of data derived from food diaries (e.g. micronutrient data) can be carried out as this is likely to be unreliable, alongside the small sample size and too few days of recorded food intake.

ITT results shown in Table 37 suggest significant difference between intakes of energy (KJ) and PUFA between baseline and post-intervention in the MD group were observed (p=0.047; 0.024), with no significant differences between study groups. Non-significant decreases in energy (kcal), fat, carbohydrate, sugars, saturated fat, MUFA and PUFA, alongside increased fibre intakes were observed in both study groups. PP analysis of macronutrient data shows a significant reduction in saturated fat intake was observed in the EG group (p=0.048). Trends for reduced energy, fat, carbohydrate, sugar, MUFA and PUFA alongside increases in fibre and cholesterol were observed in both study groups, with increases in protein and alcohol in the EG group and decreases in protein, alcohol and saturated fat in the MD. There were no statistical differences between study groups. Mean post-intervention caloric intake (average of non-fasting days) was 1469.20kcal for males and 1583.35kcal for females. Unadjusted results for ITT and PP analysis are presented in Appendix G25.

Table 37: Estimated marginal means and standard errors of macronutrient intake from general linear model repeated measures by study group adjusted for age, sex and baseline value

Dietary component (EMM±SEM)	**ITT**							**PP**						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Energy (kcal)	1968.31 ± 78.32	1797.81 ± 68.63	0.146	2063.73 ± 668.77	1863.06 ± 712.86	0.057	0.923	1798.45 ± 146.59	1568.18 ± 189.58	0.145	1831.67 ± 221.27	1549.38 ± 152.42	0.190	0.849
Energy (kj)	8261.12 ± 327.06	7551.50 ± 287.73	0.150	7927.88 ± 395.27	7041.29 ± 463.83	**0.047***	0.589	7542.55 ± 613.60	6587.09 ± 794.09	0.151	7789.50 ± 929.86	6503.04 ± 638.44	0.140	0.792
Protein (g)	82.56 ± 5.05	82.94 ± 4.09	0.947	75.58 ± 3.37	73.22 ± 5.88	0.538	0.289	71.00 ± 5.77	79.27 ± 7.11	0.280	77.00 ± 8.23	76.11 ± 6.97	0.942	0.674
Fat (g)	78.08 ± 4.15	67.52 ± 4.01	0.162	73.19 ± 7.30	67.64 ± 8.76	0.254	0.580	69.33 ± 9.84	56.46 ± 7.62	0.104	69.08 ± 7.92	61.45 ± 6.95	0.369	0.513
Carbohydrate (g)	214.50 ± 13.19	203.18 ± 10.40	0.546	212.50 ± 10.54	181.24 ± 11.11	0.073	0.319	181.55 ± 21.74	171.91 ± 21.70	0.732	209.00 ± 27.92	160.38 ± 18.45	0.137	0.540
Alcohol (g)	5.53 ± 4.74	6.93 ± 4.35	0.564	8.61 ± 1.42	6.41 ± 0.63	0.308	0.389	7.51 ± 5.29	7.83 ± 4.74	0.957	9.35 ± 7.72	7.34 ± 4.09	0.629	0.789
Sugars (g)	95.78 ± 1.56	88.74 ± 3.70	0.089	84.94 ± 5.95	71.57 ± 5.24	0.207	0.264	77.91 ± 8.24	71.44 ± 8.48	0.604	94.88 ± 20.22	73.42 ± 11.00	0.225	0.875

Dietary component (EMM±SEM)	ITT							PP						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Fibre (g)	20.84 ± 1.06	22.70 ± 1.83	0.410	17.76 ± 0.73	19.34 ± 1.19	0.139	0.579	18.96 ± 2.36	22.10 ± 2.37	0.259	17.33 ± 2.05	20.04 ± 2.96	0.333	0.777
Saturated fat (g)	28.32 ± 1.22	23.85 ± 2.60	0.204	24.24 ± 2.72	22.79 ± 3.87	0.465	0.353	27.03 ± 2.54	20.27 ± 3.65	**0.048***	23.41 ± 2.42	20.98 ± 3.19	0.485	0.490
MUFA (g)	18.43 ± 1.44	17.40 ± 1.43	0.402	22.22 ± 2.08	21.52 ± 2.49	0.200	0.408	18.03 ± 2.12	16.53 ± 2.65	0.385	19.74 ± 2.37	18.75 ± 2.07	0.699	0.568
PUFA (g)	7.81 ± 1.08	7.04 ± 0.73	0.162	11.27 ± 0.71	10.42 ± 0.65	**0.024***	0.386	8.16 ± 1.43	7.26 ± 1.15	0.248	9.90 ± 1.74	8.83 ± 1.74	0.604	0.603
Water content (g)	2724.69 ± 145.57	2569.38 ± 277.30	0.522	2192.62 ± 93.77	2130.06 ± 180.36	0.800	0.837	2439.18 ± 270.94	2549.18 ± 315.93	0.745	2329.75 ± 259.76	2364.88 ± 410.06	0.927	0.585
Cholesterol (mg)	242.60 ± 43.61	222.95 ± 34.32	0.757	167.26 ± 17.72	200.70 ± 41.67	0.351	0.664	200.10 ± 38.64	208.52 ± 43.64	0.836	163.41 ± 23.89	229.87 ± 33.41	0.115	0.583

*Significant p values are shown in bold with an asterisk
[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex
[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Table 37 cont.

7.3.7. Micronutrient intakes

Table 38 shows that after adjusting for age, sex and baseline value, ITT analysis suggests that selenium intake was significantly increased in the EG group over the course of the intervention (p=0.040), with significantly heightened intakes of potassium, iron and calcium in the MD study group (p=0.002; 0.003; 0.004). Trends were shown for increased intakes of Vitamin D and lowered sodium consumption across both groups, with the EG study group showing non-significant trends for increased intakes of potassium, iron and calcium. There were no significant differences between study groups. PP analysis showed non-significant increases in selenium, potassium, iron and calcium intakes alongside decreases in sodium across both study groups, with increased vitamin D intake in the MD group and no change in the EG group. There were no significant differences between study groups. Unadjusted data is shown in Appendix G26.

Table 38: Estimated marginal means and standard errors of micronutrient intake from general linear model repeated measures by study g roup adjusted for age, sex and baseline value

Dietary component (EMM±SEM)	**ITT**							**PP**						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Vitamin D (ug)	1.97 ± 0.39	2.76 ± 0.41	0.110	2.00 ± 0.21	2.63 ± 0.10	0.120	0.843	1.76 ± 0.51	1.73 ± 0.49	0.958	2.67 ± 0.615	2.91 ± 0.539	0.695	0.275
Selenium (ug)	34.25 ± 5.04	47.13 ± 7.06	**0.040***	36.63 ± 2.41	40.62 ± 4.17	0.371	0.389	37.96 ± 5.42	47.93 ± 7.38	0.163	40.73 ± 4.03	47.83 ± 4.09	0.134	0.358
Potassium (mg)	2322.00 ± 156.28	2467.84 ± 104.21	0.434	2135.68 ± 36.02	2338.77 ± 33.03	**0.002***	0.821	2456.18 ± 180.24	2614.63 ± 216.06	0.619	2185.25 ± 238.55	2331.92 ± 191.22	0.434	0.394
Iron (mg)	7.65 ± 0.69	7.82 ± 0.77	0.729	7.59 ± 0.23	8.51 ± 0.26	**0.003***	0.124	8.64 ± 0.63	8.90 ± 0.66	0.750	7.60 ± 0.657	8.29 ± 0.483	0.351	0.406
Calcium (mg)	558.93 ± 50.79	595.18 ± 49.50	0.659	548.15 ± 21.74	606.48 ± 24.52	**0.004***	0.749	560.09 ± 49.45	661.81 ± 69.72	0.252	543.17 ± 40.36	560.91 ± 72.54	0.775	0.342
Sodium (mg)	2005.09 ± 99.94	1676.75 ± 98.19	0.071	2147.70 ± 211.96	1997.10 ± 260.76	0.087	0.212	2081.91 ± 161.07	1796.27 ± 137.33	0.110	2285.33 ± 230.38	1963.75 ± 236.96	0.273	0.854

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

7.3.8. Fasting days

Table 39 shows dietary intake on a fasting day (from three-day food diaries) of 23 participants completing the study. Average caloric intake on fasting days amongst male participants was 852.00kcal (± 178.21) and 607.31kcal (±47.37) in females. The MD group was shown to consume significantly more MUFA on fasting days than the EG (p=0.032). There were also trends for higher consumption of energy, fat, alcohol, sugars, saturated fat, PUFA, cholesterol, vitamin D and selenium in the MD group compared to the EG.

Table 39: Dietary intake on fasting days for study completers in each intervention group

Dietary component (mean ± SD)	All participants (n= 23)	EG (n= 11)	MD (n= 12)	P value
Energy (kcal)	681.78 ± 313.62	639.18 ± 255.48	720.83 ± 365.92	0.545
Energy (kj)	2859.34 ± 1308.70	2688.63 ± 1066.80	3015.83 ± 1528.05	0.561
Protein (g)	41.42 ± 21.53	44.38 ± 16.94	38.70 ± 25.47	0.540
Fat (g)	29.16 ± 21.28	21.49 ± 17.23	36.18 ± 22.87	0.099
Carbohydrate (g)	59.84 ± 29.54	66.61 ± 25.85	53.63 ± 32.41	0.303
Alcohol (g)	1.96 ± 7.06	0.00 ± 0.00	3.76 ± 9.61	0.209
Sugars (g)	28.30 ± 20.31	26.20 ± 15.37	30.23 ± 24.53	0.646
Fibre (g)	9.18 ± 5.27	9.78 ± 5.61	8.62 ± 5.14	0.610
Saturated fat (g)	8.98 ± 7.05	7.87 ± 7.92	10.01 ± 6.32	0.481
MUFA (g)	9.53 ± 9.97	4.97 ± 4.11	13.73 ± 11.98	**0.032***
PUFA (g)	5.21 ± 4.98	3.27 ± 3.01	6.98 ± 5.84	0.074
Water content (g)	2232.74 ± 1286.64	2171.91 ± 1194.34	2288.50 ± 1416.68	0.834
Cholesterol (mg)	122.59 ± 140.36	86.39 ± 118.37	155.73 ± 155.41	0.245
Vitamin D (ug)	2.18 ± 4.09	1.51 ± 2.02	2.79 ± 5.37	0.466
Selenium (ug)	21.15 ± 23.93	16.45 ± 17.70	25.45 ± 28.60	0.379
Potassium (mg)	1352.57 ± 678.43	1338.63 ± 654.76	1365.33 ± 728.30	0.927
Iron (mg)	4.02 ± 2.22	4.25 ± 2.29	3.80 ± 2.23	0.635

Calcium (mg)	326.67 ± 262.97	333.12 ± 316.47	320.75 ± 217.20	0.913
Sodium (mg)	1072.65 ± 826.31	1355.09 ± 1071.28	813.75 ± 411.53	0.119

*Significant p values are shown in bold with an asterisk

7.3.9. Physical activity

Table 40 shows analysis of three-day accelerometer data and IPAQ results, with results adjusted for age, sex and baseline value showing that there were non-significant trends for increased overall activity (measured by vector magnitude), step count, light activity, moderate activity and very vigorous activity alongside decreased sedentary time across both study groups, alongside increased vigorous activity in the MD group. There was a significant difference in MET-mins between baseline and post-intervention in participants in the MD group (PP p=0.049 and ITT p=0.023). There were no significant differences between study groups. Unadjusted results are shown in Appendix G27.

Table 40: Estimated marginal means and standard errors of accelerometer data from general linear model repeated measures by study group adjusted for age, sex and baseline value

	ITT							**PP**						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Vector magnitude	489123.93 ± 48278.18	514278.87 ± 53910.02	0.565	652636.29 ± 45013.48	660099.10 ± 46783.86	0.889	0.591	519536.77 ± 80250.64	590632.49 ± 75986.67	0.380	620778.42 ± 63635.47	634979.28 ± 65080.91	0.875	0.806
Steps	7456.15 ± 793.39	8106.57 ± 1087.20	0.344	9547.05 ± 752.94	10043.07 ± 810.19	0.516	0.884	8586.52 ± 1201.55	10130.55 ± 1558.68	0.215	9565.58 ± 1103.84	10448.14 ± 1152.78	0.486	0.943
Sedentary time (%)	64.67 ± 1.98	62.70 ± 1.96	0.303	61.07 ± 2.86	59.19 ± 2.91	0.362	0.809	64.48 ± 3.16	60.43 ± 2.31	0.242	64.84 ± 2.55	61.86 ± 2.78	0.385	0.328
Light activity (%)	27.71 ± 2.01	28.01 ± 1.69	0.878	27.99 ± 3.35	28.30 ± 3.30	0.831	0.968	26.81 ± 3.15	27.84 ± 2.15	0.781	23.88 ± 2.69	24.38 ± 2.34	0.835	0.164
Moderate activity (%)	4.56 ± 0.76	5.44 ± 0.97	0.281	5.87 ± 0.58	6.31 ± 0.76	0.527	0.914	5.49 ± 0.87	7.08 ± 1.22	0.277	6.13 ± 0.80	6.82 ± 1.11	0.551	0.788

Vigorous activity (%)	0.68 ± 0.30	0.59 ± 0.29	0.141	0.65 ± 0.20	0.88 ± 0.27	0.384	0.232	1.03 ± 0.53	0.86 ± 0.51	0.159	0.61 ± 0.12	0.98 ± 0.37	0.407	0.358
Very vigorous activity (%)	0.03 ± 0.03	0.04 ± 0.03	0.337	0.06 ± 0.03	0.13 ± 0.08	0.367	0.350	0.00 ± 0.00	0.01 ± 0.01	0.342	0.06 ± 0.05	0.18 ± 0.12	0.395	0.470
MET-mins/ week	3845.40 ± 947.55	3537.70 ± 564.47	0.732	2705.63 ± 402.45	3589.79 ± 533.42	**0.023 ***	0.533	4778.36 ± 1677.55	4323.00 ± 884.15	0.798	2963.00 ± 494.29	4102.42 ± 726.83	**0.049 ***	0.985

*Significant p values are shown in bold with an asterisk
[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex
[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

7.3.10. Physical capability

Table 41 shows that after adjusting for age, gender and baseline value there were no significant differences in grip strength between baseline and post-intervention, however there were trends for non-significant increases in lung function. There were no significant differences between study groups in any outcomes. Unadjusted results are displayed in Appendix G28.

Table 41: Estimated marginal means and standard errors of physical capability data from general linear model repeated measures by study group adjusted for age, sex and baseline value

	ITT							**PP**						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Dominant grip strength (kg)	25.74 ± 1.30	25.71 ± 1.64	0.972	29.21 ± 2.36	29.65 ± 2.32	0.779	0.185	25.16 ± 2.00	25.00 ± 2.73	0.894	30.32 ± 3.05	30.69 ± 2.84	0.895	0.168
Non-dominant grip strength (kg)	24.03 ± 1.48	25.42 ± 1.64	0.262	26.82 ± 2.00	26.58 ± 2.20	0.760	0.674	24.08 ± 2.28	26.21 ± 2.84	0.355	26.75 ± 2.00	27.09 ± 2.69	0.768	0.824
FEV1 (L)	2.73 ± 0.17	2.84 ± 0.16	0.195	3.05 ± 0.20	3.08 ± 0.18	0.648	0.320	2.71 ± 0.23	2.79 ± 0.24	0.489	2.91 ± 0.26	2.98 ± 0.27	0.364	0.602
FVC (L)	2.87 ± 0.19	3.02 ± 0.18	0.178	3.19 ± 0.21	3.28 ± 0.21	0.220	0.360	2.84 ± 0.25	3.01 ± 0.28	0.370	3.08 ± 0.29	3.24 ± 0.32	0.165	0.610

*Significant p values are shown in bold with an asterisk
[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex
[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

7.3.11. Anthropometry and body composition

Table 42 shows that after adjusting ITT data for age, gender and baseline value there was significant difference between baseline and post-intervention waist circumference for both study groups (EG p=0.006; MD p=0.044), alongside weight, BMI and hip circumference in the MD group (p=0.004, 0.011 and 0.019). The MD was shown to decrease body fat percentage significantly more than the EG (p=0.018). PP analysis showed that significant difference between baseline and post-intervention weight values were observed in both study groups (EG p=0.049; MD p=0.000), with significant differences seen in the MD group for body fat percentage (p=0.034) and waist circumference in the EG (p=0.030). No significant differences were noted between study groups. Mean weight loss for the EG was 2.91±3.51kg (ITT) and 3.62±4.39% (PP) of baseline weight compared to 2.23±3.74kg (ITT) and 2.73±4.11% (PP) of baseline weight in the MD group. No significant differences were observed between study groups in terms of weight loss in kg (p=0.833) or percentage weight loss (p=0.761). 44.5% of participants in the EG group lost at least 5% of their baseline body weight, compared to 25% in the MD, with no significant difference between groups (p=0.326). Unadjusted results are shown in Appendix H29.

Table 42: Estimated marginal means and standard errors of anthropometric data from general linear model repeated measures by study group adjusted for age, sex and baseline value

	ITT							PP						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Weight (kg)	79.03 ± 3.17	76.63 ± 2.79	0.141	82.41 ± 3.65	79.73 ± 3.96	**0.004***	0.801	82.72 ± 4.81	78.10 ± 5.84	**0.049***	79.63 ± 2.50	76.00 ± 2.50	**0.000***	0.449
BMI (kg/m^2)	28.37 ± 0.82	27.52 ± 0.72	0.148	28.26 ± 0.60	27.41 ± 0.73	**0.011***	0.709	29.66 ± 1.10	27.92 ± 1.50	0.071	27.94 ± 0.27	26.80 ± 0.15	0.067	0.285
Body fat (%)	35.30 ± 1.01	34.84 ± 0.71	0.423	34.08 ± 1.67	32.25 ± 2.05	0.088	**0.018***	35.70 ± 0.76	34.42 ± 0.83	0.077	32.91 ± 3.23	29.84 ± 3.06	**0.034***	0.080
Waist circumference (cm)	92.01 ± 2.14	88.85 ± 1.95	**0.006***	95.10 ± 2.40	91.20 ± 1.73	**0.044***	0.972	94.77 ± 4.05	89.54 ± 4.18	**0.030***	95.00 ± 4.48	89.82 ± 2.08	0.278	0.617
Hip circumference (cm)	106.61 ± 2.09	102.78 ± 3.24	0.142	107.72 ± 1.16	105.59 ± 1.27	**0.019***	0.154	106.25 ± 4.30	102.66 ± 5.53	0.162	106.80 ± 1.91	104.01 ± 1.56	0.080	0.239
Waist-to-hip ratio	0.89 ± 0.019	0.85 ± 0.017	0.240	0.88 ± 0.029	0.84 ± 0.018	0.289	0.687	0.89 ± 0.019	0.85 ± 0.017	0.240	0.88 ± 0.029	0.84 ± 0.804	0.289	0.687

*Significant p values are shown in bold with an asterisk
[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex
[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

7.3.12. Blood lipids and blood pressure

Table 43 shows that after adjusting for age, sex and baseline value significant results were shown in ITT analysis with regards to the reduction in SBP in both study groups (p=0.001 for both), alongside HDL in the EG (p=0.033). There were also trends for reduced DBP, TC, LDL and HDL in the EG group, and reduced HDL:TC in the MD. Neither analysis showed any significant difference between study groups. PP analysis showed significant reductions in SBP across groups (p=0.002 in the EG and 0.002 in the MD). There were trends for reduced DBP, LDL in the EG; TC, TG, HDL in both groups, and HDL:TC in the MD group. There was a significant difference between groups, with SBP reducing most in the EG (p=0.021).

At baseline, just 15% and 7.5% of all participants had a SBP or DBP reading classified as high (above 140mmHg or 90mmHg respectively). Post-intervention, 7.5% had a high SBP and 10% had a high DBP reading. At baseline 27.5%, 2.5% and 25% of all participants had high TC (above 5mmol/L), TG (above 2.3mmol/L) and LDL (above 3mmol/L) respectively, alongside 5% with low HDL levels (below 1mmol/L). After intervention, 25%, 0% and 25% of all participants had high levels of TC, TG and LDL, with 7.5% showing low HDL levels. Further sub-group analysis was not carried out due to these small percentages.

Table 43: Estimated marginal means and standard errors of blood lipids and blood pressure from general linear model repeated measures by study group

	ITT							PP						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
SBP (mmHg)	126.63±3.26	118.63±1.93	**0.001***	131.65±4.41	124.28±3.11	**0.001***	0.147	133.54±4.80	120.24±2.73	**0.002***	137.96±5.74	127.60±3.82	**0.002***	**0.021***
DBP (mmHg)	72.65±2.38	70.68±1.70	0.444	76.03±2.06	76.53±2.95	0.858	0.174	77.52±3.30	72.42±2.43	0.236	78.43±2.97	79.73±4.53	0.791	0.169
TC (mmol/L)	4.50±0.16	4.33±0.17	0.054	4.62±0.18	4.62±0.20	1.000	0.326	4.49±0.15	4.24±0.16	0.116	4.83±0.22	4.81±0.27	0.884	0.260
TG (mmol/L)	1.03±0.10	1.00±0.09	0.633	1.05±0.14	1.02±0.07	0.773	0.839	1.06±0.13	1.00±0.09	0.540	1.01±0.20	1.00±0.10	0.711	0.990
HDL (mmol/L)	1.54±0.07	1.46±0.08	**0.033***	1.35±0.06	1.38±0.06	0.293	0.056	1.51±0.10	1.41±0.10	0.066	1.42±0.08	1.44±0.09	0.701	0.074

LDL (mmol/L)	2.50±0.12	2.41±0.11	0.139	2.78±0.17	2.78±0.16	1.000	0.258	2.50±0.16	2.38±0.13	0.231	2.91±0.23	2.92±0.22	0.914	0.222
HDL:TC	3.03±0.13	3.05±0.12	0.748	3.53±0.21	3.41±0.15	0.316	0.853	3.15±0.23	3.15±0.20	1.000	3.49±0.26	3.43±0.21	0.683	0.865

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

7.3.13. Links between blood lipids and body composition

Partial correlation analysis of all randomised participants is displayed in Table 44 and suggests significant positive association between TC and TG (p=0.030); TC and HDL (p=0.000), TC and LDL (p=0.000); LDL and HDL:TC (p=0.001); alongside waist change and weight change (p=0.000), with anthropometric results taken from section 7.3.11. There was also significant negative association between HDL and HDL:TC (p=0.000).

Table 45 shows significant positive association between TC and HDL (p=0.034); TC and LDL (p=0.000); LDL and HDL:TC (p=0.005); waist change and hip change (p=0.004); alongside waist change and weight change (p=0.003). There was also significant negative association between HDL and HDL:TC (p=0.002); and TG and hip change (p=0.001).

Table 44: Partial correlation analysis of blood lipids and change in weight, waist and hip controlling for age and sex (ITT)

	TG (mmol/L)	**HDL (mmol/L)**	**LDL (mmol/L)**	**HDL:TC**	**Waist change (%)**	**Hip change (%)**	**Weight change (%)**
TC (mmol/L)	P=**0.030*** R=0.373	P=**0.000*** R=0.590	P=**0.000*** R=0.889	P=0.176 R=0.238	P=0.127 R=0.267	P=0.834 R=0.037	P=0.959 R=0.009
TG (mmol/L)		P=0.150 R=0.252	P=0.531 R=0.111	P=0.431 R=0.140	P=0.622 R=0.088	P=0.250 R=-0.203	P=0.592 R=-0.095
HDL (mmol/L)			P=0.247 R=0.204	P=**0.000*** R=-0.602	P=0.294 R=0.185	P=0.641 R=-0.083	P=0.801 R=-0.045
LDL (mmol/L)				P=**0.001*** R=0.558	P=0.250 R=0.223	P=0.440 R=0.137	P=0.740 R=0.059
HDL:TC					P=0.858 R=0.032	P=0.468 R=0.129	P 0.910 R=0.020

Waist change (%)						P=0.115 R=0.275	P=**0.000*** R=0.638
Hip change (%)							P=0.136 R=0.261

*Significant p values are shown in bold with an asterisk

Table 45: Partial correlation analysis of blood lipids and change in weight, waist and hip controlling for age and sex (PP)

	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)	HDL:TC	Waist change (%)	Hip change (%)	Weight change (%)
TC (mmol/L)	P=0.272 R=0.251	P=**0.034*** R=0.464	P=**0.000*** R=0.927	P=0.137 R=0.336	P=0.970 R=0.009	P=0.718 R=-0.84	P=0.701 R=-0.89
TG (mmol/L)		P=0.873 R=-0.037	P=0.596 R=0.123	P=0.180 R=0.304	P=0.121 R=-0.349	P=**0.001*** R=-0.683	P=0.296 R=-0.239
HDL (mmol/L)			P=0.551 R=0.138	P=**0.002*** R=-0.631	P=0.592 R=-0.124	P=0.384 R=-0.200	P=0.586 R=-0.126
LDL (mmol/L)				P=**0.005*** R=0.593	P=0.575 R=0.130	P=0.609 R=0.119	P=0.991 R=-0.003
HDL:TC					P=0.717 R=0.084	P=0.539 R=0.142	P=0.942 R=-0.017
Waist change (%)						P=**0.004*** R=0.595	P=**0.003*** R=0.621
Hip change (%)							P=0.061

							R=0.416

*Significant p values are shown in bold with an asterisk

7.4. Discussion

7.4.1. Recruitment and attrition rates

Levels of interest in this pilot study and subsequent recruitment were relatively high, potentially due to trial recruitment beginning in January when many were attempting to lose Christmas weight and begin the year with healthy habits. Steady recruitment suggests acceptability of this dietary intervention and demonstrates that overweight and obese participants are seeking novel methods of weight management outside of conventional CER. Importantly, this trial involving mainly female, young, Caucasian participants had relatively low levels of drop-outs amongst those beginning the intervention, with non-completers shown to be slightly younger and heavier than those completing the study per-protocol. Attrition rates in weight management interventions can vary greatly, with a 2011 systematic review showing that there is insufficient direct research into why many participants do not remain adherent to a weight loss plan. Thirteen of the 32 included studies in this work demonstrated a link between younger age and higher risk of attrition from a weight loss study, and concluding that age, gender, marital status, education, ethnicity and socioeconomic status were not consistently associated with withdrawal from weight-related studies (Moroshko *et al.*, 2011). A 2004 study involving adherence to a hypocaloric MD amongst 1018 overweight and obese Spanish volunteers looking to lose weight showed that a male participant was 2.4 times more likely to complete the trial than a female; possibility of completion increases by 1.6% for every year increasing in age; risk of attrition increases by 21% for every unit increase in BMI at baseline; and to have previously made a weight loss attempt decreased completion probability by 37% (Bautista-Castaño *et al.*, 2004). This final factor is significant in the present study as high proportions of participants reported a history of slimming endeavours which may have impacted the reported attrition rates. The main reason for enrolling in this study was to 'lose weight and become healthier', with a study of 1781 participants suggesting that attrition rates were higher among those reporting aesthetic goals compared to those hoping for health-related weight loss which may suggest that more attention could be paid to study participants' enrolment motivation in order to reduce drop-out numbers (Dalle Grave *et al.*, 2005).

Other than a few reports of fasting regimes being too difficult to follow after changes to lifestyle circumstances (for example a participant changing from working day shifts to night shifts), the majority of participants withdrawing from the present study gave reasons unrelated to the trial protocol such as family issues or work commitments preventing them from attending final testing visits; suggesting that the intervention in both study groups was considered acceptable. These results are similar to those of a 2006 study involving 940 obese participants enrolled on a weight loss trial employing a structured post-intervention interview to ascertain reasons for study withdrawal; which showed that more than half of attrition was due to practical difficulties such as family problems, issues at work, distance from the place of testing visits, and unrelated health problems (Grossi *et al.*, 2006). Authors of various studies suggest that future interventions to tackle obesity should pay heed to the highlighted factors in attrition, rather than further focus on intervention design (Grossi *et al.*, 2006, Bautista-Castaño *et al.*, 2004), with multiple studies involving two days per week of IF showing low attrition rates and high levels of adherence to protocol (Harvie *et al.*, 2013, Schubel *et al.*, 2018, Conley *et al.*, 2018, Carter *et al.*, 2019, Panizza *et al.*, 2019).

7.4.2. Acceptability and feasibility of study diets

Responses to online feedback questionnaires suggested that participants found both the EG and MD highly acceptable, with qualitative feedback showing that participants reported noticeable dietary changes alongside motivations around nutrition. In the EG group, the least acceptable guideline seemed to be that calling for consumption of two or more portions of fish per week; although efforts were made in this study to provide simple recipes enabling participants to cook fish easily with options to mask the sometimes unpopular flavour of oily fish, for example salmon cooked in a spicy tomato sauce. Aside from flavour, potential factors influencing fish intake may be price, availability, and cooking skills alongside environmental issues (Raatz *et al.*, 2013). In the MD study group, participants stated that they would be unlikely to adhere to guidelines around wine consumption. Lack of acceptance of recommendations to consume seven glasses of wine per week is potentially due to a predominance of 'binge drinking' culture in the UK, whereby larger quantities of alcohol are consumed in one sitting rather than small volumes each day as recommended in the MD pyramid, alongside recent government recommendations to reduce alcohol consumption. Similarly, British participants are likely not consume solely red wine as recommended as other alcoholic beverages such as beers and spirits are popular and do not have the proven health benefits of red wine (Hoffman, 2018).

High numbers of participants in this study reported acceptability of IF, with a minority highlighting issues around willpower and side effects such as cravings, however many planned to continue with somewhat modified versions of the study protocol, including slightly increased caloric intake and alternative days of fasting. This is similar to a 2019 study whereby none of the 84 participants followed up after 24 months of either IF or CER were still adhering to their allocated diet, however the majority reported following the principles of these diets or certain parts which suited their lifestyles (Carter *et al.*, 2019). Few studies report serious negative side-effects of IF, with a systematic review showing that in four of the eleven included studies less than 20% of participants undergoing IF reported minor side-effects such as headaches, bad temper and feeling cold (Cioffi *et al.*, 2018). Alongside providing information about how participants eat under 'real world' situations rather than under controlled laboratory conditions, the lack of restriction on how fasting days should be structured may have increased acceptability and feasibility, and therefore also completion rates of this fasting regime, with participants able to fit fasting meals around their lifestyles and choose to fast on days that suited them.

7.4.3. Acceptability of trial design

This trial design was rated highly, with no participants reporting withdrawal due to any study design-related issues. Participants utilised the information webpages, but involvement with social media was less enthusiastic with many participants reporting that they did not normally use social media. Low-contact, Internet-based dietary interventions have been shown to be acceptable, with a 2005 trial demonstrating that participants given access to a specially-designed MD information website were significantly more positive about the study materials received than participants allocated standard nutrition information leaflets, with participants rating the website more useful, encouraging and interesting than printed brochures (Papadaki and Scott, 2005). A small number of participants in this study reported that a mid-point check in would have increased motivation. Although a formal testing visit halfway through the intervention was not included in this trial design because of a focus on acceptability and feasibility, participants were invited to contact the researcher at any time to arrange phone calls or face-to-face meetings should they have encountered any problems or have questions, however this was not utilised by any participants. A 2009 study suggested that adherence to an IF regime did not differ between a phase of the trial where all study food was provided and a phase where foods were self-selected, prepared and eaten at home, with researchers suggesting that data gathered during this phase was more indicative of the efficacy and feasibility of fasting patterns in a free-living population (Varady *et al.*, 2009). There is scope to broaden this trial in future to investigate the impact and acceptability of other intervention types, potentially including multiple contacts with the researcher or group meetings, however the present study aimed to assess acceptability and feasibility during a low-contact intervention to investigate adherence under 'real world' settings. Overall participants reported that they got what they hoped for out of the trial; that the MD, EG and IF were acceptable; and that many planned to continue with a modified regime, thus suggesting feasibility.

7.4.4. Participants' dietary changes

Results of this low-contact, low-cost pilot study included significant increases in dietary adherence in both the MD and EG study groups, suggesting that Internet-based, cost-effective interventions may be valuable in the improvement of dietary patterns and therefore in the treatment and prevention of obesity. Findings are similar to the PREDIMED-Plus trial wherein participants receiving an intensive intervention based on a MD with physical activity recommendations demonstrated an increase in MD adherence score (measured using the PREDIMED 14-item screener (Martínez-González *et al.*, 2012)) of approximately two units compared to the control group receiving usual dietary recommendations after 12 months of intervention (Salas-Salvadó *et al.*, 2019). Papadaki and Scott (2005) showed that during a six-month MD intervention, participants with access to a specially-designed website containing frequently-updated recipes, quizzes and dietary information significantly increased intakes of vegetables, fruit, legumes and MUFA:saturated fat ratio compared to the control group who only increased legume consumption after receiving healthy eating information in the form of printed brochures.

The present study also demonstrated improvements in eating patterns across both study groups, with similar results to a 2019 study during which participants showed increased consumption of some key Mediterranean foods such as fish, wholegrains and nuts alongside a decreased intake of refined cereals, sweets, cakes and red meats after both six and twelve months of intervention (Salas-Salvadó *et al.*, 2019). Notably, post-intervention food diaries from the present study showed that participants did not meet the UK's recommended daily intake of 30g of fibre, although values were above the national average of 19g (NHS, 2015). Dietary fibre can play a significant role in reducing CVD risk (Threapleton *et al.*, 2013) and has a satiating effect which can reduce caloric intake, thus showing potential for reduction in obesity risk (Hervik and Svihus, 2019) so future studies should bear in mind that the reduction in carbohydrate intake noted in the present study could be linked to insufficient fibre consumption. This intervention showed reduction in total sugar consumption across both the EG and MD study groups – a positive result considering that results of the National Health and Nutrition Examination Survey (NHANES) show an exponential escalation in CVD risk with increasing intake of calories from sugars (Yang *et al.*, 2014). The decreased sugar intake reported in participants' post-intervention food diaries may be linked to greater adherence to dietary guideline around soft drinks, with studies showing that sugar-sweetened beverages are the most significant contributors to overall added sugar intake (Yang *et al.*, 2014). Significant reductions in saturated fat intake were observed in the EG but not the MD group, potentially because of the higher baseline intakes of EG participants as post-intervention saturated fat levels were similar between groups. High percentages of EG participants reported reducing intakes of processed meats, consuming only small amounts of fats and oils, alongside making a conscious choice to select unsaturated fat sources throughout the trial, but smaller numbers of those in the MD group reported post-intervention adherence to guidelines around red meat and butter. Reductions in both MUFA and PUFA intakes were observed in each study group, potentially because even though both diets included foods such as fish and nuts which are rich in these fatty acids, these guidelines were amongst those with smallest levels of reported adherence. A 2009 study of 17,197 participants in the SUN (Seguimiento Universidad de Navarra) study showed that individuals adhering closely to a MD reported lower intakes of total fat than those with the highest level of adherence to a more Western diet type defined as a higher intake of red or processed meats, precooked or fast foods, sweetened soft drinks, full-fat dairy products and potatoes (Serra-Majem *et al*., 2009). Because MUFA and PUFA have been shown to be important in protection against CVD via many mechanisms such as reducing blood pressure and inflammatory responses (Ander *et al.*, 2003), future studies should aim to increase intakes of these healthy fats while reducing consumption of saturated fat.

Investigation of micronutrient intakes was limited as analysis showed that underreporting in food diaries was likely, however there were trends in both study groups for increased consumption of micronutrients associated with reduced CVD risk, alongside a reduction in sodium intake which has been heavily implicated in CVD incidence via increased hypertension risk, for example the INTERMAP study involving 4680 participants showing that there is direct significant influence of dietary sodium (measured via analysis of 24-hour urinary sodium excretion) on blood pressure, without attenuation after adjusting results for other dietary factors (Stamler *et al.*, 2018). It has been shown that 75% of salt consumed is added during food manufacture rather than by the individual during preparation or consumption (PHE, 2016b), therefore the reduction in sodium consumption demonstrated in this study may be due to researchers stressing the importance of home-cooking rather than reliance on convenience foods. Because Vitamin D synthesis from sunlight is not possible for much of the year in the UK, sufficient consumption of Vitamin D-rich foods is important (Spiro and Buttriss, 2014). Increased intake of Vitamin D seen more prominently in the MD group may be due to an emphasis on consumption of three or more portions of fish or seafood per week; with heightened selenium, iron and potassium observed in both study groups potentially due to increased intakes of fruits and vegetables alongside low-fat dairy products and green leafy vegetables likely providing calcium.

No statistically significant differences were observed between study groups in results adjusted for age, sex and baseline amongst completers, suggesting that recommendations to increase EG and MD adherence are equal in impact on intakes of macro- and micronutrients.

7.4.5. Dietary intakes on fasting days

Caution is advised when interpreting fasting day food diaries as these were based on a single recorded day however results suggest that even when calories were restricted, mean intakes of protein almost reached the recommended amount for females but that consumption of carbohydrates (specifically fibre) and the studied micronutrients was low. This is not surprising considering the small caloric intakes on fasting days, however it is important that reduced macro- and micronutrient intakes on fasting days are counteracted by consumption of well-balanced, nutrient-rich foods on non-restricted days to avoid deficiencies (Panizza *et al.*, 2019).

Neither male nor female participants achieved the fasting day energy goals of 625kcal and 500kcal respectively, and when the historic under-reporting of dietary intake in food diaries by overweight and obese individuals is considered (Ravelli *et al.*, 2018) these values could be considerably higher. These results are similar to a recent trial of 54 overweight East Asian Americans following a fasting regime involving two consecutive days of 70% caloric restriction for 12 weeks in which average fasting day energy intake was 929kcal compared to the mean target of 692kcal (Panizza *et al.*, 2019). These results suggest that individuals are able to dramatically lower energy intakes however such low caloric recommendations are potentially infeasible for participants under real-world conditions.

The present study does not suggest hyperphagia on unrestricted days, with food diary analysis demonstrating a reduction in caloric intake between baseline and post-intervention unrestricted days. Studies have shown that individuals do not seem to compensate for reduced caloric intake on non-fasting days (Panizza *et al.*, 2019, Cioffi *et al.*, 2018), with Harvie *et al.* (2013) reporting reduced energy consumption on non-restricted days and hypothesising that IF may cause behavioural changes, such as becoming more aware of eating patterns and understanding appetite and hunger cues. This supports findings of the present study, wherein participants reported that portion sizes on unrestricted days were influenced by their experiences of consuming less food on fasting days.

7.4.6. Physical activity

The present study suggests no change in activity levels when measured objectively using accelerometers however significant increases in IPAQ scores (measured in MET/mins) were observed, with no difference between study groups with regards to any activity outcomes. Caution should be taken when interpreting IPAQ results, as this score was derived from self-reported data which could be flawed, and does not completely concur with the objective measurement of activity employed here in the use of accelerometers. A potential reason for the lack of change in physical activity measures could be that baseline sedentary time (7.68 hours) was lower than results found from a large, multi-country study concluding that the average sedentary time was 8.65 hours per day (Van Dyck *et al*., 2015) therefore participants may not have increased activity levels by a large amount. A systematic review of 40 papers indicated that of the three publications reporting physical activity, two showed no change in activity levels from baseline, and one demonstrated significant decreases in exercise levels when energy intake was severely restricted (Seimon *et al.*, 2015). Similarly, a 2019 study showed no change to time spent sedentary or doing moderate to vigorous physical activity measured using accelerometers during a six-month MD or low-fat intervention (Mayr *et al.*, 2019). A 2019 study comparing IF with CER showed that step counts increased above baseline levels in the CER group but fell below baseline in the IF study group, with total step count remaining similar between groups after 24 months of follow-up (Carter *et al.*, 2019). Participants in the PREDIMED-Plus trial adhering to a MD with reduced caloric intake alongside promotion of exercise demonstrated increased total leisure time physical activity, decreased television viewing time and reduced total sedentary time over the 12 month trial (Salas-Salvadó *et al.*, 2019). Increasing physical activity is not always a goal in dietary interventions, with many studies recording exercise levels only to investigate its role as a co-variable of other outcomes such as weight loss. The present study was presented to participants as a lifestyle intervention, with researchers promoting daily activity and participants encouraged to wear their pedometers and keep track of their step counts. The study website also contained information about exercise, such as links to local organisations' websites and tips on how to easily incorporate more physical activity into a working day. This could explain the increase MET-mins/week reported in both study groups, however it is possible that participants over-reported their activity levels and under-reported their sedentary time when completing the IPAQ (Lee *et al.*, 2011). It is therefore important to note that participants thought they were doing more physical activity than they were, potentially meaning that further education of the public about the amounts of exercise necessary for health is required.

7.4.7. Physical capability

Results of the present study suggested no difference in grip strength in either study group between baseline and post-intervention values, with trends for slightly increased lung function. Lack of discernible change may be due to the study length, with the eight week intervention potentially too short to highlight significant alterations in physical capability. Although participants in this study reported increasing the amount of physical activity conducted, objective measurements carried out using accelerometers showed no significant change to activity levels, which may be why no significant alterations to physical capability were observed. Recommendations for increasing physical activity in this pilot study focused mainly on cardiovascular exercise such as walking to increase step count, which may not have had much impact on grip strength, but could have instigated the trends for improved lung function. Participants' age and health status could also be a factor as this was a relatively young cohort without medical issues therefore there was potentially less scope for improvement over this short period than there may be in an older or less healthy population. A meta-analysis suggested that lower grip strength was associated with increased mortality risk, however upon stratification of data association was shown to be weaker in studies involving participants below 60 years of age. Authors also highlighted the paucity of studies investigating physical capability in younger populations, and stressed that mortality may be better predicted by investigating change in physical capability rather than absolute values at a single time point, meaning that longer-term studies taking multiple measurements are required (Cooper *et al.*, 2010). Although there are few studies into the lung function of lung-healthy individuals, a 2009 study suggested that weight loss and improvements to other body composition measurements can positively impact lung function measured via spirometry (Steele *et al*., 2009), and a 2017 trial of 341 healthy participants concluded that those partaking in more physical activity (measuring using accelerometers) had higher FEV1 and FVC results than inactive individuals, with authors concluding that physical activity protects against chronic diseases and inflammation (Luzak *et al*., 2017), which may help to explain the findings of the present study.

7.4.8. Anthropometry and body composition

Results of this pilot study suggested significant decreases in weight across both the EG and MD study groups, with significantly decreased body fat in the MD group and waist circumference in the EG, alongside trends for reduction in BMI, hip circumference and WHR in both groups and a higher percentage of participants in the EG losing 5% of their baseline body weight or more. No statistically significant differences were observed between groups in ITT analysis, suggesting that both the EG and MD may improve body composition and anthropometric markers when combined with IF. As shown in section 7.3.9, although MET-mins/week (based on self-reported data) increased in the MD group, physical activity did not change dramatically throughout the trial which suggests that changes in body composition were due to dietary alternations. Previous studies have confirmed similar effects, with participants in the PREDIMED-Plus trial demonstrating a 3.7% reduction (mean 3.2kg) in body weight after 12 months of intervention compared to baseline, alongside significant decreases in body fat (-1.9kg) (Salas-Salvadó *et al*., 2019). A 2019 study coupling the MD with two consecutive days per week of 70% caloric reduction showed that participants in the intervention group showed significant improvements in body weight, BMI, waist circumference, hip circumference and body fat percentage compared to those consuming a DASH diet without energy restricted days (Panizza *et al*., 2019). An Australian intervention involving two consecutive or non-consecutive (participants' choice) days of 500kcal for women and 600kcal for men with five days of habitual eating showed a mean reduction of 4.2kg in fat mass and 3.7kg overall weight loss after 12 months, with results comparable to a fasting regime of one week restricted calorie intake followed by one week of habitual diet (Headland *et al*., 2018). A meta-analysis of 40 studies concluded that IF was consistently associated with weight loss and reductions in BMI, waist circumference, hip circumference and fat mass; with multiple studies suggesting that IF and CER promote comparable weight loss (Seimon *et al.*, 2015). Although positive results have been observed in these studies, it is important to note that few long-term trials have been carried out. Because weight loss often plateaus after six months and weight regain is not uncommon (Headland *et al.*, 2016), future work should aim to focus on maintenance of these beneficial alterations to body composition such as weight loss by implementation of lifestyle changes rather than short-term 'diets'.

7.4.9. Blood lipids and blood pressure

This pilot study suggested that adherence to the EG or MD in conjunction with IF was associated with significant reductions in SBP and trends for decreased TC and TG in both study groups; DBP, HDL and LDL in the EG; and HDL:TC in the MD group. Anthropometric changes were also associated with alterations to blood lipids, with a higher percentage change from baseline hip circumference linked to significant reduction in TG levels and trends observed for reduction in TG with higher weight and waist circumference change. Results of the PREDIMED-Plus trial confirm these findings, with adherence to the MD alongside moderate weight loss associated with a reduction in blood pressure alongside improvements in TG, HDL and LDL levels (Salas-Salvadó *et al.*, 2019). A meta-analysis of 82 studies showed that 5-10% weight loss was associated with significant beneficial changes to cardiovascular biomarkers, with every kilogram of weight lost associated with a significant reduction in SBP and DBP of 0.611mmHg and 0.296mmHg respectively after 6-12 months of intervention. Changes to HDL and TG did not become significant until after approximately 12 months of dietary intervention. This suggests that the present pilot study may not have been long enough to elicit significant results, with authors of this meta-analysis stressing that longer-term weight maintenance is imperative in improving cardiovascular biomarkers (Zomer *et al.*, 2016). Similarly, small changes to the percentages of participants categorised as having high levels of TC, TG and LDL alongside low HDL was observed in the present study, with minor modifications potentially due to the relatively low blood lipid levels at baseline of this relatively young, healthy population meaning that little impact was made by this short-term study. A recent meta-analysis showed that there were few studies investigating the impact of weight loss on cardiovascular biomarkers in younger participants but that of those, weight loss was associated with significant decreases in SBP and DBP alongside trends for reductions in TC, LDL and HDL alongside increased TG levels. This is compared to results of studies investigating adults ages above 40 years, wherein significant reductions were observed in LDL and TG alongside SBP and DBP (Zomer *et al.*, 2016). Physical activity also impacts blood pressure and blood lipids (Fogelholm, 2010), however due to the small changes in physical activity levels observed in this pilot study (reported in section 7.3.9), it is unlikely that this caused the significant decrease in SBP or trends for decreased blood lipid levels.

It is thought that improvements to cardiovascular biomarkers associated with adherence to the MD are linked to increased consumption of unsaturated fats such as olive oil, with wholegrains and fish alongside reduced intakes of red meat, desserts and high-salt processed foods (Salas-Salvadó *et al.*, 2019). The Greek-EPIC prospective cohort study involved 23,349 apparently healthy participants suggested that the observed lower mortality rates associated with a MD was most likely caused by moderate (rather than minimal or excessive) ethanol consumption, low consumption of red meat, alongside high intakes of fruits, vegetables, nuts, olive oil and legumes (Trichopoulou *et al.*, 2009). Both intervention groups in this pilot study showed increased adherence to their respective healthy eating patterns, and improvements in dietary patterns for example increased vegetable intakes and reduced red meat consumption were observed in both the EG and MD groups which may explain the modest but favourable alterations to some cardiovascular biomarkers. Furthermore, IF has been shown to impact blood-borne biomarkers of CVD, with a 2018 study involving adherence to a ‘5:2’ fasting regime associated with advantageous alterations to blood pressure (mean of reduction in SBP of 1.9mmHg and DBP of 3.0mmHg after 12 months), HDL (mean increase of 0.13mmol/L), TC (mean reduction of 0.07mmol/L) and TG (mean reduction of 0.31mmol/L) (Sundfor *et al.*, 2018). Similarly, a 2011 study of 107 participants adhering to a fasting regime involving caloric reduction to 25% of requirements for two days per week over six months showed significant reductions in TC of 0.3mmol/L, TG of 0.2mmol/L, LDL of 0.3mmol/L, SBP of 3.7mmHg and DBP of 4.3mmol/L, with no change to HDL levels (Harvie *et al.*, 2011).

7.4.10. Strengths and limitations

7.4.10.1. Overall study design

Strengths of this study include the strict randomisation protocol and broad advertisement of the study, alongside careful analysis of online questionnaires and study feedback. This is also one of few studies assessing adherence to fasting regimes outside of research settings, evaluating a combination of the MD and IF, and highlighting the importance of acceptability and feasibility of dietary patterns rather than assessing only the clinical outcomes. It should also be acknowledged that this study has limitations. Firstly, this was a pilot study so involved a small sample size which was mainly female and from a University population in the North East of England, limiting generalisability to the whole population. Similarly, this study included only participants who were driven enough to answer adverts in order to take part in the trial, meaning they may be more motivated to lose weight or become healthier than the general population. Only overweight and obese participants were involved in this study, meaning that results are not transferrable to lean individuals whose aim may not be to lose weight but to become healthier in other ways. This was a relatively short-term trial meaning that conclusions concerning these dietary patterns may not be generalisable to longer-term use. Similarly, mid-intervention measurements were not carried out therefore conclusions could not be drawn concerning points in the intervention when the largest changes occurred, for example the point in the intervention when most or least weight loss happened, which may have been useful in the design of future longer-term interventions. A lack of mid-point measurements also meant that adherence to the study protocol was not checked at mid-point.

7.4.10.2. Diet, physical activity and physical capability

Strengths of this study include the use of a validated dietary adherence scoring system for use with the MD group, and the care taken when briefing participants about completion of food diaries and their subsequent analysis. Use of accelerometers for measurement of physical activity levels is thought to be the most accurate method (Hendelman *et al.*, 2000, Brage *et al.*, 2003), and the IPAQ is a validated way of collecting information about self-reported activity with standardised analysis methodology (Craig *et al.*, 2003). It should also be stressed that there are limitations to this study, such as the self-reported nature of the IPAQ meaning that results should be taken as an estimate with a systematic review of 23 studies showing that the IPAQ frequently over-estimates physical activity (Lee *et al.*, 2011). The lack of a validated questionnaire assessing adherence to the EG meant that in order to enable comparison between study groups and between pre- and post-intervention dietary habits, a non-validated online survey was created which was piloted but has not been employed in other studies. There are well-documented issues with self-reported food diaries such as the influence of social desirability, potential to forget items consumed and misreporting sometimes caused by difficulty in reporting portion sizes or cooking methods; problems which can be solved using thorough training of participants. The longer the period of time the food diary is kept for, the more information is available to researchers including micronutrients and foods eaten less frequently however compliance with longer diaries has been shown to be poor. Weighed food diaries provide further reliable data however these increase the burden on the participant and therefore have been associated with poor compliance (Ortega *et al.*, 2015). A further issue is that in this study a single fasting day food diary was completed, meaning that an accurate picture of fasting day food consumption may not have been gained. Food diaries are frequently marred by underreporting, particularly by overweight and obese participants, which therefore may not allow a true understanding of eating habits (Ravelli *et al.*, 2018). Future trials could collect further dietary information, potentially in the form of seven-day food diaries kept at multiple points in the trial involving both fasting and non-fasting days. Food diaries kept specifically the day after a restricted day would allow investigation into any 'carry-over' effect from fasted to non-restricted days. Similarly, further research could investigate the levels of activity conducted on fasting days to assess whether or not a smaller caloric intake impacts ability or motivation to exercise. Dietary adherence was not verified in the present study, with future work potentially utilising metabolomics analysis to corroborate that participants had consumed the reported foods. Strengths of this work include the strict adherence to protocol when taking body composition and physical capability measurements, use of the same calibrated equipment for all tests, and results comparable to other studies. Handheld dynamometers are cost-efficient and portable, making them a good choice in assessment of hand grip strength. However, there are inconsistencies in literature concerning the reliability of handheld dynamometry relating mainly to problems surrounding standardisation of use, for example in the way the dynamometer is held by the participant, which would decrease usefulness of this tool (Toonstra and Mattacola, 2013). For this reason, care was taken during this trial that the standard operating procedure was followed during each use of the dynamometer. To gain accurate FEV1 and FVC results from spirometry requires participants to make maximal effort which means that inaccurate measurements can be made if participants do not inhale fully, do not form a tight seal with their mouth around the tube, pause too long before exhaling, cough during exhalation, stop exhaling early, or 'ease off' before completion of the exhale (Cooper, 2005). For these reasons, care was taken to fully explain the method to participants, demonstrate where necessary and to repeat any measurements where technique was deemed incorrect. The use of only grip strength and lung function tests may not give a complete picture of physical capability. Further physical capability tests such as the sit-to-stand test or walking speed test were not employed during this trial due to time constraints and the lack of literature concerning their use in younger populations (Cooper *et al.*, 2010) however these may be useful in future studies of this nature.

7.4.10.3. Cardiovascular biomarkers

Significant strengths of this study include the strict protocol adherence when taking anthropometrical measures and during collection of blood samples via venepuncture alongside the calibre of equipment used to analyse blood samples and the results concurrent with other similar studies. It is important to note that there are also limitations associated with this pilot study, for example the length of intervention may have been too short to observe meaningful alterations to blood lipids and blood pressure. The changes observed may have been small because blood lipid levels were relatively low at baseline, with few participants' values classified as high, therefore it is unlikely that very significant impact would be observed as a result of this short intervention. Similarly, this study involved only relatively young, healthy participants who are more likely to have favourable blood lipid levels and blood pressure. Although this study aimed to exclude as few individuals as possible, results are not generalisable to those with a BMI above 40kg/m^2 or below 25kg/m^2, older adults or those with any health conditions such as CVD as these factors were exclusion criteria in this trial. As a bathroom-type scale was used, accurate body weight measurements to fractions of kilograms were not available; an issue which would have been negated by the use of a calibrated digital scale. Waist and hip circumference measurements were taken over light clothing to minimise any embarrassment which means results were slightly inaccurate, however measurements were taken in the same way at each testing visit and between participants meaning the data is consistent and reproducible. Furthermore, care should be taken when assessing WHR as theoretically an obese and healthy weight participant could have the same WHR which may not change during weight loss or gain (de Koning *et al.*, 2007). Further work should aim to include as wide a sample group as possible so that results are generalisable to the general public. This pilot study investigates well-established blood-borne cardiovascular biomarkers and measures of body composition, however there are also further factors which could be considered in future work, such as blood insulin and glucose levels which may be impactful when examining the impact of this intervention on people with type 2 diabetes, alongside less-studied predictors of CVD for example IL-6 and TNF-α and other anthropometrical measures such as skin-fold callipers.

7.5. Conclusions

In conclusion, this pilot study suggests that a low-contact, Internet-based intervention testing a combination of the MD or EG with IF is deemed acceptable and feasible by a young, mainly female convenience sample of overweight and obese adults in the North East of England. Both study groups demonstrated improvement to dietary habits, some increase in physical activity levels and little change to physical capability markers. This study also suggested that adherence to the EG or MD in conjunction with IF was associated with significantly reduced SBP alongside trends for favourable alterations to blood lipids in both study groups, with changes to a higher number of outcomes observed in the EG than MD. Similarly, both study groups were shown to be equally effective in improving body composition measures such as weight and BMI. Weight loss and reductions to waist and hip circumferences were also shown to be associated with beneficial changes to blood lipids. Although there are limitations to the generalisability of this pilot study, this work could form the basis for further work investigating the impact of Internet-based, low-cost interventions promoting novel dietary patterns on obesity and CVD risk alongside other significant health issues such as type 2 diabetes in a wider sample group representative of the general public including different groups such as the elderly, those with medical issues such as type 2 diabetes, or adults of a healthy weight to investigate potential benefits to lean individuals.

7.6. Points covered in Chapter 7

i) This intervention seems acceptable and feasible to this sample population, with few drop-outs and positive feedback from participants.

ii) Physical activity and physical capability were not significantly changed during the intervention. However positive changes were made to dietary intakes in both study groups. Few participants met the fasting day caloric targets, however there were beneficial alterations to body composition and biomarkers of cardiovascular disease.

8. General discussion

8.1. Thesis summary

This thesis follows a series of logical phases (Figure 1) informing chapters which generate and subsequently answer research questions (Table 46). As shown in Figure 1, the first phase of this thesis was an in-depth search of existing literature to identify gaps in knowledge and to learn from previous studies. Findings suggested that obesity remains a significant global problem, with models predicting that this will not improve in the future. Alongside the economic burden, this disease has substantial impact on an individual's health, with multiple studies associating obesity with premature mortality alongside many other comorbidities (covered in section 1.1). Previous literature highlighted relatively low success rates when utilising traditional methods of obesity management and a lack of knowledge concerning novel ways to reduce weight and improve health. Research also suggested that the MD and IF have potential as healthy eating options, with both shown to positively impact body composition and blood-borne biomarkers of CVD (detailed in sections 1.2 and 1.3) although little work sought to understand the acceptability and feasibility of these eating patterns in a free-living population, with most studies conducted under strict research conditions.

The next phase of this thesis involved running a systematic review and meta-analysis to better understand the impact of the MD when employed in non-Mediterranean countries, as detailed in Chapter 2. This involved the gathering and comparison of all relevant literature according to a pre-defined protocol which amounted to 27 studies suggesting that there is a growing interest in the MD as a healthy eating pattern outside of use as the traditional diet in Mediterranean countries. This meta-analysis demonstrated that dietary interventions involving adherence to a MD for at least 12 weeks was associated with non-significant beneficial alterations to multiple CVD risk factors such as reductions in TC, TG and SBP alongside advantageous changes to body composition for example reduced body weight.

Because the MD had been shown to have beneficial impact on health, it was then important to evaluate the acceptability of this dietary pattern to the general public and to understand how readily MD guidelines were followed, as shown in Chapter iv). Response levels to the online survey disseminated to a mainly University-based population were high suggesting that this method of data collection was feasible, and results showed that respondents generally had a low level of MD adherence, with those in the overweight or obese BMI categories less likely to report high levels of adherence than their healthy weight counterparts. Similarly, the MD was perceived as a palatable way of eating, however respondents in the overweight and obese BMI categories alongside those detailing higher numbers of PBHE were less likely to report an acceptance level above the median value.

The subsequent part of phase two involving conducting a systematic review and meta-analysis to better understand the impact of IF on health, as detailed in Chapter 4. The resulting nine studies suggested that research in this area was limited, however IF was tentatively linked to significant decreases in body composition markers such as BMI and body fat percentage alongside non-significant decreases in other outcomes such as body weight, LDL, and SBP.

The aforementioned work has shown that the target population to benefit from the use of the MD and IF would be those classified as overweight or obese. Phase three involved gathering information about the potential use of the studied eating patterns in clinical practice. Chapter 5 therefore involved the design and implementation of an online survey and systematic review to investigate the use of the MD and IF by HP – both with their patients and in their own lives. The sixteen studies included in this analysis suggested that there could be improvements in HP's eating habits, and that there is little research into their MD adherence and recommendation of this diet to patients. The accompanying online survey did not garner many responses however opinion of the MD was generally positive, and HP reported that although they would like to recommend this diet, they do not have sufficient time to properly explain the MD to their patients, with the majority reporting low levels of success in bettering patients' eating habits.

Phase four involved the distillation of all gathered knowledge into the design of a dietary intervention aiming to test the hypotheses generated in this thesis. This pilot study aimed to investigate how acceptable and feasible adherence to a lifestyle intervention involving consumption of the EG or MD combined with IF alongside increased physical activity was to the general public, with further research into the impact of this intervention on body composition, physical capability, physical activity and biomarkers of CVD. Novelty lay in the low-contact, Internet-based nature of the trial as, to the author's knowledge, no previous studies into the MD and IF have been conducted under 'free-living' conditions in the North East of England. This pilot study was well-received, with randomisation of the targeted number of 40 participants suggesting that the public are interested in novel dietary patterns. Responses to online surveys collecting feedback alongside satisfactory retention rates suggested high levels of acceptability and feasibility, with analysis of food diaries and dietary adherence questionnaires suggesting that participants increased levels of adherence to both the EG and MD alongside making beneficial changes to their dietary intakes. Food diary analysis demonstrated that the majority of participants did not meet calorie targets on fasting days, but that all significantly reduced energy intakes. Beneficial alterations to body composition were observed, with significant weight loss in each study group and no significant difference between the EG and MD in terms of weight loss, alongside significant reductions in body fat percentage in the MD and waist circumference in the EG. Little change was noted in physical capability measured as grip strength, with trends for increased lung function. Similarly, there were significant increases in self-reported physical activity but no change in activity when measured objectively using accelerometers. Analysis of blood samples suggested that this intervention was linked with significantly decreased SBP alongside trends for reductions in TC and TG across both study groups, with the EG group showing benefits in a larger number of blood-related outcomes than the MD. Overall this pilot study suggested that a novel lifestyle intervention involving the EG and MD in combination with IF was shown to be acceptable and feasible to this sample population, and demonstrated beneficial impact on body composition and biomarkers of CVD, with little change to physical capability and physical activity.

8.2. Strengths and limitations

The work in this thesis adds to current understanding in this area, and is novel in several ways. Strengths include the employment of rigorous methodology both in the systematic reviews and meta-analyses alongside the online surveys and pilot study. The design of this pilot study was informed by much previous literature such as RCTs utilising findings from other sources such as epidemiological studies, and results concur with multiple trials. This work starts to fill a gap in knowledge about the use of novel dietary patterns in the treatment of obesity investigated under 'free-living' conditions, with particular emphasis on how acceptable these patterns are to the public. Limitations include the relatively small numbers of studies included in systematic reviews and meta-analyses. The pilot nature of the lifestyle intervention means that future studies are required to test this dietary pattern on a wider population for example involving older adults or those with comorbidities to allow generalisability to the UK public. Similarly, this intervention tested only a fasting regime involving two non-consecutive days per week consuming 500kcal for women and 600kcal per day for men. There is therefore scope to trial alternative regimes, for example a higher caloric intake on each day or potentially alternate-day fasting. Future studies should also investigate further outcomes such as blood insulin and glucose levels, IL-6 and TNF-α.

Table 46: Research questions generated through each chapter and their subsequent answers

Chapter	Research questions	Answers arising from chapter
2: The efficacy and effectiveness of Mediterranean dietary interventions outside Mediterranean countries: a systematic review and meta-analysis	How acceptable is this dietary pattern to the non-Mediterranean general public?	The dietary pattern was shown to be acceptable, with high completion rates reported in many studies, interventions often well received and some participants reporting planning to continue eating a MD after the study.
	What impact does consumption of the MD have on cardiovascular biomarkers and body composition?	Included studies showed that consumption of a MD has beneficial effects on cardiovascular biomarkers such as total cholesterol levels and triglyceride levels and body composition measures such as waist circumference and BMI.
3: Acceptability of and current adherence to the Mediterranean diet in the North East of England	How adherent are the general public in England to the MD, how much do they know about this dietary pattern, and how acceptable do they find the dietary guidelines?	Mean MD adherence score out of a maximum of 14 points was 5.24 ± 2.09, showing that respondents had low levels of adherence to this pattern. 43.0% of respondents stated that they 'know a little bit about the MD' and only 10.5% selected the 'I fully understand the concept of the MD' option. Levels of MD acceptability were high overall with 90.9% stating they thought a guideline of consumption of more than three portions of vegetables per day was acceptable, but only 20.9% reporting that more than four tablespoons of olive oil per day was an acceptable guideline.
	Which methods do individuals utilise in weight loss attempts, how many attempts do they make, and how successful are they?	79.7% of respondents reported making an attempt to lose weight in the past. 28.9% of participants employed diet plans with group meetings, 30.8% used diet plans without group meetings, 48.5% involved exercise plans, 21.1% used meal replacements, 14.5% used medicinal aids, 24.5% fasted, and 0.2% underwent surgery. Overall, the 439 participants who stated they had tried to lose weight in the past made on average five attempts, two of which were deemed successful.

Chapter	Research questions	Answers arising from chapter
	What are the most commonly reported perceived barriers to healthy eating?	36.7% of respondents reported ‘lack of willpower’ as a barriers to their healthy eating, 33.2% reported ‘busy lifestyle’ and 31.8% ‘giving up foods that I like’. Least commonly reported barriers were ‘feeling conspicuous amongst others’ (4.5%), ‘I don’t want to change my eating habits’ (8.0%) and ‘limited cooking facilities’ (8.7%).
	Are there links between these variables?	Cluster analysis based on perceived barriers to healthy eating showed distinct clusters of participants, with those stating that a lack of willpower was not a barrier to their healthy eating shown to be oldest, leanest, reporting the highest MD adherence score, the lowest number of PBHE and the highest MD acceptability level. Pearson correlation analysis suggested that BMI was significantly negatively associated with MD adherence score; significantly positively associated with PBHE, and non-significantly positively associated with MD acceptability. MD adherence score was negatively associated with PBHE and positively associated with MD acceptability. PBHE were significantly negatively associated with MD acceptability.
4: The impact of intermittent fasting on body composition and cardiovascular biomarkers: a systematic review and meta-analysis	How does IF impact cardiovascular biomarkers?	Results suggest that IF is linked to non-significant decreases in total cholesterol, LDL, triglycerides, SBP, DBP, serum glucose and serum insulin levels, with non-significant increases in HDL.
	How does IF impact body composition?	Results suggest that IF is linked to non-significant decreases in body weight and waist circumference alongside statistically significant decreases in both BMI and body fat percentage.

Table 46 cont.

Chapter	Research questions	Answers arising from chapter
5. Healthcare professionals and the Mediterranean diet: a systematic review and online survey	Are IF and the MD employed in weight loss strategies by healthcare practitioners?	Results of this survey suggested that 46.7% of respondents utilised the EG, 44.4% used the MD and 6.7% used IF.
	How much literature is available about the diets of healthcare practitioners?	Ten studies were included in the section of this review concerning the eating habits of HP, with 45 complete survey responses.
	How acceptable is the MD to healthcare professionals and what are their opinions on its acceptability to patients?	One study reported on MD acceptability, with 46% of surveyed doctors answering that they believed implementation of the MD could have a beneficial impact on the eating habits and lifestyle of patients. Results of the online survey suggested that the MD is deemed acceptable, but HP think the MD is less acceptable to their patients than the public thought it was to themselves.
	How healthy are healthcare professionals' diets and what are the specific dietary challenges in this group compared to the general public?	This systematic review suggested that HP are not very adherent to the MD, with generally poor dietary habits. It is hypothesised that barriers to HP's healthy eating are often based around their jobs, for example working shifts or having poor food storage facilities alongside inadequate supply of healthy meals in staff canteens.

Table 46 cont.

Chapter	Research questions	Answers arising from chapter
6: Combining the Mediterranean diet and intermittent fasting to improve health of overweight and obese adults: pilot study protocol	How should the acceptability and feasibility of a combination of the MD and IF be investigated?	The acceptability and feasibility of these dietary patterns should be investigated by the running of a low-contact, Internet-based pilot RCT, specifically using the feedback given by participants alongside analysis of recruitment and retention rates and reasons given for withdrawal from the study.
	How should dietary changes associated with adherence to this intervention be measured?	Alterations to diet should be investigated by analysing three-day food diaries and assessing adherence to study diets using dietary adherence screeners.
	How should physical activity and physical capability be measured?	Physical activity should be assessed using accelerometers, and physical capability by measurement of grip strength and lung function.
	How should body composition be assessed?	Body composition should be assessed by measuring height, weight, waist and hip circumference alongside body fat percentage.
	How should blood-borne biomarkers of CVD be investigated?	Blood samples should be taken via venepuncture, prepared for analysis by centrifuging and freezing, and then analysed at a local hospital for total cholesterol, HDL, LDL and triglycerides.
7. A pilot study investigating the impact of the Mediterranean diet and intermittent fasting in a population of healthy,	What were the characteristics of the participants taking part in this trial?	Participants were mainly young, Caucasian and female, with many university students. Participants were healthy but overweight or obese.
	How acceptable and feasible is this dietary intervention?	Results of this chapter from participant feedback and analysis of recruitment and retention rates suggest that this intervention is acceptable to participants, and that participants are able to follow the protocol without much input from researchers.

overweight and obese adults		Positive feedback was obtained, for example that the dietary changes quickly became habit and drop-out rates were low, with no participants stating that their withdrawal was because of the study protocol.
	What dietary, physical activity, and physical capability changes were associated with this trial?	Results showed that dietary adherence was significantly improved in both study groups, with the EG and MD increasing consumption of healthy foods such as vegetables and reducing soft drink intakes. There were also improvements in macro- and micronutrient intakes, with no significant differences between study groups. Although there were significant increases in self-reported activity measured using the IPAQ, objectively measured physical activity did not change in either study group across the intervention. Results suggest that that there were no significant differences in grip strength between baseline and post-intervention, however there were trends for non-significant increases in lung function in both study groups, with no significant differences between study groups in any outcomes.
	What impact did this trial have on body composition and cardiovascular biomarkers?	Results showed significant reductions in body weight in both study groups, with significant differences seen in the MD group for body fat percentage and waist circumference in the EG. Mean weight loss for the EG was 3.62±4.39% of baseline weight compared to 2.73±4.11% in the MD group. 44.5% of participants in the EG group lost at least 5% of their baseline body weight, compared to 25% in the MD, with no significant difference between groups found for any studied outcomes. Results of this section suggest that there were trends for reduced TC, TG, HDL in both groups, alongside LDL in the EG and HDL:TC in the MD group. Results suggest significant reductions in SBP and trends for reduced DBP in both study groups, with greater increases in SBP shown in the EG.

	What changes could be made if this trial was carried out again and what future work is required?	Further studies could look to collect further participant feedback, potentially asking more detailed questions. Future trials should also attempt to include a sample more representative of the UK public, for example with higher numbers of men or more older adults than were included here.

Table 46 cont.

9. References

ADAB, P., PALLAN, M. & WHINCUP, P. H. 2018. Is BMI the best measure of obesity? *BMJ,* 360**,** k1274.

ALBERT, N. M., BUTLER, R. & SORRELL, J. 2014. Factors Related to Healthy Diet and Physical Activity in Hospital-Based Clinical Nurses. *Online J Issues Nurs,* 19**,** 5.

ALBERTI-FIDANZA, A., FIDANZA, F., CHIUCHIU, M. P., VERDUCCI, G. & FRUTTINI, D. 1999. Dietary studies on two rural Italian population groups of the Seven Countries Study. 3. Trend of food and nutrient intake from 1960 to 1991. *European Journal of Clinical Nutrition,* 53**,** 854-860.

ALTHUBAITI, A. 2016. Information bias in health research: definition, pitfalls, and adjustment methods. *Journal of Multidisciplinary Healthcare,* 9**,** 211-217.

AMBRING, A., JOHANSSON, M., AXELSEN, M., GAN, L. M., STRANDVIK, B. & FRIBERG, P. 2006. Mediterranean-inspired diet lowers the ratio of serum phospholipid n-6 to n-3 fatty acids, the number of leukocytes and platelets, and vascular endothelial growth factor in healthy subjects. *American Journal of Clinical Nutrition,* 83**,** 575-581.

ANDER, B. P., DUPASQUIER, C., PROCIUK, M. A. & PIERCE, G. N. 2003. Polyunsaturated fatty acids and their effects on cardiovascular disease. *Experimental and clinical cardiology,* 8**,** 164-172.

ARANDA, K. & MCGREEVY, D. 2014. Embodied empathy-in-action: overweight nurses' experiences of their interactions with overweight patients. *Nursing Inquiry,* 21**,** 30-38.

ARÓS, F. & ESTRUCH, R. 2013. Mediterranean Diet and Cardiovascular Prevention. *Revista Española de Cardiología (English Edition)***,** 771-774.

ASH, S., REEVES, M. M., YEO, S., MORRISON, G., CAREY, D. & CAPRA, S. 2003. Effect of intensive dietetic interventions on weight and glycaemic control in overweight men with Type II diabetes: a randomised trial. *International Journal of Obesity,* 27**,** 797-802.

AUNE, D., SEN, A., PRASAD, A., NORAT, T., JANSZKY, I., TONSTAD, S., ROMUNDSTAD, P. & VATTEN, L. J. 2016. BMI and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ,* 353**,** i2156.

BACH-FAIG, A., BERRY, E. M., LAIRON, D., REGUANT, J., TRICHOPOULOU, A., DERNINI, S., MEDINA, F. X., BATTINO, M., BELAHSEN, R., MIRANDA, G., SERRA-MAJEM, L. & MEDITERRANEAN DIET FDN EXPERT, G. 2011. Mediterranean diet pyramid today. Science and cultural updates. *Public Health Nutrition,* 14**,** 2274-2284.

BACH-FAIG, A., FUENTES-BOL, C., RAMOS, D., CARRASCO, J. L., ROMAN, B., BERTOMEU, I. F., CRISTIÀ, E., GELEVA, D. & SERRA-MAJEM, L. 2010. The Mediterranean diet in Spain: adherence trends during the past two decades using the Mediterranean Adequacy Index. *Public Health Nutrition,* 14**,** 622-628.

BAULCH, J., CHESTER, A. & BRENNAN, L. 2012. Treatment Alternatives for Overweight and Obesity: The Role of Online Interventions. *Behaviour Change,* 25**,** 1-14.

BAUTISTA-CASTAÑO, I., MOLINA-CABRILLANA, J., MONTOYA-ALONSO, J. A. & SERRA-MAJEM, L. 2004. Variables predictive of adherence to diet and physical activity recommendations in the treatment of obesity and overweight, in a group of Spanish subjects. *International Journal of Obesity,* 28**,** 697-705.

BELL, D. & ESSES, V. 2002. *Ambivalence and Response Amplification: A Motivational Perspective*.

BELZA, A., TOUBRO, S., STENDER, S. & ASTRUP, A. 2009. Effect of diet-induced energy deficit and body fat reduction on high-sensitive CRP and other inflammatory markers in obese subjects. *International Journal of Obesity* 33**,** 456-64.

BHATNAGAR, P., WICKRAMASINGHE, K., WILKINS, E. & TOWNSEND, N. 2016. Trends in the epidemiology of cardiovascular disease in the UK. *Heart,* 102**,** 1945-1952.

BHF. 2018. *Cardiovascular Disease Statistics 2018* [Online]. Available: https://www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2018 [Accessed 23rd July 2019].

BHUTANI, S., KLEMPEL, M. C., KROEGER, C. M., TREPANOWSKI, J. F. & VARADY, K. A. 2013. Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans. *Obesity,* 21**,** 1370-9.

BLACKBURN, H. & JACOBS, D., JR 2014. Commentary: Origins and evolution of body mass index (BMI): continuing saga. *International Journal of Epidemiology,* 43**,** 665-669.

BLAKE, H., MO, P. K., LEE, S. & BATT, M. E. 2012. Health in the NHS: lifestyle behaviours of hospital employees. *Perspectives in Public Health,* 132**,** 213-215.

BLAKE, H. & PATTERSON, J. 2015. Paediatric nurses' attitudes towards the promotion of healthy eating. *British Journal of Nursing,* 24**,** 108-12.

BONASSA, A. & CARPINELLI, A. 2018. Intermittent fasting for three months decreases pancreatic islet mass and increases insulin resistance in Wistar rats. University of São Paulo.

BORGAN, S., JASSIM, G., MARHOON, Z. & H IBRAHIM, M. 2015. The lifestyle habits and wellbeing of physicians in Bahrain: A cross-sectional study. *Public Health,* 15**,** 655.

BRAGE, S., WEDDERKOPP, N., FRANKS, P. W., ANDERSEN, L. B. & FROBERG, K. 2003. Reexamination of validity and reliability of the CSA monitor in walking and running. *Medicine and Science in Sports and Exercise,* 35**,** 1447-54.

BRAVATA, D. M., SMITH-SPANGLER, C., SUNDARAM, V., GIENGER, A. L., LIN, N., LEWIS, R., STAVE, C. D., OLKIN, I. & SIRARD, J. R. 2007. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA,* 298**,** 2296-304.

BUTLAND, B., JEBB, S., KOPELMAN, P., MCPHERSON, K., THOMAS, S., MARDELL, J. & PARRY, V. 2007. Foresight Tackling Obesities: Future Choices – Project Report. *In:* SCIENCE, G. O. F. (ed.) 2nd ed. UK.

CAREY, I. M., COOK, D. G. & STRACHAN, D. P. 1999. The effects of adiposity and weight change on forced expiratory volume decline in a longitudinal study of adults. *International Journal of Obesity,* 23**,** 979-985.

CARTER, S., CLIFTON, P. M. & KEOGH, J. B. 2019. The effect of intermittent compared with continuous energy restriction on glycaemic control in patients with type 2 diabetes: 24-month follow-up of a randomised noninferiority trial. *Diabetes Research and Clinical Practice,* 151**,** 11-19.

CELIS-MORALES, C. A., WELSH, P., LYALL, D. M., STEELL, L., PETERMANN, F., ANDERSON, J., ILIODROMITI, S., SILLARS, A., GRAHAM, N., MACKAY, D. F., PELL, J. P., GILL, J. M. R., SATTAR, N. & GRAY, S. R. 2018. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. *BMJ,* 361**,** k1651.

CHENG, H. L. 2016. *A simple, easy-to-use spreadsheet for automatic scoring of the International Physical Activity Questionnaire (IPAQ) Short Form* [Online]. ResearchGate. [Accessed 9th July 2019].

CHUDYK, A. M., MCALLISTER, M. M., CHEUNG, H. K., MCKAY, H. A. & ASHE, M. C. 2017. Are we missing the sitting? Agreement between accelerometer non-wear time validation methods used with older adults' data. *Cogent Medicine,* 4**,** 1313505.

CIOFFI, I., EVANGELISTA, A., PONZO, V., CICCONE, G., SOLDATI, L., SANTARPIA, L., CONTALDO, F., PASANISI, F., GHIGO, E. & BO, S. 2018. Intermittent versus continuous energy restriction on weight loss and cardiometabolic outcomes: a systematic review and meta-analysis of randomized controlled trials. *Journal of Translational Medicine,* 16**,** 15.

CLAYTON, D. J., BURRELL, K., MYNOTT, G., CREESE, M., SKIDMORE, N., STENSEL, D. J. & JAMES, L. J. 2016. Effect of 24-h severe energy restriction on appetite regulation and ad libitum energy intake in lean men and women. *American Journal of Clinical Nutrition,* 104**,** 1545-1553.

CONLEY, M., LE FEVRE, L., HAYWOOD, C. & PROIETTO, J. 2018. Is two days of intermittent energy restriction per week a feasible weight loss approach in obese males? A randomised pilot study. *Nutrition & Dietetics,* 75**,** 65-72.

COOPER, B. G. 2005. Limitations to spirometry being performed in 'the office'. *Chronic Respiratory Disease,* 2**,** 113-115.

COOPER, R., KUH, D., HARDY, R. & MORTALITY REVIEW GROUP 2010. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. *BMJ,* 341**,** c4467.

CORK, S. 2018. *Expert reaction to unpublished poster presentation on diabetes and fasting as presented at the European Society of Endocrinology annual meeting, ECE 2018* [Online]. Science Media Centre. Available: http://www.sciencemediacentre.org/expert-reaction-to-unpublished-poster-presentation-on-diabetes-and-fasting-as-presented-at-the-european-society-of-endocrinology-annual-meeting-ece-2018/ [Accessed 12th November 2018 2018].

COUTO, E., BOFFETTA, P., LAGIOU, P., FERRARI, P., BUCKLAND, G., OVERVAD, K., DAHM, C. C., TJONNELAND, A., OLSEN, A., CLAVEL-CHAPELON, F., BOUTRON-RUAULT, M. C., COTTET, V., TRICHOPOULOS, D., NASKA, A., BENETOU, V., KAAKS, R., ROHRMANN, S., BOEING, H., VON RUESTEN, A., PANICO, S., PALA, V., VINEIS, P., PALLI, D., TUMINO, R., MAY, A., PEETERS, P. H., BUENO-DE-MESQUITA, H. B., BUCHNER, F. L., LUND, E., SKEIE, G., ENGESET, D., GONZALEZ, C. A., NAVARRO, C., RODRIGUEZ, L., SANCHEZ, M. J., AMIANO, P., BARRICARTE, A., HALLMANS, G., JOHANSSON, I., MANJER, J., WIRFART, E., ALLEN, N. E., CROWE, F., KHAW, K. T., WAREHAM, N., MOSKAL, A., SLIMANI, N., JENAB, M., ROMAGUERA, D., MOUW, T., NORAT, T., RIBOLI, E. & TRICHOPOULOU, A. 2011. Mediterranean dietary pattern and cancer risk in the EPIC cohort. *British Journal of Cancer,* 104**,** 1493-1499.

CRAIG, C. L., MARSHALL, A. L., SJOSTROM, M., BAUMAN, A. E., BOOTH, M. L., AINSWORTH, B. E., PRATT, M., EKELUND, U., YNGVE, A., SALLIS, J. F. & OJA, P. 2003. International physical activity questionnaire: 12-country reliability and validity. *Medicine and Science in Sports and Exercise,* 35**,** 1381-95.

CUMMINGS, J. 2016. Leading Change, Adding Value: A Framework for Nursing, Midwifery, and Care Staff. *In:* NHS (ed.). London, UK.

DA SILVA, R., BACH-FAIG, A., QUINTANA, B. R., BUCKLAND, G., DE ALMEIDA, M. D. V. & SERRA-MAJEM, L. 2009. Worldwide variation of adherence to the Mediterranean diet, in 1961-1965 and 2000-2003. *Public Health Nutrition,* 12**,** 1676-1684.

DALLE GRAVE, R., CALUGI, S., MOLINARI, E., PETRONI, M. L., BONDI, M., COMPARE, A., ., MARCHESINI, G. & GROUP, Q. S. 2005. Weight Loss Expectations in Obese Patients and Treatment Attrition: An Observational Multicenter Study. *Obesity Research,* 13**,** 1961-1969.

DANSINGER, M. L., GLEASON, J., GRIFFITH, J. L., SELKER, H. P. & SCHAEFER, E. J. 2005. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: A randomized trial. *JAMA,* 293**,** 43-53.

DAVIS, C., BRYAN, J., HODGSON, J. & MURPHY, K. 2015. Definition of the Mediterranean Diet: A Literature Review. *Nutrients,* 7**,** 9139-9153.

DAVIS, C. S., CLARKE, R. E., COULTER, S. N., ROUNSEFELL, K. N., WALKER, R. E., RAUCH, C. E., HUGGINS, C. E. & RYAN, L. 2016. Intermittent energy restriction and weight loss: a systematic review. *European Journal of Clinical Nutrition,* 70**,** 292-299.

DE KONING, L., MERCHANT, A. T., POGUE, J. & ANAND, S. S. 2007. Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *European Heart Journal,* 28**,** 850-856.

DE LORGERIL, M., SALEN, P., MARTIN, J. L., MONJAUD, I., DELAYE, J. & MAMELLE, N. 1999. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction - Final report of the Lyon Diet Heart Study. *Circulation,* 99**,** 779-785.

DELIMARIS, I. 2013. Adverse Effects Associated with Protein Intake above the Recommended Dietary Allowance for Adults. *ISRN nutrition,* 2013**,** 126929-126929.

DEN HOED, M., MARIMAN, E. C. M., BOUWMAN, F. G., WESTERTERP, K. R. & WESTERTERP-PLANTENGA, M. S. 2009. Postprandial responses in hunger and satiety are associated with the rs9939609 single nucleotide polymorphism in FTO. *The American Journal of Clinical Nutrition,* 90**,** 1426-1432.

DEVAUX, M. & SASSI, F. 2011. Social inequalities in obesity and overweight in 11 OECD countries. *European Journal of Public Health,* 23**,** 464-469.

DJURIC, Z., RUFFIN, M. T., RAPAI, M. E., CORNELLIER, M. L., REN, J. W., FERRERI, T. G., ASKEW, L. M., SEN, A., BRENNER, D. E. & TURGEON, D. K. 2012. A Mediterranean dietary intervention in persons at high risk of colon cancer: Recruitment and retention to an intensive study requiring biopsies. *Contemporary Clinical Trials,* 33**,** 881-888.

DOBBS, R., SAWERS, C., THOMPSON, F., MANYIKA, J., WOETZEL, J. R., CHILD, P., MCKENNA, S. & SPATHAROU, A. 2014. Overcoming Obesity: An Initial Economic Analysis. Jakarta: Indonesia: McKinsey Global Institute.

DONNELL, C. J. & ELOSUA, R. 2008. Cardiovascular Risk Factors. Insights From Framingham Heart Study. *Revista Española de Cardiología (English Edition),* 61**,** 299-310.

ERDRICH, S., BISHOP, K. S., KARUNASINGHE, N., HAN, D. Y. & FERGUSON, L. R. 2015. A pilot study to investigate if New Zealand men with prostate cancer benefit from a Mediterranean-style diet. *PeerJ,* 2015**,** Epub ahead of print.

ESTRUCH, R., ROS, E., SALAS-SALVADÓ, J., COVAS, M., CORELLA, D., ARÓS, F., GÓMEZ-GRACIA, E., RUIZ-GUTIÉRREZ, V., FIOL, M., LAPETRA, J., LAMUELA-RAVENTOS, R. M., SERRA-MAJEM, L., PINTÓ, X., BASORA, J., MUÑOZ, M. A., SORLÍ, J. V., MARTÍNEZ, J. A., FITÓ, M., GEA, A., HERNÁN, M. A. & MARTÍNEZ-GONZÁLEZ, M. A. 2018. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *New England Journal of Medicine,* 378**,** e34.

ESTRUCH, R., ROS, E., SALAS-SALVADO, J., COVAS, M. I., CORELLA, D., AROS, F., GOMEZ-GRACIA, E., RUIZ-GUTIERREZ, V., FIOL, M., LAPETRA, J., LAMUELA-RAVENTOS, R. M., SERRA-MAJEM, L., PINTO, X., BASORA, J., MUNOZ, M. A., SORLI, J. V., MARTINEZ, J. A., MARTINEZ-GONZALEZ, M. A. & INVESTIGATORS, P. S. 2013. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *New England Journal of Medicine,* 368**,** 1279-1290.

EYSENBACH, G. 2004. Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *Journal of Medical Internet Research,* 6**,** e34.

FAUGIER, J., LANCASTER, J., PICKLES, D. & DOBSON, K. 2001. Barriers to healthy eating in the nursing profession: Part 2. *Nursing Standards,* 15**,** 33-5.

FERENCE, B. A., GINSBERG, H. N., GRAHAM, I., RAY, K. K., PACKARD, C. J., BRUCKERT, E., HEGELE, R. A., KRAUSS, R. M., RAAL, F. J., SCHUNKERT, H., WATTS, G. F., BORÉN, J., FAZIO, S., HORTON, J. D., MASANA, L., NICHOLLS, S. J., NORDESTGAARD, B. G., VAN DE SLUIS, B., TASKINEN, M. R., TOKGÖZOĞLU, L., LANDMESSER, U., LAUFS, U., WIKLUND, O., STOCK, J. K., CHAPMAN, M. J. & CATAPANO, A. L. 2017. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *European Heart Journal,* 38**,** 2459-2472.

FICCA, G., AXELSSON, J., MOLLICONE, D. J., MUTO, V. & VITIELLO, M. V. 2010. Naps, cognition and performance. *Sleep Medicine Reviews,* 14**,** 249-258.

FOGELHOLM, M. 2010. Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. *Obesity Reviews,* 11**,** 202-221.

FRANK, E., SEGURA, C., SHEN, H. & OBERG, E. 2010. Predictors of Canadian physicians' prevention counseling practices. *Canadian Journal of Public Health,* 101**,** 390-5.

FRANK, E., WRIGHT, E. H., SERDULA, M. K., ELON, L. K. & BALDWIN, G. 2002. Personal and professional nutrition-related practices of US female physicians. *American Journal of Clinical Nutrition,* 75**,** 326-32.

GANESAN, K., HABBOUSH, Y. & SULTAN, S. 2018. Intermittent Fasting: The Choice for a Healthier Lifestyle. *Cureus,* 10**,** e2947-e2947.

GARDENER, H., WRIGHT, C. B., GU, Y. A., DEMMER, R. T., BODEN-ALBALA, B., ELKIND, M. S. V., SACCO, R. L. & SCARMEAS, N. 2011. Mediterranean-style diet and risk of ischemic stroke, myocardial infarction, and vascular death: the Northern Manhattan Study. *American Journal of Clinical Nutrition,* 94**,** 1458-1464.

GAZ, D. V., RIECK, T. M., PETERSON, N. W., FERGUSON, J. A., SCHROEDER, D. R., DUNFEE, H. A., HENDERZAHS-MASON, J. M. & HAGEN, P. T. 2018. Determining the Validity and Accuracy of Multiple Activity-Tracking Devices in Controlled and Free-Walking Conditions. *American Journal of Health Promotion,* 32**,** 1671-1678.

GORDON, D. J., PROBSTFIELD, J. L., GARRISON, R. J., NEATON, J. D., CASTELLI, W. P., KNOKE, J. D., JACOBS, D. R., JR., BANGDIWALA, S. & TYROLER, H. A. 1989. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation,* 79**,** 8-15.

GOULET, J., LAMARCHE, B., NADEAU, G. & LEMIEUX, S. 2003. Effect of a nutritional intervention promoting the Mediterranean food pattern on plasma lipids, lipoproteins and body weight in healthy French-Canadian women. *Atherosclerosis,* 170**,** 115-124.

GROSSI, E., DALLE GRAVE, R., MANNUCCI, E., MOLINARI, E., COMPARE, A., CUZZOLARO, M. & MARCHESINI, G. 2006. Complexity of attrition in the treatment of obesity: clues from a structured telephone interview. *International Journal of Obesity,* 30**,** 1132-1137.

GROSSO, G., MARVENTANO, S., YANG, J., MICEK, A., PAJAK, A., SCALFI, L., GALVANO, F. & KALES, S. N. 2017. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: Are individual components equal? *Critical Reviews in Food Science and Nutrition,* 57**,** 3218-3232.

GUASCH-FERRE, M., SALAS-SALVADO, J., ROS, E., ESTRUCH, R., CORELLA, D., FITO, M. & MARTINEZ-GONZALEZ, M. A. 2017. The PREDIMED trial, Mediterranean diet and health outcomes: How strong is the evidence? *Nutrition and Metabolism in Cardiovascular Disease,* 27**,** 624-632.

GUESS, N. 2018. *Expert reaction to unpublished poster presentation on diabetes and fasting as presented at the European Society of Endocrinology annual meeting, ECE 2018* [Online]. Science Media Centre. Available: http://www.sciencemediacentre.org/expert-reaction-to-unpublished-poster-presentation-on-diabetes-and-fasting-as-presented-at-the-european-society-of-endocrinology-annual-meeting-ece-2018/ [Accessed 12th November 2018].

HAKIM, S. A., ELDIN, W. S. & MOHSEN, A. 2016. Dietary behavior and its relation with lifestyle, rotating work shifts and job satisfaction among nurses of Ain Shams university hospitals. *The Egyptian Journal of Community Medicine,* 34**,** 75-86.

HARRIS, J. A. & BENEDICT, F. G. 1918. A Biometric Study of Human Basal Metabolism. *Proceedings of the National Academy of Sciences of the United States of America,* 4**,** 370-373.

HARRIS, L., MCGARTY, A., HUTCHISON, L., ELLS, L. & HANKEY, C. 2018. Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis. *Obesity Reviews,* 19**,** 1-13.

HARVEY, J., HOWELL, A., MORRIS, J. & HARVIE, M. 2018. Intermittent energy restriction for weight loss: Spontaneous reduction of energy intake on unrestricted days. *Food Science & Nutrition,* 6**,** 674-680.

HARVIE, M., WRIGHT, C., PEGINGTON, M., MCMULLAN, D., MITCHELL, E., MARTIN, B., CUTLER, R. G., EVANS, G., WHITESIDE, S., MAUDSLEY, S., CAMANDOLA, S., WANG, R., CARLSON, O. D., EGAN, J. M., MATTSON, M. P. & HOWELL, A. 2013. The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women. *British Journal of Nutrition,* 110**,** 1534-47.

HARVIE, M. N., PEGINGTON, M., MATTSON, M. P., FRYSTYK, J., DILLON, B., EVANS, G., CUZICK, J., JEBB, S. A., MARTIN, B., CUTLER, R. G., SON, T. G., MAUDSLEY, S., CARLSON, O. D., EGAN, J. M., FLYVBJERG, A. & HOWELL, A. 2011. The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: a randomized trial in young overweight women. *International Journal of Obesity,* 35**,** 714-727.

HAYWOOD, C. J., PRENDERGAST, L. A., LIM, R., LAPPAS, M., LIM, W. K. & PROIETTO, J. 2019. Obesity in older adults: Effect of degree of weight loss on cardiovascular markers and medications. *Clinical Obesity,* 9**,** e12316.

HEADLAND, M., CLIFTON, P. M., CARTER, S. & KEOGH, J. B. 2016. Weight-Loss Outcomes: A Systematic Review and Meta-Analysis of Intermittent Energy Restriction Trials Lasting a Minimum of 6 Months. *Nutrients,* 8.

HEADLAND, M. L., CLIFTON, P. M. & KEOGH, J. B. 2018. Effect of intermittent compared to continuous energy restriction on weight loss and weight maintenance after 12 months in healthy overweight or obese adults. *International Journal of Obesity*.

HENDELMAN, D., MILLER, K., BAGGETT, C., DEBOLD, E. & FREEDSON, P. 2000. Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Medicine and Science in Sports and Exercise,* 32**,** S442-9.

HERVIK, A. K. & SVIHUS, B. 2019. The Role of Fiber in Energy Balance. *Journal of Nutrition and Metabolism,* 2019**,** 11.

HICKS, M., MCDERMOTT, L. L., ROUHANA, N., SCHMIDT, M., SEYMOUR, M. W. & SULLIVAN, T. 2008. Nurses' body size and public confidence in ability to provide health education. *Journal of Nursing Scholarship,* 40**,** 349-54.

HIGGINS, J. P. T. & GREEN, S. 2008. Cochrane Handbook for Systematic Reviews of Interventions Chichester: Wiley-Blackwell.

HIGGINS, J. P. T., GREEN, S. & COCHRANE COLLABORATION. 2008. *Cochrane handbook for systematic reviews of interventions,* Chichester, West Sussex ; Hoboken NJ, Wiley-Blackwell.

HODGE, A. M., ENGLISH, D. R., ITSIOPOULOS, C., O'DEA, K. & GILES, G. G. 2011. Does a Mediterranean diet reduce the mortality risk associated with diabetes: Evidence from the Melbourne Collaborative Cohort Study. *Nutrition Metabolism and Cardiovascular Diseases,* 21**,** 733-739.

HOEVENAAR-BLOM, M. P., NOOYENS, A. C. J., KROMHOUT, D., SPIJKERMAN, A. M. W., BEULENS, J. W. J., VAN DER SCHOUW, Y. T., BUENO-DE-MESQUITA, B. & VERSCHUREN, W. M. M. 2012. Mediterranean Style Diet and 12-Year Incidence of Cardiovascular Diseases: The EPIC-NL Cohort Study. *Plos One,* 7.

HOFFMAN, R. M. 2018. The benefits of moderate wine consumption. *BMJ,* 361**,** 1630.

HOWE, M., LEIDEL, A., KRISHNAN, S. M., WEBER, A., RUBENFIRE, M. & JACKSON, E. A. 2010. Patient-related diet and exercise counseling: do providers' own lifestyle habits matter? *Preventive Cardiology,* 13**,** 180-5.

HOYO, C., COOK, M. B., KAMANGAR, F., FREEDMAN, N. D., WHITEMAN, D. C., BERNSTEIN, L., BROWN, L. M., RISCH, H. A., YE, W. M., SHARP, L., WU, A. H., WARD, M. H., CASSON, A. G., MURRAY, L. J., CORLEY, D. A., NYREN, O., PANDEYA, N., VAUGHAN, T. L., CHOW, W. H. & GAMMON, M. D. 2012. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. *International Journal of Epidemiology,* 41**,** 1706-1718.

JAGANNATHAN, R., PATEL, S. A., ALI, M. K. & NARAYAN, K. M. V. 2019. Global Updates on Cardiovascular Disease Mortality Trends and Attribution of Traditional Risk Factors. *Current Diabetes Reports,* 19**,** 12.

JEBB, S. A. 2016. *Expert reaction to study looking at Mediterranean diet, levels of fat and body weight* [Online]. Science Media Centre. Available: http://www.sciencemediacentre.org/expert-reaction-to-study-looking-at-mediterranean-diet-levels-of-fat-and-body-weight/ [Accessed 12th November 2018 2018].

JOHANSSON, L., SOLVOLL, K., BJORNEBOE, G. E. & DREVON, C. A. 1998. Under- and overreporting of energy intake related to weight status and lifestyle in a nationwide sample. *American Journal of Clinical Nutrition,* 68**,** 266-74.

JOHNSTONE, A. M., FABER, P., GIBNEY, E. R., ELIA, M., HORGAN, G., GOLDEN, B. E. & STUBBS, R. J. 2002. Effect of an acute fast on energy compensation and feeding behaviour in lean men and women. *International Journal of Obesity and Related Metabolic Disorders,* 26**,** 1623-8.

KEARNEY, J. M. & MCELHONE, S. 1999. Perceived barriers in trying to eat healthier--results of a pan-EU consumer attitudinal survey. *British Journal of Nutrition,* 81 Suppl 2**,** S133-7.

KELLY, M., WILLS, J. & SYKES, S. 2017. Do nurses' personal health behaviours impact on their health promotion practice? A systematic review. *International Journal of Nursing Studies,* 76**,** 62-77.

KENFIELD, S. A., DUPRE, N., RICHMAN, E. L., STAMPFER, M. J., CHAN, J. M. & GIOVANNUCCI, E. L. 2014. Mediterranean diet and prostate cancer risk and mortality in the Health Professionals Follow-up Study. *European Journal of Urology,* 65**,** 887-94.

KEOGH, J. B., PEDERSEN, E., PETERSEN, K. S. & CLIFTON, P. M. 2014. Effects of intermittent compared to continuous energy restriction on short-term weight loss and long-term weight loss maintenance. *Clinical Obesity,* 4**,** 150-6.

KEYS, A., FIDANZA, F., KARVONEN, M. J., KIMURA, N. & TAYLOR, H. L. 1972. Indices of relative weight and obesity. *Journal of Chronic Diseases,* 25**,** 329-343.

KEYS, A., MIENOTTI, A., KARVONEN, M. J., ARAVANIS, C., BLACKBURN, H., BUZINA, R., DJORDJEVIC, B. S., DONTAS, A. S., FIDANZA, F., KEYS, M. H., KROMHOUT, D., NEDELJKOVIC, S., PUNSAR, S., SECCARECCIA, F. & TOSHIMA, H. 1986. The diet and 15-year death rate in the Seven Countries Study. *American Journal of Epidemiology,* 124**,** 903-915.

KNOOPS, K. T. B., DE GROOT, L., KROMHOUT, D., PERRIN, A. E., MOREIRAS-VARELA, O., MENOTTI, A. & VAN STAVEREN, W. A. 2004. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women - The HALE project. *Journal of the American Medical Association,* 292**,** 1433-1439.

KOSTEVA, A. R., SALATA, B. M., KRISHNAN, S. M., HOWE, M., WEBER, A., RUBENFIRE, M. & JACKSON, E. A. 2012. Physician variation in perceived barriers to personal health. *International Journal of Genetic Medicine,* 5**,** 53-7.

KRIS-ETHERTON, P., ECKEL, R. H., HOWARD, B. V., ST. JEOR, S. & BAZZARRE, T. L. 2001. Lyon Diet Heart Study. *Circulation,* 103**,** 1823.

LANTZ, H., PELTONEN, M., AGREN, L. & TORGERSON, J. S. 2003. Intermittent versus on-demand use of a very low calorie diet: a randomized 2-year clinical trial. *Journal of Internal Medicine,* 253**,** 463-71.

LARA, J., EVANS, E. H., O'BRIEN, N., MOYNIHAN, P. J., MEYER, T. D., ADAMSON, A. J., ERRINGTON, L., SNIEHOTTA, F. F., WHITE, M. & MATHERS, J. C. 2014a. Association of behaviour change techniques with effectiveness of dietary interventions among adults of retirement age: a systematic review and meta-analysis of randomised controlled trials. *BMC Medicine,* 12**,** 177.

LARA, J., MCCRUM, L. A. & MATHERS, J. C. 2014b. Association of Mediterranean diet and other health behaviours with barriers to healthy eating and perceived health among British adults of retirement age. *Maturitas,* 79**,** 292-8.

LARA, J., TURBETT, E., MCKEVIC, A., RUDGARD, K., HEARTH, H. & MATHERS, J. C. 2015. The Mediterranean diet among British older adults: Its understanding, acceptability and the feasibility of a randomised brief intervention with two levels of dietary advice. *Maturitas,* 82**,** 387-393.

LAVIE, C. J., ARENA, R., ALPERT, M. A., MILANI, R. V. & VENTURA, H. O. 2018. Management of cardiovascular diseases in patients with obesity. *Nature Reviews Cardiology,* 15**,** 45-56.

LEE, J. S., CHANG, P. Y., ZHANG, Y., KIZER, J. R., BEST, L. G. & HOWARD, B. V. 2017. Triglyceride and HDL-C Dyslipidemia and Risks of Coronary Heart Disease and Ischemic Stroke by Glycemic Dysregulation Status: The Strong Heart Study. *Diabetes Care,* 40**,** 529-537.

LEE, P. H., MACFARLANE, D. J., LAM, T. H. & STEWART, S. M. 2011. Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review. *The International Journal of Behavioral Nutrition and Physical Activity,* 8**,** 115-115.

LEVITSKY, D. A. & DEROSIMO, L. 2010. One day of food restriction does not result in an increase in subsequent daily food intake in humans. *Physiology and Behaviour,* 99**,** 495-9.

LOGAN, K. J., WOODSIDE, J. V., YOUNG, I. S., MCKINLEY, M. C., PERKINS-PORRAS, L. & MCKEOWN, P. P. 2010. Adoption and maintenance of a Mediterranean diet in patients with coronary heart disease from a Northern European population: a pilot randomised trial of different methods of delivering Mediterranean diet advice. *Journal of Human Nutrition and Dietetics,* 23**,** 30-37.

LUZAK, A., KARRASCH, S., THORAND, B., NOWAK, D., HOLLE, R., PETERS, A. & SCHULZ, H. 2017. Association of physical activity with lung function in lung-healthy German adults: results from the KORA FF4 study. *Bmc Pulmonary Medicine,* 17**,** 9.

MA, C., AVENELL, A., BOLLAND, M., HUDSON, J., STEWART, F., ROBERTSON, C., SHARMA, P., FRASER, C. & MACLENNAN, G. 2017. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. *BMJ,* 359**,** j4849.

MACDIARMID, J. I., LOE, J., KYLE, J. & MCNEILL, G. 2013. "It was an education in portion size". Experience of eating a healthy diet and barriers to long term dietary change. *Appetite,* 71**,** 411-419.

MAON, S., EDIRIPPULIGE, S., WARE, R. & BATCH, J. 2012. The use of web-based interventions to prevent excessive weight gain. *Journal of Telemedicine and Telecare,* 18**,** 37-41.

MARTÍNEZ-GONZÁLEZ, M. A., GARCÍA-ARELLANO, A., TOLEDO, E., SALAS-SALVADÓ, J., BUIL-COSIALES, P., CORELLA, D., COVAS, M. I., SCHRÖDER, H., ARÓS, F., GÓMEZ-GRACIA, E., FIOL, M., RUIZ-GUTIÉRREZ, V., LAPETRA, J., LAMUELA-RAVENTOS, R. M., SERRA-MAJEM, L., PINTÓ, X., MUÑOZ, M. A., WÄRNBERG, J., ROS, E., ESTRUCH, R. & FOR THE, P. S. I. 2012. A 14-Item Mediterranean Diet Assessment Tool and Obesity Indexes among High-Risk Subjects: The PREDIMED Trial. *PLoS ONE,* 7**,** e43134.

MARTINEZ-GONZALEZ, M. A. & SANCHEZ-VILLEGAS, A. 2004. The emerging role of Mediterranean diets in cardiovascular epidemiology: monounsaturated fats, olive oil, red wine or the whole pattern? *European Journal of Epidemiology,* 19**,** 9-13.

MARTINEZ-LACOBA, R., PARDO-GARCIA, I., AMO-SAUS, E. & ESCRIBANO-SOTOS, F. 2018. Mediterranean diet and health outcomes: a systematic meta-review. *European Journal of Public Health,* 28**,** 955-961.

MATHERS, J. C. 2015. Impact of nutrition on the ageing process. *British Journal of Nutrition,* 113**,** S18-S22.

MAYR, H. L., ITSIOPOULOS, C., TIERNEY, A. C., KUCIANSKI, T., RADCLIFFE, J., GARG, M., WILLCOX, J. & THOMAS, C. J. 2019. Ad libitum Mediterranean diet reduces subcutaneous but not visceral fat in patients with coronary heart disease: A randomised controlled pilot study. *Clinical Nutrition ESPEN,* 32**,** 61-69.

MCCONWAY, K. 2016. *Expert reaction to study looking at Mediterranean diet, levels of fat and body weight* [Online]. Science Media Centre. Available: http://www.sciencemediacentre.org/expert-reaction-to-study-looking-at-mediterranean-diet-levels-of-fat-and-body-weight/ [Accessed 12th November 2018 2018].

MCMORROW, L., LUDBROOK, A., MACDIARMID, J. I. & OLAJIDE, D. 2017. Perceived barriers towards healthy eating and their association with fruit and vegetable consumption. *Journal of Public Health,* 39**,** 330-338.

MHW. 1999. *Dietary guidelines for adults in Greece* [Online]. Available: http://www.mednet.gr/archives/1999-5/pdf/516.pdf [Accessed 19th January 2018].
MIDDLETON, G., KEEGAN, R., SMITH, M. F., ALKHATIB, A. & KLONIZAKIS, M. 2015. Implementing a Mediterranean diet intervention into a RCT: Lessons learned from a non-Mediterranean based country. *Journal of Nutrition Health & Aging,* 19**,** 1019-1022.
MILÀ-VILLARROEL, R., BACH-FAIG, A., PUIG, J., PUCHAL, A., FARRAN, A., SERRA-MAJEM, L. & CARRASCO, J. L. 2011. Comparison and evaluation of the reliability of indexes of adherence to the Mediterranean diet. *Public Health Nutrition,* 14**,** 2338-2345.
MITTAL, T. K., CLEGHORN, C. L., CADE, J. E., BARR, S., GROVE, T., BASSETT, P., WOOD, D. A. & KOTSEVA, K. 2018. A cross-sectional survey of cardiovascular health and lifestyle habits of hospital staff in the UK: Do we look after ourselves? *European Journal of Preventive Cardiology,* 25**,** 543-550.
MOHER, D., LIBERATI, A., TETZLAFF, J., ALTMAN, D. G. & GRP, P. 2010. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *International Journal of Surgery,* 8**,** 336-341.
MOROSHKO, I., BRENNAN, L. & O'BRIEN, P. 2011. Predictors of dropout in weight loss interventions: a systematic review of the literature. *Obesity Reviews,* 12**,** 912-934.
MORRIS, J. N. & CRAWFORD, M. D. 1958. Coronary heart disease and physical activity of work; evidence of a national necropsy survey. *British Medical Journal,* 2**,** 1485-96.
NDUMELE, C. E., MATSUSHITA, K., LAZO, M., BELLO, N., BLUMENTHAL, R. S., GERSTENBLITH, G., NAMBI, V., BALLANTYNE, C. M., SOLOMON, S. D., SELVIN, E., FOLSOM, A. R. & CORESH, J. 2016. Obesity and Subtypes of Incident Cardiovascular Disease. *Journal of the American Heart Association,* 5.
NHS 2014a. Five Year Forward View. *In:* CARE QUALITY COMMISSION, H. E. E., MONITOR, PUBLIC HEALTH ENGLAND, TRUST DEVELOPMENT AUTHORITY (ed.). London, England: NHS England.
NHS. 2014b. *Health Survey for England: Adult Obesity and Overweight* [Online]. Available: http://content.digital.nhs.uk/catalogue/PUB19295/HSE2014-ch9-adult-obe.pdf [Accessed 2nd October 2017 2017].
NHS. 2015. *Why is fibre important?* [Online]. Available: https://www.nhs.uk/chq/pages/1141.aspx?categoryid=51 [Accessed 22nd January 2018].
NHS. 2016a. *Healthy weight* [Online]. Available: https://www.nhs.uk/live-well/healthy-weight/start-the-nhs-weight-loss-plan/ [Accessed 19th November 2018].
NHS. 2016b. *Obesity* [Online]. Available: http://www.nhs.uk/Conditions/obesity/Pages/Introduction.aspx [Accessed 17th November 2016].
NHS. 2017. *Health Survey for England 2017: Adult and child overweight and obesity* [Online]. Available: http://healthsurvey.hscic.gov.uk/media/78619/HSE17-Adult-Child-BMI-rep.pdf [Accessed 7th March 2019 2019].
NHS. 2018. *Statistics on Obesity, Physical Activity and Diet* [Online]. Available: https://files.digital.nhs.uk/publication/0/0/obes-phys-acti-diet-eng-2018-rep.pdf [Accessed 1st August 2018].
NHS. 2019a. *Hypertension* [Online]. Available: https://www.nhs.uk/conditions/high-blood-pressure-hypertension/ [Accessed 1st August 2019].
NHS 2019b. Statistics on Obesity, Physical Activity and Diet, England, 2019. *In:* NHS (ed.).
NI MHURCHU, C., WHITTAKER, R., MCROBBIE, H., BALL, K., CRAWFORD, D., MICHIE, J., JIANG, Y., MADDISON, R., WATERLANDER, W. & MYERS, K. 2014. Feasibility, acceptability and potential effectiveness of a mobile health (mHealth) weight management programme for New Zealand adults. *BMC Obesity,* 1**,** 10.
NICE 2014a. Obesity: identification, assessment and management.
NICE 2014b. Weight management: lifestyle services for overweight or obese adults (PH53). *In:* NICE (ed.). London, UK: NICE.

NICE 2015a. Obesity prevention (CG43). *In:* NICE (ed.). [online].
NICE 2015b. Preventing excess weight gain. *In:* NICE (ed.). [online].
NIKIPHOROU, E. & FRAGOULIS, G. E. 2018. Inflammation, obesity and rheumatic disease: common mechanistic links. A narrative review. *Therapeutic Advances in Musculoskeletal Disease,* 10**,** 157-167.
OLDWAYS. 2009. *Mediterranean Diet* [Online]. Available: https://oldwayspt.org/traditional-diets/mediterranean-diet [Accessed 19th January 2018].
ORTEGA, R. M., PEREZ-RODRIGO, C. & LOPEZ-SOBALER, A. M. 2015. Dietary assessment methods: dietary records. *Nutrición Hospitalaria,* 31 Suppl 3**,** 38-45.
PANIZZA, C. E., LIM, U., YONEMORI, K. M., CASSEL, K. D., WILKENS, L. R., HARVIE, M. N., MASKARINEC, G., DELP, E. J., LAMPE, J. W., SHEPHERD, J. A., LE MARCHAND, L. & BOUSHEY, C. J. 2019. Effects of Intermittent Energy Restriction Combined with a Mediterranean Diet on Reducing Visceral Adiposity: A Randomized Active Comparator Pilot Study. *Nutrients,* 11**,** 1386.
PAPADAKI, A. & SCOTT, J. A. 2005. The Mediterranean Eating in Scotland Experience project: Evaluation of an Internet-based intervention promoting the Mediterranean diet. *British Journal of Nutrition,* 94**,** 290-298.
PAPADAKI, A., VALSTA, L. M., LAMPI, A. M., PEÑALVO, J., ADLERCREUTZ, H., VARDAVAS, C. & KAFATOS, A. 2011. Differences in nutrient intake during a Greek Orthodox Christian fasting and non-fasting week, as assessed by a food composition database and chemical analyses of 7-day weighed food samples. *Journal of Food Composition and Analysis,* 24**,** 22-28.
PETERS, S. A. E., SINGHATEH, Y., MACKAY, D., HUXLEY, R. R. & WOODWARD, M. 2016. Total cholesterol as a risk factor for coronary heart disease and stroke in women compared with men: A systematic review and meta-analysis. *Atherosclerosis,* 248**,** 123-131.
PHE. 2015a. *Severe Obesity* [Online]. Available: http://www.noo.org.uk/NOO_about_obesity/severe_obesity [Accessed 10th January 2017].
PHE. 2015b. *UK and Ireland prevalence and trends* [Online]. Available: https://www.noo.org.uk/NOO_about_obesity/adult_obesity/UK_prevalence_and_trends [Accessed 10th January 2017].
PHE 2016a. Government recommendations for energy and nutrients for males and females aged 1 –18 years and 19+ years. *In:* ENGLAND, P. H. (ed.). London, UK.
PHE 2016b. National Diet and Nutrition Survey: assessment of dietary sodium Adults (19 to 64 years) in England, 2014. *In:* ENGLAND, P. H. (ed.). London, UK.
PHE. 2018a. *National Diet and Nutrition Survey* [Online]. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/699241/NDNS_results_years_7_and_8.pdf [Accessed 19th August 2019].
PHE 2018b. Physical activity: applying All Our Health *In:* ENGLAND, P. H. (ed.). Online.
PHIRI, L. P., DRAPER, C. E., LAMBERT, E. V. & KOLBE-ALEXANDER, T. L. 2014. Nurses' lifestyle behaviours, health priorities and barriers to living a healthy lifestyle: a qualitative descriptive study. *BMC Nursing,* 13**,** 38-38.
PINHO, M. G. M., MACKENBACH, J. D., CHARREIRE, H., OPPERT, J. M., BARDOS, H., GLONTI, K., RUTTER, H., COMPERNOLLE, S., DE BOURDEAUDHUIJ, I., BEULENS, J. W. J., BRUG, J. & LAKERVELD, J. 2018. Exploring the relationship between perceived barriers to healthy eating and dietary behaviours in European adults. *European Journal of Nutrition,* 57**,** 1761-1770.
POWER, B. T., KIEZEBRINK, K., ALLAN, J. L. & CAMPBELL, M. K. 2017. Understanding perceived determinants of nurses' eating and physical activity behaviour: a theory-informed qualitative interview study. *BMC Obesity,* 4**,** 18.

PSALTOPOULOU, T., SERGENTANIS, T. N., PANAGIOTAKOS, D. B., SERGENTANIS, I. N., KOSTI, R. & SCARMEAS, N. 2013. Mediterranean Diet, Stroke, Cognitive Impairment, and Depression: A Meta-Analysis. *Annals of Neurology,* 74**,** 580-591.

RAATZ, S. K., SILVERSTEIN, J. T., JAHNS, L. & PICKLO, M. J. 2013. Issues of fish consumption for cardiovascular disease risk reduction. *Nutrients,* 5**,** 1081-1097.

RAVELLI, M. N., SARTORI, M. M. P., CORRENTE, J. E., RASERA JUNIOR, I., DE SOUZA, N. P. P. & DE OLIVERIA, M. R. M. 2018. The under-reporting of energy intake influences the dietary pattern reported by obese women in the waiting list for bariatric surgery. *Revista de Nutrição,* 31**,** 235-249.

RAVNSKOV, U., DE LORGERIL, M., DIAMOND, D. M., HAMA, R., HAMAZAKI, T., HAMMARSKJOLD, B., HYNES, N., KENDRICK, M., LANGSJOEN, P. H., MASCITELLI, L., MCCULLY, K. S., OKUYAMA, H., ROSCH, P. J., SCHERSTEN, T., SULTAN, S. & SUNDBERG, R. 2018. LDL-C does not cause cardiovascular disease: a comprehensive review of the current literature. *Expert Reviews in Clinical Pharmacology,* 11**,** 959-970.

REEVES, G. K., PIRIE, K., BERAL, V., GREEN, J., SPENCER, E., BULL, D. & MILLION WOMEN STUDY, C. 2007. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *British Medical Journal,* 335**,** 1134-1139.

RICHARD, C., COUTURE, P., DESROCHES, S., LICHTENSTEIN, A. H. & LAMARCHE, B. 2013. Effect of an isoenergetic traditional Mediterranean diet on apolipoprotein A-I kinetic in men with metabolic syndrome. *Nutrition Journal,* 12.

RUHL, C. E. & EVERHART, J. E. 1999. Overweight, but Not High Dietary Fat Intake, Increases Risk of Gastroesophageal Reflux Disease Hospitalization: The NHANES I Epidemiologic Followup Study. *Annals of Epidemiology,* 9**,** 424-435.

SALAS-SALVADÓ, J., DÍAZ-LÓPEZ, A., RUIZ-CANELA, M., BASORA, J., FITÓ, M., CORELLA, D., SERRA-MAJEM, L., WÄRNBERG, J., ROMAGUERA, D., ESTRUCH, R., VIDAL, J., MARTÍNEZ, J. A., ARÓS, F., VÁZQUEZ, C., ROS, E., VIOQUE, J., LÓPEZ-MIRANDA, J., BUENO-CAVANILLAS, A., TUR, J. A., TINAHONES, F. J., MARTÍN, V., LAPETRA, J., PINTÓ, X., DAIMIEL, L., DELGADO-RODRÍGUEZ, M., MATÍA, P., GÓMEZ-GRACIA, E., DÍEZ-ESPINO, J., BABIO, N., CASTAÑER, O., SORLÍ, J. V., FIOL, M., ZULET, M. Á., BULLÓ, M., GODAY, A. & MARTÍNEZ-GONZÁLEZ, M. Á. 2019. Effect of a Lifestyle Intervention Program With Energy-Restricted Mediterranean Diet and Exercise on Weight Loss and Cardiovascular Risk Factors: One-Year Results of the PREDIMED-Plus Trial. *Diabetes Care,* 42**,** 777-788.

SARRI, K. O., LINARDAKIS, M. K., BERVANAKI, F. N., TZANAKIS, N. E. & KAFATOS, A. G. 2004. Greek Orthodox fasting rituals: a hidden characteristic of the Mediterranean diet of Crete. *British Journal of Nutrition,* 92**,** 277-84.

SCHRODER, H., MARRUGAT, J., VILA, J., COVAS, M. I. & ELOSUA, R. 2004. Adherence to the traditional mediterranean diet is inversely associated with body mass index and obesity in a spanish population. *J Nutr,* 134**,** 3355-61.

SCHUBEL, R., NATTENMULLER, J., SOOKTHAI, D., NONNENMACHER, T., GRAF, M. E., RIEDL, L., SCHLETT, C. L., VON STACKELBERG, O., JOHNSON, T., NABERS, D., KIRSTEN, R., KRATZ, M., KAUCZOR, H. U., ULRICH, C. M., KAAKS, R. & KUHN, T. 2018. Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial. *American Journal of Clinical Nutrition,* 108**,** 933-945.

SCHWINGSHACKL, L. & HOFFMANN, G. 2015. Adherence to Mediterranean diet and risk of cancer: an updated systematic review and meta-analysis of observational studies. *Cancer Medicine,* 4**,** 1933-1947.

SEIMON, R. V., ROEKENES, J. A., ZIBELLINI, J., ZHU, B., GIBSON, A. A., HILLS, A. P., WOOD, R. E., KING, N. A., BYRNE, N. M. & SAINSBURY, A. 2015. Do intermittent diets provide physiological benefits over continuous diets for weight loss? A systematic review of clinical trials. *Molecular and Cellular Endocrinology,* 418**,** 153-172.

SENEKAL, M., LASKER, G. L., VAN VELDEN, L., LAUBSCHER, R. & TEMPLE, N. J. 2016. Weight-loss strategies of South African female university students and comparison of weight

management-related characteristics between dieters and non-dieters. *BMC Public Health,* 16**,** 12.
SENTENACH-CARBO, A., BATLLE, C., FRANQUESA, M., GARCIA-FERNANDEZ, E., RICO, L., SHAMIRIAN-PULIDO, L., PEREZ, M., DEU-VALENZUELA, E., ARDITE, E., FUNTIKOVA, A. N., ESTRUCH, R. & BACH-FAIG, A. 2018. Adherence Of Spanish Primary Physicians And Clinical Practise To The Mediterranean Diet. *European Journal of Clinical Nutrition*.
SERRA-MAJEM, L., BES-RASTROLLO, M., ROMAN-VINAS, B., PFRIMER, K., SANCHEZ-VILLEGAS, A. & MARTINEZ-GONZALEZ, M. A. 2009. Dietary patterns and nutritional adequacy in a Mediterranean country. *British Journal of Nutrition,* 101 Suppl 2**,** S21-8.
SHIROMA, E. J. & LEE, I. M. 2010. Physical Activity and Cardiovascular Health. *Circulation,* 122**,** 743-752.
SILLIMAN, K., RODAS-FORTIER, K. & NEYMAN, M. 2004. *A Survey of Dietary and Exercise Habits and Perceived Barriers to Following a Healthy Lifestyle in a College Population*.
SLAVIN, J. L., MARTINI, M. C., JACOBS, D. R., JR & MARQUART, L. 1999. Plausible mechanisms for the protectiveness of whole grains. *The American Journal of Clinical Nutrition,* 70**,** 459s-463s.
SNODGRASS, S. J., GUEST, M., KABLE, A. K., JAMES, C., ASHBY, S. E., PLOTNIKOFF, R. C. & COLLINS, C. E. 2016. Weight Management Advice for Clients with Overweight or Obesity: Allied Health Professional Survey. *Healthcare,* 4**,** 14.
SOFI, F., MACCHI, C., ABBATE, R., GENSINI, G. F. & CASINI, A. 2014. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. *Public Health Nutrition,* 17**,** 2769-2782.
SPEAKMAN, J. R., RANCE, K. A. & JOHNSTONE, A. M. 2008. Polymorphisms of the FTO Gene Are Associated With Variation in Energy Intake, but not Energy Expenditure. *Obesity,* 16**,** 1961-1965.
SPIRO, A. & BUTTRISS, J. L. 2014. Vitamin D: An overview of vitamin D status and intake in Europe. *Nutrition Bulletin,* 39**,** 322-350.
STAMLER, J., CHAN, Q., DAVIGLUS, M. L., DYER, A. R., VAN HORN, L., GARSIDE, D. B., MIURA, K., WU, Y. F., UESHIMA, H., ZHAO, L. C., ELLIOTT, P. & GRP, I. R. 2018. Relation of Dietary Sodium (Salt) to Blood Pressure and Its Possible Modulation by Other Dietary Factors: The INTERMAP Study. *Hypertension,* 71**,** 631-637.
STEELE, R. M., FINUCANE, F. M., GRIFFIN, S. J., WAREHAM, N. J. & EKELUND, U. 2009. Obesity is associated with altered lung function independently of physical activity and fitness. *Obesity (Silver Spring),* 17**,** 578-84.
SUNDFOR, T. M., SVENDSEN, M. & TONSTAD, S. 2018. Effect of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk: A randomized 1-year trial. *Nutrition Metabolism and Cardiovascular Diseases,* 28**,** 698-706.
TANTON, J., DODD, L. J., WOODFIELD, L. & MABHALA, M. 2015. Eating Behaviours of British University Students: A Cluster Analysis on a Neglected Issue. *Advances in Preventive Medicine,* 2015**,** 8.
TEMPORELLI, P. L., ZITO, G. & FAGGIANO, P. 2013. Cardiovascular Risk Profile and Lifestyle Habits in a Cohort of Italian Cardiologists (from the SOCRATES Survey). *The American Journal of Cardiology,* 112**,** 226-230.
THREAPLETON, D. E., GREENWOOD, D. C., EVANS, C. E. L., CLEGHORN, C. L., NYKJAER, C., WOODHEAD, C., CADE, J. E., GALE, C. P. & BURLEY, V. J. 2013. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ : British Medical Journal,* 347**,** f6879.
THYAGARAJAN, B., JACOBS, D. R., JR., APOSTOL, G. G., SMITH, L. J., JENSEN, R. L., CRAPO, R. O., BARR, R. G., LEWIS, C. E. & WILLIAMS, O. D. 2008. Longitudinal association of body mass index with lung function: the CARDIA study. *Respiratory Research,* 9**,** 31.

TOGNON, G., LISSNER, L., SAEBYE, D., WALKER, K. Z. & HEITMANN, B. L. 2014. The Mediterranean diet in relation to mortality and CVD: a Danish cohort study. *British Journal of Nutrition,* 111**,** 151-159.

TOONSTRA, J. & MATTACOLA, C. G. 2013. Test-Retest Reliability and Validity of Isometric Knee-Flexion and -Extension Measurement Using 3 Methods of Assessing Muscle Strength. *Journal of Sport Rehabilitation,* 22**,** null.

TORQUATI, L., KOLBE-ALEXANDER, T., PAVEY, T., PERSSON, C. & LEVERITT, M. 2016. Diet and physical activity behaviour in nurses: a qualitative study. *International Journal of Health Promotion and Education,* 54**,** 268-282.

TRICHOPOULOU, A. 2005. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. *British Medical Journal,* 330**,** 991-995.

TRICHOPOULOU, A., BAMIA, C. & TRICHOPOULOS, D. 2009. Anatomy of health effects of Mediterranean diet: Greek EPIC prospective cohort study. *British Medical Journal,* 338.

TRICHOPOULOU, A., COSTACOU, T., BAMIA, C. & TRICHOPOULOS, D. 2003. Adherence to a Mediterranean diet and survival in a Greek population. *New England Journal of Medicine,* 348**,** 2599-608.

TUDOR-LOCKE, C., BARREIRA, T. V. & SCHUNA, J. M., JR. 2015. Comparison of step outputs for waist and wrist accelerometer attachment sites. *Medicine and Science in Sports and Exercise,* 47**,** 839-42.

UNIVERSITY OF YORK, N. C. F. R. A. D. 2009. *Systematic reviews: CRD's guidance for undertaking reviews in health care* [Online]. York: Centre for Reviews and Dissemination. Available: https://www.york.ac.uk/crd/guidance/ [Accessed 30th November 2016].

VAN DER RHEE, H., COEBERGH, J. W. & DE VRIES, E. 2013. Is prevention of cancer by sun exposure more than just the effect of vitamin D? A systematic review of epidemiological studies. *European Journal of Cancer,* 49**,** 1422-1436.

VAN DYCK, D., CERIN, E., DE BOURDEAUDHUIJ, I., HINCKSON, E., REIS, R. S., DAVEY, R., SARMIENTO, O. L., MITAS, J., TROELSEN, J., MACFARLANE, D., SALVO, D., AGUINAGA-ONTOSO, I., OWEN, N., CAIN, K. L. & SALLIS, J. F. 2015. International study of objectively measured physical activity and sedentary time with body mass index and obesity: IPEN adult study. *International Journal of Obesity,* 39**,** 199-207.

VARADY, K. A., BHUTANI, S., CHURCH, E. C. & KLEMPEL, M. C. 2009. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. *American Journal of Clinical Nutrition,* 90**,** 1138-43.

VARADY, K. A., BHUTANI, S., KLEMPEL, M. C., KROEGER, C. M., TREPANOWSKI, J. F., HAUS, J. M., HODDY, K. K. & CALVO, Y. 2013. Alternate day fasting for weight loss in normal weight and overweight subjects: a randomized controlled trial. *Nutrition Journal,* 12.

VERSCHUREN, W. M., JACOBS, D. R., BLOEMBERG, B. P., KROMHOUT, D., MENOTTI, A., ARAVANIS, C., BLACKBURN, H., BUZINA, R., DONTAS, A. S., FIDANZA, F. & ET AL. 1995. Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. *JAMA,* 274**,** 131-6.

VON ELM, E., ALTMAN, D. G., EGGER, M., POCOCK, S. J., GOTZSCHE, P. C., VANDENBROUCKE, J. P. & INITIATIVE, S. 2014. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for reporting observational studies. *International Journal of Surgery,* 12**,** 1495-1499.

VOS, T., BARBER, R. M., BELL, B., BERTOZZI-VILLA, A., BIRYUKOV, S., BOLLIGER, I., CHARLSON, F., DAVIS, A., DEGENHARDT, L., DICKER, D., DUAN, L., ERSKINE, H., FEIGIN, V. L., FERRARI, A. J., FITZMAURICE, C., FLEMING, T., GRAETZ, N., GUINOVART, C., HAAGSMA, J., HANSEN, G. M., HANSON, S. W., HEUTON, K. R., HIGASHI, H., KASSEBAUM, N., KYU, H., LAURIE, E., LIANG, X., LOFGREN, K., LOZANO, R., MACINTYRE, M. F., MORADI-LAKEH, M., NAGHAVI, M., NGUYEN, G., ODELL, S., ORTBLAD, K., ROBERTS, D. A., ROTH, G. A., SANDAR, L., SERINA, P. T., STANAWAY, J. D., STEINER, C., THOMAS, B., VOLLSET, S. E., WHITEFORD, H., WOLOCK, T. M., YE, P., ZHOU, M., ÃVILA, M. A., AASVANG, G. M.,

ABBAFATI, C., OZGOREN, A. A., ABD-ALLAH, F., AZIZ, M. I. A., ABERA, S. F., ABOYANS, V., ABRAHAM, J. P., ABRAHAM, B., ABUBAKAR, I., ABU-RADDAD, L. J., ABU-RMEILEH, N. M. E., ABURTO, T. C., ACHOKI, T., ACKERMAN, I. N., ADELEKAN, A., ADEMI, Z., ADOU, A. K., ADSUAR, J. C., ARNLOV, J., AGARDH, E. E., AL KHABOURI, M. J., ALAM, S. S., ALASFOOR, D., ALBITTAR, M. I., ALEGRETTI, M. A., ALEMAN, A. V., ALEMU, Z. A., ALFONSO-CRISTANCHO, R., ALHABIB, S., ALI, R., ALLA, F., ALLEBECK, P., ALLEN, P. J., ALMAZROA, M. A., ALSHARIF, U., ALVAREZ, E., ALVIS-GUZMAN, N., AMELI, O., AMINI, H., AMMAR, W., ANDERSON, B. O., ANDERSON, H. R., ANTONIO, C. A. T., ANWARI, P., APFEL, H., ARSENIJEVIC, V. S. A., ARTAMAN, A., ASGHAR, R. J., ASSADI, R., ATKINS, L. S., ATKINSON, C., et al. 2015. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet,* 386**,** 743-800.

WANG, B., ZHOU, Y., XIAO, L., GUO, Y., MA, J., ZHOU, M., SHI, T., TAN, A., YUAN, J. & CHEN, W. 2018. Association of lung function with cardiovascular risk: a cohort study. *Respiratory Research,* 19**,** 214.

WANG, T., FENG, W., LI, S., TAN, Q., ZHANG, D. & WU, Y. 2019. Impact of obesity and physical inactivity on the long-term change in grip strength among middle-aged and older European adults. *Journal of Epidemiology and Community Health,* 73**,** 619-624.

WATERLANDER, W., WHITTAKER, R., MCROBBIE, H., DOREY, E., BALL, K., MADDISON, R., MYERS SMITH, K., CRAWFORD, D., JIANG, Y., GU, Y., MICHIE, J. & NI MHURCHU, C. 2014. Development of an Evidence-Based mHealth Weight Management Program Using a Formative Research Process. *JMIR,* 2**,** e18.

WEAVER, J. U. 2008. Classical endocrine diseases causing obesity. *Frontiers of Hormone Research,* 36**,** 212-228.

WEBB, T. L., JOSEPH, J., YARDLEY, L. & MICHIE, S. 2010. Using the internet to promote health behavior change: a systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. *Journal of Medical Internet Research,* 12**,** e4.

WEN, C. P., WAI, J. P., TSAI, M. K., YANG, Y. C., CHENG, T. Y., LEE, M. C., CHAN, H. T., TSAO, C. K., TSAI, S. P. & WU, X. 2011. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet,* 378**,** 1244-53.

WHO. 2006. *Fact sheet on obesity and overweight* [Online]. Available: http://www.who.int/mediacentre/factsheets/fs311/en/ [Accessed 28th March 2019].

WHO 2008. Closing the Gap in a Generation: Health Equity Through Action on the Social Determinants of Health. Geneva, Switzerland: WHO.

WILLIAMS, K. V., MULLEN, M. L., KELLEY, D. E. & WING, R. R. 1998. The effect of short periods of caloric restriction on weight loss and glycemic control in type 2 diabetes. *Diabetes Care,* 21**,** 2-8.

WILSON, P. W., D'AGOSTINO, R. B., SULLIVAN, L., PARISE, H. & KANNEL, W. B. 2002. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Archives of Internal Medicine,* 162**,** 1867-72.

WING, R. R., BLAIR, E., MARCUS, M., EPSTEIN, L. H. & HARVEY, J. 1994. Year-long weight loss treatment for obese patients with type II diabetes: does including an intermittent very-low-calorie diet improve outcome? *American Journal of Medicine,* 97**,** 354-62.

WING, R. R., LANG, W., WADDEN, T. A., SAFFORD, M., KNOWLER, W. C., BERTONI, A. G., HILL, J. O., BRANCATI, F. L., PETERS, A. & WAGENKNECHT, L. 2011. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care,* 34**,** 1481-6.

WINSTON, J., JOHNSON, C. & WILSON, S. 2008. Barriers to healthy eating by National Health Service (NHS) hospital doctors in the hospital setting: results of a cross-sectional survey. *BMC Research Notes,* 1**,** 69-69.

WU, L. & SUN, D. L. 2017. Adherence to Mediterranean diet and risk of developing cognitive disorders: An updated systematic review and meta-analysis of prospective cohort studies. *Scientific Reports,* 7**,** 9.

YANG, Q., ZHANG, Z., GREGG, E. W., FLANDERS, W. D., MERRITT, R. & HU, F. B. 2014. Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Internal Medicine,* 174**,** 516-24.

YORK, U. O. 2009. *Systematic reviews: CRD's guidance for undertaking reviews in health care* [Online]. York: Centre for Reviews and Dissemination. Available: https://www.york.ac.uk/crd/guidance/ [Accessed 30th November 2016].

YOUNG, L. R. & NESTLE, M. 2007. Portion sizes and obesity: responses of fast-food companies. *Journal of Public Health Policy,* 28**,** 238-48.

YUSUF, S., HAWKEN, S., OUNPUU, S., DANS, T., AVEZUM, A., LANAS, F., MCQUEEN, M., BUDAJ, A., PAIS, P., VARIGOS, J. & LISHENG, L. 2004. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet,* 364**,** 937-52.

ZAPKA, J. M., LEMON, S. C., MAGNER, R. P. & HALE, J. 2009. Lifestyle behaviours and weight among hospital-based nurses. *Journal of Nursing Management,* 17**,** 853-60.

ZLATEVSKA, N., DUBELAAR, C. & HOLDEN, S. 2014. Sizing Up the Effect of Portion Size on Consumption: A Meta-Analytic Review. *Journal of Marketing*.

ZOMER, E., GURUSAMY, K., LEACH, R., TRIMMER, C., LOBSTEIN, T., MORRIS, S., JAMES, W. P. T. & FINER, N. 2016. Interventions that cause weight loss and the impact on cardiovascular risk factors: a systematic review and meta-analysis. *Obesity Reviews,* 17**,** 1001-1011.

10. Additional materials

10.1. Appendix A

Appendix A1:

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10.2. Appendix B

Appendix B3:

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	19
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	19
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	19
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	20
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	21

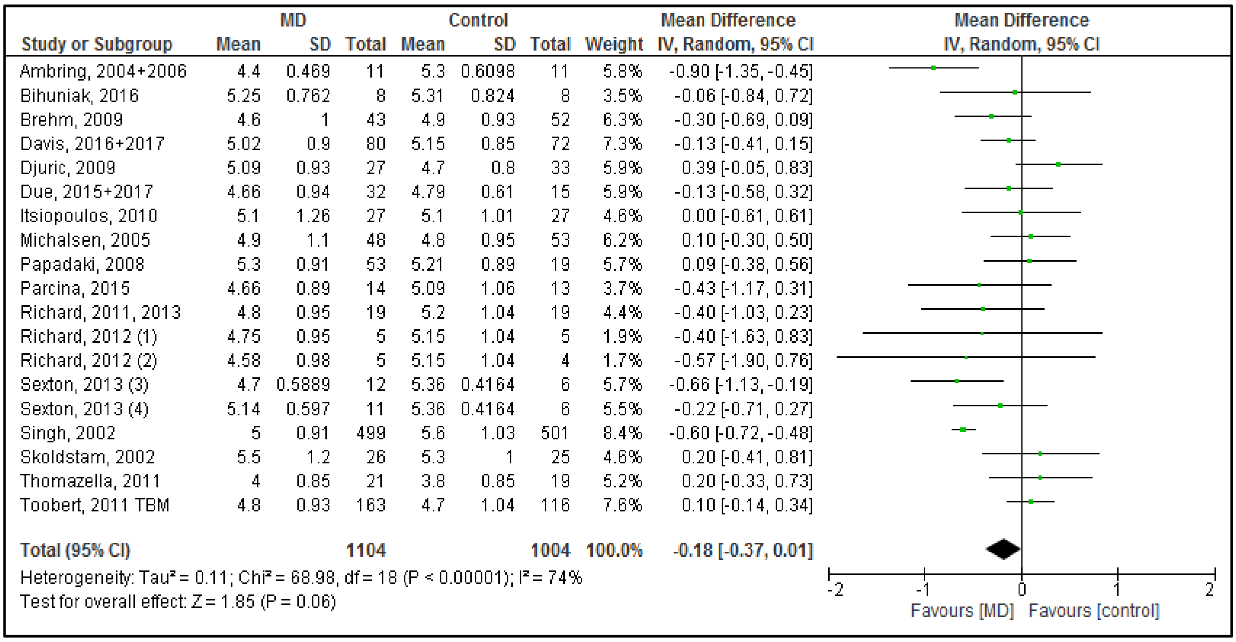
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	20
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	20
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	21
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	22
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	22
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	20
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	20
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	22
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	20
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	20
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	23
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	23
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	23

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	23
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	23
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	23
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	23
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	34
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	36
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	34
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

Appendix B3: PRISMA checklist for Chapter 2 systematic review and meta-analysis

Appendix B4:

Appendix B4 shows an example of meta-analysis results and includes results of 19 studies reporting on total cholesterol levels. The forest plot presents the results of individual studies, the weight allocated to each one of these (shown by green squares), and the overall effect size (the mean difference and 95% confidence intervals are presented and illustrated by the black diamond at the bottom of the graph). Overall, in relation with the control group, consuming a MD reduced total cholesterol by 0.18mmol/L [95% CI -0.37, 0.01], p value 0.06; and heterogeneity levels assessed by the I^2 test were high (74%).



	MD			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Ambring, 2004+2006	4.4	0.469	11	5.3	0.6098	11	5.8%	-0.90 [-1.35, -0.45]
Bihuniak, 2016	5.25	0.762	8	5.31	0.824	8	3.5%	-0.06 [-0.84, 0.72]
Brehm, 2009	4.6	1	43	4.9	0.93	52	6.3%	-0.30 [-0.69, 0.09]
Davis, 2016+2017	5.02	0.9	80	5.15	0.85	72	7.3%	-0.13 [-0.41, 0.15]
Djuric, 2009	5.09	0.93	27	4.7	0.8	33	5.9%	0.39 [-0.05, 0.83]
Due, 2015+2017	4.66	0.94	32	4.79	0.61	15	5.9%	-0.13 [-0.58, 0.32]
Itsiopoulos, 2010	5.1	1.26	27	5.1	1.01	27	4.6%	0.00 [-0.61, 0.61]
Michalsen, 2005	4.9	1.1	48	4.8	0.95	53	6.2%	0.10 [-0.30, 0.50]
Papadaki, 2008	5.3	0.91	53	5.21	0.89	19	5.7%	0.09 [-0.38, 0.56]
Parcina, 2015	4.66	0.89	14	5.09	1.06	13	3.7%	-0.43 [-1.17, 0.31]
Richard, 2011, 2013	4.8	0.95	19	5.2	1.04	19	4.4%	-0.40 [-1.03, 0.23]
Richard, 2012 (1)	4.75	0.95	5	5.15	1.04	5	1.9%	-0.40 [-1.63, 0.83]
Richard, 2012 (2)	4.58	0.98	5	5.15	1.04	4	1.7%	-0.57 [-1.90, 0.76]
Sexton, 2013 (3)	4.7	0.5889	12	5.36	0.4164	6	5.7%	-0.66 [-1.13, -0.19]
Sexton, 2013 (4)	5.14	0.597	11	5.36	0.4164	6	5.5%	-0.22 [-0.71, 0.27]
Singh, 2002	5	0.91	499	5.6	1.03	501	8.4%	-0.60 [-0.72, -0.48]
Skoldstam, 2002	5.5	1.2	26	5.3	1	25	4.6%	0.20 [-0.41, 0.81]
Thomazella, 2011	4	0.85	21	3.8	0.85	19	5.2%	0.20 [-0.33, 0.73]
Toobert, 2011 TBM	4.8	0.93	163	4.7	1.04	116	7.6%	0.10 [-0.14, 0.34]
Total (95% CI)			**1104**			**1004**	**100.0%**	**-0.18 [-0.37, 0.01]**

Heterogeneity: Tau² = 0.11; Chi² = 68.98, df = 18 (P < 0.00001); I² = 74%

Test for overall effect: Z = 1.85 (P = 0.06)

Appendix B4: Meta-analysis of 19 studies reporting on serum total cholesterol levels (mmol/L)

10.3. Appendix C

Appendix C5:

Dr John K Lodge
Applied Sciences Ethics Representative
Faculty of Health & Life Sciences
Northumberland Building
Newcastle upon Tyne
NE1 8ST

Dear Louise,

Faculty of Health and Life Sciences Research Ethics Committee

Submission Code: 892

Title: Acceptability of and current adherence to the Mediterranean diet in the North East of England: an online survey

Following independent peer review of the above proposal I am pleased to inform you that Departmental (and thus) Faculty approval has been granted for this proposal - subject to compliance with the University policies on ethics and consent and any other policies applicable to your individual research.

NB. If your research involves working with children and/or vulnerable adults you should also have recent Disclosure & Barring Service (DBS) and occupational health clearance.

The University's Policies and Procedures are available from the following web link: http://www.northumbria.ac.uk/researchandconsultancy/sa/ethgov/policies/?view=Standard

All researchers must give notice of the following:

- Any significant changes to the study design;
- Any incidents which have an adverse effect on participants, researchers or study outcomes;
- Any suspension or abandonment of the study;

Please keep this letter with your application as proof of ethical clearance and for any future auditing requirements. We wish you well in your research endeavours.

Yours sincerely,

John K Lodge

Dr John K Lodge
Department of Applied Sciences Ethics Representative

Appendix C5: Public survey ethical approval

Appendix C6:

Public opinions of the Mediterranean diet (Northumbria University)

Information sheet

Researchers: Louise Francis, Fan Liang

Contact details: louise.francis@northumbria.ac.uk, fan.liang@northumbria.ac.uk

Supervisor: Dr Jose Lara

Contact details: jose.lara@northumbria.ac.uk

What is the purpose of this project?

This research forms part of a PhD project looking at the feasibility and acceptability of the Mediterranean diet in the UK. It is therefore important to assess the views of the public on this dietary pattern. This information will inform future clinical trials aiming to assess the impact of a combination of Mediterranean diet consumption and intermittent fasting on weight loss and cardiovascular biomarkers.

Why have I been selected to take part?

You have been invited to complete an online survey as you are meet the following inclusion criteria: above 18 years of age, a UK resident and an English-speaker as the survey is written in English and no translational facilities are available.

What will I have to do?

You will be asked to complete an anonymous online survey which should take around 15 minutes. The survey will involve questions about background information such as age and height, questions about your opinions of a novel diet, and questions about how often you eat certain foods. You can save the survey part way through and complete it at another time.

Will my participation involve any physical or psychological discomfort?

Participating in this research should not involve any physical or psychological discomfort.

How will confidentiality be assured?

In order to maintain anonymity, an online survey is used which does not collect any personal data such as your name or home address. All data will be treated in accordance with the Data Protection Act, and data will only be used by members of the research team for reasons appropriate to the research question.

Has this research received appropriate ethical clearance?

This study has been given full ethical approval by the Northumbria University Ethics Committee.

Will I receive any financial reward for taking part?

No financial rewards are offered for participating in this study.

How can I withdraw from the project?

Participants are not able to withdraw from the project after their survey has been submitted as the software used does not allow identification of specific participants' data. However if you choose to withdraw from the study before the survey has been submitted, closing the browser window in which the survey is open will terminate the survey and no data will be collected.

I would like further information or to ask a question. Who do I contact and how?

For any further information, do not hesitate to contact the investigator (Louise Francis) or the project supervisor (Dr Jose Lara) using the email addresses at the top of this information sheet.

If you have any questions, please click 'Finish later' and return to this survey once your questions have been answered.

Consent form

I consent to participate in this survey, and have read and understood the Information Sheet. * *Required*

- ◯ Yes
- ◯ No

Background questions

What is your gender? * Required

- Male
- Female
- Prefer not to say

What was your age on your last birthday? * Required

What is your ethnicity? * Required

- Caucasian
- East Asian (Chinese origin)
- South Asian (non-Chinese origin)
- Black
- Other

If you selected Other, please specify:

Are you originally from a Mediterranean country (e.g. Spain, Italy, Greece etc)?

- Yes
- No

- Other

If you selected Other, please specify:

Where in the UK do you currently reside? * *Required*

- North East England
- North West England
- South East England
- South West England
- Scotland
- Wales
- Northern Ireland
- Other

If you selected Other, please specify:

What is your marital status? * *Required*

- Single
- Married
- Widowed/Divorced/Separated
- Prefer not to say
- Other

If you selected Other, please specify:

What is your employment status? * Required

- Unemployed
- Working part-time (less than 30 hours per week)
- Working full-time (more than 30 hours per week)
- Carer/Housewife/Househusband
- Retired
- Prefer not to say
- Full-time student
- Part-time student
- Other

If you selected Other, please specify:

What is your highest education level? * Required

- None
- GCSE/O-Level
- A-Level
- Diploma
- Foundation degree
- Undergraduate degree

- Postgraduate degree
- PhD/equivalent
- Prefer not to say
- Other

If you selected Other, please specify:

Are you currently a smoker, an ex-smoker, or have you never smoked? * Required

- Current smoker
- Ex-smoker
- Never smoked

Do you currently drink any alcohol? * Required

- Yes
- No

What is your weight in kilograms? Click here to open a unit conversion website in a new window - you may find it useful if you need to convert your weight in stones and pounds to kilograms. * Required

What is your height in metres? Click here to open a unit conversion website in a new window - you may find it useful if you need to convert your height from feet and inches to metres. * Required

Do you have a current diagnosis for any of the following?

	* Required	
	Yes	No
Cardiovascular disease	◌	◌
Hypertension	◌	◌
Type 2 diabetes	◌	◌
High cholesterol	◌	◌

Do you follow a special diet because of a medical condition? * Required

◌ Yes
◌ No

What health condition is your diet tailored to?

Weighing yourself

Do you have a set of scales for weighing yourself at home? * *Required*

- Yes
- No

How often do you weigh yourself/have somebody else weigh you? * *Required*

- Never
- Yearly
- Monthly
- Weekly
- Daily
- Other

If you selected Other, please specify:

At the present time, are you trying to lose weight, trying to gain weight, or not trying to change your weight? * *Required*

- Trying to lose weight
- Trying to gain weight
- Not trying to change weight

Have you ever attempted to lose weight in the past? * *Required*

- Yes
- No

Your weight loss experience

How many separate weight loss attempts have you made in the past? * *Required*

How many of these would you say were successful? * *Required*

Have you used any of the following in your attempt(s) to lose weight?

	Yes	No
Diet plans involving group meetings (e.g. Slimming World, Weight Watchers)		
Other diet plans (e.g. Lean in 15)		
Exercise plans (e.g. fitness DVDs)		
Meal replacements (e.g. Slim Fast)		
Medicinal aids (e.g. slimming tablets)		
Fasting (e.g. 5:2 diet)		
Surgical methods (e.g. gastric band)		

Your own diet

How many times do you usually eat out **per month**? (i.e. consume food not cooked at home). Please give a number * *Required*

When eating out, which of the following cuisines do you prefer? (Please choose one) * *Required*

- Indian
- Chinese
- Italian
- Spanish
- Mexican
- British
- American
- Other

If you selected Other, please specify:

Do you ever use olive oil in your diet? * *Required*

- Yes
- No

How much olive oil do you use per day, in approximate tablespoons?

Please enter a number.

Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, beef or other red meats? * Required

- Yes, I eat more white meats than red meats
- No, I eat more red meats than white meats
- I'm vegetarian/vegan

How many servings of the following foodstuffs do you consume **per day**?

	* Required								
	0	1	2	3	4	5	6	7	More than 7
Vegetables (excluding white potatoes) (1 serving = 80g, or 2 broccoli florets, three heaped tablespoons of cooked vegetables such as carrots, or 3 celery sticks)									
Fruit (1 serving = 80g, or 1 banana, 2 kiwis, or 1 heaped tablespoon of sultanas)									
Butter, margarine, or cream (1 serving = 10g)									

How many servings of the following foodstuffs do you consume **per week**?

	* Required								
	0	1	2	3	4	5	6	7	More than 7
Red meat (1 serving = 70g, or three slices of ham)	○	○	○	○	○	○	○	○	○
Soft drinks (1 serving = 150ml)	○	○	○	○	○	○	○	○	○
Wine (1 serving = 125ml)	○	○	○	○	○	○	○	○	○
Green tea (1 serving = 250ml)	○	○	○	○	○	○	○	○	○
Legumes (e.g. kidney beans, lentils or chickpeas) (1 serving = 5 heaped tablespoons cooked)	○	○	○	○	○	○	○	○	○
Fish or shellfish (1 serving = 140g)	○	○	○	○	○	○	○	○	○
Cakes, pastries or sweets, which are not homemade	○	○	○	○	○	○	○	○	○
Walnuts (1 serving = 40g)	○	○	○	○	○	○	○	○	○
Other unsalted nuts including peanuts (1 serving = 40g)	○	○	○	○	○	○	○	○	○
A meal containing vegetables, pasta, rice, or other dishes seasoned with sauces made with tomato and onion, leek or garlic, and olive oil	○	○	○	○	○	○	○	○	○

The Mediterranean diet

Which of the following statements is most true for you? * Required

- I've never heard of the Mediterranean diet
- I know a little bit about the Mediterranean diet
- I know quite a bit about the Mediterranean diet
- I fully understand the concept of the Mediterranean diet
- Other

If you selected Other, please specify:

Do you believe that your usual diet is healthy? * Required

- Yes
- No
- Prefer not to say
- Other

If you selected Other, please specify:

Are any of the following factors barriers to your healthy eating?

Please don't select more than 1 answer(s) per row.

Please select at least 20 answer(s).

	Yes	No

Irregular working hours	☐	☐
Busy lifestyle	☐	☐
Giving up foods that I like	☐	☐
Lack of willpower	☐	☐
I don't want to change my eating habits	☐	☐
Limited cooking skills	☐	☐
Healthy food is more perishable	☐	☐
Lengthy preparation of healthy food	☐	☐
Limited storage facilities	☐	☐
Limited cooking facilities	☐	☐
Increased price of healthy foods	☐	☐
Unappealing healthy food	☐	☐
Strange or unusual healthy foods	☐	☐
Feeling conspicuous among others	☐	☐
Taste preferences of family and friends	☐	☐
Not knowing enough about healthy eating	☐	☐
Experts keep changing their minds about healthy foods	☐	☐
Limited healthy choice when I eat out	☐	☐
Healthy options not available in shop or canteen at work	☐	☐
Not enough healthy food to satisfy hunger	☐	☐

The Mediterranean diet

Would you find the following Mediterranean dietary guidelines acceptable? (if you don't eat or drink something, e.g. meat or wine, please just click 'no')

	Yes	No	I don't know
Olive oil should be used as the main culinary fat source, replacing butter etc	○	○	○
At least 4 tablespoons of olive oil should be consumed per day	○	○	○
Red meat should only be consumed a maximum of twice per week (1 serving = 70g, or three slices of ham)	○	○	○
Meats such as chicken, turkey and rabbit should be chosen over beef, pork or veal	○	○	○
Sweets such as desserts, chocolate and anything else high in refined sugars should be consumed a maximum of 3 times per week	○	○	○
Carbonated or sweet drinks should be consumed a maximum of once per day (1 serving = 150ml)	○	○	○
A minimum of 2 servings of vegetables (excluding white potatoes) should be eaten per day (1 serving = 80g, or 2 broccoli florets, three heaped tablespoons of cooked vegetables such as carrots, or 3 celery sticks)	○	○	○
A minimum of 3 servings of fruit should be eaten per day (1 serving = 80g, or 1 banana, 2 kiwis, or 1 heaped tablespoon of sultanas)	○	○	○
Butter, margarine and cream (1 serving = 10g) should be eaten less than once per day	○	○	○
7 glasses of wine should be consumed per week (1 glass = 125ml)	○	○	○
More than 3 servings of legumes (e.g. kidney beans, lentils or chickpeas) should be consumed per week (1 serving = 5 tablespoons of cooked food)	○	○	○
More than 3 servings of fish or shellfish should be consumed per week (1 serving of fish = 140g, or about the size of a cheque book)	○	○	○

More than 3 servings of unsalted nuts should be consumed per week (1 serving = 40g, or a small handful)	○	○	○
A meal containing vegetables, pasta or rice served with a sauce made using tomato, garlic, olive oil and onion should be eaten at least twice per week	○	○	○

Debrief sheet

Researcher: Louise Francis, Fan Liang

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What was the aim of this project?

This project aimed to investigate the opinions of the public on the acceptability and feasibility of the Mediterranean diet in the UK.

Have I been deceived in any way during the study?

No deception was used in this study.

How will I find out about the results?

Should you wish to receive information on the results of this study, please email one of the research team using the above email addresses.

What will happen to the information I have provided?

All data will be stored securely and confidentially until a certain time after the study has finished, when it will be destroyed.

How will the results be disseminated?

This research is intended for a PhD project and therefore results may be disseminated in a scientific journal.

How would I withdraw my information after finishing the study?

Participants are not able to withdraw from the project after their survey has been submitted as the software used does not allow identification of specific participants' data. However if you choose to withdraw from the study before the survey has been submitted, closing the browser window in which the survey is open will terminate the survey and no data will be collected.

How can I register a complaint about this research?

If you have any worries about the way this study was carried out please do not hesitate to contact one of the research team using the provided email addresses.

Appendix C6: Public opinions of the MD online survey

Appendix C7:

PBHE	Adherence to MD guideline OR (95% CI); p value			
	Olive oil[1]	**Volume olive oil**[2]	**White meat**[3]	**Vegetables**[4]
Irregular working hours	0.929 (0.536-1.609); 0.792	0.915 (0.130-6.449); 0.929	3.010 (1.442-6.284); **0.003***	2.081 (1.150-3.764); **0.015***
Busy lifestyle	0.832 (0.476-1.455); 0.519	0.928 (0.138-6.261); 0.939	0.636 (0.309-1.308); 0.219	0.371 (0.201-0.683); **0.001***
Giving up foods that I like	1.194 (0.679-2.100); 0.537	0.298 (0.045-1.968); 0.209	0.774 (0.356-1.680); 0.517	0.612 (0.335-1.117); 0.110
Lack of willpower	0.663 (0.337-1.304); 0.234	0.353 (0.049-2.535); 0.301	0.797 (0.317-2.002); 0.629	0.473 (0.225-0.998); **0.049***
Lengthy preparation time of healthy foods	0.541 (0.309-0.948); **0.032***	3.041 (0.383-24.168); 0.293	0.602 (0.285-1.274); 0.185	0.736 (0.407-1.329); 0.309
Increased price of healthy foods	0.862 (0.511-1.453); 0.577	0.722 (0.119-4.390); 0.723	1.552 (0.769-3.133); 0.220	1.151 (0.659-2.012); 0.621
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter**[6]	**Red meat**[7]	**Soft drinks**[8]
Irregular working hours	1.126 (0.570-2.224); 0.732	0.862 (0.402-1.848); 0.704	0.854 (0.434-1.683); 0.649	0.933 (0.447-1.948); 0.853
Busy lifestyle	1.260 (0.632-2.511); 0.512	0.555 (0.291-1.058); 0.074	0.748 (0.380-1.474); 0.402	0.514 (0.254-1.040); 0.064
Giving up foods that I like	0.868 (0.449-1.676); 0.672	0.697 (0.368-1.318); 0.266	0.816 (0.411-1.620); 0.560	0.673 (0.330-1.373); 0.276
Lack of willpower	0.418 (0.194-0.900); **0.026**	0.862 (0.402-1.848); 0.704	1.140 (0.500-2.600); 0.756	1.263 (0.526-3.035); 0.601

Lengthy preparation time of healthy foods	0.817 (0.413-1.676); 0.560	0.703 (0.364-1.358); 0.294	0.712 (0.357-1.421); 0.335	0.824 (0.399-1.702); 0.601
Increased price of healthy foods	1.040 (0.548-1.971); 0.905	1.317 (0.709-2.449); 0.383	1.533 (0.792-2.968); 0.205	0.437 (0.221-0.866); **0.018***
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes**[10]	**Fish**[11]	**Sweets**[12]
Irregular working hours	0.350 (0.090-1.368); 0.131	1.458 (0.637-3.336); 0.372	1.719 (0.700-4.218); 0.237	0.902 (0.484-1.681); 0.746
Busy lifestyle	1.170 (0.321-4.257); 0.812	0.230 (0.104-0.509); **0.000**	0.990 (0.410-2.393); 0.983	0.804 (0.435-1.487); 0.487
Giving up foods that I like	1.299 (0.302-5.596); 0.725	1.586 (0.676-3.725); 0.289	0.959 (0.417-2.205); 0.922	0.571 (0.314-1.041); 0.068
Lack of willpower	2.356 (0.408-13.594); 0.338	0.757 (0.287-1.995); 0.573	0.540 (0.202-1.444); 0.220	0.618 (0.304-1.258); 0.185
Lengthy preparation time of healthy foods	0.828 (0.228-3.002); 0.774	0.499 (0.218-1.141); 0.100	0.759 (0.320-1.799); 0.530	0.815 (0.436-1.525); 0.523
Increased price of healthy foods	0.438 (0.121-1.589); 0.209	0.960 (0.447-2.060); 0.916	0.598 (0.267-1.338); 0.211	1.007 (0.560-1.811); 0.983
PBHE	**Adherence to MD guideline OR (95% CI); p value**			
	Nuts[13]	**Sofrito**[14]	**Overall adherence**[15]	
Irregular working hours	0.781 (0.267-2.289); 0.653	1.055 (0.457-2.438); 0.900	0.302 (0.196-0.468); **0.000***	
Busy lifestyle	0.534 (0.187-1.527); 0.242	2.080 (0.922-4.694); 0.078	0.514 (0.293-0.903); **0.021***	

Giving up foods that I like	0.350 (0.125-1.527); 0.242	1.199 (0.511-2.815); 0.677	0.694 (0.371-1.298); 0.253	
Lack of willpower	2.219 (0.619-7.957); 0.221	0.957 (0.330-2.776); 0.936	0.661 (0.322-1.359); 0.260	
Lengthy preparation time of healthy foods	0.445 (0.154-1.281); 0.133	0.222 (0.081-0.607); **0.003***	0.600 (0.320-1.123); 0.110	
Increased price of healthy foods	0.736 (0.272-1.992); 0.547	1.792 (0.813-3.952); 0.148	0.764 (0.419-1.391); 0.378	

Definitions of adherence to guideline:
use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14].
Odds ratios for MD adherence[15] refer to values above the median value of 5. P values shown in bold and with an asterisk were statistically significant (<0.05).

Appendix C7: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between the top six most commonly reported perceived barriers to healthy eating (PBHE) and adherence

BMI (kg/m²)	Adherence to MD guideline OR (95% CI); p value			
	Olive oil[1]	**Volume olive oil[2]**	**White meat[3]**	**Vegetables[4]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.683 (0.421-1.108); 0.122	2.279 (0.505-10.283); 0.284	0.779 (0.417-1.456); 0.434	0.968 (0.564-1.663); 0.908
>=30	0.924 (0.535-1.597); 0.778	2.111 (0.417-10.686); 0.366	1.429 (0.670-3.048); 0.356	1.150 (0.520-2.133); 0.657
BMI (kg/m²)	**Adherence to MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.826 (0.497-1.375); 0.463	0.828 (0.507-1.353); 0.452	0.716 (0.420-1.220); 0.219	0.541 (0.331-0.882); **0.014***
>=30	0.961 (0.546-1.694); 0.892	0.880 (0.507-1.526); 0.648	0.770 (0.422-1.403); 0.393	0.811 (0.473-1.390); 0.446
BMI (kg/m²)	**Adherence to MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	5.353 (0.698-41.071); 0.107	0.651 (0.383-1.107); 0.113	0.953 (0.511-1.778); 0.880	1.137 (0.703-1.839); 0.601
>=30	5.774 (0.710-46.937); 0.101	0.824 (0.457-1.484); 0.518	0.837 (0.409-1.711); 0.625	1.776 (1.043-3.023); **0.034***
BMI (kg/m²)	**Adherence to MD guideline OR (95% CI); p value**			

	Nuts[13]	Sofrito[14]	Overall adherence[15]	
18.50-24.99	Reference	Reference	Reference	
25.00-29.99	0.666 (0.348-1.272); 0.218	1.344 (0.652-2.769); 0.423	0.555 (0.349-0.884); **0.013***	
>=30	1.145 (0.577-2.270); 0.699	0.724 (0.342-1.536); 0.400	0.762 (0.454-1.279); 0.303	

Definitions of adherence to guideline:
use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14].
Odds ratios for MD adherence[15] refer to values above the median value of 5. P values shown in bold and with an asterisk were statistically significant (<0.05).

Appendix C8: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between BMI 25.00-29.99kg/m2 and >=30 kg/m2 in comparison to BMI 18.50-24.99kg/m2 and adherence to the MD guidelines

BMI (kg/m^2)	Acceptance of MD guideline OR (95% CI); p value			
	Olive oil[1]	**Volume olive oil[2]**	**White meat[3]**	**Vegetables[4]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.716 (0.436-1.177); 0.188	0.790 (0.455-1.372); 0.403	1.238 (0.725-2.114); 0.435	0.603 (0.242-1.503); 0.278
>=30	0.853 (0.488-1.490); 0.576	0.907 (0.490-1.677); 0.755	1.013 (0.560-1.830); 0.967	0.598 (0.221-1.615); 0.311
BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.991 (0.561-1.750); 0.974	1.070 (0.638-1.793); 0.798	1.232 (0.761-1.993); 0.396	1.136 (0.676-1.907); 0.630
>=30	1.205 (0.626-2.320); 0.576	1.084 (0.606-1.939); 0.785	1.544 (0.888-2.683); 0.124	1.427 (0.783-2.600); 0.245
BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
18.50-24.99	Reference	Reference	Reference	Reference
25.00-29.99	0.846 (0.520-1.376); 0.500	0.607 (0.366-1.004); 0.052	1.059 (0.665-1.687); 0.810	0.868 (0.489-1.543); 0.630
>=30	0.708 (0.406-1.236); 0.225	0.585 (0.335-1.023); 0.060	1.194 (0.706-2.019); 0.508	1.077 (0.558-2.080); 0.824
BMI (kg/m^2)	**Acceptance of MD guideline OR (95% CI); p value**			

	Nuts[13]	Sofrito[14]	Overall acceptance[15]	
18.50-24.99	Reference	Reference	Reference	
25.00-29.99	0.731 (0.457-1.170); 0.191	1.038 (0.579-1.858); 0.901	0.947 (0.590-1.521); 0.822	
>=30	1.007 (0.593-1.711); 0.979	1.318 (0.670-2.593); 0.425	1.195 (0.698-2.046); 0.517	

Definitions of MD guidelines:
use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14].
Odds ratios for MD adherence[15] refer to values above the median value of 5. P values shown in bold and with an asterisk were statistically significant (<0.05).

Appendix C9: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating associations between BMI 25.00-29.99kg/m2 and >=30 kg/m2 in comparison to BMI 18.50-24.99kg/m2 and acceptance of the MD guidelines

Appendix C10:

PBHE	Acceptance of MD guideline OR (95% CI); p value			
	Olive oil[1]	Volume olive oil[2]	White meat[3]	Vegetables[4]
Irregular working hours	0.709 (0.403-1.245); 0.231	0.878 (0.443-1.741); 0.710	1.761 (0.896-3.460); 0.101	0.940 (0.367-2.404); 0.897
Busy lifestyle	1.171 (0.659-2.083); 0.590	0.997 (0.495-2.005); 0.993	0.711 (0.361-1.399); 0.323	0.579 (0.216-1.551); 0.277
Giving up foods that I like	0.675 (0.382-1.195); 0.178	0.849 (0.425-1.694); 0.643	1.243 (0.632-2.444); 0.528	1.071 (0.428-2.680); 0.884
Lack of willpower	1.094 (0.955-2.840); 0.073	1.939 (0.813-4.622); 0.135	1.296 (1.046-3.784); **0.036***	1.908 (0.652-5.583); 0.238
Lengthy preparation time of healthy foods	0.430 (0.238-0.776); **0.005***	0.609 (0.309-1.201); 0.152	0.398 (0.192-0.824); **0.013***	0.625 (0.236-1.671); 0.351
Increased price of healthy foods	1.646 (0.955-2.840; 0.073	0.783 (0.411-1.492); 0.457	1.989 (1.046-3.784); 0.532	1.322 (0.549-3.182); 0.534
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Fruit[5]	**Butter[6]**	**Red meat[7]**	**Soft drinks[8]**
Irregular working hours	1.296 (0.685-2.450); 0.425	0.951 (0.525-1.722); 0.867	1.643 (0.891-3.031); 0.112	1.543 (0.826-2.882); 0.173
Busy lifestyle	0.721 (0.375-1.388); 0.328	0.751 (0.407-1.385); 0.359	1.810 (0.990-3.312); 0.054	0.737 (0.391-1.389); 0.345
Giving up foods that I like	0.659 (0.337-1.288); 0.223	1.035 (0.569-1.883); 0.910	1.535 (0.822-2.865); 0.179	0.953 (0.503-1.804); 0.882
Lack of willpower	1.168 (0.531-2.574); 0.697	0.849 (0.408-1.766); 0.661	0.651 (0.301-1.406); 0.274	1.330 (0.624-2.838); 0.460

Lengthy preparation time of healthy foods	0.920 (0.478-1.769); 0.802	0.893 (0.488-1.637); 0.715	0.315 (0.161-0.615); **0.001***	0.697 (0.364-1.336); 0.277
Increased price of healthy foods	1.038 (0.563-1.914); 0.905	1.314 (0.749-2.305); 0.341	1.416 (0.788-2.546); 0.245	0.967 (0.531-1.764); 0.914
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Wine[9]	**Legumes[10]**	**Fish[11]**	**Sweets[12]**
Irregular working hours	1.098 (0.606-1.990); 0.758	0.963 (0.550-1.687); 0.896	1.401 (0.808-2.429); 0.229	0.887 (0.460-1.712); 0.721
Busy lifestyle	1.474 (0.798-2.722); 0.216	1.352 (0.759-2.409); 0.306	1.184 (0.679-2.063); 0.552	0.892 (0.457-1.740); 0.737
Giving up foods that I like	1.151 (0.633-2.091); 0.645	1.811 (1.004-3.265); **0.048***	0.912 (0.522-1.593); 0.746	0.802 (0.411-1.562; 0.516
Lack of willpower	0.845 (0.412-1.732); 0.646	0.504 (0.248-1.023); 0.058	0.688 (0.349-1.357); 0.280	1.832 (0.831-4.043); 0.134
Lengthy preparation time of healthy foods	0.818 (0.450-1.487); 0.510	0.719 (0.405-1.278); 0.261	0.770 (0.439-0.351); 0.362	0.572 (0.285-1.149); 0.117
Increased price of healthy foods	0.690 (0.395-1.206); 0.193	0.557 (0.326-0.951); **0.032***	1.083 (0.642-1.827); 0.766	0.998 (0.534-1.865); 0.996
PBHE	**Acceptance of MD guideline OR (95% CI); p value**			
	Nuts[13]	**Sofrito[14]**	**Overall acceptance[15]**	
Irregular working hours	1.592 (0.914-2.771); 0.100	1.454 (0.686-3.080); 0.329	1.035 (0.597-1.795); 0.902	
Busy lifestyle	1.078 (0.616-1.887); 0.793	1.728 (0.816-3.659); 0.153	1.159 (0.663-2.025); 0.605	

Giving up foods that I like	1.297 (0.739-2.278); 0.364	2.238 (1.054-4.751); **0.036***	0.817 (0.467-1.430); 0.480	
Lack of willpower	0.514 (0.260-1.018); 0.056	0.236 (0.087-0.644); **0.005***	0.915 (0.465-1.800); 0.796	
Lengthy preparation time of healthy foods	0.772 (0.440-1.354); 0.367	1.261 (0.597-2.665); 0.544	0.702 (0.399-1.236); 0.220	
Increased price of healthy foods	0.729 (0.433-1.229); 0.236	1.226 (0.602-2.499); 0.575	1.045 (0.619-1.766); 0.868	

Definitions of MD guidelines:
use olive oil as main fat source[1]; volume of olive oil >=4 tbsp/day[2]; preferential consumption of white meat over red meat[3]; >=2 portions vegetables/day[4]; >=3 portions fruit/day[5]; <1 portion butter/day[6]; <1 portion red meat/day[7]; <1 soft drink/day[8]; >=7 glasses wine/week[9]; >=3 portions legumes/week[10]; >=3 fish/week[11]; <2 portions cakes or sweets/week[12]; >=3 portions unsalted nuts/week[13] and >=2 portions sofrito/week[14].
Odds ratios for MD adherence[15] refer to values above the median value of 5. P values shown in bold and with an asterisk were statistically significant (<0.05).

Appendix C10: Odds ratios (OR) and 95% confidence intervals (95% CI) derived from binary logistic regression indicating overall associations between the top six most commonly reported perceived barriers to healthy eating (PBHE) and acceptance of MD guidelines

10.4. Appendix D

Appendix D11:

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	80
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	80
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	80
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	81
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	81

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	81
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	81
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	81
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	82
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	82
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	81
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	81
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	81
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	81
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	81
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	82
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	82
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	82

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	82
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	82
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	92
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	94
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	92
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

Appendix D11: PRISMA checklist for Chapter 4 systematic review and meta-analysis

10.5. Appendix E

Appendix E12:

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	96
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	96
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	98
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	98

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	98
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	98
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	98
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	98
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	98
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	100
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	100
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	114
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	117
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	114
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

Appendix E12: PRISMA checklist for Chapter 5 systematic review

Appendix E13:

Healthcare professionals' opinions of the Mediterranean diet

Page 1: Information sheet

Researcher: Louise Francis

Contact details: louise.francis@northumbria.ac.uk

Supervisor: Dr Jose Lara

Contact details: jose.lara@northumbria.ac.uk

What is the purpose of this project?

This research forms part of a PhD project looking at the feasibility and acceptability of the Mediterranean diet in the management of obesity and type 2 diabetes in the UK. It is therefore important to gain an understanding of the current healthy eating advice given by healthcare professionals, and their thoughts on the use of the Mediterranean diet as a healthy eating plan.

This information will inform future clinical trials aiming to assess the impact of a combination of Mediterranean diet consumption and intermittent fasting on weight loss and cardiovascular biomarkers.

Why have I been selected to take part?

You have been invited to complete an online survey as you are a dietitian, nutritionist, nurse or doctor. There are no other restrictions to participating.

What will I have to do?

You will be asked to complete an anonymous online survey which should take around 15 minutes. This survey will contain questions about your job title and years of experience, your current healthy eating advice to patients, your thoughts on the Mediterranean diet, and your eating habits.

Will my participation involve any physical or psychological discomfort?

Participating in this research should not involve any physical or psychological discomfort.

How will confidentiality be assured?

In order to maintain anonymity, an online survey is used which does not collect any personal data such as your name or home address. All data will be treated in accordance with the Data Protection Act, and data will only be used by members of the research team for reasons appropriate to the research question.

Has this research received appropriate ethical clearance?

This study has been given full ethical approval by the Northumbria University Faculty of Health and Life Sciences Ethics Committee.

Will I receive any financial reward for taking part?

No financial rewards are offered for participating in this study.

How can I withdraw from the project?

If you begin the survey but decide not to complete it, closing the browser window will end the survey and your answers will not be stored or submitted. Once the survey is completed information cannot be withdrawn as individual participants cannot be identified.

I would like further information or to ask a question. Who do I contact and how?

For any further information, do not hesitate to contact the investigator (Louise Francis) or the project supervisor (Dr Jose Lara) using the email addresses at the top of this information sheet.

If you have any questions, please click 'Finish later' and return to this survey once your questions have been answered.

Page 2: Consent form

1. I consent to participate in this survey, and have read and understood the Information Sheet.
✱ *Required*

- ○ Yes
- ○ No

Page 3: Background information

2. What is your age? * Required

[ ]

3. What is your gender? * Required

- Male
- Female
- Prefer not to say

4. What is your ethnicity? * Required

- Caucasian
- Asian
- Black
- Mixed / Multiple ethnic groups
- Other

4.a. If you selected Other, please specify:

[ ]

5. What is your current job title? * Required

- Dietitian
- Dietetic Assistant
- Nutritionist

- [ ] Nutrition Assistant
- [ ] Nurse
- [ ] Hospital Doctor
- [ ] GP
- [ ] Other

5.a. If you selected Other, please specify:

6. Where do you usually work? * Required

- [ ] Hospital
- [ ] Community
- [ ] Both
- [ ] Other

6.a. If you selected Other, please specify:

7. What is the postcode of your usual place of work? * Required

Please enter a valid UK postcode.

8. How many years have you spent working in your current field? i.e. how long have you been a nurse/dietitian etc? (If less than 1 year, please state '1') * Required

9. What is your main area of work? (Please select the most relevant answer) * Required

- [ ] General practice
- [ ] Obesity
- [ ] Paediatrics
- [ ] Renal
- [ ] Gerontology
- [ ] Sports
- [ ] Diabetes
- [ ] Hypertension
- [ ] Cardiovascular
- [ ] Oncology
- [ ] Neurology
- [ ] Respiratory
- [ ] Other

9.a. If you selected Other, please specify:

Page 4: Current healthy eating recommendations

10. Do you recommend any of the following techniques to help your patients improve their eating patterns?

	✱ Required			
	Yes	No	Other	If you selected Other, please specify:
The Eatwell Guide	○	○	○	
Behaviour change therapies (eg cognitive behaviour therapy)	○	○	○	
Commercial programs (eg Weight Watchers)	○	○	○	
Meal replacements (eg Slim Fast)	○	○	○	
Surgical methods (eg gastric band)	○	○	○	

11. In your experience, what percentage of your patients are successful in improving their dietary patterns? (Please give a percentage between 0 and 100) ✱ *Required*

12. Websites such as NHS Choices, the British Heart Foundation and Diabetes UK contain information about the Mediterranean diet (MD). Do you currently utilise any Mediterranean dietary recommendations when encouraging patients to improve their dietary patterns? ✱ *Required*

- ○ Yes, always
- ○ Yes, often
- ○ Yes, sometimes
- ○ No
- ○ Other

12.a. If you selected Other, please specify:

13. There is currently much information in the media about intermittent fasting, defined as any diet which cycles between periods of fasting (eating less than 500 calories per day) and non-fasting. Do you currently recommend intermittent fasting to your patients as a tool for improving dietary patterns? * Required

- Yes, always
- Yes, often
- Yes, sometimes
- No
- Other

13.a. If you selected Other, please specify:

Page 5: Using the Mediterranean diet in healthy eating advice

14. Would **your patients** find the following Mediterranean dietary guidelines acceptable?

	Yes	No	I don't know
Olive oil should be used as the main culinary fat source, replacing butter etc	○	○	○
At least 4 tablespoons of olive oil should be consumed per day	○	○	○
Red meat should only be consumed a maximum of twice per week (1 serving = 70g, or three slices of ham)	○	○	○
Meats such as chicken, turkey and rabbit should be chosen over beef, pork or veal	○	○	○
Sweets such as desserts, chocolate and anything else high in refined sugars should be consumed a maximum of 3 times per week	○	○	○
Carbonated or sweet drinks should be consumed a maximum of once per day (1 serving = 150ml)	○	○	○
A minimum of 2 servings of vegetables (excluding white potatoes) should be eaten per day (1 serving = 80g, or 2 broccoli florets, three heaped tablespoons of cooked vegetables such as carrots, or 3 celery sticks)	○	○	○
A minimum of 3 servings of fruit should be eaten per day (1 serving = 80g, or 1 banana, 2 kiwis, or 1 heaped tablespoon of sultanas)	○	○	○
Butter, margarine and cream (1 serving = 10g) should be eaten less than once per day	○	○	○
7 glasses of wine should be consumed per week (1 glass = 125ml)	○	○	○
More than 3 servings of legumes (e.g. kidney beans, lentils or chickpeas) should be consumed per week (1 serving = 5 tablespoons of cooked food)	○	○	○
More than 3 servings of fish or shellfish should be consumed per week (1 serving of fish = 140g, or about the size of a cheque book)	○	○	○
More than 3 servings of unsalted nuts should be consumed per week (1 serving = 40g, or a small handful)	○	○	○
A meal containing vegetables, pasta or rice served with a sauce made using tomato, garlic, olive oil and onion should be eaten at least twice per week	○	○	○

15. Do **your patients** report the following factors as barriers to healthy eating? * Req

Please don't select more than 1 answer(s) per row.

Please select at least 20 answer(s).

	Yes	No
Irregular working hours	☐	☐
Busy lifestyle	☐	☐
Giving up foods that I like	☐	☐
Lack of willpower	☐	☐
I don't want to change my eating habits	☐	☐
Limited cooking skills	☐	☐
Healthy food is more perishable	☐	☐
Lengthy preparation of healthy food	☐	☐
Limited storage facilities	☐	☐
Limited cooking facilities	☐	☐
Increased price of healthy foods	☐	☐
Unappealing healthy food	☐	☐
Strange or unusual healthy foods	☐	☐
Feeling conspicuous among others	☐	☐
Taste preferences of family and friends	☐	☐
Not knowing enough about healthy eating	☐	☐
Experts keep changing their minds about healthy foods	☐	☐
Limited healthy choice when I eat out	☐	☐
Healthy options not available in shop or canteen at work	☐	☐
Not enough healthy food to satisfy hunger	☐	☐

Page 6: Your own diet

16. Do you believe that there is room for improvement in **your** usual diet? i.e. do you think y could make **your** diet more healthy? * *Required*

- Yes
- No

16.a. Do you consider the following factors barriers to **your own** healthy eating?

Please don't select more than 1 answer(s) per row.

Please select at least 20 answer(s).

	Yes	No
Irregular working hours	☐	☐
Busy lifestyle	☐	☐
Giving up foods that I like	☐	☐
Lack of willpower	☐	☐
I don't want to change my eating habits	☐	☐
Limited cooking skills	☐	☐
Healthy food is more perishable	☐	☐
Lengthy preparation of healthy food	☐	☐
Limited storage facilities	☐	☐
Limited cooking facilities	☐	☐
Increased price of healthy foods	☐	☐
Unappealing healthy food	☐	☐
Strange or unusual healthy foods	☐	☐
Feeling conspicuous among others	☐	☐
Taste preferences of family and friends	☐	☐
Not knowing enough about healthy eating	☐	☐
Experts keep changing their minds about healthy foods	☐	☐
Limited healthy choice when I eat out	☐	☐

Healthy options not available in shop or canteen at work	☐	☐
Not enough healthy food to satisfy hunger	☐	☐

17. Do you regularly use olive oil in your diet to replace other fats such as butter? * Required

- ◯ Yes
- ◯ No
- ◯ I don't know

17.a. How much olive oil do you use per day, in approximate tablespoons?

[ ]

18. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, beef or other red meats? * Required

- ◯ Yes, I eat more white meats
- ◯ No, I eat more red meats
- ◯ Not applicable, I'm vegetarian/vegan

19. How many servings of the following foodstuffs do you consume **per day**?

	* Required								
	0	1	2	3	4	5	6	7	More than 7

Vegetables (excluding white potatoes) (1 serving = 80g, or 2 broccoli florets, three heaped tablespoons of cooked vegetables such as carrots, or 3 celery sticks)	○	○	○	○	○	○	○	○	○
Fruit (1 serving = 80g, or 1 banana, 2 kiwis, or 1 heaped tablespoon of sultanas)	○	○	○	○	○	○	○	○	○
Butter, margarine, or cream (1 serving = 10g)	○	○	○	○	○	○	○	○	○

20. How many servings of the following foodstuffs do you consume **per week**?

	* Required								
	0	1	2	3	4	5	6	7	More than 7
Red meat (1 serving = 70g, or three slices of ham)	○	○	○	○	○	○	○	○	○
Soft drinks (1 serving = 150ml)	○	○	○	○	○	○	○	○	○
Wine (1 serving = 125ml)	○	○	○	○	○	○	○	○	○
Legumes (e.g. kidney beans, lentils or chickpeas) (1 serving = 5 heaped tablespoons cooked)	○	○	○	○	○	○	○	○	○
Fish or shellfish (1 serving = 140g)	○	○	○	○	○	○	○	○	○
Cakes, pastries or sweets, which are not homemade	○	○	○	○	○	○	○	○	○
Unsalted nuts (1 serving = 40g)	○	○	○	○	○	○	○	○	○
A meal containing vegetables, pasta, rice, or other dishes seasoned with sauces made with tomato and onion, leek or garlic, and olive oil	○	○	○	○	○	○	○	○	○

Page 7: Debrief sheet

Researcher: Louise Francis

Contact details: louise.francis@northumbria.ac.uk

Supervisor: Dr Jose Lara

Contact details: jose.lara@northumbria.ac.uk

What was the aim of this project?

This project aimed to investigate the current healthy eating advice, the opinions of healthcare professionals on the use of the Mediterranean diet as a novel dietary pattern and the Mediterranean dietary adherence of healthcare professionals.

Have I been deceived in any way during the study?

No deception was used in this study.

How will I find out about the results?

Should you wish to receive information on the results of this study, please email one of the research team using the above email addresses.

What will happen to the information I have provided?

All data will be stored securely and confidentially until a certain time after the study has finished, when it will be destroyed.

How will the results be disseminated?

This research is intended for a PhD project and therefore results may be disseminated in a scientific journal.

How can I register a complaint about this research?

If you have any worries about the way this study was carried out, please do not hesitate to contact one of the research team using the provided email addresses.

Appendix E13: Healthcare professionals' opinions of the MD online survey

Appendix E14:

Dr John K Lodge
Applied Sciences Ethics Representative
Faculty of Health & Life Sciences
Northumberland Building
Newcastle upon Tyne
NE1 8ST

Date: November 2017

Dear Louise

Faculty of Health and Life Sciences Research Ethics Committee

Submission Code: 726

Title: Investigating the opinions of healthcare professionals on the use of the Mediterranean diet in the treatment of obesity and Type 2 Diabetes Mellitus

Following independent peer review of the above proposal I am pleased to inform you that Departmental (and thus) Faculty approval has been granted for this proposal - subject to compliance with the University policies on ethics and consent and any other policies applicable to your individual research.

NB. If your research involves working with children and/or vulnerable adults you should also have recent Disclosure & Barring Service (DBS) and occupational health clearance.

The University's Policies and Procedures are available from the following web link: http://www.northumbria.ac.uk/researchandconsultancy/sa/ethgov/policies/?view=Standard

All researchers must give notice of the following:

- Any significant changes to the study design;
- Any incidents which have an adverse effect on participants, researchers or study outcomes;
- Any suspension or abandonment of the study;

Please keep this letter with your application as proof of ethical clearance and for any future auditing requirements. We wish you well in your research endeavours.

Yours sincerely,

Dr John K Lodge
Department of Applied Sciences Ethics Representative

Appendix E14: Northumbria University ethical approval for healthcare professionals' online survey

Appendix E15:

NHS
Health Research Authority

Dr Jose Lara
Department of Applied Sciences, Faculty of Health and Life Sciences
Northumbria University
Ellison Building, Room A324
NE1 8ST

Email: hra.approval@nhs.net

18 April 2018

Dear Dr Lara

Letter of HRA Approval

Study title:	**Investigating the opinions of healthcare professionals on the use of the Mediterranean diet in the treatment of obesity and Type 2 Diabetes Mellitus.**
IRAS project ID:	**231487**
Sponsor	**Northumbria University**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further from the HRA.

Appendix E15: Health Research Authority approval for healthcare professionals' online survey

Appendix E16:

Dear Dr Lara,

<u>**Confirmation of Capacity and Capability at The Newcastle upon Tyne Hospitals NHS Foundation Trust**</u>

Study Title: **Investigating the opinions of healthcare professionals on the use of the Mediterranean diet**
IRAS ID: **231487**
R&D Ref: **08855**
Site for Recruitment to CPMS: **The Royal Victoria Infirmary**

This email confirms that **The Newcastle upon Tyne Hospitals NHS Foundation Trust** has the capacity and capability to deliver the above referenced study. You may now begin to work on this study. Please find attached the finalised HRA Statement of Activities.

Best Wishes,

Karen Verrill
Research Governance Specialist
Newcastle Joint Research Office
Level 1, Regent Point
Regent Farm Road
Gosforth
Newcastle upon Tyne
NE3 3HD

Tel: 0191 2823070 Uni ext 21-23070
E-mail: Karen.Verrill2@nuth.nhs.uk

If your query relates to a Freedom of Information request, please re-direct your query to rec-man@ncl.ac.uk

Please consider the environment before you print this email.

NJRO Website: https://microsites.ncl.ac.uk/njro/

Newcastle Joint Research Office

Appendix E16: Newcastle City Hospitals Capacity and Capability confirmation

Appendix E17:

Dear Louise

IRAS ID: 231487
R&I Ref: 1906

Study Title: Healthcare professionals' knowledge of the Mediterranean diet -version1

This email confirms that City Hospitals Sunderland NHS Foundation Trust has the Capacity and Capability to deliver the above referenced study.

Recruitment should not start until you have been given the go ahead (green light) from the trial team. Please notify R&I of this date.

The generic patient information sheet and consent form templates must be localised using City Hospitals Sunderland letterhead and contain contact details for research staff prior to use.

PLEASE NOTE: When uploading recruitment, please use the following ODS codes to reflect site activity: for studies taking place at Sunderland Royal Hospital, please use "RLNGL" and for studies taking place at Sunderland Eye Infirmary, please use "RLNGM".

Thank you for your support.

Pauline Atkinson
Research and Innovation Officer | City Hospitals Sunderland NHS Foundation Trust
Tel: 0191 5656256 | Email: Pauline.atkinson@chsft.nhs.uk
Web: www.chsft.nhs.uk
Main office base: Ext 42143

Appendix E17: Sunderland City Hospitals Capacity and Capability confirmation

10.6. Appendix F

Appendix F18:

Dr John K Lodge
Applied Sciences Ethics Representative
Faculty of Health & Life Sciences
Northumberland Building
Newcastle upon Tyne
NE1 8ST

Dear Louise

Faculty of Health and Life Sciences Research Ethics Committee

Submission Code: 4413

Title: A pilot study investigating the acceptability and impact of the Mediterranean diet and intermittent fasting

Following independent peer review of the above proposal I am pleased to inform you that Departmental (and thus) Faculty approval has been granted for this proposal - subject to compliance with the University policies on ethics and consent and any other policies applicable to your individual research.

NB. If your research involves working with children and/or vulnerable adults you should also have recent Disclosure & Barring Service (DBS) and occupational health clearance.

The University's Policies and Procedures are available from the following web link: http://www.northumbria.ac.uk/researchandconsultancy/sa/ethgov/policies/?view=Standard

All researchers must give notice of the following:
- Any significant changes to the study design;
- Any incidents which have an adverse effect on participants, researchers or study outcomes;
- Any suspension or abandonment of the study;

Please keep this letter with your application as proof of ethical clearance and for any future auditing requirements. We wish you well in your research endeavours.

Yours sincerely,

Dr John K Lodge
Department of Applied Sciences Ethics Representative

Appendix F18: Northumbria University ethical approval for pilot study

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Templeman, 2018	Intermittent fasting, energy balance and associated health outcomes in adults: study protocol for a randomised controlled trial	1	Intermittent fasting with calorie restriction = alternate between 24-hour periods of fasting and feeding to 150% of habitual daily energy intake. Intermittent fasting without calorie restriction = alternate between 24-hour periods of fasting and feeding to 200% of habitual daily energy intake. Water, herbal teas and black tea/coffee with no sugar (i.e. unsweetened energy-free drinks) during fasting cycles.	None given.
Kessler, 2018.	A non-randomized controlled clinical pilot trial on 8 wk of intermittent fasting (24 h/wk)	1	Abstinence from solid food between 00:00 and 23:59 at minimum, and a maximum caloric intake of 300 kcal on each fasting day.	Participants in the fasting group were asked to continue their regular nutritional habits on the non-fasting days.
Arnason, 2017	Effects of intermittent fasting on health markers in those with type 2 diabetes: A pilot study	18-20 hours/day	*Ad libidum* zero-calorie coffee, tea, and water intake during fasting hours being permitted.	Participants were allowed to eat whatever they chose during non-fasting hours, but were encouraged to include at least 1/3 plate of protein to promote satiety.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Schubel, 2016	The effects of intermittent calorie restriction on metabolic health: Rationale and study design of the HELENA Trial	2 non-consecutive	Meals on the energy-restricted days are based on a list with pre-selected food items sorted by different food groups. Participants are asked to choose four food items out of the vegetable group, two out of the low-fat dairy product group and one food item out of each the meat/fish, carbohydrate and fruit group. For exact weighing of the food quantity that is required to meet the target calorie amount participants are provided with a digital kitchen scale. In general a daily intake of a minimum of 2 litres of low-energy drinks (water, caffeine-free and unsweetened beverages) is recommended.	Eu-caloric healthy balanced diet (calorie intake: 100%). For the five eu-caloric days, the dietitian provides individualized counseling regarding adherence to food choices according to the recommendations of the German Nutrition Society for a healthy balanced diet.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Zuo, 2016	Comparison of High-Protein, Intermittent Fasting Low-Calorie Diet and Heart Healthy Diet for Vascular Health of the Obese.	1	On the one IF day per week, daily energy intake consisted of 330 and 430 kcal for women and men, respectively.	High protein-low calorie (HP-LC) diet 6 days per week. In order to induce an energy deficit without compromising lean body mass, the daily macronutrient distribution (30% protein, 45% carbohydrate, and 25% fat) has been used in this phase based on our previous study (Arciero et al., 2014). Total energy intake during HP-LC was 1200 and 1500 kcal per day for females and males, respectively. (The composition for the HP-LC diet is shown in Fig. A) The eating schedule was designed to produce a regular frequency of meals and protein consumption during the weight loss and weight loss maintenance interventions. During the weight loss phase, each meal consisted of approximately 20–30 g servings of high-quality protein in either whole food or supplement form. Subjects were told to eat 4–5 meals per day on HP-LC days.
Antoni, 2016	Investigation into the acute effects of total and partial energy restriction on postprandial metabolism among overweight/obese participants	ER: participants started their fast from 20.00 hours the night before their dietary intervention	Partial (75%) ER: participants consumed four commercially available LighterLife™ FoodPacks (2638 kJ, 58 g carbohydrate (37% of total energy), 54 g protein (35% of total energy), 17 g fat (28% of total energy)), which provided approximately 25% of their estimated isoenergetic needs. The degree of ER chosen is comparable with that used by previously published IER weight loss trials.	Isoenergetic control diet (0% ER): each participant was supplied with an isoenergetic diet comprised of commonly consumed food and drinks (11 040kJ), 327g carbohydrate (55% of total energy), 99g protein (15% of total energy) and 97g fat (30% of total energy)) providing 100% of their estimated isoenergetic needs.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
		day until 08.00 hours on the morning of their study day, totalling 36 h.		
Taylor, 2015	Determining how best to support overweight adults to adhere to lifestyle change: protocol for the SWIFT study	2 non-consecutive	Energy intake cannot exceed 2 (females) – 2.5 (males) MJ. In practice, this usually means a small breakfast (e.g. plain porridge), no or limited food during the day, and non-starchy vegetables only for the evening meal, although other variations are possible.	Participants can eat *ad libitum* on the remaining days.
Teng, 2013	Improvement of metabolic parameters in healthy older adult men following a fasting calorie restriction intervention	2	Muslim Sunnah fasting combined with a reduction of 300–500 kcal/d from the habitual energy intake. During fasting day, subjects needed to take a light meal before sunrise (Sahur), no food and drink on the day was allowed (approximately for 13 h) and a complete meal after sunset (Iftar). During fasting day, smoking was also forbidden.	On the other days, subjects must reduce their dietary intake by 500 kcal/d.
Hussin, 2013	Efficacy of fasting and calorie restriction on mood and depression among ageing men	2	Muslim Sunnah fasting combined with a reduction of 300 to 500 kcal/day from baseline energy intake.	On the other days, subjects must reduce their dietary intake by 500 kcal/d.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Arciero, 2016	Protein-Pacing Caloric-Restriction Enhances Body Composition Similarly in Obese Men and Women during Weight Loss and Sustains Efficacy during Long-Term Weight Maintenance	1	Six servings of an antioxidant-rich beverage providing 120 kcals, three servings of low-glycemic protein wafers providing 90 kcal, and a 100 or 200 kcal whole-food, high protein snack for women and men, respectively. Total caloric intake on IF days was approximately 350–450 kcals for women and men, respectively. All subjects also consumed a daily micronutrient supplement pack containing a combination of minerals and vitamins, phytonutrients/antioxidants, and essential fatty acids along with a nutrient-rich herbal tonic.	None given.
Ash, 2003	Effect of intensive dietetic interventions on weight and glycaemic control in overweight men with Type II diabetes: a randomised trial	4	Liquid meal replacement formula (Modifasts, Novartis Ltd, Melbourne, Australia), providing 4180 kJ/day (1000 kcal/day),	*Ad libitum* eating similar to the dietary stabilisation phase was encouraged so that energy intake averaged 6000–7000 kJ/day (1400–1700 kcal/day) over the week.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Bhutani, 2010	Improvements in Coronary Heart Disease Risk Indicators by Alternate-Day Fasting Involve Adipose Tissue Modulations	ADF	25% of baseline energy needs. All food was provided on each fast day to ensure that subjects were meeting their energy restriction goal for that day. Provided as a 3-day rotating menu, and dietary carbohydrate, fat and protein accounted for ~55, 25, and 20% of ingested energy, respectively. The feed/fast days began at midnight each day, and all fast day meals were consumed between 12:00pm and 2:00pm to ensure that each subject was undergoing the same duration of fasting. Subjects were encouraged to drink plenty of water and were permitted to consume energy-free beverages such as tea and coffee on the fast days.	*Ad libitum.*
Eshghinia, 2013	The effects of modified alternate-day fasting diet on weight loss and CAD risk factors in overweight and obese women	3	All subjects consumed very low calorie diet (25 to 30% energy needs). Energy free beverage (such as water, tea, green tea, coffee without sugar), non-starchy vegetable (such as lettuce, cucumber, green leaf, tomato) and sugar free gums were free. Daily dietary carbohydrate, fat and protein accounted for 55, 25, and 20% of ingested energy, respectively.	Usual diet based on the "Key Recommendations of Dietary Guidelines for Americans" 1700–1800 Kcal/d. On Friday subjects consume ad libitum without limitation.
Halberg, 2005	Effect of intermittent fasting and refeeding on insulin action in healthy men	1	Each fasting period started at 2200 and ended at 1800 the following day. During the fasting periods the subjects were allowed to drink water and were instructed to maintain habitual activities.	None given.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Harvie, 2013	The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women	2 consecutive	70% energy restriction and 40g carbohydrate. 2500-2717kJ with approximately 250 g of protein foods including lean meat, fish, eggs, tofu, textured vegetable protein, three servings of low-fat dairy foods (e.g. 195ml semi skimmed milk, 150g low-fat yoghurt, 30g low-fat cheese), four portions of low-carbohydrate vegetables and one portion of low-carbohydrate fruit, at least 1170 ml of other low-energy fluids, and an over-the-counter multivitamin and mineral supplement providing the RDA for vitamins and typically 20–50% for minerals on restricted days.	Euenergetic Mediterranean-type diet that met their estimated energy requirements.
Heilbronn, 2005	Glucose Tolerance and Skeletal Muscle Gene Expression in Response to Alternate Day Fasting	ADF	Consume energy-free beverages, tea, coffee, and sugar-free gum.	Subjects were informed that they could eat whatever they wished and that double their usual intake would be required to maintain body weight.
Hoddy, 2015	Changes in hunger and fullness in relation to gut peptides before and after 8 weeks of alternate day fasting	ADF	25% of baseline energy needs. Meals were provided. The macronutrient distribution: ~24% kcal as fat, ~16% kcal as protein, and ~60% kcal as carbohydrates. Participants visited the research centre on a weekly basis to pick up their meals for the week. Subjects were allowed to consume zero-calorie beverages, such as black coffee, tea and diet soda, on the fast day.	*Ad libitum* food intake.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
Johnson, 2007	Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma	ADF	Women were instructed to consume 320 calories and men 380 calories of a commercially available canned meal replacement shake.	*Ad libitum* - whatever they normally ate and to the point of satisfaction but not to intentionally overeat.
Keogh, 2014	Effects of intermittent compared to continuous energy restriction on short-term weight loss and long-term weight loss maintenance	7	5500 kJ ER for 1 week, followed by 1 week of their usual diet.	5500 kJ ER continuously for the duration of the study. Both groups followed an energy restricted diet based upon the 'Total Wellbeing Diet' portion and recipe system from the Commonwealth Scientific and Industrial Research Organisation (CSIRO).
Klempel, 2010	Dietary and physical activity adaptations to alternate day modified fasting: implications for optimal weight loss	ADF	25% of baseline energy needs. Meals provided.	*Ad libitum* food intake.
Varady, 2009	Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and	ADF	25% of baseline energy needs. Meals provided, allowed to consume energy-free beverages, tea, coffee, and sugar-free gum and were encouraged to drink plenty of water.	*Ad libitum* - instructed to limit fat intake to <30% of energy needs by choosing low-fat meat and dairy options.

Author, year	Title	Days/week	Guidelines for fasting days	Guidelines for non-fasting days
	cardioprotection in obese adults			

Appendix F19: Data gathered to inform decision on type of fasting to investigate

Appendix F20:

Author, year	Title	Mediterranean diet	Control diet
Ambring, 2004/2006	Mediterranean-inspired diet lowers the ratio of serum phospholipid n-6 to n-3 fatty acids, the number of leukocytes and platelets, and vascular endothelial growth factor in healthy subjects	Twice the amount of fibre than the control, 3–4 times as many antioxidants, almost 3 times the amount of PUFAs and twice the amount of n–3 fatty acids, one-half the amount of saturated fat, one-half the amount of cholesterol, and a 35% reduction in the glycemic index. In addition, sterol esters were included as an ingredient in the margarine (2 g/d) only during the MID. The amount of calories, proteins, carbohydrates, and total of fat was similar between the 2 diets.	Ordinary Swedish diet i.e. macronutrient composition (16%, 48%, 34%, and 2% of energy from protein, carbohydrates, fat, and alcohol), dietary fatty acids (15%, 13%, 5%, and 1% of energy from saturated, monounsaturated, n–6 PUFAs, and n–3 PUFAs), dietary cholesterol (321 g), and fiber (17 g).
Bihuniak, 2016	Adherence to a Mediterranean-Style Diet and Its Influence on Cardiovascular Risk Factors in Postmenopausal Women	Incorporation of 3tbsp EVOO daily; 3 to 5 servings/wk of high n-3 fish (eg, salmon or tuna); 1.5 oz Diamond walnuts daily; and increased amounts of fruits, vegetables (goal of 5 servings/day), and whole grains.	Usual diet.
Brehm, 2009	One-Year Comparison of a High–Monounsaturated Fat Diet With a High-Carbohydrate Diet in Type 2 Diabetes	45% CHO, 15% protein, and 40% fat (with 20% MUFA).	High carbohydrate diet: 60% CHO, 15% protein, and 25% fat
Choudhury, 2014	An almond-enriched diet increases plasma α-tocopherol and improves vascular	Substitute any daily snack for two bags of almonds (50g).	Usual diet.

Author, year	Title	Mediterranean diet	Control diet
	function but does not affect oxidative stress markers or lipid levels		
Djuric, 2009	A Mediterranean dietary intervention in healthy American women changes plasma carotenoids and fatty acids in distinct clusters	PUFA/saturated fatty acid (SFA)/MUFA ratio of 1:2:5. Increase fruits and vegetables consumption by substituting fruits and vegetables for other carbohydrates. The fruits and vegetable goal was 7 to 9 servings per day, depending on energy intake, in specified variety: at least once serving daily from each of the following groups: vitamin C fruit, other fruit, red vegetable, dark orange vegetable, dark green vegetable, other vegetable, allium vegetable, and dark green herb.	National Cancer Institute's Action Guide to Healthy Eating.
Lee, 2015	Switching to a 10-day Mediterranean-style diet improves mood and cardiovascular function in a controlled crossover study	Increased consumption of fruits, vegetables, oily fish, low-fat dairy, and nuts, focusing on foods that provided a source of carbohydrates, protein, and healthy fats. Ensure all foods were freshly prepared, and exclude all pre-prepared, packaged, and processed foods. Abstain from consuming meat, butter and margarine, caffeinated/energy drinks, added sugars and salts, alcohol, and the use of tobacco or illicit drugs.	Usual diet.
Richard, 2011	Effect of the Mediterranean diet with and without weight	Traditional MD.	North American control, isocaloric, weight-maintaining conditions.

Author, year	Title	Mediterranean diet	Control diet
	loss on cardiovascular risk factors in men with the metabolic syndrome		
Ryan, 2013	The Mediterranean diet improves hepatic steatosis and insulin sensitivity in individuals with non-alcoholic fatty liver disease	Reconstruction of the traditional Cretan MD, using detailed descriptive food data reported in the Seven Countries Study. Traditional recipes and food preparation techniques were sourced from Cretan cook books. High in MUFA from olive oil and contained ω3PUFA from both plant and marine sources. 40% energy from fat (MUFA and ω3PUFA), 40% from carbohydrate, and 20% from protein.	Based on both the Australian National Heart Foundation Diet and the American Heart Association Diet. Low in saturated and unsaturated fat and higher in carbohydrate than the MD. The small amount of fat that was included was predominantly ω6 PUFAs. It was also high in wholegrain carbohydrate foods and had an approximate macronutrient composition of 30% energy from fat, 50% from carbohydrate, and 20% from protein.
Singh, 2002	Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial.	Less than 30% of energy from total fat, less than 10% from saturated fat, less than 300 mg of cholesterol consumed per day. 250–300g of fruit, 125–150g of vegetables, and 25–50g of walnuts or almonds. 400–500g/d of whole grains, legumes, rice, maize, and wheat daily, as well as mustard seed or soy bean oil, in 3-4 servings/d.	National Cholesterol Education Program (NCEP). This diet recommends that less than 30% of energy comes from total fat, less than 10% from saturated fat, and that less than 300 mg of cholesterol is consumed per day.
Stendell-Hollis, 2013	A comparison of Mediterranean-style and MyPyramid diets on weight loss and inflammatory biomarkers in postpartum breastfeeding women.	Plant-based; study-provided walnuts (28 g/day), 1–2 tablespoons/day of olive oil (refined or virgin), and ≥7 servings/day of fruits and vegetables. ≥6 servings of whole grains per day and ≥2 servings of fish per week and to increase consumption of legumes while limiting the intake of whole fat dairy products, red	Diet recommended for lactation as described by the USDA MyPyramid for Pregnancy and Breastfeeding.

Author, year	Title	Mediterranean diet	Control diet
		meats, processed foods, desserts, and sources of fat in the diet other than olive oil.	
Thomazella, 2011	Effects of High Adherence to Mediterranean or Low-Fat Diets in Medicated Secondary Prevention Patients.	Daily consumption of unrefined cereals and products (e.g., whole-grain bread, pasta, brown rice); fresh fruits (4 to 6 servings/day); varied raw or cooked vegetables and legumes (2 to 3 servings/day); extra-virgin olive oil (30 ml/day) as the main added fat; non-fat or low-fat dairy products (1–2 servings/day) and nuts (10 g/day); weekly consumption of fish (3 to 4 times/week), poultry (3 to 4 times/week), and eggs (0 to 4 per week) and low red meat consumption (once a week). Sweets were allowed only a few times per month; red wine consumption (250 ml/day).	Advised to follow recommendations according to the National Cholesterol Education Program Third Adult Treatment Panel: decreased fat intake, particularly saturated and trans-fatty acids; increased intake of fruits, vegetables, legumes, whole grains, fat-free and low-fat dairy products; moderate amount of lean meat, fish, or poultry; and vegetable oil for cooking.
Toobert, 2003	Long-term effects of the Mediterranean lifestyle program: a randomized clinical trial for postmenopausal women with type 2 diabetes	More bread, more root vegetables, green vegetables, and legumes, more fish, less red meat, replaced by poultry, daily fruit, and avoidance of butter and cream, to be replaced by olive/canola oil or olive/canola-based margarine.	Usual diet.
Davis, 2016	A Mediterranean diet lowers blood pressure and improves endothelial function: results from the MedLey randomized intervention trial.	>1tbsp/d extra-virgin olive oil, 5–6 servings vegetables/d, ≥2 servings fresh fruit/d, 4–6 servings wholegrain cereals/d, 4–6 servings nuts/wk, 3 servings legumes/wk, 3 servings fish (1 oily)/wk, <1	Usual diet.

Author, year	Title	Mediterranean diet	Control diet
		serving red meat/wk, limit consumption of discretionary foods to ≤3 times/wk.	
Entwhistle, 2018	Adherence to Mediterranean and low-fat diets among heart and lung transplant recipients: a randomized feasibility study.	Daily mixed consumption of a range of vegetables, fruit, wholegrains, fish/seafood, raw nuts and legumes; abundant use of extra-virgin olive oil, moderate consumption of dairy products and red wine, low intake of red and processed meats, of sweets, sweet-baked pastries and sweetened beverages.	Low-fat diet. Modified British Heart Foundation low-fat guidelines with an emphasis on consuming mainly plant-based wholefoods similar to the Mediterranean diet, with advice to minimize high-fat foods such as processed meats, commercially baked pastries and desserts, and vegetable oils and spreads.
Sotos-Prieto, 2017	Rationale and design of feeding America's bravest: Mediterranean diet-based intervention to change firefighters' eating habits and improve cardiovascular risk profiles.	Olive oil (extra virgin if possible) as main culinary fat or ≥ 4 tbsp/day, tree nuts and peanuts (peanut butter without hydrogenated fat): ≥ 3 servings/wk, fresh fruit: ≥ 3 servings/day, vegetables: ≥ 2 servings/day, fish (including fatty fish) and seafood: ≥ 3 servings/wk, legumes: ≥ 3 servings/wk, sofrito: ≥ 2 servings/wk, fresh herbs, allium: ≥ 2 servings/day, yogurt: ≤ 2 servings/day, white meat instead of red meat (2–3 servings/wk), whole grains/cereals instead of refined grains, wine with meals (optional, only for habitual drinkers): ≥ 7 glasses/wk. Soda drinks: < 1 drink/day, spread fats: < 1 serving/day, red and processed meats≤ 2 servings/wk, commercial bakery foods sweets, and pastries: < 3 servings/wk, fast food: ≤ 1/wk.	Usual diet.

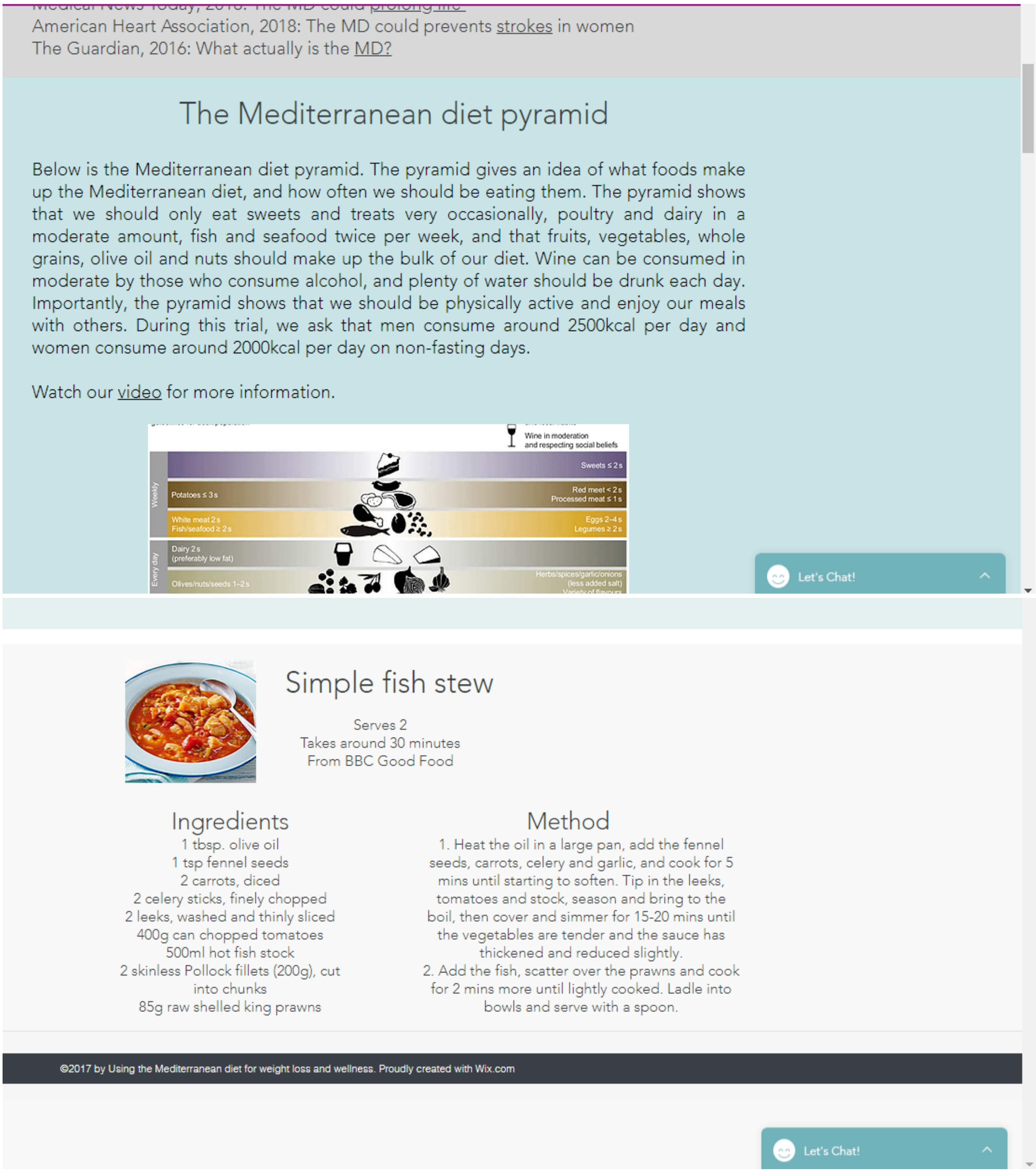
Author, year	Title	Mediterranean diet	Control diet
Tussing-Humpherys, 2017	Building research in diet and cognition: The BRIDGE randomized controlled trial	6–10 exchanges of a variety of non-starchy fruits and vegetables; 5–11 of grain foods, with an emphasis on whole grain selections; 2–4 of low-fat dairy; 5–6 oz of lean or very lean poultry, meat, or seafood; and at least one exchange of tree nuts per day and 1–2 of red wine with meal. Olive oil as the main fat; 2 tablespoons daily. Consumption of fast foods, red and processed meats, fried foods, pastries, typical snacks, refined carbohydrates, sugared beverages, and high-fat dairy foods are discouraged.	Usual diet with weekly health-related newsletters (e.g., dental health, flu facts, poison control, and sun safety).
Davis, 2017	A Mediterranean Diet Reduces F2-Isoprostanes and Triglycerides among Older Australian Men and Women after 6 Months	High in extra-virgin olive oil, vegetables, fruit, nuts, whole grains, legumes, and fish as core foods. Moderate in red wine and dairy foods (primarily cheese and yogurt) and contained small amounts of red meat, small goods (salami, mettwurst, bacon, and other processed meats), and discretionary foods.	Usual diet.
Due, 2017	The effect of three different ad libitum diets for weight loss maintenance: a randomized 18-month trial	Moderate fat (35–45 E%), high in MonoUnsaturated Fatty Acid (>20 E%).	35% of energy from fat with >15% of energy from saturated fatty acid.
Torres-Peña, 2018	Mediterranean diet improves endothelial function in patients with diabetes and prediabetes:	Rich in fat from olive oil, with 35% of calories from fat (22% monounsaturated, 6% polyunsaturated, 7% saturated), and 50% from carbohydrates. Abundant use of virgin olive oil for cooking and dressing of	Low-fat diet, with 28% of calories from fat (12% monounsaturated, 8% polyunsaturated, 8% saturated) and 55% of calories from carbohydrates.

Author, year	Title	Mediterranean diet	Control diet
	A report from the CORDIOPREV study.	salads, consumption of two or more servings (125 g/serving) per day of vegetables (at least one of them as salad), three or more servings (125 g/serving) per day of fresh fruit, three or more servings (40 g/serving) per week of legumes; three or more servings (150 g/serving) per week of fish or seafood, three or more servings (25 g/serving) per week of nuts or seeds, white meats instead of red meats or processed meats and regular preparation of a homemade sofrito. Optionally a moderate consumption of red wine (7 glasses/week). Avoid and limit the consumption of butter, cream, fast food, sweets, pastries and sugar-sweetened beverages.	
Assaf-Balut, 2017	A Mediterranean diet with additional extra virgin olive oil and pistachios reduces the incidence of gestational diabetes mellitus (GDM): A randomized controlled trial: The St. Carlos GDM prevention study.	≥2 servings/day of vegetables, ≥3 servings/day of fruit (avoiding juices), three servings/day of skimmed dairy products, wholegrain cereals, 2-3 servings of legumes/week, moderate to high consumption of fish; a low consumption of red and processed meat, avoidance of refined grains, processed baked goods, pre-sliced bread, soft drinks and fresh juices, fast foods and precooked meals.	Given MD guidelines, but advised by midwives to restrict consumption of dietary fat, including EVOO and nuts. These recommendations are provided in local antenatal clinics as part of the available guidelines in pregnancy standard care.
Estruch, 2013	Primary Prevention of Cardiovascular Disease with a Mediterranean Diet.	High intake of olive oil, fruit, nuts, vegetables, and cereals; a moderate intake of fish and poultry; a low intake of dairy products, red meat, processed meats,	Low-fat diet.

Author, year	Title	Mediterranean diet	Control diet
		and sweets; and wine in moderation, consumed with meals.	
Maiorino, 2016	Mediterranean diet cools down the inflammatory milieu in type 2 diabetes: the MÉDITA randomized controlled trial.	No more than 50% of daily energy from carbohydrates and no less than 30% energy from fat.	Low fat diet with no more than 30% of energy from fat.

Appendix F20: Table of MD intervention trials published since 2000 used to decide upon MD and control diet employed in pilot study

Appendix F21:


American Heart Association, 2018: The MD could prevents strokes in women
The Guardian, 2016: What actually is the MD?

The Mediterranean diet pyramid

Below is the Mediterranean diet pyramid. The pyramid gives an idea of what foods make up the Mediterranean diet, and how often we should be eating them. The pyramid shows that we should only eat sweets and treats very occasionally, poultry and dairy in a moderate amount, fish and seafood twice per week, and that fruits, vegetables, whole grains, olive oil and nuts should make up the bulk of our diet. Wine can be consumed in moderate by those who consume alcohol, and plenty of water should be drunk each day. Importantly, the pyramid shows that we should be physically active and enjoy our meals with others. During this trial, we ask that men consume around 2500kcal per day and women consume around 2000kcal per day on non-fasting days.

Watch our video for more information.

Simple fish stew

Serves 2
Takes around 30 minutes
From BBC Good Food

Ingredients
1 tbsp. olive oil
1 tsp fennel seeds
2 carrots, diced
2 celery sticks, finely chopped
2 leeks, washed and thinly sliced
400g can chopped tomatoes
500ml hot fish stock
2 skinless Pollock fillets (200g), cut into chunks
85g raw shelled king prawns

Method
1. Heat the oil in a large pan, add the fennel seeds, carrots, celery and garlic, and cook for 5 mins until starting to soften. Tip in the leeks, tomatoes and stock, season and bring to the boil, then cover and simmer for 15-20 mins until the vegetables are tender and the sauce has thickened and reduced slightly.
2. Add the fish, scatter over the prawns and cook for 2 mins more until lightly cooked. Ladle into bowls and serve with a spoon.

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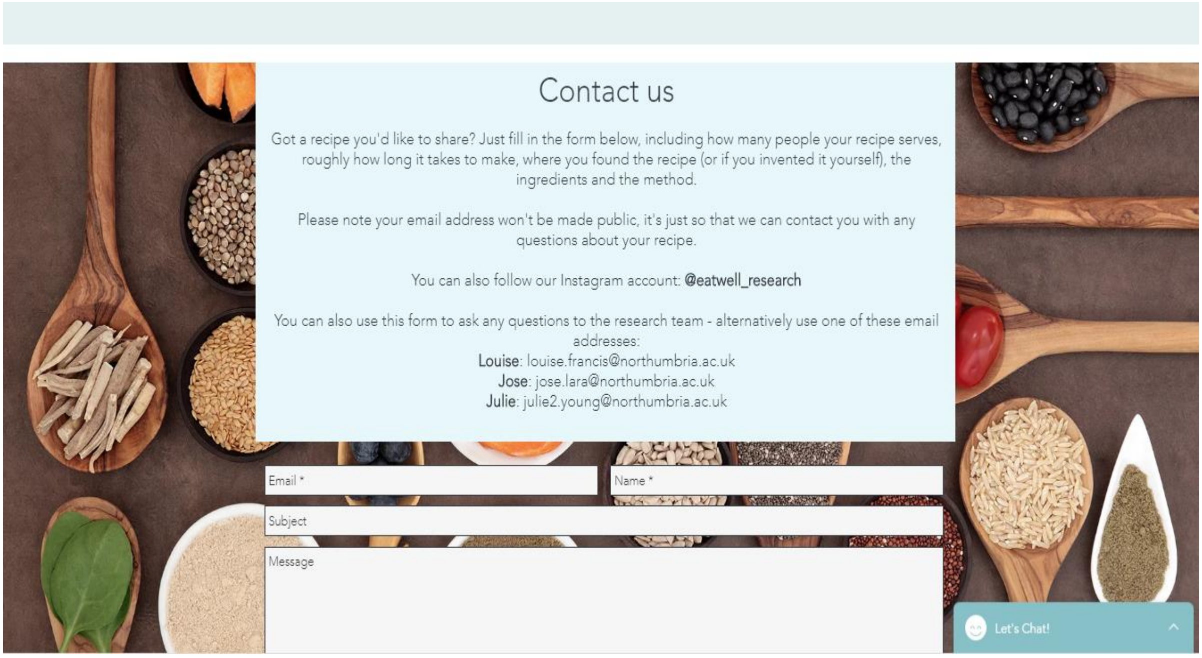
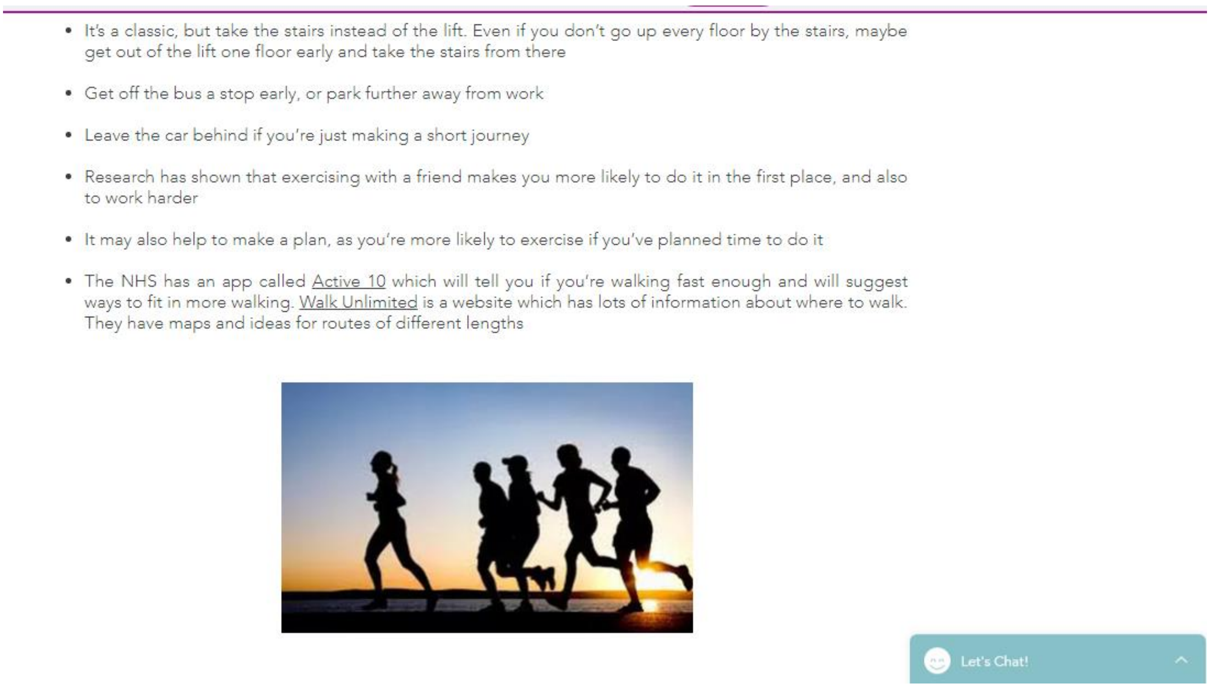
Appendix F21: Example screenshots from the MD website, showing a recipe and dietary information

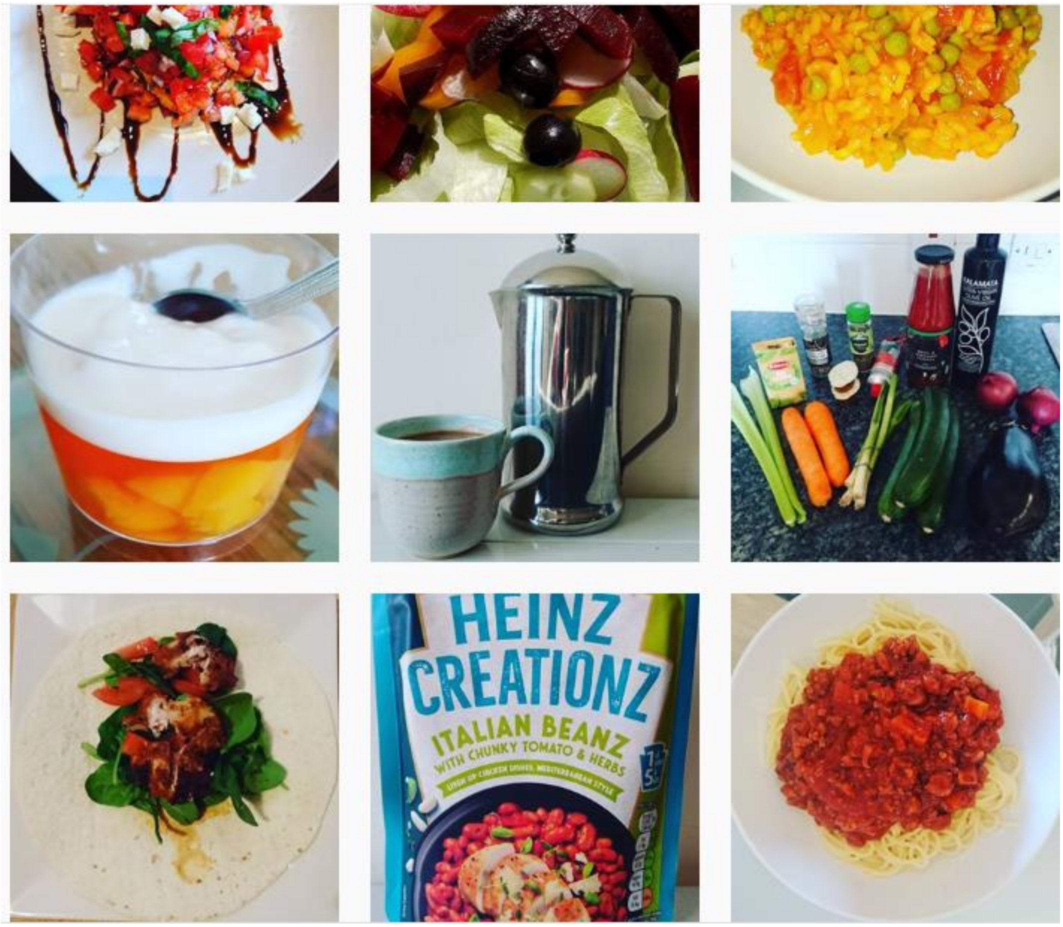
Appendix F22:





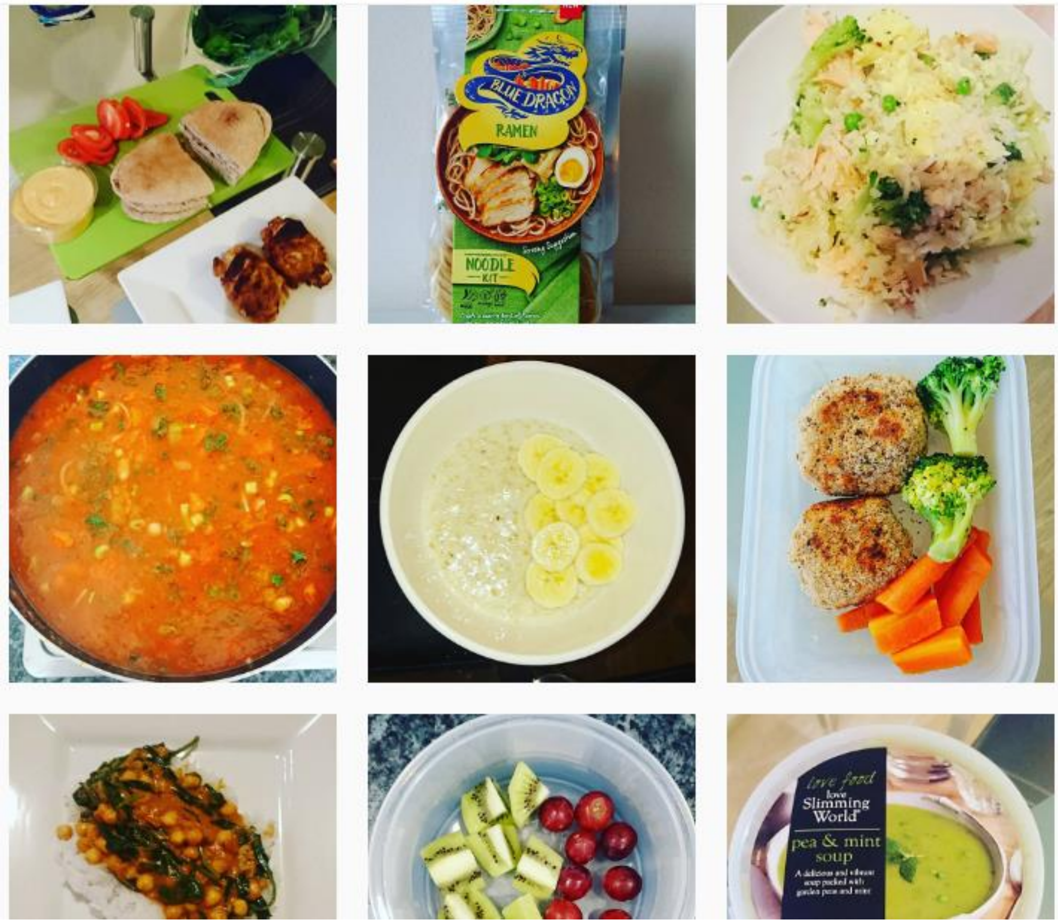
Appendix F22: Example screenshots from the EG website, showing physical activity information and the 'contact us' page

Appendix F23:



Appendix F23: Example photographs uploaded to the MD social media account

Appendix F24:



Appendix F24: Example photographs uploaded to the EG social media account

10.7. Appendix G

Appendix G25:

Dietary component (EMM±SEM)	ITT							PP						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Energy (kcal)	1932.40 ± 101.50	1765.30 ± 126.33	0.052	2155.80 ± 363.62	1980.92 ± 361.00	0.155	0.576	1798.46 ± 143.72	1568.18 ± 172.13	0.118	1831.67 ± 218.20	1549.37 ± 146.29	0.173	0.934
Energy (kj)	8107.60 ± 425.71	7413.80 ± 530.00	0.054	7740.10 ± 575.90	6945.68 ± 430.56	0.123	0.497	7542.55 ± 601.43	6587.10 ± 720.54	0.124	7789.50 ± 924.91	6503.04 ± 612.32	0.136	0.930
Protein (g)	80.25 ± 4.42	82.00 ± 4.90	0.696	72.90 ± 5.18	72.31 ± 4.75	0.931	0.164	71.00 ± 5.25	79.27 ± 6.40	0.227	77.00 ± 7.71	76.11 ± 6.89	0.939	0.741
Fat (g)	75.38 ± 6.03	65.88 ± 6.23	**0.030***	72.00 ± 5.77	67.11 ± 5.52	0.314	0.884	69.32 ± 9.01	56.46 ± 7.52	0.076	69.07 ± 8.07	61.45 ± 6.92	0.353	0.630
Carbohydrate (g)	203.10 ± 16.00	196.35 ± 15.83	0.637	207.75 ± 17.89	180.08 ± 13.22	0.125	0.435	181.55 ± 21.54	171.91 ± 19.43	0.719	209.00 ± 28.02	160.38 ± 16.85	0.119	0.657
Alcohol (g)	8.50 ± 3.65	8.32 ± 3.23	0.950	7.83 ± 4.51	5.96 ± 2.50	0.441	0.566	7.51 ± 4.80	7.83 ± 4.26	0.952	9.35 ± 7.49	7.34 ± 4.00	0.616	0.935

Sugars (g)	90.65 ± 8.90	85.19 ± 9.12	0.384	84.81 ± 12.20	72.08 ± 7.08	0.212	0.264	77.91 ± 8.09	71.44 ± 7.62	0.571	94.88 ± 19.15	73.42 ± 10.26	0.212	0.880
Fibre (g)	19.91 ± 1.54	22.07 ± 1.73	0.160	17.30 ± 1.26	19.09 ± 1.76	0.263	0.235	18.96 ± 2.12	22.10 ± 2.34	0.229	17.33 ± 1.98	20.04 ± 2.81	0.317	0.584
Saturated fat (g)	27.95 ± 2.14	23.22 ± 2.82	**0.015***	24.21 ± 1.88	22.66 ± 2.34	0.428	0.879	27.03 ± 2.43	20.27 ± 3.48	**0.031***	23.41 ± 2.32	21.00 ± 3.18	0.468	0.881
MUFA (g)	18.41 ± 1.34	16.80 ± 1.71	0.146	21.75 ± 2.20	21.17 ± 1.86	0.767	0.091	18.03 ± 1.98	16.53 ± 2.44	0.349	19.74 ± 2.84	18.75 ± 1.94	0.763	0.481
PUFA (g)	7.87 ± 0.81	7.00 ± 0.75	0.056	10.73 ± 1.29	10.03 ± 1.23	0.603	**0.042***	8.15 ± 1.37	7.26 ± 1.12	0.201	9.90 ± 1.85	8.83 ± 1.65	0.643	0.451
Water content (g)	2667.65 ± 183.60	2564.20 ± 246.78	0.697	2123.55 ± 203.89	2149.42 ± 269.50	0.900	0.263	2439.18 ± 148.12	2549.18 ± 361.56	0.787	2329.75 ± 253.11	2364.88 ± 389.62	0.921	0.734
Cholesterol (mg)	237.01 ± 31.74	211.00 ± 30.37	0.460	161.92 ± 23.93	201.44 ± 29.53	0.188	0.823	200.100 ± 35.44	208.52 ± 39.77	0.830	163.42 ± 25.22	229.87 ± 36.11	0.188	0.694

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix G25: Unadjusted estimated marginal means and standard errors of macronutrient intake from general linear model repeated measures by study group for ITT and PP

Appendix G26:

Dietary component (EMM±SEM)	ITT							PP						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 11)			MD (n= 12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Vitamin D (ug)	1.88 ± 0.40	2.50 ± 0.72	0.285	2.06 ± 0.40	2.59 ± 0.38	0.205	0.909	1.76 ± 0.51	1.73 ± 0.49	0.958	2.67 ± 0.615	2.91 ± 0.539	0.695	0.275
Selenium (ug)	33.74 ± 3.70	45.16 ± 5.95	**0.043***	37.44 ± 3.57	40.48 ± 4.75	0.514	0.540	37.96 ± 5.42	47.93 ± 7.38	0.163	40.73 ± 4.03	47.83 ± 4.09	0.134	0.358
Potassium (mg)	2312.75 ± 119.10	2485.70 ± 156.18	0.351	2165.08 ± 179.44	2375.33 ± 141.30	0.157	0.603	2456.18 ± 180.24	2614.63 ± 216.06	0.619	2185.25 ± 238.55	2331.92 ± 191.22	0.434	0.394
Iron (mg)	7.60 ± 0.48	7.76 ± 0.61	0.745	7.65 ± 0.61	8.63 ± 0.47	0.108	0.267	8.64 ± 0.63	8.90 ± 0.66	0.750	7.60 ± 0.657	8.29 ± 0.483	0.351	0.406
Calcium (mg)	563.75 ± 38.14	611.25 ± 43.14	0.351	540.45 ± 42.20	609.33 ± 52.40	0.205	0.978	560.09 ± 49.45	661.81 ± 69.72	0.252	543.17 ± 40.36	560.91 ± 72.54	0.775	0.342
Sodium (mg)	2006.50 ± 112.40	1698.25 ± 120.29	**0.014***	2124.15 ± 160.62	1980.78 ± 158.10	0.401	0.163	2081.91 ± 161.07	1796.27 ± 137.33	0.110	2285.33 ± 230.38	1963.75 ± 236.96	0.273	0.854

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix G26: Unadjusted estimated marginal means and standard errors of micronutrient intake from general linear model repeated measures by study group for ITT and PP

Appendix G27:

	ITT							PP						
	EG (n= 20)			MD (n= 20)			P value[b]	EG (n= 20)			MD (n= 20)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Vector magnitude	489123.93 ± 48278.18	514278.87 ± 53910.02	0.565	652636.29 ± 45013.48	660099.10 ± 46783.86	0.889	0.591	519536.77 ± 72172.99	590632.49 ± 78977.07	0.395	620778.42 ± 59204.12	634979.27 ± 64786.58	0.865	0.666
Steps	7456.15 ± 793.39	8106.57 ± 1087.20	0.344	9547.05 ± 752.94	10043.07 ± 810.19	0.516	0.884	8586.52 ± 1193.48	10130.55 ± 1601.05	0.229	9565.58 ± 1044.83	10448.14 ± 1092.92	0.449	0.870
Sedentary time (%)	64.67 ± 1.98	62.70 ± 1.96	0.303	61.07 ± 2.86	59.19 ± 2.91	0.362	0.809	64.48 ± 2.90	60.43 ± 2.97	0.247	64.84 ± 2.52	61.86 ± 2.62	0.351	0.721
Light activity (%)	27.71 ± 2.01	28.01 ± 1.69	0.878	27.99 ± 3.35	28.30 ± 3.30	0.831	0.968	26.81 ± 2.90	27.84 ± 2.56	0.768	23.88 ± 2.66	24.38 ± 2.16	0.832	0.310
Moderate activity (%)	4.56 ± 0.76	5.44 ± 0.97	0.281	5.87 ± 0.58	6.31 ± 0.76	0.527	0.914	5.49 ± 0.79	7.08 ± 1.25	0.291	6.13 ± 0.73	6.82 ± 1.01	0.511	0.872
Vigorous activity (%)	0.68 ± 0.30	0.59 ± 0.29	0.141	0.65 ± 0.20	0.88 ± 0.27	0.384	0.232	1.03 ± 0.52	0.86 ± 0.49	0.149	0.61 ± 0.27	0.98 ± 0.36	0.394	0.836

Very vigorous activity (%)	0.03 ± 0.03	0.04 ± 0.03	0.337	0.06 ± 0.03	0.13 ± 0.08	0.367	0.350	0.00 ± 0.00	0.01 ± 0.01	0.341	0.06 ± 0.04	0.18 ± 0.12	0.354	0.195
MET-mins/ week	3845.40 ± 947.55	3537.70 ± 564.47	0.732	2705.63 ± 402.45	3589.79 ± 533.42	**0.023***	0.533	4778.36 ± 1590.27	4323.00 ± 823.62	0.778	2963.00 ± 541.26	4102.42 ± 817.78	**0.040***	0.851

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix G27: Unadjusted estimated marginal means and standard errors of physical activity data from general linear model repeated measures by study group for ITT and PP

Appendix G28:

	ITT							PP						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Dominant grip strength (kg)	25.74 ± 1.30	25.71 ± 1.64	0.972	29.21 ± 2.36	29.65 ± 2.32	0.779	0.185	25.16 ± 2.00	25.00 ± 2.73	0.894	30.32 ± 3.05	30.69 ± 2.84	0.895	0.168
Non-dominant grip strength (kg)	24.03 ± 1.48	25.42 ± 1.64	0.262	26.82 ± 2.00	26.58 ± 2.20	0.760	0.674	24.08 ± 2.28	26.21 ± 2.84	0.355	26.75 ± 2.00	27.09 ± 2.69	0.768	0.824
FEV1 (L)	2.73 ± 0.17	2.84 ± 0.16	0.195	3.05 ± 0.20	3.08 ± 0.18	0.648	0.320	2.71 ± 0.23	2.79 ± 0.24	0.489	2.91 ± 0.26	2.98 ± 0.27	0.364	0.602
FVC (L)	2.87 ± 0.19	3.02 ± 0.18	0.178	3.19 ± 0.21	3.28 ± 0.21	0.220	0.360	2.84 ± 0.25	3.01 ± 0.28	0.370	3.08 ± 0.29	3.24 ± 0.32	0.165	0.610

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix G28: Unadjusted estimated marginal means and standard errors of physical capability data from general linear model repeated measures by study group for ITT and PP

10.8. Appendix H

Appendix H29:

	ITT							PP						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
Weight (kg)	79.03 ± 3.17	76.63 ± 2.79	0.141	82.41 ± 3.65	79.73 ± 3.96	**0.004***	0.801	80.54 ± 5.05	76.14 ± 5.11	**0.011***	79.68 ± 2.56	75.91 ± 2.42	**0.002***	0.969
BMI (kg/m^2)	28.37 ± 0.82	27.52 ± 0.72	0.148	28.26 ± 0.60	27.41 ± 0.725	**0.011***	0.709	29.17 ± 1.18	27.60 ± 1.26	**0.013***	27.85 ± 0.80	26.66 ± 0.882	**0.002***	0.545
Body fat (%)	35.30 ± 1.01	34.84 ± 0.71	0.423	34.08 ± 1.67	32.25 ± 2.05	0.088	**0.018***	35.97 ± 2.23	34.96 ± 2.33	0.212	32.89 ± 2.68	29.81 ± 3.00	**0.014***	0.196
Waist circumference (cm)	92.01 ± 2.14	88.85 ± 1.95	**0.006***	95.10 ± 2.40	91.20 ± 1.73	**0.044***	0.972	93.91 ± 3.82	88.17 ± 3.98	**0.000***	94.84 ± 2.51	89.45 ± 2.12	**0.006***	0.774
Hip circumference (cm)	106.61 ± 2.09	102.78 ± 3.24	0.142	107.72 ± 1.16	105.59 ± 1.27	**0.019***	0.154	105.68 ± 4.52	101.46 ± 4.69	**0.003***	107.43 ± 2.43	104.27 ± 2.46	**0.016***	0.592
Waist-to-hip ratio	0.89 ± 0.019	0.85 ± 0.017	0.240	0.88 ± 0.029	0.84 ± 0.018	0.289	0.687	0.89 ± 0.017	0.85 ± 0.018	0.209	0.89 ± 0.027	0.84 ± 0.017	0.246	0.761

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex
[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix H29: Unadjusted estimated marginal means and standard errors of body composition data from general linear model repeated measures by study group for ITT and PP

Appendix H30:

	ITT							PP						
	EG (n=20)			MD (n=20)			P value[b]	EG (n=11)			MD (n=12)			P value[b]
	Baseline	Post	P value[a]	Baseline	Post	P value[a]		Baseline	Post	P value[a]	Baseline	Post	P value[a]	
SBP (mmHg)	126.62±3.35	118.60±1.90	**0.001***	131.65±4.46	124.28±3.14	**0.001***	0.132	133.54±4.79	120.24±2.75	**0.001***	137.96±6.25	127.60±4.10	**0.003***	0.158
DBP (mmHg)	72.65±2.31	70.68±1.70	0.428	76.03±2.26	76.63±2.82	0.855	0.084	77.52±3.20	72.42±2.37	0.222	78.43±3.15	79.93±4.19	0.776	0.153
TC (mmol/L)	4.50±0.18	4.33±0.18	**0.061***	4.62±0.21	4.62±0.24	0.110	0.326	4.50±0.21	4.24±0.22	0.094	4.83±0.27	4.81±0.31	0.871	0.152
TG (mmol/L)	1.03±0.10	1.00±0.09	0.623	1.05±0.13	1.02±0.07	0.758	0.839	1.06±0.12	1.00±0.09	0.516	1.06±0.18	1.00±0.09	0.683	0.995
HDL (mmol/L)	1.54±0.08	1.46±0.08	**0.031***	1.35±0.70	1.38±0.08	0.303	0.476	1.51±0.11	1.41±0.12	0.058	1.43±0.08	1.44±0.10	0.701	0.831

LDL (mmol/L)	2.49±0.14	2.41±0.12	0.235	2.78±0.20	2.78±0.20	1.000	0.114	2.50±0.20	2.38±0.16	0.309	2.91±0.27	2.93±0.27	0.906	0.103
HDL:TC	3.03±0.16	3.05±0.12	0.826	3.53±0.20	3.41±0.16	0.304	0.080	3.15±0.27	3.15±0.20	1.000	3.49±0.26	3.43±0.23	0.666	0.356

*Significant p values are shown in bold with an asterisk

[a]p value compares baseline and post-intervention values within study groups, adjusted for age and sex

[b]p value compares post-intervention values between study groups, adjusted for age, sex and baseline value

Appendix H30: Unadjusted estimated marginal means and standard errors of blood data from general linear model repeated measures by study group for ITT and PP