METABOLIC SYNDROME AND ABDOMINAL OBESITY: WAIST MEASUREMENT AND LIFESTYLE EDUCATION TO REDUCE CARDIOVASCULAR AND DIABETES RISK

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**Metabolic syndrome and abdominal obesity:
waist measurement and lifestyle education
to reduce cardiovascular and diabetes risk**

Abstract

The overall aim was to contribute to the development of effective self-management lifestyle education for management of cardiovascular and diabetes risk in people with metabolic syndrome (MetS). An additional aim was to elicit views on the use of waist circumference measurement to assess health risk due to overweight and obesity, and identify strategies to promote waist measurement.

A qualitative study was conducted to determine the knowledge and attitudes of patients and primary care health practitioners concerning waist size measurement. A systematic review (and meta-analysis) was conducted to review the existing evidence on effectiveness of interventions for reducing diabetes and cardiovascular risk in people with MetS. An evidence based group lifestyle education programme was developed and tested in a randomised controlled trial: The Reversal Intervention for Metabolic Syndrome (TRIMS) study.

Key findings:
- Healthcare professionals were generally aware of a link between a large waist size and health risks; practical barriers to using waist measurement included lack of time, extra workload and financial implications. For patients, being given an explanation of the assessment appeared to be what was most important to them.
- The benefits of both lifestyle and pharmacological interventions to reverse MetS were indicated, by the meta-analysis, with lifestyle being the most effective.
- The TRIMS education programme was well received; people felt positive about making lifestyle changes and improving their future health.
- After 6-months follow-up the TRIMS programme was effective at reducing waist size, hip circumference, weight, and body mass index, and increasing unsaturated fat intake; reversal of MetS was not significantly different between the intervention and control groups.

Based on the findings from this programme of work, recommendations are provided for future research and clinical practice in order to promote better management of cardiovascular and diabetes risk in people with MetS.

List of publications arising from this thesis

Original articles:

Dunkley AJ, Davies MJ, Stone M A , Taub NT, Troughton J, Yates T, Khunti K. The Reversal Intervention for Metabolic Syndrome (TRIMS) study: rationale, design, and baseline data. *TRIALS* 2011;12:107

Dunkley A J, Stone M A, Patel N, Davies MJ, Khunti K. Waist circumference measurement: knowledge, attitudes and barriers in patients and practitioners in a multi-ethnic population. *Family Practice* 2009; 26(5):365-371

Review articles:

Dunkley AJ, Davies MJ, Khunti K. Metabolic Syndrome. *General Practice UPDATE* 2008;1(3):32-39.

Published abstracts:

Dunkley AJ, K Charles, M Castro, KR Abrams, J Camosso-Stefinovic, MJ Davies, K Khunti. Prevention of Type 2 diabetes and cardiovascular disease in people with metabolic syndrome: a systematic review and meta-analysis. *Diabetic Medicine* 2009:24(Suppl 1) :95

Dunkley AJ, Stone MA, Khunti K, Davies MJ. Waist size measurement: views of patients, doctors and nurses. *Diabetic Medicine* 2008;25(Suppl1):150.

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Abbreviations are written in full the first time that they are used in each chapter.

Initials	Full text
ACE	Angiotensin converting enzyme inhibitor
ACR	Albumin creatinine ratio
Af-Am	African-American
ARB	Angiotensin-II receptor blocker
ATO	Atorvastatin
BMI	Body mass index
BOCF	Baseline observation carried forward
BP	Blood pressure
C	Control group
CCB	Calcium channel blocker
CI	Confidence interval
CRD	Centre for Reviews and Dissemination
CVD	Cardiovascular disease
D	Diet
DESMOND	Diabetes Education and Self-Management for Ongoing and Newly Diagnosed
DINE	Dietary Instrument for Nutrition Education
DPP	(US) Diabetes Prevention Programme
DPS	(Finnish) Diabetes Prevention Study
EA	Exercise advice
EQ-5D	EuroQol EQ-5D questionnaire
F	Female
FEN	Fenofibrate
FFA	Free fatty acid
FINDRISC	Finnish Diabetes Risk Score
FPG	Fasting plasma glucose
FSA	Foods Standards Agency
GP	General Practitioner
GSE	General Self Efficacy Scale

HADS	Hospital Anxiety and Depression Scale
HbA1c	Glycated haemoglobin
HCP	Healthcare professional
HDL	High density lipoprotein
Hisp	Hispanic
hs-CRP	High-sensitivity-C-reactive protein
I	Intervention group
ID	Individualised or intensive dietary advice
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGR	Impaired glucose regulation
IGT	Impaired glucose tolerance
IL-6	Interleukin-6
IMD	Indices of Multiple Deprivation
IPAQ	International Physical Activity Questionnaire
IQR	Interquartile range
ITT	Intention to treat
LDL	Low density lipoprotein
LOCF	Last observation carried forward
LOV	Lovastatin
M	Male
MET	Metformin
MetS	Metabolic syndrome
MRC	Medical Research Council
MTC	Mixed treatment comparison
NA	Not applicable
NCEP	National Cholesterol Education Program
NICE	National Institute for Health and Clinical Excellence
NR	Not reported
NS-SEC 5-class	National Statistics Socio-economic Classification 5-class version
NT	No treatment
NVQ	National Vocational Qualification
ODES	Oslo Diet and Exercise Study

OGTT	Oral glucose tolerance test
OR	Odds ratio
PAI-1	Plasminogen activator inhibitor-1
Pharm	Pharmacological
PICOS	Population, intervention, comparator, outcomes, study design
PL	Placebo
PN	Practice nurse
PRA	Pravastatin
PREPARE	Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement
PT	Patient
QoF	Quality and Outcomes Framework
RCT	Randomised controlled trial
RIM	Rimonabant
ROS	Rosiglitazone
RR	Relative risk
SA	South Asian
SD	Standard deviation
SE	Standard error
SES	Supervised exercise sessions
SIB	Sibutramine
SIGN	Scottish Intercollegiate Guidelines Network
STA	Standard advice
T2DM	Type-2 diabetes
TNF-α	Tumour necrosis factor-alpha
TRIMS	The Reversal Intervention for Metabolic Syndrome
VAS	Visual Analogue Scale
VLDL	Very-low density lipoprotein
WE	White European
WHO	World Health Organisation
WHR	Waist-to-hip ratio

Chapter 1. Introduction and guide to thesis

1.1 Rationale and aims

The predicted global increase in type-2 diabetes (T2DM) and cardiovascular disease (CVD), and associated morbidity and mortality, are a growing public health burden.[1, 2] This is largely due to rising levels of obesity, and sedentary lifestyles.[3] Additionally, the disease burden in certain ethnic groups such as South Asians (UK census categories Indian, Pakistani and Bangladeshi[4]) is significantly higher than for White Europeans (white British, Irish or other European background).[5, 6] Strategies to reduce the development of CVD and T2DM in high risk individuals are a priority.

People who are centrally obese often have a clustering of additional cardiovascular and diabetes risk factors such as elevated blood pressure (BP), dyslipidaemia and impaired glucose metabolism, which have been linked to insulin resistance and collectively termed metabolic syndrome (MetS). [7, 8] UK data suggest that approximately 30 - 34% of adults aged 40 to 75 years have MetS,[9] and this number is likely to grow as the population continue to become increasingly inactive and obesity levels rise.[10]

Waist circumference is one of the essential criteria for diagnosing MetS and is the anthropometric measurement most closely correlated with central / visceral adiposity.[11] Recent national guidance recommends including waist circumference measurement as part of both vascular risk assessment and obesity management.[12, 13] Despite this, waist measurement is not routinely

carried out in clinical practice. At present body mass index (BMI) is widely used to identify individuals with a health risk due to being overweight or obese.[14] There is currently a lack of reseach evidence relating specifically to health practitioners' and patients' knowledge and attitudes about waist size measurement. This includes the importance of waist size and associated health risk, and possible barriers to carrying out this assessment in a multi-ethnic setting.

MetS could be a useful concept for healthcare professionals and patients to focus on when addressing the health risks associated with obesity.[15] Despite some debate about the prognostic significance of MetS[16] and its usefulness to clinical practice, there is evidence that MetS is linked to an increased risk of developing both CVD and T2DM.[17-19] It also precedes T2DM and CVD by several years.[16] MetS is, therefore, potentially of great importance to public health; people with MetS could be an important group to target for primary prevention of T2DM and CVD.[16, 20] It is therefore important to develop a pragmatic early intervention that can be easily implemented to a large number of people in primary care.

Evidence from clinical trials is limited regarding the effectiveness of strategies aimed at primary prevention of T2DM and/or CVD in people with MetS. However, a recent meta-analysis of a number of trials has suggested that intensive lifestyle programmes targeted at people with pre-diabetes, who are at high risk of T2DM, are effective in reducing the incidence of diabetes by more than 50%.[21] Nonetheless, targeting dysglycaemia in isolation may not be the

best approach if the ultimate aim is to reduce the rate of cardiovascular complications. Research is therefore needed into the efficacy of lifestyle interventions for primary prevention of T2DM and CVD that can be applicable to people with MetS in primary care. Given the ethnic diversity of the UK population,[22] it is also important to consider the applicability of lifestyle interventions in multi-cultural settings.

Therefore, the overall aims of the programme of work in this thesis are to:

- contribute to the development of effective self-management lifestyle education for management of cardiovascular and diabetes risk in people with MetS;

- elicit views on the use of waist size measurement to assess health risk due to overweight and obesity, and identify strategies to promote waist circumference measurement.

Specific objectives of the programme of work described were:

1) To determine the knowledge and attitudes of patients and primary healthcare practitioners (general practitioners and practice nurses) concerning waist circumference measurement, with particular reference to exploring barriers to waist circumference measurement in a multi ethnic population.

2) To conduct a systematic review and consolidate existing evidence of the effectiveness of interventions for reducing diabetes and cardiovascular risk in people with MetS.

3) To develop an evidence based lifestyle education programme to improve cardiovascular risk and dysglycaemia in people with MetS in primary care.

4) To investigate the hypothesis that delivery of a group self-management education programme designed to encourage lifestyle changes in individuals identified with MetS would be a feasible, acceptable, and effective strategy for primary prevention of CVD and T2DM.

The remainder of this introductory chapter:

- Firstly, considers the development of complex interventions to improve health (section 1.2) and outlines the Medical Research Council's (MRC) framework for developing and evaluating complex interventions.[23, 24] This framework helped inform the plan of work for this thesis, and ultimately guided the development of the lifestyle educational intervention reported in Chapter 5.

- Secondly, presents an overview of the programme of work undertaken for this thesis (section 1.3). This includes a summary of the organisation of the content of this thesis (section 1.3.1) and an outline of the scope of data presented (section 1.3.2).

1.2   Development of complex interventions

1.2.1 The nature of complex interventions

Interventions in health services research and public health that are aimed at promoting changes in behaviour are usually complex in nature. The MRC defines complex interventions as being "built up from a number of components, which may act both independently and inter-dependently".[23] However,

complexity relates not only to the design of an intervention but also to the delivery, evaluation and longer term implementation. Some of the key characteristics of complex interventions are outlined in Box 1-1.[25]

- Number of interacting components within the intervention(s)
- Number and difficulty of behaviours necessitated for people delivering or receiving the intervention
- Number of groups or organisational categories that intervention is aimed at
- Number and variability of outcomes
- Degree of flexibility allowed by the intervention   *(adapted from Craig 2008)[25]*

Box 1-1: Characteristics of a complex intervention

1.2.2 Medical Research Council guidance on developing and evaluating complex interventions

1.2.2.1 The original MRC framework

In 2000 the MRC published a framework to help researchers and funders address the challenges of developing and evaluating randomised controlled trials (RCTs) of complex interventions[23] (Figure 1-1). This framework has been widely used; however, subsequently, it was recognised that there were limitations to this original guidance. Suggested limitations[25] included the adoption of a model that closely mirrored the phases of drug development; the diagram illustrating the model implied a linear process; an over emphasis on clinical trials; and a lack of an evidence base. The framework has since been updated and extended to address these points.
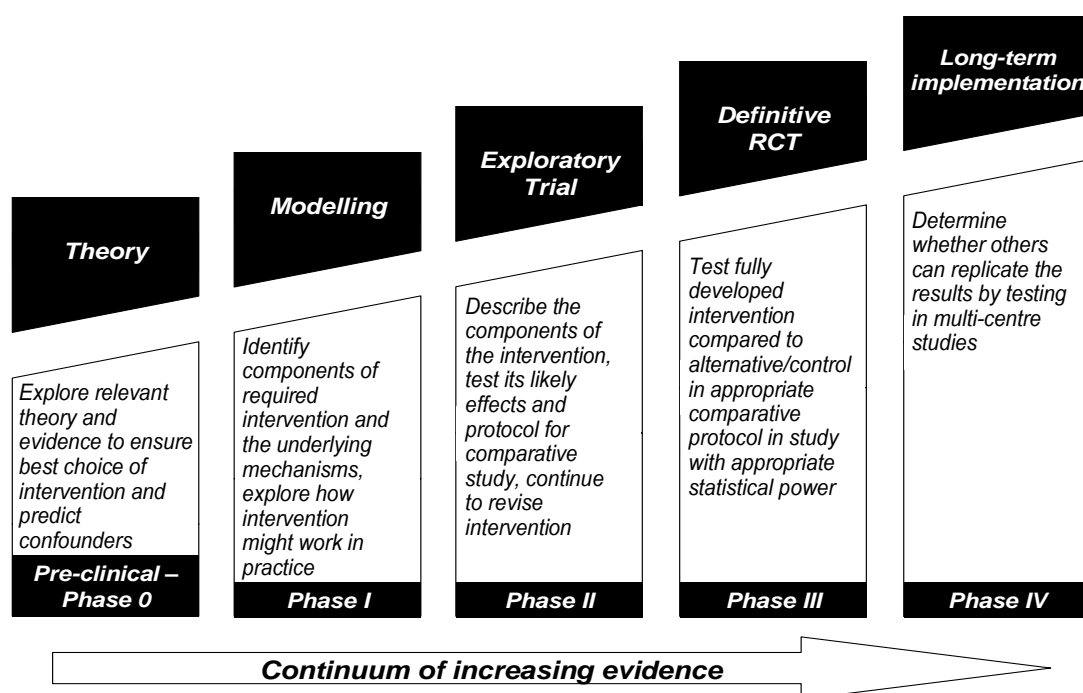
Figure 1-1: The original Medical Research Council framework for the evaluation of complex interventions

1.2.2.2 The updated MRC framework

The current 2008 MRC guidance emphasises a more flexible process.[25] In the new framework all the suggested phases are seen as being equally important; including development and implementation which was previously underplayed. In addition, despite suggested connections between the different phases, it is acknowledged that the process may not adhere to a cyclical or a linear sequence. The guidance suggests using an iterative approach which may at any stage involve going back to an earlier phase. The main stages and key activities are summarised in Figure 1-2. Reporting is seen as being vital at every stage of the process.
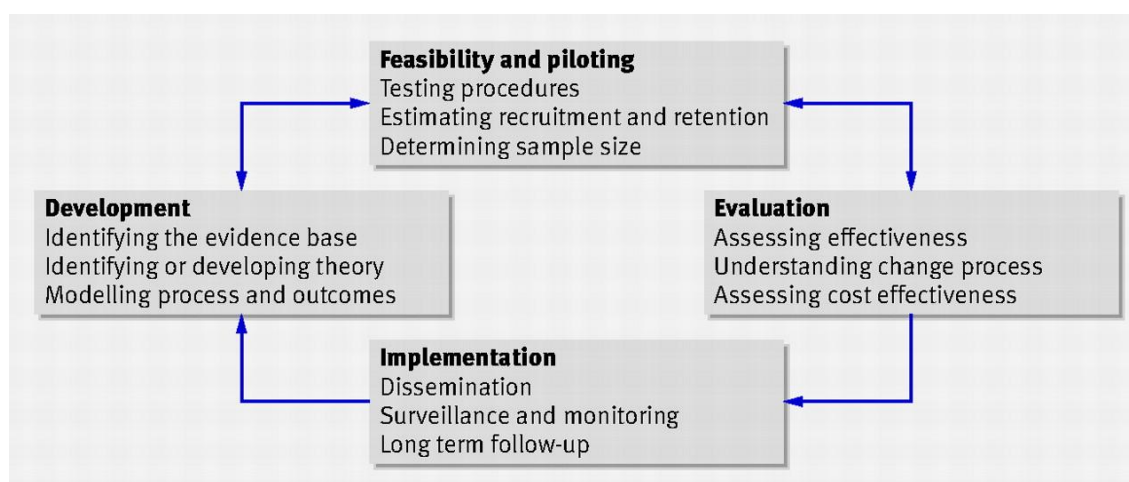
(Ref: Craig 2008)[24]

Figure 1-2: The new Medical Research Council framework for developing and evaluating complex interventions

Development

The development phase includes:

1) Identifying the existing evidence about similar interventions and methods; this may include conducting a systematic review.

2) Identifying and developing theory related to the likely process of change; existing evidence and theory should be utilised but this stage could involve undertaking new primary research.

3) Modelling processes and outcomes, including the design of the intervention and identifying suitable assessment measures and long term outcomes. This could involve paper based modelling, a primary study or economic modelling.

Feasibility and piloting

The feasibility and piloting phase may include:

1) Testing the delivery of the intervention, including acceptability and compliance.

2) Estimating rates of recruitment and retention.

3) Determining effect and sample sizes.

Both quantitative and qualitative methods are likely to be required.

Evaluation

The evaluation phase includes:

1) Assessing effectiveness. A randomised method should be considered but may not be a feasible approach for evaluating the study outcomes. An alternative experimental or non-experimental design may be preferable.

2) Understanding processes and process evaluation. Recommendations include following appropriate reporting guidelines for different study types.[24] This should ensure that interventions are described in enough detail to enable replication and that any variations in implementation are reported.

3) Assessing cost-effectiveness by conducting an economic evaluation to estimate potential cost benefits.

Implementation

The implementation phase includes:

1) Active dissemination using a multi-faceted approach. Findings should be published in the research literature but also disseminated more widely and include specific recommendations for practice or policy. Involving

stakeholders at the design stage, to ensure relevance, may later assist the process of implementation.

2) Surveillance, monitoring and long-term follow-up, to determine whether benefits inferred from the intervention are transferrable into different settings and/or are maintained after the original study. This may involve building into the study design plans to obtain consent and collect appropriate long-term outcome data.

The way in which the various parts of the programme of work undertaken for this thesis relates to the current MRC framework is considered in the final chapter (Chapter 8, section 8.4, Figure 8-1).

1.3 Overview of the programme of work undertaken

1.3.1 Organisation and scope of the thesis

The remainder of the thesis consists of the following chapters:

- Chapter 2 provides background about MetS, including the potential relevance to public health.

- Chapter 3 describes a qualitative interview study exploring the knowledge and attitudes of patients and primary care practitioners regarding waist circumference measurement and associated health risks.

- Chapter 4 presents a systematic review collating the evidence on the effectiveness of interventions for reducing T2DM and CVD risk in people with MetS.

- Chapter 5 describes the development of a group lifestyle education programme which was developed for an RCT aimed at reducing diabetes

and CVD risk factors in people with MetS: The Reversal Intervention for Metabolic Syndrome (TRIMS) study.

- Chapter 6 presents the design and methods used to conduct the TRIMS study.

- Chapter 7 details the results of the evaluation of the TRIMS intervention based on 6-months of follow-up, as explained in section 1.3.2.

- Chapter 8 summarises the main findings of the overall programme of work for the thesis. The implications for clinical practice and recommendations for future research are also discussed.

- The references, appendices and publications associated with this programme of work are included at the end of this thesis.

1.3.2 Scope of data presented in this thesis for the TRIMS RCT

One of the main objectives of the programme of work undertaken for this thesis is to evaluate the delivery of an education programme designed to encourage lifestyle changes in individuals with MetS. The methods used to evaluate the education programme (Chapter 6) include the collection of 12 month follow-up data, and it was originally anticipated in the study proposal that the required sample size would be recruited to the TRIMS study within 3 to 4 months. However, the recruitment phase of the study overran due to delays with recruiting general practices; it took a total of 9 months to enrol the required number of partcipants to the study. Therefore, the data presented in this thesis for the evaluation of the TRIMS RCT (Chapter 7) are limited to baseline and 6-month follow-up data, see Figure 1-3. The 12-month follow-up data will be analysed outside the timescale of the PhD.
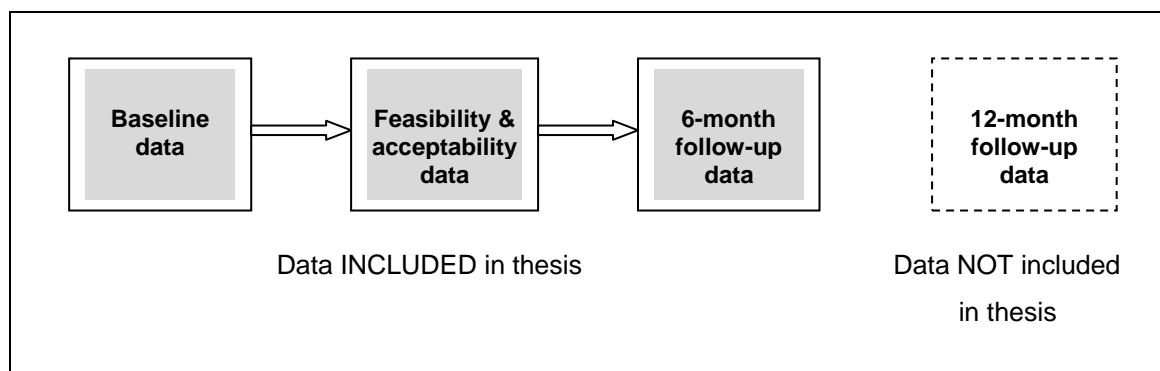
Figure 1-3: Outline of data presented in this thesis for the TRIMS study

1.4   Concluding remarks

This chapter has outlined the rationale and aims (section 1.1), and presented an overview of the programme of work undertaken for this thesis (section 1.3). The MRC framework for developing and evaluating complex interventions, which was used to guide the overall programme of work undertaken for this thesis, was also considered (section 1.2). The following chapter (Chapter 2) provides background to the thesis including an overview of MetS and the importance to public health.

Chapter 2. Metabolic syndrome: an overview

2.1   Introduction

2.1.1 Chapter overview

This chapter provides additional background by presenting an overview of metabolic syndrome (MetS). Firstly, the current definitions for MetS are outlined (section 2.2) and the prevalence of MetS and associated risk factors are then discussed (section 2.3). The proposed mechanisms underlying MetS, including the role of insulin resistance and the importance of abdominal obesity, are explained in section 2.4. The role of MetS for identifying people at high future risk of type-2-diabetes (T2DM) and cardiovascular disease (CVD), and the validity of MetS as a concept are then outlined (section 2.5). Next the use of waist measurement to identify MetS in clinical practice is considered (section 2.6). Finally, management of risk and prevention of T2DM and CVD in people with MetS are outlined, (section 2.7).

2.2   Defining metabolic syndrome

MetS is characterised by a clustering of adverse risk factors for CVD and T2DM, which are generally suggestive of a sedentary lifestyle and excess calories. MetS was initially described by Reaven in 1988 as Syndrome X[26] (patients with hypertension who were insulin resistant, hyperglycaemic, and hyperinsulinaemic), and it was subsequently termed Insulin Resistance Syndrome.[27, 28] In 1999 the World Health Organisation (WHO) attempted to define MetS[29] (Table 2-1), and there have since been numerous other proposed

definitions. Attempts have been made to agree on an exact definition but currently there is no global consensus.[16]

An essential requirement of the WHO definition is the diagnosis of diabetes, impaired glucose tolerance or insulin resistance.[29] Inclusion of a formal measure of insulin resistance was initially considered a strength of the WHO definition. However, the requirement to carry out an oral glucose tolerance test and/or an euglycaemic clamp has since been seen as major drawback.[30] Presently, the definitions most widely referred to were formulated by the National Cholesterol Education Program (NCEP)[7, 31] and the International Diabetes Federation (IDF),[8] Table 2-1. These current definitions for MetS are aimed at being easy to use in the clinical setting and share similar diagnostic criteria. However, the NCEP definition[7, 31] has been the one most commonly used in previous epidemiological studies.

Compared to the WHO definition, the NCEP definition is focused more towards identifying CVD risk. In the NCEP definition no single factor is highlighted and MetS is diagnosed if any 3 out of the following 5 criteria are present: raised fasting plasma glucose (FPG), raised triglycerides, low high density lipoprotein (HDL) cholesterol, hypertension or central obesity. The original NCEP definition[7] has lately been updated to include any pharmacological treatment for abnormal lipids or blood pressure (BP) and a lower FPG threshold.[31] However, the applicability of the NCEP waist circumference criteria to different populations has been criticised.[30]

Despite similarities to the NCEP definition, in the more recent IDF definition the role of abdominal obesity is central. [8] Lower thresholds are stipulated for the central obesity criterion and the waist circumference values provided are also ethnic specific,[8] due to differences in risk between certain ethnic groups for a given waist size / body mass.[32] Some experts fear that the IDF pre-requisite of abdominal obesity and the focus of waist circumference as a surrogate measure of insulin resistance may lead to the exclusion of some people who are non-obese but insulin resistant and the inclusion of individuals who are obese but insulin sensitive.[33] However, the number of people this could potentially effect is likely to be small, (see section 2.3.2).

WHO (1999)[29]	NCEP (2005)[31]	IDF (2005) [8]
ESSENTIAL REQUIREMENT **Diabetes, IGT, or insulin resistance**		**ESSENTIAL REQUIREMENT** **Central obesity** **Waist circumference** ≥ 94 cm[†] (males) ≥ 80 cm[†] (females)
+ *ANY 2 out of the following 4* ⬇	*ANY 3 out of the following 5* ⬇	**+** *ANY 2 out of the following 4* ⬇
	1) Raised fasting plasma glucose: $\geq$ 5.6 mmol/l*	**1) Raised fasting plasma glucose:** $\geq$ 5.6mmol/l
1) Dyslipidaemia: Triglycerides > 1.7mmol/l and/or HDL < 0.9 (males) < 1.0 (females)	**2) Raised triglycerides:**** $\geq$ 1.7mmol/l and/or **3) Low HDL cholesterol:**** < 1.03 (males) < 1.29 (females)	**2) Raised triglycerides:** $\geq$ 1.7mmol/l *(or specific treatment for)* and/or **3) Reduced HDL cholesterol** < 1.03 (males) < 1.29 (females), *(or specific treatment for)*
2) Hypertension: BP $\geq$140/90 mmHg	**4) Hypertension:**** BP $\geq$130/85 mmHg	**4) Raised blood pressure:** BP $\geq$130/85 mmHg (or treatment for previously diagnosed hypertension)
3) Obesity: BMI > 30 kg/m^2 and/or WHR > 0.9 (males) >0.85 (females)	**5) Central obesity:** Waist circumference ≥ 102 cm (males) ≥ 88 cm (females)	
4) Microalbuminuria: Urinary albumin excretion rate $\geq$ 20mcg/min or albumin: creatinine ratio $\geq$ 30mg/g		
	Updated from the original NCEP 2001definition[7]; **fasting plasma glucose value ($\geq$6.1 mmol/l) was updated to include a lower value;* *** was updated to include drug treatment.*	*[†]Waist circumference ethnic-specific for Europid men & women; Waist circumference for South Asians (Chinese, Malay, & Asian Indian): $\geq$90cm (males), & $\geq$80 cm (females).*
Abbreviations: **BMI** (body mass index); **BP** (blood pressure); **HDL** (high density lipoprotein); **IDF** (International Diabetes Federation); **IGT** (impaired glucose tolerance); **NCEP** (National Cholesterol Education Program); **WHR** (waist-to-hip ratio); **WHO** (World Health Organisation)		

Table 2-1: The most commonly referred to definitions of metabolic syndrome

2.3 Prevalence and risk factors for metabolic syndrome

2.3.1 Prevalence

Recent global prevalence estimates for MetS indicate that, for most regions worldwide, around 20 – 30% of the adult population could have MetS.[10] However, it is difficult to accurately determine the prevalence of MetS as it varies according to the criteria used and the population surveyed.[34] In developing countries, it has been suggested that between 13 – 30% of people could have MetS but in rural areas this could be lower.[35] In high-income nations such as the US, the prevalence of MetS is thought to be around 39%.[36]

However, despite the difficulties of obtaining precise prevalence rates, it has consistently been demonstrated that the prevalence of MetS increases with age.[37] For example, US data indicate that the prevalence of MetS increases from 7% to 44%, for ages 20 – 29 years and 60 - 69 years respectively.[38] This is also thought to at least partially explain the lower prevalence of MetS in some less developed regions such as Southeast Asia, where there is a predominance of younger adults.[10] The prevalence of MetS also shows ethnic variation.[39] Genetic / racial factors are thought to partially account for higher prevalence rates in India compared to some other Asian countries, and also to higher rates of MetS in the Hispanic population in the US.[10]

Gender related differences in prevalence have been shown in some previous studies, with MetS rates being higher for males than for females.[36, 40] However, the evidence is inconsistent and observed differences appear to be generally related to the ethnic and racial mix of the population.[41]

Recent UK data suggest that approximately 1 in 3 adults aged 40 to 75 years could have MetS (30 and 34% according to the NCEP and IDF definitions respectively).[9] This number is likely to rise as lifestyles continue to become increasingly inactive and as a consequence of an ageing population.[10]

2.3.2 Risk factors for developing metabolic syndrome

Both genetic and environmental factors are associated with an increased risk of MetS (Box 2-1). Obesity, in particular abdominal obesity, and insulin resistance, either due to a genetic component or secondary to obesity are acknowledged as the main causative factors.[8, 31] These are discussed further in section 2.4.

However, the emphasis that previous definitions of MetS have put on obesity has differed.[15] It is generally acknowledged that a small proportion of people who develop metabolic irregularities may not be obese; additionally, a small proportion of individuals may stay metabolically healthy despite being obese. However, the numbers of people with high levels of body fat who remain healthy are likely to be small.[15] The reasons for these anomalies are possibly due to genetic differences between individuals[42] and differing levels of physical activity/cardio-respiratory fitness.[43]

Abdominal or central obesity	Ageing
Insulin resistance	Genetic predisposition
Physical inactivity / sedentary behaviour	Ethnicity
Endocrine dysfunction / hormonal changes	Socio-economic inequalities
Anti-psychotic medication	Low household income / wealth
	Lower educational attainment

Box 2-1: Risk factors for developing metabolic syndrome

Sedentary behaviour is associated with an approximately 2-fold risk of developing MetS. Recent data suggest that people who undertake no moderate or vigorous leisure-time physical activity are approximately twice as likely to have MetS (OR 1.90, 95% CI: 1.22 – 2.97) than people who do ≥150 minutes per week of activity.[44] Additionally, both low and moderate levels of cardio-respiratory fitness have been shown to be associated with a substantially higher risk of MetS in men (RR 4.6, 95% CI: 2.7 – 7.8 and RR 2.7, 95% CI: 1.5 - 4.6, respectively), when compared to high levels of cardio-respiratory fitness, after adjustment for age.[43]

Socio-economic inequalities have also been linked to the development of MetS. Evidence from several studies suggests that there is an inverse association between prevalent MetS and the following: household income/wealth,[45] educational level/achievement,[36, 46, 47] and socio-economic status.[47] Additionally, neuroendocrine dysfunction/hormonal changes,[48] and long-term use of medication such as anti-psychotic medications,[49] have also been linked to the development of MetS, possibly due to alterations in body fat distribution.

2.4 Mechanisms underlying the metabolic syndrome

2.4.1 Insulin resistance

In healthy individuals, insulin normally stimulates the uptake of glucose in the skeletal muscles, liver and adipose tissue and additionally induces lipogenesis (formation of fatty acids and other lipids).[50] When insulin resistance develops, initially the cells are less sensitive but eventually they may become increasingly resistant to the effects of insulin. However, insulin resistance is often described using a glucocentric view of elevated blood glucose levels and corresponding increased insulin production to maintain euglycaemia. In MetS, an overabundance of circulating free fatty acids (FFAs), derived mainly from excess calories and an expanded adipose tissue mass, is thought to be a key contributor to insulin resistance.[37]

2.4.2 Abdominal obesity

Adipose tissue is primarily composed of adipocytes (fat cells) whose main function is to store excess calories as triglycerides and release FFAs in response to the body's energy needs.[51] Subcutaneous adipose tissue is situated just under the skin and is generally where the vast majority of body fat is stored. Visceral adipose tissue (intra-abdominal fat) is found primarily in the omentum and mesentery.[52] The main differences between subcutaneous and visceral adipose tissue are outlined in Box 2-2.

.

Subcutaneous adipose tissue	**Visceral adipose tissue**
Drains through the systemic veins	Drains directly to the liver through the portal vein
Smaller sized adipocytes • More insulin sensitive • Greater capacity to absorb FFA and glycerol – prevents deposition in non-adipose tissue	More larger adipocytes • Greater capacity to generate FFAs (hyperlipolytic) • Resistant to anti-lipolytic effect of insulin • Remains sensitive to glucose uptake

(Ref:Ibrahim 2010)[52]

Box 2-2: Anatomical and physiological differences between subcutaneous and visceral adipose tissue

Physiologically, subcutaneous adipose tissue exerts a protective effect against circulating FFAs and triglycerides by acting as a "buffer or sink".[53] However, when the storage capacity is exceeded or there is impaired production of new adipocytes, fat begins to accumulate elsewhere.[52] There is much individual variation in the accumulation of adipose tissue stores particularly in the amount of visceral adipose tissue, including ethnic and genetic differences.[53] In White Europeans (WEs) the subcutaneous adipose tissue compartment is thought to have a much larger capacity than for South Asians (SAs); it is unclear if this is due to a lower number of adipocytes or a lessened ability to take up FFAs. Additionally, less subcutaneous adipose tissue coupled with a corresponding larger amount of visceral adipose tissue is thought to account for increasing metabolic abnormalities in SAs at a given body mass index (BMI) compared to WEs.[54, 55]

Current definitions of MetS[8, 31] include waist size criteria as a proxy for abdominal obesity. Evidence from imaging studies in overweight and obese people, suggests that metabolic changes associated with abdominal obesity are correlated with excess visceral adipose tissue (intra-abdominal fat) rather than subcutaneous abdominal fat.[48]

2.4.3 Adipose tissue as an endocrine gland

In addition to its role in energy storage, it is now thought that adipose tissue acts as an endocrine gland and secretes numerous bioactive mediators which are collectively referred to as adipokines (adipocytokines).[56] Adipokines are thought to be involved in the regulation of metabolism, lipid uptake, immune response and inflammatory processes.[51] Excess visceral adipose tissue is associated with[51]:

1) Increased levels of inflammatory cytokines, including TNF-alpha (TNF-α), interleukin-6 (IL-6);

2) Altered secretion of metabolic regulators, including increased leptin production, and a decrease in adiponectin (which is thought to have a protective effect against CVD and T2DM).

As a result of these changes, metabolic disturbances occur, leading to dyslipidaemia, reduced glucose metabolism, decreased insulin sensitivity, increased inflammation and accelerated atherosclerosis.[37]

2.4.4 Pathogenesis: possible casual relationships in MetS

2.4.4.1 The role of visceral adipose tissue

Despite it being generally acknowledged that insulin resistance and abdominal obesity play a significant part in the development of MetS[8] the underlying casual mechanisms are not yet completely clear. Three explanations have been suggested,[48] (see Figure 2-1):

1) The hyperlipolytic state of the omental adipose tissue

    - The omental (visceral) adipose tissue is resistant to the anti-lipolytic effect of insulin. As a result, excessive amounts of FFAs go directly to the liver and this impairs several metabolic processes.

2) The role of adipose tissue as an endocrine organ

    - The altered production of adipokines due to visceral obesity contributes to the development of an altered metabolic state.

3) The inability of subcutaneous adipose tissue to expand.

    - An enlarged amount of visceral adipose tissue is just a marker or partial marker for subcutaneous adipose tissue being unable to expand further or becoming dysfunctional. As a result, fat starts to be stored ectopically.

However, it is suggested that MetS may develop due to a combination of all three processes linked to visceral obesity or dysfunctional adipose tissue, resulting from a mixture of excess calories, a sedentary lifestyle and/or a genetic predisposition.[48]
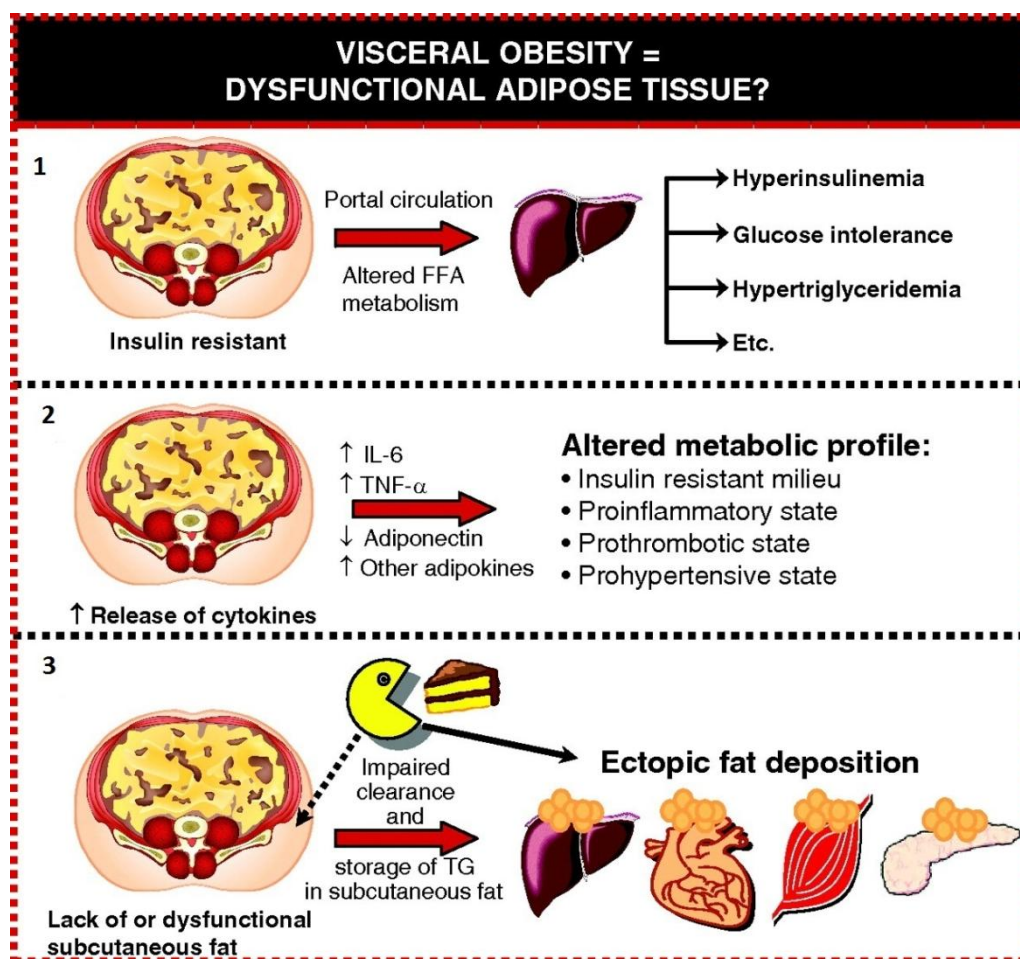
(adapted from Despres 2008)[48]

Figure 2-1: Proposed mechanisms which link visceral obesity to atherothrombotic-inflammatory abnormalities of insulin resistance

The concept of a combination of interacting processes collectively contributing to the pathogenesis of MetS is further illustrated in Figure 2-2.[37] The proposed resulting metabolic abnormalities and associated mechanisms, include:

- Dyslipidemia
  - An abundance of FFAs reaching the liver leads to an increased production of apolipoprotein-B, which is triglyceride rich and contains very low density lipoproteins (VLDL).

- o This results in a combination of raised triglyceride levels, reduced HDL levels, and an increase in small dense low density lipoproteins (LDLs). This combination is particularly atherogenic.

- Impaired glucose regulation

  - o An excess of circulating FFAs leads to 1) decreased insulin-mediated uptake of glucose (and conversion to glycogen) in the muscles, 2) increased hepatic production of glucose, and 3) reduced insulin clearance

  - o This results in elevated glucose levels and increased insulin secretion

- Elevated BP

  - o Increased circulating insulin (hyperinsulinaemia) is thought to raise BP through intensified activity of the sympathetic nervous system and greater sodium reabsorption

  - o Higher levels of FFAs may also directly contribute to raised BP

- Pro-inflammatory state

  - o Heightened secretion of inflammatory cytokines (e.g. IL-6, TNF-α), and decreased production of anti-inflammatory adiponectin, leads to 1) increased insulin resistance and release of FFAs, and 2) increased inflammation as indicated by elevated levels of high sensitivity C-reactive protein (hs-CRP).

  - o This also leads to a pro-thrombotic state due to increased levels of fibrinogen and plasminogen activator inhibitor-1 (PAI-1).

Many of the resulting metabolic abnormalities currently form part of the diagnostic criteria for MetS, see section 2.2. However, some of the additional

factors, although not officially part of any current definitions, are recommended as supplementary MetS criteria for research purposes,[8] see Box 2-3.
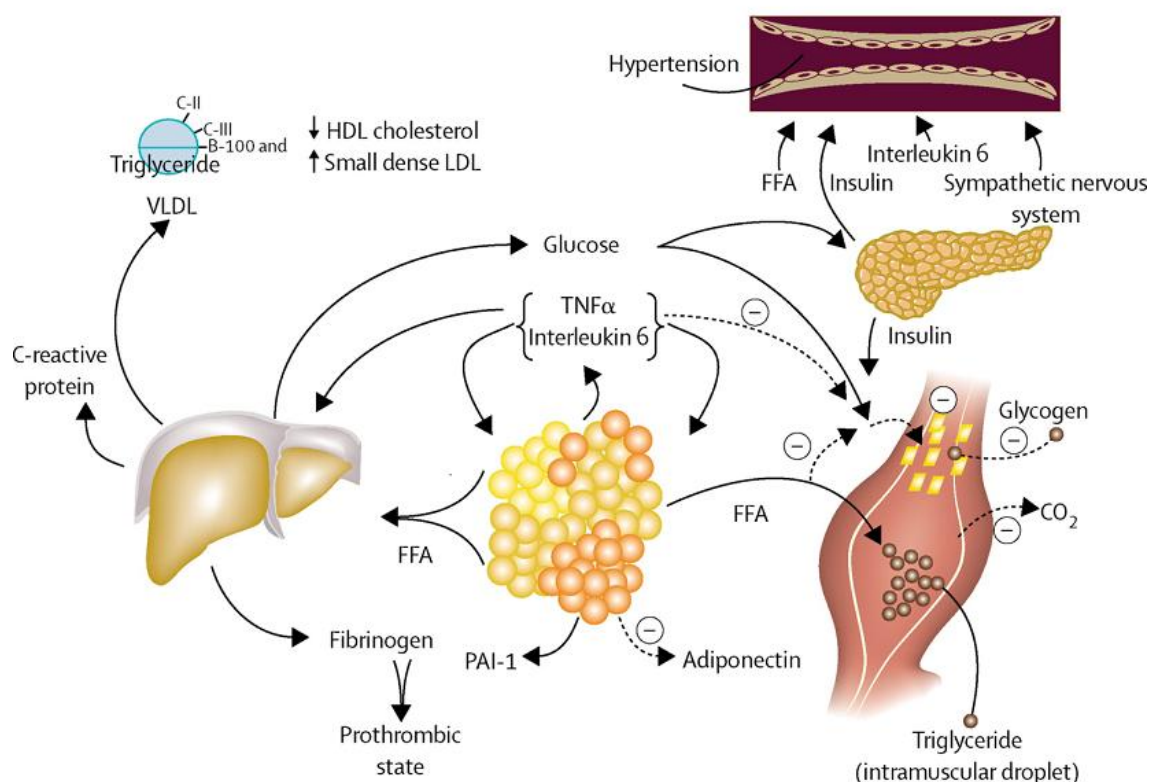
(adapted from Eckel 2005)[37]

Figure 2-2: Pathophysiology of the metabolic syndrome (insulin resistance).

Adipose tissue biomarkers:	Adiponectin, Leptin
Inflammatory markers:	hs-CRP, IL-6, TNF-α
Thrombotic markers:	PAI-1, Fibrinogen
Atherogenic dyslipidaemia:	Apoliporotein-B, Small LDL particles
Dysglycaemia:	Oral glucose tolerance test (2 hour glucose)
Insulin resistance:	Fasting insulin
Vascular dysregulation:	Microalbuminuria
Other:	Liver fat content, Pituitary-adrenal axis

(adapted from Alberti 2005)[8]

Box 2-3: Additional factors for inclusion in research into metabolic syndrome

2.5 Importance of metabolic syndrome

2.5.1 Increased risk of diabetes and CVD

MetS is linked to an increased risk of developing both T2DM and CVD. Estimates vary but current evidence from two recently conducted meta-analyses indicate that individuals with MetS are approximately twice as likely to develop CVD compared to people without MetS.[18, 19] MetS also confers an approximately 3.5 to 5 times greater risk of developing T2DM.[17] Due to their increased risk profile, people with MetS could, therefore, be an important group to target for prevention of T2DM and CVD.[16, 20]

2.5.2 Evaluation and assessment of risk

Lack of a consensus definition and concerns about whether the risk conveyed by the syndrome as a whole exceeds the total risk associated with individual components, have led to debate about the prognostic significance of MetS.[16, 57] Findings from two recent prospective studies indicate a strong association between MetS (NCEP[7]) and incident diabetes (RR 7·47 [4·90 to 11·46]) and a modest association with CVD (RR 1·27 [1·04 to 1·56]).[58] However, in both studies, despite all five componants of MetS being associated with risk of developing T2DM, waist circumference, triglycerides, and glucose criteria were not associated with risk of developing CVD.

The usefulness of MetS in clinical practice compared to existing risk assessment tools such as the Framingham CVD risk score,[59, 60] has also been questioned.[57, 61] Existing evidence is inconclusive as to whether the addition of metabolic syndrome to convential methods improves CVD risk prediction.[62]

Furthermore, some experts have questioned the utility of attempting to define criteria that predict increased risk for both T2DM and CVD simultaneously.[58, 63] Incorporating additional factors into current risk prediction models has been suggested as the prefered method.[62]

However, tools such as the Framingham risk score were designed to measure absolute risk (global risk) of CVD and identify people who have a high 10 year risk and therefore warrant drug treatment for risk factor reduction.[59] The role of MetS in risk assessment relates to the identification of people who have a comparatively high long-term risk for both T2DM and CVD.[8, 15] Additionally, the identification of people with MetS in clinical practice does not preclude the use of traditional methods of CVD risk assessment. The IDF currently advocate intensive lifestyle advice/intervention to reduce long term risk for individuals with MetS; however, they also recommend that absolute risk assessment should be undertaken to determine the need for drug therapy.[8]

2.5.3 Individual versus population risk

Despite current suggestions by the WHO that MetS has limited utility in clinical practice as a diagnosis or management tool, they also concede that MetS may be a useful concept for the focus of local or national public health campaigns.[63] Globally, population-wide strategies aimed at targeting common risk factors, such as smoking, decreasing physical activity levels and unhealthy diet, are seen as vital to address the growing burden of non-communicable diseases including T2DM and CVD, particularly in developing countries.[64] However, total population strategies alone will not have an immediate impact on CVD mortality

and morbidity but need to be combined with approaches that identify high-risk communities and individuals.[64] Additionally, in developing countries where resources are more limited, it is vital to target those people who are most likely to benefit from intervention.[65] High risk individuals have most to gain from intensive modification of multiple risk factors and at an individual level MetS provides a way to identify and manage multiple risk factors for both CVD and T2DM.[16, 66] However, if resources are available, this approach should be supplemented with population-focused prevention strategies which take into account the specific context and needs of the local population.[63]

2.6 Waist circumference measurement

Waist circumference is the anthropometric measurement most closely correlated with visceral adipose tissue[11] and central adiposity.[67] Some studies have shown that waist circumference is a better indicator of future risk than waist-to-hip ratio[68] and BMI.[67] Waist size is also one of the essential criteria for identifying MetS.[8, 31]

2.6.1 Reproducibility of waist measurement

Despite the evidence for a strong link between waist circumference and outcomes, there is currently no consensus as to how or where to measure waist size. Protocols for conducting waist measurement, that are reported in existing research literature, are broadly based on identifying bony landmarks (last rib, iliac crest, or midpoint) or external landmarks (narrowest or largest abdominal circumference, umbilicus, or 1 cm or 1 inch above the umbilicus).[69] The four sites which are commonly utilised for waist measurement include: (1) the mid-

point between the lowest rib and the iliac crest; (2) at the level of the umbilicus; (3) the minimal waist; and (4) immediately above the iliac crest.[69]

There is evidence to suggest that absolute waist size value differs according to where the measurement is taken, particularly for women[69-71]; some investigators have expressed concern that this may result in the incorrect identification of central obesity and corresponding health risk in some people.[69] However, despite this variability, the site utilised for waist measurement appears not to have any substantial influence on the association between waist circumference and health outcomes.[69, 71]

Concerns have previously been raised by experts about the variability of waist measurements, both intra-operator (variability in measurements taken by the same healthcare professional) and inter-operator (variability between healthcare professionals).[70, 72] However, generally evidence suggests that there is good reproducibility of waist size measurements at all sites.[70, 73] Furthermore, a recent study found that inter-operator variability was eliminated once healthcare professionals were given guidance (written instruction) on how to measure waist circumference.[74] What appears to be most important, particularly if MetS is to be correctly identified, is the consistency of measuring waist size at the site specified by each diagnostic guideline.[71] For example, the IDF and WHO definitions of MetS[8, 29] suggest the mid-point as the level for waist measurement and the NCEP definition[7, 31] stipulates measurement immediately above the iliac crest.

2.6.2 Identifying metabolic syndrome

The IDF definition of MetS[8] was developed to be simple to use and encourage the early identification of MetS, with a view to facilitating primary prevention of T2DM and CVD. All the components of MetS can be easily measured in primary care and currently, lipids and BP are commonly measured in many patients. However, generally, waist circumference is not routinely measured in clinical practice.[14] Measurement of waist circumference could be incorporated into existing health monitoring/screening.[12, 13]

Additional considerations are whether it needs to be a health professional who measures a person's waist size, and whether patients could be involved with assessing their risk of having MetS. The IDF propose that an individual could initially measure their own waist and, if it was raised, their BP, FPG, triglycerides and HDL could then be checked by a health professional.[8] The Finnish Diabetes Risk Score (FINDRISC), a simple self-assessment tool which includes measurement of waist circumference, has proved a reliable method for predicting future risk of T2DM[75]; higher FINDRISC scores have also been shown to be strongly associated with an increased prevalence of MetS.[75] This suggests that engaging people in assessing their own risk by self-measuring of waist size, with further follow-up assessments by health professionals as necessary, could be a useful approach to identifying MetS.

2.7 Recommendations for management of metabolic syndrome

2.7.1 What do we do with patients we identify?

It has been suggested that MetS could be a useful concept for both healthcare professionals and patients to focus on when addressing the health risks associated with abdominal obesity.[15] Additionally, the ability to identify people with MetS in primary care, in order to intervene early and reduce future health risk, is potentially of great importance.[20] However, currently patients with established CVD and/or T2DM receive aggressive management of their individual risk factors. This is not the case for people whose MetS has not progressed to overt atherosclerotic disease or diabetes but who remain at high long term risk. By identifying people with MetS, healthcare professionals should be able to target individuals who are most likely to benefit from early intervention.[16] Once MetS is identified, the aim should be to reduce the future risk of T2DM and CVD and management needs to be focused on addressing all the components of the syndrome.[8]

2.7.2 Current guidance: lifestyle advice and pharmacotherapy

Lifestyle changes (diet and physical activity) are recommended as the initial approach for individuals with MetS, with the addition of pharmacotherapy to treat elevated BP and/or dyslipidaemia if lifestyle alone is ineffective and/or the person has a high CVD risk.[8, 31] No specific pharmacological agents are currently available to treat MetS "as a whole" and pharmacotherapy is currently not recommended for treatment of hyperglycaemia or insulin resistance in individuals with MetS. However, there is evidence that drug therapy can be

effective in reducing cardiovascular events and CVD mortality in people with MetS.[8] The IDF currently advise using either fibrates or statins to reduce dyslipidaemia, but no specific therapy is recommended for hypertension.[8]

In UK clinical practice, there is no specific guidance for risk reduction in individuals with MetS, and the optimal way to promote healthy lifestyle changes is also unclear. Brief information, in the current Scottish Intercollegiate Guidelines Network (SIGN) guidelines on CVD risk estimation and prevention,[76] specifically recommends offering all people with MetS professional advice on exercise, weight monitoring, and a cardio-protective diet, with regular follow-up depending on their progress and CVD risk.

Recent, international, evidence based guidelines, specifically for primary prevention of CVD and T2DM in people with MetS, recommend that healthcare professionals include lifestyle modification as part of the clinical management of at risk patients.[77] The overall emphasis of the guidance includes:

- Reducing calories to promote a weight loss of 5 – 10%;
- Lowering total and saturated fat, and increasing fibre;
- Increasing moderate physical activity to ≥ 30 minutes (but ideally 45 – 60 minutes) 5 to 7 times per week.

Additional recommendations are provided for commencing medication according to assessment of 10-year global CVD risk; targets include:

- Treating BP to <140/90;
- Aspirin prophylaxis;

- Lipid lowering therapy to reduce LDL and non-HDL cholesterol, and raise HDL cholesterol.

2.7.2.1 Research evidence

In MetS, there is a lack of existing systematic review evidence to inform management guidelines, including guidance related to the primary prevention of T2DM and/or CVD in people with MetS. In spite of this, the rising prevalence of MetS combined with its possible role in the context of diabetes and CVD prevention, has resulted in an increasing research interest focused upon possible interventions. Current evidence of the effectiveness of lifestyle and pharmacological interventions for reducing diabetes and cardiovascular risk in people with MetS will be considered in detail in the systematic review presented in Chapter 4.

2.8   Concluding remarks

This chapter has provided an overview of the concept of MetS, in order to provide a backdrop to the work presented in the following chapters. The next chapter (Chapter 3) describes a qualitative study exploring the knowledge and attitudes of both patients and primary care health professionals towards waist size measurement.

Chapter 3. Views on waist size measurement a qualitative study

3.1 Introduction

3.1.1 Chapter overview

This chapter presents a qualitative study conducted to explore the views of both patients and primary care health professionals towards waist size measurement. It explores people's knowledge of the importance of waist size as a measure of abdominal obesity and associated health risk and attitudes to carrying out assessment of waist size in a multi-ethnic setting. The introduction (section 3.1) highlights current recommendations for waist circumference measurement, outlines the rationale for conducting the study and states the aims. The methods used to conduct the study are then described (section 3.2) and the key themes identified are presented in the results section (0). Finally, the findings are discussed and the key implications identified (section 3.4).

3.1.2 Background and rationale

There have been calls for a greater emphasis to be placed on measuring waist size when assessing obesity and associated health risk.[67] Recent guidelines on vascular risk assessment published by the National Screening Committee recommend including waist circumference measurement in risk assessment both for population based screening and for screening those at risk.[12] The National Institute for Clinical Excellence (NICE) also recommends that waist circumference measurement may be useful in addition to body mass index

(BMI) for obesity management in people whose BMI is less than 35kg/m^2.[13] Additionally, waist circumference measurement is of great importance to metabolic syndrome (MetS), as outlined in Chapter 2, as a proxy measure for visceral adipose tissue[11] and central adiposity[67]; it is one of the criteria for diagnosing MetS.[7, 8]

The primary health care team are ideally suited to identify risk using waist circumference measurement.[20] However, despite the evidence for a strong link between waist size and outcomes, and waist circumference being a relatively simple measure, this assessment is not routinely carried out in general practices. A recent survey suggests that only 12% of practice nurses (PNs) in England measure waist circumference in a typical week compared to 96% who measure BMI,[14] but currently there is a lack of research evidence relating specifically to practitioner barriers to carrying out waist circumference measurement.

There is also a lack of knowledge about patients' understanding of the importance of waist size. Evidence from a recent study suggests that very few people know what the cut off point is at which waist size confers an increased health risk.[78] However, this was a questionnaire survey and people's knowledge and views were not explored in depth. Additionally, although patient concerns about some physical examinations by healthcare professionals (HCPs) have previously been explored,[79-83] little is known about patient perceptions about waist measurement.

There is an increasing body of evidence that certain ethnic groups are at higher risk of developing type-2 diabetes (T2DM) and cardiovascular disease (CVD),[5, 6] and that abdominal obesity may be an important contributing factor.[84] In South Asian (SA) populations abdominal adiposity is much higher compared with many other ethnic groups (including White Europeans (WEs)) for a given waist size.[32, 85] Despite this, there is limited research evidence relating to the use of waist circumference measurement to detect increased risk in migrant populations including SAs. This includes a lack of information regarding potential cultural barriers.

Table 3-1 illustrates the ethnic diversity of the population of Leicester City[86] and Leicestershire County,[87] from where the population for this study were sampled, compared to the population of England.[88] The Asian population in Leicester has a much higher proportion of people of Indian origin (mainly from either Gujarat in India, or via East Africa) compared to the Asian population in England as a whole. Additionally, 75% of Leicester's Indian community are Hindu and 25% are Muslim.[86]

Ethnicity	Leicestershire County (2006 estimates)	Leicester City (2007 estimates)	England (2007 estimates)
White European	93%	60%	88%
Asian (Indian)	5% (4%)	31% (28%)	6% (3%)
Black	1%	8%	3%
Other	2%	2%	3%
Estimates provided may total >100% due to rounding of data			

Table 3-1: Ethnic diversity of Leicester, Leicestershire and England

3.1.3 Aims and objectives

The aims of the study were to elicit and explore the knowledge and attitudes of both patients and primary care health professionals towards waist size measurement, including identification of possible barriers to carrying out this assessment in a multi-ethnic setting.

3.2 Methods

This study was conducted in accordance with the approval granted by Leicestershire, Northamptonshire and Rutland NHS research ethics committee (see letter in Appendix 2).

3.2.1 Design and initial recruitment

A qualitative study using purposive sampling and in-depth semi-structured interviews was conducted. A provisional quota of recruiting 10 HCPs and 20 patients was set, to facilitate capture of a range of views. The final number would be based on reaching saturation in terms of the emergence of new themes. All general practices in Leicestershire, UK, were sent an invitation to participate and general practices were selected from those who volunteered. The final sample of nine practices was based on including a range in terms of: list size, urban or rural location, ethnic background of patients, teaching/training status, and the number of general practitioners (GPs) and PNs working at the practice. Subsequently, interviewees were recruited by letter or in person from the selected practices. For HCPs, practice managers were given a study information pack to distribute to each of the GPs and PNs working in their practice. For patients, each practice was given posters to publicise the study

and study information packs to give out to interested patients. At practices that had a high proportion of people of SA ethnicity on their register, Gujarati translated versions were also supplied.

All GPs and PNs in participating practices were eligible to take part. Patient volunteers were required to be:

(1) able to speak and understand English and/or Gujarati, as Gujarati is the most common SA language spoken in Leicester and an experienced interviewer with Gujarati skills was available.

(2) aged 25 to 75 years, as this is the likely age range to be included in any screening programme targeting ethnically diverse populations ($\geq$ 25 years for SAs and $\geq$ 40 years for WEs).

For both professionals and patients, a sampling frame was used to purposively select a diverse sample to be interviewed from those who volunteered. We sought to capture a range of views in terms of ethnic background, age, and gender. To further inform the selection process, volunteers were also invited to provide the following information: for patients, frequency of visiting their general practice, previous experience of having their waist measured, and weight/BMI (optional); and for HCPs, length of time working in primary care, and whether their current role involved waist circumference measurement.

3.2.2 Data collection and recording

Topic guides to assist with directing the interviews were developed through discussion between the members of the research team and input from relevant

stakeholder groups (HCPs and patients).To assist with development of the HCP topic guide a small group of professionals including a GP, dietician, PN, and specialist nurse were approached. For the patient topic guide, we involved a sample of administration and support staff from within our department; individuals were sent a brief description of the study and an outline of possible questions and areas for exploration and asked for feedback. Both the stakeholder groups consulted comprised people from a range of ethnic backgrounds including SAs.

Draft versions of the topic guide were then piloted with known contacts and any revisions indicated were made at this stage. Changes to the draft patient topic guide included exploration of experience of having waist measured in a non-health care setting, for example when being measured for clothes by a tailor; additions to the HCP topic guide included exploration of perceived usefulness of waist measurement compared to BMI and weight, and reliability of waist measurement. Subsequently, topic guides continued to be revised as any new issues emerged from the interviews during the data collection process. For example the notion of usefulness of waist measurement was incorporated as an additional area to explore in both patient and HCP interviews. In addition, the concept of MetS was explored more specifically in later interviews with patients following the emergence of this topic during HCP interviews. The topics included for discussion are outlined in Table 3-2 (see Appendix 2 for the interview topic guides).

Interviews were carried out between October 2007 and April 2008. Patient interviews were conducted in the participant's home and HCPs were interviewed at the general practice where they worked. Written consent to participate in the study was obtained immediately prior to the interview. All interviews were audio-recorded and transcribed verbatim. The author conducted all the HCP interviews and the patient interviews for people whose first language was English; transcription of these interviews was carried out by an independent professional transcriber. An experienced qualitative researcher with appropriate language skills and who has received extensive training in qualitative interviewing in both English and Gujarati conducted all the interviews with patients whose first language was Gujarati, and later simultaneously transcribed the interviews from Gujarati to English where appropriate (see Appendix 1 for further details of the individual researchers involved). Both interviewers additionally kept reflective diaries.

Topics for discussion with patients:	Topics for discussion with HCPs:
• Previous experience of body shape/size assessment	• Assessment of obesity related health risks
• Knowledge of the importance of waist size and associated health risks	• Knowledge of waist size as a risk factor
• Emotional feelings related to being measured	• Feelings related to measuring patients
• Potential barriers	• Perceived barriers
• Perceived usefulness of measurement	• Usefulness of waist measurement

Table 3-2: Areas for possible discussion included in the topic guides

3.2.3 Data analysis

Transcripts from patient and practitioner interviews were analysed separately and the results subsequently compared. A constant comparative approach[89] was adopted throughout. To develop an initial coding frame, three HCP interviews and three patient interviews were open-coded independently by the author and a senior researcher with extensive qualitative experience (see Appendix 1), either manually or using QSR-N6 free nodes.[90] Progressive focusing was then carried out in order to develop descriptive and conceptual (interpretive) categories. The coding scheme developed was then used as a guide to systematically code the other interview transcripts using the software QSR-N6.[90] In line with our constant comparative approach, as transcripts were analysed the coding frame was modified in response to new data. Exploration and interpretation of the coded data involved two researchers to ensure validity and included comparison of themes and concepts. We purposively examined whether the views of GPs were different from those of PNs, and whether there were differences in views between SA and White European (WE) patients.

3.3 Results

3.3.1 Characteristics of the sample

Interviews were conducted with 18 patients (6 SA) and 10 HCPs, in line with our quota sampling frame. The SA patients interviewed were all from the local Gujarati Hindu community, of whom two opted to be interviewed in Gujarati, possibly suggesting a lesser degree of acculturation. Table 3-3 and Table 3-4 show additional details of characteristics of the sample interviewed.

Characteristics of lay-participants interviewed *(n = 18)*	n
Age group:	
25 – 39 years	2
40 – 59 years	5
60 – 75 years	11
Sex:	
Female	11
Male	7
Frequency of visiting general practice:	
Monthly	8
6 monthly	1
Yearly	7
No information	2
Ethnicity:	
White	11
South Asian	6
Other*	1
Approximated BMI category, *ethnic specific:*	
Normal	3
Overweight	8
Obese	6
No information	1
* Ethnic group not defined	

Table 3-3 Characteristics of lay-participants interviewed

Characteristics of HCPs interviewed *(n = 10)*	n
Profession:	
Practice Nurse	4
General Practitioner	6
Age group:	
25 – 39 years	2
40 – 59 years	8
Sex:	
Female	7
Male	3
Number of years working in primary care:	
1 – 5 years	2
6 – 10 years	2
> 10 years	6
Practice currently measures waist circumference:	
Regularly	2
Occasionally	7
Never	1
Ethnicity,	
White	5
South Asian	4
African	1

Table 3-4 Characteristics of healthcare professionals interviewed

We identified varying experiences of the types of patients targeted for waist circumference measurement by HCPs, the method used, and the frequency of measuring waist size. Only one practice routinely carried out waist circumference measurement for all patients but a few practices measured waist size in specific patient groups, usually for people with diabetes or for obesity management. Most patients had no experience of waist circumference measurement by a HCP but some had been measured by a family member or a

tailor in relation to buying or fitting clothes. Generally patients had limited experience of measuring their own waist.

3.3.2 Themes identified from the interviews

Two overarching themes were identified from the patient and HCP interviews: understanding of waist size measurement to assess or monitor risk (theme 1), and attitudes related to perceived barriers and facilitators to waist measurement (theme 2). Overall, no clear differences emerged when comparing the views of SA and WE patients, or GPs and PNs. Quotations to illustrate themes 1 and 2 are coded as follows: PT (patient), interview number, gender (male / female (M/F)), SA (if South Asian); or HCP (health care professional), interview number, profession (GP/PN).

3.3.2.1 *Understanding of waist size measurement to assess or monitor risk*

Generally PNs and GPs demonstrated, without specific prompting, an awareness of the link between a large waist size and risk of diabetes.

> *"The bigger the waist the more at risk they are of certain conditions like glucose intolerance and diabetes." (HCP, 10, PN)*

A link with CVD was less frequently mentioned spontaneously but was generally acknowledged after prompting. However, the concept of central obesity, including metabolic syndrome and its association with risk, was less commonly raised. Most HCPs suggested specific values for a healthy waist size but there was a high level of variation, (74 – 88 cm cited for females and 90 – 100 cm for

males). Awareness of ethnic specific recommendations for waist size values due to increased health risks in certain ethnic groups was poor. However, health professionals frequently acknowledged that there were differences in waist size or health risks for certain ethnic groups, particularly Asians.

"Well we understand ... that certain ethnic populations have higher risks, some of our Asian populations have a much higher risk of heart disease ... a larger waist is a pre-disposing factor." (HCP, 08, PN)

"Even if their body mass index is lower, my understanding is Asian people seems to have a larger waistline than Caucasians." (HCP, 07, GP)

Around half of all patients interviewed demonstrated no knowledge of the importance of waist size or of any associated health risks.

"I do know that as you get older your fat sort of settles here, okay, and that's as much as I know. I don't know how dangerous it is or whether you should be aware of it." (PT,08, F)

Of those patients who demonstrated an awareness of health problems associated with a large waist size, very few specifically mentioned the risk of developing heart disease and / or diabetes. However, a few people talked about an apple shaped body being unhealthy and a pear shaped body being more healthy.

"Certain body shapes are supposed to be more healthy than others ... I think the apple shape's supposed to be the unhealthy one." (PT,12 F)

Additionally, some patients remarked that people who have a large waist size or who are overweight are not necessarily unhealthy. In some cases this perception appeared to lead to denial of the link between body size and health.

"I have been in contact with a lot of fat people, they've never had no problems and I mean not just fat, but fat as in fat. They've never had no problems so the two don't connect." (PT,01,M,SA)

"Well I know some blokes who have got big stomachs and that, and they're as fit as fleas, you know what I mean" (PT,07,M)

In later interviews, of those patients who were specifically asked about the term MetS, all were unfamiliar with the concept. Furthermore, the two people who speculated about the meaning of the term MetS, both assumed that it must be linked to a person's ability to lose or gain weight.

"I think some people have a high metabolism, they can eat, drink and do what they like. If you've got a low metabolism you can put weight on very easily." (PT,10,F)

3.3.2.2 Attitudes related to perceived barriers and facilitators to waist measurement

Issues emerging from the patient and HCP interviews in relation to perceived barriers and facilitators were categorised as a number of sub-themes as presented below.

Standardisation and training needs

Most HCPs indicated that they had not received any specific training in how to carry out waist circumference measurement. Concerns related to the need for training included difficulties in positioning the tape, lack of repeatability, operator variability and interpretation of results. A commonly raised issue was the need for a standardised and nationally accepted method.

"I mean it sounds quite easy on the face of it but some people, it can be quite difficult in some patients … so a written instruction and standardisation of how to measure it will be helpful." (HCP,07,GP)

"If I get a patient that moves in, how do I know that their waist measurements from the previous surgery are conducted the same way we're doing here." (HCP,08,PN)

Perceived usefulness

The majority of HCPs felt that waist circumference measurement was more useful than BMI or that it was advantageous to carry out this assessment as well as BMI.

"BMI is just a figure, it doesn't tell their right risk factor … if you are going to target obesity without waist circumference what are you looking at?" (HCP,02,GP)

"Yeh, well I think the BMI is important but that's not everything. I think you should take (it) in context with the BMI." (HCP,07,GP)

However, the view was also expressed that there may be no need to measure body size at all.

> *"Take your clothes off and stand in front of a mirror if you want to know whether you're fat or not 'cos that's all you need to do really. It's pretty damned obvious normally." (HCP,03,GP)*

Differing views were expressed by HCPs regarding the perceived usefulness of waist measurement to patients. Some felt that patients are not familiar with waist size and may not understand how it relates to risk.

> *"I don't think people are as aware of waist circumference measurement as they are of weight" (HCP,06,GP)*

> *"Not a lot of patients know that it is important ... you have to sell it." (HCP,14,GP)*

Others thought that a waist measurement was something that could motivate patients to make lifestyle changes.

> *"They go oh my goodness I used to be a thirty-six, you know. It sometimes can bring them up short and make them think actually I should do something about this. We'll chat about what's a healthy diet and what goals to make." (HCP,13,PN)*

When the topic of using waist circumference measurement to predict risk was raised with patients, the majority felt that having their waist size measured by a

HCP would be useful for themselves in terms of identifying health problems, getting advice, and facilitating positive lifestyle changes. Overall, patients also thought that it would be beneficial for their doctor/nurse to know their waist size.

"The earlier I can find something that's wrong with me and start treatment to get it put right, the better. So yeah, the more examinations the better, so far as I'm concerned." (PT,13,M)

"Well it might get me to look at my diet … and try to lose some weight you know." (PT,04,F)

"They can assess your health, what you are or what problems it can create in the future." (PT,19,M,SA)

Self-measurement of waist size was also explored. The majority of patients' thought that it would be useful for them to measure their own waist size. However, the importance of providing some guidance related to where to measure and how to interpret the measurement was emphasised.

"Some sort of diagram to indicate that I'm measuring the right part of my body, where the waist is … something to say why I'm measuring it.."
(PT,13,M,)

"I would want to know … where to measure it, what I'm looking for. Perhaps the first time the nurse could show you exactly the spot where you should be measuring … then you keep your eye on it yourself." (PT 08,F)

<u>Personal feelings</u>

For some HCPs, the perceived intimate nature of waist circumference measurement appeared to present a barrier, although for others this was not an issue.

"It's personal to go up and start putting your arms around a patient."

(HCP,10,PN)

"I think it's less invading for a patient to have them standing on a scale than

to measure their waist circumference." (HCP,06,GP)

HCPs also perceived that patients might feel uncomfortable or be embarrassed about having their waist measured.

"All your women that have babies and have ended up with massive stretch

marks ... even those with normal weight don't like revealing themselves."

(HCP,13,PN)

"Not many will say no but if they are really obese they won't feel nice so

...you have to make them comfortable and if I am in their place I won't feel

comfortable, I won't come to my clinic again because it's very embarrassing."

(HCP,01,PN)

Furthermore, a few HCPs demonstrated preconceived ideas about cultural groups, specifically SA women, for example in relation to removal of clothing.

"A big Asian lady, …I mean it would be easier to weigh her and she wouldn't mind that. To ask her to remove her clothes, well … she (would) need to ring the husband to get permission for you to do that" (HCP,14,GP)

"Depends on the individual circumstances. Some patients don't care, but if you're a Muslim woman and very strict about it you wouldn't want anybody other than a woman touching you so it depends on your individual ethnic preferences and your personal preferences as well." (HCP,03,GP)

"Depends on their person … and their culture you know er … some of the women not wanting to expose themselves all the time but erm … I would still be able to do it." (HCP,13,PN)

In contrast, most patients, including SAs, said that they did not think that they would be embarrassed or feel uncomfortable about having their waist measured.

"I wouldn't feel anything about it, wouldn't think about it 'cos they are doing their job and that's it." (PT,19,M,SA)

"Wouldn't bother me… Don't have a problem with it at all." (PT,08,F)

Two patients, both WE females, expressed concerns when they were asked specifically about loosening or removing any clothing, although there was no indication that this would lead to them actually refusing to have their waist measured.

"I wouldn't be happy if I'd gotta take a skirt or trousers too far down... I don't

mind it being on my waist but I'm not sure I'd want to strip off for that."

(PT,10,F)

" A bit embarrassed ... I'm a bit podgy round the waist now." (PT,04,F)

In addition, a few women, both SA and WE, cited a preference for being measured by a female HCP but this was not seen as essential, and the need for a chaperone was not perceived as important.

"I'd be more comfortable with a female, but it wouldn't matter if there was

just you know a male available, but I would prefer a female." (PT,10, F)

Overall, what appeared most important to patients was that the HCP should provide them with an explanation of what the measurement involved and why it was being conducted.

"I would expect them to tell me that without me having to ask, you know. I'd

like to measure your waist because, you know, and this is how we'll do it."

(PT,08,F)

"I'd agree as long as they were telling me why they were doing it ... you know,

so there was a reason." (PT,16,F.)

Practical considerations

Time was specifically mentioned as a barrier by the majority of HCPs in relation to the length of appointments and the extra workload involved if measurements and associated discussions were to be carried out regularly.

"Time constraints in consultations if you wanted to do it in consultations."

(HCP,03,GP)

"I wouldn't mind but it's extra work for me…there's so much pressure of work

…workload will increase a lot you know." (HCP,01,PN)

"You don't just take the measurement, you have to explain what it means so in

itself it doesn't take a moment does it, but then you've got quite a good length

of topic of conversation to explain it." (HCP,06,GP)

The topic of finance was frequently raised by HCPs either as a barrier in terms of cost implications for the practice, or as a facilitator when asked about possible methods of encouraging the use of waist circumference measurement. Three people, all GPs, specifically mentioned inclusion of this assessment in the Quality and Outcomes Framework (QoF)[91] as a potential incentive.

"Well if it ends up as a QoF point no doubt it will be done because they're

worth a lot of money … I don't think it would be done voluntarily."

(HCP,06,GP)

In addition, some HCPs suggested organisational incentives for carrying out waist circumference measurement. These included the addition of waist

circumference to all patient templates, targeting new patients, or policy changes at practice or primary care trust level.

Practical considerations mentioned by patients were generally related to concerns about having their waist measured when they were not expecting to have this assessment. These concerns included perceptions about hygiene, for example in terms of showering before the appointment; the need to wear appropriate clothing; time implications if the assessment added to the length of the appointment; and a perceived need for the opportunity to consider whether it would be appropriate to bring children to the appointment.

3.4   Discussion

3.4.1 Key findings

In the sample we interviewed, no clear differences emerged when comparing the views of patients from two different ethnic groups (SA, n = 6; WE, n = 11; not defined, n = 1), or GPs (n = 6) and PNs (n = 4). HCPs were generally aware of a link between a large waist size and health risks, although, knowledge of ethnic specific recommendations for waist size was poor. Additionally, the concept of central obesity, including MetS and its association with risk, was not commonly raised. Most HCPs had not received specific training in how to carry out waist circumference measurement and did not routinely carry out this assessment. Generally, they felt that there were advantages to using waist circumference measurement alongside or instead of BMI. However, a few felt uncomfortable about carrying out waist circumference measurement and some perceived that patients might be embarrassed. Practical barriers suggested

included lack of time and extra workload. Financial implications were seen as both a barrier and a potential incentive.

Around half of all patients interviewed had no previous knowledge of the importance of waist circumference measurement, although, a few people talked about which body shape they thought was healthier. Additionally, when specifically asked about the term MetS, no one was familiar with the concept. Despite this general lack of knowledge, the majority of patients indicated that having their waist size measured would be useful for both themselves and their doctor or nurse. Furthermore, most patients felt that self-measurement of waist size would be useful, provided that they received some guidance. Generally, patients perceived a lack of embarrassment about waist circumference measurement although a few women expressed a preference for a female to measure them. What appeared most important to patients was being provided with an explanation of what the measurement involved and why it was being carried out. Practical barriers for patients were related to having the measurement carried out without prior warning.

3.4.2 Comparison with other studies

A small number of quantitative studies have considered knowledge and experience of waist circumference measurement, but there is a lack of qualitative evidence. A large survey which included the UK suggested that only 58% of primary care physicians recognise that abdominal obesity is a significant risk factor for heart disease.[78] Although an association between a large waist size and CVD was not frequently mentioned spontaneously by the HCPs we

interviewed, this link was generally acknowledged after prompting. However, the concept of central obesity, including MetS and its association with risk, was not commonly raised by our HCPs. Results from a survey of practitioners in Scotland similarly suggest that GPs' and PNs' awareness of the link between waist size and intra-abdominal obesity is poor.[92]

In addition, around half of the patients we interviewed demonstrated a lack of any understanding of the importance of waist size in relation to health risks. Previous evidence from cross sectional studies also suggests that few patients know what the cut-off point is at which waist size confers an increased risk,[78] and that patients tend to perceive the size of their own waist to be significantly smaller than the actual value when measured by a HCP.[93] In this study a few people were aware of the potential health risks associated with certain body shapes but perceptions of others appeared to lead to denial of a link between body size and health. The concept of MetS was also something that patients were unfamiliar with when specifically asked in later interviews. Previous evidence from a large US population survey similarly found that people generally lack knowledge and awareness of MetS.[94]

In this study HCPs' perceptions about the views of patients were not necessarily an accurate reflection of the feelings expressed by patients themselves, particularly in relation to patients' perceived embarrassment at having their waist size measured. Findings from a small number of previous cross sectional studies have also noted a difference between patients' attitudes and professionals' perceptions about these attitudes, specifically in relation to

patient views towards CVD risk detection,[95] and the emotional impact to patients of having T2DM.[96]

Other authors have highlighted patient concerns about other physical examinations such as breast,[79] rectal[80] and genital examination,[80] and cervical screening,[79, 81, 82] but there is a lack of literature related directly to patient attitudes to waist circumference measurement. In our study, patients did not perceive the need for a chaperone for waist circumference measurement. This is consistent with a questionnaire study conducted in primary care in the US which found that, although patients indicated a preference for a chaperone for some examinations, it was not seen as necessary for examination of the heart/lungs and abdomen.[83]

Some of the practical considerations raised as potential barriers to carrying out waist circumference measurement by the HCPs we interviewed show similarities with the results of two previous cross sectional studies examining implementation of evidence based recommendations. These include lack of time, particularly limitations associated with a heavy workload,[97] and lack of reimbursement.[98]

3.4.3 Strengths and limitations

The use of sound qualitative methodology, including purposive sampling and a flexible topic guide, ensured that data were collected from a range of people and enabled in depth exploration of their views and experiences. It is acknowledged that the group of administration and support staff used to

represent patients' perspectives during the development of a topic guide was a non-representative group. However, this opportunistic sample enabled the appropriateness of the proposed lines of questioning to be tested on people without a healthcare professional background. The actual sample of patients interviewed for the study itself was drawn widely from people attending general practices.

A further strength of the study is inclusion of the views of both practitioners and their patients. However, only GPs and PNs were involved rather than a wider range of HCPs and previous cross sectional evidence suggests that, compared to GPs and PNs, dieticians are more aware of the importance of waist size to intra-abdominal obesity.[92] It is therefore acknowledged that it could have been useful to include dieticians working in primary care in our sampling strategy.

By including patients from different ethnic groups, the study provides insight into relevant attitudes in a diverse ethnic setting. However, it is acknowledged that people from minority ethnic backgrounds living in the UK are not a homogenous group. Our sample of Gujarati Hindus represents a specific sub-group of migrant SAs and the views they expressed may differ to other non-English speakers who were excluded from taking part. The transferability of the findings to other sub-groups of SAs and other ethnic groups would need testing through further research. For example, it may be surmised, though it should not be assumed, that Muslim women might have different attitudes to having their waists measured. Indeed, one of the HCPs interviewed in our study suggested that Muslim women might not want anybody other than a woman touching them

(HCP, 03, GP). However, as the study has shown in relation to potential embarrassment, HCPs' perceptions about the attitudes of their patients are not necessarily an accurate reflection of the views expressed by patients themselves.

3.4.4 Implications of study findings

Some of the findings from the study described in this chapter have been used to help inform the development and delivery of the group educational intervention described in Chapter 5. In particular, findings related to patients lack of prior understanding of MetS and views about self-assessment of waist size were considered relevant to curriculum development (for details see Chapter 5, section 5.4.1).

General implications for practice arising from the broader remit of the study will be discussed in Chapter 8 (final chapter).

3.5   Concluding remarks

In addition to its specific role in the development of the intervention described later in this thesis (Chapters 5 and 6), the study also contributes more broadly to an area of research where there has been a paucity of qualitative studies. This study adds to our understanding of barriers and facilitators regarding waist size measuring in a multi-ethnic population, highlighting factors for consideration if waist circumference measurement is to be facilitated in routine practice. The following chapter presents a systematic review and meta-analysis

which was conducted to review the evidence on interventions for reducing

diabetes and CVD risk in people with MetS.

Chapter 4.   Effectiveness of lifestyle and pharmacological interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: a systematic review

4.1   Introduction

4.1.1   Chapter overview

This chapter reports a systematic review conducted to review the existing evidence for primary prevention of type-2-diabetes (T2DM) and cardiovascular disease (CVD) in people with metabolic syndrome (MetS). Keys findings from a meta-analysis are also reported. The introduction (section 4.1) briefly outlines the rationale for carrying out the systematic review and states the aims. The methods used to conduct the systematic review are then described (section 4.2). The details of the data synthesis are then presented in the results section (4.3). The findings of the review and the key implications that informed the development work in Chapter 5 are then discussed (section 4.4).

Appendix 1 details the contributions of people involved in the systematic review and meta-analysis. The systematic review, including the extraction and collation of all data, was conducted by the author of this PhD thesis. However, in order to ensure that guidelines for best practice[99] were followed the review involved some collaborative work with a team of people. More specifically, the author contributed to the meta-analysis by extracting and collating the relevant data

and was also involved in interpreting the results of the analysis, but the direct pairwise and Baysian mixed treatment comparison meta-analysis reported as part of this chapter were conducted by an expert statistician.

Recognising the author's contribution, and the fact that the findings supported the rationale for the intervention to be tested in the trial (Chapters 6 and 7), a summary of the methods used and the key results, from the meta-analysis, are included in the current chapter. Additional details of both the methodology used for the meta-analysis and the results obtained, are included in Appendix 3 rather than in the main body of the thesis.

4.1.2 Background and rationale

The rising prevalence of MetS, combined with its possible role in the context of diabetes and CVD prevention (as outlined in Chapter 2) has resulted in an increasing research interest focused on possible interventions. Several randomised controlled trials (RCTs) of interventions (lifestyle and/or pharmacological) aimed at reducing T2DM and CVD risk in people with MetS have been conducted. However, a literature search suggested that no systematic review of the evidence had previously been published.

4.1.3 Aims

- The overall aim of the work described in this chapter was to review the evidence on interventions for reducing diabetes and CVD risk in primary prevention populations with MetS.

- If sufficient data were available, an additional aim was to conduct a meta-analysis relating to the outcomes of incidence of T2DM, CVD events or mortality, and reversal of MetS.

4.2 Methods

To collate (and potentially quantify) the evidence, a systematic review was undertaken; this included trials investigating the effectiveness of interventions for reversing MetS or for primary prevention of CVD and/or T2DM, in populations with MetS

4.2.1 Inclusion criteria

The inclusion and exclusion criteria are summarised in Table 4-1.

PICOS	Inclusion criteria	Exclusion criteria
P - population	- People with MetS (identified using any recognized definition) - Adults ≥18 years	- MetS induced by medication (i.e. anti-retroviral therapy, anti-psychotics) - People with existing CVD and/or T2DM (10% permitted)
I - intervention	- Lifestyle - Pharmacological - Surgical	
C - comparator	- Usual care - Active control (drug or lifestyle) - Placebo	
O - outcomes	- Incidence of T2DM - CVD events or mortality - Reversal of MetS	- Changes in individual components of MetS - Prevention of MetS
S - study design	- RCT or - Post-hoc analysis of an RCT	Quasi- or non-randomised trials

Table 4-1: Inclusion and exclusion criteria for systematic review

Studies were eligible for inclusion if they were RCTs that compared lifestyle, pharmacological, or surgical interventions, and had a minimum follow-up of 24 weeks. Because the focus of the review was primary prevention, studies where >10% of the population had existing CVD and/or diabetes were excluded. No language restrictions were applied but only studies published as full-length articles were included.

4.2.2 Search strategy and selection

A range of electronic bibliographic databases were searched. These included: EMBASE (1980 to Jan 2010), MEDLINE (1950 to Jan 2010, and In-Process), CINAHL (1982 to Jan 2010), BNI (1985 to Jan 2010), The Cochrane Library (Issue 1, 2010), Science Citation Index (Web of Knowledge) (1980 to Jan 2010), and PubMed (2004 to Jan 2010). In order to construct an effective search strategy, specific elements of the review question were identified and categorised according to the PICOS approach (Population, Intervention, Comparators, Outcomes, Study design)[99], see Table 4-1. MeSH terms and keywords were then combined with the CRD/Cochrane Highly Sensitive Search Strategy RCTs filter[100] and tailored to individual bibliographic databases. The final search strategy (see Box 4-1) included only terms related to the target population and the study design. A scoping search, carried out prior to undertaking the review, suggested that this was the most appropriate approach. The main search for the systematic review was initially conducted in June 2007 and later updated in January 2010.

```
Database: EMBASE <1980 to 2010 Week 03>        Search Strategy:
--------------------------------------------------------------------------------------------
1     exp Metabolic Syndrome X/ (13926)
2     (metabolic adj syndrome).ti,ab. (12644)
3     (android adj obesity).ti,ab. (104)
4     (syndrome adj affluence).ti,ab. (0)
5     (plurimetabolic adj syndrome).ti,ab. (39)
6     (cardiometabolic adj syndrome).ti,ab. (65)
7     GHO syndrome.ti,ab. (0)
8     (glucose adj intolerance adj syndrome).ti,ab. (2)
9     (obesity adj syndrome).ti,ab. (165)
10    ((hypertension and obesity) adj syndrome).ti,ab. (8)
11    (central adj obesity adj syndrome).ti,ab. (2)
12    reaven syndrome.ti,ab. (3)
13    syndrome X.ti,ab. (1234)
14    insulin resistance syndrome.ti,ab. (1300)
15    reaven.ti,ab. (46)
16    hyperinsulin$ syndrome.ti,ab. (13)
17    (insulin resistance adj hyperinsulin$ adj syndrome).ti,ab. (4)
18    atherothrombogenic syndrome.ti,ab. (3)
19    (metabolic adj cardiovascular adj syndrome).ti,ab. (40)
20    dead$ quartet.ti,ab. (33)
21    (dysmetabolic adj syndrome).ti,ab. (67)
22    MetSyn.ti,ab. (53)
23    or/1-22 (19227)
24    Randomized Controlled Trial/ (179441)
25    RANDOMIZATION/ (27401)
26    crossover procedure/ (22267)
27    double blind procedure/ (75637)
28    single blind procedure/ (8937)
29    (random$ adj3 trial$).ti,ab. (105179)
30    exp controlled trial/ (3088069)
31    drug comparison/ (81258)
32    exp clinical trial/ (583869)
33    ((sinlg$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).ti,ab. (90627)
34    or/24-33 (3477941)
35    23 and 34 (9190)
36    letter.pt. (470536)
37    case study/ (6774)
38    animal experiment/ (1335163)
39    editorial.pt. (244048)
40    or/36-39 (2051395)
41    35 not 40 (8009)
42    RANDOM.tw. (91404)
43    PLACEBO.mp. (188748)
44    DOUBLE-BLIND.tw. (84348)
45    or/42-44 (302245)
46    23 and 45 (1549)
47    RANDOM.tw. (91404)
48    CLINICAL TRIAL.mp. (597507)
49    exp TREATMENT OUTCOME/ (522044)
50    or/47-49 (1072816)
51    23 and 50 (3870)
52    51 not 40 (3604)
```

Box 4-1: Example search strategy for the systematic review - EMBASE

Two reviewers, including the author of this thesis, independently assessed abstracts and titles for eligibility and retrieved potentially relevant articles, with differences resolved by a third reviewer where necessary. If foreign language papers were identified, partial translations were obtained to ascertain whether they met the inclusion criteria and full translations were obtained if indicated. Where studies met all the inclusion criteria but data were incomplete, authors were contacted for additional data and/or clarification. The reference lists of included papers and relevant reviews were examined in order to determine whether there were any further papers not identified through electronic searching. Experts in the field of MetS and first authors of included papers were also contacted.

4.2.3 Data extraction

Two reviewers, including the author, independently extracted data, using a form designed specifically for this review (see Appendix 3), and subsequently liaised to check for consistency. Data extracted included sample size, population demographics, intervention details and length of follow-up. Where available, outcome data were recorded for reversal of MetS (proportion), incidence of T2DM, and cardiovascular events or mortality. All papers relating to a particular study were retrieved, including those on design and methodology (if reported separately) or the original trial results for sub-group analyses. Data reported in the text were checked against data in tables, for each paper. Where minor discrepancies were apparent (one paper only[101]) data were taken from the tables.

4.2.4 Quality assessment

The quality of included studies was evaluated using an approach based on the Delphi list,[102] as suggested by the Centre for Reviews and Dissemination.[103] This scoring system was selected in preference to the Jadad score[104], as it includes assessment of allocation concealment in addition to several other crucial indicators related to the risk of bias and internal validity in RCTs. One mark was awarded for each criterion met, giving a possible total score of nine. Where baseline characteristics were only partially reported, or blinding to study intervention was possible for some but not all participants (studies with both a lifestyle and a pharmacological intervention group), the criterion was classed as being partially met and half a mark was given.

4.2.5 Descriptive data synthesis: lifestyle interventions

Detailed data relating to the components of the lifestyle interventions, for studies included in the systematic review, were summarised and evaluated to help to inform the development work presented in Chapter 5. Comparison was made of the behavioural strategies utilised including who facilitated the intervention, where it was delivered, the number of sessions, and any theories underpinning the intervention. Stratified comparisons were also made separately for exercise and nutritional components.

4.2.6 Quantitative data synthesis: meta-analysis

There were insufficient trials reporting CVD events or mortality, or incidence of T2DM, for a meta-analysis of these outcomes. Direct pairwise comparison

meta-analyses and Bayesian mixed treatment comparison meta-analyses were conducted to examine the effectiveness of interventions in studies where data were available to assess reversal of MetS. Each type of analysis was conducted on both a collapsed data set where the interventions were grouped into 4 treatment categories (control, lifestyle, pharmacological, and lifestyle and pharmacological combined), and on the actual ungrouped study intervention data. Further details of the methods used for the meta-analysis are presented in Appendix 3.

4.3 Results

4.3.1 Identification of studies

Results relating to identification and selection of eligible trials are summarised in Figure 4-1.
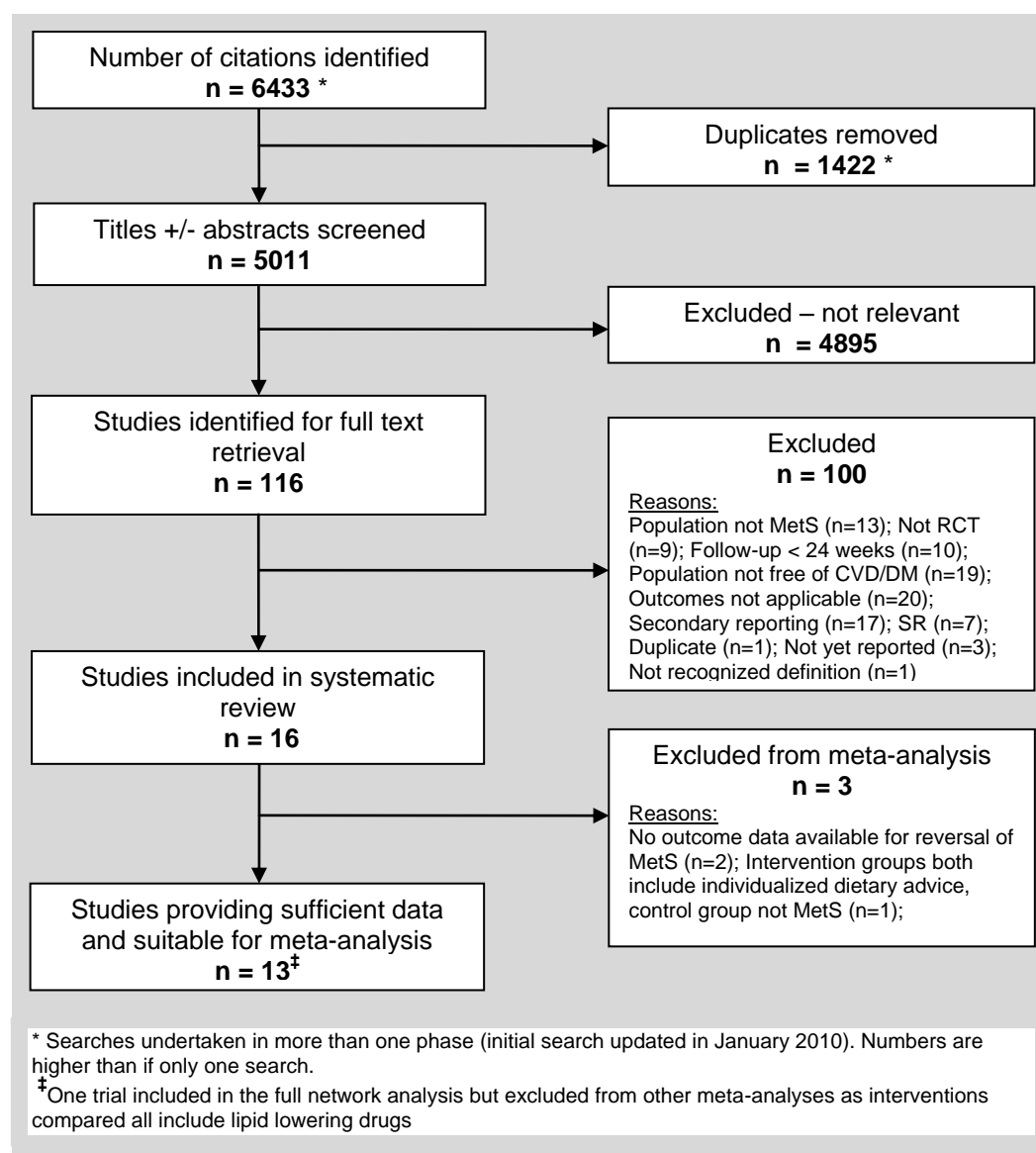
Figure 4-1: Flow chart of selection of studies from search to final inclusion

Searches yielded 6433 citations and subsequently 5011 unique abstracts were screened for eligibility. Following on from this, 116 potentially relevant studies

were identified for full text retrieval, and authors of 19 of these studies were contacted in order to clarify eligibility criteria and/or for additional outcome data. Replies were received for 10 studies, seven of which were subsequently included in the 16 studies that met the review criteria. Letters sent to experts yielded four responses; however, the four trials suggested by these respondents had already been identified and excluded.

4.3.2 Summary of studies included in the systematic review

Sixteen studies met the review criteria[101, 105-119] and are summarized in Table 4-2 and Table 4-3. Study interventions (alone or in combination) included: 1) individualized/intensive dietary advice, 2) supervised exercise sessions, 3) exercise advice, 4) metformin, 5) rosiglitazone, 6) atorvastatin, 7) pravastatin, 8) lovastatin, 9) fenofibrate, 10) sibutramine, and 11) rimonabant. Standard/brief advice on diet and/or exercise was considered to be comparable with usual care and was not judged to be an active intervention. Seven trials focused solely on the effectiveness of lifestyle interventions (two diet alone, two exercise alone, three combined diet and exercise), six studies compared the effectiveness of pharmacological interventions alone (four lipid lowering, one anti-diabetic, one anti-obesity), and three studies had combined lifestyle and pharmacological interventions. No studies considered the efficacy of surgical interventions. Twelve of the studies were subgroup analyses, eight of these were not pre-specified but undertaken post hoc and published separately from the main trial. All papers were published in the previous seven years in the English language.

Studies were conducted in the US, India, Iran and several European countries; however, ethnicity was poorly reported. The number of participants with MetS ranged from 24 to 3,196 and 11 studies each randomised at least 100 people with MetS. The majority of studies utilised the National Cholesterol Education Program (NCEP) definition[7] of MetS, one study adopted the earlier World Health Organisation (WHO) definition,[29] and one used the more recent International Diabetes Federation (IDF) criteria.[8] Length of follow-up varied from 26 weeks to 10 years. The mean age and body mass index (BMI) of participants ranged from 41 to 70 years and 26 to 39 kg/m^2 respectively, and the proportion of males ranged from 21 to 100%. Outcome data for reversal of MetS were reported (or obtained from the authors) for the majority of studies (14/16), see Table 4-4. Two papers additionally reported the incidence of diabetes[106, 112] and only three papers reported cardiovascular mortality and events.[108, 118, 119] Overall, there was considerable heterogeneity between studies in respect to key characteristics such as the population, setting, intervention and follow-up period.

Author & Year	Definition of MetS	Focus of intervention	Nº randomised main trial	Nº randomised with MetS	Follow-up period	Sub-group	Outcome reversal MetS	Other outcomes
Studies included in meta-analysis								
Anderssen, 2007	IDF	**Lifestyle** *(Diet & supervised exercise)*	188	137	1 year	Yes (post hoc)	Yes	-
Athyros, ‡ 2005	NCEP	**Atorvastatin** **Fenofibrate**	300	300	1 year	No	Yes	-
Bo, 2007	NCEP	**Lifestyle** *(Diet & exercise advice)*	335	239	1 year	Yes (prespecified)	Yes	Incidence of T2DM
Esposito, 2004	NCEP	**Lifestyle** *(Diet)*	180	180	2 years	No	Yes	-
Esposito, 2006	NCEP	**Rosiglitazone**	100 (C not MetS)	100	1 year	No	Yes	-
Geluk, 2005	NCEP	**Pravastatin**	864	228	4 years	Yes (post hoc)	Yes	CVD event or mortality
Johnson, 2007	NCEP (2005)	**Lifestyle** *(Supervised exercise)*	334 (227 completers) (171 MetS data)	69 (data available)	8 months	Yes (post hoc)	Yes	-
Orchard, 2005	NCEP	**Lifestyle** *(Diet & exercise advice)* **Metformin**	3324	1711	3 years	Yes (post hoc)	Yes	-
Phelan, 2007	NCEP	**Lifestyle** *(Diet & exercise advice)* **Sibutramine**	224	78	1 year	Yes (post hoc)	Yes	-
Ramachandran 2006	WHO	**Lifestyle** *(Diet & exercise advice)* **Metformin**	531 (502 completers)	233 (data available)	3 years	Yes (post hoc)	Yes	Incidence of T2DM
Stewart, 2005	NCEP	**Lifestyle** *(Supervised exercise)*	115 (104 complete data)	44 (data available)	26 weeks	Yes (unclear)	Yes	-
Van Gaal, 2005	NCEP	**Rimonabant**	1507	564	1 year	Yes	Yes	-
Villareal, 2006	NCEP	**Lifestyle** *(Diet & supervised exercise)*	27	24	26 weeks	Yes (unclear)	Yes	-
Studies not included in meta-analysis								
Azadbakht, 2005	NCEP	**Lifestyle** *(Diet)*	76 (Control not MetS)	76	6 months	No	Yes	-
Clearfield, 2005	NCEP[††]	**Lovastatin**	6605	3196	5 years trial, 10 yr FU	Yes (post hoc)	No	CVD event or mortality
Sattar, 2003	NCEP[††]	**Pravastatin**	6595	1691	5 years	Yes (post hoc)	No	CVD event or mortality

Abbreviations **NCEP**: National Cholesterol Educational Programme; **WHO**: World Health Organisation; **IDF**: International Diabetes Federation.
References: NCEP[7]; NCEP (2005)[31]; WHO[29]
[††]definition modified (BMI threshold substituted for waist circumference); ‡ Trial included only in the full network meta-analysis

Table 4-2: Characteristics of studies included in the systematic review

Author & Year	Country	Ethnicity	Age, mean (SD)	Male %	BMI, mean kg/m^2	Main eligibility criteria
Studies included in meta-analysis						
Anderssen, 2007	Norway	NR	45 (2.5)	100	29	Physically inactive; BMI >24; dyslipidaemia
Athyros, ‡ 2005	Greece	NR	NR	63	31	Consecutive patients
Bo, 2007	Italy	NR	56**	42**	30	Dysmetabolic patients
Esposito, 2004	Italy	NR	44	55	28	Sedentary (< 1 hr/wk physical activity); stable weight in previous 6 months.
Esposito, 2006	Italy	NR	46 (4.5)	54	28	Sedentary (< 1 hr/wk physical activity); stable weight in previous 6 months.
Geluk, 2005	Netherlands	96% Caucasian	55 (11)**	70**	29	Persistant microalbuminuria
Johnson, 2007	US	NR	53 (7)**	53**	30	Sedentary; BMI 25 – 35; dyslipidaemia
Orchard, 2005	US	55% White, 20% Af-Am, 16% Hisp, 9% other	51 (10.7)**	32**	34	Increased BMI; IFG or IGT
Phelan, 2007	US	(80% White, 18% Afn-Am, 3% Hisp.)	48 (9.9)	37	38	BMI 30 - 45
Ramachandran 2006	India	Native Asian Indian	46**	79**	26	IGT
Stewart, 2005	US	87% white, 11% Af-Am, 2% other	64 (5.7)**	49**	30	Untreated hypertension
Van Gaal, 2005	Europe/US	94% white	45**	21**	36	BMI > 30; or BMI > 27 & dyslipidaemia & hypertension
Villareal, 2006	US	85% white	70**	33**	39	BMI > 30; mild to moderate physical frailty; stable body weight for 1 yr prior; sedentary lifestyle
Studies not included in meta-analysis						
Azadbakht, 2005	Iran	NR	41 (12.3)	29	30	Overweight or obese; stable weight previous 6 months
Clearfield, 2005	US	89% white	58**	85**	27	Dyslipidaemia
Sattar, 2003	UK	NR	55.2 (5.5)	100	28	Hypercholesterolaemia

**data stated is for main trial, NOT available for sub-group.
Abbreviations: **BMI**: Body Mass Index; **IFG**: Impaired Fasting Glucose; **IGT**: Impaired Glucose Tolerance; **NR**, not reported; Ethnicity: **Af-Am** = African-American, **Hisp** = Hispanic. ‡ Trial included only in the full network meta-analysis

Table 4-3: Characteristics of study populations

Author & Year	Intervention		Nº Randomised with MetS in each study group	MetS reversed	
				n	%
Studies included in meta-analysis					
Anderssen, 2007	Lifestyle *(Diet & supervised exercise)*	ID v	34	12	35.3
		SES v	34	8	23.5
		ID + SES v	43	29	67.4
		NT	26	3	11.5
Athyros, ‡ 2005	Atorvastatin	ATO + STA v	100	75	75.0
	Fenofibrate	FEN + STA v	100	76	76.0
		ATO + FEN+ STA	100	77	77.0
Bo, 2007	Lifestyle *(Diet & exercise advice)*	ID + EA v	119	69	58.0
		STA	120	28	23.3
Esposito, 2004	Lifestyle *(Diet)*	ID v	90	60	66.7
		STA	90	18	20.0
Esposito, 2006	Rosiglitazone	ROS + STA v	50	20	40.0
		PL + STA	50	5	10.0
Geluk, 2005	Pravastatin	PRA v	114	46	40.4
		PL	114	47	41.2
Johnson, 2007	Lifestyle *(Supervised exercise)*	SES (low amount / moderate) [†]	18*	11	61.1
		SES (low amount / vigorous) [†]	17*	5	29.4
		SES (high amount / vigorous) [†]	18*	11	61.1
		NT	16*	3	18.8
Orchard, 2005	Lifestyle *(Diet & exercise advice)* Metformin	ID + SES v	549	209	38.1
		MET-F + STA v	570	131	23.0
		PL + STA	592	107	18.1
Phelan, 2007	Lifestyle *(Diet & exercise advice)* Sibutramine	ID + EA v	18	13	72.2
		SIB v	19	7	36.8
		SIB + ID + EA v	21	13	61.9
		SIB + STA	20	3	15.0
Ramachandran 2006	Lifestyle *(Diet & exercise advice)* Metformin	ID + EA v	58*	22	37.9
		MET-F v	57*	25	43.9
		MET-F + ID + EA v	56*	13	23.2
		STA	62*	13	21.0
Stewart, 2005	Lifestyle *(Supervised exercise)*	SES + STA v	22*	9	36.0
		STA	22*	8	33.3
Van Gaal, 2005	Rimonabant	RIM 20mg v	228	144	63.2
		RIM 5mg v	228	105	46.1
		PL	108	48	44.4
Villareal, 2006	Lifestyle *(Diet & supervised exercise)*	ID + SES v	15	10	66.7
		NT	9	0	0
Studies not included in meta-analysis					
Azadbakht, 2005	Lifestyle *(Diet)*	ID (DASH diet) v	38	13.3	35.0
		ID (wt reducing diet)	38	7.2	19.0
Clearfield, 2005	Lovastatin	LOV + STA v	1632	NR	NR
		PL + STA	1564		
Sattar, 2003	Pravastatin	PR + STA v	847	NR	NR
		PL + STA	844		

<u>Interventions:</u> **ID** = individualized &/or intensive dietary advice; **EA** = exercise advice; **SES** = supervised exercise; **STA** = standard &/or brief advice (diet &/or exercise); **MET-F** =metformin; **SIB** = sibutramine; **LOV** = lovastatin; **ATO** = atorvastatin; **FEN** = fenofibrate; **PRA** = pravastatin; **RIM** = rimonabant; **ROS** = rosiglitazone; **PL** = placebo; **NT** = no treatment; **NR** - Not reported; **NA** - Not applicable (lifestyle intervention). *complete data available; [†]exercise arms combined for meta-analysis; ‡ Trial included only in the full network meta-analysis

Table 4-4: Outcome data for reversal of metabolic syndrome

4.3.3 Study quality

Details of study quality are presented in Table 4-5. Seven of the included studies attained a Delphi score of at least six (range 2.5 to 7.5). Eligibility criteria were satisfactorily reported for all trials. The majority also provided a measure of variability for the study's primary outcome and analysed data on an intention-to-treat basis. However, randomisation methods and allocation concealment were more poorly reported. Generally, studies involving lifestyle interventions attained lower quality scores due to the difficulties of blinding participants and care providers.

Trial	Method of randomisation	Allocation concealment	Eligibility criteria	Groups similar at baseline	Participants blinded	Care provider blinded	Out-come assessors blinded	Point estimate & measure of variability	Analysis ITT	Delphi score
Studies included in meta-analysis										
Anderssen, 2007	1	1	1	1	NA	NA	NR	0	1	**5.0**
Athyros, ‡ 2005	NR	NR	1	1	NR	NR	NR	0	1	**3.0**
Bo, 2007	1	1	1	1	NA	NA	1	1	1	**7.0**
Esposito, 2004	1	1	1	1	NA	NA	NR	1	1	**6.0**
Esposito, 2006	NR	NR	1	0.5	1	1	NR	1	1	**5.5**
Geluk, 2005	1	NR	1	1	1	1	NR	1	1	**7.0**
Johnson, **2007**	1	NR	1	1	NA	NA	NR	1	0	**4.0**
Orchard, 2005	1	1	1	0.5	0.5	0.5	0	1	1	**6.5**
Phelan, 2007	NR	NR	1	0.5	No	No	NR	1	1	**3.5**
Ramachandran 2006	NR	NR	1	0.5	No	NR	NR	1	0	**2.5**
Stewart, 2005	NR	NR	1	1	NA	NA	NR	1	0	**3.0**
Van Gaal, 2005	1	1	1	0.5	1	1	NR	1	1	**7.5**
Villareal, 2006	1	NR	1	0.5	NA	NA	1	1	1	**5.5**
Studies not included in meta-analysis										
Azadbakht, 2005	1	NR	1	0.5	NA	NA	NR	1	1	**4.5**
Clearfield, 2005	NR	NR	1	0.5	1	1	1	1	1	**6.5**
Sattar, 2003	1	NR	1	0.5	1	1	No	1	1	**6.5**

NR - Not reported; **NA** - Not applicable (lifestyle intervention). ‡ Trial included only in the full network meta-analysis

Table 4-5: Study quality of trials included in the review

4.3.4 Descriptive data synthesis: lifestyle interventions

4.3.4.1 Behavioural strategies

The overall details of the behavioural strategies utilised in the lifestyle interventions are summarised in Table 4-6. The majority of studies used either a combination of small group and individual sessions or just group sessions. Two studies also used phone calls in addition to face-to-face contact.[112, 117] Other details of how interventions were delivered were poorly reported; for example, some studies mentioned using manuals or leaflets but details were lacking.

Information about the person(s) involved with the delivery of the intervention was provided for most of the studies. For studies incorporating a dietary component, most involved a nutritionist / dietician or somebody who had received appropriate training. However, only some of the studies that included supervised exercise sessions specified that an appropriately skilled person was involved. The venue for the intervention sessions was also poorly described. Descriptions of schedules frequently lacked detail, but the information provided suggested that there was considerable variation in the intensity of interventions between studies in terms of the total contact time, and number and frequency of contacts that participants received.

The theoretical basis of most programmes was unclear. Only four studies[106, 110, 111, 113] reported the evidence base/guidelines[120-124] that underpinned lifestyle messages and goals. Additionally, only one study[105] mentioned that the intervention was informed by a specific behavioural theory (Social Cognitive

Theory).[125] However, the approach used by many studies was consistent with other theoretical methodologies such as the Theory of Planned Behaviour.[126]

Author & Year	Focus of intervention	Nº sessions & length of intervention	Who delivered intervention	Where delivered (setting)	Other advice	Goal setting	Theory base
Anderssen, 2007	**Diet and/or exercise** • Individualised dietary counselling • Group exercise sessions	• **Diet**: 3 sessions (initial with spouse, alone at 3 & 9 months) • **Exercise**: group (14 – 20 people), 60mins x 3 per wk, • 1 yr follow-up	**Exercise**: qualified instructor	Unclear	Smoking cessation. Cholesterol risks discussed at 3 & 9 months	**Exercise**: Evaluation & goal setting after 2 months, 4 months & 1 year.	**Exercise**: motivational strategy based on Bandera's theory of self-efficacy;
Azadbakht, 2005	**Dietary modification** • Individualised dietary advice • Behavioural & psychological counselling offered	• Monthly visits (45-60 mins) • Monthly group sessions (all) • Daily phone contact with nutritionist (DASH diet group) • 6 month follow-up	Nutritionist	Home & outpatients	NR	NR	NR
Bo, 2007	**Diet, exercise, & behaviour modification** • Individualised detailed verbal & written recommendations • Group behavioural counselling & practical lifestyle tips	• 5 sessions ≥ 60 mins • 1st session individual • 4 subsequent group sessions (10 - 12 people) • 1 yr follow-up	Trained professionals (nutritionists, specialists in endocrinology & internal medicine)	Unclear	NR	Individualised diet, weight loss, & physical activity goals	Structured core with flexibility in presentation. Recommendations based on US National Institutes for Health guidance[127]
Esposito, 2004	**Mediterranean style diet** • Individually tailored dietary advice • Behavioural & psychological counselling offered	• 5 sessions of at least 60 mins • Monthly small group sessions for 1 yr • Yr 2, 2 monthly • 2 yrs follow-up	Nutritionist	Outpatients	NR	Personal goal setting; self-monitoring using food diaries;	NR
Johnson, 2007	**Exercise training** • Prescribed energy expenditure • 3 treatment groups (high amount & intensity, low amount & high intensity, low amount & moderate intensity)	• Group sessions • 2 – 3 month run-in, then 6 months supervised	NR	Unclear	Maintain dietary intake	Prescribed weekly expenditure (time & distance) but dependent on treatment arm	NR
Orchard, 2005	**Lifestyle modification, or metformin** • Reduce weight & increase activity • Behaviour modification	• 16 lesson curriculum individually over 24 wks • Monthly contact thereafter • Group sessions • 5 yrs maximum follow-up	Person trained in nutrition, exercise, or behaviour modification	Unclear	Smoking cessation	Yes Structured core protocol but flexible approach if difficulty achieving weight loss or exercise goals	Based on previous literature[124] & dietary guidance on NCEP Step I diet[123]
Phelan, 2007	**Lifestyle modification to achieve wt loss and/or sibutramine** • Prescribed energy restricted diet • Encouraged to exercise • Sibutramine	• Weekly,(wks 1 - 18) • Bi-weekly,(wks 20-40) • Follow-up wk 52 • 1 yr follow-up • Group meetings (7-10 people) • 90 mins sessions	Led by trained psychologists	Primary care	NR	Prescribed energy deficit diet Participants completed daily food & activity records (reviewed weekly).	Programme followed published weight control[121] and weight maintenance[122] guidelines

Author & Year	Focus of intervention	Nº sessions & length of intervention	Who delivered intervention	Where delivered (setting)	Other advice	Goal setting	Theory base
Ramachandran 2006	**Lifestyle modification &/or metformin** • Advice on healthy diet and regular physical activity Metformin	• Individually in person at randomisation • Letter or phone at 2 wks • Then monthly phone calls & personal sessions 6 monthly, (for 3 years total)	Unclear	Unclear	NR	NR	NR
Stewart, 2005	**Exercise training** • Prescribed supervised exercise sessions	• 3 per wk x 26 weeks (or 6 months); • If compliance <62 (80%) sessions given extra month • 6 month follow-up	unclear	Unclear	All participants asked to maintain normal calorie intake & given written exercise & dietary guidance	Prescribed exercise targets according to baseline exercise test and on-going heart rate	Followed American College of Sports Medicine guidelines[120]
Villareal, 2006	**Diet induced weight loss & exercise** • Prescribed low calorie diet • Behavioural therapy • Supervised exercise training programme:	• Exercise sessions 90 mins x 3 per wk for 26 wks • Weekly behavioural therapy • 6 months follow-up	Dietician & physical therapist	University & physicians laboratory		Individualised diet and weight loss goals Behavioural programme included goal setting, self monitoring, problem solving skills, & relapse prevention training	NR

Abbreviations: **NCEP**, National Cholesterol Education Programme; **NR**, not reported;

Table 4-6: Overall details of lifestyle interventions

4.3.4.2 Nutrition

Details of the dietary components of the lifestyle interventions are outlined in Table 4-7. Generally papers reported some specific elements of dietary advice given to participants but the amount of detail varied. All studies focused on energy restriction with the aim of weight loss and a few studies specified targets for weight loss. The majority also focused on reducing total and/or saturated fat intake, and around half aimed to increase fibre intake and reduce consumption of refined carbohydrates. Inclusion of other elements such as moderating alcohol intake or reducing salt consumption was specified by very few studies.

Only a small number of studies reported using additional resources or activities such as food diaries, food composition, eating out and food shopping.

Dietary Components	Studies & focus of lifestyle interventions							
	Anderssen	Azadbakht	Bo	Esposito	Orchard	Phelan	Ramachandran	Villareal
	Diet & exercise	*Diet*	*Diet & exercise*	*Diet*	*Diet & exercise*	*Diet & exercise*	*Diet & exercise*	*Diet & exercise*
Energy restriction if appropriate	✓	✓	✓	✓	✓	✓	✓	✓
Weight loss target	0.5 – 2 kg per month			7%				10% in 6 months
INCREASE CONSUMPTION:								
Fish / fish products	✓							
Low fat dairy		✓						
Fruit &/or vegetables	✓	✓						
Wholegrains / complex carbohydrates	✓	✓	20 – 30 g fibre		Fibre rich foods			
Legumes				✓				
Nuts				walnuts				
Olive oil				✓				
DECREASE CONSUMPTION:								
Total fat		✓	✓	✓	✓	✓	✓	✓
Saturated fat	✓	✓		✓			✓	
cholesterol	✓	✓						
Red meat		✓		✓				
Simple sugars / refined carbohydrates	✓	✓	✓				✓	
Salt			✓					
Alcohol			✓		✓			
OTHER:								
Heavy meal in evening	✓							
Portion control			✓					
Food composition			✓					
Food pyramid			✓		✓			
Food diary				✓	✓			
Eating out & food shopping			✓					
Recommended proportions: FAT			<30%,	<30%		30%	≤20g/day	≤30%
CARBOHYDRATE			50–60%	50-60%		55%		50%
PROTEIN			15–20%	15–20%		15%		20%

Table 4-7: Nutritional advice details for interventions involving diet only or diet combined with exercise or pharmacology

4.3.4.3 Exercise

The physical activity/exercise components of the lifestyle interventions are presented in Table 4-8. Generally, both for the exercise advice components and for the content of supervised exercise programmes, only brief details were provided. Around half of the papers mentioned the inclusion of individualised exercise goals but generally no further details were given about how this was achieved. Interventions that were restricted to exercise advice all advised participants to undertake moderate activity such as brisk walking. However, the specified amount of time and the number of times per week varied; two studies recommended 30 minutes per day and two studies recommended 150 minutes per week. Only one paper[111] mentioned using activity records (logbooks) and no studies specified that additional tools, such as pedometers, were used to promote physical activity. For the supervised exercise programmes, most provided three sessions per week. However, the length of time varied from 45 to 90 minutes per session and the intensity differed.

Exercise components	Studies & focus of lifestyle interventions							
	Anderssen *Diet & exercise*	**Bo** *Diet & exercise*	**Johnson** *Exercise*	**Orchard** *Diet & exercise*	**Phelan** *Diet & exercise*	**Ramachandran** *Diet & exercise*	**Stewart** *Exercise*	**Villareal** *Exercise*
Individualised exercise goals	✓	✓	Prescribed intensity &/or amount, according to treatment arm	✓	Unclear	N/R	✓	Unclear
Exercise advice **Time & intensity**	N/R	Moderate intensity (brisk walks) >150 mins per wk	N/R	Moderate intensity (brisk walking or bicycling) 150 mins per wk (30 mins 5 times per wk)	Walking 30 mins per day most days	Continue if involved in physical labour, walking/cycling, regular exercise for >30 mins per day, If sedentary advised & motivated to walk briskly >=30 mins per day.	N/R	N/R
Supervised activity	Exercise: group (14-20 people) 60mins, 3 times/week Aerobics, circuit training, or fast walking/jogging; Given oral & written information at first session; Encouraged to exercise unsupervised / home	N/A	Supervised session or verified by heart monitor Asked to use 2 out of 3 machines (treadmill, elliptical machine, cycle ergometer) 3 treatment groups: mean time ranged 128 – 205 mins (19 – 32 km) per wk	Optional supervised sessions provided 2 per wk Flexibility in choosing type of exercise Optional loan of home exercise equipment or enrolling in class at an exercise facility	N/A	N/A	45 mins 3 times per wk for 6 months Warm up, resistance training (2 sets of 10-15 repetitions, & aerobic exercise (45 mins). Given written guide to exercise	90 mins, 3 times per wk Focused on improving flexibility (15 mins warm up), endurance (30 mins), strength (30 mins), & balance (15 mins)

Abbreviations: **N/R**: not reported; **N/A**: not applicable

Table 4-8: Physical activity details for lifestyle interventions involving exercise only or diet and exercise combined

4.3.5 Key results from the quantitative data synthesis: meta-analysis

Thirteen studies[101, 105-116] with outcome data for reversal of MetS involving 3907 participants (estimated 42% male) were included in the meta-analysis, see Table 4-4. One of these studies was included only in the full network meta-

analysis but excluded from the other meta-analyses as it had no comparator arm in the grouped network; this trial contained only pharmacological interventions.[116] Two additional studies were excluded as outcome data were only available for CVD events or mortality,[118, 119] and one study was excluded as both intervention groups involved individualised dietary advice.[117] Generally, the results of the meta-analyses indicate that lifestyle interventions are more effective at reversing MetS than pharmacological therapies.

The direct pairwise meta-analysis on the grouped network shows that lifestyle interventions increase the odds of MetS reversal by nearly 4-fold (OR 3.81, 95% CI 2.47 to 5.88) and pharmacological interventions by 60% (OR 1.59 95% CI 1.04 to 2.45), compared to control, with moderate levels of heterogeneity (Table 4-9). The mixed treatment comparison results indicated that lifestyle had the largest probability (87.4%) of being the best intervention.

The direct pairwise results for the full network indicate that anti-diabetic drugs, diet, exercise, and diet and exercise combined all increased the odds of MetS reversal compared to control (Table 4-10 and Figure 4-2). However, a high level of heterogeneity was seen for the anti-diabetic drug versus control comparison (I^2 = 78.4%). The results of the mixed treatment comparison analysis showed similar results to the pairwise analysis (Table 4-10). Diet and exercise (33.8%), anti-obesity drugs with lifestyle advice (31.4%) and diet alone (17.5%) had the largest probabilities of being the best interventions.

Despite being unable to conduct a meta-analysis on incidence of T2DM and CVD due to insufficient reporting, two trials reported incident diabetes[106, 112] and three trials reported cardiovascular mortality and events. [108, 118, 119] The Bo et al trial conducted in Italy demonstrated that a lifestyle intervention significantly reduced the incidence of diabetes after one year of follow-up compared to the control group.[106] Additionally, findings from the Indian diabetes prevention programme[112] after three years of follow-up suggest that lifestyle and/or metformin are effective at reducing the incidence of diabetes. Furthermore, subgroup analyses of people with MetS from three large trials of statin therapy,[108, 118, 119] found that treatment reduced cardiovascular mortality and morbidity after follow-up periods ranging from four to ten years. However, treatment effects were statistically significant in only two of the trials.[108, 118]

Comparison	Direct meta analysis			Mixed treatment comparison analysis	
	Nº trials	OR (95% CI)	I²	Nº comparisons	OR (95% CI)
Lifestyle vs. Control	8	**3.81 (2.47 to 5.88)**	56.8%	8	**4.43 (2.36 to 9.16)**
Pharm vs. Control	5	**1.59 (1.04 to 2.45)**	69.1%	5	1.73 (0.73 to 3.80)
Lifestyle & Pharm vs. Control	1	1.14 (0.48 to 2.72)	-	1	2.16 (0.63 to 8.29)
Pharm vs. Lifestyle	3	0.49 (0.20 to 1.24)	80.8%	3	0.39 (0.16 to 0.90)
Lifestyle & Pharm vs. Lifestyle	2	0.53 (0.26 to 1.06)	0%	2	0.49 (0.14 to 1.74)
Lifestyle & Pharm vs. Pharm	2	1.31 (0.11 to 15.13)	91.9%	2	1.25 (0.36 to 4.49)
Abbreviations: **Pharm,** Pharmacological;					

Table 4-9: Results of the direct and mixed treatment comparison meta-analysis on the grouped network

Comparison	Direct meta analysis			Mixed treatment comparison analysis	
	Nº trials	OR (95% CI)	I²	OR (95% CI)	% best
Control		Reference		Reference	0
Anti-diabetic drug	3	**2.56 (1.07 to 6.13)**	78.4%	**3.63 (1.28 to 11.91)**	5.4
Anti-diabetic drug & Lifestyle	1	1.14 (0.48 to 2.72)	-	1.74 (0.31 to 10.47)	2.4
Anti-obesity drug	1	1.50 (0.99 to 2.29)	-	1.20 (0.27 to 5.39)	0.2
Anti-obesity drug & Lifestyle	0	-	-	5.10 (0.59 to 47.13)	31.4
Diet	2	**7.07 (3.84 to 13.0)**	0%	**4.64 (1.25 to 18.52)**	17.5
Exercise	3	**2.22 (1.03 to 4.78)**	0%	2.05 (0.62 to 7.27)	1.1
Exercise & Diet	5	**4.08 (2.33 to 7.16)**	21.2%	**6.73 (3.05 to 17.95)**	33.8
Fenofibrate	0	-	-	1.03 (0.06 to 15.71)	3.6
Statin	1	0.96 (0.57 to 1.64)	-	0.97 (0.14 to 6.55)	0.4
Statin & Fenofibrate	0	-	-	1.09 (0.07 to 17.22)	4.2

Table 4-10: Results of the direct and mixed treatment comparison meta-analysis of the full network
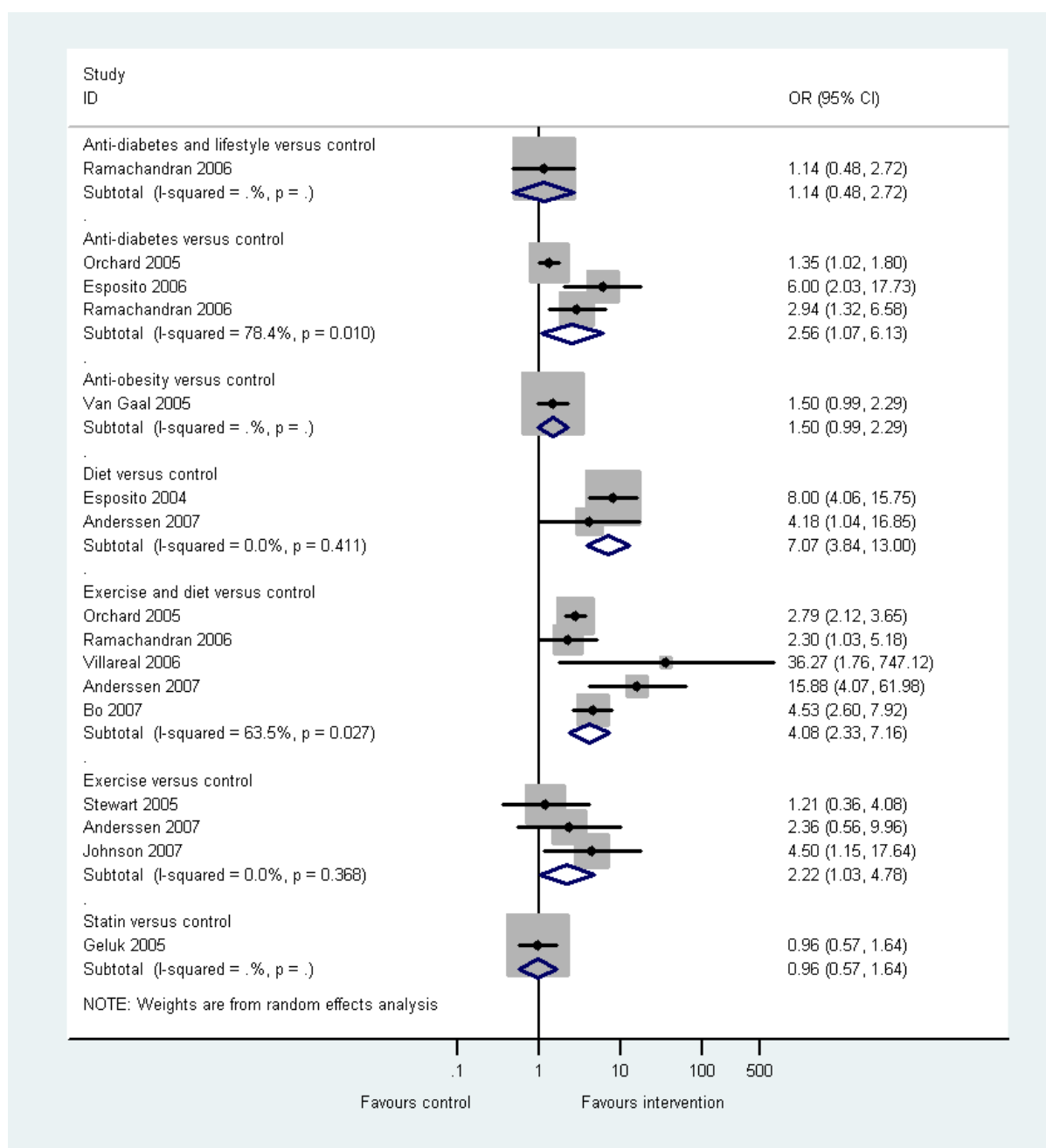
Figure 4-2: Forest plot illustrating treatment effect for invention versus control

4.4 Discussion

4.4.1 Key findings

Overall, the details of the behavioural strategies utilised by lifestyle programmes were poorly reported, although the majority involved some small group sessions. Interventions with a nutritional focus all emphasised energy restriction to lose weight; interventions involving exercise advice all promoted moderate physical activity such as brisk walking. The other components incorporated into lifestyle programmes varied. The trials were too heterogeneous to be able to make firm conclusions about which aspects of lifestyle interventions, at a detailed level, are most effective. However, the meta-analysis of 13 studies including 3907 participants with MetS indicates the benefits of both lifestyle and pharmacological interventions to reverse MetS, with lifestyle interventions appearing to be the most effective.

4.4.2 Strengths and limitations

There has been no previously published systematic review and meta-analysis of the evidence regarding interventions aimed at reversing MetS; this review therefore addressed a gap in the literature. The methods used for the review were robust, including strategies for obtaining all relevant outcome data that were available to study authors even when not reported.

There was considerable clinical diversity between the interventions included in the trials identified by the review. For lifestyle interventions, lower intensity programmes seemed to be no less effective than comparatively more intensive ones. However, differences between populations, follow-up period, and

treatment of control group subjects hinder comparisons. It is also acknowledged that trials may have achieved higher levels of compliance among participants than would be the case in routine practice. For pharmacological interventions, several different types of therapy were identified including lipid lowering, anti-diabetic and anti-obesity medications. However, some of these therapies (rimonabant, sibutramine, rosiglitazone) are currently suspended from use in routine clinical practice following concerns over safety.[128-130]

Although trials complied with some of the Delphi quality indicators, there was a variation in the overall quality of studies. In general, allocation concealment was poorly reported and this has been linked to an increased likelihood of reporting significant findings.[131] Additionally, studies investigating lifestyle interventions tended to achieve lower quality scores due to the difficulty of blinding participants and care providers. Furthermore, although the potential benefit of interventions included within this review is clear, much of the evidence came from subgroup analyses. Most of these analyses were not specified in advance; consequently, the findings should be interpreted with caution.

4.4.3 Other studies

No previously published systematic review had been identified as providing evidence relating to the effectiveness of interventions for primary prevention of T2DM and CVD in people with MetS. However, there is evidence that both intensive lifestyle programmes and drug treatment targeted at people with pre-diabetes, who are at high risk of T2DM, are effective in reducing the incidence of diabetes.[21] In addition, a recently published meta-analysis suggests that

adherence to the Mediterranean diet is associated with a reduced risk of MetS; however, the review included studies that considered development of MetS in people who were free of the syndrome at baseline and also populations who had existing diabetes and/or CVD.[132]

4.4.4 Implications of evidence from the systematic review

One of the stages recommended in the Medical Research Council (MRC) guidance for the development of complex interventions to improve health[25] (described in Chapter 1) involves "identifying the existing evidence base". Conducting a systematic review is advocated as part of this process. The review and meta-analysis described in this chapter provided an evidence base to help inform development of the group education programme (described in Chapter 5), which was developed for use in an RCT: The Reversal Intervention for Metabolic Syndrome (TRIMS) study.

For example:

- The systematic review and meta-analysis provided evidence of the effectiveness of lifestyle interventions for reversing MetS and reducing CVD and diabetes risk, and supports the rationale for testing an educational intervention to reverse MetS. Additionally, the analysis revealed that lifestyle interventions were more effective than pharmacological interventions for reversing MetS.

- Additionally, details from the lifestyle interventions (in conjunction with other evidence sources outlined in Chapter 5 informed both: 1) the key

behavioural goals of the TRIMS programme; and 2) the corresponding components to incorporate in the TRIMS curriculum.

4.5 Concluding remarks

This chapter has presented a systematic review and meta-analysis that was conducted to investigate the effectiveness of interventions for reducing diabetes and CVD risk in populations with MetS. The wider implications for practice and research from the evidence of effectiveness will be discussed in Chapter 8.

The following chapter presents the development work carried out to develop the TRIMS education programme.

Chapter 5. Development of a lifestyle intervention for reversing metabolic syndrome

5.1 Introduction

5.1.1 Chapter overview

This chapter describes the development of an educational programme which was developed for a randomised controlled trial (RCT): The Reversal Intervention for Metabolic Syndrome (TRIMS) study. The systematic review reported in Chapter 4 and the qualitative study reported in Chapter 3 helped to inform the development of the intervention. The introduction (5.1) outlines the rationale and states the aims of the TRIMS study. Section 5.2 presents the background related to the curriculum development and the educational approach utilised by the TRIMS programme. The related key behavioural change theories are then described (5.3). Section 5.4 details an in-depth development and feasibility phase that was carried out to ensure that the design of the lifestyle intervention was appropriate for people with metabolic syndrome (MetS).

5.1.2 Background and rationale for undertaking the TRIMS RCT

As outlined in Chapter 1 and Chapter 2, recent attention has focused on strategies to combat the current and forecast epidemic of type-2-diabetes (T2DM) and cardiovascular disease (CVD). People with MetS could be an important group to target for primary prevention of T2DM and CVD due to their increased risk profile.[16, 20] Additionally, MetS could be a useful concept for

healthcare professionals and patients to focus on when addressing the health risks associated with abdominal obesity.[15] It is therefore important to develop a pragmatic early intervention that can be easily implemented to a large number of people in primary care.

Several trials aimed at reversal of MetS or primary prevention of T2DM and/or CVD in people with MetS have been published, as described in Chapter 4. However, no studies have been conducted in a multi-ethnic UK population. Research is therefore needed into the effectiveness of pragmatic lifestyle interventions for reducing diabetes and CVD risk that can be applicable to multi-ethnic populations with MetS in a primary care setting.

5.1.3 Aims

The aim of the TRIMS study was to investigate the hypothesis that delivery of a group self-management education programme designed to encourage lifestyle changes in individuals identified with MetS would be a feasible, acceptable, and effective strategy for primary prevention of CVD and T2DM in an ethnically diverse population including strong representation of people of South Asian (SA) origin.

Specific objectives of the study were to:

- develop an evidence based patient education programme to improve management of cardiovascular and diabetes risk factors in people with MetS in primary care;

- determine the impact of attending an education programme on features of MetS and well being after 12 months of follow-up;

- assess acceptability, uptake, and feasibility of implementing a group self-management education programme in an ethnically diverse population of individuals with MetS.

These objectives are addressed in the current chapter and the two following chapters (Chapters 6 and 7).

5.2 Background related to development of the TRIMS curriculum

Part of the development phase outlined by the Medical Research Council (MRC) framework[25] for developing and evaluating complex interventions (Chapter 1), includes - identifying and developing theory related to the likely process of change. However, the framework suggests that, if it is appropriate, existing evidence and theory should be utilised. Therefore, as part of the development process for the TRIMS intervention, it was decided to adapt an existing theory-based education programme, which was originally developed for people with pre-diabetes (Let's Prevent[133]). Using this existing curriculum as a framework, the TRIMS curriculum was revised to make it more suitable for people with MetS, who may or may not be dysglycaemic, and include additional emphasis on management of cardiovascular risk. Permission to adapt the pre-diabetes programme was granted by the DESMOND collaborative.[134] Full details of the adaptation of the Let's Prevent curriculum and development of the

TRIMS programme are included in section 5.4 (Development and feasability phase).

5.2.1 Brief overview of the Let's Prevent programme and the DESMOND approach to patient education

The Let's Prevent programme, which was adapted for the TRIMS study, was designed as a group lifestyle education programme for people with pre-diabetes, and has previously undergone extensive piloting and development work.[133] The key nutritional and physical activity messages of the Let's Prevent programme are based on evidence from previous diabetes prevention trials, including: the US Diabetes Prevention Programme (DPP)[135]; the Finnish Diabetes Prevention Study (DPS)[136]; and the Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement (PREPARE) study.[137] The style and process of the Let's Prevent programme are based on the DESMOND[134, 138] approach to patient self-management education.

The DESMOND approach draws on a range of concepts from health psychology and education[125, 139, 140], which are outlined in section 5.3, and its philosophy is centred on patient empowerment. In addition, DESMOND meets nationally agreed standards for patient education[141]; these include having a structured programme with a written curriculum, using trained and accredited educators to deliver the programme, and having processes for quality assurance.

The overall details of the DESMOND and Let's Prevent programmes are summarised in Table 5-1.

	DESMOND	Let's Prevent programme
Differences between the programmes	• Aimed at people with **type-2 diabetes** • Research based: programme has undergone extensive piloting and has been **previously** evaluated by a large scale RCT • National programme – currently commissioned by numerous primary care trusts / healthcare organisations	• Aimed at people with **pre-diabetes** • Research based: programme has undergone extensive piloting and is **currently** being evaluated by a large scale RCT
Shared by both programmes	• Meets national standards for patient education • Underpinned by the DESMOND theoretical and philosophical basis • Empowerment – supports person to become the expert and puts them in control • Detailed written curriculum developed by a multi-disciplinary team (psychologist, dietician, nurse, exercise therapist) • Small group sessions • Delivered by healthcare professionals • Educators trained in the DESMOND approach and philosophy • Training and quality development programme for educators	

Table 5-1: Key information about the DESMOND and Let's Prevent patient education programmes

5.3 Behaviour change theories

The key theories underpinning the DESMOND and Let's Prevent programmes are: 1) Leventhal's Common Sense Model[140]; 2) Chaiken's Dual Processing Theory[139]; and 3) Bandura's Social Cognitive Theory.[125] These theories encompass many of the psychological concepts that are currently recommended by the National Institute for Health and Clinical Excellence (NICE) for informing the structure and content of planned behaviour change activities or programmes.[142] Concepts advocated include outcome

expectancies, self-efficacy, personal relevance, subjective norms / social approval, intention (goal) formation, behaviour change plans, and relapse prevention / coping skills.

Lifestyle changes can potentially have an important impact on reversal of MetS and associated health risks, as suggested by the systematic review and meta-analysis presented in Chapter 4. Therefore, due to the relevance of Leventhal's, Chaiken's and Bandura's theories to encouraging behaviour change, a self-management education programme underpinned by these theories was judged to be appropriate for reversal of MetS.

The following sections (5.3.1, 5.3.2, 5.3.3) present the main points of the three behaviour change theories. A summary of how each theory informs the DESMOND and Let's Prevent style and approach to group self-management education, which was adopted by the TRIMS study, is then outlined in Table 5-2, page 116.

5.3.1 Common sense model

Leventhal's common sense model of illness representations focuses both on how people perceive or view their health status and how they respond to health problems/threats.[143] The model considers that individuals construct a cognitive representation or definition of their illness, and then form plans and strategies for coping based on this representation. This in turn influences their behaviour and health outcomes,[144] (Figure 5-1).
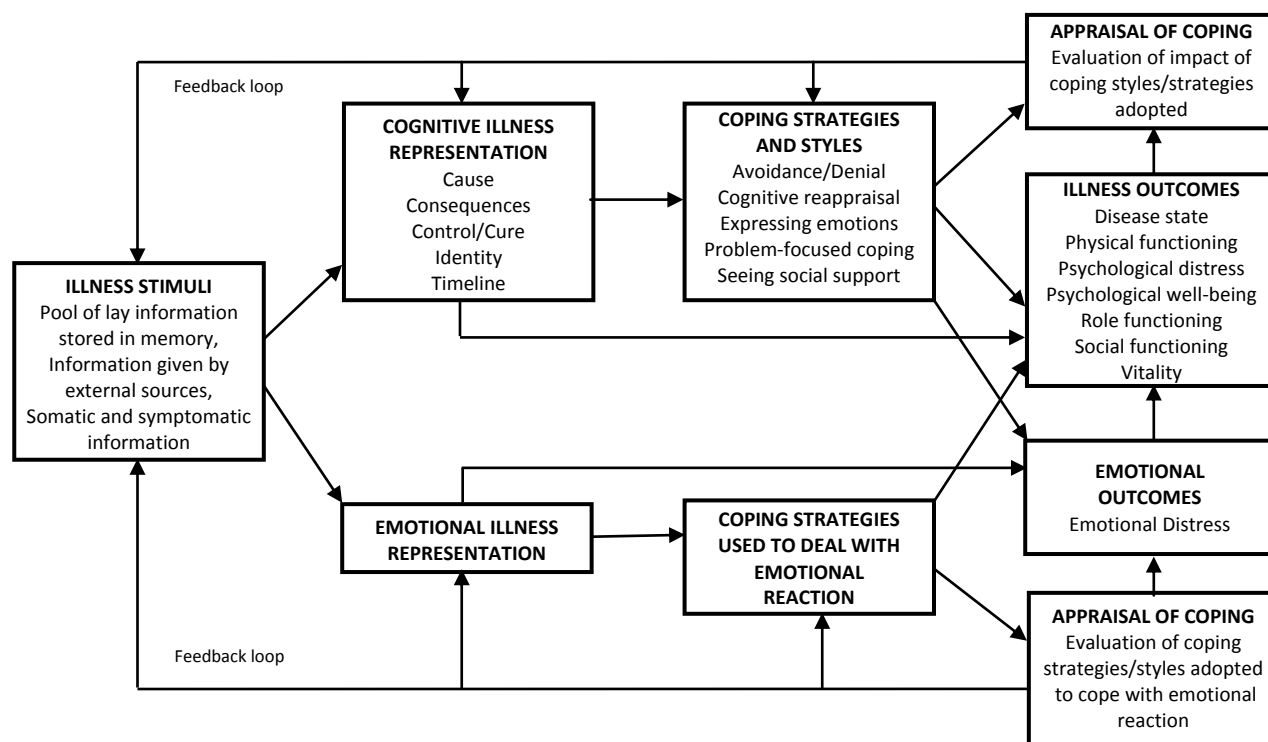
(adapted from Hagger 2003)[145]

Figure 5-1: Schematic representation of Leventhal's Common Sense Model of Illness Representations

Illness representations or 'lay beliefs about illness' are thought to have five components:[140]

1) Identity – the name or label attached to the condition and associated symptoms.

2) Cause – perceptions regarding the possible causes of the condition.

3) Time-line – how long an individual believes the condition could last and timescale of illness symptoms.

4) Consequences – beliefs about the long term impact of the condition, including physical or functional capacity, social consequences, and quality of life.

5) Curability / controllability – perceptions about whether the condition can be controlled or cured, and how an individual views their role and involvement in this process.

Overall, three sources of information are thought to shape or influence an individual's illness representation[140]:

- firstly, general 'lay' information a person has already assimilated about the illness from social interactions and cultural sources;

- secondly, information acquired from significant people such as family and friends, or authoritative sources such as a healthcare professional;

- thirdly, their current experience of the illness based on perceived symptoms and on previous knowledge, including the effectiveness of prior methods they may have used to cope with similar health problems.

The perception and interpretation of information from these different sources contribute to the construction of the illness representation. Leventhal describes this as a two-level process where connections are created between concrete and abstract/conceptual sources of information.[140] For example, initially an individual links the symptoms that they are experiencing (concrete) to previous diagnoses or illness labels (abstract). Next the person forms a schematic representation of their illness that is associated with the illness label. This process of linking symptoms with a label is considered to be spontaneous and intuitive.[145] In addition to cognitive illness representations Leventhal also proposes that people form simultaneous emotional illness representations, as shown in Figure 5-1.

A link between illness representations and coping behaviours and strategies is also emphasised in the common sense model.[140] Evidence suggests that if a person's illness is viewed as uncontrollable and highly symptomatic this is likely to lead to negative coping strategies such as denial and avoidance. Conversely, perceiving an illness as controllable is associated with positive coping strategies such as problem-focused coping.[145] It is therefore important to try to elicit people's illness beliefs as part of any health behaviour change programme.

5.3.2 Dual processing theory

Chaiken's dual processing theory is concerned with how people assess and judge the validity of information and messages.[139] The theory proposes that individuals use two different methods of assessing information: heuristic processing and systematic processing.

Heuristic processing

With heuristic processing, people apply previously held or learnt "judgement rules" to the information being considered. For example, "consensus opinions are correct", and "experts' statements can be trusted".[146] The cognitive demands of heuristic processing are minimal, and labels associated with heuristic thinking include automatic, intuitive and reflexive.[147] However, heuristic processing can involve both conscious and unconscious processes.[146]

Systematic processing

In contrast, systematic processing requires both cognitive ability and capacity, and is generally a conscious process.[146] People judge the validity of information

in the context of their prior knowledge about the issue or topic.[139] Attributes attached to systematic thinking include controlled, analytic and reflective.[147]

Both of these types of processing are affected by cognitive and motivational factors.[146] Examples of cognitive factors include time constraints, attention span, the amount of effort required, mood, and memory. Motivational influences generally fall into three groups:

1) Accuracy motivation

- Individuals are motivated to hold accurate attitudes and beliefs.

2) Defense motivation (personal relevance)

- individuals selectively aim to preserve their "self-concept and associated world views". They embrace beliefs and attitudes that are compatible with their perceived values, social identity (e.g. occupation) and personal attributes (e.g. intelligence).

3) Impression motivation (social acceptability)

- individuals usually consider both the social context and any associated possible consequences before they express particular beliefs or judgements. They desire to hold beliefs and attitudes that meet with their present social aspirations and goals.

Chaiken's dual processing model considers that attitudes which are formed or changed using systematic processing are more predictive of future behaviour change than if heuristic processing alone is used.[139] However, how messages are communicated is also key; analytic factors including the content of messages and the credibility of the source have been shown to influence

people's intentions to adopt healthy behaviours.[148] Furthermore, systematic processing of information is facilitated when individuals are encouraged to take an active role in their learning.

5.3.3 Social cognitive theory

Bandura's social cognitive (learning) theory (Figure 5-2) views most behaviour as being driven by goals that: 1) reflect expectancies about the outcomes of potential actions; and 2) provide the motivation to initiate actions or behaviours.[149] Outcome expectations reflect a person's belief that that a specific behaviour will lead to a particular outcome.[125] However, even if people believe that a strategy will deliver certain outcomes, they often question whether they can take the necessary course of action. Individuals are inclined to avoid situations that they think surpass their capabilities and favour activities that they consider themselves able to carry out.[149]
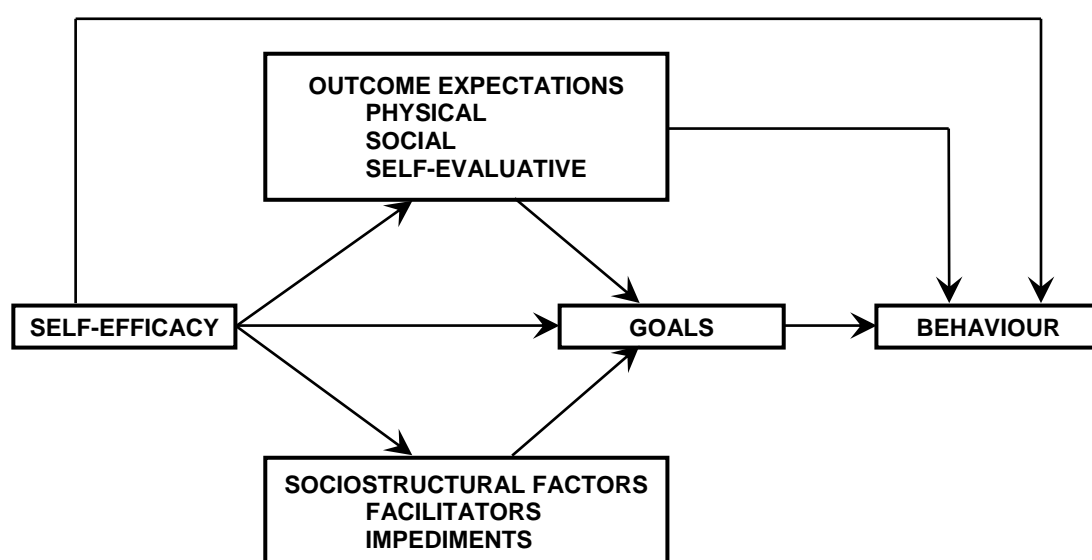
(adapted from Bandura 2004)[150]

Figure 5-2: Bandura's diagrammatic representation of social cognitive theory

Self-efficacy is seen as the key to successful self-regulation of behaviour. Self-efficacy expectations reflect a person's belief that they can successfully carry out the behaviour required to enable a desired outcome,[125] and affect both the initiation and the continuation of behaviour change, including goal setting and achievement of goals.[149]

Perceived sociostructural factors can also affect goal setting by acting as barriers (impediments) and opportunities (facilitators). Sociostructural factors exist within all environmental, cultural, economic, political, and healthcare systems. However, how people view these opportunities or barriers depends on their self-efficacy beliefs. Individuals who have strong self-efficacy perceive that they are able to exert control and focus on opportunities and overcome obstacles.[151]

Most theorists agree that if behaviour change is to be facilitated goals need to be specific and achievable.[151] However, social cognitive theory also makes a distinction between distal (long-term) goals and proximal goals (sub-goals).[152] Distal goals are seen as remote and too far in the future to act as incentives or guide behaviour. They encourage individuals to postpone taking action. In contrast, as part of a series of sub-goals in pursuit of a distal goal, proximal goals can both prompt a person to take action and also guide and direct their efforts. By successfully accomplishing proximal goals individuals can increase their self-efficacy beliefs and enhance their motivation.[152]

Theory	Key elements of the theory	How these elements are applied in group education
Common sense model	- People tend to conceptualise a health threat / problem according to 5 domains: - Identity; Cause; Timeline; Consequences; Control / cure - Influenced by: - Social and cultural factors - Significant people and authoritative sources - Perceived symptoms and prior knowledge	- Important to elicit these beliefs as thought to influence coping behaviours and strategies - Health information needs to be aimed at targeting all 5 domains. If not: - Individual is likely to acquire the missing information from another source - Risk of forming spurious health beliefs - Could negatively impact subsequent coping behaviour
Dual process theory	- People use two different methods of assessing information: - Systematic and heuristic - Processing affected by both cognitive and motivational factors - Attitudes formed or changed using systematic processing more predictive of future behaviour change	- Systematic processing of information is encouraged - Individuals are encouraged to take an active role in their learning and work things out and ask questions - The educator uses open questions to elicit information, rather than lecturing the group
Social cognitive (learning) theory	- Most behaviour is driven by goals - Behavioural change, including goal setting and achievement of goals, is influenced by: - Self-efficacy beliefs - Outcome expectancies - Perceived social structural factors (barriers and opportunities) - A distinction is made between distal (long-term) goals and proximal goals (sub-goals)	- Social modelling of knowledge and competencies - People learn from interaction with others. - Helps a person to realise what they already know - Cultivates new competencies - Instils behavioural outcome expectations - The educator supports individuals - Interactive group activities provide people with direct (mastery) experiences and indirect (vicarious) experiences - Enhances self-efficacy

References: Common Sense Model[140] ; Dual Process Theory[139]; Social Cognitive Theory[125] .

Table 5-2: Summary of how behaviour change theories inform the group education self-management approach, which was adopted by the TRIMS intervention

5.4 Development and feasibility phase

The TRIMS study was designed as a 12 month RCT that compared the effectiveness of structured group lifestyle education (intervention) with usual care (control).

5.4.1 Development of the initial curriculum

A multi-faceted approach was adopted to inform the detailed development of the TRIMS education programme, including adaptation of the Let's Prevent curriculum, to make it suitable for people with MetS.

Firstly, existing evidence regarding the effectiveness of lifestyle interventions for reversing MetS was collated by conducting a systematic review and meta-analysis, as reported in Chapter 4. Secondly, currently published guidelines and recommendations were reviewed, some specifically for MetS and others providing more general guidance related to management of CVD risk, and diet and nutrition.[7, 8, 12, 31, 76, 77, 153-156] A combined approach was used to ensure that the lifestyle behaviour modifications recommended by the TRIMS programme were evidence based and also in line with current UK practice guidance. There was agreement between the different sources of evidence to support all of the specific lifestyle elements outlined in Table 5-3.

Additionally, relevant findings from the qualitative study reported in Chapter 3 (section 3.3) were used to inform the development. For example:

- One of the main aims of the TRIMS programme was to increase people's knowledge and understanding of MetS, including raising awareness of possible future health risk. Waist size is one of the recommended criteria for identifying MetS. However, the findings appeared to indicate that patients were generally unaware of the importance of waist size and of any associated health risks including MetS. Development of the appropriate sections of the curriculum and the pre-course leaflet and handbook,

therefore, assumed a starting point of no knowledge. Explanations provided were pitched appropriately.

- Another aim of the TRIMS programme was to focus on personal risk, and optional behavioural goals included losing weight / reducing waist size. As part of this section of the curriculum, it was planned to promote self-monitoring of waist size. The findings suggested that patients were not reluctant to have their waist measured and additionally felt that self-measurement of waist size could be useful, provided that they received some guidance. Therefore, a small section on waist measurement was incorporated into the programme. This included appropriate explanations and an opportunity for participants to be shown how and where to measure their waist.

Modifiable lifestyle factors	Key lifestyle elements
PHYSICAL ACTIVITY	Increase physical activity
WEIGHT / WAIST SIZE	Sustained weight loss Moderate calorie restriction
DIETARY FACTORS	<u>Dietary consumption:</u>
Fibre	Increase wholegrains (reduce refined carbohydrates) Increase legumes Increase fruit and vegetables
Fats	Moderate reduction in total fat Reduce saturated fat Increase mono-unsaturated fat
Omega-3	Increase fish / oily fish
Salt	Reduce salt
Alcohol	Alcohol in moderation
SMOKING	Cessation of smoking
Sources of evidence: MetS systematic review (Chapter 4); MetS specific guidelines & recommendations[7, 8, 31, 77]; Other guidelines & recommendations[12, 76, 153-156].	

Table 5-3: Key lifestyle messages included in the TRIMS education programme

Subsequently, an initial curriculum was developed by a multi-disciplinary team, which included a nurse and a dietician. Additional resources were also developed including a handbook for patients to reinforce what they had learnt on the course and use as a resource in the future. The main aims of the TRIMS programme were: to increase knowledge and understanding of MetS, including raising awareness of possible future health risk and of potential prevention strategies; and to enhance self-efficacy and self-regulatory skills in order to promote healthy lifestyle behaviours.

The key behavioural goals that the programme aimed to promote included:

1) Increasing physical activity, $\geq$ 45 minutes of moderate intensity activity (or an extra 4,500 steps) per day;

2) Losing weight (reducing waist size), a reduction of between 5 - 10% of initial body weight through increasing physical activity and/or reducing calorie intake;

3) Increasing dietary fibre consumption, particularly wholegrains, legumes, fruits and vegetables;

4) Reducing consumption of saturated fats;

5) Reducing salt intake;

6) Increasing intake of omega-3 fatty acids;

7) Smoking cessation.

However, despite suggested targets, the emphasis of the programme was on enabling participants to set their own realistic personalised goals for behaviour change.

Additionally, brief discussion of relevant medication (i.e. anti-hypertensives, lipid lowering therapy) was included as part of the appropriate sections of the curriculum. However, prescribing guidance was not given; people were advised to consult their primary healthcare practitioner if they had specific concerns.

5.4.2 Piloting

Permission to pilot the education sessions within primary care was obtained from Leicester City Primary Care Trust. One large general practice in the city was subsequently approached and agreed for their patients to be involved. From this practice a sample of patients who were on the hypertension register and also met the criteria for MetS were sent a letter and information sheet by their general practitioner (GP), identifying them as having MetS and inviting them to attend the education sessions. This was followed-up by a telephone call from their GP approximately one week later.

The structured group education programme was delivered as two 3-hour, afternoon sessions held two weeks apart, at the health centre where the GP's practice was based. Two health educators (a nurse and a dietician), who had previously been trained as DESMOND educators and were experienced in using this approach to patient education, led the sessions. The sessions were designed to encourage participation and included games/activities. Participants were also supported to identify personal risk factors that they wished to change and to formulate a self-management plan. As part of the education sessions the participants were provided with a pedometer and activity logbook to use as

motivational tools, and a handbook to use during sessions and then take away as a resource for the future.

Six people initially agreed to attend the education programme. The main reason given by those declining the invitation was the difficulty of taking time off work. On the day, a total of three volunteers attended the first session and four people (2 male, 2 female) attended the second session held two weeks later. Uptake in terms of those who attended all or part of the programme as a proportion of those invited was therefore 20% (4/30).

A range of methods was used to evaluate the education sessions and collect feedback. These included observations recorded during the sessions by an experienced researcher, reflections from the two educators leading the programme, and semi-structured interviews conducted by telephone with volunteers who had attended the education sessions. Qualitative data from these sources were collated using Framework Charting.[157]

Observations and feedback indicated that, at the start of the education programme, people found it difficult to comprehend MetS as it was an unfamiliar concept. However, with repeated explanations and reinforcement throughout the programme, the sessions helped individuals to understand the condition, including the role of abdominal obesity (waist size) and possible future health risks. This was something people said that they valued and it enabled them to focus on their own personal risk. Key messages that people felt they had taken away from the sessions included: making healthier food choices, reading food

labels, and using a pedometer and log-book to help to increase activity levels. For some parts of the curriculum, some individuals expressed a preference for a more direct approach, with the educator talking more and less group discussion, specifically for topics with which people were less familiar. Overall, learning as part of a group was viewed favourably by individuals as they felt they benefited from the questions that other people asked and the sharing of experiences.

5.4.3 Modifications to the intervention as a result of piloting

Findings from the pilot of the intervention were used to help refine the curriculum, resources and style of delivery of the programme. The content and structure of the final TRIMS education programme used for the main trial is outlined in Table 5-4 and Table 5-5, (see Appendix 4 for an example of a section of the curriculum).

Revisions made after piloting included:

- Changes to the introduction section at the start of the education programme, to ensure that educators made participants aware of the non-didactic approach that would be used. This included emphasising the benefits of the style of delivery to be used, including group participation and facilitation of learning through the use of open questions, games and activities. This reinforced explanations given in a pre-course booklet that introduced people to what they could expect when they attended the group sessions.

- Another revision to the programme involved simplifying the way in which MetS was explained. The part of the curriculum related to understanding MetS was amended, particularly the sections focusing on how the body uses

and stores energy from food (fats and carbohydrates) and the role of insulin resistance. Additional prompts were also added, to help educators to link explanations about MetS to any prior perceptions and beliefs that participants may have shared as part of the patient story section. The accompanying resources were also modified.

- Additionally, in response to feedback, a food diary was added to the participant handbook so that people could optionally record their daily food intake. This complemented the physical activity logbook already provided.

PART 1 – First week	Overview of the main aims and activities	Theory
A: INTRODUCTION AND HOUSEKEEPING (5 minutes)	To inform participants of the aims of the course, main topics to be covered, and the style of delivery	
B: THE PATIENT STORY (20 minutes) 1) Names 2) How did you find out you had metabolic syndrome? 3) What do you think it is? Causes? 4) What will it mean for my health? Treatments? 5) Have you a question?	To elicit an individual's experiences, perceptions and health beliefs Participants are encouraged to share their experiences and beliefs with the rest of the group, and identify any questions they have	Common sense model
C: METABOLIC SYNDROME AND INSULIN RESISTANCE 1) Understanding metabolic syndrome (55 minutes) • Energy from food – food groups • Healthy metabolism – energy used / stored • Abdominal obesity and insulin resistance • Cholesterol • Blood pressure 2) How does metabolic syndrome affect me? (40 minutes) • Understanding your personal results • Causes • Reversing metabolic syndrome and reducing the risk of T2DM and CVD	To help participants understand what metabolic syndrome is, possible causes, what it means to their health, and possible ways to reduce their future health risk Participants are helped to work through what is happening in the body with metabolic syndrome, complete their own personal health profile, and consider how they were identified as having metabolic syndrome	Common sense model Dual process theory
D: PHYSICAL ACTIVITY (40 minutes) 1) Benefits 2) Recommendations 3) Measuring activity 4) Barriers and facilitators	To facilitate exploration of the recommendations and benefits of physical activity, and possible barriers Participants are: • encouraged to consider ways to increase their activity levels (including their own personal activity targets)and how this could reduce future health risk • shown and discuss how they can use a pedometer and logbook as a motivational tool and encouraged to go away and use them before their next session	Common sense model Dual process theory Social cognitive (learning) theory
E: HOW AM I DOING? (5 minutes)	Participants are encouraged to reflect on the main messages so far and start to think about possible lifestyle changes	Social cognitive (learning) theory
Throughout the sessions a combination of open questions, analogies, visual aids, games, activities and a personal handbook are used by the educators to assist participant learning. Each week included a 15 minute break.		

Table 5-4: Outline plan of the TRIMS education programme: Part 1

PART 2– Second week	Overview of the main aims and activities	Theory
F: REFLECTIONS (5 minutes)	Participants are encouraged to reflect on issues that have come up and share these with the group	Social cognitive (learning) theory
G: WEIGHT MANAGEMENT AND FOOD CHOICES (1) (35 minutes) 1) Factors influencing food choices 2) Monitoring weight / shape 3) Energy balance 4) Losing weight / reducing waist size 5) Food messages • Fat, alcohol, fruit and vegetables	To help participants explore factors involved in weight management, and consider food choices. Participants are: • encouraged to consider practical ways to lose weight / reduce waist size • helped to work through what factors can cause changes in weight and which foods are higher sources of calories • shown and discuss how they could use a food diary to record what they eat and drink and identify possible changes they could make.	Common sense model Dual process theory Social cognitive (learning) theory
H: FOOD CHOICES (2) (75 minutes) 1) Types of fats 2) Omega-3 3) Fibre 4) Salt 5) Making healthier food choices	To facilitate exploration of the recommendations and benefits of making healthier food choices, and how these relate to metabolic syndrome and individual risk factors. Participants are encouraged to consider ways to make healthier food choices (including reading food labels) and how this could reduce future health risk	Common sense model Dual process theory Social cognitive (learning) theory
I: METABOLIC SYNDROME SELF-MANAGEMENT PLAN (40 minutes) 1) Additional risk factors – smoking, depression 2) Behaviour change 3) Identifying personal risk factors & completing an action plan	To help participants to identify a behavioural goal they can aim for to improve their risk profile / reverse metabolic syndrome, and make a realistic plan of action for this behaviour change Participants are helped to: • identify things they want to change based on their personal health profile, • explore possible options utilising information from previous sessions • identify personal barriers • develop their own personal action plan	Social cognitive (learning) theory
J: QUESTIONS AND FUTURE CARE (10 minutes)	To ensure that all questions previously raised by participants have been answered fully, and that they know how to access ongoing care and support	Common sense model
Throughout the sessions a combination of open questions, analogies, visual aids, games, activities and a personal handbook are used by the educators to assist participant learning. Each week included a 15 minute break.		

Table 5-5: Outline plan of the TRIMS education programme: Part 2

5.5   Concluding remarks

This chapter has described the development and feasibility phase that was carried out in order to develop a lifestyle education programme (TRIMS). The following chapter (Chapter 6) reports the methods used to conduct the TRIMS RCT.

Chapter 6. Design and methods used to conduct a randomised controlled trial of a lifestyle intervention for reversing metabolic syndrome

6.1 Introduction

6.1.1 Chapter overview

This chapter describes the design and methods used to conduct a randomised controlled trial (RCT): The Reversal Intervention for Metabolic Syndrome (TRIMS) study. The overall aims of the TRIMS study were described in detail in the previous chapter (Chapter 5); the objectives that relate specifically to this chapter are outlined in section 6.1. Section 6.2 describes in detail the design and methods including recruitment, randomisation, delivery of the intervention, collection of data and assessment of outcomes.

6.1.2 Objectives

In order to evaluate the TRIMS intervention, the specific objectives were to:

- determine the impact of attending the TRIMS education programme;
- assess the acceptability, uptake, and feasibility of implementing the TRIMS programme.

6.2 Methods: Design of the TRIMS randomised controlled trial

The TRIMS study was designed as a single-centre, 2 arm, parallel, 12 month RCT, to compare the effectiveness of structured group lifestyle education (intervention) with usual care (control) for improving management of

cardiovascular and diabetes risk factors in people with metabolic syndrome (MetS).

6.2.1 Participant recruitment

Local ethics and research governance approvals were obtained prior to conducting the main TRIMS RCT (Appendix 5). General practices (in Leicestershire, UK) who were already taking part in local population based diabetes screening studies[158-160] were approached to participate. Potential participants aged 40 – 74 years, from volunteer practices, were then recruited by postal invitation.

Two different recruitment strategies were employed:

- Firstly, eligible people identified as having MetS, International Diabetes Federation (IDF) definition,[8] according to their previous screening results, were sent a postal invitation via their general practitioner (GP).

- Secondly, people who had consented to be approached with details of other research studies, when they participated in a screening study, and who met the inclusion criteria, were sent a letter of invitation by the principal investigator of the screening study.

Exclusion criteria included:

- previous history of type-2-diabetes (T2DM) or cardiovascular disease (CVD);

- pregnancy and/or breast feeding;

- life-limiting terminal illness;

- lack of capacity to give informed consent;

- being housebound or residing in a nursing/care home;

- inability to understand, speak and read English.

Respondents were asked to attend for an initial appointment having fasted overnight for at least 8 hours. Written informed consent was obtained from volunteers by a research nurse prior to carrying out any tests or measurements. Participants underwent a 75g oral glucose tolerance test (OGTT), [161] and had additional demographic and bio-medical data collected in a standardised way, according to the schedule in Table 6-1. Data collected included measurements to confirm MetS status; however, if relevant blood tests for glucose and lipids had been conducted for screening within the last 3 months, these were not repeated and the initial screening values were used as the baseline values.

Collected by research nurse	Baseline	6-months	12-months
Bloods & biomedical data			
FPG	✓	✓	✓
2 hour glucose	✓	✓	✓
HbA1c	✓	✓	✓
Total cholesterol	✓	✓	✓
HDL	✓	✓	✓
Triglycerides	✓	✓	✓
Albumin:creatinine ratio (urine)	✓	✓	✓
Blood pressure	✓	✓	✓
Waist circumference	✓	✓	✓
Hip circumference	✓	✓	✓
Height	✓	✗	✗
Weight	✓	✓	✓
Medical history	✓	✓	✓
Current medication	✓	✓	✓
Smoking status	✓	✓	✓
Biomarkers			
Insulin, Hs-CRP, Adiponectin	✓	✗	✓
Demographic details			
Age	✓	✗	✗
Sex	✓	✗	✗
Ethnicity *(adapted from classification used for 2001 UK census)*	✓	✗	✗
Current employment status *(working, retired, unemployed, long term sick/disabled, never worked, other)*	✓	✗	✗
Education *(age finished full time education, & highest level of qualification held)*	✓	✗	✗
Socio-economic classification *(NSSEC 5-Class)* [162]	✓	✗	✗
Deprivation score *(IMD score, 2007)* [163]	✓	✗	✗
Self-reported data			
Questionnaires			
Physical activity *IPAQ (short form)* [164]	✓	✓	✓
Anxiety & depression *HADS* [165]	✓	✓	✓
Quality of life *EQ-5D* [166]	✓	✓	✓
Dietary habits *DINE* [167]	✓	✓	✓
General self-efficacy *GSE* [168]	✓	✓	✓
Ambulatory activity	✓	✓	✓
Abbreviations: **FPG** (fasting plasma glucose); **HbA1c** (glycated haemoglobin); **HDL** (high density lipoprotein); **Hs-CRP** (high-sensitivity-C-reactive-protein); **NS-SEC 5-Class** (National Statistics Socio-economic Classification 5-Class version); **IPAQ** (International Physical Activity Questionnaire); **HADS** (Hospital Anxiety & Depression Score); **EQ-5D** (EuroQol EQ-5D questionnaire); **DINE** (Dietary Instrument for Nutrition Education); **GSE** (General Self Efficacy); **IMD** (Indices of Multiple Deprivation)			

Table 6-1: Data collection schedule and outcome measures

6.2.2 Randomisation

Following their baseline appointment, eligible volunteers were randomised to either the study intervention arm (routine care plus TRIMS group education programme) or control arm (routine care) using computer-generated block randomisation. The researcher who held the randomisation sequence had no involvement with the recruitment of participants or baseline data collection. After completion of recruitment the block size was revealed to the author. The sequence was alternate blocks of four and six, with each block having an equal intervention and control group allocation.

Blinding of participants was not possible due to the nature of the study. Participants were informed of their group allocation by a letter sent in the post and volunteers' GPs were also provided with this information. People in the intervention group were informed that they would be given their bio-medical results as part of the TRIMS education and the control group were asked to contact their GP if they wanted any information about their results.

6.2.3 Delivery of the TRIMS intervention

Intervention group participants were contacted by telephone within one to two weeks of their baseline assessment and invited to attend the TRIMS education programme within the following two months. The education sessions were held Monday to Saturday, at various local community venues and consisted of six hours of contact time spread over two 3-hour sessions, held approximately two weeks apart. Participants were also invited to bring a friend or relative for both social and practical support. Two trained/experienced educators (the author

plus dietician/additional nurse) facilitated the groups. The approximate proportions of the curriculum devoted to specific topics are outlined in Chapter 5 (Table 5-4 and Table 5-5). In addition to attending the initial group education, at six months people were given the option of receiving additional support from an educator, via the telephone, to answer any queries and concerns and to help participants update their self-management education resources.

6.2.4 Primary and secondary outcomes

The primary outcome was reversal of MetS according to the IDF criteria in the intervention group compared to the control group, after 12-months of follow-up. Taking into account the ethnic diversity within our target population, the IDF criteria were chosen in preference to the National Cholesterol Education Program (NCEP) definition due to the provision of ethnic specific cut points for waist circumference and central obesity (Chapter 2, Table 2-1). Secondary outcomes, compared at 6-months and 12-months versus baseline, and for the intervention group versus the control group include changes in: 1) the prevalence of MetS according to NCEP criteria; 2) individual components of the MetS (fasting plasma glucose, triglycerides, high density lipoprotein (HDL) cholesterol, blood pressure (BP), waist circumference), and 2-hour glucose; and 3) other anthropometric, biomedical and lifestyle outcome measures as outlined in Table 6-1.

6.2.5 Data collection and assessment of outcomes

Routine laboratory methods were used for all biochemical measurements. Serum total cholesterol, HDL cholesterol, and triglycerides; plasma fasting and

2-hour glucose; and urine albumin and creatinine, were measured using a Siemens Adiva 2400 analyser (Siemens Healthcare Diagnostics, Camberley, UK). Glycated haemoglobin (HbA1c) was measured using a Tosoh G7 analyser (Tosoh Bioscience Ltd, Redditch, UK). Low density lipoprotein cholesterol (LDL) was estimated using the Friedewald equation.[169] If participants gave consent, additional blood was taken at baseline (and 12-months) for measurement of bio-markers that are linked to MetS (high-sensitivity C-reactive protein (hs-CRP), adiponectin and insulin).[170] After processing, the serum for bio-markers was stored in aliquots at -80°c and these samples will be analysed as a single batch at the end of the study. Analysis of bio-markers does not form part of the work described in this thesis.

Resting BP was measured using an Omron automatic BP monitor, (Omron Healthcare UK Ltd) and a mean value was calculated from the last two measurements in a series of three. Waist circumference was measured midway between the costal margin and the iliac-crest, in the mid-axillary line, over minimal clothing and at the end of expiration, and was recorded to the nearest mm. Hip circumference was measured at the widest point over the buttocks and to the nearest mm. Weight in light clothing and no shoes was recorded to the nearest 0.1kg using a digital scale, and height to the nearest cm using a stadiometer and with head placed in the Frankfurt plane. Additional data were collected on physical activity [164], anxiety and depression [165], health related quality of life [166], dietary habits [167] and general self-efficacy [168] using validated questionnaires that were self-completed by participants, as outlined in Table 6-1. Ambulatory activity was measured using a CW-700 Yamax Digi-Walker

electronic pedometer with a 7-day memory (Yamax Corporation, Tokyo, Japan) and an average step count per day was calculated from measurements from at least three days.

6.2.5.1 Feasibility and acceptability

Acceptability of the TRIMS education programme was measured by obtaining qualitative feedback. Topics explored included: ease of understanding; views about the content of the programme and style of delivery; and usefulness and relevance, including cultural relevance (see Appendix 6 for topic guide). An independent researcher conducted semi-structured interviews via the telephone. Information about the interviews and a reply slip was given in person or posted to participants who attended the education sessions. A convenience sample of subjects was then selected to be interviewed from those who volunteered. Written consent was obtained in advance by post and confirmed verbally at the time of the interview. Feasibility was assessed through identification and consideration of problems encountered during implementation of the intervention, and uptake was measured by comparing the number of responses to the number of invitations.

6.2.5.2 Follow-up data collection

The control and intervention groups were recalled at 6 months and 12 months for repeat measurements (Table 6-1). All persons involved in the collection of follow-up data were independent and blinded to study group allocation.

6.2.6 Sample size

Although the data presented in this thesis are restricted to 6-months of follow-up, the TRIMS study was powered to detect a between group difference of 30% in the proportion of people with prevalent MetS at 12-months (prevalence of MetS reduced to 60% in the intervention group and 90% in controls, alpha = 0.05, power = 0.80). Allowing for 20% loss to follow up, 80 participants were required in total, 40 people in each of the control and intervention arms. The power calculation was based on the results of the ODES trial[105] which achieved a difference of 55% between the diet and exercise group and the control group. With our less intensive group lifestyle programme a more modest difference of 30% was assumed. The TRIMS study is not powered to see a significant between group difference at 6-months follow-up.

Bearing in mind the ethnic diversity in the population from which the TRIMS study participants were to be recruited, the IDF definition[8] of MetS was considered to be appropriate due to its provision of ethnic-specific cut-off points for waist circumference and central obesity. However, there is a lack of evidence from previous lifestyle intervention trials that have used the IDF definition to identify MetS; the majority of previous trials have used the NCEP definition.[7, 31] The rationale for basing the power calculation on the ODES trial was its use of the IDF definition to identify MetS.

6.2.7 Data analysis

6.2.7.1 Baseline data

For continuous outcome variables, independent-sample t-tests or Mann Whitney-U tests were used to compare between group differences at baseline; chi-square tests were used to compare categorical variables.

6.2.7.2 Follow-up data

Analysis of 6-month follow-up data was conducted on an modified intention-to-treat basis. Data for all participants were analysed according to the group to which they were randomised and, for those in the intervention group, regardless of whether they received none, some, or all of the intervention. However, the analysis did not include those lost to follow-up. Baseline observation carried forward (BOCF) was not used as a substitute for missing data, for those lost to follow-up, as this method is currently not favoured due to the possible introduction of bias.[171-173] Bi-variate and multi-variate analyses were conducted to compare differences between study groups, and 95% confidence intervals (CIs) were calculated for treatment effects, corresponding to the statistical testing.

- The proportions of subjects with MetS were compared using the chi-square test, followed by logistic regression modelling to adjust for possible confounders. For the regression models, recommended rules that relate to the required number of cases (n) per included co-variate, were adhered to.[174]

- Further study outcomes were compared using similar methods and linear modelling or logistic modelling as appropriate, to adjust for baseline values.

Significance was assessed at the 5% level. The other statistical assumptions made that relate to the data-analysis are outlined in Box 6-1. PASW Statistics version 18.0 (SPSS Inc.) was used to conduct all statistical analyses. Similar methods will be used to analyse 12-month follow-up data.

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<u>Continuous outcome variables</u>

- Normality of continuous variables was based on the significance of Shapiro-Wilks test due to the small sample size
- Independent-sample t-tests were used to compare between group differences for normally distributed data and provide an indication of the size of the treatment effect
  - The significance of Levene's test for equality of variance was used to indicate which variant of the test to use
- Mann Whitney-U tests were used to compare between group differences for data which were not normally distributed
  - Hodges Lehmann median difference and CI were calculated to assess the size of the treatment effect
- Linear regression modelling was conducted with the baseline variable as a co-variate in order to adjust for baseline values.

<u>Categorical variables</u>

- Chi-square tests were used to compare categorical variables; Yates' continuity correction was used for 2 x 2 tables, and Fisher's exact test if the expected count in any of the cells was <5.
- For binary categorical variables, logistic regression modelling was conducted with the baseline variable as a co-variate, in order to adjust for baseline values and provide odds ratios and 95% confidence intervals

</div>

Box 6-1: Assumptions made relating to the conduct of data-analyses

6.2.7.3 *Qualitative feedback*

Qualitative feedback collected in order to gauge the acceptability of the TRIMS programme was analysed using a thematic approach including the use of charting [157] to collate the data.

6.3   Concluding remarks

This chapter has presented the methods used to conduct the TRIMS study. The following chapter (Chapter 7) reports the quantitative and qualitative results for the TRIMS RCT, including baseline and 6-month follow-up data.

Chapter 7. Results of The Reversal Intervention for Metabolic Syndrome (TRIMS) study

7.1 Introduction

7.1.1 Chapter overview

This chapter reports the results of the quantitative and qualitative evaluation of The Reversal Intervention for Metabolic Syndrome (TRIMS) study. Although the trial was conducted and designed with 12 months of follow-up, as previously outlined in Chapter 1 the findings presented in this chapter include only baseline and 6-month follow-up data.

7.2 Results of quantitative evaluation

7.2.1 Presentation of results

For all variables, the numbers of available data (n =) are provided in the tables. This is to ensure transparency as to who was included in each analysis, as recommended by the current CONSORT guidelines.[173, 175]

7.2.2 Recruitment

Participants were recruited to the main TRIMS randomised controlled trial (RCT) between November 2009 and July 2010 (Figure 7-1). In total, 322 potentially eligible people were invited to participate from 8 different general practices. Of those people who were invited, 129 (40%) volunteered to participate, 52 (16%) refused, and 141 (44%) did not reply. Reasons given by those who declined to participate (n = 52) included lack of time due to work or

other commitments (n = 12), no perceived need for additional advice or health checks (n = 15), and other health problems (n = 3). Overall, 82 people were enrolled onto the study, 42 to the intervention group and 40 to the control.
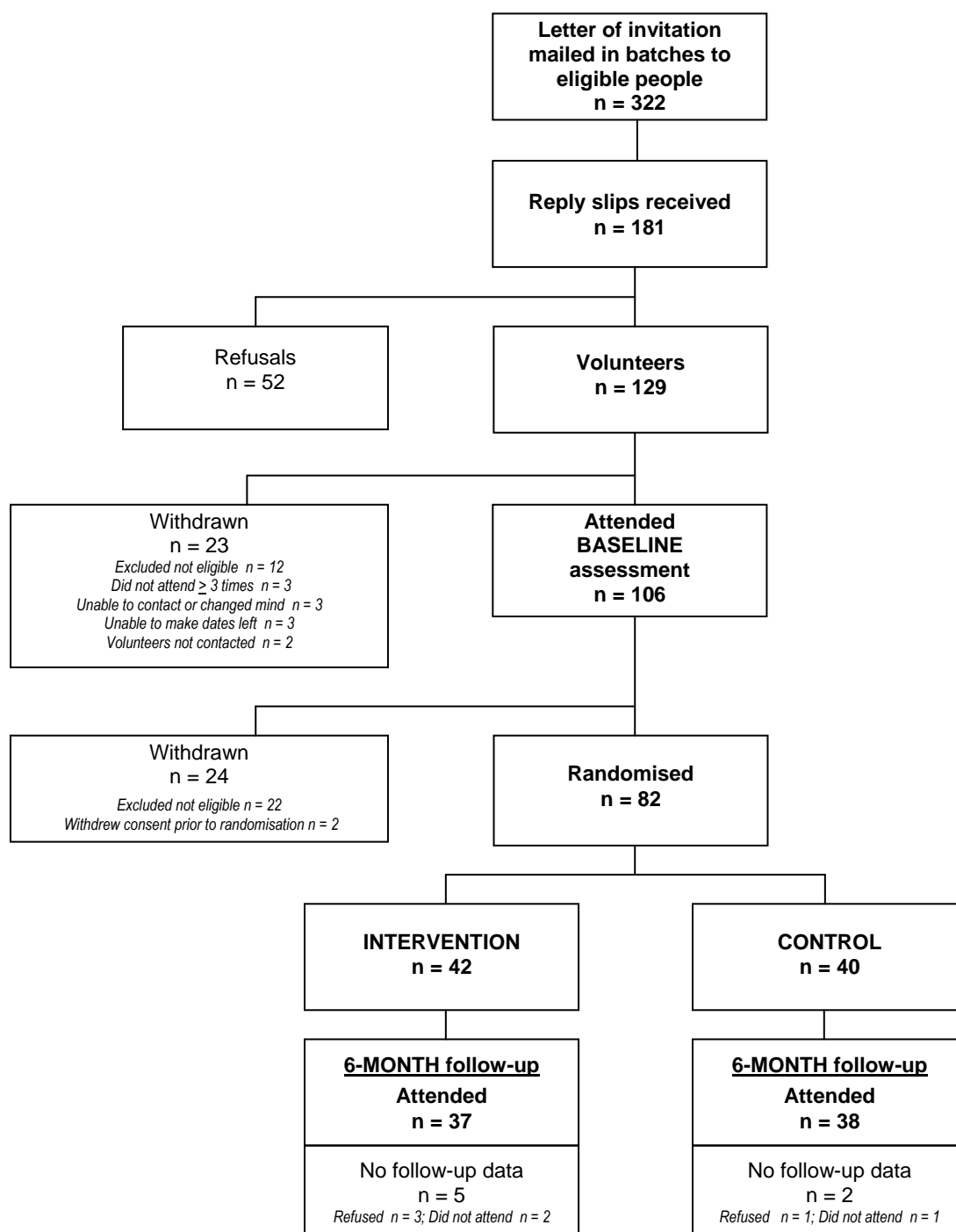
Figure 7-1: Flow chart of recruitment, randomisation and follow-up

7.2.3 Baseline characteristics

The baseline characteristics for the overall study population and by treatment group are presented in Table 7-1, Table 7-2, Table 7-3, and Table 7-4. The randomisation procedure led to balanced samples in the intervention and control groups, with no statistically significant differences in the demographic or clinical characteristics between the study arms.

7.2.3.1 Demographic characteristics

Of the 82 participants, 36 (44%) were male, 18 (22%) were of South Asian (SA) ethnicity, and the median age was 63 years (IQR 57 to 67), (Table 7-1).

7.2.3.2 Anthropometric and bio-medical measures

The mean waist size was 106 cm (SD $\pm$11) and median body mass index (BMI) 30 kg/m2 (IQR 28 to 33). According to the International Diabetes Federation (IDF) definition for metabolic syndrome (MetS), 25 people (31%) met 3 criteria, 44 (54%) met 4 criteria, and 13 (16%) met 5 criteria. The MetS values for the individual criteria for blood pressure (BP), high density lipoprotein (HDL) and triglycerides were met by 80 to 90% of people. However, only 22 participants (27%), 12 (29%) intervention and 10 (25%) control, met the criterion for raised fasting plasma glucose (FPG). Overall, the prevalence of MetS according to the updated National Cholesterol Education Program (NCEP) criteria[31] was 94%, 93% intervention group and 95% control (p = 1.000).

7.2.3.3 Current medication and medical history

Fifty-four participants (66%) had a history of previously diagnosed hypertension and 52 (64%) of previously diagnosed hyperlipidaemia. Forty-two participants (51%) were prescribed a statin and 42 (51%) an anti-hypertensive.

7.2.3.4 Lifestyle and well-being

According to pedometer measurements, the median number of steps/day for participants was 5762 (IQR 3365 to 8592). Self-reported time spent sitting was 300 mins/day (IQR 180 to 360). Dietary data indicated that 34 people (46%) were classified as having a low fibre intake; 9 (14%) as having a high fat intake; 48 people (59%) consumed ≤ 3 portions of fruit, salad or vegetables per day; and 34 (46%) were classed as having a lower unsaturated fat intake. Ten participants (12%) were current smokers.

Characteristics	n	All (n = 82)	n	Intervention (n = 42)	n	Control (n = 40)
Age (yrs)[‡]	82	63 [57 - 67]	42	65 [55 – 68]	40	62 [58 – 67]
Sex: Male	82	36 (43.9)	42	21 (50.0)	40	15 (37.5)
Ethnicity:	82		42		40	
South Asian		18 (22.0)		11 (26.2)		7 (17.5)
White		62 (75.6)		31 (73.8)		31 (77.5)
Other		2 (2.4)		0 (0.0)		2 (5.0)
IMD score (2004)[‡]	82	19.50 [14.04 – 33.74]	42	21.49 [14.04 – 21.49]	40	18.59 [13.55 – 32.96]
Employment status:	82		42		40	
Full time		21 (25.6)		10 (23.8)		11 (27.5)
Part time		17 (20.7)		11 (26.2)		6 (15.0)
Retired		40 (48.8)		19 (45.2)		21 (52.5)
Unemployed		1 (1.2)		0 (0)		1 (2.5)
Long term sick		3 (3.7)		2 (4.8)		1 (2.5)
Age finished full-time education (yrs)[‡]	82	15.0 [15.0 – 16.3]	42	15.5 [15.0 – 17.0]	40	15.0 [15.0 – 16.0]
Age finished full-time education	82		42		40	
≤ 16		62 (75.6)		33(78.6)		29 (72.5)
17 - 18		12 (14.6)		7 (16.7)		5 (12.5)
≥ 19		8 (9.8)		2 (4.8)		6 (15.0)
Qualifications:	82		42		40	
0		32 (39.0)		19 (45.2)		13 (32.5)
1		25 (30.5)		14 (33.3)		11 (27.5)
2		13 (15.9)		4 (9.5)		9 (22.5)
3		12 (14.6)		5 (11.9)		7 (17.5)
NS-SEC-5 class:	82		42		40	
1		17 (20.7)		9 (21.4)		8 (20.0)
2		19 (23.2)		7 (16.7)		12 (30.0)
3		10 (12.2)		6 (14.3)		4 (10.0)
4		15 (18.3)		8 (19.0)		7 (17.5)
5		21 (25.6)		12 (28.6)		9 (22.5)

[‡]**Nonparametric continuous data** are expressed as median [IQR]; **Categorical data** as number (%).
Other ethnicity category: 1 Caribbean Indian, 1 mixed Caribbean/White British.
Qualifications: 0 (None); 1 (O-level, NVQ level 1 & 2, or equivalent); 2 (A-level, NVQ 3, or equivalent); 3 (Degree, professional qualification, or equivalent).
NS-SEC-5 class: 1 (Managerial & professional occupations); 2 (Intermediate occupations); 3 (Small employers & own account workers); 4 (Lower supervisory & technical occupations); 5 (Semi-routine & routine occupations).
Abbreviations: **IMD** (Indices of Multiple Deprivation); **NS-SEC** (National Statistics Socio-economic Classification); **NVQ** (National Vocational Qualification)

Table 7-1: Baseline demographic characteristics for all participants and by study group

Characteristics	n	All (n = 82)	n	Intervention (n = 42)	n	Control (n = 40)
Anthropometric & bio-medical measures						
Waist circumference(cm)*	82	105.5 $\pm$ 10.8	42	103.9 $\pm$ 10.2	40	107.2 $\pm$ 11.2
Hip circumference (cm) ‡	82	108.5 [103.7 – 114.6]	42	106.2 [103.5 – 113.6]	40	112.0 [104.5 – 117.6]
Weight (kg)‡	82	83.1 [75.5 – 93.6]	42	81.1 [75.0 – 90.8]	40	86.8 [77.5 – 97.6]
BMI (kg/m^2) ‡	82	30.2 [28.1 – 33.1]	42	29.3 [27.8 – 32.2]	40	30.9 [28.8 – 34.1]
Systolic BP (mmHg)*	82	132.4 $\pm$ 15.4	42	134.9 $\pm$ 13.2	40	129.8 $\pm$ 17.3
Diastolic BP (mmHg)*	82	85.9 $\pm$ 9.5	42	85.6 $\pm$ 9.7	40	86.1 $\pm$ 9.5
Total cholesterol (mmol/l)*	82	4.99 $\pm$ 0.86	42	4.82 $\pm$ 0.77	40	5.17 $\pm$ 0.93
LDL cholesterol (mmol/l)*	80	2.92 $\pm$ 0.74	42	2.80 $\pm$ 0.68	38	3.05 $\pm$ 0.80
HDL cholesterol (mmol/l) ‡	82	1.20 [1.00 – 1.50]	42	1.20 [1.00 – 1.53]	40	1.20 [1.03 – 1.48]
Triglycerides(mmol/l) ‡	82	1.60 [1.20 – 2.00]	42	1.45 [0.98 – 1.93]	40	1.60 [1.40 – 2.08]
HbA1c (%) ‡	80	6.00 [5.80 – 6.10]	40	5.90 [5.70 – 6.08]	40	6.05 [5.80 – 6.20]
HbA1c (mmol/l) ‡	80	42.0 [40.0 – 43.0]	40	41.0 [39.0 – 42.8]	40	42.5 [40.0 – 44.0]
FPG (mmol/l)*	82	5.21 $\pm$ 0.56	42	5.23 $\pm$ 0.44	40	5.19 $\pm$ 0.66
2 hour glucose (mmol/l)*	81	5.80 $\pm$ 1.65	41	5.65 $\pm$ 1.43	40	5.95 $\pm$ 1.85
Urine ACR (mg/mmol)‡	81	1.00 [0.60 – 1.80]	41	1.00 [0.60 – 1.65]	40	1.05 (0.60 – 2.85)
Metabolic Syndrome						
Proportion who met IDF criteria for:						
BP	82	73 (89.0)	42	37 (88.1)	40	36 (90.0)
FPG	82	22 (26.8)	42	12 (28.6)	40	10 (25.0)
HDL	82	72 (87.8)	42	35 (83.3)	40	37 (92.5)
Triglycerides	82	67 (81.7)	42	35 (83.3)	40	32 (80.0)
Total N° of IDF criteria met:	82		42		40	
3		25 (30.5)		13 (31.0)		12 (30.0)
4		44 (53.7)		23 (54.8)		21 (52.5)
5		13 (15.9)		6 (14.3)		7 (17.5)

*Parametric continuous data are expressed as mean $\pm$ S.D; ‡Nonparametric continuous data as median [IQR]; Categorical data as number (%).
Abbreviations: ACR (albumin creatinine ratio); BMI (body mass index); BP (blood pressure); FPG (fasting plasma glucose); HbA1c (glycated haemoglobin); HDL (high density lipoprotein); IDF (International Diabetes Federation); LDL (low density lipoprotein).

Table 7-2: Baseline anthropometric, bio-medical measures and metabolic syndrome criteria

Characteristics	n	All (n = 82)	n	Intervention (n = 42)	n	Control (n = 40)
Prior medical history						
Hypertension	_82_	54 (65.9)	_42_	27 (64.3)	_40_	27(67.5)
Hyperlipidaemia	_82_	52 (63.4)	_42_	26 (61.9)	_40_	26 (65.0)
Pre-diabetes	_82_	3 (3.7)	_42_	2 (4.8)	_40_	1 (2.5)
Current medication						
Statin	_82_	42 (51.2)	_42_	22 (52.4)	_40_	20 (50.0)
BP medication prescribed	_82_	42 (51.2)	_42_	19 (45.2)	_40_	23 (57.5)
Beta-blocker	_82_	9 (11.0)	_42_	5 (11.9)	_40_	4 (10.0)
ACE-inhibitor	_82_	15 (18.3)	_42_	5 (11.9)	_40_	10 (25.0)
ARB	_82_	12 (14.6)	_42_	7 (16.7)	_40_	5 (12.5)
Thiazide	_82_	18 (22.0)	_42_	8 (19.0)	_40_	10 (25.0)
CCB	_82_	16 (19.5)	_42_	5 (11.9)	_40_	11 (27.5)
Alpha-blocker	_82_	1 (1.2)	_42_	0 (0.0)	_40_	1 (2.5)
Nº of BP meds <u>if prescribed</u>:	_42_		_19_		_23_	
1		19 (45.2)		10 (52.6)		9 (39.1)
2		18 (42.9)		7 (36.8)		11 (47.8)
3		2 (4.8)		1 (5.3)		1 (4.3)
4		3 (7.1)		1 (5.3)		2 (8.7)
Steroids (inhaled, topical, oral)	_82_	6 (7.3)	_42_	3 (7.1)	_40_	3 (7.5)
Thyroid medication	_82_	12 (14.6)	_42_	5 (11.9)	_40_	7 (17.5)
Anti-coagulant (aspirin, warfarin)	_82_	12 (14.6)	_42_	7 (16.7)	_40_	5 (12.5)
Impaired glucose regulation	_81_		_41_		_40_	
Diabetes		0 (0)		0 (0)		0 (0)
IFG		3 (3.7)		1 (2.4)		2 (5.0)
IGT		5 (6.2)		2 (4.9)		3 (7.5)
Both		3 (3.7)		1 (2.4)		2 (5.0)
Normal		70 (86.4)		37 (90.2)		33 (82.5)

Categorical data are expressed as number (%).
Abbreviations: **ACE** (angiotensin-converting enzyme); **ARB** (angiotensin receptor blocker); **BP** (blood pressure); **CCB** (calcium-channel blocker); **IFG** (impaired fasting glucose); **IGT** (impaired glucose tolerance).

Table 7-3: Baseline medical history, current medication and classification of impaired

glucose regulation

Characteristics	n	All (n = 82)	n	Intervention (n = 42)	n	Control (n = 40)
Current smoker: *yes*	*82*	10 (12.2)	*42*	4 (9.5)	*40*	6 (15.0)
<u>Dietary intake</u>						
Fibre intake:	*74*		*38*		*36*	
Low		34 (45.9)		18 (47.4)		16 (44.4)
Medium		29 (39.2)		15 (39.5)		14 (38.9)
High		11 (14.9)		5 (13.2)		6 (13.7)
Total fat intake:	*65*		*34*		*31*	
Low		43 (66.2)		22 (64.7)		21 (67.7)
Medium		13 (20.0)		7 (20.6)		6 (19.4)
High		9 (13.8)		5 (14.7)		4 (12.9)
Unsaturated fat intake	*79*		*41*		*38*	
Higher		43 (54.4)		20 (48.8)		23 (60.5)
Lower		36 (45.6)		21 (51.2)		15 (39.5)
Portions of fruit & vegetables:	*82*		*42*		*40*	
≥ 4 per day		34 (41.5)		17 (40.5)		17 (42.5)
≤ 3 per day		48 (58.5)		25 (59.5)		23 (57.5)
<u>Physical activity</u>						
Pedometer counts (av steps/day)[‡]	*72*	5762 [3365 – 8592]	*39*	6829 [3224 – 8596]	*33*	4774 [3522 – 8653]
Self-reported energy expenditure: [‡]						
Total MET mins/week	*49*	2190 [842 – 3554]	*26*	2592 [1246 – 3499]	*23*	1272 [594 – 4639]
Walk MET mins/week	*58*	693 [462 – 2079]	*32*	941 [470 – 2599]	*26*	693 [446 – 1386]
Time spent sitting mins/day	*66*	300 [180 – 360]	*34*	270 [165 – 360]		300 [240 – 360]
IPAQ category:	*49*		*26*		*32*	
Low		9 (18.4)		3 (11.5)	*23*	6 (26.1)
Moderate		24 (49.0)		14 (53.8)		10 (43.5)
High		16 (32.7)		9 (34.6)		7 (30.4)
<u>Well-being</u>						
EQ-5D score:	*82*		*42*		*40*	
Higher		37 (45.1)		21 (50.0)		16 (40.0)
Lower		45 (54.9)		21 (50.0)		24 (60.0)
EQ-5D VAS[‡]	*81*	80.0 [70.0 – 90.0]	*41*	80.0 [70.0 – 90.0]	*40*	80.0 [61.3 – 90.8]
GSE*	*80*	3.23 + 0.41	*41*	3.22 + 0.47	*39*	3.23 + 0.33
HADS: Anxiety score*	*79*	7.28 + 3.63	*40*	7.45 + 3.70	*39*	7.10 + 3.60
HADS: Depression score[‡]	*82*	4.00 [2.00 – 6.25]	*42*	4.00 [2.00 – 7.00]	*40*	4.00 [2.25 – 6.00]

*****Parametric continuous data** are expressed as mean $\pm$ S.D; **[‡]Nonparametric continuous data** as median [IQR]; **Categorical data** as number (%).

Unsaturated fat intake (higher means consume more unsaturated fat, lower means consume more saturated fat).

EQ-5D score (higher means score >0.800, lower means score <0.800)

Abbreviations: **EQ-5D** (EuroQol EQ-5D questionnaire); **GSE** (General Self Efficacy scale); **HADS** (Hospital Anxiety & Depression Scale); **IPAQ** (International Physical Activity Questionnaire); **MET** (metabolic equivalent); **VAS** (Visual Analogue Scale);

Table 7-4: Baseline lifestyle and well-being characteristics

7.2.4 Uptake of education sessions

A total of seven full TRIMS education programmes were run between December 2009 and August 2010, at four different community venues (one health centre, three community centres). Figure 7-2 outlines the number of people who attended the programme. If people did not attend one or both of their scheduled sessions they were contacted to arrange a new appointment. A total of 39 people (93%) in the intervention group attended at least one of the education sessions and 33 people (79%) attended the complete programme. Only one person expressly refused to attend any sessions and only one person refused to attend the second session. The median number of weeks between baseline appointment and attendance at a TRIMS education session was 5 weeks (IQR 3 to 8).
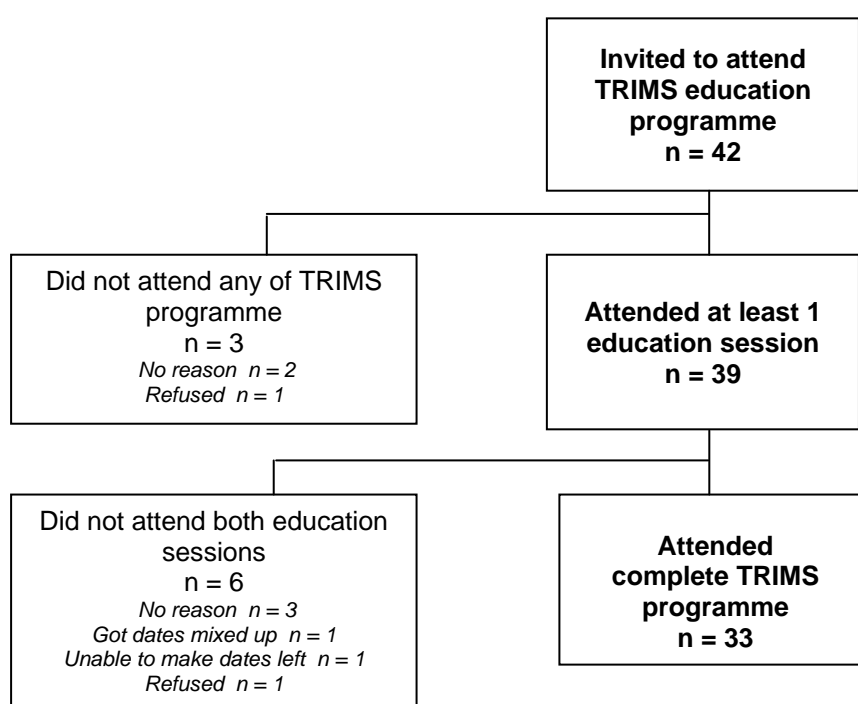
Figure 7-2: Flow chart of people attending the TRIMS education programme

7.2.5 Analysis of six month follow-up data

A total of 75 people (91%), comprising 37 (88%) in the intervention group and 38 (95%) in the control, attended for collection of 6-month follow-up data (Figure 7-1). The mean length of follow-up was 27 weeks (SD ± 3.5). Reasons for participants being lost to follow-up included, other health problems (n = 2), illness of a family member (n = 2), and repeated non-attendance (n = 3). The median age of the seven people who were not followed up was 67 years (IQR 60 to 73), 5 (71%) were female, and all were of White European (WE) ethnicity. Additionally, overall, comparison of baseline values for the main outcome measures showed no statistically significant differences between attendees and those lost to follow-up.

For most variables, data were available for 91% of participants. However, for some variables, particularly when data were collected by self-completion questionnaires, the proportion of available data was lower. For example, the availability of physical activity data recorded on the International Physical Activity Questionnaire (IPAQ) and dietary data recorded on the Dietary Instrument for Nutritional Education (DINE) questionnaire ranged from 68 to 90% and 76 to 90% respectively, mainly due to missing responses for some of the questions. Additionally, pedometer counts were available for only 62 people (76%) at 6-months follow-up. Of the 13 people (9 control, 4 intervention) with missing data, only one 1 person in the control group refused to wear a pedometer. However, around half of those who did not return their pedometer at 6-months also did not return them at baseline.

7.2.5.1 *Reversal of metabolic syndrome*

At 6-months follow-up MetS had reversed for 7 people (19%) in the intervention group compared to 6 (16%) in the control group (Table 7-5). Logistic regression modelling suggested that people in the intervention group had approximately 20% less risk of prevalent MetS compared to people in the control (Table 7-6). However, any differences were not statistically significant. Furthermore, sensitivity analysis conducted to adjust for ethnicity, gender, BP medication, lipid medication and current smoking showed no significant association between study group and prevalence of MetS.

7.2.5.2 *Other metabolic syndrome outcomes*

The number of IDF MetS criteria that people met, and the proportion of people who met the individual MetS criteria for BP, waist circumference, HDL, FPG or triglycerides, also showed no significant between group differences (Table 7-5). The proportion of individuals who were classified as having MetS according to the updated NCEP definition also showed no significant change at 6-months.

A similar proportion of people in the intervention (49%) and control groups (50%) were prescribed statins at 6-months, but less people were prescribed anti-hypertensives in the intervention group compared to the control (46% vs. 55%). However, any differences were not statistically significant and prescribing had changed very little from baseline. For BP medication, therapy had been newly prescribed for one person in the intervention group, and one person in the control had an additional hypertensive medication prescribed. For statins,

one person in each of the intervention and control groups had stopped statin therapy, and one person in the control group had been started on statins.

7.2.5.3 Impaired glucose regulation

At 6-month follow-up one person in the control group had developed diabetes (Table 7-5). Additionally, a slightly higher proportion of people met the criteria for pre-diabetes (impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or both) in the control group (18%) than the intervention group (5%). However, this was similar to baseline and any differences between the groups were not statistically significant.

7.2.5.4 Anthropometric and bio-medical measures

Unadjusted between group comparisons of change at 6-months indicated no significant difference for BP, lipids and glucose control (Table 7-7). However, waist circumference, hip circumference, and BMI were all significantly lower in the intervention compared to the control group. Furthermore, these differences remained after adjusting for baseline values, - 2.3cm (95% CI: - 4.1 to -0.5, p = 0.013), - 2.0cm (95% CI: - 3.6 to - 0.4, p = 0.014), - 0.6kg/m^2 (95% CI: - 1.1 to – 0.1, p = 0.015) for waist, hips, and BMI respectively. Additionally, after baseline adjustment, weight showed a significant reduction for individuals in the intervention group versus the control group (-1.73 kg; 95% CI: - 3.29 to - 0.16, p = 0.031). At 6-months follow-up urine albumin creatinine ratio (ACR) levels were within normal range for all people with most values being at or close to zero; these data are therefore not presented in the tables as no meaningful comparison could be made.

7.2.5.5 Physical activity

After 6-months of follow-up, there was a trend towards a higher increase in physical activity in the intervention group compared to the control (Table 7-8). Self-reported energy expenditure, as measured by total MET minutes/week and walk MET minutes/week, was higher, median difference 332 and 396 respectively (13 and 309 after adjustment for baseline values); however, any differences were not statistically significant. The average number of steps per day, as measured by pedometer counts, was initially significantly higher in the intervention versus control group, median difference 2113 (95% CI: 363 to 3800, p = 0.020). However, after adjustment for baseline the difference was no longer statistically significant (1217 steps, 95% CI -770 to 3205, p = 0.225).

7.2.5.6 Dietary intake

Differences between the proportions of people who were classified as having a medium or high fibre intake, or a low or medium fat intake suggested that individuals in the intervention group had a lower total fat intake and a higher fibre intake at 6-months compared to the control group (Table 7-8). However, these differences were not statistically significant. Intake of fruit and vegetables showed no statistical difference between the two groups. However, the proportion of people who were classed as having a higher intake of unsaturated fat was significantly higher in the intervention group (64%) versus the control group (42%), OR 2.96 (95% CI 1.02 to 8.55, p = 0.045) after adjustment for baseline values.

7.2.5.7 Smoking

The proportion of people who were current smokers was slightly lower in the intervention (8%) than control (13%) at 6-months follow-up but any differences were not statistically significant and was similar to at baseline (Table 7-8). Only one person, who was in the control group, had given up smoking at 6-months follow-up.

7.2.5.8 Well-being

There were no significant changes in health related quality of life (EQ5D), general self-efficacy (GSE), or anxiety and depression (HADS) at 6-months follow-up (Table 7-9).

Characteristics	n	Intervention 6-months	n	Control 6-months	Unadjusted between group comparison			Adjusted between group comparison		
					Odds ratio I vs C	95% CI	p value	Odds ratio I vs C	95% CI	p value
Metabolic Syndrome										
Prevalence of MetS (IDF) [#]	*37*	30 (81.1)	*38*	32 (84.2)	0.80	0.24 to 2.67	p = 0.958	---	---	---
Proportion who met IDF criteria for:										
WC	*37*	37 (100.0)	*38*	37 (97.4)	----	---	p = 1.000	---	---	---
BP	*37*	31 (83.8)	*38*	32 (84.2)	0.97	0.28 to 3.33	p = 1.000	1.14	0.27 to 4.83	p = 0.859
FPG	*37*	5 (13.5)	*38*	10 (26.3)	0.44	0.13 to 1.43	p = 0.273	0.34	0.09 to 1.33	p = 0.120
HDL	*37*	28 (75.7)	*38*	30 (78.9)	0.83	0.28 to 2.45	p = 0.950	1.00	0.30 to 3.34	p = 0.998
Triglycerides	*37*	25 (67.6)	*38*	26 (68.4)	0.96	0.36 to 2.54	p = 1.000	0.64	0.16 to 2.55	p = 0.527
Total Nº of IDF criteria met:	*37*		*38*		---	---	p = 0.434	---	---	---
0		0 (0.0)		1 (2.6)						
1		2 (5.4)		0 (0.0)						
2		5 (13.5)		5 (13.2)						
3		8 (21.6)		9 (23.7)						
4		20 (54.1)		17 (44.7)						
5		2 (5.4)		6 (15.8)						
Prevalence of MetS (NCEP) [#]	*37*	28 (75.7)	*38*	31 (81.6)	0.70	0.23 to 2.14	p = 0.732	0.75	0.23 to 2.49	p = 0.638
Current medication										
Statin [#]	*37*	18 (48.6)	*38*	19 (50.0)	0.95	0.38 to 2.34	p = 1.000	0.49	0.04 to 5.72	p = 0.573
BP medication prescribed [#]	*37*	17 (45.9)	*38*	21 (55.3)	0.69	0.28 to 1.71	p = 0.565	---	0 to ---	p = 0.998
Nº of BP meds, <u>if prescribed</u>:	*17*		*21*		---	---	p = 0.841	---	---	---
1		10 (58.8)		9 (42.9)						
2		5 (29.4)		9 (42.9)						
3		1 (5.9)		1 (4.8)						
4		1 (5.9)		2 (9.5)						
Impaired glucose regulation:	*37*		*38*		---	---	p = 0.331	---	---	---
Diabetes		0 (0.0)		1 (2.6)						
IFG		1 (2.7)		3 (7.9)						
IGT		1 (2.7)		2 (5.3)						
Both		0 (0.0)		2 (5.3)						
Normal		35 (94.6)		30(78.9)						

Categorical data are expressed as number (%); Chi-square test conducted to compare between group differences & provide p value.
[#] **Binary categorical data:** Logistic regression analysis conducted to provide OR & CI for unadjusted between group comparisons

Binary categorical data: Logistic regression analysis conducted to adjust for baseline values.

--- (used if unable to calculate or model wouldn't converge)
Abbreviations: **MetS** (metabolic syndrome); **BP** (blood pressure); **FPG** (fasting plasma glucose); **HDL** (high density lipoprotein); **IDF** (International Diabetes Federation); **IFG** (impaired fasting glucose); **IGT** (impaired glucose tolerance; **NCEP** (National Cholesterol Education Panel); **WC** (waist circumference)

Table 7-5: Comparison of 6-month follow-up data: metabolic syndrome, medication and glucose regulation

Logistic regression models	Variables adjusted for	Number of cases in the model	Odds ratio OR (95% CI)	p value
Model 1	-------	75	0.80 (0.24 to 2.67)	p = 0.958
Model 2	Ethnicity	73	0.85 (0.25 to 2.84)	p = 0.787
Model 3	Gender & ethnicity	73	0.75 (0.22 to 2.60)	p = 0.652
Model 4	Gender	75	0.69 (0.20 to 2.38)	p = 0.559
Model 5	Gender, ethnicity, BP medication	73	0.75 (0.20 to 2.84)	p = 0.670
Model 6	Gender, ethnicity, lipid medication	73	0.51 (0.12 to 2.25)	p = 0.373
Model 7	Gender, ethnicity, BP medication, lipid medication	73	0.47 (0.10 to 2.15)	p = 0.326
Model 8	Gender, ethnicity, BP medication, lipid medication, current smoker	73	0.63 (0.13 to 3.14)	p = 0.570

Dependant variable prevalent MetS at 6-months follow-up; Independent variable study treatment group (reference category control group)

Table 7-6: Association between study treatment group and prevalent metabolic syndrome

Characteristics	n	Intervention 6-months	n	Control 6-months	Unadjusted between group comparison			Adjusted between group comparison		
					Difference I vs C	95% CI	p value	Difference I vs C	95% CI	p value
Anthropometric & bio-medical measures										
Waist circumference(cm) *	37	99.3 ± 8.8	38	104.4 ± 11.1	-5.18	-9.80 to -0.56	p = 0.028	-2.29	-4.08 to -0.49	p = 0.013
Hip circumference (cm) ‡	37	106.0 [102.0 – 111.8]	38	114.4 [104.5 - 120.0]	-6.00	-10.00 to -1.00	p = 0.013	-2.02	-3.62 to -0.42	p = 0.014
Weight (kg) ‡	37	80.4 [70.3 – 89.45]	38	85.6 [76.7 – 97.7]	-6.30	-12.20 to 0.30	p = 0.058	-1.73	-3.29 to -0.16	p = 0.031
BMI (kg/m^2) ‡	37	28.2 [27.1 – 30.8]	38	31.1 [28.4 – 33.6]	-2.1	-3.75 to -0.30	p = 0.022	-0.63	-1.14 to -0.13	p = 0.015
Systolic BP (mmHg) *	37	133.1 ± 17.6	37	127.1 ± 14.6	6.0	-1.5 to 13.5	p = 0.115	2.9	-3.3 to 9.0	p = 0.360
Diastolic BP (mmHg) *	37	84.6 ± 10.8	37	82.6 ± 9.6	2.0	-2.4 to 6.7	p = 0.403	2.3	-1.9 to 6.4	p = 0.280
Total cholesterol (mmol/l) *	37	4.56 ± 0.76	38	4.90 ± 0.98	-0.34	-0.74 to 0.07	p = 0.104	-0.07	-0.36 to 0.22	p = 0.620
LDL cholesterol (mmol/l) *	37	2.62 ± 0.67	37	2.82 ± 0.78	-0.19	-0.53 to 0.14	p = 0.255	-0.01	-0.24 to 0.22	p = 0.963
HDL cholesterol (mmol/l) ‡	37	1.30 [1.05 – 1.50]	38	1.20 [1.10 – 1.40]	0.00	-0.10 to 0.10	p = 0.638	0.00	-0.10 to 0.10	p = 0.964
Triglycerides(mmol/l) ‡	37	1.40 [1.00 – 1.65]	38	1.50 [1.30 – 1.75]	-0.20	-0.50 to 0.00	p = 0.099	-1.00	-1.18 to 1.10	p = 0.579
HbA1c (%) *	37	5.86 ± 0.36	38	5.92 ± 0.34	-0.07	-0.23 to 0.09	p = 0.408	-0.01	-0.13 to 0.11	p = 0.922
HbA1c (mmol/l) ‡	37	41.0 [37.5 – 43.0]	38	41.0 [39.0 – 43.0]	-1.00	-2.00 to 1.00	p = 0.530	-1.01	-1.04 to 1.02	p = 0.547
FPG (mmol/l)*	37	5.19 ± 0.33	38	5.23 ± 0.53	-0.04	-0.24 to 0.17	p = 0.718	-0.06	-0.23 to 0.11	p = 0.480
2 hour glucose (mmol/l) ‡	37	5.30 [4.65 – 6.25]	38	5.35 [4.53 – 7.05]	-0.10	-0.80 to 0.50	p = 0.656	-0.21	-0.75 to 0.32	p = 0.429

*Parametric continuous data are expressed as mean ± S.D; t-tests conducted to compare between group difference, and provide mean difference, p value and CI.
‡Nonparametric continuous data are expressed as median [IQR]; Mann-Whitney-U tests conducted to compare between group difference and provide p value; Hodges Lehmann median difference & associated CI provided.

Linear regression conducted to adjust for baseline values

Abbreviations: **BMI** (body mass index); **BP** (blood pressure); **FPG** (fasting plasma glucose); **HbA1c** (glycated haemoglobin); **HDL** (high density lipoprotein); **LDL** (low density lipoprotein).

Table 7-7: Comparison of 6-month follow-up data: anthropometric and bio-medical measures

Characteristics	n	Intervention 6-months	n	Control 6-months	Unadjusted between group comparison			Adjusted between group comparison		
					OR or difference I vs C	95% CI	p value	OR or difference I vs C	95% CI	p value
Current smoker: yes	*37*	3 (8.1)	*38*	5 (13.2)	0.58	0.13 to 2.63	p = 0.711	---	0 to ---	p = 0.998
Dietary intake **Fibre intake:**	*31*		*38*		---	---	p = 0.728	---	---	---
Low		11 (35.5)		17 (44.7)						
Medium		11 (35.5)		11 (28.9)						
High		9 (29.0)		10 (26.3)						
Total fat intake:	*25*		*35*		---	---	p = 0.225	----	----	----
Low		18 (72.0)		24 (68.6)						
Medium		7 (28.0)		7 (20.0)						
High		0 (0.0)		4 (11.4)						
Higher unsaturated fat intake: yes[#]	*33*	21 (63.6)	*38*	16 (42.1)	2.41	0.92 to 6.27	p = 0.116	2.96	1.02 to 8.55	p = 0.045
Portions of fruit & vegetables: ≥ 4/day[#]	*36*	18 (50.0)	*38*	19 (50.0)	1.00	0.40 to 2.49	p = 1.000	1.09	0.38 to 3.12	p = 0.872
Physical activity **Pedometer counts (av steps/day)** [‡]	*33*	7474 [4845 – 9698]	*29*	4740 [3163 – 8259]	2113	363 to 3800	p = 0.020	1217	-770 to 3205	p = 0.225
Self-reported energy expenditure:[‡]										
Total MET mins/week	*26*	4248 [2049 – 5522]	*30*	2813 [1181 – 6359]	332	-1521 to 1905	p = 0.718	13	-1827 to 1854	p = 0.988
Walk MET mins/week	*31*	1782 [792 – 2772]	*31*	1188 [594 – 2376]	396	0 to 1188	p = 0.101	309	-387 to 1005	p = 0.376
Time spent sitting (mins/day)	*30*	255 [180 – 428]	*30*	285 [180 – 360]	0	-90 to 60	p = 0.755	11	-68 to 90	p = 0.782
IPAQ category:	*26*		*30*		---	---	p = 0.246	---	---	---
Low		1 (3.8)		5 (16.7)						
Moderate		8 (30.8)		11 (36.7)						
High		17 (65.4)		14 (46.7)						

[‡]**Nonparametric continuous data** are expressed as median [IQR]; Mann-Whitney-U tests conducted to compare between group difference and provide p value; Hodges Lehmann median difference & associated CI provided.
Categorical data are expressed as number (%); Chi-square tests conducted to compare between group differences & provide p value.
[#]**Binary categorical data:** Logistic regression analysis conducted to provide OR & CI for unadjusted between group comparisons.

Continuous variables: Linear regression conducted to adjust for baseline values.
Binary categorical data: Logistic regression analysis conducted to adjust for baseline values.

--- (used if unable to calculate or model wouldn't converge)
Abbreviations: **IPAQ** (International Physical Activity Questionnaire); **MET** (metabolic equivalent); **n/a** (not applicable: unable to calculate or model wouldn't converge)

Table 7-8: Comparison of 6-month follow-up data: lifestyle (smoking, diet, physical activity)

Characteristics	n	Intervention 6-months	n	Control 6-months	Unadjusted between group comparison			Adjusted between group comparison		
					OR or difference I vs C	95% CI	p value	OR or difference I vs C	95% CI	p value
Well-being										
EQ-5D score: higher #	37	15 (40.5)	37	13 (35.1)	1.26	0.49 to -3.23	p = 0.811	0.97	0.31 to 3.05	p = 0.952
EQ-5D VAS ‡	36	82.0 [70.0 – 90.8]	38	80.0 [70.0 – 90.0]	0	-5.0 to 10.0	p = 0.605	-1.8	-7.0 to 3.4	p = 0.495
GSE ‡	36	3.30 [2.93 – 3.68]	38	3.20 [3.00 – 3.53]	0	-0.20 to 0.20	p = 0.996	0.00	-0.15 to 0.15	p = 0.977
HADS: Anxiety score *	37	7.08 ± 4.06	37	6.73 ± 3.53	0.35	-1.41 to 2.12	p = 0.692	0.06	-1.01 to 1.13	p = 0.914
HADS: Depression score ‡	37	3.00 [1.00 – 6.50]	37	3.00 [1.50 – 5.50]	0	-1.00 to 1.00	p = 0.819	0.31	-0.65 to 1.26	p = 0.526

Parametric continuous data are expressed as mean ± S.D; t-tests conducted to compare between group difference, and provide mean difference, p value and CI.
‡*Nonparametric continuous data* are expressed as median [IQR]; Mann-Whitney-U tests conducted to compare between group difference and provide p value; Hodges Lehmann median difference & associated CI provided.
#*Binary categorical data* are expressed as number (%); Chi-square tests conducted to compare between group differences & provide p value; logistic regression analysis conducted to provide OR & CI.for unadjusted between group comparisons

Continuous variables: Linear regression conducted to adjust for baseline values.
Binary categorical data: Logistic regression analysis conducted to adjust for baseline values.

EQ-5D score (**higher**, means score >0.800).

Abbreviations: **EQ-5D** (EuroQol EQ-5D questionnaire); **VAS** (Visual Analogue Scale); **GSE** (General Self Efficacy scale); **HADS** (Hospital Anxiety & Depression Scale)

Table 7-9: Comparison of 6-month follow-up data: wellbeing

7.3 Qualitative evaluation: acceptability of TRIMS education programme

7.3.1 Characteristics of participants interviewed

Following their attendance at the education sessions, 16 participants volunteered to be interviewed. Telephone interviews were successfully arranged with 13 people. The characteristics of the sample interviewed were in line with the sampling frame and are shown in Table 7-10. The average length of time that had elapsed between completion of the TRIMS programme and the interview was 4.3 weeks [IQR 2.9 to 5.1].

Characteristics of participants interviewed *(n = 13)*	n
Age group:	
40 – 49 years	1
50 – 59 years	3
60 – 69 years	7
70 – 74 years	2
Sex:	
Female	4
Male	9
Ethnicity:	
White	10
South Asian	3

Table 7-10: Characteristics of participants interviewed following their attendance at TRIMS education programme

7.3.2 Key findings from the participant interviews

Quotations to illustrate the key findings from the interviews are coded as follows: interview (INT) and number, ethnicity (SA or WE), gender (male (M) / female (F)), age group.

7.3.2.1 *Overall acceptability of the TRIMS intervention*

Findings from the participant interviews indicated that the TRIMS education programme was overall well received. The practicalities of the education programme were generally acceptable in terms of the venue and the timing (time of day / day of the week). Most people thought that the number of sessions and the length were appropriate.

7.3.2.2 *Understanding of metabolic syndrome*

<u>Impact on knowledge and understanding of metabolic syndrome</u>

Overall, before people attended the TRIMS programme the term MetS did not mean anything to them. Additionally, some people specifically mentioned feeling surprised or worried when they were first informed that they had MetS.

> *"I didn't really know what it was ... didn't know anything about it." (INT 02, WE, F, 70–74)*

> *"I was a bit shocked, a bit surprised ... when I first heard about it." (INT 10, WE, F, 60-69)*

However, a few people said that they were not surprised and it made sense, for example, because of their current lifestyle habits and weight.

"I know that I'm overweight and I don't have any exercise because of the job that I do ... so it kind of made sense ... It was just putting a name to all the things that I probably knew I had." (INT 07, WE, F, 50-59)

After attending the education programme, those interviewed all demonstrated increased knowledge of MetS, including greater awareness of what happens in the body and possible future health risks. However, their depth of understanding varied.

"It's a number of things that people have ... high blood pressure ... dimension around the waist ... triglyceride levels, cholesterol levels, and what was the other one... when people have a combination of these and they are above a certain level then obviously it comes as metabolic syndrome ... it's the fat around the internal organs that can cause you problems." (INT 04, WE, M, 60-69)

"It brings on diabetes and heart attacks and there's a layer of fat in the middle." (INT 02, WE, F, 70–74)

Additionally, for some people, perceptions associated with MetS following the programme included being in control, and either having the ability to prevent things from getting worse or being able to reverse MetS.

"What I've learnt was that I could do things to improve my health and the likelihood of contracting heart disease and diabetes." (INT 06, WE, M, 50-59)

Views on usefulness of the label metabolic syndrome

When people were specifically asked about the usefulness of being given the label MetS their views were mixed.

"It's not really a disease as such it's a condition, so I think it's probably good in as much as you've got something to call it." (INT 06, WE, M, 50-59)

"I would think it's fine (being given a label) *because that's what it is and it's something to work towards to say right I'm going to try and reverse it, and if you've had a heart attack, you've had a heart attack, that's the end of that. So it's the same sort of thing, so you've got to learn to accept it." (INT 03, SA, M, 40-49)*

"I've told a lot of people I know, my friends and relations, that I'm suffering from metabolic syndrome and they look at me gone out…. Nobody seems to know the term. When you say metabolic syndrome what are we actually saying….. It's not like a broken leg or it's not like saying you've got type-1 diabetes or type-2 is it?" (INT 05, WE, M, 70-74)

7.3.2.3 *Recall of sessions and key messages*

Participants' recall of specific sections of the programme varied but was reasonable overall.

Physical activity

Generally, people's recall of the physical activity messages was good, including their recollection of recommended activity targets (i.e. time, frequency, step counts).

"The minimum is 10 minutes each time. Brisk walking is better for you, hoovering is better for you if it it's a fast one you know, window cleaning, it's all good, but a slow walk … doesn't count as exercise. You should do 10,500 (steps)." (INT 08, SA, M, 50-59)

Some people had been surprised by the suggested targets but most thought that the physical activity messages were useful.

"I was very surprised, I thought I did quite well at walking and when I found out how many steps you should be doing I was really shocked." (INT 10, WE, F, 60-69)

<u>Food choices</u>

Recollection of the food and dietary messages was good and included all the key nutritional goals that the TRIMS programme aimed to promote.

"The messages were not to eat certain types of fat, to eat the monofats, to eat fruit and vegetables, low salt intake … whole grains, eat those." (INT 05, WE, M, 70-74)

The usefulness of reading food labels was also frequently mentioned.

"The constituents of food and actually looking at the packaging… either the traffic lights on them, the actual figures, the percentages. I found that interesting, as well it's a bit of an eye opener." (INT 04, WE, M, 60-69)

Reducing waist size

Recall of information related specifically to weight management / reducing waist size varied, although, the benefits of making small changes (100 calories or two biscuits less per day) was mentioned by a few people.

"The real message was about the two digestive biscuits, you know, cut two of those out a day and you'll lose a tremendous amount of weight, well not a tremendous amount but you know it's a small, I think the food message is small changes you make can have a positive impact." (INT 17, WE, M, 50-59)

Action planning

Only some people specifically recalled the action planning section of the programme including making a personal plan and setting goals. However, most people talked generally during their interview about targets or things that they wanted to change, particularly in relation to physical activity goals.

"I used to do a little bit (of exercise), but now I'm trying to get there, to do an hour a day." (INT 03, SA, M, 40-49)

"I'm trying to reach you know 50,000 (steps) a week you know if I can." (INT 15, WE, M, 60-69)

7.3.2.4 Format of the intervention: resources and style of delivery

Resources

Overall, the resources were well received. There was variation in terms of how much the take-home resources had been used but all were useful for at least some people.

Almost everybody was regularly using the pedometer and some people additionally liked keeping records of their activity in the physical activity logbook.

*"I use it (*pedometer*) every day now ... it is very useful, from that I can work it out how much I walked plus how much I have to walk and everything." (INT 16, SA, M, 60-69)*

People's views differed on the usefulness of the food diary. A few people had regularly used it but others did not feel the need as they tended to make a mental note instead of writing down what they had eaten.

"I've not actually done a written down exercise at all, I've got it down in my own mind what I'm looking for." (INT 04, WE, M, 60-69)

The participant handbook had been a useful source of information for most people since they attended the education sessions, and some had shared it with their family and friends.

"I've looked at it (handbook) quite a lot, I've regularly looked at it, and the family have been very interested in it as well." (INT 05, WE, M, 70-74)

The majority of people also felt that the handbook addressed all their information needs.

"I was very impressed ... I can't think of anything extra that would need to be in there." (INT 04, WE, M, 60-69)

However, one (South Asian) participant would have liked additional information to be included on the amount of calories in other types of foods, specifically in Asian foods.

"The only thing I would like to know more is, you know, the food chart you gave us in the file ... it would be great if we could know more about other foods, y'know like because I'm Asian. So some of the things we don't know what the calories have ... it does help, but a bit more would be great." (INT 08, SA, M, 50-59)

The health profile was also generally viewed as being useful and something that people would use again in the future to compare / plot results and measurements.

"I am using them (health profile) now,....I shall use again when the measurements are taken" (INT 06, WE, M, 50-59)

However, people appeared undecided about the usefulness of the action plans and how likely they were to use them in the future.

"At the moment I am monitoring myself in a diary, not actually using a plan, which is similar to the plan I suppose." (INT 07, WE, F, 50-59)

Style of delivery

Generally, people enjoyed learning as part of a group and felt that they gained a lot from being able to hear the experiences and views of other participants.

"I think it was great to be in a group, you get more ideas and everyone different thinking." (INT 08, SA, M, 50-59)

"We were able to share ideas, share surprises, share learning." (INT 17, WE, M, 50-59)

Additionally, most people thought that the games and activities used with the group were a good way of learning, by involving the members of the group.

"I mean it (the activities/games) got people going, like you know, it gets you going." (INT 10, WE, F, 60-69)

Some people specifically mentioned that topics were well explained and appropriate language was used, and that this had facilitated their understanding.

"Fairly easy to understand actually, I mean I am not a medical person but the way it was explained in sort of lay man's terms I understood you know ... I found it quite easy to understand." (INT 05, WE, M, 70-74)

Furthermore, the majority of people felt that the pace of the sessions was appropriate and helped with their understanding.

"I think it takes time to get into it because my memory is not that, not pretty good, so if somebody said to me once I wouldn't say I'd remember everything ... because they keep coming round to it, it helped me out quite a bit." (INT 08, SA, M, 50-59)

7.3.2.5 Reported impact on behaviour

<u>Changes to behaviour</u>

The most common changes that people reported making to their behaviour included:

- Increasing exercise or physical activity

- Trying to lose weight around the middle / reduce waist size

- Looking at food labels

- Less alcohol

- Reducing portion sizes

- Making changes to the types of foods bought and eaten

    o Avoiding higher fat foods

    o Eating less "junk" food

    o Changing to mono-unsaturated oils or spreads

    o Cutting down salt intake

    o Eating more fish (particularly oily fish)

    o Eating more salad

    o Increasing intake of fruit (particularly as a replacement for less healthier snacks)

Typical reports regarding behaviour change included:

"I used to eat a hell of a lot of cakes and things like that. I don't eat, I perhaps have one or two a week, where I'd have it every day." (INT 15, WE, M, 60-69)

"I've changed my routine every day. I get up early every morning, I start walking." (INT 16, SA, M, 60-69)

"You look for the green labels (traffic lights) because they have less sugar in them and less salt and things like that." (INT 02, WE, F, 70-74)

<u>Barriers</u>

The most frequently mentioned barriers preventing people from changing their behaviour or making it difficult included:

- Factors related to physical activity -

    o Cold weather

    o Lack of time / busy working

    o Sedentary job

- Factors related to food -

    o Not responsible for doing the shopping

    o Love food / enjoy eating

- General issues -

    o Hard at the start, need to get used to lifestyle changes

    o Previous problems trying to lose weight

    o Wary or negative attitude of husband or wife towards change

    o Previous problems with motivation

For example, participants described barriers as follows:

"It's the hard to make changes …all I do is I fall out of the house, I fall into the car and I fall into my office because my office is so far away." (INT 07, WE, F, 50-59)

"I don't do the shopping. I've said to the wife, you need to be careful on this and that, or the other. We still tend to eat the same sort of products, so not been able to implement that part of the education very well." (INT 17, WE, M, 50-59)

"I am never able to lose … I've tried to lose weight for ages, years and years,

since I was about 21,22, and instead of losing I've always gained it." (INT 08,

SA, M, 50-59)

7.3.2.6 Take home messages

When people were specifically asked about what the most important thing was that they had learnt from the course, the views of those interviewed were focused around three areas:

1) The majority of people interviewed mentioned positive perceptions about their ability to make healthy lifestyle changes and being able to influence future health outcomes.

   "I could do things to improve my health and the likelihood of contracting

   heart disease and diabetes." (INT 06, WE, M, 50-59)

2) The significance of discovering what MetS meant including possible future consequences to their health was mentioned by a few people.

   "What it exactly means and what it could do if you don't start taking care."

   (INT 03, SA, M, 40-49)

3) Increased knowledge about different types of foods and healthier eating habits were cited by a small number of participants.

   "That you can change things without going on a diet, you know it's changing

   the way you eat." (INT 14, WE, F, 60-69)

7.4 Discussion

7.4.1 Summary of main findings

it is acknowledged that the TRIMS study is not powered to see a significant between group difference for outcomes at 6-months follow-up. Results from the analysis of 6-month follow-up data indicate that the number of people for whom MetS had reversed was not significantly different between the intervention and control groups, 19% and 16% respectively. However, results suggest that the TRIMS education programme (six hours, delivered over two sessions) was effective at reducing waist circumference (-2.3cm), hip circumference (-2.0cm), weight (-1.73kg), and BMI (-0.6kg/m^2), all of which significantly decreased in the intervention compared to the control group after adjustment for baseline values. Additionally, people in the intervention group had substantially increased odds of consuming a higher intake of unsaturated fat (OR 2.96, 95% CI 1.02 to 8.55, p = 0.045) compared to the control group. Furthermore, the trend for a number of additional outcomes was in the right direction for people in the intervention group even if any differences were not statistically significant, for example, physical activity levels increased (step count, total MET minutes, walk MET mins).

The qualitative evaluation of the TRIMS education programme indicates that, overall, the programme was well received. People's knowledge of MetS improved, including awareness of possible health risks. In addition, after attending the course, people generally perceived that they would be able to make beneficial changes to their lifestyle and so improve their future health. Commonly reported behaviour changes included: increasing physical activity;

trying to lose weight around the middle / reduce waist size; making changes to the types of foods bought and eaten; and reducing portion size.

7.4.2 Comparison with other studies

Combined evidence from studies by other authors (as reported in the systematic review and meta-analysis presented in Chapter 4), suggests that lifestyle advice (diet and/or exercise) is effective for reversing MetS (OR 3.81, 95% CI 2.47 to 5.88). However, the scope for comparing TRIMS 6-month follow-up data with findings from individual studies of lifestyle interventions included in the meta-analysis is limited for a number of reasons, for example, as the follow-up period for the majority of included studies was one to three years. Additionally, for some studies the populations were highly selected, for example all participants had impaired glucose regulation,[110, 112] or were sedentary/physically inactive.[101, 105, 109, 115] Furthermore, interim data and secondary outcomes (e.g. waist circumference, weight) were poorly reported and none of the studies objectively measured changes in physical activity.

Findings from one of the studies in the review, which did report 6-month follow-up, and which was aimed at promoting dietary changes in people with MetS in Iran, suggest that both a weight reducing dietary intervention and a modified Mediterranean type dietary intervention (DASH diet) significantly reduced the prevalence of MetS compared to control (19%, 35% and 0% respectively, p<0.05).[117] However, the control group was not determined by randomisation but consisted of matched cases. Furthermore, the population was much younger (mean age 41 years) and more highly selected than for the TRIMS

study, and people who smoked or were on medication for lipids or BP at baseline were excluded. In addition, the interventions were more intensive with participants receiving monthly individual dietary advice sessions and daily phone calls. The reduced prevalence of MetS in the weight reducing diet arm (19%) is similar to the reduction in the TRIMS intervention arm at 6-months. Unadjusted reductions in waist size were also similar in the Iranian trial compared to TRIMS, at around 5cm. However, unadjusted weight loss was much greater (estimated median differences -15kg (DASH), -13kg (weight reducing diet), -6kg (TRIMS intervention)).

Two small trials which were conducted in the US in mixed ethnic but predominately white (>85%) populations, and were included in the meta-analysis, also reported 6-month data.[113, 115] Both of the studies involved supervised exercise sessions, and one trial additionally involved dietary advice.[115] In the exercise only study,[113] as for the TRIMS study, there was no significant between group difference for reversal of MetS. However, reversal of MetS was higher than for the TRIMS RCT, around 35% of people no longer had MetS after 6-months, but people recruited to the exercise study all had untreated hypertension at baseline. Unfortunately no further comparison could be made, people with MetS were a sub-group (n = 44, approximately 42%) of the trial population and no separate data were reported for changes in weight or individual components of MetS.

In the diet and exercise study[115] MetS reversed for a large proportion of people in the intervention group (67%) compared to 0% in the control group. However,

the control group comparison was "no treatment". Additionally, after adjustment for age and baseline values, the diet and supervised exercise intervention substantially decreased waist size -11cm (95% CI: -18 to -2, p<0.05) and significant changes were seen for glucose, triglycerides and BP compared to control. Similarly to TRIMS, no significant changes were seen for HDL cholesterol. However, the trial data published included changes in bio-medical values for a small number of people who did not have MetS at baseline (control n = 1, 10%; intervention n = 2, 12%). Furthermore, the participants in the diet and supervised exercise study had a mean BMI ($39kg/m^2$) at recruitment that was much higher than for the TRIMS study (median BMI $30kg/m^2$) and their eligibility criteria included a previously sedentary lifestyle.

A previous study involving one 3-hour group lifestyle education session supplemented with a pedometer (PREPARE),[137] and conducted in a UK population with a similar age and ethnic profile to the TRIMS study sample, was found to be effective at increasing physical activity by almost 2,000 steps per day at 6-months follow-up. Similar to the findings from the TRIMS study the PREPARE programme did not significantly improve BP or lipid profile. In contrast, PREPARE did not promote weight loss or a reduction in waist size, but was effective at improving glycaemic control. However, the PREPARE population all had IGT, while, only 7% of participants in the TRIMS study had IGT at baseline. Furthermore, the design of the PREPARE programme was based mainly on promoting physical activity rather than dietary changes and weight management.

7.4.3 Strengths and limitations

The group based education programme developed for the TRIMS intervention, includes a detailed evidence based curriculum, underpinned with appropriate learning and health-behaviour theories. The in-depth development and evaluation of the TRIMS programme was guided by the current Medical Research Council (MRC) framework for the development, evaluation and implementation of complex interventions to improve health.[25]

Holding the education groups in local community venues and ensuring that a choice of various days and times were provided for sessions, including weekends, helped to maximise participant attendance. Less than 10% of those invited did not attend any of the programme and approximately 80% attended the full programme. An additional strength is the qualitative evaluation that was conducted to gauge the acceptability of the TRIMS programme. However, it is acknowledged that the recruitment strategy for the qualitative evaluation did not include methods of collecting information from people who were invited but did not attend the education sessions.

To help minimise bias, all data were collected according to standard operating procedures, and all persons involved in collection of follow-up data were blinded to study group allocation. Quantitative analysis of 6-month follow-up data was conducted using robust methods, including adjustment for baseline values and sensitivity analysis for the main study outcome. Follow-up data were available for a high proportion of people at 6-months, comprising >90% of participants overall. It is acknowledged that the analysis did not include participants who

were lost to follow-up; however, there were only seven people (8.5% of the total sample) in this category, and overall they were broadly similar to the people included in the analysis.

It is difficult to elucidate the reasons for non-attendance at 6-months and, therefore, whether data were either: (1) "missing completely at random" or "missing at random" and potentially ignorable, or (2) "missing not at random" and non-ignorable.[176] Therefore, a conservative approach, which considered that missing values could be a potential source of bias, was adopted. Last observation carried forward (baseline value) was not used as a substitute for missing data as this method is not currently recommended due to the risk of introducing bias .[171, 172] Potential bias includes over or under estimating treatment effects and/or the variability of parameter estimates.[171, 172] Additionally, alternative strategies such as imputing missing values with the worst or best case values were not adopted as both methods are thought to share similar drawbacks to last observation carried forward.[176] It is acknowledged that these methods may be useful if sensitivity analyses are performed. Instead, full details were provided to enable transparency as to who was included in each analysis, as recommended by the current CONSORT guidelines.[173, 175] It is recognised that multiple imputation or hierarchical linear modelling are proposed as the preferred methods for dealing with missing data,[171, 172] and use of these methods will be considered when the primary analysis of 12-month data is conducted. However, these strategies were not considered to be indicated for the interim analysis presented in this thesis.

It is recognised, that people who were recruited to the TRIMS study had previously participated in diabetes screening studies. It is therefore possible that involvement in these research studies may have motivated people in the control group to make lifestyle changes and this could account for some of the improvement in the control group including the small proportion for whom MetS reversed (16%). This observation is consistent with the findings of some other authors who have noted reversal of MetS in control groups (see Chapter 4, Table 4-4). Additionally, for most of the screening studies from which the TRIMS participants were recruited, those people who had been identified as having pre-diabetes had been offered follow-up as part these studies; therefore, they were not eligible for recruitment to the TRIMS study. Since people invited to participate in the TRIMS study were those who were not originally identified as having impaired glucose regulation, large improvements in glycaemic control were not anticipated over the study period.

It is acknowledged that by recruiting people to the study who were prescribed medication to lower BP or lipids on an "on-going" basis, individuals could still be classed as meeting the corresponding criteria for MetS at follow-up even if their BP or lipids had fallen below the value for MetS. Therefore, it may be less likely that MetS would reverse for these people. However, there is no reason to assume that this would affect one group more than the other. At 6-months there were no significant differences in BP or lipid values between the two groups and medication use was virtually unchanged from baseline.

The emphasis of the TRIMS programme was on enabling participants to set their own personalised goals for behaviour change; however, there were several key messages that the programme aimed to promote (Chapter 5, p114). It is acknowledged that providing participants with too much choice could be seen as a possible weakness and translate into small changes in a number of different risk factors which may not reach statistical significance. However, the TRIMS programme was aimed at promoting realistic changes which can hopefully be sustained by people in the longer-term. Additionally, in terms of prevention of T2DM and CVD, there may be overall benefit from small changes that may not be statistically significant. The TRIMS 6-month follow-up data suggest that there were small non-significant changes in lipids and glucose regulation in the right direction in the intervention group compared to the control after adjustment for baseline values (see Table 7-7).

The majority of previous epidemiological studies and clinical trials have used the NCEP definition[7, 31] to identify MetS. However, bearing in mind the ethnic diversity in the TRIMS study population, provision of ethnic-specific cut-off points for waist circumference and central obesity within the IDF definition [8] led to preferential selection of this definition for our trial. Additionally, secondary outcome measures for the TRIMS study include the prevalence of MetS according to NCEP criteria. Analysis of 6-month follow-up data suggested that there were no significant differences between the study groups for this outcome, which mirrored our findings using the IDF definition.

It could be argued that the Oslo Diet and Exercise Study (ODES trial[105]), on which the power calculation for this study was based, differs from the TRIMS study in a number of ways. Firstly, there are some differences in the demographic profile of the TRIMS population. In the ODES trial the population were all males and a younger age group (41 to 50 years, ODES; 40 to 75 years TRIMS). However, at baseline participants in both trials had a similar BMI and waist circumference; 29kg/m^2 and 105.4cm respectively for ODES and 30 kg/m^2 and 105.5cm for TRIMS. Additionally, the ODES study was conducted in a Norweign population but comparison of potential ethnic differences is hindered as ethnicity was not reported in the ODES trial. Secondly, the lifestyle intervention developed for the TRIMS study is less intensive than the diet and exercise intervention in the ODES trial. However, if the prevalence of MetS is in the region of 30%[9], one-to-one counselling is unlikely to be feasible in a primary care setting. The TRIMS intervention is a pragmatic group based education programme, with broad inclusion criteria and designed to be appropriate to be delivered in the "real world setting". Additionally, this study was not powered for a difference of 55% as found in the ODES trial but a more modest difference of 30% between the intervention and control groups. Furthermore, the ODES study used the IDF definition for MetS. It is acknowledged that conducting a pilot study before the main TRIMS RCT could have been useful for estimating sample size and for highlighting potential factors influencing recruitment. However, it was not considered feasible due to the time lines of the project as a whole.

Based on the results of the 6-month follow-up data, it is acknowledged that the TRIMS study may be underpowered to justify using resolution of MetS as the primary outcome at 12-months follow-up, and to speculate that a significant result will not be seen at 12-months. However, a lack of published data for reversal of MetS at multiple time points, including at 6-months and 12-months follow-up, hinder comparison and make it difficult to speculate on likely changes after 12-months follow-up.

It could also be argued that a longer follow-up period may be needed to see significant between group changes for reversal of MetS. Evidence from a sub-group of participants with MetS in the Diabetes Prevention Programme (DPP) indicates that cumulative reversal of MetS was significantly higher (p = 0.002) in the lifestyle arm (38%) compared to placebo (18%) after three years of follow-up.[110] In contrast, one year follow-up data showed only small differences between reversal of MetS in the three study groups, with lifestyle appearing to have a lower reversal rate than both placebo and metformin.[110]

The TRIMS study excluded people who were unable to understand, speak and read English. It is acknowledged that this could potentially have an impact on the study findings; health outcomes may differ between English speakers and non-English speakers of the same ethnic minority background. This may limit the generalisability of study findings. However, our study population includes a subset of the SA population in the UK (English speaking people mainly of Indian origin), and overall 22% of participants were of SA ethnicity. Additionally, we took steps to address cultural needs, for example by including foods commonly

eaten in the SA community. If the education programme is found to be successful at 12-months, adapting it for non-English speakers and ethnically diverse populations would be considered. A modified version would be needed to fully address cultural needs, including language and literacy,[177] but this is beyond the scope of this thesis.

7.4.4 Implications

Potential implications for clinical practice and future research are discussed in the following chapter (Chapter 8).

7.5 Concluding remarks

This chapter has reported the 6-month evaluation of the TRIMS study which compared the effectiveness of a structured group lifestyle education programme with usual care, in people with MetS. The following chapter (Chapter 8), reflects on the overall programme of work undertaken.

Chapter 8. Overall discussion: summary, implications and recommendations

8.1 Chapter overview

This chapter summarises the main findings of the programme of work undertaken for this thesis. Recommendations for future research and the implications for clinical practice are also discussed. Additionally, I review what I have learnt whilst completing this PhD and consider how I can build on this programme of research.

8.2 Summary

The overall aim of the programme of work in this thesis was to contribute to the body of knowledge relating to self-management lifestyle education for management of cardiovascular and diabetes risk in people with metabolic syndrome (MetS). An additional aim was to elicit views on waist size measurement and strategies to promote use of the measurement for assessment of obesity related health risk.

Chapter 1 provided the rationale for this thesis and outlined the aims and objectives of the programme of work and provided background on the Medical Research Council (MRC) Framework for developing and evaluating complex interventions.[25] Chapter 2 provided the more detailed background.

The qualitative study described in Chapter 3 explored in-depth the knowledge and attitudes of both patients and primary care health professionals towards measuring waist size in a multi-ethnic setting. Healthcare professionals (HCPs) were generally aware of a link between a large waist size and health risks; however, the concept of MetS and its association with risk, was not commonly raised. For patients, a few people talked about waist size in relation to "healthier body shapes" but no one was familiar with the term MetS. Practical barriers to using waist circumference measurement raised by HCPs included lack of time, extra workload and financial implications. A particularly salient finding was that patients generally raised few barriers to waist circumference measurement; being given an explanation of the assessment appeared to be what was most important to them.

Chapter 4 presented a systematic review (and meta-analysis) consolidating the evidence on the effectiveness of interventions for reducing type-2 diabetes (T2DM) and cardiovascular disease (CVD) risk in people with MetS. The meta-analysis indicated the benefits of both lifestyle and pharmacological interventions to reverse MetS, with lifestyle interventions appearing to be the most effective. In addition to contributing to the growing body of work around primary prevention of T2DM and CVD in high risk populations, the meta-analysis supported the rationale for testing an educational intervention to reverse MetS.

The in-depth development of a structured group lifestyle educational programme designed to improve management of CVD and T2DM risk factors in

people with MetS in primary care, was described in Chapter 5. The programme was developed to be tested in a randomised controlled trial (RCT): The Reversal Intervention for Metabolic Syndrome (TRIMS) study. The detailed design and methods used to conduct the TRIMS RCT were described in Chapter 6.

The quantitative and qualitative evaluation of the TRIMS study was reported in Chapter 7. Analysis of 6-month follow-up data indicated that reversal of MetS was not significantly different between the intervention and control groups. However, the TRIMS education programme was effective at reducing waist size, hip circumference, weight, and body mass index (BMI), and promoting a higher intake of unsaturated fat. The qualitative evaluation indicated that, overall, the TRIMS programme was well received. After attending the course, people generally perceived that they had already, or would be able to, make beneficial changes to their lifestyle and so improve their future health. Analysis of the 12-month follow-up data will be conducted outside the timescale of this thesis as outlined in Chapter 1.

8.3 Recommendations

8.3.1 Implications for clinical practice

8.3.1.1 Qualitative findings regarding waist circumference measurement

Recent guidelines on vascular risk assessment published by the National Screening Committee recommend including waist size measurement in risk assessment both for population based screening and screening those at risk.[12] The National Institute for Clinical Excellence (NICE) also recommends waist

measurement in addition to BMI for obesity management.[13] Additionally, recent research suggests that people who are overweight are increasingly likely to fail to recognise their body size as a cause for concern.[178] Waist measurement and discussion of associated risks as part of appropriate consultations could provide an opportunity to address this issue. This is an area of research focus for some current trials looking at primary prevention of diabetes and CVD.[179] Despite this, waist circumference measurement is not routinely carried out in primary care.

If the use of waist circumference measurement is to be facilitated in routine practice, barriers and facilitators highlighted by our patient and HCP interviews should be considered. There is a clear need for training in how to carry out waist circumference measurement, and if HCPs feel embarrassed or uncomfortable about this assessment ways of addressing this should be included. Further considerations include adopting a standardised method for waist circumference measurement, increasing the length of patient appointments, and recognition of workload implications at both practice and primary care trust level. Potential facilitators include the use of financial incentives and/or possible inclusion in the Quality and Outcomes Framework.[180] Implications for practice that relate directly to patients include the need for HCPs to provide patients with an explanation of the importance of waist measurement and what it involves. Additional concerns are ensuring that patients feel comfortable about being measured, possibly providing them with a choice of the gender of HCP, and planning when the measurement is to be carried out so that patients can address any barriers related to the measurement being unexpected.

8.3.1.2 Systematic review evidence regarding the effectiveness of interventions for people with metabolic syndrome

The review (presented in Chapter 4) suggests benefits from interventions aimed at promoting lifestyle changes and also those based on pharmacological therapies, although lifestyle is superior. However, there may be difficulties associated with translating this evidence into practice. MetS is not routinely identified in clinical practice.[14] Controversy exists regarding the clinical value of MetS and whether or not its detection provides incremental benefit beyond existing risk algorithms such as the Framingham risk score,[59, 60] for identifying those at high risk of CVD. Additionally, some HCPs will be hesitant to adopt the use of pharmacotherapy for what might be perceived as a lifestyle problem. However, they may also be cautious due to the potential for detrimental side effects; for example, in a recent study rosiglitazone was found to be effective at reducing incident diabetes in people with impaired glucose regulation after three years follow-up but also increased the risk of developing heart failure.[181] Furthermore, rosiglitazone and some of the other pharmacological therapies identified by the review (rimonabant, sibutramine) are currently suspended from use in routine clinical practice following concerns over safety.[128-130]

The optimal mode of delivering an intervention to promote lifestyle changes in people with MetS in practice is unclear. There was considerable variation in the design and intensity of lifestyle interventions included in the review. Furthermore, despite the recognised clinical value of intensive lifestyle programmes such as the US Diabetes Prevention Programme (DPP),[110] which

was included in the review, subsequent questioning of cost-effectiveness has highlighted the need to investigate less expensive pragmatic interventions.[182] In contrast, it is encouraging that a comparatively less intensive intervention, such as that in the study by Bo et al,[106] was shown to be effective for both reversing MetS and preventing T2DM.

However, the ability to implement these findings in practice may be hampered by a lack of service provision. Lifestyle changes (diet and exercise) are currently recommended as the initial management approach for people with MetS, with the addition of pharmacotherapy if lifestyle alone is ineffective and/or individuals are at high CVD risk.[7, 8, 76, 77] The importance of structured education for people with T2DM is generally recognised[183] and programmes in the UK include DESMOND[184] and X-PERT.[185] Currently, no similar programmes are generally available in routine primary care for individuals who are at high risk of T2DM, including people with MetS. Improving provision of, and access to, interventions of known efficacy is important if the benefits of interventions received by trial participants are to be extended to population level.

8.3.1.3 Evidence relating to the effectiveness of the TRIMS lifestyle education programme

With rising levels of obesity[2] and a predicted increase in the prevalence of MetS,[10] evidence relating to the effectiveness of the TRIMS education programme is potentially highly relevant in terms of public health. This brief (six hours contact time, two sessions) relatively low cost intervention was effective at promoting a modest reduction in weight, BMI, hip circumference and waist

size, and promoting a higher intake of unsaturated fat which could potentially be important to future practice. Existing evidence suggests that in terms of prevention of T2DM weight loss is of primary importance; secondary analysis of data from the intensive lifestyle arm of the DPP, which included people with MetS,[110] indicated a 16% reduction in risk of developing T2DM for each kilogram of weight lost, after adjustment for physical activity and dietary changes.[186]

Additionally, overall, the TRIMS programme was well received and people perceived that they were able to make healthy behaviour changes. However, it will remain to be seen whether the benefits of the TRIMS intervention are sustained at 12-months follow-up or beyond. Findings from studies aimed at weight loss, generally suggest that following an intervention participants regain between 30 to 50% of the weight that they initially lose, but weight maintenance is also important and evidence suggests that at two years follow-up people have not gained weight from baseline.[187] Evidence from the Finnish Diabetes Prevention Study (DPS), which included a sub-group of people (74%) with MetS, suggests that a mean weight change of 4.5kg in the intervention group at one year follow-up translated into a sustained weight change of -3kg after four years.[188] Additionally, a recent systematic review considering the long term effectiveness of interventions promoting physical activity in healthy adults suggests that beneficial behavioural changes can be sustained in the longer term. However, reminders (telephone, postal, or internet) may be needed to help improve long term effectiveness.[189]

8.3.2 Implications for future research

8.3.2.1 Qualitative findings regarding waist circumference measurement

The qualitative study addressed only one aspect of waist measurement. There is more scope for future research in this area to consider the views of other HCPs involved in obesity management, for example dieticians. Additionally, it would be useful to elicit the views of a more diverse range of patient groups; for example, people from other ethnic groups and sub-groups.

8.3.2.2 Systematic review evidence regarding the effectiveness of interventions for people with metabolic syndrome

Although the meta-analysis provides evidence of the benefits of interventions for reversal of MetS, there is a need for more rigorously designed trials providing information on long-term clinical outcomes, including CVD events and incidence of T2DM, and data on cost effectiveness. Individuals with MetS could perhaps be recruited as pre-planned subgroups of larger trials, to negate the present dispute concerning the clinical value of MetS and the cost implications of trials involving long-term clinical end-points and associated economic evaluations.

8.3.2.3 Evidence relating to the effectiveness of the TRIMS lifestyle education programme

At recruitment 44% of people who were invited to participate in the TRIMS study did not reply to their invitation letter. It may be helpful for future research to explore the reasons for non-participation in trials involving this type of

intervention, for example, using qualitative methods. The usefulness of being given the 'label' MetS was considered in the TRIMS feedback interviews, but the exploration was limited to intervention group participants. A possible area of interest for future trials would be perceptions about being given the label in the context of being assigned to the control group. Gauging HCPs' views on the usefulness of giving patients the 'label' MetS may also be of interest.

The TRIMS programme was designed as a pragmatic intervention, delivered in community settings and the comparator arm was routine primary healthcare. However, we do not have detailed information about the care provided, including possible lifestyle advice, given that MetS is not routinely identified in practice. At baseline around 50% of people were prescribed a statin and the same proportion an antihypertensive, and of those who were followed-up at 6-months prescribing was virtually unchanged. Future research could incorporate a detailed review of GP medical records and/or exploratory interviews with HCPs, in order to compare the care provided by primary care health professionals to participants in the control and intervention arms.

The TRIMS study involved a subset of people who had already participated in diabetes screening and who were not identified as having impaired glucose regulation at the time of that screening. Additionally, the TRIMS study population were mainly White Europeans (WEs) and South Asians (SAs) of Indian origin. There is scope to test the intervention in other patient groups. However, in order to include people who are unable to understand, speak and

read English, further work would need to be carried out to adapt the TRIMS programme and fully address cultural needs, including language and literacy.

8.4 Strengths and limitations of the overall programme of work

The robust programme of work carried out for this PhD thesis involved the use of a variety of research methods which included both quantitative and qualitative methodologies and a systematic review of the evidence. In addition the MRC framework on developing and evaluating complex interventions[25] (outlined in Chapter 1, section 1.2.2) was used to help inform the plan of work for this thesis. Figure 8-1 illustrates how the various parts of the programme of work relate to the MRC framework, and ultimately contributed to the development of a lifestyle education programme for management of CVD and diabetes risk in people with MetS.

A further strength is that the programme of work considers areas which are under researched. There was a lack of research evidence relating to HCP and patient knowledge and attitudes to waist circumference measurement, including potential barriers to carrying out this assessment. No previous systematic review had been published that consolidated the evidence on interventions for reducing T2DM and CVD risk in populations with MetS; and no prior studies had been conducted in a multi-ethnic UK population to test the effectiveness of a pragmatic lifestyle intervention for reducing T2DM and CVD risk in people with MetS.
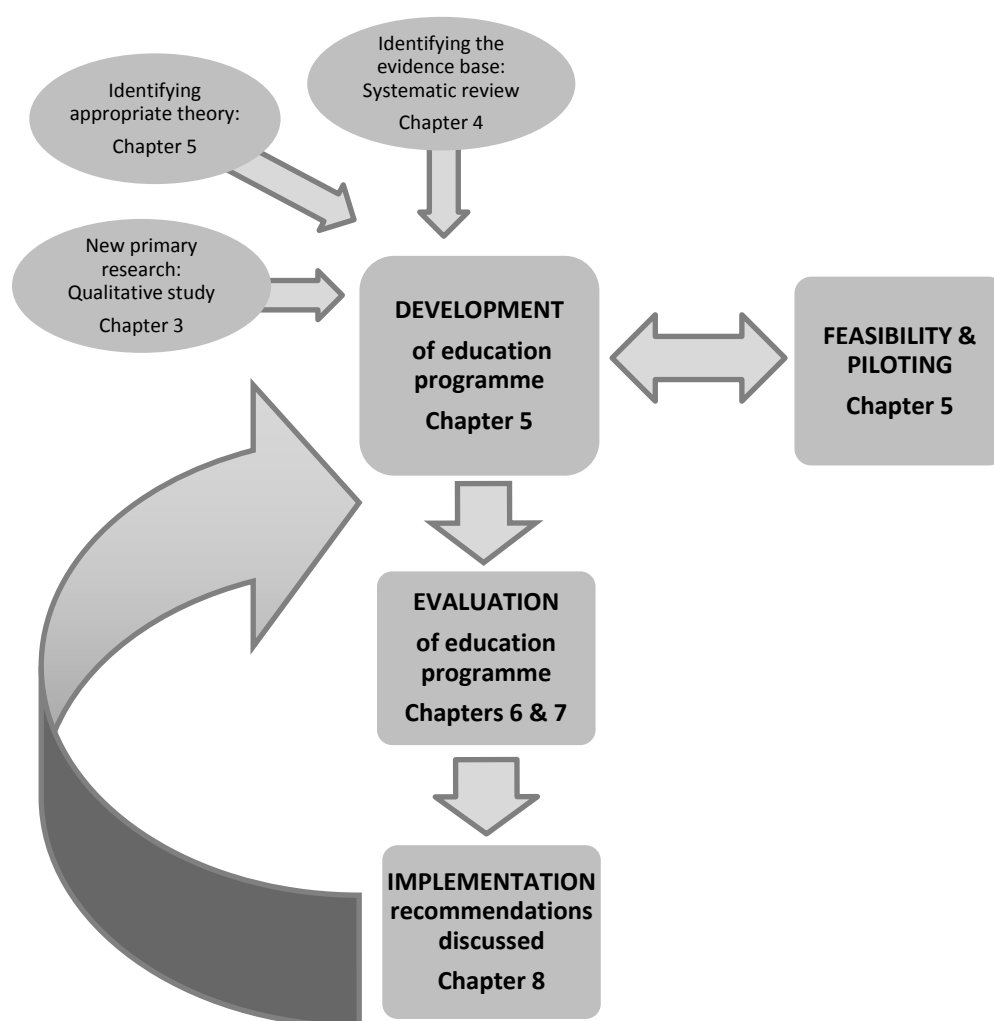
Figure 8-1: How the programme of work for this thesis relates to the Medical Research Council Framework

It is acknowledged that both the qualitative study (Chapter 3) and the TRIMS RCT (Chapters 6 and 7) were conducted at a single centre comprising a specific geographical area (Leicester and Leicestershire) and patient participants were mainly WEs and SAs of Indian origin. This may limit the generalisability of findings. In addition, it is recognised that the current debate about the usefulness of the term MetS,[16] among HCPs and researchers, may

limit the value of the programme of work. However, qualitative evaluation of the TRIMS programme indicated that, in the context of prevention of T2DM and CVD, the majority of people interviewed had positive perceptions about their ability to make healthy lifestyle changes and influence future health outcomes, once they had been made aware of the risks associated with being categorised as having MetS.

Adapting an existing educational programme for use as an intervention (Chapter 5) could potentially be seen as both a strength and a weakness. The Let's Prevent programme,[133] which was adapted, was designed for use in a different patient group, people with pre-diabetes. However, the programme had previously undergone extensive piloting and development work and is based on the recognised DESMOND approach to patient-self management education.[134, 138] Additionally, there is considerable overlap between the nutritional and physical activity recommendations for pre-diabetes and MetS. Furthermore, a thorough in-depth development phase and feasibility phase was carried out to ensure that the TRIMS programme was suitable for people with MetS.

Only 6-month follow-up data and not 12-month were able to be considered in this thesis. However, in terms of contributing to the body of knowledge pertaining to self-management education for management of cardiovascular and diabetes risk in people with MetS, the 6-month data are still valuable, particularly when coupled with the detailed qualitative evaluation of the programme.

8.5   Personal statement

Undertaking the programme of work for this PhD thesis has enabled me to develop immensely as a researcher. I have both acquired new skills and improved upon existing experience to develop an extensive portfolio of research skills.

General skills developed, that relate to both the quantitative and qualitative research conducted, include: writing a study protocol; making submissions for NHS ethical and research governance approvals; developing relevant study documentation, for example, study information sheets, consent forms, and tools for data collection; recruiting general practices; recruiting participants; and gaining informed consent. Generic skills that apply to the whole programme of work undertaken include: writing a research proposal; searching for evidence; critically appraising evidence; recognising when best practice requires collaborative working; time management; project management; presentation skills; and writing for publication in peer reviewed journals.

Specific qualitative research skills that are associated with the study reported in Chapter 3 and the qualitative evaluation reported in Chapter 7 include: developing an interview topic guide; conducting in-depth qualitative interviews with health care professionals and patients; and analysing qualitative data.

Skills that are specifically linked to the systematic review incorporate: designing a search strategy for use with various electronic databases; identifying

appropriate papers; contacting authors and experts in the field; extracting data, including quality assessment; and collating relevant evidence.

Competencies developed that are associated with the design, conduct and evaluation of the TRIMS RCT (Chapters 5 to 7) comprise: developing an educational intervention, including adapting/writing a curriculum and developing resources; collecting data, including bio-medical data; delivering a structured educational intervention; maintaining a study database, including data-entry; and analysing baseline and 6-month follow-up data. Additionally, the skills developed that relate to curriculum design, and patient education will be invaluable if the programme of work is to be taken forward and transferred to other patient groups and settings.

A list of publications arising from this programme of work is included after the abstract for this thesis (p2), and copies of the relevant published manuscripts are included in Appendix 7.

8.6   Next steps

The immediate task following the PhD is to complete the 12-month evaluation of the TRIMS RCT, including the analysis of bio-markers (high-sensitivity C-reactive protein, adiponectin, and insulin). The implications of the definitive findings of the RCT will then be considered and the way in which the research is taken forward will depend on these results.

If the TRIMS lifestyle education programme is found to be effective at reducing T2DM and CVD risk examples of possible follow-up work would be:

- Implementation of the intervention into clinical practice outside of the research setting with existing staff, such as practice nurses or dieticians, facilitating sessions and/or providing supplementary on-going support. Work conducted would need to include practical considerations about staff availability and training.

- Longer-term follow-up to confirm whether changes are sustained and translate into reduced incidence of T2DM and/or CVD.

- Cost effectiveness of the intervention in relation to health benefits achieved, including longer term cost-effectiveness on major clinical outcomes.

- Transferability to other groups of people such as non-English speakers and ethnically diverse populations.

If the intervention is not effective possible additional work might include:

- Looking for explanations, including exploration of possible barriers and enablers to behaviour change.

- Alternative methods of recruitment.

- Different methods of delivering the education programme, including the number and length of sessions, flexibility, and additional reinforcement of behaviour change messages.

- Involving service users in identifying and developing alternative interventions, for example, an internet-based intervention.

8.7 Concluding remarks

This programme of research has made a unique contribution by bridging some of the gaps in the previous body of knowledge around management of cardiovascular and diabetes risk in people with MetS. More specifically, the findings: (1) add to our understanding of HCP and patient views towards waist circumference measurement as a way of assessing obesity related health risk, including MetS; (2) provide evidence of the effectiveness of lifestyle and pharmacological interventions to reverse MetS; and (3) provide evidence on the feasibility, acceptability and effectiveness of a pragmatic evidence based lifestyle intervention for reducing T2DM and CVD risk in people with MetS, in a multi-ethnic UK primary care population.

Appendices

Appendix 1:

Collaborative work: contributions made by people

Appendix 2:

Letters and documents related to the qualitative study reported in Chapter 3

Appendix 3:

Supplementary material related to the systematic review and meta-analysis

reported in Chapter 4

Appendix 4:

Supplementary material related to the TRIMS education program

Appendix 5:

Letters and documents related to the conduct of and recruitment to the TRIMS

randomised controlled trial

Appendix 6:

Letters and documents related to the evaluation of the TRIMS randomised

controlled trial

Appendix 7:

Copies of published manuscripts

Appendix 1:

Collaborative work: contributions made by people

1) Key to contributors

2) Overall programme of work

3) Qualitative study: Chapter 3

4) Systematic review and meta-analysis: Chapter 4

5) Development of the TRIMS education programme: Chapter 5

6) Conduct and evaluation of the TRIMS study: Chapters 6 and 7

1) Key to contributors

Initials	Name	Role
AD	Alison Dunkley	Author of PhD thesis
AN	Anbar Nazir	Clinical Research Assistant
HF	Harriet Fisher	Researcher
JB	Jane Brela	Clinical Research Assistant
JCS	Janette Camosso-Stefinovic	Information Specialist
JT	Jacqui Troughton	Dietician (patient educator)
KC	Kathryn Charles	Researcher
KK	Kamlesh Khunti	PhD Supervisor
LB	Lesley Bryan	Clinical Research Assistant
LG	Laura Gray	Medical Statistician
LJ	Lesley Julian	Transcriber
MAS	Margaret Stone	PhD Supervisor
MJD	Melanie Davies	PhD Supervisor
NP	Naina Patel	Researcher
NT	Nick Taub	Medical Statistician
SC	Sandra Campbell	Nurse (patient educator)
TY	Tom Yates	Researcher (physical activity expert)

2) Overall programme of work

The author of this thesis, Alison Dunkley (AD), designed the research protocol for all the studies included in the programme of work in conjunction with her PhD supervisors, with additional support for individual studies (KC, TY, JT, NT). AD was also responsible for obtaining ethical and other approvals, designing study documentation, and recruitment of general practices and participants.

3) Qualitative study: Chapter 3

AD, NP and MAS developed the interview topic guides. AD conducted the healthcare professional interviews. NP conducted interviews with South Asian patients and also transcribed the interviews. AD conducted all other patient interviews and the interviews with healthcare professionals; LJ transcribed the interviews. AD and MAS developed an initial coding frame and AD analysed all interview transcripts.

4) Systematic review and meta-analysis: Chapter 4

AD, KC and JCS developed the search strategy, and JCS ran the searches including translating search terms for different databases. AD and KC reviewed abstracts, and selected and retrieved relevant papers. AD met with translators, and wrote and sent letters to authors/experts. KK, AD and KC made the final decisions regarding inclusion/exclusion of all papers. AD and KC designed the data extraction tool, and carried out extraction of data and quality assessments. AD conducted the qualitative evidence synthesis including tabulating details of study populations and interventions. LG conducted the meta-analyses.

5) Development of the TRIMS education programme: Chapter 5

AD, JT, NP, MAS, KK and MJD were involved with developing the initial curriculum and resources. AD and JT delivered the pilot education sessions. AD and NP developed the interview topic guide used to gauge participant feedback. NP evaluated the education sessions (observations of sessions and semi-structured telephone interviews with participants). AD analysed and collated the evaluation data, and AD and JT modified the curriculum and resources following the evaluation.

6) Conduct and evaluation of the TRIMS study: Chapters 6 & 7

AD gained informed consent from participants. AD, AN, and JB collected baseline data. MAS randomized participants. AD, JT and SC delivered the TRIMS education programme. AD and NP developed the interview topic guide used to gauge participant feedback. HF conducted semi-structured telephone interviews with participants and transcribed interview transcripts. AD and MAS developed an initial coding frame and AD analysed the interview transcripts. LB collected 6-month (and 12-month) follow-up data. AD carried out the analysis of baseline and 6-month follow-up data. NT provided statistical advice for the TRIMS study.

Appendix 2:

Letters and documents related to the qualitative study reported in Chapter 3

- Copy of funding letter from Royal College of General Practitioners

- Copy of ethics committee approval letter

- Documents for recruiting practices

  o Letter of invitation

  o Reply slip

  o Information sheet

- Poster advertising study

- Documents for recruiting patients

  o Letter of invitation

  o Reply slip

  o Information sheet

  o Consent form

  o Example of translated document: Letter of invitation (Gujarati)

- Documents for recruiting healthcare professionals

  o Letter of invitation

  o Reply slip

  o Information sheet

  o Consent form

- Topic guides for initial interviews

  o Healthcare professional interviews

  o Patient interviews

Letter 1 — Royal College of General Practitioners

14 Princes Gate • Hyde Park • London SW7 1PU
Tel: 020 7581 3232 • Fax: 020 7225 3047
Email: info@rcgp.org.uk • Website: http://www.rcgp.org.uk
Patron: His Royal Highness the Duke of Edinburgh. Registered Charity Number 223106

Royal College of General Practitioners

Professor Greg Rubin FRCGP
Honorary Secretary - Scientific Foundation Board

Mrs Alison Dunkley
Department of Health Sciences
(Division of General Practice & PHC)
University of Leicester
Leicester General Hospital
Leicester LE5 4PW

22 November 2006

Dear Mrs Dunkley,

REFERENCE SFB/2006/09
Waist circumference measurement: patient and practitioner perspective.

Thank you for your application to the Scientific Foundation Board for a grant for the above project which was considered by the Board at its meeting on 15th November 2006. I am pleased to inform you that the Board has agreed to support your application, to be funded under the Board's current partnership arrangement with Roche Products Limited, up to a maximum of £9,996.00.

The Board thought the topic guide for the interviews, as it appeared in your proposal, was rather limited and members thought you should consider incorporating some quantitative measures of knowledge into the interviews. We would welcome your response to this point.

Please note that recipients of awards from the Scientific Foundation Board are required to make their first claim against their award within six months of the date of this confirmatory letter. Failure to do so can result in the withdrawal of the grant. We also ask that recipients complete and return a short return 6 months after the date of this confirmatory letter and a copy of the form to be used for this is enclosed.

I note from your application that you have yet to obtain ethical approval for your study. The Board is unable to release grants until ethical approval has been obtained and so I would be grateful if you could let the Clerk to the Board at the College, have a copy of the letter of approval when it is received. Arrangements will then be made to notify you of how to claim your grant.

In the event that delays occur in obtaining ethical approval which mean that you could exceed the six month limit referred to above, please note that you must write to me, via the Research Office at the College, explaining the circumstances and requesting an extension.

Promoting Excellence in Family Medicine

Letter 2 — NHS National Research Ethics Service

NHS

National Research Ethics Service
Leicestershire, Northamptonshire & Rutland Research Ethics Committee 1

1 Standard Court
Park Row
Nottingham
NG1 6GN

Telephone: 01159123344 Ext: 68575
Facsimile: 01159123300

06 June 2007

Mrs Alison Dunkley
Research Nurse Primary Care Nursing
Department of Health Sciences, University of Leicester
Leicester General Hospital
Leicester, LE5 4PW

Dear Mrs Dunkley,

Full title of study:	Waist circumference measurement: views of patients, doctors, and nurses.
REC reference number:	07/Q2501/88

Thank you for your letter of 24 May 2007, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The Committee has designated this study as exempt from site-specific assessment (SSA). There is no requirement for other Local Research Ethics Committees to be informed or for site-specific assessment to be carried out at each site.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Application		04 April 2007
Investigator CV		02 April 2007
Protocol	1	20 March 2007

University of Leicester

The VOW Study,
Department of Health Sciences
(Division of General practice & PHC),
University of Leicester,
Leicester General Hospital,
Leicester,
LE5 4PW

Dear Practice Manager,

I am writing to invite your practice to volunteer to take part in a qualitative research (interview) study to determine the knowledge and attitudes of patients and primary healthcare practitioners (GPs and practice nurses) towards waist circumference measurement.

Enclosed is an information sheet which explains the purpose of the study and what will be required if you agree to take part. If after having read this information your general practice would like to volunteer to take part in this study, please complete the reply slip enclosed with this letter. The reply slip also asks for some additional information about your practice. This is so we can include different types of general practices in the study, for example practices with differing numbers of patients' on their lists. To help to achieve this, we would like as many practices as possible to volunteer at this stage, but please note that we may not need to use all those that volunteer.

We hope you will agree to participate.

Yours sincerely

Alison Dunkley
(Research Nurse)

Letter of invitation to practice: Version 2, 24/05/2007
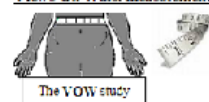
University of Leicester

The VOW Study, Department of Health Sciences
(Division of General practice & Primary Health Care),
University of Leicester, Leicester General Hospital,
Leicester, LE5 4PW.
Telephone: 0116 258 4437, E-mail: ajd38@le.ac.uk.

PRACTICE REPLY SLIP

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

Principal investigator: Alison Dunkley (Research Nurse), Co-investigators: Dr M Stone (Senior Research Fellow), Dr K Khunti (Clinical Senior Lecturer and GP), Prof M Davies (Professor of Diabetes Medicine).

I would be willing for my practice to volunteer to take part in the above study as described in the study information sheet (Practice Information Sheet, Version 1, dated 26/02/2007).

Name (PRINT) _____ Signature _____ Date _____

Role in the practice _____

Practice name _____

Practice address _____

_____

Please could you provide us with the following information? This information will help us to include a range of different general practices in the research study.

1) What is the approximate number of patients registered at your practice? _____

2) How many GPs work at your practice? _____

3) How many practice nurses work at your practice? _____

4) What are the approximate percentages of South Asian and White European patients registered at your practice?

South Asian	%		White European	%

5) Does your general practice currently carry out waist circumference measuring?

(please tick one box only)

Yes, <u>regularly</u> ☐   Yes, <u>occasionally</u> ☐   No, <u>never</u> ☐

6) Are you a teaching / training practice?

Yes / No *(please delete as appropriate)*

Practice Reply Slip: Version 1, 26/02/2007.

PRACTICE INFORMATION SHEET

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

Currently body mass index (BMI) is widely used in clinical practice to identify individuals with a health risk due to being overweight or obese. However, waist circumference is considered by many to be a better indicator of health risk than BMI. Despite the evidence for the strong link between waist circumference and outcomes, and it being a relatively simple measure, waist circumference measurements are not routinely carried out in primary care. It is generally accepted by patients and practitioners that body size is assessed by measuring height and weight, in order to estimate BMI.

There is currently a lack of evidence regarding knowledge and understanding of the role of waist circumference measurement and possible barriers to carrying out this in primary care. Our research therefore aims to determine the knowledge and attitudes of patients and primary healthcare practitioners concerning waist circumference measurement. We are particularly interested in exploring possible barriers in a mixed ethnic population. Qualitative in-depth semi-structured interviews will be conducted to determine the views of primary healthcare practitioners and patients. Interviews will be conducted in English or Gujarati.

Recruitment to the study is in 2 stages:
1) All general practices in Leicestershire are being sent a letter of invitation to participate in the research and a reply slip. From those practices who return their reply slip 10 general practices will be selected to take part, on the basis of: list size, ethnic background of patients, teaching/training status, number of GPs and practice nurses, and if practice currently measures waist circumference. A researcher will then arrange to visit the practices that are selected.
2) Interviewees will be recruited by letter or in person from the selected practices, up to 20 patients and 10 practitioners (GPs and practice nurses). We will aim to choose a diverse sample of people to be interviewed within these 2 groups, from those who volunteer in terms of ethnic background, age, and gender. Additional selection criteria will be: for patients, frequency of visiting their general practice, previous experience of having their waist measured, and body mass index (optional); for healthcare professionals, length of time working in primary care, and if their current role involves waist circumference measuring. This should enable us to capture a range of views.

Patient interviews will be conducted in the participant's home, or if they prefer somewhere that is private at the University. Health professionals will normally be interviewed at the general practice surgery they work at. All interviews will be audio-recorded.

If you agree for your practice to participate in this study please complete the reply slip attached. A reply paid envelope is enclosed.

If you still have any questions about the study please feel free to contact:
Alison Dunkley (Research Nurse), Division of General Practice & PHC, Department of Health Sciences, University of Leicester, Leicester General Hospital, Leicester, LE5 4PW.
Telephone: 0116 258 4437. E-mail: ajd38@le.ac.uk

Practice Information Sheet: Version 1, 26/02/2007

Waist Measurement

The Department of Health Sciences at the University of Leicester is doing some research about people's attitudes to having their waist size measured

This research involves interviewing people, and we are looking for volunteers over the age of 25

If you would like to volunteer or you think you know another adult who is registered at your general practice who might be interested, please ask for an information sheet at the reception desk

You will NOT be asked to have your waist measured. We just want to find out what you think

University of Leicester

Division of General Practice & PHC, Department of Health Sciences, University of Leicester, Leicester General Hospital, Leicester, LE5 4PW

(Please note a Gujarati version will also be available)

Views On Waist measurement

The VOW study

To be printed on General Practice headed paper

(Please note a Gujarati version of the patient reply slip will also be available)

Views On Waist measurement

The VOW study

University of Leicester

The VOW Study, Department of Health Sciences
(Division of General practice & Primary Health Care),
University of Leicester, Leicester General Hospital,
Leicester, LE5 4PW.
Telephone: 0116 258 4437, **E-mail**: ajd38@le.ac.uk.

PATIENT REPLY SLIP

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

Dear Patient,

This practice is taking part in a study with researchers at the University of Leicester. The purpose of this research is to find out what people think about having their waist measured, as a way of finding out if they are at risk of future health problems such as diabetes and heart problems.

Enclosed is an information sheet which explains more about the study and what will happen if you agree to help us. Once you have read this information, if you would like to volunteer to take part please complete the reply slip enclosed with this letter. The reply slip also asks for some information about you. This is so we can include different types of patients in the study, for example patients in differing age groups. To help to achieve this, we would like as many patients as possible to volunteer at this stage, but please note that we may not need to interview all those who volunteer.

We hope you will agree to take part.

Yours sincerely

Alison Dunkley
(Research Nurse)

I would like to volunteer to take part in this study, and I agree to a researcher contacting me by telephone to arrange an appointment to be interviewed.

SIGNATURE: _____ DATE: _____

NAME: _____

ADDRESS: _____

_____

TELEPHONE NUMBER: _____

To help us to choose a range of different types of people, it would be very helpful if you could provide the following information about yourself:

1) Are you? Male / Female *(please delete as appropriate)*

2) What is your age? *(please tick one box only)*

i) 25 – 39 ☐   ii) 40 – 59 ☐   iii) 60 – 75 ☐

3) Approximately how often do you go to see the doctor or nurse at your general practice? *(please tick one box only)*

i) Weekly ☐   ii) Monthly ☐   iii) Yearly ☐   iv) Less often ☐

4) Have you _ever_ had your waist measured by a doctor or nurse at your general practice?

Yes / No *(please delete as appropriate)*

5) How would you describe your ethnic origin? *(please tick one box only)*

i) White ☐   ii) Asian ☐   iii) Afro-Caribbean ☐   iv) Other ☐

This last question is optional

6) What is your height and weight?   Height _____   Weight _____

Letter of invitation to patient: Version 2, 24/05/2007

Patient reply slip: Version 1, 26/02/2007

(Please note a Gujarati written and audio version of the patient information sheet will be available)

Views On Waist measurement

University of Leicester

The VOW Study, Department of Health Sciences (Division of General practice & Primary Health Care), University of Leicester, Leicester General Hospital, Leicester, LE5 4PW. Tel: 0116 258 4437, E-mail: ajd38@le.ac.uk.

The VOW study

PATIENT INFORMATION SHEET

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

You are being invited to volunteer to take part in a research study. Before you decide you need to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends, relatives, or your GP if you wish. Please ask us if there is anything that is not clear or you would like more information. Please note that we may not need to use everybody who volunteers.

Why is this research being done?
We are trying to find out what people think about having their waist size measured, as a way of finding out if they are at risk of future health problems such as diabetes and heart problems.

What will be involved if I take part?
We are looking for volunteers who will agree to being interviewed about waist measuring. The interviews will normally be carried out in people's homes and will be recorded using a tape recorder. You will NOT be asked to have your waist measured. We just want to know what you think.

Who can volunteer?
Anyone aged over 25 and registered at your general practice.

Will the interview be confidential?
The audio-recording will be treated in the strictest confidence and will be stored without your name on it. Anyone who takes part can request a copy of their interview tape if they wish. The audio-recording will be destroyed at the end of the study and your name will not be mentioned in the results. Your contact telephone number will be deleted from our records once you have done the interview. Your doctor or practice nurse will not know what you have said in the interview.

What will happen to the results of the study?
The results of the study may be published in a medical journal or presented at research meetings or conferences.

Who is organising and funding this research?
The principal investigator for this study is Alison Dunkley (Research Nurse) at the University of Leicester. This research is being funded by a grant from the Royal College of General Practitioners.

Who has reviewed this study?
To protect your safety, rights, well-being and dignity, all research involving patients is looked at by an independent group of people, called a Research Ethics Committee. This study has been reviewed by the appropriate ethics committee in accordance with local regulations.

Patient Information Sheet: Version 2, 24/05/2007

What if I am harmed by the study?
It is very unlikely that this research will cause harm to anyone, but if you wish to complain or have any concerns about the way you have been approached or treated in connection with the study, the normal National Health Service complaints mechanisms would be available to you.

Do I have to take part?
No, we are looking for volunteers. Even if you volunteer and agree to take part, you can change your mind at any time, without giving a reason.

What do I do if I decide to volunteer?
If you have decided to volunteer to take part in the study, please send the reply slip to the university research team in the envelope provided. This does not need a stamp. We will probably not need to use everyone who volunteers: we will choose people so that we interview different types of people, for example people in different age groups.

If you still have any questions about the study please feel free to contact:
Alison Dunkley (Research Nurse),
Division of General Practice & PHC,
Department of Health Sciences,
University of Leicester,
Leicester General Hospital,
Leicester,
LE5 4PW.
Telephone: 0116 258 4437. E-mail: ajd38@le.ac.uk

Patient Information Sheet: Version 2, 24/05/2007

Please note the consent form will be verbally translated for non English speakers

Gujarati

Views On Waist measurement

The VOW study

University of Leicester

The VOW Study, Department of Health Sciences
(Division of General practice & Primary Health Care),
University of Leicester, Leicester General Hospital,
Leicester, LE5 4PW.
Telephone: 0116 258 4437, E-mail: ajd38@le.ac.uk.

Views On Waist measurement

The VOW study

To be printed on General Practice
headed paper

PATIENT CONSENT FORM

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

Principal investigator: Alison Dunkley (Research Nurse), Co-investigators: Dr M Stone (Senior Research Fellow),
Dr K Khunti (Clinical Senior Lecturer and GP), Prof M Davies (Professor of Diabetes Medicine).

Please write your initials in each box

1) I confirm that I have read and understood the information sheet (Version 2, dated 24/05/2007) for the above study and have had the opportunity to ask questions.
[1]

2) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my medical care or legal rights being affected.
[2]

3) I understand that the interview will be audio-recorded but that all information will remain strictly confidential.
[3]

4) I agree that all information collected about me as part of the study can be stored and analysed by the research team at the University of Leicester, and that small parts of what I say may be quoted anonymously when the results of the research are reported.
[4]

5) I give permission for a summary of the results of the research to be sent to my contact address.
(this is optional)
[5]

6) I agree to take part in the above study
[6]

_____   _____   _____
Name of participant (PRINT)   Signature   Date

_____   _____   _____
Name of researcher (PRINT)   Signature   Date
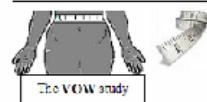
Patient Consent Form: Version 2, 24/05/2007   **1 for researcher**

માનનીય દર્દીઓ

આ પ્રેક્ટીસ(સર્જરી) યુનિવર્સિટી ઓફ લેસ્ટરનાં એક અભ્યાસનાં સંશોધનકારો સાથે ભાગ લઈ રહી છે. આ અભ્યાસનો હેતુ એ જાણવાનો છે કે લોકોને કમ્મરનું માપ લેવા વિષે શો અભિપ્રાય છે, કે જે લેવાથી ભવિષ્યમાં નેઓની નંદુરસ્તીની મુશ્કેલીઓ જેવી કે ડાયાબિટિસ અને હૃદયરોગોનાં જોખમો છે કે નહીં નેનો ખ્યાલ આવી શકે.

આ સાથે માહિતી પત્રિકા મોકલીયે છીએ જેમાં આ અભ્યાસ વિષે અને તમે જો ભાગ લેવા માટે કબૂલ થાઓ પછી શું કરવામાં આવશે ને વિષે માહિતી આપવામાં આવી છે. એક વખત આ માહિતી વાંચી લો પછી જો તમને નેમાં ભાગ લઈને વોલ-ટીયર(સ્વંસેવક) તરીકે જોડાવું હોય નો આ સાથે મોકલાવેલી રીપ્લાય સ્લીપ(વળનો જવાબ આપવાનું ફોર્મ)બરીને મોકલવા વિનંતિ. આ રીપ્લાઈ સ્લીપમાં નમારે વિષે કેટલીક માહિતી પુછવામાં એટલા માટે આવી છે કે જેથી જુદા જુદા પ્રકારનાં દર્દીઓનો આ અભ્યાસમાં સમાવેશ કરી શકીયે, દા.ત. જેમકે વિવિધ ઉંમરનાં દર્દીઓ. આ મેળવવા માટે અમને આ નબક્કે વધારેમાં વધારે વોલ-ટીયર્સની જરૂર છે પરંતુ એ ઘ્યાનમાં રાખો કે કદાચ અમારે એ બધા જ વોલ-ટીયર્સનાં ઈન્ટરવ્યુ લેવાની જરૂર ન પણ પડે.

અમે આશા રાખીયે છીએ કે તમે ભાગ લેવા માટે કબૂલ થાઓ.
લિ.

એલીસન ડન્કલિ-Alison Dunkley

(રીસર્ચ નર્સ-Research Nurse)
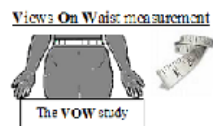
Translated by Nij Translators Tel: 0116 2202372   vowlet07

The VOW Study,
Department of Health Sciences
(Division of General practice & PHC),
University of Leicester,
Leicester General Hospital,
Leicester,
LE5 4PW

The VOW Study, Department of Health Sciences
(Division of General practice & Primary Health Care),
University of Leicester, Leicester General Hospital,
Leicester, LE5 4PW.
Telephone: 0116 258 4437, **E-mail:** ajd38@le.ac.uk.

Dear Healthcare Professional,

This practice is taking part in a study with researchers at the University of Leicester. The purpose of this research is to find out what primary care health professionals think about using waist circumference measurement as a way of finding out if patients are at risk of future health problems such as diabetes and cardiovascular disease.

Enclosed is an information sheet which explains the purpose of the study and what will be required if you agree to take part. If after having read this information you would like to volunteer to take part in this study, please complete the reply slip enclosed with this letter. The reply slip also asks for some additional information about you. This is so we can include different types of healthcare professionals in the study, for example professionals with differing number of years experience working in primary care. To help to achieve this, we would like as many healthcare professionals as possible to volunteer at this stage, but please note that we may not need to interview all those who volunteer.

We hope you will agree to participate.

Yours sincerely

Alison Dunkley
(Research Nurse)

Letter of invitation to healthcareprofessional: Version 2, 24/05/2007
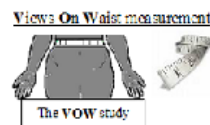
HEALTHCARE PROFESSIONAL REPLY SLIP

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

I would like to volunteer to take part in this study, and I agree to a researcher contacting me by telephone to arrange an appointment to be interviewed.

SIGNATURE: _____ DATE: _____

NAME: _____

ADDRESS: _____

_____

TELEPHONE NUMBER: _____

To help us to choose a range of different types of people, it would be very helpful if you could provide the following information about yourself:

1) Are you? Male / Female *(please delete as appropriate)*

2) What is your profession? Practice Nurse / GP *(please delete as appropriate)*

3) What is your age? *(please tick one box only)*

i) 25 – 39 ☐   ii) 40 – 59 ☐   iii) 60 – 75 ☐

3) Approximately how long have you worked in primary care ? *(please tick one box only)*

i) Less than 1 year ☐   ii) 1 – 5 years ☐   iii) 6 – 10 years   iv) More than 10 years ☐

4) Does your general practice currently carry out waist circumference measuring?
(please tick one box only)

Yes, regularly ☐   Yes, occasionally ☐   No, never ☐

5) How would you describe your ethnic origin? *(please tick one box only)*

i) White ☐   ii) Asian ☐   iii) Afro-Caribbean ☐   iv) Other ☐

Healthcare professional reply slip: Version 1, 26/02/2007

University of Leicester

The VOW Study, Department of Health Sciences (Division of General practice & Primary Health Care), University of Leicester, Leicester General Hospital, Leicester, LE5 4PW. Tel: 0116 258 4437, E-mail: ajd38@le.ac.uk

HEALTHCARE PROFESSIONAL INFORMATION SHEET

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

You are being invited to volunteer to take part in a research study. Before you decide you need to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask us if there is anything that is not clear or you would like more information. Please note that we may not need to use everybody who volunteers.

Why is this research being done?
We are trying to find out what primary care health professionals think about using waist circumference measurement as a way of finding out if patients are at risk of future health problems such as diabetes and cardiovascular disease.

What will be involved if I take part?
We are looking for volunteers who will agree to being interviewed about waist circumference measuring. The interview will normally be carried out at the general practice where you work. The interview will be audio-recorded.

Who can volunteer?
Anyone who works as a practice nurse or GP at your general practice.

Will the interview be confidential?
The audio-recording will be treated in the strictest confidence and will be stored without your name on it. Anyone who takes part can request a copy of their interview if they wish. The audio-recording will be destroyed at the end of the study and your name will not be mentioned in the results. Your contact telephone number will be deleted from our records once you have done the interview.

What will happen to the results of the study?
The results of the study may be published in a medical journal or presented at research seminars or conferences.

Who is organising and funding this research?
The principal investigator for this study is Alison Dunkley (Research Nurse) at the University of Leicester. This research is being funded by a grant from the Royal College of General Practitioners.

Who has reviewed this study?
This study has been reviewed by the appropriate Research Ethics Committee in accordance with local regulations.

Do I have to take part?
No, we are looking for volunteers. Even if you volunteer and agree to take part, you can change your mind at any time, without giving a reason.

What do I do if I decide to volunteer?
If you have decided to volunteer to take part in the study, please send the reply slip to the university research team in the envelope provided. This does not need a stamp. We will probably not need to use everyone who volunteers: we will choose people so that we interview different types of people, for example people in different age groups.

If you still have any questions about the study please feel free to contact:
Alison Dunkley (Research Nurse),
Division of General Practice & PHC,
Department of Health Sciences,
University of Leicester,
Leicester General Hospital,
Leicester,
LE5 4PW.
Telephone: 0116 258 4437. E-mail: ajd38@le.ac.uk

Health Professional Information Sheet: Version 2, 24/05/2007

Views On Waist measurement

The VOW study

University of **Leicester**

The VOW Study, Department of Health Sciences
(Division of General practice & Primary Health Care),
University of Leicester, Leicester General Hospital,
Leicester, LE5 4PW.
Telephone: 0116 258 4437, **E-mail**: ajd38@le.ac.uk.

HEALTHCARE PROFESSIONAL CONSENT FORM

Views On Waist measurement (the VOW study)

(Waist circumference measurement: views of patients, doctors and nurses)

Principal investigator: Alison Dunkley (Research Nurse), Co-investigators: Dr M Stone (Senior Research Fellow),
Dr K Khunti (Clinical Senior Lecturer and GP), Prof M Davies (Professor of Diabetes Medicine).

Please write your initials in each box

1) I confirm that I have read and understood the information sheet (Version 2, dated 24/05/2007) for the above study and have had the opportunity to ask questions. [1]

2) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my medical care or legal rights being affected. [2]

3) I understand that the interview will be audio-recorded but that all information will remain strictly confidential. [3]

4) I agree that all information collected about me as part of the study can be stored and analysed by the research team at the University of Leicester, and that small parts of what I say may be quoted anonymously when the results of the research are reported. [4]

5) I give permission for a summary of the results of the research to be sent to my contact address. *(this is optional)* [5]

6) I agree to take part in the above study [6]

_____   _____   _____
Name of participant (PRINT)   Signature   Date

_____   _____   _____
Name of researcher (PRINT)   Signature   Date

Healthcare Professional Consent Form: Version 2, 24/05/2007.   **1 for researcher**

HEALTHCARE PROFESSIONAL TOPIC GUIDE

1. Previous experience

a. Do you or anybody else at the surgery currently carry out waist circumference measuring? [For any reason?]

<u>if YES</u>

Who does the waist measuring?
- o [Yourself, a colleague, practice nurse, GP, healthcare assistant]

Do you target particular groups of patients?
- o [Perhaps patients with particular chronic diseases?]

How often are patients' waists measured?
- o [regularly? occasionally?]

Is a particular method or way of measuring used?
- o [Does everybody measure the same way?]

How long have you been measuring waist size?
- o [self? surgery?]

<u>if NO currently</u>

How do you currently assess patients to see if their health is at risk due to overweight or obesity?
- o [Do you measure weight and height, and calculate BMI, or something else?]
- o [How do other colleagues at the practice measure a patient's body size/shape?]

b. Do you have you any previous experience of measuring patients' waist size?
[It may have been at another surgery or a hospital?]
- o When was this?
- o Where was this?
- o How often did you measure patients' waists?
- o Did you use a particular method or way of measuring?
- o What sort of patients did you measure?

2. Knowledge

a. Do you know anything about the importance of waist size?
- o [Have you ever seen anything in a journal, heard anything at a study day, or from a colleague?]
- o [Anything on the television, radio, or in a magazine or newspaper?]

<u>if YES</u>

Can you tell me how you know this?
- o [When and where from?]
- o [Was it something you read, or heard, or were told?]
- o When?

<u>If NO or not mentioned</u>

Do you think there is a link between waist size and being healthy, or not?

b. What size do you think someone's waist should be?
[I don't need to know an exact figure, just what you think]
- o Do you think that would be the same for everybody?
- o Some people have said that it might depend on a patient's height, or if they're a man or a woman. What do you think?
- o What about different ethnic groups? Do you think that makes a difference?

c. Do you think waist size is something practice nurses and GPs think about?

---

3. How practitioner feels about waist measuring

<u>If DOES measure</u>	or	<u>If does NOT measure</u>

a. How do you feel about measuring a patient's waist size?

b. How would you feel if you had to measure a patient's waist when they attended the surgery?

- o If a patient came to see you for something else (like flu or a blood test etc), would you feel comfortable asking them if you could measure their waist size, or not?
- o If you were required to target particular groups of patients, how would you feel? Say all pts over 45.
- o Some people have said they feel uncomfortable when positioning the tape measure, as they have to touch a patient and get very close. What do you think?
- o Some people have said they have enough measurements to do without anymore. What do you think?

c. Who do you think should carry out waist measuring?
- o Should it be a doctor or a nurse, or doesn't it matter?
- o What about someone else like a healthcare assistant?
- o Should the person be male or female, or doesn't it matter?

4. Potential barriers to measuring

a. What things might prevent you from measuring a patient's waist? (or do prevent you?)
[Anything at all that might discourage you or put you off?]
[It might be related to the surgery, a patient, or yourself?]
- o Some people have said lack of time may prevent them, what do you think?
- o Would it make a difference if it was a patient you were familiar with, or not?
- o Would the patients attitude make a difference, or not?

b. Are there any things that might encourage you to carry out waist measuring?
[In terms of the practice, a patient, or yourself?]

5. Usefulness of waist measuring

<u>If surgery DOES measure</u>

a. Is it useful for you to have a waist size measurement for a patient, or not?
- o Do you think it helps you to identify if their health might be at risk, or not?

<u>If surgery does NOT measure</u>

b. Do you think you would find it useful if you measured a patient's waist size to identify health risk, or not?
- o Would it be useful in patients who may be at risk of diabetes or cardiovascular disease, or not?
- o What about certain age groups, or certain ethnic groups?

c. How reliable do you think a waist measurement is?
- o [Do you think someone's waist size would be the same each time it is measured, or not?]
- o Some people have said it may vary depending on who does the measuring, what do you think?

d. Some people have said that it is a difficult measurement to do, what do you think?

e. Do you think it would be useful if a patient measured their own waist in order to identify if their health might be at risk, or not?
- o If patients' measured their waist and were asked to come for a check up if they had a waist circumference above a certain size, would that be useful to you, or not?

<u>If NOT raised earlier</u>

Some research has shown that a large waist can increase the risk of getting diabetes or heart disease. Have you ever heard that?
[What do you think?]   [Do you think a big waist is related to diabetes or heart disease, or not?]

PATIENT TOPIC GUIDE

1. Previous Experience
a. Has anyone ever weighed or measured you at your doctors surgery or the hospital? if YES
  - When was that?
  - Who measured you?
  - How?
  - Why?
  - How did you feel about that?

b. Have you ever had your waist size measured?
[It might have been somewhere other than the doctors or hospital. Some people have said when they had clothes fitted]
  if YES
  - When was that?
  - Who measured you?
  - Where was that?
  - Why?
  - How did they measure you? [Was it under or over clothing?]
  - How did you feel about having your waist measured?
  If NO
  - What do you think having your waist measured would involve?
  - [Do you think it would be measured under or over clothing?]

c. Have you ever measured your own waist?
  if YES
  - When was that?
  - What made you measure your waist?
  - Did you measure it under or over clothing?
  If NO
  I don't need to know what your waist size is, but have you any idea what it is?

d. Have any of your family or friends ever talked to you about having their waist measured? if YES
  - Can you remember what they said about it?

2. Knowledge
a. Do you know anything about the importance of waist size?
  if YES
  - Tell me how you know this?
  - Where from?
  - Who from?
  - When?
  If NO
  Have you seen anything on the television, heard anything on the radio, or read anything in a magazine or newspaper?
  Do you think there is a link between waist size and being healthy, or not?

b. What size do you think someone's waist should be?
[I don't need to know an exact figure, just what you think]
  - Do you think that would be the same for everybody?
  - Some people have said that it might depend on your height, or if you are a man or a woman. What do you think?

c. Do you think someone's waist size would be the same each time it is measured, or not?
[What if it was measured 3 times in the same week?]
  - Why do you think that might be?

3. How patient feels about waist measuring
a. Do you think waist size is something people think about?

IF PREVIOUSLY HAD WC MEASURED: [You've already told me about when you had your waist measured before but.........]
b. How would you feel if somebody at your doctors surgery or the hospital wanted to measure your waist?
  - If you went to see the doctor or nurse for something else (like flu or a blood test etc), would you mind if they measured your waist, or not?

c. How would you feel if you had to loosen or move your clothing about so that your waist could be measured?
  - Some people have said that they wouldn't mind but others have said they may feel uncomfortable. What do you feel about that?

d. Would you mind who it was that measured your waist, or not?
  - Would you feel more comfortable with a male or female, or wouldn't you mind?
  - What about a doctor or a nurse, would you mind about that or not?

e. Would you feel more comfortable if someone else was there with you, or don't you think that is necessary?
  - Maybe another member of staff at the practice, or a friend or relative?

4. Potential barriers to measuring
a. Are there any things that might put you off having your waist measured?
  - Some people have said...... What do you think?
  - You mentioned earlier......... Anything else

b. Are there any things that might encourage you to have your waist measured?
  - Some people have said...... What do you think?
  - You mentioned earlier....... Anything else

5. Usefulness of waist measuring
a. Do you think it would be useful to you to have your waist measured to find out if your health might be at risk, or not?
[If the measurement indicated if you were healthy or unhealthy would that be useful, or not?]
b. Do you think it would be useful for doctors and nurses to know?

c. Do you think it would be useful if you measured your own waist in order to find out if your health might be at risk, or not?
[If you were asked to go for a check up at the surgery if your waist was above a certain size, would that be useful or not?]

6. Finally - IF IT HASN'T BEEN RAISED EARLIER
• Some research has shown that a large waist can increase the risk of getting diabetes or heart disease. Have you ever heard that?
[What do you think?]
[Do you think a big waist is related to diabetes or heart disease, or not?]
[If a doctor/ nurse could tell you if you were likely to get diabetes or heart disease by measuring the size of your waist, would that be useful, or not?]

If they ask or are concerned:
• I am unable to give you any advice about your waist size
• There is a lot of information available on waist size i.e. websites (Diabetes UK)
• If there is anything that you are worried about you need to speak to your GP or Practice Nurse
---

Appendix 3:

Supplementary material related to the systematic review and meta-analysis reported in Chapter 4

- Data extraction form

- Supplementary information about the quantitative data synthesis (meta-analysis)
  - o Supplementary methods for the meta-analysis
  - o Supplementary results from the meta-analysis

Systematic review of interventions for metabolic syndrome
Data extraction form

ELIGIBILITY CHECKLIST	YES	NO	NOTES
Population or sub-group has MetS			If no, exclude
Population >= 18 years			If no, exclude
Population free of CVD at baseline			If no, exclude if total population has CVD
Population free of DM at baseline			If no, exclude if total population has DM
RCT			If no, exclude
Follow-up period >= 24 weeks			If no, exclude
Outcomes – incidence CVD/DM and/or prevalence MetS			If no, exclude

STUDY DETAILS

First author	
Title of paper	
Journal	
Publication date	
Language and country of first author	
Important notes (include any significant issues here: eg validity, areas of uncertainty etc)	

POPULATION

Definition of MetS used	
Any modification to MetS definition applied (eg BMI instead of waist circumference)	
Country/countries	

1

Setting (eg OPD, GP)	
Eligibility criteria	
Exclusion criteria	

Numbers randomised	Total	Intervention 1	Intervention 2	Intervention 3	Control
Total					
Men					
Women					
Mean age (+/- SD)					
Ethnicity					
Recruitment dates/period					

METHODS

Type of RCT (eg parallel, crossover)	
Post hoc and/or sub-group	YES / NO \ If yes, pre-specified or exploratory:
Method of recruitment (eg how patients invited/selected to participate)	

Intervention group 1	Details
Focus of intervention	
Content of intervention	

2

Paper:
Researcher's initials:

Where intervention conducted	
How delivered	
Duration of intervention (time from start to completion)	
Training given to person(s) conducting intervention	
How compliance monitored	
How safety monitored	
Intervention group 2	**Details**
Focus of intervention	
Content of intervention	
Where intervention conducted	
How delivered	
Duration of intervention (time from start to completion)	
Training given to person(s) conducting intervention	
How compliance monitored	
How safety monitored	
Intervention group 3	**Details**
Focus of intervention	

3

Paper:
Researcher's initials:

Content of intervention	
Where intervention conducted	
How delivered	
Duration of intervention (time from start to completion)	
Training given to person(s) conducting intervention	
How compliance monitored	
How safety monitored	
Control group	**Details**
Information on control group intervention (eg placebo/usual care). Include information on compliance if applicable.	

QUALITY CRITERIA (* Delphi)

Method of randomisation*	
Allocation concealment*	Adequate / Unclear / Inadequate / Not undertaken State how (if applicable):
Eligibility criteria specified*	Yes / No

4

| Paper: |
| Researcher's initials: |

Groups similar at baseline*	Yes / No / Unclear If not, were adjustments made?
A priori sample size calculation?	Yes / No Give details:
Intervention and control groups treated identically apart from intervention	Yes / No / Unclear
Patients blinded*	Yes / No / Unclear / Not possible
Care provider(s) blinded*	Yes / No / Unclear / Not possible
Pathology staff blinded	Yes / No / Unclear / Not applicable
Outcome assessor(s) blinded*	Yes / No / Unclear
Point estimate and measure of variability given for primary outcome*	Yes / No
Analysis on ITT basis*	Yes / No
Analysis of drop-outs compared with participants who completed the intervention	Yes / No
Flow diagram charting number of participants from beginning to end of trial	Yes / No
Number of Delphi criteria met	

RESULTS/OUTCOMES

	Intervention 1	Intervention 2	Intervention 3	Control group
Compliance with intervention(s)				
Drop out rate (no and %)				
Safety of intervention(s)				
Adverse events				

5

| Paper: |
| Researcher's initials: |

PRIMARY OUTCOMES: Mortality

Period of follow-up: Interim/final outcome:

Population: Total / Sub-group (If sub-group, specify:)

OUTCOME MEASURE		
CV mortality (binary)		
Definition		
Method of measuring		
Statistical test used		
	Intervention group	**Control group**
Number of deaths		
Percentage		
HR/OR (inc CI and p value)		
All-cause mortality (binary)		
Definition		
Method of measuring		
Statistical test used		
	Intervention group	**Control group**
Number of deaths		
Percentage		
HR/OR (inc CI and p value)		

6

| Paper: |
| Researcher's initials: |

PRIMARY OUTCOME: Cardiovascular events

Period of follow-up: Interim/final outcome:

Population: Total / Sub-group (If sub-group, specify:)

THIS SHEET WILL BE REVISED FOLLOWING SELECTION OF PAPERS DEPENDING ON WHETHER TRIALS REPORT FIGURES FOR DIFFERENT EVENTS OR IN AGGREGATE ONLY.

OUTCOME MEASURE		
CV events - eg non-fatal MI/stroke, angina, CABG, PTCA (count)		
Definition		
Method of measuring		
Statistical test used		
	Intervention group	Control group
Number of events		
Number of person years of follow-up		
Event rate (%)		
HR/OR (inc CI and p value)		

| Paper: |
| Researcher's initials: |

PRIMARY OUTCOME: Incidence of type 2 diabetes/prevalence of MetS

Period of follow-up: Interim/final outcome:

Population: Total / Sub-group (If sub-group, specify:)

OUTCOME MEASURE				
Onset of diabetes (binary)				
Definition				
Method of measuring				
Statistical test used				
	Intervention 1	Intervention 2	Intervention 3	Control
Number of patients with new diagnosis of diabetes				
Percentage				
HR/OR (inc CI and p value) compared with control				
Prevalence of MetS (binary)				
Definition				
Method of measuring				
Statistical test used				
	Intervention 1	Intervention 2	Intervention 3	Control
Number of patients no longer diagnosed with MetS				
Percentage				
HR/OR (inc CI and p value) compared with control				

7

8

Paper:
Researcher's initials:

Paper:
Researcher's initials:

SECONDARY OUTCOMES

PERIOD OF FOLLOW-UP: INTERIM/FINAL OUTCOME:

OUTCOME MEASURE				
Waist circumference	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Body Mass Index	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Weight	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Fasting blood glucose	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
HDL	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Triglycerides	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				

Systolic BP	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Diastolic BP	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Other...........................	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Other...........................	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Other...........................	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				
Other...........................	Intervention 1	Intervention 2	Intervention 3	Control
Mean (Change or Actual)				
Standard deviation				
Statistical test used				

9

10

Supplementary information about the quantitative data synthesis (meta-analysis)

Supplementary methods for the meta-analysis

For the direct pairwise comparisons, random effects models were used to estimate the odds ratios for MetS reversal. Heterogeneity was assessed using the I^2 statistic and publication bias using contour enhanced funnel plots and the Peters' test. The direct pairwise meta-analyses were performed in Stata version 11.1 (StatCorp, College Station, Texas, US).

To compare all treatments for MetS reversal within a single model, mixed treatment comparison methods were used. This allowed both direct and indirect comparisons (where no head to head trials were available) to be made. Comparisons were checked to make sure they formed closed networks and a logistic regression model was used to combine data. In all cases a burn-in of 10,000 simulations was discarded and the results presented were based on a further 50,000 simulations. Convergence was checked visually using the history plots and the residual deviance was used to check the goodness of fit. Vague priors were used for all parameters. For each treatment type, the percentage of times that treatment gained the highest rank across all of the simulations was also calculated. All the mixed treatment comparison analysis was conducted using a Bayesian Markov chain Monte Carlo method using the Bayesian software, WinBUGS version 1.4.3 (Medical Research Council, Cambridge, UK).

Supplementary results from the meta-analysis

The restricted network grouped by treatment category and the full network of trial interventions are shown in Figure A and Figure B respectively (following page).
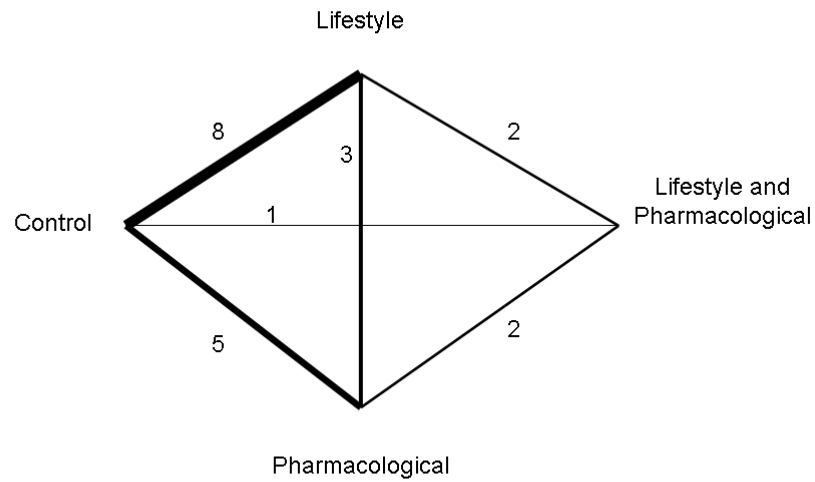
Figure F: The restricted (grouped) network of trial interventions
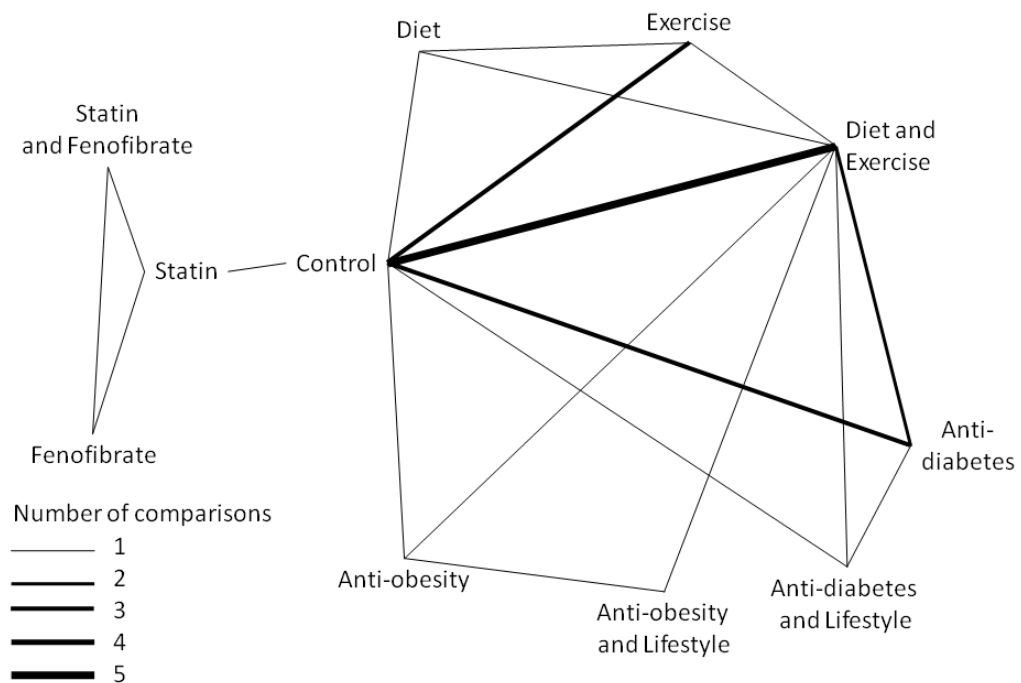
Figure G: The full network of trial interventions

Publication bias was assessed, for the direct pairwise comparison results for the grouped data, only for the lifestyle versus control comparison; no significant publication bias was seen (p=0.84), see Figure C.
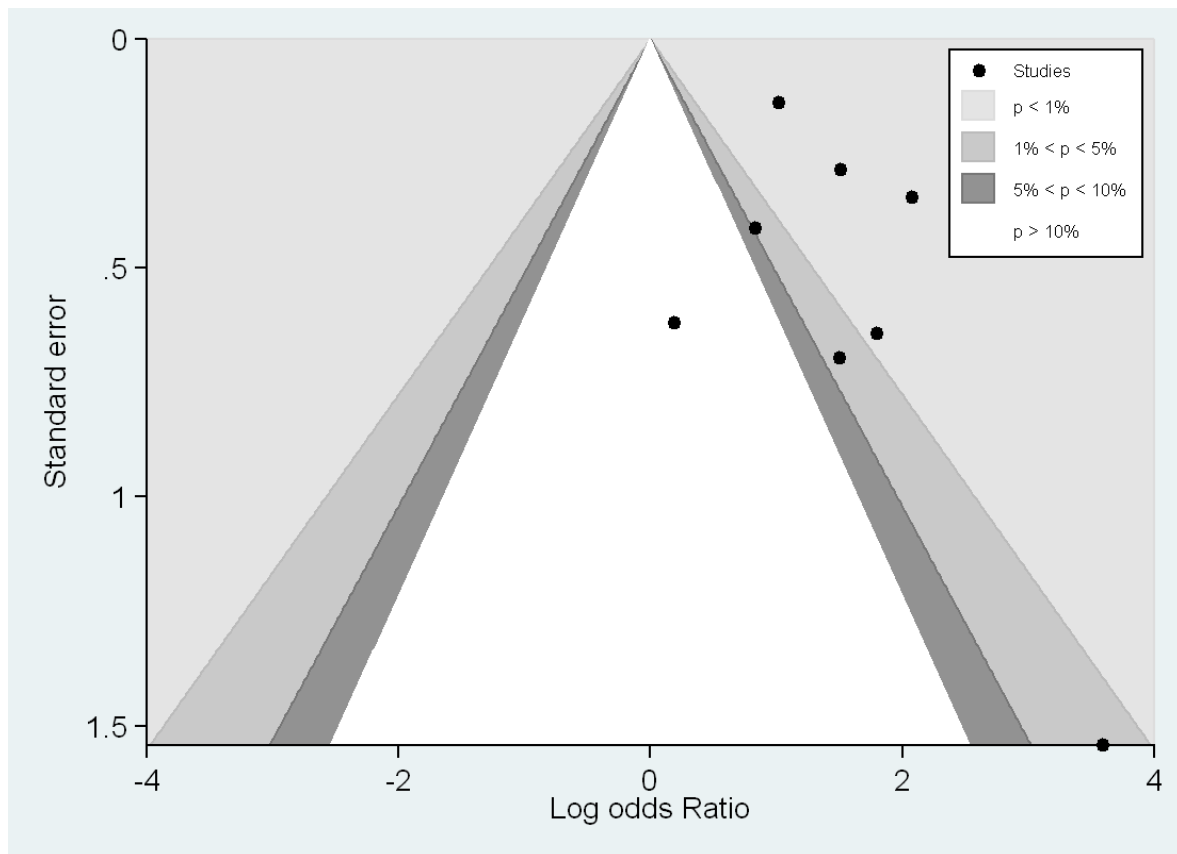
Figure H: Contour enhanced funnel plot for the lifestyle versus control direct comparison

When comparing all possible direct comparisons to the full mixed treatment comparison results (Table A), the mixed treatment comparison results generally agreed with those from the direct analysis but tended to be more conservative. All the mixed treatment comparison results except one fell within the 95% confidence intervals of the direct estimates, giving a high level of consistency. The two mixed treatment comparison models had an acceptable level of fit, with the residual deviance being roughly equal to the number of unconstrained data points in both cases.

					Mixed Treatment Comparison Results					
Control	**3.63** **1.28-11.91**	1.74 0.30-10.47	1.20 0.27-5.39	5.10 0.59-47.13	**4.64** **1.25-18.52**	2.05 0.62-7.27	**6.73** **3.05-17.95**	1.03 0.06-15.71	0.97 0.14-6.55	1.09 0.07-17.22
2.56 **1.07-6.13**	**Anti-diabetic drug**	0.48 0.08-2.78	0.33 0.05-1.89	1.39 0.13-14.46	1.27 0.22-6.78	0.56 0.11-2.70	1.84 0.59-6.23	0.28 0.01-4.98	0.27 0.03-2.26	0.30 0.01-5.32
1.14 0.48-2.72	0.39 0.17-0.87	**Anti-diabetic drug & LS**	0.69 0.07-6.25	2.94 0.19-44.45	2.67 0.30-22.73	1.18 0.14-9.81	3.85 0.70-24.03	0.59 0.02-14.85	0.55 0.04-7.10	0.63 0.02-15.63
1.50 0.99-2.29			**Anti-obesity drug**	4.24 0.56-34.29	3.86 0.54-28.11	1.70 0.26-11.90	**5.57** **1.32-28.16**	0.86 0.04-18.6	0.80 0.08-8.97	0.91 0.04-20.04
			4.71 **1.51-14.69**	**Anti-obesity drug & LS**	0.91 0.07-11.16	0.40 0.03-4.87	1.32 0.17-11.66	0.20 0.01-6.18	0.19 0.01-3.29	0.21 0.01-6.92
7.07 **3.84-13.00**					**Diet**	0.44 0.09-2.29	1.45 0.35-6.84	0.22 0.01-4.53	0.21 0.02-2.06	0.23 0.01-4.91
2.22 **1.03-4.78**					0.56 0.20-1.63	**Exercise**	3.27 0.85-14.15	0.51 0.02-9.63	0.47 0.05-4.30	0.53 0.03-10.25
4.08 **2.33-15.95**	1.72 0.13-22.76	2.02 0.89-4.57	**7.54** **2.14-26.51**	1.60 0.41-6.21	**3.80** **1.47-9.82**	**6.73** **2.43-18.62**	**Exercise & diet**	0.15 0.01-2.42	0.14 0.02-1.06	0.16 0.01-2.60
								Fenofibrate	0.93 0.13-6.88	1.06 0.14-7.66
0.96 0.57-1.64								0.95 0.50-1.80	**Statin**	1.12 0.15-8.18
								1.06 0.55-2.03	1.12 0.58-2.14	**Statin & Fenofibrate**

(Row-spanning label: "Pair-wise Meta-analysis" appears vertically along the left of the pairwise (lower-triangle) section.)

Pairwise comparisons are in bold text; Mixed treatment comparisons are in normal text

Table K: Comparison of the pair-wise and mixed treatment comparison results for the full network

Appendix 4:

Supplementary material related to the

TRIMS education program

- Pre-course leaflet

- Examples of parts of the curriculum

    o Overall plan of the curriculum

    o Session C: Metabolic Syndrome and Insulin Resistance

- Examples of parts of the handbook

    o Cover page

    o Contents page

    o Health Profile

    o Action Plan
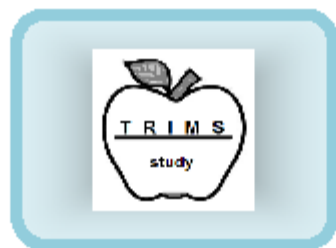
Preparing for TRIMS education sessions

This booklet aims to answer some basic questions about metabolic syndrome and gives you a better idea of what coming to a TRIMS course is all about

Preventing DIABETES & HEART DISEASE

What is TRIMS?

- A way of finding out more about metabolic syndrome.
- A way of supporting you to make healthy lifestyle changes.
- An opportunity to meet and share experiences with others

What's involved?

You are being invited to join a small group of people on a TRIMS education programme. The group will consist of 6 – 8 people who have also recently been diagnosed with metabolic syndrome and will be led by 2 experienced health professionals (nurses and/or dieticians). You can bring a partner, relative or friend with you.

The education programme will be run as 2 half-day sessions lasting around 3 hours each and held 1-2 weeks apart.

The education sessions are designed to help increase your knowledge and understanding of metabolic syndrome, to enable you to meet and talk to others in the same situation, and to support and motivate you to make healthy lifestyle changes.

Topics covered will include what metabolic syndrome is, risks and complications from having metabolic syndrome, food choices and physical activity. You will be given a booklet to accompany the education sessions and to take away with you.

2

What is metabolic syndrome?

- Metabolic syndrome is a relatively new term that describes a combination of things that together show how likely someone is to develop diabetes, heart disease, and strokes in the future.

- Metabolic syndrome is diagnosed/ identified from a series of blood tests and measurements.

- People are identified as having metabolic syndrome if they have both:
  (1) a large waist size
      31.5" (80cm) or larger for women
      37" (94cm) or larger for men (35" (90cm) if South Asian ethnicity); and
  (2) any two (or more) of the following four risk factors
      High blood pressure (or on medication for)
      High fasting blood sugar
      Low HDL cholesterol (good cholesterol)
      High triglycerides (blood fat).

- In metabolic syndrome something goes wrong with the body's metabolism (how the body functions). This is thought to be mainly due to excess weight/fat around the middle (abdominal obesity). This is why waist size is so important.

- Metabolic syndrome is something that has started to happen to the body before diabetes or heart disease has fully developed.

3

What can I do about metabolic syndrome?

You may be feeling surprised, frustrated or angry, or worried about being told you have metabolic syndrome. But the good news is that there is a lot you can do to reverse metabolic syndrome and reduce your risk of developing diabetes, heart disease and strokes in the future.

The best way you can reduce your risk is by making changes to your lifestyle. These changes include:

- Losing weight (reducing waist size)

- Being more physically active

- Making changes to what we eat and drink

- Stopping smoking

This can sometimes be hard work and you might want help.

The TRIMS programme helps you to get started with looking after your health.

4

What can I do to get ready for TRIMS?

You may feel that you have enough to think about right now and would just like to come along on the day, and that's fine. If you want to prepare for your TRIMS programme, you may want to think about the following:

What do you want to know?

What are the questions that you or your family have at the moment about metabolic syndrome? Are you unsure as to how it will affect your life?

You could write down your questions below – it's easy to forget them on the day.

Questions:

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Being active

You may be aware that physical activity plays a large part in helping you to be healthy. It might help you to think a little about how physically active you are before you start the TRIMS programme. Being physically active does not mean that you need to join a gym, it is about trying to move around as much as you can and as often as you can.

At the moment we are all recommended to do 30 minutes of moderately intensive activity at least 5 times a week. Moderately intensive activity leads to breathing harder and getting warmer than normal. It can include walking, housework, gardening etc. The 30 minutes does not have to take place all in one go. It can be done in smaller chunks e.g. 3 x 10 minutes or 2 x 15 minutes.

You might find it helpful to have a go at answering the questions below:

▪ I do some activity in my home most days (housework, gardening, washing the car etc)	√	x
▪ I try to do 30 minutes of activity most days	√	x
▪ I try to avoid driving if it is possible to walk	√	x
▪ I always use the stairs instead of the lift	√	x
▪ I am active as part of my daily routine or job	√	x

Circle either TRUE (√) or FALSE (x)

How did you do? Maybe your answers to the questions have highlighted the areas where you are doing well. They may have also helped you to think about where you could fit more activity into your life. These are things you can discuss at the TRIMS sessions.

5

6

Food choices

What you eat can also play a large part in helping you to be healthy. This does not mean that you can't eat foods that you enjoy but small changes can make a great deal of difference. We don't often think about what we eat, but spending a little time reflecting on your main food choices may help you to get the most from your TRIMS sessions.

You might find it helpful to record the most common types of meals you have in the table below. Think about the main meals that you have in a day. Often people have similar foods each day.

Breakfast:
What would you normally have for breakfast?

Midday meal:
What would you normally have for midday meal?

Evening meal:
What would you normally have for evening meal?

Supper and snacks:
What would you normally have for super and snacks?

Are there any questions you have about your food and metabolic syndrome? This may have helped you to think about changes that you could make to improve your health. These are things to discuss at the TRIMS sessions.

7

How are you feeling?

How you feel, your mood, can affect how you look after your health.

The questions on the next page will help you check how positive or depressed you are feeling. Do complete the questions if you can. It will be useful for when you attend the TRIMS sessions.

Please circle the number for each statement that best describes how often you felt or behaved this way during the past week. Don't take too long over your responses. Your first reaction to each statement will probably be more accurate than if you spend a long-time thinking about it.

8
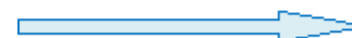
During the past week	Rarely or none of the time (less than 1 day)	Some or a little of the time (1 to 2 days)	Occasionally or a moderate time (3 to 4 days)	Most or all of the time (5 to 7 days)
I was bothered by things that don't usually bother me	0	1	2	3
I did not feel like eating: appetite = poor	0	1	2	3
I felt that I could not shake off the blues even with help from friends or family	0	1	2	3
I felt that I was just as good as other people	3	2	1	0
I had trouble keeping my mind on what I was doing	0	1	2	3
I felt depressed	0	1	2	3
I felt that everything I did was an effort	0	1	2	3
I felt hopeful about the future	3	2	1	0
I felt tearful	0	1	2	3
My sleep was restless	0	1	2	3
I was happy	3	2	1	0
I talked less than usual	0	1	2	3
I felt lonely	0	1	2	3
People were unfriendly	0	1	2	3
I enjoyed life	3	2	1	0
I had crying spells	0	1	2	3
I felt sad	0	1	2	3
I felt that people disliked me	0	1	2	3
I could not 'get going'	0	1	2	3

Your score is the total of all the numbers you have circled

TOTAL SCORE

9

What do the numbers mean? The lower your total score the more positive you will be feeling.

0 – 16
This indicates you are likely to be positive and unlikely to be depressed. However, if there are worries you wish to share and/or help you feel you need, do make an appointment to see your doctor or nurse.

17 – 24
This indicates that you are possibly depressed – that is, it is possible that you may be going through a period of depression.

If you have felt like this for several months or more this is a good indicator that you may be going through an episode of depression. However, you may be feeling like this because you have just been identified as having metabolic syndrome, or because of some other factors in your life at present. If you have only been feeling this way for a short time it may be worth looking at this again in a couple of months.

25 and above
This indicates probable depression – that is, if you are scoring in this area it is likely that you are going through an episode of depression, especially if you have felt like this for a few weeks. Even if this is caused by events going on in your life at present, or has been made worse by being told you have diabetes, it is worth discussing this with someone such as your doctor or nurse.

10

**And finally ....**

You now probably have the information you need. If you have any urgent questions you need answering before you come to the TRIMS education programme please contact your doctor or nurse or Alison Dunkley (Research Nurse) on 01162523212.

We look forward to welcoming you to TRIMS.

T R I M S
study

TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

Preventing

DIABETES & HEART DISEASE

11

TRIMS Curriculum
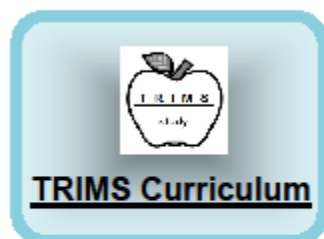
OVERALL PLAN OF SESSIONS

PART 1

- **Session A: Introduction and Housekeeping**
Duration: 5 minutes
1) Room preparation:
2) On arrival:
3) Introduction:

- **Session B: The Patient Story**
Duration: 20 minutes
1) Names
2) How did you find out you had it?
3) What do you think it is? Causes.
4) What will it mean for my health? Treatments.
5) Have you got a question?

- **Session C: Metabolic Syndrome and Insulin Resistance**
Duration: 55 minutes + 40 minutes
C.1) UNDERSTANDING METABOLIC SYNDROME – 55 minutes
  i) Defining metabolic syndrome
  ii) Healthy "metabolism" – energy from food
  iii) Healthy "metabolism" – carbohydrates and fats
  iv) Abdominal obesity and what goes wrong with glucose and fats in metabolic syndrome
  v) Cholesterol
  vi) Blood Pressure
  vii) Clarification / checking understanding
  -------------------- 15 minute break --------------------
C.2) HOW DOES METABOLIC SYNDROME AFFECT ME? – 40 minutes
  i) What measurement / level is metabolic syndrome
  ii) Understanding your personal results
  iii) What causes metabolic syndrome
  iv) Reversing metabolic syndrome and reducing the risk of developing type 2 diabetes and cardiovascular disease (heart attack/stroke)
  v) Summary

- **Session D: Physical Activity**
Duration: 40 minutes
  i) Benefits of physical activity
  ii) Recommendations - amount, frequency and intensity
  iii) Measuring activity
  iv) Barriers to physical activity and facilitators
  v) Summary

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- **Session E: How Am I Doing?**
Duration: 5 minutes
i) Review of main messages so far
ii) Starting to think about possible changes

PART 2

- **Session F: Reflections**
Duration: 10 minutes
i) Welcome back
ii) Content of the Following Sessions

- **Session G: Weight management and Food Choices (1)**
Duration: 30 minutes
i) Introduction
ii) Factors influencing food choices
iii) Monitoring weight/ shape
iv) Energy balance
v) Calorie deficit
vi) Losing weight (reducing waist size) – practical suggestions and benefits
vii) Summary and specific food messages

- **Session H: Food Choices (2) – Fat, Omega-3, Fibre and Salt**
  - **Making healthier choices**

Duration: 55 minutes + 20 minutes
i) Introduction
ii) Types of fat
iii) Omega-3   – 55 minutes
iv) Fibre
v) Salt
—————— 15 minute break ——————
vi) Making healthier choices – 20 minutes
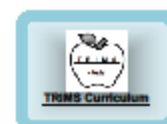
- **Session I: Metabolic Syndrome Self-Management Plan**
Duration: 40 minutes
i) Introduction
ii) Behaviour change section
iii) Identifying risk factors to change
iv) Completing an action plan

- **Session J: Questions and Future Care**
Duration: 10 minutes
i) Review of questions
ii) Closing and thanks

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Session C: Metabolic Syndrome and Insulin Resistance

Duration: 55 minute session (C.1) and 40 minute session (C.2)
(with 15 minute break in the middle)

Resources required	Flip charts generated

• Flip chart and pens
• Blue/ white tac
• Food groups GAME
   ○ 3 coloured pieces card
   ○ Selection of foods
   ○ Labels – carbohydrates, fats, proteins
• Energy used and energy stored, board and parts to demonstrate 'healthy blood glucose control and blood fats', and 'what goes wrong in metabolic syndrome.
• My Health Profile (found in handbook)
• A1 Health Profile
• Causes GAME
	• 'What is metabolic syndrome'
	• ''Food Groups'
	• 'Reversing metabolic syndrome'

Participant learning opportunities
Participants will:
- Be clear that a diagnosis of metabolic syndrome is made according to the results of a cluster of unhealthy body measurements and abnormal laboratory test results (large waist size plus any 3 out of: high blood pressure*; raised triglycerides*; low HDL*; or raised fasting blood glucose). *N.B. *or specific treatment for.*
- Understand the importance of waist size / abdominal obesity
- Describe how excess energy is stored as fat
- Understand what types of food (food groups) are normally used for energy
- Understand where glucose comes from
- Understand how glucose is normally used by the body for energy and how any excess is stored as glycogen and fat
- Understand how fat from food is normally used and stored by the body
- Know that the term triglyceride refers to blood fat
- Understand how stored energy is released and used by the body when we haven't eaten for a while
- Understand how insulin allows the use of glucose for energy and promotes the storage of fat, and how a fall in insulin levels encourages the release of stored energy
- Work out what goes wrong in the body in metabolic syndrome to make the levels of blood glucose and triglycerides rise to unhealthy levels, and understand the role of abdominal obesity/ excess stored fat
- Know how Type 2 diabetes is caused
- Know what cholesterol is normally used for in the body and the two main types (HDL and LDL)
- Understand what happens to blood vessels in metabolic syndrome (atherosclerosis).
- Understand the importance of blood pressure
- Understand the link between atherosclerosis and cardiovascular disease (heart attacks and strokes)
- Describe what are metabolic syndrome levels for: waist size, blood pressure, blood glucose levels, HDL (good) cholesterol and triglycerides

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- Know what their personal results are for metabolic syndrome
- Work out the causes of metabolic syndrome
- Know what factors contributed to causing their metabolic syndrome
- Know the risk of developing Type 2 Diabetes and cardiovascular disease
- Understand how to reverse metabolic syndrome (and all the components) and reduce the risk of developing type 2 diabetes and cardiovascular disease

Content covered
- How Metabolic syndrome is identified/ diagnosed
- Importance of waist size / abdominal obesity
- How excess energy is stored as fat
- What the main food groups are and what foods are normally used for energy
- What is glucose
- How glucose is normally used by the body for energy and how any excess is stored as glycogen and fat
- How fat from food is normally used and stored by the body
- That the term triglyceride refers to blood fat
- How stored energy is released and used by the body when we haven't eaten for a while
- How insulin allows the use of glucose for energy and promotes the storage of fat, and how a fall in insulin levels encourages the release of stored energy
- What goes wrong in the body in metabolic syndrome to make the levels of blood glucose and triglycerides rise to unhealthy levels, and understand the role of abdominal obesity/ excess stored fat
- How Type 2 diabetes is caused
- What cholesterol is normally used for in the body and the two main types (HDL and LDL)
- What happens to blood vessels in metabolic syndrome (atherosclerosis).
- The importance of blood pressure
- The link between atherosclerosis and cardiovascular disease (heart attacks and strokes)
- What are metabolic syndrome levels for: waist size, blood pressure, blood glucose levels, HDL (good) cholesterol and triglycerides
- What person's personal results are for metabolic syndrome
- What are the causes of metabolic syndrome
- The risk of progression of metabolic syndrome to Type 2 Diabetes and cardiovascular disease
- How to reverse metabolic syndrome and reduce the risk of developing type 2 diabetes and cardiovascular disease
- How to reduce waist size, blood pressure, blood glucose and triglycerides, and raise HDL-cholesterol

Educator activity
- Asks open questions to enable participants to explore the cause and effects of metabolic syndrome
- Asks open questions to elicit information from participants so as to develop a picture of what happens in the body with metabolic syndrome
- Uses visual tools to assist participants to understand what happens in the body
- Uses open questions to assist participants to explore misconceptions and gaps in knowledge
- Ensures that all participants are able to contribute in a way in which they feel comfortable by acknowledging all contributions and thanking them for their contributions
- Enables participants to work out how metabolic syndrome may change over time and the consequences this may have
- Enables participants in knowing ways in which metabolic syndrome can be monitored
- Enables participants in working out how they can reduce their risk of developing Type 2 diabetes and cardiovascular disease
- Uses open questions to check understanding
- Uses participants' words/phrases and analogies when working through the session content
- Refers participants to comments on the flip charts at appropriate points

- Uses the appropriate resources/activities

Participant activity
- Explores how metabolic syndrome is identified / diagnosed
- Work out why and where fat is stored
- Explores the role of abdominal obesity in metabolic syndrome
- Explores what types of food are used for energy
- Explores where the glucose in the blood stream comes from
- Explores how glucose is normally used by the body for energy and how/where any excess is stored
- Explores how fat from food is normally used and stored by the body
- Explores how stored energy is released and used by the body when we haven't eaten for a while
- Explores the role of insulin
- Work out what goes wrong in the body in metabolic syndrome to make the levels of blood glucose and triglycerides rise to unhealthy levels, and understand the role of abdominal obesity/ excess stored fat
- Explores the concept of insulin resistance (glucose and fats)
- Works out why pancreatic beta cell failure may occur and how this contributes to the progressive nature of diabetes
- Explore what cholesterol is normally used for in the body and the two main types (HDL and LDL)
- Understand what happens to blood vessels in metabolic syndrome (atherosclerosis).
- Explore what blood pressure is
- Explore the link between atherosclerosis and cardiovascular disease (heart attacks and strokes)
- Considers their personal results and how they were identified as having metabolic syndrome
- Works out what may have caused their metabolic syndrome and how this knowledge may help them to manage their future risk of diabetes and cardiovascular disease
- Explores how metabolic syndrome may change over time and the consequences this may have.
- Works out that metabolic syndrome can be reversed and the risk of developing type 2 diabetes and cardiovascular disease can be reduced through food choices, physical activity, stopping smoking, losing weight (reducing waist size) and medication
- Works out how waist size, blood pressure, blood glucose and triglycerides can be reduced, and HDL-cholesterol raised.

Session Plan

This section describes one way to get through all the information. This is an example of the content and the process. If you find it more comfortable to build up the story in a different way, that is acceptable, as long as the process of 'building up' is carried out through the same sort of story format used in the modelling you experienced during your initial training, and does not become didactic

The main thing is to get all the information across by assisting the group to work it out as much as they can by themselves, with occasional prompting by you and provision of new knowledge only as necessary to keep the story moving

During this session tell the group as little as you possibly can. Give them plenty of opportunity to attempt to work things out themselves.

As a guide, for every piece of information you give them, you should ask them at least one question.

C.1) UNDERSTANDING METABOLIC SYNDROME – 55 mins

In your own words explain that the group is going to try and make sense of most of the information they have just shared to try and understand what metabolic syndrome is and how they can actively self-manage their metabolic syndrome. Explain to the group that they are going to start by thinking about how our body normally uses energy from food, and then work out what is going on with glucose and insulin and fat in someone who does not have metabolic syndrome by working through a picture they are going to help you to build up.

i) Defining metabolic syndrome

Aim to build up a FLIP CHART. Explain to the group that you will complete the chart bit by bit as go through the whole of this session

So, what is metabolic syndrome?
Prompt if no answers are forthcoming; reflect back to the "What do you think it is?" FLIP CHART from the patient story.

Metabolic syndrome	
ALL	Any 2
Waist size	BP
	HDL
	Triglycerides
	FPG

Metabolic syndrome is a collection of medical problems or risk factors.

What problems did you mention earlier? What problems have you all got in common?
Hopefully someone will mention waist size / shape, if not you will have to introduce. "Has anybody heard about different body shapes, apples and pears?"

How does having weight around you middle affect your health?

In metabolic syndrome something goes wrong in the way the body functions. This is thought to be mainly due to excess weight/fat around the middle (central obesity). This is why waist size is so important.
This makes the levels of fat in the blood (cholesterol), glucose and blood pressure all rise too high for good health. Metabolic syndrome is something that has started to happen to the body before diabetes or heart disease has fully developed.

Don't worry if participants don't mention all the components at the start. You can complete the flip chart as you go through this section but ensure that participants understand that a large waist size/weight around the middle is metabolic syndrome.

As a reminder:
What is metabolic syndrome
- Large waist size (all, plus any 2 out of))
- High blood pressure   Raised triglycerides   Low HDL cholesterol   Raised fasting glucose

ii) Healthy "metabolism" – energy from food

Before we consider in more detail what goes wrong in metabolic syndrome and what it means to you individually. Going to look first at "healthy metabolism" and how our body normally maintains a healthy weight / shape and then we can work out what is happening in somebody who has got metabolic syndrome.

Food groups - game
Preparation:
Place 3 large sheets (A3) of coloured paper/card on a table.
Select one piece of food from each of the 3 food groups (carbohydrates, fats, proteins) and place each type in the centre of a different colour.
Do NOT place food group labels at this stage.

Either place the rest of the food on the table or hand out to the group.

Explain:
This activity is aimed at trying to get you to think about the main types of food or food groups that our body needs to be healthy.

First of all, I'd like you to look at a selection of foods and decide which foods are similar. Which types of foods go together? We've put a few foods down to give you a clue.

Facilitate a discussion if needed until all the foods are placed correctly.

When all the foods are placed correctly ask the group to identify which food group is which by placing the labels.
Prompt (if needed): What type of food is ......
"What type of food are bread/potatoes; what is butter; what is meat/ milk?"
"What foods are carbohydrates - starchy, sugary foods ; what are proteins; what are fats?"

CARBOHYDRATES	PROTEINS	FATS
Potatoes	meat	butter
Wholemeal bread	fish	oil
Rice	chicken	margarine
Pasta	meat substitute	double cream
Sugar	eggs	
Naan bread		
Coke		
Jelly beans		

<u>Next introduce some composite foods.</u> *Ask the group where they belong. Facilitate a discussion and try to get the group to say that they belong to more than one group*

Nuts – mainly fat/protein (small carbs),　　　　　　Fruit mostly carbohydrate
Baked beans – carbohydrate/protein,　　　　　　　Cake – mainly carbohydrate/fat,
Lentils - carbohydrate/protein,
Hard cheese - approx half protein half fat,　　　　Cottage cheese – mainly protein
Skimmed milk – equal protein/carbohydrate
Semi-skimmed milk - protein/ carbohydrate (small amount of fat)
Full fat milk – equal fat/protein/carbohydrate

Which food group does our body normally use for energy (fuel)?

Which food group does our body mainly use for growth and repair?

Carbohydrates are used as the first choice for energy (fuel), quick source.
Fat can be used as energy but it is converted very slowly.
Protein's main role is healthy growth and repair of body tissue / cells,

When focusing on metabolic syndrome we are particularly interested in fats and carbohydrates. The way the body uses carbohydrates and fat (the metabolism) are closely linked.

iii) Healthy metabolism – carbohydrates and fats

Going to focus first on how the body **normally** uses carbohydrates and fats. When someone doesn't have metabolic syndrome.

Explain what each piece/ picture represents before you place it on the board

Let's start off thinking about what usually happens to the food that we eat.
Put up the normal label

Normal

So, when you eat some food where does it go?
START to build up a picture

That's right. It goes into the stomach and then the intestines. It gets broken down (digested) into smaller parts so that it can be absorbed.
Place pictures of mouth & intestines, and food on the board.

What do you think happens to the food once it is broken up and digested?

Yes, you are right; it gets taken into the blood stream so it can get to where it's needed in the body.
Place picture of blood vessel on the board

Blood vessel

So, what happens to carbohydrates (starchy/sugary foods) when we eat them? What do they get broken down into?

Glucose, it is a type of sugar. The form of sugar found in the blood.
Place pictures of sugar cubes into the blood vessel   *SUGAR CUBES*

What does glucose do, what is it used for in our bodies?

For energy

Yes, that's right. Glucose acts as a fuel or energy for cells. Cells are the tiny components that make up all the parts of our body, such as our heart, brain and muscles.
If necessary prompt the group by recapping back to the food game that carbohydrates are the body's first choice for energy (although some glucose can come from the breakdown of fats and protein)
Continue picture. Put up the label 'For energy' and picture of cell and red arrow (from blood vessel to muscle.

What might affect how much glucose the body uses for energy?

Sleeping, resting, activity.

What does the body do with the rest of the glucose not required for energy?

To store

Stores it for use at a another time. *Continue picture. Put up label 'To store'.*

Where does the body store excess energy from glucose?

A small amount goes to the liver to be stored (as glycogen) for when we are not eating. But after that any glucose left is converted and stored as fat.
The body banks the excess glucose to use when we're not eating.
Continue picture. Put up pictures of liver and fat cells & put red arrow going to liver and fat cells.

Now thinking of fat that we eat in food.

What does fat do? What are fats used for in our bodies?

Some fats are necessary for us to stay healthy – skin, hair, cell functioning, and we do need some fat in our diet to give us energy.
If necessary prompt the group by recapping back to the food game that carbohydrates are the body's first choice for energy but fat can also be used for energy.

So, what happens to fats when we eat them?

They are broken down in the body to smaller bits called triglycerides *(may have to introduce this term)*. Triglycerides is a special name for fat in the blood.
The group may mention cholesterol – explain that although triglycerides are linked to cholesterol they are different but that cholesterol will be covered later in the session.

Continue picture. Picture of blood vessel, put in fat globules
If the body has enough glucose (not needed immediately for energy) they are taken to the fat cells (adipose tissue) to be stored.

Where do the triglycerides (fat) go next in the body?

If the body does not need any more energy as it has enough glucose, the triglycerides are taken to the fat cells in the adipose tissue to be stored.

<u>Recap to diagram</u>
So when we've eaten. Some glucose (carbohydrate) is used for energy, small amount of glucose goes to liver to be stored, and any extra energy whether originally from fat or carbohydrate is stored as fat.

Completed picture for glucose and fat
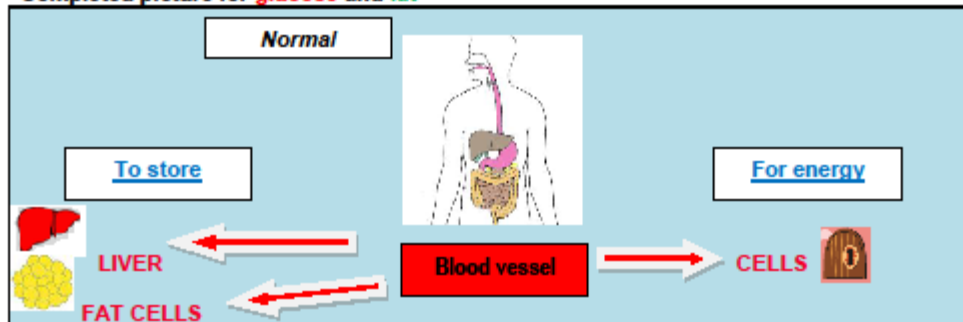
This sounds like a complicated process. Does anyone know how this process might be controlled? How do you think the glucose and triglycerides get into the cells?

Prompt: it's controlled by a very important hormone, a substance that the body normally secretes when we've eaten.
There are various factors that influence it but the main one is INSULIN.

Now, if we think of cells as having a door to let things in or let things out but normally the doors are locked. *On the board, indicate the door on the picture of the cell.*

So what would you normally need to unlock a door, (say your front door)?
Prompt the group until they come up with a key.

Ask the group "In our bodies what might be the key to open the cell door?"
(They can usually work out it's insulin).

Where does insulin come from?

The pancreas. *Place picture of pancreas on the board above blood vessel, and put some keys inside*

How does the pancreas know to produce insulin?

It produces insulin when we eat food and the level of blood glucose goes up.
Move keys into blood vessel and swap picture of cell with closed door to one with key in and put picture of door with key next to liver and fat.
Then glucose and fat can be used for energy or stored.

How does the pancreas know when to stop producing insulin?

As the level of blood glucose goes down insulin stops being produced

So that's what happens normally when we've eaten.
But the body needs a constant supply of energy in order to stay alive.
So what might happen between meals when we haven't eaten for a while or overnight?

Stored energy is released from the liver.
If you were to go longer still without eating stored energy would be released from fat cells.

Liver releases stored glucose into the blood (limited amount) - initially
Fat is released into the blood from fat cells and goes to the liver and muscles for energy (amount released depends on amount of stored fat in the body) – after a longer time

Recap:
So our body is continually renewing and releasing these energy stores
Insulin (keys):
1) allows the body to use glucose (for energy)
2) encourages the body to store extra glucose and fat

iv) Abdominal obesity and what goes wrong with glucose and fats (triglycerides) in metabolic syndrome?

OK so that is what is happening when someone does NOT have metabolic syndrome. Now want to work out what might go wrong in someone who has metabolic syndrome.

So, what happens if you often eat more than your body needs or stop doing as much activity or exercise as you used to?

You'd put on weight, weight goes up

How is the extra weight normally stored?

As fat

Where exactly does the body store this fat?

Stored in fat cells both under the skin (subcutaneously) and deeper in the abdomen around the internal organs (heart, liver, etc). Some also stored in muscles.
Think of fat cells like a balloon/ plastic bag. When the body stores fat it doesn't make more fat cells but existing fat cells just get fuller – almost unlimited capacity.

How does this stored fat affect your health?

We used to think that fat was just an energy store. It is now thought that fat stored around your middle secretes substances which interfere with how the body functions. Fat stored around the middle can lead to high blood pressure, high blood sugar (glucose), and unhealthy blood fat or cholesterol.

It is the excess fat particularly in the abdomen / around the middle that causes problems in metabolic syndrome. This is why waist size is so important.

Looking back at this picture/diagram, can you work out where things might go wrong in someone who has metabolic syndrome?

If people come up with suggestions that are not quite correct see if you can guide them to the correct answers

Because of this excess fat stored around the middle (abdominal obesity) the body isn't able to use or store energy as normal.

Two things can happen: *point to magnetic board*
- The fat around the middle secretes substances that can start to interfere with the way insulin (keys) work.
  - Think of this as the locks becoming rusty.
- As the amount of fat stored in the body increases (especially around the middle) it becomes less effective at storing both existing and new fat.

So if they keys are not working, what do you think might happen to the amount of fat and glucose in the blood?

The amount of triglycerides and glucose in the blood will increase

So what do you think might happen to the locks if there are a lot of fatty triglycerides in the blood?

The fat blocks the locks.

In metabolic syndrome insulin (keys) can't work properly.
We say that people have become insulin resistant
- One way of thinking of this is that insulin (keys) are unable to unlock or lock the cell doors as the locks are not working very well; they have either become rusty or become blocked with fat, or both

If there are a lot of fatty triglycerides in the body, what will the body try to do with it?

It will try and store the triglycerides

What happens to fat (triglycerides) if it can't be stored properly?

The body will try to store the triglycerides in many places where it would not usually be stored. It begins to store inside the internal organs (heart, liver, pancreas).

> *Important that they understand that something goes wrong with the way the body both uses and stores, glucose and fat.*
>
> *INSULIN RESISTANCE is a very important key message.*
> *May be useful to put up the labels Metabolic Syndrome and Insulin Resistance.*

Do you think that insulin resistance, rusty or blocked locks, will affect everybody in the same way?

Everybody is different so the level of glucose and fat in the blood will vary between individuals.

What else may make a difference?

The amount of saturated fat someone eats and how active a person is can affect how rusty the locks become

Don't worry if the group do not come up with this. Explain that we will be talking more about physical activity and food choices during the rest of today and next time.

So what might your body do if insulin (keys) aren't working properly?
Keep prompting them until someone suggests that you make more insulin.

Yes, as the key (insulin) you are making is not working well at opening the locks, the pancreas tries to overcome this by making more keys (insulin). So the level of insulin in the blood stays very high.

But if we think of the pancreas as being like an insulin-producing factory, what do you think happens to workers in a factory if they have to work overtime all day every day?

Yes, everyone would start to get tired, would not be working very well and production would start to fade. This is one of the things we think happens when people develop type 2 diabetes. Because your pancreas (factory) is working extra hard to produce more insulin, it starts getting tired and not producing enough insulin for your body's needs.

Recap:

- People who have metabolic syndrome have too much fat around their middle

- This fat around the middle can make the insulin keys work less well and can also block the cell doors. This is called insulin resistance.

- Insulin resistance affects the way the body both uses and stores both glucose and triglycerides

- These problems can cause the blood glucose levels and blood triglycerides to rise above normal, and fat starts to be stored in and around the internal organs (especially the liver).

Too much information may confuse participants. Some extra information is given below for educators. Only use as part of the explanation if it is appropriate and if it is likely to help with the groups understanding.

Glucose levels can increase.
- **Muscle cells IR less glucose able to enter muscles to be used or stored.**
- **Liver IR continues to release stored glucose even when fed after a meal.**
Triglyceride levels can increase.
- **Increased amount of fat released between meals due to large fat stores (obesity) and impaired reabsorption.**
- **Later fat less able to be stored especially in the subcutaneous fat (fat under the skin).**

---

v) Cholesterol)

Have you heard of any other type of fat that is carried in the body?

Some one may have mentioned this earlier?

Cholesterol..

Why do we have cholesterol?

We all need some cholesterol. It is very important to make our cell walls. Unlike triglycerides, cholesterol cannot be used for energy.

Draw picture of a blood vessel clogging up

What have you heard about different types of cholesterol?
Explore and explain (if needed) about the two types of cholesterol which makes up total cholesterol:
LDL (Low Density Lipoprotein) or 'bad ' cholesterol – like a ferry takes cholesterol from the liver to where it's needed in the body.
HDL (High Density Lipoprotein) or 'good' cholesterol – like a hoover, sucks up all the excess cholesterol.

Where does cholesterol come from?

Cholesterol (lipids) most are made by our body in the liver (75-80%)
If anyone mentions food, explain that although a small amount of cholesterol comes from the food that we eat (animal products) it is thought that the cholesterol we eat does not make a big difference to the level of cholesterol in our body.
Cholesterol can be made from any food. However, eating saturated fats can cause the body to produce more LDL (bad cholesterol) than is healthy.

So what happens to the blood vessels (arteries) in someone who has a lot of bad cholesterol?

Draw bits on inside of picture of pipe
Yes that's correct, they fur up.
This causes them to narrow – atherosclerosis

So what might happen as a result of this?

Clogged arteries can eventually lead to heart attacks and strokes

Why are we particularly mentioning this in metabolic syndrome?

Due to unhealthy levels of cholesterol and triglycerides the blood vessels/ arteries are more likely to fur up.

Also substances secreted by abdominal fat cause inflammation in the blood vessels and make them more likely to fur up

How do we know if our cholesterol or triglycerides are too high or low? Does it give any symptoms?

You can usually only know your levels by means of a blood test. Unhealthy cholesterol or triglycerides levels do not usually give us symptoms.
Explain will do more about cholesterol / triglycerides and reducing risk later.

vi) Blood Pressure

Recap on flipchart components of metabolic syndrome mentioned so far (glucose, triglycerides, HDL cholesterol, waist size. Say still one thing left to mention. If it hasn't already been written on flip-chart will need to add BLOOD PRESURE in the appropriate place.

Let's talk about blood pressure; does anyone know what blood pressure is and what it does?
Prompt people's understanding by helping them reflect on what they are feeling when they feel their pulse. (mention 2 figures systolic & diastolic)

Your blood pressure is the pressure on the walls of your arteries. As people get older and as arteries fur up, they become stiffer, and this pressure increases. Higher pressure means more stress on the artery wall, which can lead to damage. *Recap to cholesterol*

Why is blood pressure so important?

As blood pressure increases, so does the risk of heart attacks, strokes, and premature death. Lowering blood pressure reduces these risks.

How do we know if our blood pressure is high? Does it give any symptoms?

High blood pressure only rarely gives rise to symptoms. The only accurate way to tell your blood pressure is to measure it.

vii) Clarification / checking understanding

How has this helped you understand what has gone wrong in metabolic syndrome?
Listen carefully to check understanding. Answer questions or clarify any points of confusion. At this point check that all the components of MetS have been entered onto flip chart.
Metabolic syndrome is something that has started to happen to the body before diabetes or heart disease has fully developed.

---------- If people need a break could split at this point (15 MINUTES) ----------
Explain to people that after a short break they are going to look at their individual results for all the components of metabolic syndrome.

C.2) How Does Metabolic Syndrome Affect Me? – 40 mins

Now going to look in more detail at what your individual results for metabolic syndrome are and what values mean metabolic syndrome.

i) What measurement / level is metabolic syndrome?

Recap back to flipchart and show the A1 **My Health Profile** *and personal* **'My Health Profile'**

Metabolic syndrome	
ALL	**Any 2 of**
Waist size	**BP**
	HDL
	Tri
	FPG

So, we've said that metabolic syndrome is a collection of medical problems. But how high or low do your measurements or blood results need to be, for metabolic syndrome?

Aim to discuss what the Health Profile means & how it can be used.

Explain the Health Profile
- the green area indicates healthy values
- the values in the orange zone indicate metabolic syndrome
- the red area indicates values that are more unhealthy still and reaching the level for diabetes or seriously increasing your risk of heart disease & strokes

Ensure point out
- what value is metabolic syndrome for each of the components
- what types of fat or cholesterol are unhealthy in metabolic syndrome
- different values for men and women (waist size & HDL).
- different values for South Asians (waist size)

If people mention 2 hour glucose acknowledge that although important it is not how metabolic syndrome is diagnosed. Talk briefly about the OGTT if appropriate.

The other things on the profile that aren't metabolic syndrome – smoking, activity, depression – will be discussed in other parts of the curriculum.

ii) Understanding your personal results

Now want you to look at your own results for metabolic syndrome and mark them on your health profile.

Give out results for waist size, blood pressure, fasting blood glucose, triglycerides, HDL.

Discuss and get them to mark results on their profile.

Acknowledge that if they are on medication for blood pressure this component would be classed as metabolic syndrome

Acknowledge that if they are on medication for cholesterol HDL & triglycerides would be classed as metabolic syndrome

After plotted all

All of you should have a waist measurement that is metabolic syndrome but the values you have for other things will vary.

How many unhealthy measurements do you need to have metabolic syndrome?

A diagnosis of metabolic syndrome is made when you have a large waist size plus 2 (or more) out of 4 other unhealthy measurements. You do not have to have all three blood tests (fasting glucose, HDL-cholesterol, triglycerides) in the metabolic syndrome range to be diagnosed with metabolic syndrome.

Example: If you have high blood pressure (or are on treatment for) you would be diagnosed even if only one of the other tests were in the metabolic syndrome range.

Elicit responses and acknowledge that in addition to a large waist size some participant's may have 3 or 4 results in the metabolic syndrome range and some may only have 2 results in the metabolic syndrome range.

Do you think it makes any difference whether you have 3, 4 or 5 measurements that are metabolic syndrome?

The more results you have in the metabolic syndrome range the more at risk (the higher the chance) of developing problems with your health in the future.

Could use the analogy of a small rowing boat or dinghy:
"Could think of it, like if you had a small rowing boat. If 2 people are in the boat it would float fine, but the more people that get in the boat in the greater the chance / the more likely it is to sink".

iii) What Causes Metabolic syndrome?

 So, now we have considered what metabolic syndrome is.

Before we consider what this means to your health and what you can do to help we are going to look at the possible causes of metabolic syndrome.

Does anyone know what might cause metabolic syndrome in the first place?

The group has already given you their ideas in the 'Patient Story' so refer back to these.

 Use the causes resource: What causes metabolic syndrome?

If people suggest the correct answer put up the appropriate picture and discuss. Could use the pictures as prompts if needed.

Discuss the relative role of each of the suggestions below.

1. **Obesity (especially weight around the middle/ apple shaped)**
2. *Genetics (predisposition to insulin resistance) – Family History/ethnicity*
3. *Diet high in saturated fat (and trans fats)*
4. *Diet high in refined carbohydrates (low wholegrains, low fruit & veg, low fibre)*
5. *Being less active*
6. *Getting older / ageing*
7. *Certain medication (anti-psychotic medication / antiretroviral therapy in HIV)*

If anybody mentions is sugar a direct cause.
Discuss how sugar may influence weight/ shape and insulin production but it is not a direct cause of metabolic syndrome. However, a diet high in refined carbohydrates (low fibre) is associated with metabolic syndrome (refer back to causes).

iv) Reversing metabolic syndrome and reducing the risk of developing type 2 diabetes and cardiovascular disease (heart attack/stroke)

 What do you think the benefit might be of you knowing that you have got metabolic syndrome?

Elicit answers and acknowledge response.
Answers may include:
I can then do something about it
I can reduce the risk of further damage
I can get treatment

If you did nothing about your metabolic syndrome, what do you think the chance is of you developing diabetes or having a heart attack or a stroke?

People with metabolic syndrome have a cluster of risk factors (large waist size, high blood pressure, high triglycerides, low HDL (good) cholesterol, high blood glucose).

Recent evidence suggests that people with metabolic syndrome are at increased risk of developing both Type 2 diabetes and heart disease and strokes (cardiovascular disease).

If you have metabolic syndrome you are twice as likely to develop heart disease, have a stroke or die from cardiovascular disease than people who do not have metabolic syndrome.

Also you are 3 times as likely to develop Type 2 diabetes.

Do you think that there is anything that you can do to reverse metabolic syndrome and prevent yourself from developing type 2 diabetes or having a heart attack or a stroke or is it inevitable?

Good news is that by making changes you can reverse metabolic syndrome and if you reverse metabolic syndrome you will reduce your risk (your chances) of going onto develop diabetes and heart disease in the future.

Flip chart 'Reversing metabolic syndrome'

Aim to have 2 flip charts side by side with 6 rows and 5 columns.
Write in the heading reversing metabolic syndrome in the first column and the components of metabolic syndrome as headings in the other columns.

Has anyone got any ideas what you might do to reverse metabolic syndrome and delay or reduce your chances of developing diabetes or having a heart attack or stroke?
Prompt for as many answers as you can get initially without comment or discussion and aim to complete the first column (Reversing metabolic syndrome)

You may need to reflect back to the patient story, game of 'causes' and the Energy used and energy stored, board.

Reversing metabolic syndrome	Reducing waist size	Reducing blood glucose	Reducing Blood pressure	Blood fats: reducing triglycerides & raising good cholesterol	
Losing weight (waist)	√	√	√	√	
Being more physically active	√	√	√	√	
Making changes to what eat and drink	√	√	√	√	
Stopping smoking	////	////	√	√	
Medication	////	////	√	√	

People may mention specific ways of making those changes acknowledge all suggestions and if feel appropriate write in space to right, but don't need to generate detail as will cover in more detail in next few sessions.

Once completed discuss how the changes you can make to reverse metabolic syndrome relate to each of the components (waist size, blood glucose, blood pressure, triglycerides & HDL-cholesterol) and put ticks in the appropriate places.
Here are some prompt questions

How does being active help to reverse metabolic syndrome (and prevent type 2 diabetes and CVD)?

That's right being more active helps to reduce insulin resistance and oil those rusty locks to allow the glucose and fat to get into the cells.
Uses up energy. So no Xs to be stored as fat.

How does losing weight and reducing your waist size help to reverse metabolic syndrome (and prevent type 2 diabetes and CVD)?

That's right, losing weight helps to reduce insulin resistance and oil those rusty locks to allow glucose and fats to get into the cells

Do you think that it is possible to change all these things at once?
Elicit answers and acknowledge that to change everything at once is not achievable for most people

It is hard to change all these things at once but there is evidence that the more of these things you manage to change, over time, the more you reduce your risk of developing type 2 diabetes and CVD.

If you make changes metabolic syndrome is something that can be reversed. If you reverse metabolic syndrome you will reduce your risk of going on to have type 2 diabetes, and heart disease and strokes in the future.

v) Summary

Try to elicit from the group the main messages of the session so far by asking the question:

What have you gained from the last 2 sessions that has helped you understand metabolic syndrome more?

You may find it helpful to list the key messages and clarify any confusing messages. This approach will help you identify possible gaps.

This has been a lot to run through. Well done

Getting to grips with METABOLIC SYNDROME

Your Personal Handbook

Preventing DIABETES & HEART DISEASE

How to use this handbook

This handbook is for people who have recently found out that they have something called metabolic syndrome, and are taking part in the TRIMS study.

You will be using some of the information in the booklet during your TRIMS education sessions. We also hope that you will find the information useful in the future to help you look after your health.

Contents

Understanding metabolic syndrome

- What is metabolic syndrome?
- What can I do about metabolic syndrome?
- Understanding your results

Taking control

- Food choices
- Physical activity
- Other things you can do

Making lifestyle changes

Resources for you

- Health profile
- Action plan

PERSONAL HEALTH PROFILE
METABOLIC SYNDROME   Name _____   Date of Birth _____   TRIMS study

Waist Size/Shape

Waist - Male	93cm (36.5") or less	94cm (37")*		102cm (40") or more
Waist - Female	79cm (31") or less	80cm (31.5")		88cm (35") or more

Blood Pressure

BP Systolic	120	130**	140	160 or more
BP Diastolic	80	85**	90	100 or more

Blood Fats

Triglycerides	1.6 or less	1.7**	2.2	5.6 or more
HDL - Male	1.5 or more	1.0** or less		
HDL - Female	1.5 or more	1.3** or less	1.2	1.0 or less

Blood Glucose

Fasting Level	5.5 or less	5.6	6.1 to 6.9	7.0 or more

Smoking

Smoking	NON	PASSIVE	SMOKER

Physical Activity

Physical Activity	More than 10,500	7,500	Less than 5,000

Depression

Depression	0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40+

* South Asian Male 90cm or more; ** or on medication for.

What am I going to do now?

Date
_____

Name
_____

Which risk factor do I want to focus on?

WAIST SIZE / SHAPE

HIGH BLOOD PRESSURE

HIGH TRIGLYCERIDES

LOW HDL CHOLESTEROL

HIGH BLOOD GLUCOSE

SMOKING

PHYSICAL ACTIVITY

DEPRESSION

What would affect this?

- ....
- ....
- ....

Which of these am I going to tackle?
You may chose one or more of the above to start with

- ....
- ....
- ....

How am I going to do this?

- ....
- ....
- ....

What's going to stop me?

- ....
- ....
- ....

What will I do about that?

- ....
- ....
- ....

How confident do I feel that I can do this?
Choose a number between 1 and 10 (where 1 is not at all confident and 10 is very confident)

The number I choose is:

....

Appendix 5:

Letters and documents related to the conduct of and recruitment to the TRIMS randomised controlled trial

- Copy of ethics committee approval letter

- Clinical trial registration

- Documents for recruiting practices
    - Letter of invitation
    - Reply slip
    - Information sheet

- Documents for recruiting participants
    - Letter of invitation
    - Reply slip
    - Information sheet
    - Consent form

NHS

National Research Ethics Service

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30 December 2008

Professor Kamlesh Khunti
Professor of Primary Care Diabetes and Vascular Medicine
University of Leicester
22-28 Princess Road West
Leicester
Leicestershire
LE1 6TP

Dear Professor Khunti

Full title of study: A randomised controlled trial to investigate the effects of a structured self-management education programme for people with metabolic syndrome

REC reference number: 08/H0402/142

Thank you for your letter of 19 December 2008, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form. Confirmation of approval for other sites listed in the application will be issued as soon as local assessors have confirmed they have no objection.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

This Research Ethics Committee is an advisory committee to East Midlands Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within the
National Patient Safety Agency and Research Ethics Committees in England

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review –guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

08/H0402/142	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

[signature]

Mr Ken Willis / Miss Jeannie D McKie
Chair / Committee Coordinator

Email: jeannie.mckie@nottspct.nhs.uk

Enclosures: "After ethical review – guidance for researchers" SL-AR1 for CTIMPs
Site approval form

Copy to: Mr Graham Howitt
R&D office for NHS care organisation at lead site – Leicester PCT

Headed notepaper PI of screening study

University Hospitals of Leicester NHS
NHS Trust
Department of Diabetes Research
Leicester Royal Infirmary

University of Leicester

The TRIMS Study
Department of Health Sciences
(Division of General practice & PHC)
University of Leicester
22-28 Princess Road West
Leicester
LE1 6TP
Tel: 0116 2523212
E-mail: ajd38@le.ac.uk

T R I M S
study

PRACTICE REPLY SLIP

TRIMS (The Reversal Intervention in Metabolic Syndrome) Study

TRIMS (The Reversal Intervention in Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

Dear Practice Manager,

I am writing to you as the University of Leicester are currently conducting a randomised controlled trial to investigate the effects of a structured self-management education programme for people with metabolic syndrome (TRIMS Study).

With your permission we would like to invite some of the patients registered at your practice to participate in the TRIMS Study. The patients we would like to send a letter of invitation to are those who have been identified as having metabolic syndrome as part of the _____ study, which your practice has been identified as taking part in.

Enclosed is an information sheet which explains the purpose of the TRIMS Study and what will be required if you agree to take part. If after having read this information your general practice agrees that we can approach those patients identified as having metabolic syndrome, please complete the reply slip enclosed with this letter.

We hope you will agree to this.

Yours sincerely

Name
(Principal Investigator of screening study)

1) Our practice would like to volunteer to take part in the TRIMS study, and I agree to a member of the research team contacting me by telephone in order to arrange an appointment to visit the practice.

SIGNATURE: _____ DATE: _____

FULL NAME: _____

ROLE IN THE PRACTICE: Practice Manager / General Practitioner / Practice Nurse
(please delete as appropriate)

ADDRESS: _____

_____

_____

TELEPHONE NUMBER: _____

2) Please indicate generally what is the best day of the week and/or time of day to contact you by telephone					
MON	TUES	WED	THURS	FRI	No preference
Time(s):					

3) In order for us to check how representative volunteer practices are, please could you answer the following questions:		
a) Are you currently a teaching / training practice?	YES /NO	
b) How many patients do you currently have registered at your practice?	YES /NO	
c) What proportion of your patients are of:	South Asian ethnicity	%
	White European ethnicity	%

GENERAL PRACTICE LETTER OF INVITATION   Version1, dated 01/09/2008
TRIMS_LetterofinvitationtoGeneralPractices_Version1.doc   Last saved:16/09/2008
Revised:

GENERAL PRACTICE REPLY SLIP   Version 1, dated 01/09/2008
TRIMS_PracticetReplySlip_Version1.doc   Last saved: 16/09/2008
Revised:

University Hospitals of Leicester **NHS**
NHS Trust
Department of Diabetes Research

University of Leicester

The TRIMS Study,
Department of Health Sciences,
University of Leicester,
22-28 Princess Road West,
Leicester, LE1 6TP.
E-mail: ajd38@le.ac.uk.

PRINCIPAL INVESTIGATOR: Prof Kamlesh Khunti

PRACTICE INFORMATION SHEET

TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

What is metabolic syndrome?
Metabolic Syndrome consists of a group of factors that increase the risk of cardiovascular disease and Type 2 diabetes. Abdominal/central obesity and insulin resistance are thought to be the main underlying causes. People with metabolic syndrome are 2 - 3 times more likely to develop cardiovascular disease than those without metabolic syndrome and 3 – 5 times more likely to develop Type 2 diabetes. Metabolic syndrome is a major public health concern: 25% of the UK population fulfil the criteria, and this will increase as people continue to be less active and levels of overweight/obesity rise. There is no global consensus for defining metabolic syndrome. The criteria we are using to define metabolic syndrome for the TRIMS study are those of the International Diabetes Federation (IDF) where central obesity is an essential requirement. The IDF additionally provide ethnic-specific cut offs for waist circumference. People are identified as having metabolic syndrome if they have both:

- (1) a large waist size
  - o 31.5" (80cm) or larger for women
  - o 37" (94cm) or larger for men (35" (90cm) if South Asian ethnicity); and
- (2) any two of the following four risk factors
  - o High blood pressure, $\geq$130/85 (or on medication for)
  - o Raised fasting plasma glucose, $\geq$5.6mmol/l
  - o Low HDL- cholesterol, <1.03 mmol/l males or <1.29mmol/l females(or specific treatment for).
  - o High triglycerides, $\geq$1.7mmol/l (or specific treatment for).

Why is this research being done?
There is some evidence that if people make changes to their lifestyle (diet and exercise) they can reverse metabolic syndrome. However, no studies have been carried out in the UK. The TRIMS study is a 1 year randomised controlled trial comparing a lifestyle intervention with usual/routine care. The aim of our study is to see if people with metabolic syndrome who attend a group self-management education programme based on lifestyle changes (dietary and increased physical activity) can lessen their risk of having diabetes and cardiovascular disease in the future. Overall, we hope that this type of education will reduce the number of people who have metabolic syndrome.

Recruitment of general practices
A letter of invitation to participate in this research is being sent to all practices in Leicester City PCT and Leicestershire County and Rutland PCT who have been identified as having patients who have previously been involved in a screening study adopted by South East Midlands Diabetes Research Network. If you return the reply slip to express an interest in taking part, the research team will arrange to visit the practice for a full discussion about the research study and what is involved. Practices that express an interest in taking part will be able to withdraw at this stage if they wish. All practices that volunteer will be eligible for inclusion in the study.

How will people be recruited to the study?
We aim to recruit 80 volunteers with metabolic syndrome, aged 40–74 years and free of existing diabetes or CVD. A letter of recruitment and information sheet describing the study will be sent to people who have recently been screened and either (1) given their consent to be approached with details of other research studies or (2) identified by the practice as somebody with metabolic syndrome. People need to be able to speak and understand English (the intervention will be made appropriate for ethnically diverse populations, but individuals who are unable to understand, speak and read English will be excluded at this stage).

What will be involved for participating general practices?
Those people who have previously given their permission to be approached will be contacted directly by the principal investigator (PI) of the screening study. In order to identify other people participating practices will be asked to carry out searches of their practice database to identify eligible patients. The research team will provide stamped information packs ready to be sent out to random samples of the people identified until we have recruited the total number required for the study (approximately 80 patients). The invitation to participate will include some questions to confirm patients' eligibility.

What will the study involve for your patients?
Volunteers will be asked to attend for 3 appointments at: baseline, 6 months, and 1 year. Appointments will be held at the University Hospitals of Leicester (Leicester Royal Infirmary or Leicester General Hospital) or in the community. Baseline data (if not collected when previously screened or unavailable) will include: biomarkers (optional) for insulin, adiponectin, and hs-CRP; HbA1c, OGTT; urine for albumin-creatinine ratio; height, weight, BMI, hip circumference; ambulatory activity (measured by pedometer); smoking status, occupation, ethnicity; self completion questionnaire data covering psychological well-being, depression scale, health beliefs and self-efficacy, physical activity, and food/dietary habits. If it is longer than 3 months since people were originally screened the measurements related to classifying metabolic syndrome will be repeated. If these repeat measurements indicate that people no longer meet the criteria for metabolic syndrome they will not be eligible to take part in the study. This will be explained to the patient and they will be thanked for volunteering. At 6 and 12 months the control and intervention groups will be recalled for repeat blood tests, measurements and questionnaires. Practices will be sent the results of their patients' laboratory blood tests and physical measurements in the post. If these results are abnormal we may inform you earlier by telephone. This will be determined according to the study's standard operating procedures.
Intervention - After their first visit people will be randomly allocated to either the study intervention (routine care plus group self-management education) or the control group (routine care). They have an equal chance of being allocated to either of the groups. People randomised to the intervention group will be asked to attend for 2 group education sessions lasting around 3 hours each. People randomised to the control group will not receive an intervention and will be asked to see their GP for usual care.
Qualitative feedback - We will be asking for some volunteers who have been involved in the group education sessions to take part in semi-structured interviews shortly after delivery of the intervention, to give us feedback about their experiences.

Will the practice be reimbursed for participating in the study?
The TRIMS study will pay the postage costs for sending out invitation letters.

What do I do if the practice decides to participate?
If the practice decides to volunteer to take part in the study, please send the reply slip to the university research team in the envelope provided. This does not need a stamp.

<u>**If you would like more detailed information about the study or if you would like to ask any questions before deciding whether to volunteer, please feel free to contact:**</u>

Professor **Kamlesh Khunti** or Mrs Alison Dunkley (Research Nurse), Department of Health Sciences, University of Leicester. Tel: 0116 252 3212 or E-mail: ajd38@le.ac.uk.

PRACTICE INFORMATION SHEET   Version1, Dated: 01/09/2008
TRIMS_GP_PracticeInformationsheetVersion1.doc   Last saved: 03/10/2008
Revised: 1

PRACTICE INFORMATION SHEET   Version1, Dated: 01/09/2008
TRIMS_GP_PracticeInformationsheetVersion1.doc   Last saved: 03/10/2008
Revised: 2

GP headed paper or letterhead for principal investigator screening study

Name
Address
Address
Address

Date

INVITATION LETTER

Dear **Name (D.O.B)**

Following the results of tests and measurements that you had whilst participating in the _____ study, you have been identified as having something called metabolic syndrome. Metabolic syndrome consists of a group of risk factors, and people who have metabolic syndrome are at increased risk of developing diabetes and heart disease in the future. More information is given on the enclosed information sheet.

We would like to invite you to take part in a study for people with metabolic syndrome being conducted by researchers at the University of Leicester. The study involves an educational intervention. The purpose of this research is to see if people with metabolic syndrome who attend a group education programme based on lifestyle changes (dietary and increased physical activity) can lessen their risk of having diabetes and heart disease in the future.

Enclosed is an information sheet that explains more about the study and what will happen if you agree to participate. Once you have read this information, if you would like to volunteer to take part please complete the reply slip enclosed with this letter. The reply slip also asks for some information about you. This is so we can check if you are eligible to take part in the study.

We hope you will agree to take part.

If you do not want to volunteer, it would be helpful if you could let us know by completing and returning the reply slip for people who do not want to take part.

Yours sincerely

GP or Principal Investigator of screening study

PARTICIPANT LETTER OF INVITATION	Version 1, dated 01/09/2008
TRIMS_Initial_ PatientLetterofInvitation_Version1.doc	Last saved: 03/10/2008
Revised:	

University Hospitals of Leicester **NHS**
NHS Trust
Department of Diabetes Research
Leicester Royal Infirmary

University of Leicester

The TRIMS Study
Department of Health Sciences
University of Leicester
22-28 Princess Road West
Leicester
LE1 6TP
Tel: 0116 2523212
E-mail: ajd38@le.ac.uk

T R I M S study

Study ID N°

PARTICIPANT REPLY SLIP

TRIMS (The Reversal Intervention in Metabolic Syndrome) Study
(A randomised controlled trial to investigate the effects of a structured self-management education programme for people with metabolic syndrome)

1) I would like to volunteer to take part in this study, and agree to a member of the research team contacting me by post or telephone in order to arrange an appointment.

SIGNATURE: _____ DATE: _____

FULL NAME: _____

ADDRESS: _____

_____

TELEPHONE NUMBER: _____

2) Appointments will be in a morning. Please indicate which day you would prefer (if we are able to give you a choice).

MON	TUES	WED	THURS	FRI	No preference

3) To help us to check if you are eligible to take part in the study, please could you answer the following questions:

a) Are you aged 40 to 74?		YES /NO
b) Do you have a life-limiting terminal illness?		YES /NO
c) Do you have any serious mental health problems?		YES /NO
d) Do you have a learning disability?		YES /NO
e) Are you housebound?		YES /NO
f) Do you live in a nursing or care home?		YES /NO
g) Are you taking part in any other research or clinical trials? _If yes please give details:_		YES /NO
h) Have you got or ever had any of the following illnesses?	Diabetes	YES /NO /DON'T KNOW
	Stroke or Transcient Ischaemic attack (TIA)	YES /NO /DON'T KNOW
	Heart Attack (MI)	YES /NO /DON'T KNOW
	Angina	YES /NO /DON'T KNOW
	Heart bypass surgery	YES /NO /DON'T KNOW
	Angioplasty	YES /NO /DON'T KNOW
	Peripheral arterial disease	YES /NO /DON'T KNOW
i) Are you pregnant or breast-feeding?		YES / NO / NOT APPLICABLE

PARTICIPANT REPLY SLIP	Version 1, dated 01/09/2008
TRIMS_PatientReplySlip_Version1.doc	Last saved: 16/09/2008
Revised:	

University Hospitals of Leicester NHS
NHS Trust
Department of Diabetes Research
Leicester Royal Infirmary

University of Leicester
TRIMS Study,
Department of Health Sciences,
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22-28 Princess Road West,
Leicester, LE1 6TP.
Tel: 0116 252 3212
E-mail: ajd38@le.ac.uk.

PARTICIPANT INFORMATION SHEET

TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured self-management education programme for people with metabolic syndrome)

You are being invited to take part in a research study. Before you decide you need to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends, relatives, or your GP if you wish. Please ask us if there is anything that is not clear or you would like more information. Take time to decide whether or not you wish to take part.

What is metabolic syndrome?
Metabolic syndrome is a relatively new term that describes a combination of factors that together provide an indicator of a person's risk for diabetes, heart disease, stroke and other cardiovascular conditions. People are identified as having metabolic syndrome if they have both:
- (1) a large waist size
  - 31.5" (80cm) or larger for women
  - 37" (94cm) or larger for men (35" (90cm) if South Asian ethnicity); and
- (2) any two of the following four risk factors
  - High blood pressure (or on medication for)
  - High fasting blood sugar
  - Low HDL cholesterol (good cholesterol)
  - High triglycerides.

Why is this research being done?
People who have metabolic syndrome are at increased risk of going on to develop diabetes and/or heart disease and strokes in the future. The number of people who have metabolic syndrome is likely to increase in the future as people continue to be less active and levels of overweight and obesity rise. There is some evidence that if people make changes to their lifestyle (diet and exercise) they can reverse metabolic syndrome. However, no studies have been carried out in the UK. The aim of our study is to see if people with metabolic syndrome who attend a group education programme based on lifestyle changes (dietary and increased physical activity) can lessen their risk of having diabetes, heart disease and strokes in the future. Overall, we hope that this type of education will reduce the number of people who have metabolic syndrome.

Why have I been chosen?
You have been asked to join this study because you were screened recently as part of another research study and your test results showed you had metabolic syndrome. A letter has been sent to you because either (1) you have given your consent to be approached with details of other research studies or (2) your GP identified you as somebody with metabolic syndrome. Any information passed onto the TRIMS team at the University of Leicester at this stage is confidential. Unless you have already consented to be approached with details of other research studies no one other than the staff at your GP surgery is able to identify you. The TRIMS team will only hold your details if you return the reply slip to say that you are willing to take part in the study.

Who can volunteer?
Anybody who has been invited can volunteer if they are able to understand, speak and read English (this is because in this study we will be running the education sessions in English).

Do I have to take part?
No, we are looking for volunteers. If you do decide you want to take part in the study you will be given this information sheet to keep and you will be asked to sign a consent form at your first appointment before any tests or measurements are carried out. You will be given a copy of the signed consent form to keep for your own records. Even if you volunteer and agree to take part, you can change your mind at any time, without giving a reason. If you decide not to take part at any stage this will not affect the standard of care you would expect to receive.

What will be involved if I take part?
If you return the reply slip you will be asked to attend for 3 appointments. We will invite you to attend for your first appointment straight away. Your second appointment would be after 6 months and your third appointment after 1 year. At these appointments, with your permission, we would like to carry out various tests and measurements, ask you some questions, and ask you to complete some questionnaires (see below). Each appointment could take up to 3 hours and would be in a morning. Appointments will be held at the University Hospitals of Leicester (Leicester Royal Infirmary or Leicester General Hospital) or in the community.

TESTS & MEASUREMENTS
- Blood tests for: cholesterol & blood sugar
- Extra blood (optional) to be stored and tested at a later date
- Oral Glucose Tolerance Test
- Waist and hip measurements
- Height and weight
- Blood pressure x 3
- Urine sample
- Physical activity/walking, (involves wearing a pedometer and posting back to us)

WE WILL ASK YOU ABOUT
- Your past medical history
- Eating habits
- Exercise and physical activity
- Your feelings and well being
- Smoking
- Ethnicity and occupation

At your first appointment you may not need to have all the tests and measurements. If you have already had some of these carried out as part of another research study within the last 3 months we may be able to use those results instead. At your second appointment we will not ask to take extra blood to be stored. At your third appointment, with your permission we would like to repeat all the tests, measurements, questions and questionnaires. The total amount of blood we would like to take at each appointment is about 13ml (2 ½ teaspoonfuls) or if you chose to have extra blood taken to be stored and tested in the future (not applicable to 6 month appointment) this will be about 22ml (4 ½ teaspoonfuls). Which ever you chose you will normally have 2 blood samples taken from your arm using a needle and syringe at each appointment.
On the evening before all 3 of your appointments you will need to fast from 12 midnight (NO food or drink after midnight). You are allowed to have water to drink.

Sometimes because we do not know which way of treating patients is best, we need to make comparisons. After your first visit you will be allocated to either the intervention group or the control group in the study. This is done randomly, that is by chance like flipping a coin. A computer that has no information about you selects the groups. Patients in each group then have a different treatment and these are compared. You have an equal chance of being allocated to either of the groups. We will let you know by a letter or telephone call which group you have been allocated to.

INTERVENTION GROUP – Group education
If you are randomised into the intervention group you will also be asked to attend for 2 half-day group education sessions lasting around 3 hours each and held 1-2 weeks apart. The sessions will

be held in either the morning or afternoon at the Leicester Royal Infirmary, Leicester General Hospital or a local venue (if there is a demand). The group will consist of 6 – 8 people who have also recently been diagnosed with metabolic syndrome and will be led by 2 experienced health professionals (nurses and/or dieticians). You can bring a partner, relative or friend with you. The education sessions are designed to help increase your knowledge and understanding of metabolic syndrome, to enable you to meet and talk to others in the same situation, and to support and motivate you to make healthy lifestyle changes. Topics covered will include what metabolic syndrome is, risks and complications from having metabolic syndrome, food choices and physical activity. You will be given a booklet to accompany the education sessions and to take away with you.

CONTROL GROUP – Routine care
If you are randomised to the control group you will not receive any intervention. You will be asked to see your GP for usual care.

Following this we will be asking for some people who have attended the group education sessions to volunteer to be interviewed to give us feedback about their experiences (optional). Extra information about volunteering to be interviewed (intervention group only) will be given to people when attending the education sessions or sent in the post.

Travel expenses
Travel costs will be reimbursed up to a maximum of £15, which includes car park charges and public transport. Please keep all your receipts. If driving you will need to record your mileage.

What happens to any extra blood taken for storage and testing at a later date, if I agree?
Any extra blood taken (at your first appointment and your 12 month appointment) will be frozen and stored so that they can be tested all together at the end of the study. The stored bottles will only have an ID number on them. The blood will only be tested for certain proteins (bio-markers) related to diabetes and heart disease and you or your GP will not be given the results of any of these tests. Any unused blood samples remaining after the end of the study will be destroyed.

What is an Oral Glucose Tolerance Test (OGTT)?
An OGTT involves having a small sample of blood taken from your arm (2.7ml, less than a teaspoon) to measure the level of sugar in your blood after you have fasted from midnight the night before, and then drinking a sugary drink (lucozade). You then have to wait 2 hours before we take another sample of blood. This second sample of blood tells us how well your body is dealing with the sugar you drank.

Will there be any side effects?
You may suffer slight discomfort while the blood samples are being taken from your arm and some people do experience bruising after blood samples have been taken.

What if something goes wrong?
If you are harmed by taking part in this research project there are no special compensation arrangements. If you are harmed due to someone's negligence then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you.

Will my GP be informed?
If you decide to volunteer to take part in the TRIMS study we will need to inform your GP. Your GP will receive a copy of your results in the post within 1 month of each appointment. If these results are abnormal we may inform your GP earlier by telephone. We will also ask for your permission to access your medical records for information related to the current study (essential), and long-term follow-up (optional). All information collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital/surgery will have your name and address removed so that you cannot be recognised from it.

What will happen to the results of the study?
The results of the study may be published in a medical journal or presented at research seminars or conferences. Participants will not be identified in any report or publication.

Who is organising and funding this research?
The principal investigator for this study is Professor Kamlesh Khunti (Professor of Primary Care Diabetes & Vascular Medicine) at the University of Leicester. This research is being jointly funded by the University of Leicester, local NHS organisations and the Department of Health.

Who has reviewed this study?
All research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be approved by an independent group of people, called a Research Ethics Committee before it goes ahead. Approval does not guarantee that you will not come to any harm if you take part. However, approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision. This study has been reviewed by an appropriate NHS ethics committee in accordance with local regulations.

What do I do if I decide to volunteer?
If you have decided to volunteer to take part in the study, please send the reply slip to the university research team in the envelope provided. This does not need a stamp.

If you still have any questions about the study please feel free to contact:
Alison Dunkley (Research Nurse), Department of Health Sciences, University of Leicester, 22-28 Princess Road West, Leicester, LE1 6TP. Tel: 0116 252 3212 or E-mail: ajd38@le.ac.uk.

Summary of what will be involved if you decide to take part
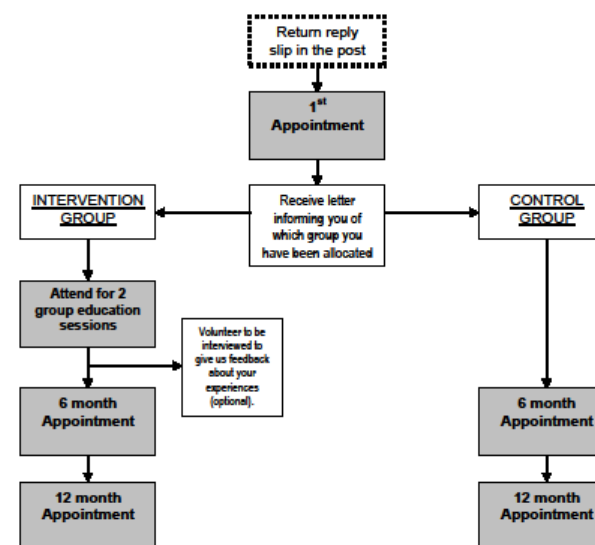
PARTICIPANT CONSENT FORM
(Version 2, 19th December 2008)

University of Leicester
Department of Health Sciences

Study ID Nº

University Hospitals of Leicester **NHS**
NHS Trust
Department of Diabetes Research

TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

Principal investigator: Prof K Khunti (Professor of Primary Care Diabetes & Vascular Medicine, & GP)
Co-investigators: Alison Dunkley (Research Nurse), Prof M Davies (Professor of Diabetes Medicine)

[Please write your initials in each box]

1) I confirm that I have read and understood the information sheet for the above study (Version 2, dated: 19/12/2008) and have had the opportunity to ask questions.

2) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my medical care or legal rights being affected.

3) I consent for the TRIMS research team to have access to my biomedical data, that was collected as part of the screening study from which I was identified as having metabolic syndrome.

4) I give permission for individuals from the TRIMS research team to have access to my NHS medical records for additional data collection relevant to the current research study.

5) I understand that my general practitioner (GP) will be informed of my participation in the TRIMS study and be sent copies of my biomedical results collected as part of the study.

6) I agree to take part in the above study.

NAME OF PARTICIPANT (PRINT)   SIGNATURE   DATE

NAME OF RESEARCHER (PRINT)   SIGNATURE   DATE

a) I consent to being approached with information about an interview   YES ☐ NO ☐
(optional) *please tick,*

b) I consent for some of my blood samples to stored and tested all together at the end of the study.
(optional) *please tick,*   YES ☐ NO ☐

c) I give permission for the TRIMS research team to have access to my NHS medical records for long-term follow-up data collection in the future.   (optional) *please tick,*   YES ☐ NO ☐

d) I would like to receive a summary of the results of the study and agree to them being posted to the address on my patient pack.   (optional) *please tick,*   YES ☐ NO ☐

e) I give permission for retention of my contact details for contact at a later stage for invitation to participate in follow-up or related studies.   (optional) *please tick,*   YES ☐ NO ☐

PARTICIPANT CONSENT FORM
Version 2, Dated 19/12/2008

When completed: 1 copy (original) for research file,
1 copy for GP notes,
1 copy for patient

Appendix 6:

Letters and documents related to the evaluation

of the TRIMS randomised controlled trial

- Example of Case Report Form (CRF): Baseline

- Self-completion questionnaires

  - o EQ5D – Health questionnaire and visual analogue scale (VAS)

  - o DINE – Eating habits questionnaire

  - o GSE – General Self-Efficacy Scale

  - o HADS – Hospital Anxiety and Depression Scale

  - o IPAQ – International Physical Activity Questionnaire, short version

- Documents for qualitative evaluation

  - o Letter of invitation

  - o Information sheet

  - o Reply slip

  - o Consent form

  - o Interview topic guide

University of Leicester University Hospitals of Leicester **NHS**
NHS Trust
Department of Cardiovascular Research
Leicester Hospitals

Participant ID No: ⬚⬚⬚⬚⬚⬚⬚⬚

Participant ID Nº: ⬚⬚⬚⬚⬚⬚⬚

Date of appointment: ⬚⬚ / ⬚⬚ / ⬚⬚

TRIMS Study

Baseline - Case Report Form

Booklet to be completed by nurse / researcher

CHECKLIST

Fasting bloods	⬚	Health & demographic questions	⬚
Lucozade	⬚	Blood pressure	⬚
Urine	⬚	Height	⬚
2 hour bloods	⬚	Weight	⬚
Last blood samples due at:		Waist & hips	⬚
		Self-completion questionnaires	⬚
⬚ : ⬚		Given pedometer & instructions	⬚

At end of clinic:

CRF checked for completion	Blood & urine to lab	Blood to freezer
⬚ *(sign initials)*	⬚ *(sign initials)*	⬚ *(sign initials)*

Baseline_CRF_TRIMS_version1a_12thJan2010.doc   Version 1a, dated 12/01/2010

This section should be completed prior to the baseline appointment

Availability of previous screening data

Date of previous screening appointment: ⬚⬚ / ⬚⬚ / ⬚⬚

Date arranged for baseline appointment: ⬚⬚ / ⬚⬚ / 1 0

		Less than 3 months since screened ↓ Is screening data available? ↓				>3 months since screened ↓ Collect ALL baseline data ↓
BLOODS	FPG	YES	*Do NOT collect*	NO	*Collect*	
	Lipids	YES	*Do NOT collect*	NO	*Collect*	
	HbA1c	YES	*Do NOT collect*	NO	*Collect*	
		YES	*Do NOT collect*	NO	*Collect*	*Collect*
URINE	Albumin: creatinine ratio	YES	*Do NOT collect*	NO	*Collect*	*ALL*
MEASUREMENTS	Waist circumference	YES	*Do NOT collect*	NO	*Collect*	
	Hip circumference	YES	*Do NOT collect*	NO	*Collect*	
	Height	YES	*Do NOT collect*	NO	*Collect*	
	Weight	YES	*Do NOT collect*	NO	*Collect*	
All remaining data including demographics, medical history & self-completion questionnaires		*Collect for ALL participants*				

Please circle as appropriate

2

Participant ID No: ☐ ☐ ☐ ☐ ☐ ☐ ☐

This section must be completed prior to obtaining informed consent

Date of birth: ☐☐ / ☐☐ / ☐☐☐☐   **Sex:** | Male *1* | Female *2* |

Inclusion / exclusion criteria:

1. Confirm that the volunteer is aged 40 – 74 years   NO ☐ (exclude)   YES ☐   AGE ☐

2. Confirm that the volunteer does not have or is not doing any of the following:

a) Do you have a life-limiting terminal illness?   NO ☐   YES ☐ (exclude)

b) Are you taking part in any other research/clinical trials   NO ☐   YES ☐ (exclude if trial involves an intervention)
(if YES please give details)

_____

c) Have you got or ever had any of the following illnesses?	Diabetes	NO	YES	(exclude if answers yes to any of these questions)
	Stroke or Transient Ischaemic attack (TIA)	NO	YES	
	Heart Attack (MI)	NO	YES	
	Angina	NO	YES	
	Heart bypass surgery	NO	YES	
	Angioplasty	NO	YES	
	Peripheral arterial disease	NO	YES	

If applicable:
d) Are you pregnant or breast-feeding?   NO ☐   YES ☐ (exclude)

Participant ID No: ☐ ☐ ☐ ☐ ☐ ☐ ☐

Obtain consent

Consent

Consent obtained: YES ☐

Consent for stored samples: YES ☐   NO ☐   *(Do NOT take brown 9ml)*

Baseline samples

Fasting Bloods

Yellow 2.7ml (glucose)   YES ☐

Brown 5ml (lipids)   YES ☐

Purple 2.7ml EDTA (HbA1c)   YES ☐

Brown 9ml (for freezer)   YES ☐   ← *(Only take if consent obtained for stored samples)*

OGTT

Lucozade 410ml   YES ☐   TIME started ☐ . ☐

Sample spinning

Blood samples spun   YES ☐   Stored in box _____

INSTRUCTIONS:
- leave to clot for 30 mins
- spin for..............
- pipette into 4 x 1ml vials (brown lids) & freeze

Numbers: ☐ ☐
☐ ☐

Urine

Albumin : creatinine   YES ☐

2 hour bloods

Yellow 2.7ml   YES ☐   TIME taken ☐ . ☐

Tick boxes to indicate which data have been collected OR strike through & write DNC if NOT to be collected

3   4

Participant ID No: ☐☐☐☐☐☐☐

Baseline measurements

Blood Pressure

Arm circumference: ☐☐ cm   BP Cuff size: **Large** ☐   **Med** ☐
                                                      32-42cm   22-32cm

Arm used for Blood Pressure: **LEFT** ☐   **RIGHT** ☐

1st reading: ☐☐☐ / ☐☐☐
              Systolic   Diastolic

Comments:

2nd reading: ☐☐☐ / ☐☐☐
              Systolic   Diastolic

3rd reading: ☐☐☐ / ☐☐☐
              Systolic   Diastolic

Average of 2nd & 3rd reading:

☐☐☐ / ☐☐☐
Systolic   Diastolic

(round up to whole number, ≤ 0.4 round down / ≥ 0.5 round up)

Height   **Waist circumference**

☐ . ☐☐ m (round up or down to the nearest cm)   ☐☐☐ . ☐ cm (measure to the nearest mm)

Weight   **Hips**

☐☐☐ . ☐ kg   ☐☐☐ . ☐ cm (measure to the nearest mm)

Record values where data have been collected OR strike through & write DNC if NOT to be collected

Participant ID No: ☐☐☐☐☐☐☐

Ethnicity

Q1) How would you describe your ethnic origin?   _Tick one box_

WHITE: BLACK (including Black British):

White British or Irish   ☐ 1   Black Caribbean   ☐ 7

Any other white background ☐ 2   Black African   ☐ 8

ASIAN OR ASIAN BRITISH: OTHER:

Indian   ☐ 3   Chinese   ☐ 9

Pakistani   ☐ 4   Mixed ethnicity ☐ 10

Bangladeshi   ☐ 5   ——————— (give details)

Any other Asian background ☐ 6   Any other ethnic origin ☐ 11

                                         ——————— (give details)

Smoking

Q2 Do you currently smoke or have you ever smoked in the past? (cigarettes, cigars or pipe)

Tick ONE box only

CURRENT REGULAR SMOKER	(→go to Q3)	☐ 1
CURRENT OCCASIONAL SMOKER (<1 per day)	(→go to Q3)	☐ 2
EX REGULAR SMOKER	(→go to Q4)	☐ 3
EX OCCASIONAL SMOKER (<1 per day)	(→go to Q4)	☐ 4
NEVER SMOKED	(→go to Q5)	☐ 0

Office use coding

Ask smokers:
Q3) How many cigarettes/ cigars/ pipes do you usually smoke per day?   ☐
(If <1 per day enter 0)

Ask ex-smokers:
Q4) How long ago did you stop smoking?   ☐   OR   ☐
                                       Years if < 1 year Months

5   6

Participant ID No:								

Participant ID No:								

Significant medical / surgical history

Q5) Have you ever been diagnosed with any of the following medical problems?

(please tick yes or no as appropriate)

	(0)	**(1)**		**If yes**
High blood pressure	**NO**	**YES**	Year diagnosed?	Currently prescribed medication? **YES / NO** *(circle)*
High cholesterol	**NO**	**YES**	Year diagnosed?	Currently prescribed medication? **YES / NO** *(circle)*
Pre-diabetes	**NO**	**YES**		
Women only:				
Gestational diabetes	**NO**	**YES**		
Polycystic ovary syndrome	**NO**	**YES**		

Q6) Have you got or had any other significant medical problems/history?

Specify:		Past / current
Specify:		**Past / current**
Specify:		**Past / current**
Specify:		**Past / current**
Specify:		**Past / current**

(circle as appropriate)

Medication

Q7) Do you currently take any medication (prescribed by a dr or nurse)?

NO [ ]   YES [ ]   *If yes enter details below*

Name of medication	**Dose** (if for cholesterol or high BP)	**Reason for use**	**Office use coding** (circle)
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3
			Lipid lowering: 1 2 Antihypertensive: 1 2 3 4 5 6 Other: 1 2 3

	Drug category (coding)		**.......... Ending in**
	Lipid lowering:		
	Statin	(1)	.....astatin
Office	Fibrate	(2)	......fibrate, ...fibrozil
use	**Anti-hypertensive:**		
	β-blocker	(1)	....olol
coding	ACE	(2)	....pril
key	ARB	(3)	....sartan
	Diuretic	(4)	....azide, ...amide
	Ca-blocker	(5)	....pine, ...amil, ...azem
	α-blocker	(6)	....zosin

7

8

Current employment status

Q8) Can I ask, do you currently work?
Which best describes participant's current employment status (probe if necessary). *Tick ONE box only*

WORKING <u>FULLTIME</u> (>30 hours per week)   □   1

WORKING <u>PART TIME</u> (<30 hours per week)   □   2

RETIRED   □   3

UNEMPLOYED (currently seeking work)   □   4

LONG TERM SICK / DISABLED   □   5

NEVER WORKED   (→go to Q4)   □   6

OTHER   □   7
.... specify

Office use coding

Occupation - *Participant's current main job (or if not working now their last main job).*

Q9) Do (did) you work as an employee or are (were) you self-employed? *Tick one only*

EMPLOYEE	SELF-EMPLOYED with employees	SELF-EMPLOYED / FREELANCE without employees
□	□	□
go to Q10(a)	go to Q10(b)	go to Q12

Q10(a) How many people work(ed) for your employer at the place you work(ed)?

1 to 24 □   25 or more □
↓ now go to Q11

Q10(b) How many people do (did) you employ?

1 to 24 □   25 or more □
↓ now go to Q12

Q11) Do (did) you supervise any other employees?

Yes □   No □
↓ now go to Q12

Q12) What sort of work do you (did you) do as your job? *Tick ONE box only*
Which best describes participant's work (or if not working now what did in their last main job).

Modern professional occupations
such as: teacher - nurse - physiotherapist - social worker - welfare officer - artist - musician - police officer (sergeant or above) - software designer   □   1

Clerical and intermediate occupations
such as: secretary - personal assistant - clerical worker - office clerk - call centre agent - nursing auxiliary - nursery nurse   □   2

Senior managers or administrators
(usually responsible for planning/ organising/ co-ordinating work & for finance) *such as:* finance manager - chief executive   □   3

Technical and craft occupations
such as: motor mechanic - fitter - inspector - plumber - printer - tool maker - electrician - gardener - train driver   □   4

Semi-routine manual and service occupations
such as: postal worker - machine operative - security guard - caretaker - farm worker - catering assistant - receptionist - sales assistant   □   5

Routine manual and service occupations
such as: HGV driver - van driver - cleaner - porter - packer - sewing machinist - messenger - labourer - waiter / waitress - bar staff   □   6

Middle or junior managers
such as: office manager - retail manager - bank manager - restaurant manager - warehouse manager - publican   □   7

Traditional professional occupations
such as: accountant - solicitor - medical practitioner - scientist - civil / mechanical engineer   □   8

Education

Q13) At what age did you leave school or finish full time education?   □

Q14) Which best describes any qualifications you may have? *Tick ONE box only*
Includes academic and vocational qualifications

'O' Levels/ CSEs/ GCSEs/ School certificate
Apprenticeships/ City & Guilds Craft/ RSA Diploma/
BTEC First Diploma/ NVQ level 1 or 2/ or equivalent   □   1

'A' Levels/ Higher school certificate/
City & Guilds Advanced Craft/ ONC/ OND/
RSA Advanced Diploma/ BTEC National/ NVQ level 3/ or equivalent   □   2

Degree (eg BA, BSc, MA, PhD, PGCE)/
Professional qualifications (eg teaching, nursing, accountancy)/
HNC/ HND/ RSA Higher Diploma/ BTEC Higher Level/ NVQ Level 4-5/   □   3

None of the above   □   0

Office use: page to be completed later …………………...…… NS-SEC coding completed: YES / NO

Derivation of 5-class NS-SEC from occupational & employment status

Participant ID No:
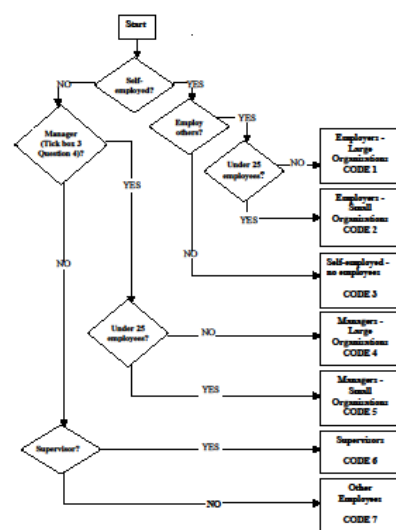
Step 1: (use flowchart) - From answers to Q9-11, & if manager Q12 - derive employment status/size of organisation & circle CODE from 1-7 in matrix table below.

Step 2: From answer to Q12, circle respondents' occupation in matrix table

Step 3: (use matrix table) to assign NS-SEC five-class code & *code in variable table below*

NS-SEC 5-Class Code	Label
1	Managerial & professional occupations
2	Intermediate occupations
3	Small employers & own account workers
4	Lower supervisory & technical occupations
5	Semi-routine & routine occupations

Office use coding: circle one only ENTER this code onto database

NS-SEC SELF-CODED MATRIX DERIVATION TABLE: FIVE CLASSES

Self-coded Occupation 2ND: From answer to Q4, circle respondents' occupation	Employment status / size of organisation 1ST: Use flowchart. Derive from answers Q1-3, & if manager Q4						
	CODE 1 Employers - large organisations	CODE 2 Employers - small organisations	CODE 3 Self employed - no employees	CODE 4 Managers - large organisations	CODE 5 Managers - small organisations	CODE 6 Supervisors	CODE 7 Other employees
1 Modern professional	1	1	1	1	1	1	1
2 Clerical & intermediate	1	3	3	1	1	1	2
3 Senior managers or administrators	1	3	3	1	1	1	1
4 Technical and craft	1	3	3	1	1	4	4
5 Semi-routine manual & service	1	3	3	1	1	4	5
6 Routine manual & service	1	3	3	1	1	4	5
7 Middle or junior managers	1	3	3	1	1	1	1
8 Traditional professional occupations	1	1	1	1	1	1	1

Office use: page to be completed later
………………………………………………...………….

Office use: page to be completed later …………………………………………………………...……….

Initial Results

Results back, date:	☐☐ / ☐☐ / 2010		
Results checked	MetS confirmed	No longer MetS	Urgent action required ↓
Participant randomised		////	Contact GP / Pt according to SOPs
Letter to participant			
Results letter to GP			

Additional Results

HbA1c result back		Sent to GP	
Urine ACR result back		Sent to GP	

Data entry

RESULTS PUT ONTO DATABASE ☐

DATA ENTRY COMPLETED for baseline CRF ☐

Participant ID №:

Date of appointment:

☐☐☐☐☐☐☐   ☐☐ / ☐☐ / ☐☐

TRIMS Study

Self-completion Questionnaires

Booklet to be completed by volunteer

INSTRUCTIONS

Whilst you are waiting please could you answer the questionnaires in this booklet.

When you have finished please could you check that you haven't missed any answers

THANK YOU

EQ5D QUESTIONNAIRE

EQ5D - Health Questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities _(e.g. work, study, housework, family or leisure activities)_

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

EQ5D_selfcompletionquestionnaire_TRIMSstudy   1

Best
imaginable
health state

100

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

90

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

80

70

60

**Your own
health state
today**

50

40

30

20

10

0

Worst
imaginable
health state
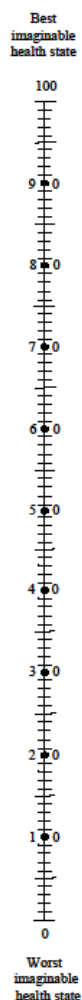
Eating Habits Questionnaire

<u>Purpose</u>

The purpose of this questionnaire is to get an idea of your usual eating habits. For the listed foods, we would like to know how many servings you eat in a typical day or week. A serving is an average portion that would be served at a meal. If you usually eat more than one serving of the food at a time, you should count all the servings you eat.

<u>Instructions</u>

For each food listed, tick the box that describes the number of servings that you usually eat. If you never eat a particular food, tick the box under "None".

Please do not leave any lines blank.

About how many pieces or slices per day do you eat of the following types of bread, rolls, or chapattis? (Please tick one box on each line)

Breads & Rolls	None	Less than 1 a day	1 to 2 a day	3 to 4 a day	5 or more a day
1. White bread or rolls, chapattis or parathas					
2. Brown bread or rolls, or brown chapattis, or parathas					
3. Wholemeal bread or rolls, chapattis, or parathas					

About how many servings per week do you eat of the following types of breakfast cereal or porridge? (Please tick one box on each line)

Breakfast cereals	None	Less than 1 a week	1 to 2 a week	3 to 5 a week	6 or more a week
4. <u>Sugared type</u>: Frosties, Coco Pops, Ricicles Sugar Puffs <u>Rice or Corn type</u>: Corn Flakes, Rice Krispies, Special K					
5. <u>Porridge</u> or Ready Brek <u>Wheat type</u>: Shredded Wheat, Weetabix, Fruit 'n Fibre, Puffed Wheat, Nutri-grain, Start <u>Muesli type</u>: Alpen, Jordan's					
6. <u>Bran type</u>: All-Bran, Bran Flakes, Sultana Bran					

About how many **servings per week** do you eat of the following foods?
(Please tick one box on each line)

	Vegetable foods	None	Less than 1 a week	1 to 2 a week	3 to 5 a week	6 to 7 a week	8 to 11 a week	12 or more a week
7.	Pasta, rice, or dishes made from grains such as millet, semolina and cornmeal INCLUDE: plain boiled rice, rice and peas, pilau and biryani							
8.	Potatoes (excluding chips), yams, cassava, plantains, breadfruit, sweet potatoes or taro/eddo							
9.	Peas, lentils (dhal) or beans (including baked beans)							
10.	Other types of vegetables (cooked or raw as in salads)							
11.	Fruit (including fresh, frozen or canned fruit)							

About how many **servings per week** do you eat of the following foods?
(Please tick one box on each line)

		None	Less than 1 a week	1 to 2 a week	3 to 5 a week	6 or more a week
12.	Cheese (any except cottage)					
13.	Beef, pork, or lamb (for vegetarians: nuts) INCLUDE: burgers, sausages, bacon, ham, meat pies, meat curries, casseroles, and processed meat					
14.	Chicken or turkey (including processing types)					
15.	Fish (NOT fried fish)					
16.	ANY fried food INCLUDE: fried fish, fried chicken, chips, fried breakfast, samosas, West Indian soup or stew, fried rice, puris, and bhajis					

		None	Less than 1 a week	1 to 2 a week	3 to 5 a week	6 or more a week
17.	Cakes, pies, puddings, pastries or Indian sweets					
18.	Sweet or savoury snacks such as chocolate, crisps, biscuits, Bombay mix, sev and chanachur					

About how much of the following types of milk do you yourself use in a day, for example in cereal, tea, or coffee? (Please tick one box on each line)

	Milks	None	Less than a quarter pint	About a quarter pint	About half a pint	1 pint or more
19.	Full cream (silver top) or Channel Islands (gold top)					
20.	Semi-skimmed (green or red striped top)					
21.	Skimmed (blue checked top)					

About how many **rounded teaspoons per day** do you usually use of the following types of spreads, for example on bread, sandwiches, toast, potatoes, or vegetables?

	Spreads	None	1 a day	2 a day	3 a day	4 a day	5 a day	6 a day	7 or more
22.	Butter, ghee or margarine such as sunflower or olive spread, Flora, Vitalite, Clover, Olivio, Stork, Utterly Butterly								
23.	Low fat spreads (e.g. Shape, Delight, Flora Lite, half fat butter, half fat ghee, etc)								

What type of fat do you usually use for the following purposes?
(Please tick one box on each line)

		Butter, lard, or dripping	Solid cooking fat (White Flora, Cookeen) Half-fat butter Hard margarine (Stork) or ghee	Soft margarine (sunflower, soya) Reduced fat spread (olive, Flora Buttery, Olivio)	Vegetable oil or Low fat spread (Flora Light, Olivite, St. Ivel Gold) or peanut oil	No fat used
24.	As a spread on bread, chapattis, vegetables etc					
25.	For frying					
26.	For baking or cooking					

About how many portions of fruit, vegetables, or salad do you usually eat in a day?

Fruit, vegetables or salad	None	1 a day	2 a day	3 a day	4 a day	5 a day	6 a day	7 or more
Include: fresh, frozen, chilled, dried, canned or 100% juice. (NOT potatoes)								

GENERAL SELF-EFFICACY SCALE QUESTIONNAIRE

General Self-Efficacy Scale (GSE)

Please read each statement and then circle the most appropriate number to indicate how you feel right now, at this moment

		Not at all true	Hardly true	Moderately true	Exactly true
1)	I can always manage to solve problems if I try hard enough	1	2	3	4
2)	If someone opposes me, I can find the means and ways to get what I want	1	2	3	4
3)	It is easy for me to stick to my aims and accomplish my goals	1	2	3	4
4)	I am confident that I could deal efficiently with unexpected events	1	2	3	4
5)	Thanks to my resourcefulness, I know how to handle unforeseen situations	1	2	3	4
6)	I can solve most problems if I invest the necessary effort	1	2	3	4
7)	I can remain calm when facing difficulties because I can rely on my coping abilities	1	2	3	4
8)	When I am confronted with a problem, I can usually find several solutions	1	2	3	4
9)	If I am in trouble, I can usually think of a solution	1	2	3	4
10)	I can usually handle whatever comes my way	1	2	3	4

GSEscale_selfcompletionquestionnaire_TRIMSstudy

Hospital Anxiety and Depression Scale (HADS)

GL assessment
the measure of potential

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more.

This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

A D
                                                                                                A D

I feel tense or 'wound up'
Most of the time
A lot of the time
From time to time, occasionally
Not at all

I still enjoy the things I used to enjoy
Definitely as much
Not quite so much
Only a little
Hardly at all

I get a sort of frightened feeling as if something awful is about to happen
Very definitely and quite badly
Yes, but not too badly
A little, but it doesn't worry me
Not at all

I can laugh and see the funny side of things
As much as I always could
Not quite so much now
Definitely not so much now
Not at all

Worrying thoughts go through my mind
A great deal of the time
A lot of the time
Not too often
Very little

I feel cheerful
Never
Not often
Sometimes
Most of the time

I can sit at ease and feel relaxed
Definitely
Usually
Not often
Not at all

I feel as if I am slowed down
Nearly all the time
Very often
Sometimes
Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach
Not at all
Occasionally
Quite often
Very often

I have lost interest in my appearance
Definitely
I don't take as much care as I should
I may not take quite as much care
I take just as much care as ever

I feel restless as if I have to be on the move
Very much indeed
Quite a lot
Not very much
Not at all

I look forward with enjoyment to things
As much as I ever did
Rather less than I used to
Definitely less than I used to
Hardly at all

I get sudden feelings of panic
Very often indeed
Quite often
Not very often
Not at all

I can enjoy a good book or radio or television programme
Often
Sometimes
Not often
Very seldom

Now check that you have answered all the questions

A D

TOTAL [ ] [ ]

f:\institut\cultadep\project4480\study4480\questionnaire\original\forproject\hadsukorig03_mapi.doc_16/01/08_aja

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE
SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the <u>last 7 days</u>. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

    _____ days per week

    ☐ No vigorous physical activities ➡ *Skip to question 3*

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

    _____ hours per day

    _____ minutes per day

    ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

    _____ days per week

    ☐ No moderate physical activities ➡ *Skip to question 5*

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

    _____ hours per day

    _____ minutes per day

    ☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

    _____ days per week

    ☐ No walking ➡ *Skip to question 7*

6. How much time did you usually spend **walking** on one of those days?

    _____ hours per day

    _____ minutes per day

    ☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

    _____ hours per day

    _____ minutes per day

    ☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

University Hospitals of Leicester **NHS**
NHS Trust
Department of Diabetes Research
Leicester Royal Infirmary

University of Leicester

The TRIMS Study
Department of Health Sciences
University of Leicester
22-28 Princess Road West
Leicester
LE1 6TP
Tel: 0116 2523212
E-mail: ajd38@le.ac.uk

INTERVIEW - INVITATION LETTER

Dear **Name DOB**

Thank you for taking part in the TRIMS study and recently attending the group education sessions for people with metabolic syndrome.

In order to get your feedback and find out what you thought about the education sessions, we would like to invite you to be interviewed.

Enclosed is an extra information sheet that explains more about the interview and what will happen if you agree to participate. Once you have read this information, if you would like to volunteer to be interviewed please complete the reply slip enclosed with this letter. The reply slip also asks for some information about you. This is so we can include different types of patients in the study, for example patients in differing age groups. To help to achieve this, we would like as many patients as possible to volunteer at this stage, but please note that we may not need to interview all those who volunteer.

We hope you will agree to be interviewed.

Yours sincerely

Alison Dunkley
Research Nurse
Tel: 0116 252 3212,
E-mail: ajd38@le.ac.uk

Prof Kamlesh Khunti
Professor of Primary Care Diabetes
& Vascular Medicine, & GP

Prof Melanie Davies
Professor of Diabetes
Medicine

INTERVIEW LETTER OF INVITATION
Qualitativefeedback_TRIMS_Letterofinvitation1.doc
Revised:

Version 1, dated 01/09/2008
Last saved: 03/10/2008

University Hospitals of Leicester **NHS**
NHS Trust
Department of Diabetes Research
Leicester Royal Infirmary

University of Leicester

TRIMS Study,
Department of Health Sciences,
University of Leicester,
22-28 Princess Road West,
Leicester, LE1 6TP.
Tel: 0116 252 3212
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TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured self-management education programme for people with metabolic syndrome)

EXTRA PARTICIPANT INFORMATION – Qualitative feedback

You are being invited to give us feedback of your experiences of attending the group education sessions. Please take time to read the following information carefully. Please ask us if there is anything that is not clear or you would like more information. This information is extra to the original participant information sheet you were given (Version 1, dated: 01/09/2008) for the TRIMS study.

Why are you asking for feedback?
We are trying to find out what people think about their experiences of attending the group education sessions for people with metabolic syndrome.

What will be involved if I take part?
If you return the reply slip one of the researchers will contact you by telephone and arrange a convenient time and date to interview you. The interviews will normally be carried out over the telephone, in people's homes or at the place where the education sessions were held. Interviews will last about half an hour and will be recorded using an audio recorder.

Do I have to take part?
No, we are looking for volunteers. It is possible that we may not need to use everyone who volunteers for the interviews, but if you offer to be interviewed and we find that we don't need you, we will let you know this. However, we would like as many people as possible to offer to be interviewed so that we can select a good variety of people, for example, men and women and people of different age groups. Even if you volunteer and agree to take part, you can change your mind at any time, without giving a reason.

Who can volunteer?
Any participant who attended the group education sessions.

Will the interview be confidential?
The audio-recording will be treated in the strictest confidence and will be stored without your name on it. Anyone who takes part can request a copy of their interview tape if they wish. The audio-recording will be destroyed at the end of the study and your name will not be mentioned in the results.

What do I do if I decide to volunteer?
If you have decided to volunteer to take part in the study, please sign the enclosed consent form and return it to the university research team in the envelope provided. This does not need a stamp.

If you still have any questions about the study please feel free to contact:
Alison Dunkley (Research Nurse), Division of General Practice & PHC, Department of Health Sciences, University of Leicester, 22-28 Princess Road West, Leicester, LE1 6TP. Tel: 0116 252 3212 or E-mail: ajd38@le.ac.uk.

EXTRA PARTICIPANT INFORMATION – QUALITATIVE FEEDBACK
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Revised:

Version 1, Dated: 01/09/2008
Last saved: 16/09/2008
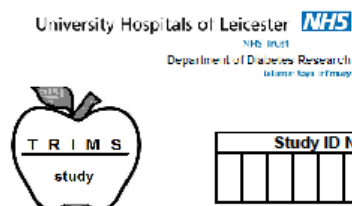
University Hospitals of Leicester NHS

NHS Trust

Department of Diabetes Research

University of Leicester

The TRIMS Study
Department of Health Sciences
University of Leicester
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Leicester
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T R I M S study

Study ID N°

INTERVIEW REPLY SLIP

TRIMS (The Reversal Intervention in Metabolic Syndrome) Study
(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

1) I would like to volunteer to be interviewed as part of the TRIMS study. I agree to a member of the research team contacting me by telephone to arrange an appointment to be interviewed.

SIGNATURE: _____ DATE: _____

FULL NAME: _____

ADDRESS: _____

TELEPHONE NUMBER: _____

2) *We may not need to interview everyone who volunteers. To help us to choose a range of different types of people for the interviews, it would be very helpful if you could provide the following information about yourself:*

i) What is your age group? 30-39 [ ]   40-49 [ ]   50-59 [ ]   60-69 [ ]

ii) Are you? Male [ ]   Female [ ]

ii) How would you describe your ethnic origin? White [ ]   Asian [ ]   Other [ ]

PLEASE NOTE: The information you have given us will be destroyed when no longer needed for choosing people to be interviewed and for contacting volunteers. If you volunteer but are not selected for the interview, we will let you know.

Thank you very much for offering to help us in this way. Please return this form to the University of Leicester in the envelope provided, which does not need a stamp.

INTERVIEW REPLY SLIP   Version 1, dated 01/09/2008
Qualitativefeedback_TRIMS_InterviewReplySlip_Version1.doc   Last saved: 16/09/2008
Revised:

PARTICIPANT CONSENT FORM
(INTERVIEW)   (Version 2, 19th December 2008)

University of Leicester
Department of Health Sciences

Study ID N°

University Hospitals of Leicester NHS

N-S Trust
Department of Diabetes Research

TRIMS (The Reversal Intervention for Metabolic Syndrome) Study

(A randomised controlled trial to investigate the effects of a structured
self-management education programme for people with metabolic syndrome)

Principal investigator: Prof K Khunti (Professor of Primary Care Diabetes & Vascular Medicine, & GP)
Co-investigators: Alison Dunkley (Research Nurse), Prof M Davies (Professor of Diabetes Medicine)

Please write your initials in each box

1) I confirm that I have read and understood the extra information sheet for qualitative feedback (Version 1, dated: 01/09/2008). [1]

2) I consent to being interviewed about the group self-management education programme for people with metabolic syndrome. [2]

3) I agree to the interview being audio-recorded and used anonymously for research purposes. [3]

4) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, and without my medical care or legal rights being affected. [4]

5) I agree that all information collected about me as part of the interview can be stored and analysed by the research team at the University of Leicester, and that small parts of what I say may be quoted anonymously when the results of the research are reported. [5]

6) I have had an opportunity to ask questions and I understand what taking part involves. [6]

NAME OF PARTICIPANT (PRINT) _____ SIGNATURE _____ DATE _____

NAME OF RESEARCHER (PRINT) _____ SIGNATURE _____ DATE _____

INTERVIEW – FEEDBACK - PARTICIPANT CONSENT FORM   Version 2 Dated 19/12/2008
InterviewQualitativefeedbackTRIMSPatientConsentFormVersion2.doc   Last saved: 19/12/2008
Revised: 19/12/2008

Interview Topic Guide - Patients attending the TRIMS group education sessions

1. Prior to the course

A. Feelings and understanding

i. When you were told that you had metabolic syndrome, how did you feel about that?

ii. Before you came onto the course, what did you know about metabolic syndrome?

Probe:
- Did you understand what it meant or not?

B. Pre-course materials

i. What did you think of the booklet/leaflet that was sent to you before you started the course?

2. Practicalities

i. What did you think of the place where the education sessions were held?

ii. What about the time of day when the education sessions were held?

iii. What about how long they lasted, were they too long, too short or about the right length of time?

iv. What about the number of sessions?

3. Specific aspects of the course

I now want to ask you about particular bits/parts of the course, different things that were covered. You may not be able to remember everything, and that's ok. Don't worry if you can't. It's not a test.

A. Patient Story

i. At the start of the course you were asked to share your experiences and thoughts about metabolic syndrome with the rest of the group.

Prompt - the educator asked each person in the group their name, what they knew or had heard about metabolic syndrome, any questions they had.

Probe:
- How did you feel about this?
- Was it useful to hear others experiences or not?

B. Understanding metabolic syndrome

i. Can you remember the section of the course on what metabolic syndrome is? What goes wrong in the body to cause metabolic syndrome?

Prompt
- the educator used a magnetic board to build up a picture of how the body uses and stores energy – fats and glucose

Probe:
- Can you tell me what you remember about how weight around the middle (large waist size) affects your health?
- Can you tell me what you remember about insulin resistance, rusty or blocked locks?
- How easy or difficult was this bit of the course to understand?

Interview Topic Guide - Patients attending the TRIMS group education sessions

ii. Do you feel it important or not important to have this explained?

Probe: Why is that? How does it help you?

C. Health profile / results

i. Can you remember being given your blood test results and measurements, and plotting them on your own health profile?

Probe:
- How did you feel about this?
- Was it useful or not?

ii. Are you likely or unlikely to use the extra health profiles you were given in your handbook?

Probe: Why is that?

D. Physical activity

i. There were some activities/games on the first week about physical activity?
What messages about physical activity can you remember?

Prompt: Can you remember anything that you were told about ....
- *How much activity/exercise you should aim to do each day?*
- *Amount of time*
- *Number of steps*

Probe:
- Do you feel these messages were useful or not?
- Anything in particular you found useful?

ii. How likely or not are you to carry on using the pedometer and logbook you were given?

Probe:
- Why is that?

E. Food games

i. A lot of the activities/games on the second week were about making changes to what you eat and drink.
What messages about food can you remember?

Prompt: Can you remember anything that you were told about..........
- *Fat*
- *Alcohol*
- *Fruit/salad/veg*
- *Fibre*
- *Salt*
- *Omega-3 / Oily fish*
- *Portion size*

Probe:
- Do you feel these messages were useful or not?
- Anything in particular you found useful?

ii. How likely or not are you to use the food diary you were given?

Probe:
- Why is that?

1

2

Interview Topic Guide - Patients attending the TRIMS group education sessions

~~E. Action planning / behaviour change~~

i. Can you remember the last part of the course when you identified one thing that you wanted to change and made a plan of how you were going to do this?

Prompt – you wrote it down and gave yourself a score for how successful you thought you'd be.

Probe:
- How did you feel about this?
- Was it useful or not?

ii. Do you think you are likely or unlikely to use the extra action plans you were given in your handbook?

Probe: Why is that?

iii. What do you think about showing or discussing the plan with your dr or nurse or not?

Probe: Why is that?

4. Handbook

i. As part of the course you were given a handbook (some leaflets in a folder) to keep. Can I check if you've looked at it since the course?

YES
Probe:
- Do you think it's useful or not useful?
- Would you've liked any extra information in the handbook? What?

NO
Probe:
- Do you think you will you look at it in the future or not?
- Why

5. Delivery of the course

I am now going to ask you about the educators and how the course was delivered

i. How did you find the course, was it difficult or easy to understand?

ii. How did you find the speed at which the course was delivered?

iii. How did you feel when the educator asked the group for their ideas, experience and questions?

iv. Overall how did you find the games and activities? Was that a good way of learning?

v. Did you feel uncomfortable about anything in the way the course was delivered or didn't feel like that all?

vi. Do you think you learnt anything from the other people in the group or would you have preferred one to one education sessions?

6. Overall

i. After attending the course, do you feel as if you know more about metabolic syndrome than you did before or not?

ii. Do you now think you are able to do something to improve your future health or not?

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Interview Topic Guide - Patients attending the TRIMS group education sessions

i. Some people have said that going on a course like this, has given them the skills and confidence to make changes to their lifestyle (diet and exercise). Do you feel the same way?

ii. If you were being very honest with yourself, are you likely to make any changes after attending the TRIMS course or not?

YES
Probe:
- What things do you think you'll change?

FINALLY
What do you think is the most important thing that you've learnt from the course?

....

THANK YOU.......................................

(If participants ask, research nurse will arrange an appointment to repeat blood tests and measurements in approx 6 months.)
(Any questions or concerns can ring Alison, tel:. 0116 2523212)

....

Additional probes
- How did you feel about that?
- What did you think about that?
- Why?

4

Appendix 7:

Copies of published manuscripts

Please note, the full versions of published articles are included in the print version of this thesis, which is available to view at the University of Leicester's David Wilson library.

Dunkley AJ, Davies MJ, Stone M A , Taub NT, Troughton J, Yates T, Khunti K. The Reversal Intervention for Metabolic Syndrome (TRIMS) study: rationale, design, and baseline data. TRIALS 2011;12:107

Available at: http://www.trialsjournal.com/content/12/1/107

Dunkley A J, Stone M A, Patel N, Davies MJ, Khunti K. Waist circumference measurement: knowledge, attitudes and barriers in patients and practitioners in a multi-ethnic population. Family Practice 2009; 26(5):365-371

Available at: http://fampra.oxfordjournals.org/content/26/5/365.full

Dunkley AJ, Davies MJ, Khunti K. Metabolic Syndrome. General Practice UPDATE 2008;1(3):32-39.

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