NIHR HTA Programme

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The NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), based at the University of Southampton, manages evaluation research programmes and activities for the NIHR

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DETAILED PROJECT DESCRIPTION (Protocol version 3, 25/09/2012)

1. PROJECT TITLE
SYSTEMATIC REVIEWS AND INTEGRATED REPORT ON THE QUANTITATIVE AND QUALITATIVE EVIDENCE BASE FOR THE MANAGEMENT OF OBESITY IN ADULT MEN

2. PLANNED INVESTIGATION

2.1 Aim
The aim is to systematically review evidence-based management strategies for treating obesity in men, and how to engage men in these obesity services.

2.2 Research objectives
The overarching objective is to integrate the quantitative and qualitative evidence base for the management and engagement of men with obesity in weight loss services, researching concurrently to systematically review:

- The effectiveness and cost-effectiveness of interventions for obesity in men, and men in contrast to women.
- The effectiveness and cost-effectiveness of interventions to engage men in their weight reduction.
- Qualitative research with men about obesity management, and providers of such services for men.

2.3 Existing research
2.31 Burden of disease
More men than women are overweight or obese in the UK and this gender difference is projected to continue. In the Health Survey for England 2008 65.9% of men had a body mass index (BMI) of 25kg/m^2 or over (overweight or obese) whilst 56.9% of women fell into this category (NHS, 2009). The Foresight Report (Government Office for Science, 2007) predicted that 36% of men and 28% of women could be obese by 2015 and 60% of men and 50% of women could be obese by 2050. Although the Foresight Report predicts that future costs to the NHS of elevated BMI could be £6.4 billion/y by 2015 and £9.7 billion/y by 2050, no breakdown by gender is given, despite there being clear gender differences for the risk of diseases related to obesity, such as coronary heart disease and type 2 diabetes. Men are less likely to realise they have a weight problem (Kamel & McNeill, 2000) and less likely to come forward for help with weight loss (Gray *et al.*, 2009). In the Counterweight programme for obesity management in 65 general practices in seven UK regions only 23% of participants were men (Counterweight Project Team, 2008). Compared to women, men are likely to have different knowledge of cooking skills and nutrition, and different perceptions of and responses to group-based approaches (Allan *et al.*, 2010) and predominantly female weight management advisors.

2.32 Existing reviews
In an extensive search we have been unable to find any previous systematic reviews, ongoing reviews, or parts of systematic reviews or guidance (e.g. National Institute for Health and Clinical Excellence, NICE, 2006; Scottish Intercollegiate Guidelines Network, SIGN, 2010) which have specifically examined the engagement and management of men with obesity for weight loss. Two of us systematically reviewed health promoting interventions for men (Robertson *et al.*, 2008), which covered a range of health behaviours (e.g. smoking, attending

for prostate cancer screening) but not weight loss in obese men. NICE obesity guidance (NICE, 2006) discusses seven randomised controlled trials (RCTs) in men only, but did not bring these reports together to provide guidance for men. The Men's Health Forums convened a conference in 2005 of 23 health and social policy researchers about men and weight issues; the outcomes of this conference were subsequently published in a book (White & Pettifer, 2007). Evidence of effective interventions was not reviewed, although several examples of innovative approaches in the UK were presented. The conclusions from the book included a need to invest in 'male sensitive approaches', that 'men's attitudes to weight and weight loss need to be more fully understood' and that the "existing, broadly 'unisex', approach is failing men".

2.33 Current practice

In Scotland we have recently completed a survey on the provision of weight loss services including the NHS and commercial sector. We identified only three programmes specifically for men (Wrieden & Avenell, 2010).

2.4 Research methods

2.41 Design

The systematic reviews to be undertaken concurrently are:

1. Systematic review of RCTs of interventions (lifestyle and/or the UK licensed medication orlistat) with men only who are obese with BMI of $\geq$30kg/m^2 (or overweight with BMI $\geq$28 kg/m^2 with cardiac risk factors based on orlistat guidance) with follow up of at least one year, any setting.
2. Systematic review of RCTs of interventions, as above, including women who are obese with BMI of $\geq$30kg/m^2 (or overweight with BMI $\geq$28 kg/m^2 with cardiac risk factors based on orlistat guidance) where results are presented separately by gender in the same trial, using the same inclusion criteria for both genders, in any setting.
3. Systematic review of interventions for men with obesity in the UK, any setting, any study design, any duration.
4. Systematic review of interventions to increase engagement of men with services for obesity management, any study design.
5. Systematic review of qualitative research with men, or men in contrast to women with obesity; health professionals and commercial organisations managing obesity.

2.42 Health technologies being assessed

Technologies to be reviewed are (a) lifestyle (e.g. diet, physical activity, behaviour change techniques or combinations of any of these) and drug interventions for the management of obesity in men, and (b) interventions to increase participation of men in any services aiming to reduce obesity, e.g. community outreach services, incentive schemes and web-based initiatives. The technologies in (a) are currently in use, and have in the past been reviewed by NICE in 2006 and SIGN in 2010, with no guidance with respect to gender. Increasing the uptake of services by men would increase total costs (but is in keeping with legislation on Gender Equality Duty), assuming that there was no change to uptake of services by women. Orlistat for weight loss have been estimated by NICE to cost £24431/Quality Adjusted Life Year (QALY) and lifestyle interventions £174-£9971/QALY (NICE, 2006). We may be able to identify ineffective interventions, which may save NHS costs.

2.43 Search strategy

The search strategy for RCTs and economic evaluations will be based on our previous systematic review (Avenell *et al.*, 2004), using the databases Medline, Embase, Cinahl, The

Cochrane Controlled Trials Register, Cochrane Systematic Reviews, Database of Abstracts of reviews of Effectiveness (DARE), Health Technology Assessment database, NHS Health Library, Psycinfo, NHS Economic Evaluations Database (NEED). We will search the Applied Social Sciences Index and Abstracts (ASSIA), British Nursing Index, Anthropology Plus and Social Science Citation Index, reference lists of included studies. We will search the Picker and Joanna Briggs Institutes for grey literature. We will contact the Men's Health Forums (MHFs) in the UK, Association for the Study of Obesity (ASO), Dietitians in Obesity Management (DOM) and commercial organisations to identify unpublished UK studies. We will search the internet for online weight loss programmes specifically targeted at men (e.g. http://www.fatmanslim.com). We will contact authors of the identified studies for published and unpublished qualitative research. There will be no language restrictions, but studies must be relevant to the UK and full text reports.

2.44 Quantitative reviews methodology

Inclusion and exclusion criteria

Study design

Systematic reviews 1 and 2 will include only RCTs or quasi-randomised trials (including trials with a cluster design) with a mean or median duration of 52 weeks or over for all groups. This duration of follow-up for data is to ensure that long-term weight loss and maintenance interventions are evaluated, with their associated effects on obesity-related morbidities (Avenell *et al.*, 2004). This was also the minimum duration of studies adopted by NICE for its review (NICE, 2006).

For systematic review 3, addressing reports of UK interventions for men, any study design and length of intervention will be considered in order to include and evaluate as much UK relevant research as possible. In the event that few eligible studies of men only are identified we will include data for men from studies reporting outcomes for men and women to maximise our available UK evidence base, and relevant data from abstracts and posters.

For systematic review 4 we will include any study design that examines interventions to increase engagement of men with services for obesity management.

For systematic review 5, we will include any study reporting qualitative research with men, or men in contrast to women with obesity; health professionals and commercial organisations managing obesity. This review will also include any relevant qualitative data identified in reports of studies in systematic reviews 1-4.

Participants

Studies must include men with a mean or median age of 16 years or over, with no upper age limit. Studies particularly examining men with obesity related to psychotropic medication, learning disability or diagnosed eating disorder will not be included. All groups of participants in studies for the systematic reviews 1, 2 and 3 must have a mean or median BMI of $\geq$30kg/m^2 ($\geq$28 kg/m^2 with cardiac risk factors based on criteria for orlistat). Where the BMI is not provided, but body weight is provided we will calculate BMI using relevant population data for heights (Avenell *et al.*, 2004). We recognise that the BMI of men being targeted in systematic reviews 4 and 5 may not be clearly stated, and may include men with a BMI below these cut-offs. Studies with these participants will be included in systematic reviews 4 and 5.

Interventions

For systematic reviews 1-3 we will include interventions in the form of orlistat (but not sibutramine or rimonabant, which no longer have UK licences), diet, physical activity, behaviour change techniques or combinations of any of these. Complementary therapy, e.g. acupuncture, and non-diet products promoted for weight loss available solely over the counter will also not be included. Studies evaluating bariatric surgery will also not be included. Weight loss or weight gain prevention must be explicitly stated as the main outcome of the studies. Studies examining a combination of interventions, e.g. smoking cessation and weight loss at the same time will not be included.

Systematic review 4 will examine any form of intervention to increase engagement of men with services for obesity management, with any study design.

Systematic review 5 will examine qualitative data from interventions eligible for systematic reviews 1-4, but also any other qualitative research reports either linked or not linked to specific interventions.

Setting

All settings for the lifestyle and drug interventions will be reviewed, including hospital, primary care, community (including community pharmacy), commercial organisations, voluntary sector, leisure centres, workplaces, internet and other digital domains, e.g. mobile phone networks. This is because there is increasing collaboration between the NHS and non-NHS organisations in delivery of services, and it may also be that increasing participation of men in obesity services may require their engagement in settings outside primary and secondary care.

Outcomes

The quantitative outcomes to be reported in the systematic reviews will include changes in weight, waist circumference, cardiovascular risk factors (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, fasting glucose, HbA1c, systolic and diastolic blood pressure), disease specific outcome measures including those particularly relevant to men such as erectile function, adverse events and quality of life outcomes. We will also collect process outcomes (e.g. staff involvement, setting, type of intervention, timing, frequency, individual and/or group setting, couple or family setting, proportion recruited and dropping out, participants' evaluations). Data on costs and economic evaluations will be collected (see page 14 for details of protocol for cost-effectiveness systematic review). Outcomes to be collected will be developed in consultation with the project advisory group.

Quantitative reviews data collection and analysis

The methods we will follow are based on those of our previous review (Avenell *et al.*, 2004).

Selection of studies

One reviewer will review the titles and abstracts of potentially eligible reports identified in the searches and a second researcher will screen these before full copies are obtained for assessment. Differences in opinion will be resolved by consensus or discussion with a third member of the team, if required. References will be stored using Reference Manager software.

Data extraction and management

One reviewer will extract details of study design, methods, participants, interventions, settings and outcomes, which will be checked by a second member of the team. Data entry into

Review Manager software (Version 5.0.24 or later as appropriate) will also be checked by a second member of the team.

Quality assessment

We will assess methodological quality of individual randomised controlled trials using a quality assessment tool adapted from the Cochrane Collaboration's tool for assessing risk of bias (Higgins *et* al., 2011). The methods used for assessing quality in non-randomised studies reporting quantitative data will be based on those used by the Health Services Research Unit, HSRU (University of Aberdeen) for technology assessment reviews (TARs) for NICE. A 14 question checklist will be used to assess the quality of RCTs (Verhagen *et al*., 1998) and a 17 question checklist for non-randomised comparative studies and case series. The development of both checklists was led by HSRU in partnership with the Review Body for Interventional Procedures for NICE. The checklists rate bias, generalisability, sample definition and selection, description of the intervention, outcome assessment, adequacy of follow-up, and performance of the analysis. One reviewer will extract the data and a second will check the data extraction. Differences in opinion will be resolved by consensus or discussion with a third member of the team, if required.

Statistical analysis

We will report means or changes in means or proportions between groups. For continuous outcomes we will report mean difference or standardised mean difference (different scales for the same outcome), and risk ratio for dichotomous data, with 95% confidence intervals.

Previous experience has shown that standard deviations for weight and risk factor data, required for meta-analysis, are sometimes missing. We will therefore use the methods we previously developed for assumed values (Avenell *et al.*, 2004), if we are unable to obtain these data from authors within one month of contacting them.

We will use Review Manager software (Version 5.0.24 or later as appropriate) for data synthesis for RCTs. Interventions will be categorised for analysis according to our previous review (Avenell *et al.*, 2004). Previous experience of reviewing trials of obesity interventions has revealed considerable heterogeneity in the studies assessed. We will therefore use random effects meta-analysis throughout. In studies with data at multiple follow-up times we will report data in meta-analyses with time periods aggregated to the nearest six months.

Subgroup analyses will explore whether the effectiveness of interventions differs according to whether all participants are selected on the basis of newly diagnosed or pre-existing obesity related co-morbidities (e.g. diabetes, hypertension) or not. If sufficient data are available, we will also explore the effect of deprivation, age, and ethnicity on effectiveness. In sensitivity analyses we will explore the effect of assumed values for weight and cardiovascular risk factor outcomes on meta-analyses.

We will use visual inspection and the I^2 statistic to assess heterogeneity in forest plots (Higgins *et al*., 2011). We will undertake funnel plots to analyse reporting biases for forest plots with 10 or more studies which report mean differences.

The role of gender as a treatment modifier will be explored by conducting a meta-analysis of the treatment by gender interaction effect across trials. Using standard methods, the interaction effect can be calculated for an individual trial where outcome data have been reported by gender (Altman & Bland, 2003).

The methods for incorporating economics evidence into the reviews will follow those recommended in The Cochrane Handbook (Higgins *et al*., 2011), and a narrative synthesis will be presented.

2.45 Qualitative synthesis methodology (systematic review 5)

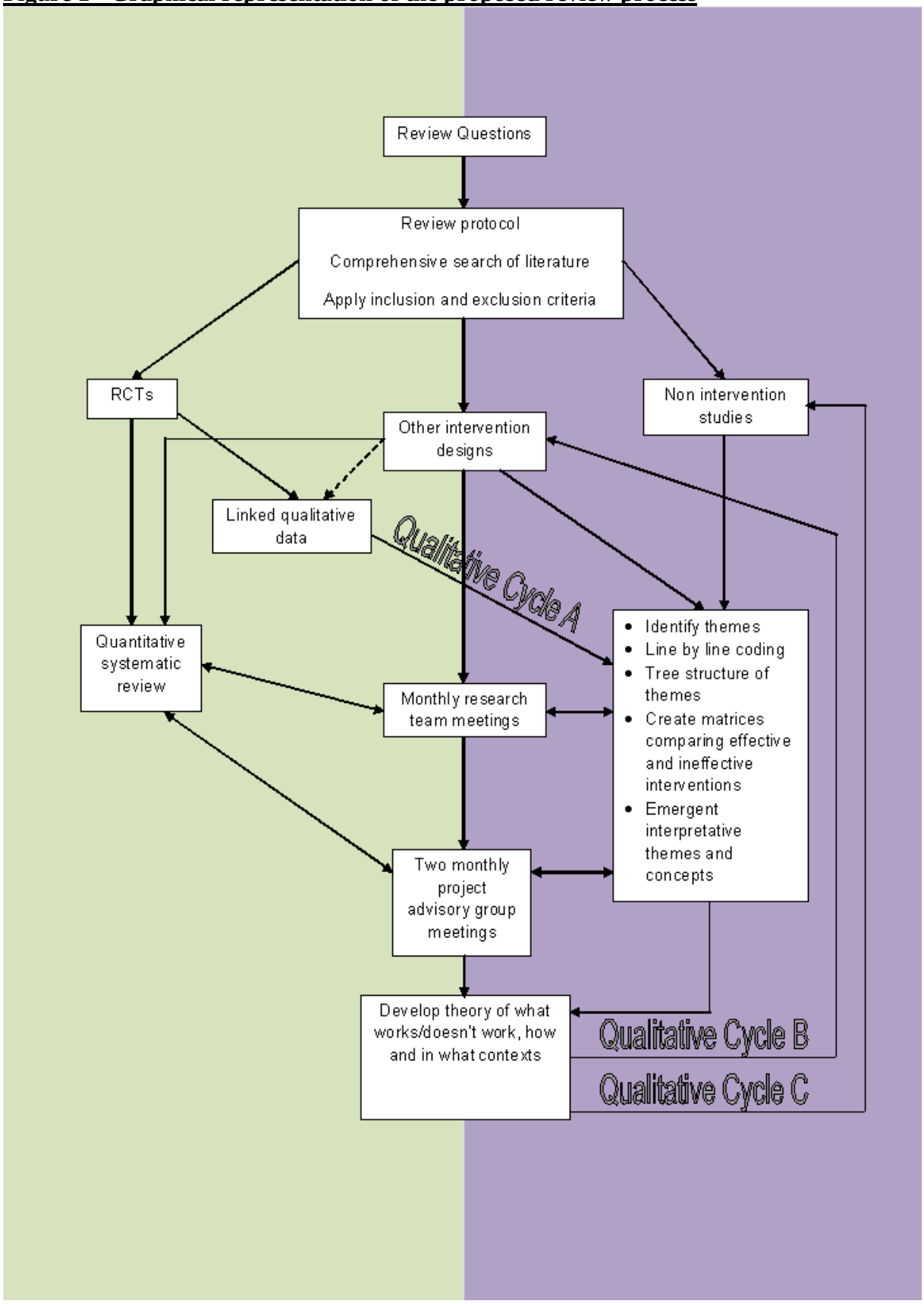
There is no single agreed method for synthesising and integrating quantitative and qualitative research evidence in a systematic review, and this is a rapidly developing field (Pope *et al.*, 2007). In recent years, the field of synthesising evidence from qualitative primary studies has also witnessed the emergence of a number of different approaches; each is based on a different epistemological viewpoint (Barnett-Page & Thomas, 2009; Spencer *et al.*, 2003). As Barnett Page & Thomas (2009) argue, the products of some qualitative synthesis reviews can be complex and conceptual and (in their opinion), tend to require further interpretation by policy makers and practitioners. Furthermore, some methods can be very time and resource intensive. To address these criticisms and in recognition that there are ongoing debates about the inherent strengths and limitations of methods used to synthesise quantitative and qualitative evidence, we propose a tailored approach, which specifically intends to inform policy and practice.

Our own overall philosophical position might be best described as one that corresponds most closely to a 'realist' perspective (Pawson, 2006; Spencer *et al.*, 2003), as we are concerned with trying to find out not only 'what works' for men in terms of weight management, but also 'for which men, and under what circumstances'. At the same time, our team of researchers span a range of clinical, sociological and social science disciplines, which represents a broad range of perspectives. Our pragmatic approach is informed by and uses aspects of review methods such as critical interpretative synthesis (Dixon-Woods *et al.*, 2007); thematic synthesis (Thomas & Harden, 2005); framework synthesis (Brunton *et al.*, 2006), and analytical approaches developed from methods of inquiry such as grounded theory (Strauss & Corbin, 1994). We intend to employ deductive and inductive analytical approaches throughout the review process.

As such, we have defined *a priori* research questions, but we also aim to generate new research questions inductively from the data to build theory (about what works, for whom, etc.) using, for example, constant comparative method, and searching for disconfirming evidence to falsify any emerging theory or theories.

The following steps have been identified to guide our iterative review process, but these may be modified depending on the studies we identify and the themes, concepts and/or issues that emerge. Modification of study design, mid-review, has been described elsewhere by Thomas & Harden (2008). (See Figure 1 for a graphical representation of the proposed review process.)

Figure 1 - Graphical representation of the proposed review process



Step 1: A priori research questions
We aim to uncover how effective interventions work (if they exist), and describe key intervention ingredients, processes, environmental and contextual factors that contribute to effectiveness (Pawson, 2006). We also aim to identify the barriers and facilitators men experience when engaging with a weight management intervention. The specific research questions are:

1. What are the best evidence-based management strategies for treating obesity in men?
2. How can men's engagement in obesity services be improved?

Step 2: Literature search (see also section 3.43)
We intend to use multiple strategies to identify qualitative research as recommended by Shaw *et al.* (2004) and Grant (2004). As we are likely to identify a high number of 'false positives', we will need an information specialist to assist with this process. We will contact authors of RCTs and intervention studies to assist in identifying linked qualitative data.

Step 3: Apply inclusion and exclusion criteria to the study abstracts
All studies must include male participants, and must have overweight and weight management as the prime focus for the study. We will include studies that have taken place in developed countries only, and which are relevant to the UK. Two researchers will independently screen abstracts and where there is disagreement, the full paper will be obtained. Where consensus cannot be reached, it will be discussed at a research team meeting. All eligible study reports will be entered onto qualitative data management software.

Step 4: Use purposive sampling to group eligible studies into three categories
Two researchers will independently group the identified studies into the following categories:

A. Qualitative and mixed method studies linked to the identified RCTs, including any qualitative data reported as part of papers reporting quantitative outcomes, as recommended in critical interpretive synthesis (Dixon Woods *et al.* , 2007)
B. Qualitative and mixed method studies linked to RCTs not identified before as well as to the identified non-randomised intervention studies including any qualitative data reported as part of papers reporting quantitative outcomes.
C. Qualitative studies that are not linked to any specific intervention. This will include UK-based studies that contain men-only samples, drawing on the views, attitudes and perceptions of men who have had prior experience of taking part in formal weight management programmes and interventions, or who have attempted to reduce or mange their weight in other ways.

Separating intervention studies from non intervention studies is a feature of the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre) mixed synthesis process (EPPI-Centre, 2007). Synthesis of qualitative research has been criticised for de-contextualising the findings of individual studies (Thomas & Harden, 2008). As the focus of this review is to assess the evidence for weight management interventions, we believe that grouping the studies in this way will assist in maintaining the research and intervention and facilitate the integration of the quantitative and qualitative review processes.

A cyclical, sequential analysis will then proceed. During Qualitative Cycle A, qualitative data from Category A studies (RCTs of efficacy) will be analysed (see Steps 5 and 6 below for details) using the constant comparative method to indentify and understand the aspects of the intervention processes and context that relate to our research questions. Then, during

Qualitative Cycle B, using theoretical sampling, Category B studies (non-randomised intervention studies) will be identified and analysed in the same way and will confirm or refute the emerging themes and concepts identified during Qualitative Cycle A. During Qualitative Cycle C, Category C (non-intervention studies) will be theoretically sampled and analysed to further refine and validate our emerging analysis and theory.

Step 5: Quality assessment of included studies

There are many criteria for assessing the quality of qualitative research and little consensus, with some arguing about whether qualitative research can and should be assessed (Dixon Woods *et al.*, 2007). In line with common practice that has emerged amongst researchers conducting reviews that use thematic and framework approaches, two researchers will independently apply the Critical Appraisal Skills Programme, CASP, (Public Health Research Unit, 2006) quality appraisal criteria and consider the potential contribution of the studies to the review. If consensus cannot be reached, wider discussion with the research team will occur.

Step 6: The analysis cycle and thematic synthesis

The proposed analysis cycle will be repeated sequentially for each category of study. It will involve: coding the qualitative data; developing initial descriptive themes; and a final stage that involves the development of higher order analytical and interpretive themes and concepts. We believe this cyclical and iterative process will identify the promising 'ingredients' of interventions more likely to be effective in male weight reduction, both in terms of essential and necessary contextual/environmental variables, and intervention processes. Weekly local meetings and monthly teleconferences of the quantitative and qualitative researchers will ensure integration and fit between the qualitative and quantitative synthesis throughout the analytical cycle.

Development of a thematic index

Two researchers will independently code line by line the findings reported in the included qualitative studies (or qualitative data from quantitative studies) for content and meaning. After doing this for a sample of around five to eight studies with diverse interventions and differing outcomes (from Categories A and B) each qualitative researcher will independently develop a descriptive thematic index. The thematic index will enable us to remain close to the reported study findings. The thematic indices will be discussed with the full project team and through consensus a single thematic index with a tree structure of themes with sub-themes will be agreed.

One researcher will then apply the thematic index by coding line by line the findings reported in the category of qualitative studies (or qualitative data from quantitative studies) under consideration. The project review team will have access to qualitative data management software (NVivo), which will help manage and support the coding process and facilitate project review team discussion and quality control.

The development of interpretive themes

We will then generate interpretive themes or concepts from studies in each category. In meta-ethnography these are called 'third order interpretations' (Noblit, 1988). Qualitative researchers will independently develop interpretive themes for effective management of obesity in men and the barriers and facilitators for engaging in weight management programmes. In addition to the *a priori* questions specified for this review, it is anticipated that new relevant questions may emerge from either the quantitative or qualitative synthesis.

This is an inherent property of qualitative research and particularly a grounded theory approach where data collection and analysis proceed iteratively to confirm or refute an emerging theory. Project review team meetings and advisory group meetings will discuss (i) the findings; (ii) any new research questions arising from the quantitative and qualitative syntheses; and (iii) strategies for further interrogation of the data. Charts or matrices will be constructed for comparison of the emergent themes for effective and non-effective interventions. Studies may be grouped according to study design or by other characteristics which emerge from the analysis as important to theory development, Matrices will facilitate using the constant comparative method to search for patterns, relationships and assist with developing theory. After completing the analytical cycle for Category A and then B studies, Category C studies will then be read and include if they add a new a perspective or provide disconfirming evidence, following the principles of grounded theory. This will test the robustness of the synthesis as recommended in narrative synthesis methods (Pope *et al.*, 2007). These theoretically sampled studies will be systematically analysed according to the cycle described above. Finally, theoretical sampling will be used to search for disconfirming data or alternative perspectives in other reports. We do not envisage a linear process to this synthesis, but it will be an iterative process of asking new questions of the data and the analysis, to build and test theory. Our wide ranging literature search and review process will ensure the most recent developments to obesity interventions are included.

The project advisory group of Men's Health Forums' stakeholders will be formed to: ensure that the review is conducted in a systematic and transparent manner; to check for over-interpretation of data; to provide expert opinion on the credibility and plausibility of the thematic index and other emergent issues; and potentially, be able to provide sources for disconfirming data.

We will report our findings as a narrative synthesis combining and juxtaposing quantitative and qualitative findings.

2.5 Expected output of research

Our work will identify the existing evidence with which to develop guidance for the NHS on the subject of men and obesity management. The individual reviews and integrated report will also provide guidance on whether further research is needed to develop better methods for engaging and retaining men in obesity interventions. At least three research papers and two European and three UK conference presentations will result from this research and results will be widely disseminated to the lay community, policy-makers at regional and national level, NHS professionals and researchers, including contributors to the project.

2.6 Project timetable and milestones

Months 0-2: Protocol development, first project advisory group meeting.
Months 0-12: Literature searching; contacting interest groups for reports; quantitative and qualitative data extraction and quality assessment, data synthesis, monthly advisory meetings.
Months 13-15: Report preparation, conference abstract submissions and peer-reviewed papers.

3. STAFF

The project will be led from the Health Services Research Unit (HSRU) at the University of Aberdeen by Dr Alison Avenell (chief investigator). Principal investigators are Dr Flora Douglas (Population Health, University of Aberdeen), Dr Pat Hoddinott (HSRU, University

of Aberdeen), and Professor Edwin van Teijlingen, School of Health and Social Care, Bournemouth University).

The applicants, researchers and project advisory group (see below) will meet in person at the beginning of the project to discuss the protocol and sources of information. The same group will have teleconferences every two months with a particular focus on the interpretation of the emerging evidence. In the final three months of the project a further face-to-face meeting will discuss the draft final report and presentation of the findings to as wide an audience as possible.

All applicants and researchers will have monthly teleconferences, and there will be weekly meetings at the University of Aberdeen with the researchers and local applicants in Aberdeen.

4. PROJECT ADVISORY GROUP

We will link with three representatives from the Men's Health Forums England and Wales, Scotland, and Ireland, who will provide a project advisory group, as there is no relevant UKCRN. They will provide lay insights to enhance the utility and relevance of the research. Ms Douglas and Prof van Teijlingen had a productive collaboration with the Men's Health Forum Scotland on a project evaluating well men health services' pilots for Scottish Government Social Research. The Men's Health Forums previously convened and reported on a conference discussing weight issues in men (White & Pettifer, 2007), and supported the production of a practical guide for healthy living and weight loss in men (Banks, 2005).

5. ETHICAL ARRANGEMENTS

Ethical approval is not required for this project.

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ROMEO STUDY COST-EFFECTIVENESS PROTOCOL FOR SYSTEMATIC REVIEW

1. OBJECTIVES

To report costs, outcomes and cost-effectiveness of alternative strategies for the management of obesity in adult men.

2. SEARCH STRATEGY

Studies that report both costs and outcomes of alternative strategies of weight loss, providing a distinct and interpretable focus on strategies for the management of male obesity (this will include studies of male and female, where male results are reported separately) will be identified from randomised controlled trials. An extensive electronic search will be carried out to identify reports of relevant published and ongoing studies as well as grey literature. A highly sensitive search strategy will be developed using both appropriate subject headings and text word terms to identify reports on costs and weight loss strategies for the management of male obesity. The following databases will be searched:

- MEDLINE (1990 –current)
- MEDLINE-in-Process
- Embase (1990 – current)
- Health Management Information Consortium (1990 – current)
- NHS Economic Evaluations Database
- Cost-effectiveness Analysis Registry
- Research papers in economics

There will be no language restrictions but the search will be limited to studies published since 1990. The strategy that will be used for the multi-file search of Medline and Embase is detailed in the appendix 1.

One reviewer will screen the titles and, when available, abstracts of all reports identified by the search strategies. All potentially relevant reports will be retrieved in full and assessed independently by two reviewers. Any disagreement that cannot be resolved by consensus will be referred to a third party.

3. ELIGIBILITY CRITERIA

3.1 Types of studies

Full text studies that compare both costs and outcomes for interventions for the management of obesity in adult men will be included. Studies will be excluded if they do not attempt to relate cost to outcome data. The following types of papers will also be excluded: methodological papers, papers which review economic evaluations (although their reference lists will be checked for additional papers to include), discursive analysis of costs/benefits, partial evaluation studies such as cost analysis, efficacy or effectiveness evaluations and cost of treatment/burden of illness papers.

3.2 Participants

Studies must include men with a mean or median age of 16 years or over, with no upper age limit. Studies particularly examining men with obesity related to psychotropic medication or diagnosed eating disorder, or with learning disabilities, will not be included. All groups of participants must have a mean or median BMI of $\geq$30kg/m^2 or ($\geq$28 kg/m^2 with cardiac risk

factors based on criteria for orlistat). Where the BMI is not provided, but body weight is provided we will calculate BMI using relevant population data for heights[5])1 (Avenell *et al.*, 2004).

3.3 Types of intervention

We will include interventions in the form of orlistat[5])2 (but not sibutramine or rimonabant, which no longer have UK licences), diet, physical activity, behaviour change techniques or combinations of any of these. Complementary therapy, e.g. acupuncture, and non-diet products promoted for weight loss available solely over the counter will also not be included. Studies evaluating bariatric surgery will not be included. Weight loss or weight gain prevention must be explicitly stated as the main outcome of the studies. Studies examining a combination of interventions, e.g. smoking cessation and weight loss at the same time will not be included.

3.4 Types of outcomes

The outcomes of the review will be costs (regardless of how estimated), effects (no matter how these have been specified) and incremental costs per unit of effect gained.

Additional, more specific secondary outcomes of the review will be included where reported in the studies. These will include but will not be limited to:

1. Incremental costs per unit change in intermediate outcome measures (e.g. unit weight / waist circumference change)
2. Incremental costs per life year gained over the trial outcome period
3. Incremental cost per life year gained over the model time horizon (if applicable)
4. Incremental costs per additional QALY gained over the trial outcome period
5. Incremental costs per additional QALY gained over the model time horizon (if applicable).

We will also collect process outcomes (e.g. staff involvement, setting, type of intervention, timing, frequency, individual and/or group setting, couple or family setting, proportion recruited and dropping out, participants' evaluations). Resource use data and outcomes to be collected will be developed in consultation with the project advisory group.

4 METHODS

4.1 Data extraction strategy

Data extraction will be undertaken by the project health economist. Data extraction will focus on two key areas: (i) the results of the economic evaluations in terms of estimates of costs and effects; and (ii) the methods used to derive the results. Examples of the type of data to be extracted from the included studies are described below.

1. <u>The study characteristics</u>
    - The research question
    - The study design
    - The comparison
    - The setting
    - The time horizon of the study
    - The discount rate applied (if appropriate)

- The basis of costing (i.e. the perspective of the analysis – health services / personal / societal)

2. Characteristics of the study population
   - Numbers receiving or randomised to each intervention
   - Other systematic differences in clinical management
   - Inclusion/exclusion criteria
   - Dates to which data on effectiveness and costs related
   - Year of costing, inflated to 2012 pounds sterling where appropriate

3. Duration of follow-up for both costs and effectiveness

4. Results
   - Summary of effectiveness and costs (point estimate and if reported range or standard deviation, together with confidence intervals and / or P-Values as appropriate)
   - Summary of cost-effectiveness/utility (point estimate and if reported range or standard deviation together with confidence intervals and / or P-Values as appropriate)
   - Sensitivity analysis together with confidence intervals and / or P-Values as appropriate
   - Probabilistic sensitivity analysis, if reported in economic models (including details of the probability of each considered intervention being cost-effective at threshold values of willingness to pay for a one unit improvement in outcome (e.g. probability of cost-effectiveness at a willingness to pay of £20,000 per QALY))

5. Conclusions
   - As reported by the authors
   - Implications / recommendations for future research.

In order to estimate the secondary outcomes described above, data will also be extracted (where reported and if not the primary outcome of the paper) for each screening intervention considered on. Should any of the required data not be explicitly reported, these will be calculated from the studies where possible:

1) The change in average weight and waist circumference for each group from baseline to the primary follow-up time point
2) Average life years gained for each group over follow-up
3) Average life years gained for each group over the time horizon of the model (if applicable)
4) Average number of QALYs for each group over follow-up
5) Average number of QALYs for each group over the model time horizon (if applicable)

4.2 Quality assessment strategy

The methodological quality of the retrieved studies will be assessed by using the Evers checklist for health economic evaluations[3] (Evers, 2005). Where the economic evaluation has been based on a modelling exercise, additional data extraction will be performed to describe the source of parameter estimates and the methods used to combine these estimates in the

economic model. The criteria which will be used to appraise modelling studies will be based on those developed by Phillips and colleagues (Phillips 2004)[4].

4.3 Data synthesis

No attempt will be made to synthesise quantitatively the studies that are identified, nor will an economic model be constructed. Data from the included studies will be summarised in order to identify common results, variations and weaknesses between studies. A narrative review of the included studies will be presented. If a study only reported average cost-effectiveness ratios (ACERs) then, where possible, the data will be reanalysed to provide estimates of incremental cost-effectiveness. If the data allow, we will investigate the impact on cost-effectiveness for appropriate subgroups (e.g. obesity with or without obesity related co-morbidities). If sufficient data are available, we will also explore the effect of deprivation, age, and ethnicity on cost-effectiveness outcomes. Therefore, separate summaries will be developed where possible for each set of studies that consider the same patient group. Where possible the data extracted from the included studies will be used to provide estimates of the secondary outcomes described above.

References

1. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, *et al*. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess 2004; 8(21): 1-458.

2. National Institute for Health and Clinical Excellence. Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children. London: NICE; 2006. http://guidance.nice.org.uk/CG43/Guidance/Section (accessed 6th August 2010).

3. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care 2005; 21(2): 240-5.

4. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al*. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. Health Technol Assess 2004;8(36).

Appendix 1 – Cost-effectiveness MEDLINE search strategy.

MEDLINE/Embase draft search strategy

1. exp "costs and cost analysis"/
2. cost-benefit analysis/
3. quality-adjusted life years/
4. economics,pharmaceutical/
5. exp budgets/
6. exp models, economic/
7. exp decision theory/
8. monte carlo method/
9. markov chains/
10. exp health status indicators/
11. cost$.ti.
12. (cost$ adj2 (effective$ or utilit$ or benefit$ or minimis$)).ab.
13. economic$ model$.tw.
14. (economic$ or pharmacoeconomic$ or pharmaco-economic$).tw.
15. (price$ or pricing).tw.
16. (financial or finance or finances or financed).tw.
17. ((value adj2 money) or monetary).tw.
18. markov$.tw.
19. monte carlo.tw.
20. (decision$ adj2 (tree? or analy$ or model$)).tw.
21. (standard adj1 gamble).tw.
22. trade off.tw.
23. or/1-22
24. *obesity/
25. *overweight/
26. obesity, morbid/ use prmz
27. morbid obesity/ use oemez
28. (obes$ or overweight).tw.
29. weight loss/ use prmz
30. weight reduction/ use oemez
31. (weight adj1 (los$ or reduc$ or maint$ or control or manag$)).tw.
32. (obesity adj1 management).tw.
33. (anti obesity or antiobesity).tw.
34. or/24-32
35. (men or male or males).tw.
36. *obesity/ec
37. *overweight/ec
38. or/36-37
39. (women not men).tw.
40. (female not male).tw.
41. 38 not (39 or 40)
42. 23 and 34 and 35
43. 41 or 42
44. exp animals/ not humans/
45. 43 not 44