Systematic Reviews of Interventions to Treat and Prevent Obesity

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Abstract

Systematic Reviews of Interventions to Treat and Prevent Obesity

Aim

To systematically review lifestyle interventions to treat and prevent obesity in adults, children and vulnerable subgroups.

Methods

Cochrane methodology and a 'best available evidence' approach were adopted to produce a series of published systematic reviews.

Results

Adults: diets alone and with exercise and/or behaviour therapy compared with control significantly reduced weight for up to three years (weighted mean difference weight change 4 to 13 kg at one year) and prevented weight gain for up to seven years. Exercise as an adjunct to diet and also meal replacements may be effective in the long-term maintenance of weight loss. 600 kcal/day deficit or low-fat diet; diet and exercise with/without behaviour therapy; significantly reduced the risk of hypertension, type 2 diabetes and metabolic syndrome compared with control.

School-children: 39% of school-based interventions significantly improved mean body-mass index compared with control. Combined diet and physical activity interventions were most effective. It is unclear what elements of interventions are consistently effective in preventing excessive weight gain. There can be significant prevention of weight gain in children from interventions not conceptualized as obesity prevention interventions.

Vulnerable subgroups: lifestyle interventions can prevent excessive weight gain in pregnancy and help weight-concerned women stop smoking. Diet and exercise can reduce weight in postmenopausal women. There is insufficient evidence to inform how interventions need to be modified to meet the needs of pre-school children or ethnic minority groups within the UK.

Conclusions

This evidence underpins national guidance, informs government policy and influences clinical practice. Population-wide recommendations may be effective in preventing a population increase in prevalence of obesity only as part of a government strategy that includes environmental change and is coupled with targeted interventions to reduce the prevalence of obesity caused at least in part by social inequalities.

Statement of objectives, sources and assistance

This thesis puts into context a series of published systematic reviews of obesity research. The aim of this body of work is to systematically and comprehensively review the evidence for the effectiveness of interventions to prevent and treat obesity in adults and children and in subgroups of the population who are at increased risk of obesity.

Following from these aims, this body of work has several key objectives. These are:

- **O1** to evaluate the effectiveness of interventions in terms of improving weight status, risk factors for disease and disease;
- **O2** to identify study characteristics, process indicators and contextual factors that may affect the outcomes of interventions;
- **O3** to develop methodology to synthesize evidence from different study designs;
- **O4** to assess how the evidence has informed national strategies and clinical practice.

The candidate confirms that appropriate credit has been given where reference has been made to the work of others.

Collaborative work

The submitted work consists of nine published documents on a series of systematic reviews of obesity research produced as part of collaborative group projects. Appendix 1 contains letters from all co-authors of these published documents which confirm the candidate's individual level of contribution to the work. The nine published documents are contained within the Appendices (Appendices 2 to 10).

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I dedicate this thesis to all my children, Alexander, Charlotte and Victoria; thank you for being yourselves.

Executive Summary

Systematic Reviews of Interventions to Treat and Prevent Obesity

Introduction

Obesity is a major threat to public health; the prevalence and severity of overweight is increasing exponentially. Two in three adults and one in three children in the UK are overweight, including obese. Obesity significantly contributes to chronic disease, the rates of which are rapidly increasing. The last decade has seen the emergence of the early onset of type 2 diabetes, stroke and cardiovascular disease that previously had only manifested in adults. The future health and cost burden to society and the NHS are daunting.

The dietary and inactivity risk factors for developing obesity are modifiable and thus obesity is potentially preventable. Behaviour change to improve diet and increase physical activity forms the foundation of any intervention to prevent and treat obesity.

There is a need to revisit the evidence as a whole; in order to use the best available evidence to underpin national centralized guidance and inform a national strategy to manage obesity within the UK.

Aim

To systematically and comprehensively review lifestyle interventions to treat and prevent obesity in adults and children and in subgroups of the population who are at increased risk of obesity.

Objectives

- **O1** to evaluate the effectiveness of interventions in terms of improving weight status, risk factors for disease and disease;
- **O2** to identify study characteristics, process indicators and contextual factors that may affect the outcomes of interventions;
- **O3** to develop methodology to synthesize evidence from different study designs;
- **O4** to assess how the evidence has informed national strategies and clinical practice.

Methods

Systematic review methodology based upon methods of the Cochrane Collaboration, plus the development of a 'best available evidence' approach which involved synthesizing different types of data. If sufficient high quality and up-to-date evidence was identified for a specific research question then older studies or those using weaker study designs were not examined. In the case of limited evidence from high quality studies then the 'best available' evidence was used and graded according to quality and relevance to the research question.

The submitted work consists of systematic reviews for the NHS Research and Development Health Technology Assessment Programme, National Preventative Research Initiative, Cochrane Collaboration and the National Institute for Health and Clinical Excellence. Also, five peer-reviewed journal publications (Journal of Human Nutrition and Dietetics, Menopause International and Obesity Reviews) including a short science review for Foresight the Government Office for Science.

Results

Currently there is more evidence of benefit from obesity treatment interventions compared with prevention interventions, from studies in adults compared with children and about short-term intermediary outcomes compared with longer-term clinical outcomes. There is very limited evidence from UK-based studies, interventions in pre-school children, ethnic minority or other vulnerable groups of people living in the UK. There is insufficient evidence to inform how interventions need to be modified in order to be targeted and tailored to the needs of these vulnerable groups.

Diets alone and with the addition of exercise and/or behaviour therapy compared with control significantly reduced weight in adults for up to three years (WMD weight change in the range of 4 to 13 kg at one year) and prevented weight gain in adults for up to seven years (WMD weight change in the range of 0.5 to 7 kg at two years).

Adding drugs, exercise or behaviour therapies to diet significantly reduced weight in adults for up to three years (WMD weight change in the range of 1 to 8 kg at one year). Adding either exercise or behaviour therapy was effective but both in combination did not significantly improve weight loss.

Adding behaviour therapy to a prevention intervention produced greater weight loss compared with adding exercise. However exercise as an adjunct to diet may be better in the longer term. Meal replacements may be a useful tool in the long-term maintenance of weight loss.

Compared to control: combinations of a 600 kcal/day deficit or low-fat diet; diet and exercise with and without behaviour therapy; significantly reduced the risk of hypertension, type 2 diabetes and the metabolic syndrome. Diet and behaviour therapy compared to control, significantly reduced the risk of ovarian cancer.

In the most recent and comprehensive review of school-based interventions for obesity prevention, 39% of interventions were effective in significantly improving mean BMI compared with control. Interventions which combined diet and physical activity had the greatest percentage of effective studies compared with diet alone and physical activity alone. It is unclear what elements of interventions are consistently effective in preventing excessive weight gain in children.

Lifestyle interventions can help prevent excessive weight gain in pregnancy and may help to reduce weight retention between pregnancies and prevent overweight in the offspring. Weight gain prevention interventions incorporated into smoking cessation programmes may help women who are concerned about their weight to stop smoking. Diet and exercise can help to reduce weight in post-menopausal women who are at increased risk of cardiovascular disease.

Most studies failed to report effectiveness stratified by demographic characteristics or information about process or contextual factors.

Evidence shows there can be significant weight gain prevention in children from interventions not conceptualized as obesity prevention interventions, which is opposite to evidence from interventions in adults that appear more successful when specifically aimed at weight loss.

Conclusions

The evidence contained within this submitted body of work underpins national guidance, informs government policy and influences clinical practice.

A more flexible approach to producing a systematic review is required when the purpose of the review is to develop guidance to help clinical practice or to help develop an intervention. In addition to effectiveness, public health decision makers require evidence of appropriateness, implementation, feasibility, acceptability and sustainability and the context of individual behaviour change within the wider community and socio-political environment.

A ‘best available evidence’ approach provides the flexibility to include more evidence which can be graded in terms of quality and relevance to the research question. Combining quantitative and qualitative evidence can add context, provide corroboration and increase understanding, particularly with regard to complex public health interventions. Modeling future predictions of the potential impact of obesity interventions can provide justification to implement public health interventions even when the evidence from systematic reviews is limited.

A comprehensive, coherent and sustainable public healthy obesity prevention strategy is beginning to come into force which is underpinned by the best available evidence. Whilst both prevention and treatment are necessary to manage obesity; the priority of any comprehensive strategy should be prevention by behavioural change; beginning at the stage of pre-conception. Population-wide recommendations may be effective in preventing a population increase in prevalence of obesity only as part of a government strategy that includes environmental change and is coupled with targeted interventions to reduce the prevalence of obesity caused at least in part by social inequalities.

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Appendix 4
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Appendix 7
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Appendix 8
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Appendix 9
T. Brown and C. Summerbell. Systematic review of school-based interventions that focus on changing dietary intake and physical activity levels to prevent childhood obesity: An update to the obesity guidance produced by the National Institute for Health and Clinical Excellence. Obesity Reviews 2009; 10: 110-141

Appendix 10
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Abbreviations

BMEGs	black and minority ethnic groups
BMI	body mass index
CCT	controlled clinical trial
CI	confidence interval
CVD	cardiovascular disease
EU	European Union
GDG	guideline development group
HTA	health technology assessment
IOTF	International Obesity Taskforce
LCD	low-calorie diet
NCMP	National Child Measurement Programme
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NPRI	National Prevention Research Initiative
OECD	Organisation for Economic Cooperation and Development
OR	odds ratio
PCT	primary care trust
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses
PROBIT	Promotion of Breastfeeding Intervention Trial
PSMF	protein-sparing modified fast
RCT	randomised controlled trial
UK	United Kingdom
UNICEF	United Nations International Children's Emergency Fund
USA	United States of America
VLCD	very low-calorie diet
WMD	weighted mean difference

Chapter 1

1 Introduction

1.1 Aims and objectives

The overarching theme of this body of work is obesity; including the prevention and treatment; in adults and children; by diet, physical activity, behavioural and pharmacological interventions; from a public health perspective. The method is systematic review, including synthesis of quantitative and qualitative research.

The aim of this body of work is to systematically and comprehensively review the evidence for the effectiveness of interventions to prevent and treat obesity in adults and children and in subgroups of the population who are at increased risk of obesity.

Following from these aims, this body of work has several key objectives. These are:

- **O1** to evaluate the effectiveness of interventions in terms of improving weight status, risk factors for disease and disease;
- **O2** to identify study characteristics, process indicators and contextual factors that may affect the outcomes of interventions;
- **O3** to develop methodology to synthesize evidence from different study designs;
- **O4** to assess how the evidence has informed national strategies and clinical practice.

1.2 Definition and measurement

The biological definition of being obese is to be very fat, where weight exceeds optimal weight for height by about 30% and excess weight is stored as body-fat[1]. Obesity is a chronic and progressive condition which poses a serious threat to health[2].

Body mass index (BMI) is a measure of weight relative to height and is defined as weight (kg) divided by height (m^2). BMI measures the extent of being overweight; cut-off points are applied to BMI to classify weight in adults, which are correlated with risk for serious disease (table 1).

The use of BMI to measure weight in children is more complicated compared with adults because children are growing and the relationship between BMI and being overweight varies by age, height and gender. United Kingdom (UK) growth data from 1990 (derived from a representative sample of 37,700 children constructed by combining data from 17 separate surveys) is used to express BMI as a percentile based on the BMI distribution and adjusted for skewness, age and sex. 'Underweight' is less than or equal to the 2nd percentile; 'overweight' is greater than or equal to the 85th percentile but less than the 95th percentile; 'obese' is greater or equal to the 95th percentile[3].

Table 1. World Health Organisation (WHO) classification of weight in adults[4]:

Classification	BMI (kg/m2)	Associated health risks
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.5 – 24.9	Average
Preobese	25.0 – 29.9	Increased
Obese class I	30.0-34.9	Moderately increased
Obese class ii	35.0 – 39.9	Severely increased
Obese class iii	40 or higher	Very severely increased

In 1999 the International Obesity Task Force (IOTF) recommended the use of age and sex-specific cut-off points for BMI to define being overweight and obese in children. Centile curves were developed that were based on data of children's growth from six different populations and extrapolated from adult BMI cut-off points. Median BMI is 13 kg/m^2 at birth, 17 kg/m^2 at age one, 15.5 kg/m^2 at age six and 21 kg/m^2 at age 20. The centile curves pass through the points of 25kg/m^2 and 30kg/m^2 at age 18[5].

Classification of a child as overweight therefore depends on which reference population is used and what points on the distribution are selected for classification. The universal approach of the international reference values is initially appealing. However the international reference values may not detect real differences in body composition and therefore the relationship between body composition and disease that exist within populations[6].

The limitations of BMI mainly relate to its accuracy in measuring obesity within individuals and its applicability to different subgroups of the population. For example, the incidence of obesity is difficult to measure in children as the ratio of weight gain to height gain changes during normal growth. In addition, BMI is an indirect measure of body-fat. Children with different amounts of body-fat can have similar BMI; for the equivalent BMI, girls aged 7 to 17 years have greater amounts of body-fat than boys of the same age[7].

BMI cut-off points may not be applicable to certain ethnic groups due to differences in body composition and distribution of body-fat. BMI is not an equivalent measure of percentage body-fat in different race-sex groups; for the equivalent BMI, white children aged 7-17 years have more body-fat than black children[7]. British South Asian adolescents aged 14-17 years have significantly more body-fat than white European adolescents, with more central fat[8].

The distribution of body-fat is associated with risk-factors for disease; abdominal fat in adults is particularly associated with risk factors for cardiovascular disease (CVD). Multiple measures of body-fat such as BMI and waist circumference can provide a more accurate prediction of disease risk in individuals and certain subgroups[9]; however BMI is a useful measure to assess prevalence of obesity from a public health perspective[10].

1.3 Prevalence

Obesity is a global threat to public health and the most significant public health issue in the UK; which has experienced a dramatic increase in both the prevalence and severity of overweight. In 1980, rates of obesity in England were 6% in men and 8% in women[11]; the latest trends show that 24% of adults are obese. Rates of being overweight amongst English children aged 7-11 years are four times higher than 30 years ago. In England, 16.5% of children (aged 2-15 years) are obese. An additional 41% of men, 32% of women and 14% of children are overweight. Mean BMI is 27.1 kg/m^2 for men, 26.8 kg/m^2 for women and 18.4 kg/m^2 for children[12]. The rate of obesity increases steadily with age; peaks at age 45-54 years and declines from 75 years[13]. Incidence rates of maternal obesity have also increased with approximately 18% of women of childbearing age (16-44 years) being obese[14].

The National Child Measurement Programme (NCMP) figures for 2007/08 indicate that obesity is twice as high in children aged 10-11 years compared with children aged 4-5 years. Of children aged 4-5 years, 9.6% are obese and an additional 13% are overweight; 18.3% of children aged 10-11 years are obese and an additional 14.3% are overweight[15].

The increase in prevalence of obesity is reflected across the world and in most age groups including the very young. The IOTF estimates that 10% of children aged 5-17 years are overweight worldwide including 2.3% obese; which equates to 155 million overweight school-children worldwide including 30-45 million school-children who are obese[16]. England has one of the highest prevalence rates of obesity amongst the Organisation for Economic Cooperation and Development (OECD)[17]. In 2004 the European Union (EU) average for percentage of obesity was 13.4% for adults aged 15 years and over; England had the second highest rate of 22.7% [13].

The Foresight report on obesity[18] predicts that by 2050, 60% of males and 50% of females could be obese.

1.4 Vulnerable groups and life stages

Specific subgroups of the population are at increased risk of obesity and obesity-related diseases. Children of all ethnic groups, with the exception of Chinese, have a higher proportion of obesity than white children at ages 4-5 and 10-11 years. ‘Black or Black British’ children have 26.4% obesity at age 10-11 years compared with 17.3% ‘White' children[15]. Irish and Black Caribbean men and Black Caribbean, Black African and Pakistani women are at increased risk of obesity[19].

The link between socioeconomic status and obesity in the UK is complex and maybe associated with the degree of relative social inequality rather than absolute levels of

income[18]. There is a clear relationship between 'equivalised household income' and obesity for women and girls but not men and boys; 19% of women are obese in the highest equivalised household income quintile and the percentage rises in each of the other four quintiles to 32% obesity in the lowest quintile[13]. There appears to be a strong positive relationship between deprivation (Index of Multiple Deprivation) and prevalence of obesity in children, with 64-65% higher prevalence of obesity in the most deprived rank compared with the least deprived[15].

People with disability are particularly vulnerable to obesity. Obesity is linked to muscular-skeletal conditions, mental health disorders and learning difficulties in adults and children[20].

Childhood is a crucial life stage for the development of obesity; children with natural parents who are obese are at increased risk of being obese themselves and children who are obese in childhood are more likely to be obese in adulthood[13 21]. For children aged 5-17 years and between the 85th and 94th percentiles (i.e. overweight); about half were found to be obese at age 18-37 years[22]. There is some evidence that obesity in adolescence has a stronger relationship with adult obesity than obesity in younger children[23].

Other life stages associated with increased risk of weight gain include smoking cessation, pregnancy and menopause[24;25].

1.5 Aetiology

The aetiology of obesity is complex however in simplistic biological terms, weight gain occurs due to an imbalance between the amounts of energy (calories) consumed and the amount of energy expended through physical activity. If more calories are consumed than the body requires and uses through physical activity, then weight gain will occur.

The prevalence of obesity has risen rapidly over a relatively short time, suggesting that environmental and behavioural factors have played a greater role than genetics in causing this rise[11].

It is probable that in the last three or four decades there has been both an increase in the intake of more high fat and high calorie foods and an increase in time spent in sedentary activities combined with a decrease in physical activity. At the very least, energy intake has not been reduced to compensate for the reduced energy needs caused by current low levels of physical activity.

The evidence regarding any change in energy intake and expenditure is inconsistent, mainly because energy intake is underestimated in food intake surveys and physical activity is difficult to accurately measure. Prentice and Jebb summarize UK evidence and conclude that excessive food intake relative to energy needs has lead to initial weight

gain, but most importantly the reduction in physical activity has greatly reduced energy needs and lead to the development of obesity[26].

All energy intake comes from food, whereas 20-40% of energy expenditure is through modifiable physical activity. A relatively small excess intake of calories will lead to a relatively large cumulative weight gain over a long period of time. An average daily increase in net energy intake of 150 calories is enough to explain the rise in obesity prevalence in the United States of America (USA) during 1980 to 2000[27].

In 2006, 40% of men and 28% of women met the recommendation of at least 30 minutes moderate physical activity on at least five days a week. In 2007, 72% of boys and 63% of girls met the recommended target of at least 60 minutes daily physical activity. Three out of ten adults and two out of ten children consume a recommended five or more daily portions of fruit and vegetables. The average fat content of secondary school meals is 41% despite a recommended target of 35%[13].

Diet and physical activity are integral parts of the energy balance equation and are behaviours which can be modified to prevent and reverse excessive weight gain. However the energy balance equation needs to be viewed within the context of an obesogenic environment with environmental, social and cultural factors influencing what children and adults eat and do.

1.6 Clinical implications for health

The amount and distribution of fat determines the risk of obesity-related diseases and in general the more overweight the greater the risk. In 1998, 6% of all deaths in England were attributable to obesity[11] and obesity is estimated to cause an average of seven years reduction in life expectancy[28].

Obesity causes dyslipidaemia, hypertension, impaired glucose tolerance, metabolic and hormonal changes, which in turn contribute to cardiovascular disease, cancers (ovary, breast, uterus, prostate, colorectal); metabolic and endocrine diseases such as type 2 diabetes and other chronic disease such as osteoarthritis. In 1998, 36% of cases of hypertension, 47% of cases of type 2 diabetes and 15% of cases of angina were attributable to obesity[11].Women who are obese are nearly 13 times more likely to have type 2 diabetes compared with women who are normal weight[13]. Maternal obesity increases the risk of caesarean and instrumental delivery, haemorrhage and infection[14]. Obesity can exacerbate changes to the lipoprotein profile experienced during menopause, which are associated with increased risk of CVD[29].

Alarmingly, during the last decade, obesity-related disease has been identified in children. Unlike in the adult population, there is currently a lack of longitudinal data linking childhood BMI to childhood health outcomes[22]. However cross-sectional data

shows that there has been an increase in the incidence of risk factors for CVD, type 2 diabetes and the metabolic syndrome in adolescents[30-33;] . Vascular abnormalities, increased blood lipids, glucose intolerance and type 2 diabetes, hypertension and increases in liver enzymes are more common in children with obesity[34]. Obesity in adolescence is associated with increased overall mortality, CVD and type 2 diabetes in adulthood[22].

1.7 Cost burden

As well as the considerable and increasing health burden, the future health cost implications of these disease trends for the National Health Service (NHS) are daunting. In 1998 the estimated direct cost to the NHS in England of treating obesity was £9.4 million and £470 million for treating obesity-related diseases which amounted to 1.5% of the total NHS expenditure in England[11]. In 2002 the estimated direct cost of GP consultations, hospital activity and anti-obesity drugs to the NHS in England was £45.8 - £49.0 million. The cost of treating obesity-related conditions was estimated at £945 - £1,074 million, which was 2.5% of the total NHS expenditure in England. When the cost of loss of income attributable to obesity-related illness and death were included the total cost to society was estimated at £3.3 - £3.7 billion[35].

In 2007/08, there were over 5000 NHS hospital admissions with a primary diagnosis of obesity, almost seven times greater than ten years earlier. In 2007 there were over a million prescription items for drugs for the treatment of obesity in England, nearly ten times the number prescribed in 1999[13]. The Foresight report on obesity[18] predicts that by 2050 the annual NHS cost of obesity and its consequences could rise from £1 billion to £6.5 billion.

1.8 Public health perspective

The overarching goals of public health are to improve the health of the population and reduce inequalities in health outcomes. These two goals are inter-dependent because increasing health inequalities affects the overall health of the whole population[36].

The degree of relative social inequality and risk of obesity are inextricably linked and the obesity epidemic is contributing significantly to the wider socioeconomic inequalities in health. Obesity interventions targeted and tailored to individuals with the highest risk of obesity will help to reduce the prevalence of obesity (caused at least in part by social inequalities) and may help to reduce inequalities in health, but only as part of a national strategy to tackle the underlying social, economic and environmental determinants of health.

Evidence from obesity interventions needs to be viewed within the context of an obesogenic environment. Behaviour change in terms of eating healthier and exercising more is influenced by economic, environmental and social factors which are often beyond the control of the individual.

From a public health perspective; both prevention and treatment interventions are necessary to manage obesity; however, the priority of any comprehensive strategy should be prevention which begins at the stage of pre-conception. Focusing solely on treatment of obesity is insufficient to reduce the prevalence, because as people with obesity are being treated, other people are becoming obese. Treatments to reduce obesity will only ever provide a partial solution. It is preferable for children and adults to attain and remain a normal weight, rather than require treatment for being overweight. Prevention of obesity in childhood will reduce the prevalence of adult overweight and associated diseases. Children may also be more amenable to change in dietary and activity habits since their lifestyle habits are still developing.

Interventions to improve diet and increase physical activity are indispensable elements of any intervention for the treatment and prevention of obesity. Changing behaviour to improve public health has the potential for the greatest benefit to health yet is probably the most challenging type of intervention.

1.9 Summary

Obesity is a major threat to public health; the prevalence and severity of overweight is increasing exponentially. Two in three adults and one in three children in the UK are overweight including obese. Obesity significantly contributes to chronic disease, the rates of which are rapidly increasing. The last decade has seen the emergence of the early onset of type 2 diabetes, stroke and CVD that previously had only manifested in adults. The future health and cost burden to society and the NHS are daunting.

The dietary and inactivity risk factors for developing obesity are modifiable and thus obesity is potentially preventable. Behaviour change relating to diet and physical activity must form the foundation of any intervention to prevent and treat obesity; however behaviour change interventions need to appreciate the influence of the obesogenic environment.

From a public health perspective, BMI adequately measures the prevalence of obesity and is a useful tool to measure the effectiveness of interventions to prevent or treat obesity. Interventions may need to be targeted at vulnerable groups such as children and adults of lower socioeconomic status and ethnic minorities; and during vulnerable life stages such as when stopping smoking, being pregnant and experiencing the menopause.

There is great potential for health improvement in terms of improved quality of life, increased life expectancy, and cost savings that could be directed towards other healthcare needs.

1.10 Structure and outline of the submitted work

1.10.1 The submitted work

The submitted work provides a comprehensive and systematic review of the evidence of lifestyle interventions to prevent and treat obesity within the whole population and within particularly vulnerable groups.

When this body of work was initiated there was a clear and urgent need for national centralized guidance for the management of obesity, based on the best available evidence. Unlike other chronic diseases, there was no integrated system within the NHS for managing obesity and obesity was only managed clinically in the presence of obesity-related co-morbidities[11]. As the issue of obesity came to dominate public health; this body of work intended to inform the issue of obesity and provide future direction for public health decision making with regard to a comprehensive obesity strategy within the UK. During the development of this body of work, the National Institute for Health and Clinical Excellence (NICE) commissioned reviews of the evidence of interventions to manage obesity[24], including reviews contained within this research, in order to develop national guidelines on the prevention and management of obesity that were published in 2007[37].

In the last decade there have been numerous systematic reviews assessing the effectiveness of interventions to manage obesity. These reviews have applied different inclusion criteria which varied with regard to study design, setting, duration, definition of excess weight and the types of outcomes reported, making it difficult to summarize the evidence. There is a need to revisit the evidence as a whole and to use the best available evidence; which is the premise underpinning this body of work.

Seven systematic reviews were produced in the following format; a report for the NHS Research and Development Health Technology Assessment (HTA) Programme[38]; a report for the National Prevention Research Initiative (NPRI)[39]; a systematic review for the Cochrane Collaboration[40]; three reviews for NICE[24] and a review personally requested by the editor of the Menopause International journal[41]. Other outputs from these systematic reviews are four publications in peer-reviewed journals[42;43]; including an update of the NICE review of school-based interventions[44] and a short science review for Foresight the Government Office for Science[45].

The following is a reference list of the papers which form the submitted work, the order of which mirrors the presentation in chapter 2:

Systematic reviews of the treatment and prevention of obesity in adults

Treatment

HTA Report

Avenell A, Broom J, Brown TJ**,** Poobalan A, Aucott L, Stearns SC, Smith WCS, Jung RT, Campbell MK, Grant AM. 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. http://www.hta.ac.uk/1187 (Appendix 2)

Linked publications

Avenell A, Brown TJ**,** McGee MA, Campbell MK, Grant AM, Broom J, Jung RT, Smith WCS. What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomised controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. Journal of Human Nutrition and Dietetics 2004; 17(4): 293-316. (Appendix 3)

Avenell A, Brown TJ**,** McGee MA, Campbell MK, Grant AM, Broom J, Jung RT, Smith WCS. What are the long-term benefits of weight reducing diets in adults? A systematic review of randomised controlled trials. Journal of Human Nutrition and Dietetics 2004; 17 (4): 317-335. (Appendix 4)

Prevention

NPRI Review

Brown T, Avenell A, Edmunds LD, Moore H, Whittaker V, Avery L and Summerbell C for the PROGRESS team. Systematic Review of Long-term Lifestyle Interventions to Prevent Weight Gain and Morbidity in Adults. Obesity Reviews 2009; 10(6):627-38. Epub 2009 Sep 14. DOI: 10.1111/j.1467-789X.2009.00641.x (Appendix 5)

Systematic reviews of the prevention of obesity in children

Cochrane Review

Summerbell CD, Waters E, Edmunds LD, Kelly S, Brown T, Campbell KJ. Interventions for Preventing Obesity in Children. The Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD001871.pub2. DOI: 10.1002/14651858.CD001871.pub2. (Appendix 6)

NICE Guideline

National Institute for Health and Clinical Excellence. Obesity: The Prevention, Identification, Assessment and Management of Overweight and Obesity in Adults and Children. Clinical guideline. CG43 Obesity; full guideline, section 3- prevention: evidence statements and reviews. National Institute for Health and Clinical Excellence, 2006. http://www.nice.org.uk/guidance/CG43. (Appendix 7)

Specifically;

8. Prevention evidence summary: interventions for pre-school children and family-based interventions ('early years'), p287-295.

9. Prevention evidence summary: school-based interventions, p296-316.

Linked publications

Brown T, Kelly S, Summerbell C. Prevention of obesity: a review of interventions. Short Science Review. Foresight Tackling Obesities: Future Choices. Obesity Reviews 2007; 8 (Suppl 1): 127-130. http://www.foresight.gov.uk. (Appendix 8)

T. Brown and C. Summerbell. Systematic review of school-based interventions that focus on changing dietary intake and physical activity levels to prevent childhood obesity: An update to the obesity guidance produced by the National Institute for Health and Clinical Excellence. Obesity Reviews 2009; 10: 110-141. (Appendix 9)

Systematic reviews of obesity interventions targeted at black, minority ethnic groups, vulnerable groups and individuals at vulnerable life-stages

NICE Guideline

National Institute for Health and Clinical Excellence. Obesity: The Prevention, Identification, Assessment and Management of Overweight and Obesity in Adults and Children. Clinical guideline. CG43 Obesity; full guideline, section 3- prevention: evidence statements and reviews. National Institute for Health and Clinical Excellence, 2006. http://www.nice.org.uk/guidance/CG43. (Appendix 7)

Specifically;

13. Prevention evidence summary: interventions aimed at black, minority ethnic groups, vulnerable groups and vulnerable life stages ('BMEGs'), 365-390.

Invited publication

Brown Tamara J. Health benefits of weight reduction in postmenopausal women: a systematic review. Menopause International 2006;12(4): 164-171. (Appendix 10)

1.10.2 Relationship between the submitted reviews

As well as evaluating the effectiveness of interventions, systematic reviews can provide an overview of the evidence in context and highlight any gaps in research where evidence is limited which can stimulate further research. The reviews included in this submission are linked by the research recommendations made in response to the gaps in the evidence highlighted by each antecedent review.

In 2000 the HTA programme commissioned the 'Systematic Review of Long-Term Effects and Economic Consequences of Treatments for Obesity and Implications for Health Improvement'[38] in response to identifying this as a key gap in the evidence needed by the NHS. Outputs from the HTA report include two peer-reviewed journal articles[42;43]. The HTA report recommended that a review of prevention interventions be carried out and in response the 'Systematic Review of Long-Term Lifestyle Interventions to Prevent Obesity in Adults' was produced[39].

In 2004 NICE commissioned a series of rapid reviews which formed the supporting evidence for their Obesity Guidance[37]. The candidate was responsible for five of these rapid reviews including three submitted in this body of work; interventions for pre-school children and family-based interventions; school-based interventions; and interventions aimed at black, minority ethnic groups, vulnerable groups and vulnerable life stages[24].

The NICE Obesity reviews[24] brought together all the evidence accumulated within the existing reviews[38;40]. A short science review was published[45] which underpinned the evidence gathered for the Foresight report into tackling obesities[18]. A 'Systematic review of school-based interventions that focus on changing dietary intake and physical activity levels to prevent childhood obesity: an update to the obesity guidance produced by the National Institute for Health and Clinical Excellence' has since been published[44]. In addition the systematic review: 'Interventions for Preventing Obesity in Children' was updated for the Cochrane Collaboration[40].

The NICE review of cohorts[24;25] to assess key determinants of weight gain highlighted smoking cessation, pregnancy and menopause as key life-stages associated with increased risk of excessive weight gain. In response to these findings, a systematic review of health benefits of weight reduction in postmenopausal women[41] was conducted. A review of interventions targeted at black, minority ethnic groups, vulnerable groups and vulnerable life stages was commissioned on behalf of NICE and carried out by the candidate[24;46].

The reviews are also linked through systematic review methodology which has developed in symbiosis with the obesity research. For example, the NICE obesity reviews applied a 'best available evidence' approach[47] which was developed in response to the limitations of the evidence gathered within the Cochrane obesity prevention

review[40]. The 'best available evidence' approach enabled inclusion of lesser quality studies, studies not aimed specifically at obesity prevention and studies of shorter duration. It also included corroborative evidence to provide information about context and process in order to enrich the effectiveness data. This 'best available evidence' approach has become a prerequisite for systematic reviews which are used to inform guidance and practice in public health.

1.10.3 Professional development – a chronology

In 2001 I began my career as a research assistant on the HTA review[38] where I did the bulk of the searching, data extraction and meta-analysis by following a pre-set protocol and guidance from the lead reviewer. In 2002 I gained an MSc by Research in Public Health. Following the completion of the HTA review I co-wrote two papers[42;43] and undertook consultancy in obesity research whilst I became Research Associate then Research Fellow.

In 2005 I became lead reviewer at the Obesity Collaborating Centre for NICE at the University of Teesside where I managed a team to produce five rapid reviews[24] and presented evidence to the Guideline Development Group (GDG). I also began to focus on developing methodology to deal with the increasing complexity of evidence within systematic reviews which was required by decision-makers. I was asked by Foresight to write a short report[45] on the main results from the NICE reviews which were used to underpin the Foresight report into tackling obesity[18].

Based on the knowledge gained from producing the NICE reviews of interventions to prevent obesity in children[24] I became a collaborator on the Cochrane update of interventions to prevent obesity in children[40] and made significant contributions to the protocol and discussion. Following this, I updated the NICE schools review of interventions to prevent obesity in school-children and produced a publication as first author[44]. The editor of Menopause International invited me to write a paper on the health benefits of weight reduction in postmenopausal women of which I was single author of the publication[41].

On the strength of my experience I was asked to produce another large-scale systematic review of obesity interventions for the University of Aberdeen as part of the NPRI. I am first-author of a paper on this work which has recently been published in Obesity Reviews[39].

My experience has led to being invited to act as peer reviewer, speak at conferences, contribute to scoping and briefing events and write a book chapter. As well as managing review teams I now train students in systematic review methodology.

1.10.4 Presentation of the submitted work

CHAPTER 2 presents both the methods and results for the treatment and prevention of obesity in adults; the prevention of obesity in children; and for interventions targeted at black, minority ethnic groups, vulnerable groups and individuals at vulnerable life stages. CHAPTER 3 discusses and puts into context the results from chapter 2 with particular reference to methods of evaluating effectiveness.

CHAPTER 4 provides the conclusion to this body of work. This chapter summarizes the main findings according to the objectives and highlights the contribution of the submitted body of work to the overall body of knowledge.

CHAPTERS 2, 3 & 4 provide interlinking passages between the submitted body of work which is presented and discussed as a whole.

Chapter 2

2 Systematic Reviews of Interventions to Treat and Prevent Obesity

2.1 Systematic reviews of treatment and prevention of obesity in adults

2.1.1 Methodology

Treatment

The HTA review[38;42;43] was underpinned by a pre-specified protocol which was devised using the methods of the Cochrane Collaboration[48]. Study inclusion criteria were; randomised controlled trials (RCTs) with a minimum duration of one year; in adults with a mean age of at least 18 years and a mean BMI of 28 kg/m^2 or greater. Types of included interventions were drugs, diets, exercise and behaviour therapy. Drugs used to aid weight loss in the UK at the time of the HTA review are detailed in Table 2. Weight loss or the prevention of weight gain had to be explicitly stated as a main outcome of the study and the primary outcome measure was weight change.

The search strategy included weight and obesity related terms and text words combined with a strategy for identifying RCTs. Thirteen electronic databases were searched and specific journals were hand searched. Data extraction was carried out using a form generated from the outcomes pre-specified in the review protocol. Quality assessment included the quality of random allocation concealment, whether the analysis was based on an intention-to-treat and blinding of outcome assessors.

Where results from studies could be quantitatively combined, a statistical meta-analysis of the data was performed to determine the effect size of the intervention. For continuous data (such as weight change) a weighted mean difference (WMD) was calculated (weighted by the inverse of the variance) and a fixed effects approach was adopted. If data could not be combined quantitatively it was assessed qualitatively.

Meta-analysis requires a mean and standard deviation of the change between two time-points; change sometimes needed calculating from actual values. Missing standard deviations were imputed by means of linear regression for weight and from the means of reported standard deviations in the case of risk factors.

Prevention

The NPRI review[39] was based on the methods used in the HTA review[38] and the data extraction form was adapted according to the NPRI review protocol. Study inclusion criteria were; RCTs, with a minimum duration of two years; in adults aged 18 to 65 years with BMI less than 35 kg/m^2. Types of included interventions were diets, exercise and behaviour therapy. The primary outcome measure was weight change and the study did not have to be aimed at obesity prevention and could include the prevention of disease or improvement of health.

Interventions were categorised as interventions with definite intention to lose weight and interventions with no definite intention to lose weight. Key systematic reviews and eight electronic databases were searched for relevant studies and two journals were hand searched.

Table 2. Pharmacotherapy used for weight loss when HTA report produced.

Name of drug	Action of drug
Acarbose (Glucobay® manufactured by Bayer)	Inhibits digestion of starch and sucrose, used to improve blood glucose control in people with diabetes.
Metformin (Glucophage® manufactured by Lipha; Glucamet® manufactured by Opus)	Decreases release of glucose into the circulation, increases glucose uptake into the tissues, improves blood glucose control in people with diabetes.
Orlistat (Xenical® manufactured by Roche)	Inhibits all gastrointestinal lipases needed to absorb dietary fat. By reducing absorption; caloric intake is decreased.
Sibutramine (Reductil® and Meridia® manufactured by Abbott)	Reuptake inhibitor of noradrenaline, serotonin and dopamine, reduces food intake by producing a feeling of satiety.
Selective serotonin reuptake inhibitors; Fluoxetine (Prozac® manufactured by Dista; Felicium® manufactured by Opus) Sertraline (Lustral® manufactured by Pfizer).	Inhibits the uptake of serotonin by the brain and also inhibit appetite. Primarily used to treat depression.

2.1.2 Results

Eighty-four RCTs assessed the effects of lifestyle and drug treatments for obesity in adults with a BMI of 28 kg/m^2 or greater, at least one year from randomisation[38;42;43]. Thirty-nine RCTs examined lifestyle interventions to prevent weight gain in adults with a BMI less than 35 kg/m^2 at least two years from baseline[39]. Some studies were included in both reviews[38;39].

Weight

Treatment

Intervention versus control

All six comparisons produced significant benefit in terms of weight loss for the intervention group (Table 3).

Table 3. Table of summary estimates for weight changes from RCTs of weight reduction - Intervention versus (vs) control ((WMD and 95% confidence interval (CI), in kg)).

Comparison	12 months	18 months	24 months	30 months	36 months	60 months
600 kcal/day deficit or low-fat diet vs control	-5.31* (-5.86, -4.77)	-1.15 (-2.76, 0.45)	-2.35* (-3.56, -1.15)		-3.55* (-4.54, -2.55)	-0.20 (-2.03, 1.63)
LCD vs control	-6.25* (-9.05, -3.45)		-7.00* (-10.99, -3.01)		-6.10* (-10.71, -1.49)	
VLCD vs control	-13.40* (-18.43, -8.37)					
Diet and exercise vs control	-4.78* (-5.41, -4.16)		-2.70* (-3.60, -1.80)			
Diet and behaviour therapy vs control	-7.21* (-8.68, -5.75)		-1.80 (-4.77, 1.17)			
Diet, exercise and behaviour therapy vs control	-4.00* (-4.46, -3.54)	-3.40* (-3.84, -2.97)	-3.00* (-3.59, -2.40)	-4.68* (-6.08,-3.28)	-2.00* (-2.66, -1.34)	

* Significant difference

At 12-months follow-up, WMD weight change ranged from -4.00 kg (95% CI; -4.46,-3.54) in the diet, exercise and behaviour therapy intervention versus control, to -13.40 kg (95% CI; -18.43,-8.37) in the VLCD intervention versus control. In descending order, the greatest WMD weight change was;

Very low-calorie diet (VLCD) versus control

Diet and behaviour therapy versus control

Low-calorie diet (LCD) versus control

600 kcal/day deficit or low-fat diet versus control

Diet and exercise versus control

Diet, exercise and behaviour therapy versus control

Diet alone can produce similar weight loss to diet in combination with exercise and/or behaviour therapy when compared to no-treatment control for up to three years.

Adjuncts to diet only, diet and behaviour therapy, diet and exercise

Three of the five drug adjuncts (Orlistat, Sibutramine, Acarbose) and two of the three lifestyle adjuncts (exercise, behaviour therapy) produced significant benefit in terms of weight loss for the intervention group at 12 months (Table 4).

Table 4. Table of summary estimates for weight changes from RCTs of weight reduction – adjuncts to diet (WMDs and 95% CI, in kg).

Comparison	12 months	18 months	24 months	36 months	60 months
Adjuncts to diet					
Orlistat and diet vs diet	-3.01* (-3.48,-2.54)		-3.26* (-4.15,-2.37)		
Sibutramine and diet vs diet	-4.12* (-4.97,-3.26)				
Selective serotonin reuptake inhibitor and diet vs diet	-0.33 (-1.49,0.82)				
Metformin and diet vs diet	-1.09 (-2.29,0.11)		-0.50 (-4.02,3.02)		-0.12 (-1.13, 0.89)
Acarbose and diet vs diet	-0.79* (-1.53,-0.05)				
Exercise and diet vs diet	-1.95* (-3.22,-0.68)	-7.63* (-10.33,-4.92)		-8.22* (-15.27,-1.16)	
Behaviour therapy and diet vs diet	-7.67* (-11.97,-3.36)	-4.18* (-8.32,-0.04)		-2.91 (-8.60,2.78)	1.90 (-3.76, 7.56)
Exercise and behaviour therapy and diet vs diet	-0.67 (-4.22,2.88)	-2.06 (-5.57,1.45)	-1.40 (-5.01,2.21)		
Other adjuncts					
Exercise and behaviour therapy and diet vs diet and behaviour therapy	-3.02* (-4.94,-1.11)		-2.16* (-4.20,-0.l2)		
Behaviour therapy and exercise and LCD vs LCD and exercise	-10.69* (-14.22,-7.16)				

* Significant difference

In terms of adjuncts to diet only, at 12 months follow-up there was significant WMD weight change which ranged from -0.79 kg (95% CI; -1.53,-0.05) in the Acarbose and diet versus diet only intervention, to -7.67 kg (95% CI; -11.97,-3.36) in the behaviour therapy and diet versus diet alone intervention. Behaviour therapy added to a low-calorie diet and exercise combination produced the greatest WMD weight change of -10.69 kg (95% CI; -14.22,-7.16) at 12 months.

In descending order, the greatest WMD weight change was;

Behaviour therapy and exercise and LCD versus LCD and exercise

Behaviour therapy and diet versus diet

Sibutramine and diet versus diet

Exercise and behaviour therapy and diet versus diet and behaviour therapy

Orlistat and diet versus diet

Exercise and diet versus diet

Acarbose and diet versus diet

The addition of exercise or behaviour to diet was associated with improved weight loss however when adding both exercise and behaviour therapy to diet, weight loss was not significantly improved.

Adding behaviour therapy to a diet (-7.67 kg, 95% CI; -11.97,-3.36) or diet plus exercise intervention (-10.69 kg, 95% CI; -14.22,-7.16) produced greater weight loss compared with adding exercise to a diet (-1.95 kg, 95% CI; -3.22,-0.68) or diet plus behaviour therapy intervention (-3.02 kg, 95% CI; -4.94,-1.11). However exercise as an adjunct to diet may be better in the longer term as exercise (-8.22 kg, 95% CI; -15.27, -1.16) but not behaviour therapy (-2.91 kg, 95% CI; -8.60, 2.78) demonstrated significant weight loss when added to diet at three years.

Head-to-head comparisons

All comparisons of different types of diet failed to showed any significant difference between groups for weight at any time except protein-sparing modified fast (PSMF) versus VLCD at 18 months when the VLCD group lost more weight (Table 5).

Table 5. Table of summary estimates for weight changes from RCTs of weight reduction – head-to-head comparisons (WMDs and 95% CI, in kg).

Comparison	12 months	18 months	24 months	36 months	60 months
LCD vs 600 kcal/day or low-fat diet	1.63 (-1.26,4.52)				
VLCD vs 600 kcal/day or low-fat diet			-4.70 (-11.79,2.39)		
VLCD vs LCD	-0.15 (-2.73,2.43)	-1.13 (-5.32,3.06)			
PSMF vs LCD	-3.57 (-7.36,0.22)	0.69 (-1.58,2.96)	-2.17 (-4.88,0.54)	-1.51 (-5.43,2.41)	0.20 (-5.68,6.08)
PSMF vs VLCD		2.73* (0.07,5.39)			

Prevention

Intervention versus control

Five of eight comparisons demonstrated significant benefit in terms of weight loss for the intervention group in studies that were specifically aimed at weight loss (Table 6).

Table 6. Table of summary estimates for weight changes from RCTs of weight prevention – Intervention vs control (WMDs and 95% CI, in kg).

Comparison	24 months	30 months	36 months	48 months	54 months	72 months	90 months
Intention to lose weight							
600 kcal/day deficit or low-fat vs control	-0.76 (-2.41, 0.89)	0.70 (-1.78, 3.18)	-3.49* (-4.63, -2.35)				
LCD vs control	-7.00* (-10.99, -3.01)		-6.10* (-10.71, -1.49)				
Weight Watchers vs control	-2.70* (-3.95, -1.45)						
VLCD + meal replacements vs low-fat control	-4.70 (-11.79, 2.39)						
Behaviour therapy (telephone) vs control	-0.34 (-0.95, 0.27						
Behaviour therapy (mail) vs control	-0.14 (-0.75, 0.47)						
Diet and exercise vs control	-2.56* (-3.34, -1.77)						
Diet, exercise and behaviour therapy vs control	-2.47* (-3.18, -1.77)		-2.04* (-2.70, -1.39)		-2.50* (-3.59, -1.41)		
No intention to lose weight							
Low-fat non-reducing diet vs control	-1.42* (-2.10, -0.74)						
Behaviour therapy vs control	-1.30 (-2.83, 0.23)						
Diet and behaviour therapy vs control	-1.01* (-1.34, -0.68)		-1.77* (-1.94, -1.59)	-0.52* (-0.85, -0.19)		0.20 (-0.26, 0.66)	-0.70* (-0.90, -0.50)
Diet, exercise and behaviour therapy (clinic) vs control	-1.40 (-3.12, 0.32)		-0.80 (-2.35, 0.75)				
Diet, exercise and behaviour therapy (home) vs control	-1.50 (-2.20, 1.20)		0.60 (-1.16, 2.36)				

* Significant difference

Two of the five comparisons that were not specifically aimed at weight loss did demonstrate significant weight loss for the intervention group although the amount of weight loss (WMD weight change 0.5 kg to 2.8 kg) was less than in studies specifically aimed at weight loss (WMD weight change 2.0 kg to 7.0 kg).

At two years follow-up WMD weight change ranged from -1.01 kg (95% CI; -1.34,-0.68) in the diet and behaviour therapy versus control intervention to -7.00 kgs (95% CI; -10.99,-3.01) in the low-calorie diet versus control intervention. In descending order, the greatest WMD weight change at 12 months was;

LCD versus control

Weight Watchers versus control

Diet and exercise versus control

Diet, exercise and behaviour therapy versus control

Low-fat non-reducing diet versus control

Diet and behaviour therapy versus control

Interventions combining diet with additional elements compared to control were not always associated with greater weight loss. Both diet and exercise (-2.56 kg, 95% CI; -3.34,-1.77) and diet, exercise and behaviour therapy (-2.47 kg, 95% CI; -3.18,-1.77) versus control produced similar WMD weight change, which was less than some of the diets alone versus control. There was no evidence assessing the effectiveness of exercise alone compared to control on weight.

Adjuncts to diet

At two years there was no additional benefit to weight of adding exercise to diet or adding exercise plus behaviour therapy to diet (Table 7). Meal replacements in addition to diet produced significant improvement in weight at 51 months but not at 27 months. Meal replacements in addition to diet combined with exercise and behaviour therapy produced significant improvement in weight at 24 months.

Table 7. Table of summary estimates for weight changes from RCTs of weight prevention – Adjuncts to diet (WMDs and 95% CI, in kg).

Comparison	24 months	27 months	29/33 months	51 months
Intention to lose weight				
Diet, exercise and behaviour therapy vs diet	-1.40 (-5.01,2.21)			
Diet and meal replacement vs diet		-2.70 (-6.89,1.49)		-5.40* (-8.97, -1.83)
Diet, exercise, behaviour therapy and meal replacement vs diet, exercise, behaviour therapy	-6.00* (-10.19,-1.81)			
Diet, exercise, behaviour therapy and food provision vs diet, exercise, behaviour therapy	0.55 (-2.96,4.06)			
Diet, exercise, behaviour therapy and financial incentive vs diet, exercise and behaviour therapy	1.30 (-2.16,4.76)			
Diet, exercise, behaviour therapy, food provision and financial incentive vs diet, exercise and behaviour therapy	1.30 (-2.16,4.76)			
Diet, exercise, behaviour therapy and food provision vs diet, exercise, behaviour therapy and financial incentive	-0.75 (-3.85,2.35)			
Diet, exercise, behaviour therapy, food provision and financial incentive vs diet, exercise, behaviour therapy and food provision	0.00 (-3.05, 3.05)			
No intention to lose weight				
Diet and exercise vs diet			-0.74 (-3.06, 1.59)	

* Significant difference

Head-to-head comparisons

Direct comparisons of active interventions failed to show significant effect on weight, with one exception (Table 8). A Mediterranean diet plus behaviour therapy compared to a low-fat diet produced significant improvement in weight at two years (WMD weight change -2.8 kg, 95% CI; -3.06,-2.54).

Table 8. Table of summary estimates for weight changes from RCTs of weight prevention – head-to-head comparisons (WMDs and 95% CI, in kg).

Comparison	24 months	29/33 months	36 months
Intention to lose weight			
Diet, exercise (2500kcals/wk), behaviour therapy and social support vs diet, exercise (1000kcals/wk) and behaviour therapy		-1.96 (-4.70,0.78)	
Behaviour therapy (telephone) vs behaviour therapy (mail)	-0.20 (-0.81,0.41)		
Diet, exercise, behaviour therapy and meal replacement (group dietitian) vs diet, exercise, behaviour therapy and meal replacement (individual nurse/physician)	-4.40 (-9.62,0.82)		
No intention to lose weight			
Mediterranean diet and behaviour therapy vs low-fat diet	-2.80* (-3.06,-2.54)		
Low-fat non-reducing vegan diet vs low-fat non-reducing diet	-2.30 (-6.22,1.62)		
Clinic diet, exercise and behaviour therapy vs home diet, exercise and behaviour therapy	-0.90 (-2.43,0.63)		-1.40 (-3.13,0.33)
Group higher-intensity exercise vs Individual higher-intensity exercise	0.71 (-1.27, 2.68)		
Lower-intensity home-based exercise vs higher-intensity home-based exercise	-0.53 (-2.56, 1.51)		
Structured exercise and behaviour therapy vs lifestyle exercise and behaviour therapy	-0.74 (-2.0,0.52)		
Diet and exercise (8.4MJ/wk) vs diet and exercise (4.2MJ/wk)		-3.30 (-1.04,7.64)	
Diet and walking exercise vs diet and resistance training exercise		1.00 (-4.04,6.04)	

* Significant difference

Clinical outcomes

Treatment[38;42;43]

Orlistat was associated with less weight loss than sibutramine but had a more beneficial impact on risk factors. Metformin significantly reduced mortality in 700 obese diabetics at ten year follow-up. A 600 kcal/day deficit/low-fat diet was associated with benefits to weight, risk factors, prevention of type 2 diabetes and improvement in hypertension, with effects persisting at three years. Diet plus exercise interventions; with and without behaviour therapy suggested improvement in type 2 diabetes and control of hypertension.

Prevention[39]

A 600 kcal/d deficit/low-fat diet can reduce the incidence of type 2 diabetes, improve blood pressure control and reduce the need for antihypertensive medication for up to three years. Diet plus exercise reduces the risk of type 2 diabetes for up to six years

compared to control. Diet combined with exercise and behaviour therapy can reduce the risk of type 2 diabetes, hypertension and the metabolic syndrome. The addition of exercise to diet can reduce the risk of metabolic syndrome in men. Diet and behaviour therapy showed reduced risk of ovarian cancer risk in the final four years of an eight year study of 48,000 women; however type 2 diabetes risk was not significantly reduced at eight years.

2.1.3 Discussion

The pattern of results followed expectations; more studies of active versus control interventions demonstrated significant weight difference between groups compared to studies evaluating additional elements or head-to-head comparisons.

The aim of individual studies appears to influence results as there are more effective studies and a greater amount of weight loss in studies specifically aimed at weight loss compared to studies which focus on healthy eating or increased exercise.

Adults receiving placebo plus diet in the Orlistat and Sibutramine trials, lost less weight compared with adults receiving a 600 kcal/day deficit or low-fat diet (in the diet versus control trials). This suggests that participants receiving placebo did not adhere to the dietary advice and this might have over-estimated the effect of the addition of weight-loss drugs to diet compared with diet alone.

Although few studies followed up participants for longer than three years; the majority of studies that produced significant improvement in weight and continued to follow-up participants, showed that weight loss was sustained, in some cases for over four years.

Study interventions were heterogeneous which made the classification of studies difficult. The comparisons were underpinned by few studies making it difficult to generalize about effective interventions. There was limited evidence of the effect of weight loss on risk factors or clinical outcomes. Approximately 25% of the prevention studies and the majority of non-drug treatment studies reported weight outcomes only. Few studies were powered to detect differences in morbidity and mortality.

Risk factor data were limited and inconsistent within and between studies. Risk factors and clinical outcomes could improve despite lack of weight loss. For example in one study of 700 obese diabetics; Metformin in addition to diet was associated with non-significant weight change (WMD -0.37 kgs 95% CI; -1.67, 0.93) but significant reduction in mortality ((odds ratio (OR) 0.62, 95% CI; 0.42, 0.91)) at 10 years. Risk factors can improve independently from weight loss through drug action or improved fitness from exercise.

In some participants some risk factors significantly improved whilst other risk factors did not (with or without concomitant weight change). Significant improvements in some risk

factors were small changes in absolute values and the clinical value of these improvements maybe limited.

Risk factors often showed no improvement despite significant weight loss. Possible reasons for this include insufficient weight loss to impact on risk factors, insufficient power or duration of study to detect significant differences. There did not appear to be any pattern between intensity of the intervention and weight change.

Studies that were sufficiently powered and reported risk factor or clinical outcome data were mainly in populations with or at high risk of obesity-related co-morbidities such as type 2 diabetes, metabolic syndrome or hypertension. Participants with CVD, hypertension or type 2 diabetes appear to lose more or less weight than participants without co-morbidities however the pattern is not consistent. More research is required into how and why interventions vary in effectiveness in different types of populations. There is limited evidence of lifestyle interventions to prevent weight gain in healthy normal weight adults within the community.

2.1.4 Conclusion

In terms of treatment; diets alone and with the addition of exercise or behaviour therapy significantly improved weight loss (WMD weight change 4 to 13 kg in first year) compared to no-treatment control for up to three years. Adjuncts including drugs, exercise or behaviour therapy increased weight loss (WMD weight change 1 to 11 kg in first year). Regarding prevention interventions; diet, alone and with the addition of exercise and/or behaviour therapy demonstrated significant weight loss (WMD weight change 0.5 to 7 kg) compared to control at a minimum of two years. Exercise and meal replacements may be useful tools in the long-term maintenance of weight loss.

Additional elements (behaviour therapy or exercise) did not always produce better results compared with diet alone versus control. Adjuncts to diet were not always more beneficial than diet alone. On the whole, direct comparisons of different diets, different types and amounts of exercise and varying who and where the intervention was provided produced no significant benefit to BMI between groups.

Diet alone and in combination with exercise and/or behaviour therapy can significantly reduce the risk of hypertension, metabolic syndrome and type 2 diabetes compared to no treatment control.

Obesity interventions in adults appear more effective when they are specifically aimed at prevention of weight gain compared with interventions which focus more generally on healthier eating and increased physical activity.

2.2 Systematic reviews of the prevention of obesity in children

2.2.1 Methodology

The methods of the Cochrane review[40] were based on the methods of the Cochrane Collaboration[49] and guidelines for systematic reviews in health promotion and public health[50]. Study inclusion criteria were; controlled trials with a minimum duration of 12 weeks; in children with a mean age of less than 18 years. Types of included interventions were diet and nutrition; exercise and physical activity; lifestyle and social support. Studies had to report a stated aim to prevent excessive weight gain. The setting could be community, school or clinic. At least one of the following measures had to be reported at baseline and follow-up: weight and height; percent fat content; BMI; ponderal index; skin-fold thickness.

The search strategy included terms and text words for weight and obesity, intervention and setting, combined with a strategy for identifying controlled trials, which was narrowed to include only studies that included children. Five electronic databases and various websites were searched and experts were contacted. A data extraction form including quality assessment was designed, based on the Effective Public Health Practice Project Quality Assessment Tool for quantitative studies[51].

The main changes to the methods of the Cochrane review update compared with the previous version were to include studies of a shorter duration, widen the search strategy and number of databases searched and to include information about context, theory and process.

The methods of the NICE reviews (interventions for pre-school children and school-based interventions)[24;52] included a 'best available evidence' approach where 'best' refers to evidence from RCTs. If sufficient high quality and up-to-date evidence was identified for a specific research question then older studies and/or those using weaker study designs were not examined. In the case of limited evidence from high quality studies then the 'best available' evidence was used[47]. For evidence of effectiveness; both systematic reviews and primary studies of RCTs and controlled clinical trials (CCTs) were sought that measured weight (however measured) or dietary intake or physical activity levels, at least before and after the intervention, which had to be at least 12 weeks duration. Included interventions were diet, physical activity, behaviour therapy or combinations of such interventions types. Studies were not excluded based on the aim of the study. Evidence from qualitative studies based in the UK was also sought for corroborative evidence.

The systematic review of school-based interventions[44] which updated the NICE review of school-based interventions used identical methodology and inclusion criteria to the NICE

methodology with one exception; the updated review only included studies that reported a weight outcome.

Results from the studies of children could not be quantitatively combined, mainly due to heterogeneity of outcomes and types of interventions. Each study was summarized and described according to the characteristics of participants; interventions; follow up and outcomes measured.

2.2.2 Results

In addition to differences in methodology; the reviews differed by inclusion age and so the results are presented by age.

Included studies

All children under 18[40]

Twenty-two studies were included, 19 were school or preschool-based interventions, one was a community-based intervention targeting low-income families and two were family-based interventions targeting non-obese children of overweight parents. Twelve studies lasted less than one year and ten studies lasted longer than a year.

Children aged two to five years[24;45;52]

Five studies were included, none of which were UK-based. One study was clinic-based and the remainder were conducted in a nursery or childcare setting. All interventions included family involvement of varying degrees.

School-children aged four to 16 years[24;44;45;52]

Thirty-eight studies were included in the update[44]; 15 new studies and 23 studies included within the NICE obesity reviews[24]. Seventeen studies were US-based and three were UK-based. Two studies were based in pre-school settings, 23 studies were set in primary schools and 13 studies were based in secondary schools. Twenty-two studies had follow-up less than one year. Mean baseline BMI ranged from 15.5 kg/m^2 to 27.6 kg/m^2 where reported (23 studies).

Weight

All children under 18[40]

Four of 22 (18%) studies were effective in preventing weight gain.

Long-term (12 months or longer)

Six studies combined dietary education and physical activity interventions; five resulted in no difference in overweight status between groups and one (Planet Health) resulted in improvements for girls receiving the intervention, but not boys. Planet Health aimed to

improve diet and increase physical activity and reduce television viewing. The adjusted OR showed significant improvement in percentage obesity in girls but not boys at 18 months (girls; OR 0.47; 95% CI 0.24 to 0.93, p = 0.03). Two studies focused on physical activity alone of which one appeared to be effective in preventing obesity. Two studies focused on nutrition education alone, but neither was effective in preventing obesity.

Short-term (less than one year)

Two of four physical activity interventions produced minor reductions in overweight status in favour of the intervention. An aerobic dance intervention demonstrated significant improvement in mean BMI at 12 weeks in intervention girls compared with control girls (-0.8 kg/m^2 vs 0.3 kg/m^2, respectively). An intervention to reduce television and video use showed significant difference in mean BMI between groups at 6 months (-0.45 kg/m^2, 95% CI -0.73 to -0.17, p = 0.002). The other eight studies were combined diet and physical activity interventions and none had a significant impact on weight.

Children aged two to five years[24;45;52]

Three of the five studies (two diet and exercise interventions and one diet intervention) found some evidence that the intervention prevented unhealthy weight gain leading to obesity, compared with controls.

School-children aged four to 16 years[24;44;45;52]

Fifteen of 38 studies (39%) were effective. One of three diet studies, five of 15 physical activity studies and nine of 20 combined diet and physical activity studies demonstrated significant and positive differences between intervention and control for BMI.

2.2.3 Discussion

The studies were heterogeneous in terms of design, participants, intervention and outcome measures; making it impossible to combine study findings using statistical methods. It is difficult to generalize about which interventions are effective and how the range and extent of intervention components influence effectiveness.

The Cochrane review[40] included only studies specifically aimed at preventing weight gain and demonstrated lack of significant benefit to weight (particularly from combined diet and activity interventions) from the limited available evidence. The NICE review[24] and its update[44] (which included studies not specifically aimed at preventing weight gain) demonstrated optimistic but inconsistent results. These differences in review conclusions demonstrate the importance of what evidence is considered when assessing the effectiveness of interventions.

Limited evidence from the Cochrane review[40] suggests that many diet and exercise interventions to prevent obesity in children are not effective in preventing weight gain, but can be effective in promoting a healthy diet and increased physical activity levels. Half (3/6) of the physical activity interventions showed a small but positive impact on BMI status.

Limited evidence from the NICE review[24] of pre-school children indicates that interventions which focus on the prevention of obesity through improvements to diet and activity appear to have a small but important impact on body weight that may aid weight maintenance.

Findings from the most recent review of school-children[44] are inconsistent and mainly short-term, but overall suggest that combined diet and physical activity school-based interventions may help prevent children becoming overweight in the long-term. Physical activity interventions, particularly in girls in primary schools, may help to prevent these children from becoming overweight in the short term. However the same interventions were not tested across a range of ages and effectiveness could be due to the type of interventions used in this age group rather than the age per se.

Despite lack of conclusive results in terms of weight, the majority of studies demonstrated significant improvement in diet and activity behaviours such as increasing fruit and vegetable intake, promoting water consumption, increasing active play and physical education in schools. Possible reasons why studies could show significant benefit in terms of behaviour change but not BMI is uncertain. Some studies were not adequately powered to detect differences between groups and some of the interventions were not of sufficient length or intensity to produce a change in BMI. Assessment of effectiveness can also be exacerbated by weaknesses in assessment measures.

2.2.4 Conclusion

The findings are inconsistent and mainly short-term, but overall suggest that combined diet and physical activity school-based interventions may help prevent children becoming overweight in the long-term. It is unclear what elements of interventions are consistently effective.

The aim of individual studies within reviews appears to impact on reported outcomes and therefore overall review conclusions. Results for BMI appear less effective if confined to studies specifically aimed at weight gain prevention in children rather than improving healthy eating and physical activity.

2.3 Systematic reviews of obesity interventions targeted at black, minority ethnic groups, vulnerable groups and individuals at vulnerable life stages

2.3.1 Methodology

The methods of the NICE reviews of interventions aimed at black, minority ethnic groups, vulnerable groups and vulnerable life stages[24;46] adopted a 'best available evidence' approach in line with NICE methodology (discussed in 2.2.1). For evidence of effectiveness; both systematic reviews and primary studies of RCTs and CCTs were sought that measured weight (however measured) or dietary intake or physical activity levels, at least before and after the intervention which had to be at least 12 weeks duration. Studies were not excluded based on the aim of the study. Evidence from qualitative studies based in the UK was also sought for corroborative evidence.

Black and minority ethnic groups included minority population groups with relatively high rates of obesity within the UK[53]. Vulnerable groups included populations with relatively high risk of obesity based on inequality (for example inequality of income or education) along with children in care and in special schools and adults in institutions. Other vulnerable groups included individuals with learning difficulties, special needs and developmental disorders[53]. Vulnerable life-stages included smoking cessation, pregnancy and menopause[25;53].

The review of postmenopausal women[41] included both systematic reviews and primary studies of RCTs and CCTs with a minimum duration of 24 weeks (because the focus was on long-term health outcomes). All women were required to be postmenopausal and have a BMI of at least 25 kg/m^2 at baseline. The search strategy used the keywords 'weight loss' and 'weight reduction' combined with 'postmenopaus$' and phase I of the Cochrane search terms for identifying RCTs[54]. The search was run in MEDLINE, EMBASE, PsychINFO and CINAHL from database conception to May 2006.

Both reviews included interventions of diet, physical activity, behaviour therapy or combinations of such interventions types. Each study was summarized and described according to the characteristics of participants; interventions; follow up and outcomes measured.

2.3.2 Results

Included studies [24;46]

Black and minority ethnic groups

No studies were identified that assessed lifestyle interventions in BMEGs or low-income groups in the UK.

Vulnerable groups

Two studies in adults with disabilities and one study in children with disability were identified.

Vulnerable life stages

Three ante-natal interventions and seven smoking cessation studies were identified. Two systematic reviews and one long-term RCT in peri-menopausal women were included.

Weight

Vulnerable groups

Disability[24;46]

A 12-month intervention to reduce obesity using health practitioner input with adults with learning difficulties in Manchester, UK, showed that in the control group obesity levels deteriorated in 10.2%, remained the same in 81.6% and improved in 8.2%. In the intervention group 10.5% deteriorated, 63.2% remained the same and 26.3% improved. Mean BMI did not appear to significantly differ from baseline or between groups at one year.

A 12-week cardiovascular and strength exercise programme in obese adults with Down's syndrome based in the USA showed a significant difference in weight but not BMI between groups at 12 weeks. There was a slight reduction in weight at 12 weeks in the intervention group whereas weight increased in the control group.

A 9-month aerobic exercise programme (45 minutes, four times per week) in 20 nine year old children with spastic cerebral palsy, based in Germany, reported 'no changes' in fat mass compared with an average 1.1 kg increase in the control group. This small study was not powered to detect significant changes in weight.

Vulnerable life stages

Pregnancy[24;46]

Three studies (all based in the USA) assessed antenatal interventions, two in low-income women. Two studies were specifically aimed at preventing excessive weight gain during pregnancy, one study was an RCT, one was a CCT and one study used historical controls for the comparison group.

The RCT significantly reduced the percentage of normal-weight women (but not overweight women) that exceeded the weight gain goal, however the intervention had no significant effects on average weight gain from pre-pregnancy to delivery and weight gains were comparable between black and white women.

The CCT showed that women in the exercise intervention group gained less weight in the latter stages of pregnancy (although still within normal range). The women in this study were physically active at baseline and were self-selecting in choosing whether to continue exercising (intervention group) or to reduce exercise during pregnancy (control). In the study using historical controls, there was significant reduction in excessive weight gain in the low-income women and significant reduction in the risk of weight retention women who were overweight.

Smoking[24;46]

Seven studies assessed interventions to prevent excessive weight gain during and after smoking cessation programmes. Three studies were diet plus exercise interventions, two were exercise interventions; one was a food replacement intervention and one a cognitive-behavioural therapy intervention for women with 'weight concerns'. The majority of the studies were small, based in the USA; included women aged 30 to 40 years who smoked 19 to 32 cigarettes a day.

Three of the seven interventions significantly improved abstinence rates, three showed no significant difference in abstinence rates and in one study both an individualised and non-individualised diet plus aerobic exercise intervention increased the risk of smoking compared to control at 12 months.

In six studies the diet and/or exercise intervention did not significantly reduce weight gain compared to control. Weight gain ranged from 1 to 9kg across all the groups in the seven studies. Cognitive-behavioural therapy for weight concerns significantly attenuated weight gain (and improved smoking abstinence) compared with standard smoking cessation in women concerned about their weight (2.5 kg vs 7.7 kg respectively). A third comparison group which included a 500 kcal/day deficit diet did not show significant difference in weight compared to control (5.4 kg vs 7.7 kg respectively).

Menopause[24;41;46]

A systematic review of 18 good quality RCTs of at least eight weeks duration, assessed the effect of exercise in over 1800 healthy postmenopausal women (aged 50–65 years). Body composition showed improvement in nine studies and most studies showed a small loss of weight and body-fat. The most effective results were accomplished in three studies with overweight participants who used weight-reducing diets in combination with

exercise training. The mean weight loss ranged from 2 to 10 kg between 12 weeks to one year.

Evidence from one high quality RCT suggests that a tailored programme with a behavioural element addressing both dietary intake and physical activity can prevent excess weight gain in perimenopausal women. At 54 months, 55% of the intervention women were at or below their baseline weight compared with 26% in the control. The intervention demonstrated significant improvement in weight, waist circumference, BMI, percent body-fat and fat-free mass compared with control at 54 months.

The systematic review of postmenopausal women[41] included four RCTs, one CCT and one systematic review. All active-treatment arms demonstrated significant improvements in weight and body composition from baseline. Weight loss in active-treatment arms varied from 1.5 kg to 9 kg over 6 to 12 months. Significant effects between treatment groups were shown only in intervention versus control studies. Significant weight loss was not accompanied by beneficial changes in cardiovascular risk factors in the majority of studies. None of the studies reported disease outcomes.

Summary[24;41;46]

The effectiveness of interventions among BMEGs, lower-income groups and other vulnerable groups in the UK is unknown. There is a dearth of evidence on the effectiveness of interventions among individuals with a disability. Limited short-term evidence suggests that a cardiovascular and strength exercise intervention may prevent excessive weight gain in overweight adults with Down's syndrome.

The antenatal studies varied in terms of aim, quality and population. The evidence is limited but suggests that antenatal interventions aimed at reducing excessive weight gain can be effective in low-income pregnant women but the impact of baseline weight remains unclear. Antenatal interventions including exercise, diet alone and in combination, can reduce excessive weight gain in pregnant women. Excessive weight gain during pregnancy is correlated with postpartum weight retention and so antenatal interventions may help to curb the increasing level of obesity amongst women. Since the NICE review[24] was produced, an RCT of a dietary intervention has been published which showed a significant reduction in excessive weight gain in obese pregnant white women between 15 and 36 weeks gestation compared with control[55]. This evidence strengthens the above conclusions.

Smoking cessation interventions incorporating weight management interventions may increase continuous abstinence rates but the long-term impact on weight remains unclear.

Weight-reducing diets in combination with exercise training can significantly improve body composition in overweight postmenopausal women. A diet, exercise and behavioral therapy intervention significantly improved BMI and other anthropometric measures in women experiencing the menopause, with effects sustained at 54 months.

Lifestyle interventions can produce significant weight loss compared to no-treatment control in overweight postmenopausal women and have the potential to improve disease outcomes associated with overweight. Significant weight loss was not accompanied by beneficial changes in cardiovascular risk factors in the majority of studies. Many of the studies were probably underpowered and too short in duration to detect change in risk factors. The study that produced the greatest weight loss demonstrated improvements in risk factors and it may be that only this one study produced sufficient weight loss to significantly improve risk factors.

2.3.3 Discussion

There is a severe lack of evidence from lifestyle interventions to prevent excessive weight gain that are targeted and tailored to ethnic minority groups and other vulnerable groups at increased risk of obesity who are living within the UK. The need for intervention is greatest amongst these groups who are at increased risk of obesity.

In this case, results of studies based outside the UK are not generalizable to minority ethnic groups in the UK. The link between socioeconomic status and obesity in the UK is complex and maybe associated with the degree of relative social inequality rather than absolute levels of income[18]. The socio-political context of low-income populations within the UK (which often includes ethnic minority groups with higher risk of obesity) is different from low-income and ethnic minority populations in other countries.

Pregnant women are at increased risk of obesity and obesity impacts on reproductive health and increased risk to health during pregnancy (caesarian, haemorrhage, infection)[14]. Preventing excessive weight gain during pregnancy and reducing overweight prior to conception will improve the health of these women and the health of their children. Obese pregnant women are less likely to breastfeed and to breastfeed for a shorter duration compared with normal weight women[56]. Breastfeeding exclusively for six months is associated with reduced obesity in children however this evidence is mainly derived from observational studies. The largest (17 000 infants) and longest (6.5 years) breastfeeding intervention to date, did not reduce obesity and CVD risk factors at six years despite significantly increasing breastfeeding[57]. The Promotion of Breastfeeding Intervention Trial (PROBIT) was a cluster-randomised trial of a breastfeeding promotion intervention based on the World Health Organisation (WHO)/United Nations International Children's Emergency Fund (UNICEF) Baby-Friendly Hospital Initiative.

Exclusive breastfeeding for six months may not constitute an effective public health strategy for reducing obesity but may contribute to an obesity prevention strategy by helping new mothers to reduce weight retention and establishing good weaning practices.

Weight gain prevention interventions incorporated into smoking cessation programmes may help women who are concerned about their weight to give up smoking.

More research is needed into the timing and intensity of diet and exercise interventions to prevent excessive weight gain during and post-menopause. Post-menopausal women are at increased risk of CVD and require long-term follow-up to assess the effects of weight gain prevention on clinical outcomes.

2.3.4 Conclusion

There is no evidence regarding whether or how obesity interventions need to be modified for ethnic minority groups and other vulnerable groups living in the UK. There are social inequalities in the prevalence of obesity. Interventions addressing obesity on a population-wide scale may appear beneficial but may in fact be widening health inequalities between groups that vary in risk for obesity.

Future interventions need to be targeted and tailored to high-risk groups such as minority ethnic groups and those with low-income and limiting disabilities.

Interventions to prevent excessive weight gain during pregnancy, menopause and smoking cessation all have the potential for significant health benefits.

Chapter 3

3 Methods of evaluating effectiveness

3.1 Why results from similar systematic reviews may differ

What evidence is included and how the evidence is assessed has important implications for the evaluation of the effectiveness of obesity interventions.

Differences in review protocols

Studies specifically aimed at preventing weight gain might be expected to have a greater likelihood of demonstrating effectiveness in terms of benefit to weight than studies not specifically targeting obesity prevention. Evidence from studies in adults in the NPRI review[39] showed that the effective interventions included a greater proportion of studies that intended adults to lose weight compared with studies not aimed at weight loss. These studies that intended to produce weight loss also produced a greater amount of weight loss.

This does not appear to be the case in the reviews of children. There were a smaller percentage of effective studies that aimed to prevent weight gain compared with studies not specifically targeting weight (18% effective studies in Cochrane review[40], 39% effective studies in updated review of school-based interventions[44]).

A similar review of obesity prevention in children[58] included studies not specifically aimed at preventing weight gain and this contributed to a greater percentage of studies which showed effectiveness compared to the Cochrane review[40]. The review by Doak et al.[58] included 24 studies with 17 categorised as effective (71%) whereas in the Cochrane review[40] only four of the 22 studies were categorised as effective (18%). Both reviews[40;58] share similar aims; however only ten studies appeared in both reviews due to differences in inclusion criteria and assessment of outcome[59].

Whether to include studies with aims not specific to preventing weight gain is a contentious issue and partially explains the discrepancy between the results of the two reviews[59]. Applying identical inclusion criteria to both reviews showed that 50% of 30 included interventions were effective and excluding studies not aimed at preventing weight gain showed that 42% (10/24) of interventions were effective[59].

Differences in outcome measures

Triallists report various anthropometric measures including percentage body-fat, percentage overweight, percentage obese, BMI, BMI z-score, BMI percentile, waist circumference, waist-hip-ratio, skinfold thicknesses and weight. The use of such assorted outcome measures makes comparisons between studies difficult. As discussed in

Chapter 1; from a public health perspective, BMI is a good measure of prevalence however other measures of excess fat maybe important when assessing an individual, particularly a child or a person of ethnic minority status.

Even if one measure of excess fat is used in studies, differences in results also relate to the methods used within studies to classify weight status of children. The most commonly applied thresholds for overweight and obesity are derived from the IOTF[5] and the 1990 British centile charts[60]. The IOTF reference population is much larger and more representative of different ethnic groups however it is more stringent and usually produces a lower percentage of obesity (even when the UK population is used) compared to the 1990 British centile charts. One methodology applied universally would eliminate discrepancy in prevalence due to the use of different classifications and enable more reliable comparisons of data between studies.

Obesity prevention interventions aim to reduce the number of people becoming overweight and prevent the amount of overweight from increasing within those already overweight (i.e. mean BMI and prevalence of overweight). In order to evaluate the effectiveness of an obesity prevention strategy it is crucial to assess how change in prevalence and change in mean BMI has occurred. For example if prevalence change is due to weight loss in the overweight or reduction in mean BMI is due to reduced incidence in normal weight.

Prevalence of obesity can change significantly without affecting the mean BMI because prevalence involves a minority of the sample being above the specified cut-off point, whereas the mean BMI includes every participant in the sample. For example, over time a few participants could increase their BMI enough to cross the cut-off point and become overweight. There will be a smaller number of participants who lose BMI and cross the cut-off threshold in the opposite direction, but the change in prevalence is the balance of these two shifts. Relative few participants would need to reduce their BMI to compensate for the rising BMI of participants who have crossed the cut-off threshold, so mean BMI would stay the same but prevalence would increase.

Discrepancy between results of reviews can arise from differences in assessment of outcome measures. The Cochrane review[40] classified an intervention as effective if mean change in BMI was statistically significant and in favour of the intervention. A study was classified as not effective if, for example, prevalence was significantly reduced but mean BMI was not. The review by Doak et al.[58] classified an intervention as effective if any outcome measure (of weight) showed significant benefit in favour of the intervention. When comparing the ten studies included in both reviews this discrepancy in assessment becomes clear: the Cochrane review[40] assessed three out of the 10 (30%) studies as effective whereas the review by Doak et al.[58] assessed six out of the same 10 (60%) interventions as effective[59].

In determining the effectiveness of an obesity intervention it is difficult to decide which outcome measures to focus on. One method is to assess the effectiveness of the outcome measure which best matches the individual study aim. Another method involves grading the outcomes by using a hierarchy so that clinical outcomes take precedence over behaviour change outcomes which in turn take precedence over change in knowledge or attitudes. Another method is to choose an outcome measure which is considered most relevant to obesity prevention (usually a measure of weight). If there is inconsistency between the effects of multiple outcome measures within a study, then overall effectiveness can be based on the balance and grade of the individual outcomes.

Differences in assessment of participants

Differences in results can arise depending on whether all participants are assessed according to the groups they were randomised into (known as 'intention to treat') or whether only participants who completed the study were assessed. Some studies only assess participants who adhered to the treatment protocol and so groups become almost self-selected.

'Intention to treat' studies do not exclude any participant; participants who are lost to follow-up (drop-outs) can have their last observed outcome measurements carried forward to the end of the assessment period. If there are significant differences between participants who have dropped-out and those that have completed the trial this can bias the results. For example if the majority of drop-outs do so because they have reached a plateau and are failing to lose any more weight, their last measurements could be when weight loss was greatest. Failure to maintain weight loss and weight regain is common (usually seen after six months in weight loss trials in adults) and so including these participants in final assessment - by carrying the last observation forward – will tend to produce a more favourable result for the intervention.

In reality some participants will drop-out or not adhere to an intervention and a major focus of public health interventions is how they perform in real life across the whole population. By studying the characteristics of participants who do not adhere to an intervention, future interventions can be targeted and tailored more appropriately.

3.2 Synthesizing different types of data

'Best available evidence' approach

For the HTA review, conducted in 2001, it was relevant to employ the methods of the Cochrane Collaboration[49] because the review was a first attempt at synthesizing a relatively large amount of evidence from RCTs of effectiveness of obesity treatments in adults. As a research assistant I was involved in every process of the HTA review[38] post protocol.

Since the HTA review[38] there has been increasing awareness that end-users require a variety of evidence. The systematic reviews commissioned by NICE[24;47;53] aimed to provide an evidence base for the development of guidance to enable decision makers and practitioners to implement effective public health obesity interventions and so a 'best available evidence' approach was adopted which involved synthesizing different types of data. If sufficient high quality and up-to-date evidence was identified for a specific research question then older studies and/or those using weaker study designs were not examined. In the case of limited evidence from high quality studies then the 'best available' evidence was used[47].

I adopted a 'best available evidence' approach partly because of my experience of limited evidence from obesity interventions in children, also to include information on process outcomes and context, and in order to enable the GDG to develop guidance. I believe the end-users of systematic reviews are of paramount importance because they help to define the purpose of a review and reviewers should consider the needs of the end-user throughout the review process. This belief was reinforced during the production of the NICE reviews[24] when I presented evidence in person to the GDG. The GDG required minute detail about individual interventions and this emphasized the importance of the need to question the relevance of evidence to practice, in order to translate it into practice.

The NICE reviews[24] had additional research questions (as well as effectiveness) which were crucial in order to develop guidelines for practice. As lead reviewer for the Obesity Collaboration Centre at Teesside University I understood that it would be unhelpful to the GDG to conclude in areas of limited evidence that 'there was a lack of high-quality evidence' and more constructive to appraise what evidence existed and additionally, to gain insight into what types of interventions have the potential to be effective.

Evidence from the HTA review[38] and the Cochrane review[40] highlighted the discrepancy and lack of long-term data for children compared to adults. A 'best available evidence' approach meant that the NICE protocol for the obesity reviews could reflect this; RCTs of at least one year were included in the NICE review of treatments for adults and lesser quality studies of shorter duration and not specifically aimed at obesity prevention, were included in the NICE reviews of prevention interventions for children.

My experience of using a 'best available evidence' approach for the NICE reviews[24] enabled me to appreciate the value to the end-user of incorporating process outcomes and widening the inclusion criteria for evidence. In response I made changes to the protocol of the Cochrane update of obesity prevention interventions in children[40] to reflect the broader approach of public health reviews in terms of the information it provides for public health decision makers. The search strategy was widened and the number of databases searched was increased, studies of shorter duration were included and details regarding theory, process and context were extracted.

Following the update of the Cochrane review[40] I undertook an update of the schools review[44] and a review of weight reduction in postmenopausal women[41], in which I was responsible for each stage of the reviews, from conception to publication. Both reviews are useful to the end-user for different reasons. The update of the schools review[44] builds on the evidence base by capturing a relatively large number of studies published since the NICE review[24]. The update strengthens the evidence that school-based interventions combining diet and exercise can significantly prevent excessive weight gain in school children. In contrast, the review of weight reduction in postmenopausal women[41] highlights that there is still a dearth of evidence of interventions amongst vulnerable groups which may have the greatest need for intervention.

In the area of obesity research there is an ever increasing plethora of reviews and to avoid duplication of effort it may be more sensible to build on the evidence contained within these reviews rather than search databases and journals for primary studies. One potential weakness in using existing reviews for identifying relevant studies is reliance that these reviews were produced in a systematic and robust manner and captured all relevant evidence. A systematic review of systematic reviews can make this method more robust however to have confidence that all relevant studies have been captured it is often necessary to systematically search for both reviews and primary studies.

The 'best available evidence' approach[47] used in the NICE obesity reviews[24] enabled the inclusion of both systematic reviews and individual studies from one systematic search for both types of evidence. I have since modified this approach for the NPRI review[39] by first searching for reviews then searching for individual studies published after the NICE guidance; which were used to 'top up' the evidence found within the systematic reviews.

Combining evidence

Quantitatively combining results from RCTs by statistical meta-analysis of the data provides a 'gold standard' for quantitative synthesis. However public health interventions are often complex and not amenable to meta-analysis; individual behaviour change outcomes are insufficient to assess such interventions. If there is limited evidence from good quality studies then there is a case for considering evidence from other study

designs. In addition there is an inherent danger of separating the effectiveness of an intervention from its context.

Systematic reviews need to address additional research questions to those regarding effectiveness such as information on process (including appropriateness, implementation, feasibility, acceptability and sustainability) and the context of individual behaviour change in relation to the community and wider socio-political environment[61]. Effectiveness can be influenced by how the intervention is provided, who provides it and where it is provided. End-users require both outcome and process data and I believe that methods of combining these two types of data can enhance understanding of why and how interventions can work.

There are two main ways of synthesizing qualitative and quantitative data either in addition or instead of meta-analysis. Textual narrative describes the study findings by grouping similar studies together whereas thematic synthesis attempts to find common elements across the different study designs. Both methods have strengths and weakness, textual narrative is better at describing the scope and strength of the evidence but can read rather like 'telling a story' and be rather cumbersome when dealing with a large number of studies. A thematic approach may be more interesting for the reader and more appropriate for hypothesis testing but may obscure heterogeneity and study quality[62].

My initial approach to combining data was a combination of textual narrative and thematic synthesis which involved describing the interventions and comparing similarities and differences to assess any emerging patterns. However the end-user requires an appraisal of the strength of the evidence and this spurred further methodological development.

When using a 'best available evidence' approach, evidence can be graded by levels in terms of its applicability to the research question. For example when evaluating studies modified for BMEGs in the UK, 'level one' evidence could be studies directly related to this population, 'level two' evidence could be other vulnerable groups such as low-income families in the UK and 'level three' evidence could be from other BMEGs and low-income populations outside the UK. Effectiveness could be assessed and stratified by the level of evidence within which the individual studies could be graded by quality and type of outcome (clinical, behavioural, knowledge). In addition to using all the available evidence and identifying any gaps; this approach helps to compare interventions modified for BMEGs with interventions in majority populations.

The 'best available evidence' approach[47] used within the NICE obesity reviews[24] enabled qualitative and quantitative evidence to be combined. Where there was limited evidence from high quality studies, lower quality evidence was used for corroboration and to provide information on process indicators which added context and improved

understanding relating to the effectiveness of interventions. Specifically with regard to the NICE review of black, minority ethnic groups; evidence from ethnic minorities in the USA was used in the absence of UK-based evidence. As evidence from outside the UK is not directly relevant in this case, the evidence was 'downgraded' in that caution was applied in making any generalizations about the results of these interventions. Thus the strength of the evidence helps in terms of assessing the level of confidence in the effectiveness of an intervention.

'Mapping' the evidence.

It is often useful in reviews of complex public health interventions to map the included studies according to the spheres of influence that the intervention aims to impact upon. For example an intervention could focus on individual behaviour change, change within the family, changes to the immediate environment such as healthier food in school canteens or changes to the wider environment such as improved food labeling in supermarkets and free access to leisure facilities or an intervention could focus on all or some of these spheres. By mapping the studies in this way we can see where there is the most evidence and where there is limited evidence and whether effectiveness varies according to the spheres of influence of an intervention.

In practical terms, mapping the evidence helps to organize the data so that similarities between effective interventions can be highlighted and differences between effective and non-effective interventions can be compared and any emerging themes can be described. Where lack of data are highlighted this can lead to further searching for evidence further down the quality hierarchy. Non-intervention evidence from cohort, survey or other qualitative studies can be used to corroborate effectiveness data[63]. It can add context and improve understanding about why an intervention is effective or not.

My current method of combining evidence in includes a 'stepped approach' which is a flexible approach whereby evidence from various study types is initially identified and then I grade the evidence by quality and relevance to the research question and 'map' the evidence by spheres of influence. I compose a hierarchy of theoretical evidence (which prioritizes evidence at the top) and then match the identified evidence within the hierarchy. This enables the best available evidence to be combined, provides corroborative evidence to aid understanding, highlights gaps in the research and enables the reviewer to appraise the strength of all available evidence.

Summary

Without these developments in methodology I would have reported and concluded on a lack of available evidence to answer many of the research questions and the evidence-base would have remained limited. These developments in methodology have enabled more constructive work because in areas where there is severely limited evidence I have

been able to suggest potential beneficial elements of interventions which require further investigation. Combining corroborative evidence with effectiveness evidence and information on process and context has provided insight into how and why interventions have the potential to produce beneficial behaviour change.

By grading the evidence by relevance to the research questions I have been able to ensure reviews remain focused on the original research questions and avoided the inherent danger of focusing on areas which are less relevant because stronger evidence exists. Combining and appraising the best available evidence has enabled decision-makers to produce policy and practice guidance which is graded by the strength of the evidence. Without mapping the spheres of influence of interventions, the reviews would have failed to capture the importance of the obesogenic environment and the context within which individual behaviour change is constrained.

3.3 Modeling of potential interventions

Significant change in behaviour in terms of improvement in healthy eating or increase in physical activity, does not necessarily demonstrate improvement in weight in children. Significant improvement in weight is not always accompanied by beneficial changes in risk factors or clinical outcomes in adults. Lack of effectiveness can be due to inadequate sample size, duration or intensity of an intervention. A study might not have been sufficiently powered to detect differences in clinical outcomes, or the intervention could have been too short, or the amount of behaviour change insufficient to impact on weight.

When we don't know what type of intervention will be effective (and this is currently the situation with regard to children) we can look at the evidence from a different angle; how effective would an intervention need to be in order to have a beneficial impact on population weight and health? Also what amount of behaviour change is required in order to produce this benefit to weight and health?

In the absence of longer-term data from interventions and the use of intermediary measures such as dietary intake and activity levels, modeling becomes a useful tool. Modeling of weight change in relation to energy intake and output can be used to predict the effect of an obesity intervention on population weight. Modeling enables targets to be established within public health interventions that will help to prevent excessive weight gain at population level.

Modeling techniques vary and produce different estimates of the energy gap required (in terms of kcals/day) to prevent excessive weight gain[64;65]. Hill et al.[64] estimate that an energy deficit of 100 kcals/day is required to prevent excessive weight gain in adults and Butte et al.[65] estimate the energy gap may need to be around 260 kcals/day in children. More detailed evaluation of the behaviour change achieved within interventions and comparison with the estimates used within these modeling techniques would enable

assessment of whether the behaviour change was enough to impact on weight and the amount of weight change that could be expected over a certain period of time.

A minority of obesity intervention trials in adults (and even less in children) report risk factor outcomes. The HTA review[38] of obesity treatment in adults modeled the impact of weight reduction on change in risk factors. Regression analysis demonstrated that a weight loss of 10 kg was associated with a fall in total cholesterol of 0.25 mmol/L (about 5%) and a weight loss of 10% was associated with a reduction in systolic blood pressure of 6.1 mmHg. More weight loss was associated with greater improvement in lipids.

Modeling the impact of change in behaviour on weight and the effect of weight change on risk factors are crucial in order to assess the cost-effectiveness of an intervention and enable decision makers to implement effective public health interventions. It is sometimes necessary to take a 'leap of faith' that interventions which show a significant improvement in healthy eating and/or physical activity and thus significant improvement in the right direction, will prevent obesity and obesity-related diseases in the long-term. Modeling allows practitioners to appreciate the clinical significance of statistically significant changes in weight, or indeed behaviour, which are reported in systematic reviews of obesity interventions.

3.4 Conclusions

Systematic reviews need to be user-friendly and flexible to the demands of the research question. Preliminary mapping of all available evidence should be an explicit part of the review process. Both outcome and process evaluations are crucial elements which need reporting in studies and in systematic reviews. Continuing development of methodology is required with regards to combining evidence from different types of study design. Future methodological development is needed to evaluate environmental change and policy driven interventions.

My reviews have focused on the end-user, mainly decision-makers for policy and practice and in doing so they have become more relevant to practice. There is an increased awareness of the needs of public health decision-makers and this is reflected in a broader approach now taken to producing systematic reviews of public health interventions. Using the 'best available evidence' enables the sharing of appraised evidence rather than censoring of evidence which is not of the highest quality and this is a constructive approach to public health research.

My reviews have encouraged better reporting of process evaluations, context and the impact of the environment, which is demonstrated in recent publications of obesity interventions. My reviews have highlighted a lack of evidence of interventions in vulnerable groups and studies are now being conducted in pre-school and other vulnerable groups within the UK which hold promise for the future of obesity research.

The methodology which I have developed which reflects the importance of using best available evidence, corroborative evidence and evidence about process and context, together with methods of combining such evidence, is recognised within the wider research community. The Cochrane Collaboration has developed guidelines specifically for conducting systematic reviews within public health[50].

In addition the 'Preferred Reporting Items for Systematic reviews and Meta-Analyses' (PRISMA) published in July 2009[66] reflect the recognition that systematic reviewing is an iterative process which requires a flexible protocol that can be modified if necessary in response to the nature of the identified evidence. It is important to point out that this is opposite to developing a protocol to identify only a selection of evidence. PRISMA includes a flow diagram which details the number of studies included in both quantitative and qualitative analysis and reflects the importance of doing both.

The Foresight report[18] concluded that the length of time needed to fill the evidence gaps was at odds with the need for urgent action and I would argue that any action needs to be properly evaluated especially if there is a move away from evidence-based practice towards practice-based evidence. Developments are needed in methods to evaluate the effect of new policy interventions such as the population-wide social marketing campaign 'Change4Life'[67] which promotes lifestyle change to prevent obesity. This provides an opportunity to develop methods to evaluate the impact of population-wide interventions on the complex interaction between social inequality and obesity over the life-course.

3.5 Professional development - reflections

Between 2001 and 2005 I progressed in my career from research assistant on the HTA review[38] to lead reviewer at the Obesity Collaborating Centre at the University of Teesside.

My professional development has been underpinned by an evolving awareness and understanding of the complexity of producing high quality user-friendly systematic reviews within obesity research. As this awareness has occurred I have moved away from a medical model of health (which does not account for the role of social factors in health) and adopted a public health perspective. This perspective has helped me to view the individual and their behaviour within the context of an obesogenic environment and to 'make sense' of the evidence derived from interventions. My developments in methodology are underpinned by this perspective.

I find myself in a distinctive position of having acquired a comprehensive knowledge of the current state of obesity intervention research. I feel privileged to have had the opportunity to use my skills as a systematic reviewer to enable the GDG to develop guidance to combat obesity[24] and experience first-hand the impact that my work has had in influencing this process and thereby influencing practice.

During this time I came to realise that the production of a systematic review is never a stand-alone activity but rather it is one element in the process of translating evidence into practice and it is therefore vital that each review is user-friendly and fit for purpose.

Chapter 4

4 Conclusions

4.1 Review of aims and objectives

This chapter summarizes the main findings according to the objectives defined in the introduction (page 1) and highlights the contribution of the submitted body of work to the overall body of knowledge.

O1 to evaluate the effectiveness of interventions in terms of improving weight status, risk factors for disease and disease

Diets alone and with the addition of exercise and/or behaviour therapy compared with control significantly reduced weight in adults for up to three years and were associated with a WMD weight change in the range of 4 to 13 kg. Adding drugs, exercise or behaviour therapies to diet significantly reduced weight in adults for up to three years and were associated with a WMD weight change in the range of 1 to 8 kg. Adding one adjunct (either exercise or behaviour therapy) was effective but both in combination did not significantly improve weight loss. A 600 kcal/day deficit or low-fat diet; diet and exercise with and without behaviour therapy significantly reduced the risk of type 2 diabetes and hypertension when compared with control.

Diets alone and with the addition of exercise and/or behaviour therapy compared with control significantly prevented weight gain in adults for up to seven years and were associated with a WMD weight change in the range of 0.5 to 7 kg. Compared to control, a 600 kcal/day deficit or low-fat diet; diet and exercise; diet and exercise and behaviour therapy; significantly reduced the risk of type 2 diabetes. Compared to control, a 600 kcal/day deficit or low-fat diet; diet and exercise and behaviour therapy significantly reduced the risk of hypertension. Risk of the metabolic syndrome was significantly reduced with diet and exercise (in men); and with diet and exercise and behaviour therapy compared to control. Diet and behaviour therapy compared to control, significantly reduced the risk of ovarian cancer but not type 2 diabetes.

Adding behaviour therapy to a prevention intervention produced greater weight loss compared with adding exercise. However exercise as an adjunct to diet is perhaps better in the longer term, as exercise, but not behaviour therapy, demonstrated significant weight loss when added to diet at three years. Meal replacements may be a useful tool in the long-term maintenance of weight loss.

In the most recent and comprehensive review of school-based interventions for obesity prevention, 39% of interventions were effective in significantly improving mean BMI compared with control. Interventions which combined diet and physical activity had the

greatest percentage of effective studies compared with diet alone and physical activity alone.

Lifestyle interventions can help prevent excessive weight gain in pregnancy and may help to reduce weight retention between pregnancies and prevent overweight in the offspring. Weight gain prevention interventions incorporated into smoking cessation programmes may help women who are concerned about their weight to stop smoking. Diet and exercise can help to reduce weight in post-menopausal women who are at increased risk of CVD.

Currently there is more evidence of benefit from obesity treatment interventions compared with prevention interventions, from studies in adults compared with children and about short-term intermediary outcomes compared with longer-term clinical outcomes.

Children and adults of ethnic minority status, low-income or disability are at increased risk of obesity. Evidence for effective interventions in these groups (with arguably the greatest need for intervention) is severely limited particularly from UK-based studies. There is also very limited evidence from interventions in pre-school children. It is unknown if and how interventions need to be modified in order to be targeted and tailored to the needs of these vulnerable groups.

An important and under-researched area is lifestyle interventions for the treatment of morbid obesity. Demand for obesity surgery from adults that are morbidly obese is likely to outstrip resources in the UK, with 0.8% of all adults aged 16-24 years being morbidly obese[12]. A systematic review of diet, exercise and behaviour therapy interventions to treat morbid obesity is required to assess which adults are more likely to successfully lose weight without resorting to surgery.

O2 to identify study characteristics, process indicators and contextual factors that may affect the outcomes of interventions

There does not appear to be any clear pattern emerging from the data, in that both simple and complex interventions have demonstrated effectiveness. Longer-term, more intensive and theory-driven interventions have not always produced better results.

Adults with CVD, hypertension or type 2 diabetes appear to lose more or less weight than participants without co-morbidities however the pattern is not consistent. There is limited evidence of lifestyle interventions to prevent weight gain in healthy normal weight adults within the community.

With regard to prevention interventions in children; it is unclear what elements of interventions are consistently effective. Physical activity interventions appear more effective in girls in primary schools compared with boys and children in secondary

school. However, similar interventions were not tested across a range of ages and effectiveness could be due to the type of interventions used in this age group rather than the age itself.

Most studies failed to report effectiveness stratified by demographic characteristics or information about process or contextual factors. More research is required into how and why study characteristics impact on effectiveness.

Interventions may fail to show significant beneficial effect on weight because they are truly not effective or because methods of assessment and study design hamper evaluation of effectiveness. Lack of evidence should not be confused with lack of effectiveness. In order to evaluate effectiveness it is crucial that the relevant research questions are asked and the relevant evidence is identified and evaluated in terms of the outcomes which best match the research questions.

It is likely that the range and intensity of the components of an intervention, the duration of the intervention along with the type of setting and provider, all influence effectiveness. The demographics of the population in terms of age, gender, socio-economic status and ethnicity may all influence the effectiveness of an intervention as well as individual motivation to change behaviours. The aim of an intervention may also influence the outcome and in different ways, as demonstrated when comparing the reviews of children with the reviews of adults. The protocol of a systematic review influences which studies are included and how they are evaluated which impact on the overall assessment of effectiveness. Future evaluation of such effect modifiers will help towards producing optimal effective interventions including interventions modified for vulnerable subgroups[68].

Evidence shows there can be significant weight gain prevention in children from interventions not conceptualized as obesity prevention interventions which is opposite to evidence from interventions in adults which appear more successful when specifically aimed at weight loss.

O3 to develop methodology to synthesize evidence from different study designs

A more flexible approach to producing a systematic review is required when the purpose of the review is to develop guidance to help clinical practice or to help develop an intervention. In addition to effectiveness, public health decision makers require evidence of appropriateness, implementation, feasibility, acceptability and sustainability and the context of individual behaviour change within the wider community and socio-political environment.

A ‘best available evidence’ approach[47] provides the flexibility to include more evidence which can be graded in terms of quality and relevance to the research question. Combining quantitative and qualitative evidence can add context, provide corroboration

and increase understanding, particularly with regard to complex public health interventions. Modeling future predictions of the potential impact of obesity interventions can provide justification to implement public health interventions even when the evidence from systematic reviews is limited.

Developments in the methodology of searching and synthesizing evidence that have evolved within this submitted body of work have been applied in a recent systematic review[69] conducted by the candidate. The aim of this review was to systematically review the effectiveness of diet and physical activity interventions to maintain a healthy weight and prevent overweight, that have been modified for South Asian pregnant women and/or children up to the age of 5 years, living in the UK.

The search strategy included searching key systematic reviews; an electronic search to identify primary studies published after the NICE guidance on obesity[37]; a search of the 'grey literature' and contact with experts. A stepped approach which included the 'best available evidence' was applied in anticipation that there would be limited evidence from RCTs. All types of study design, including corroborative evidence, were included and the types of evidence prioritized by quality and relevance. Each study was assessed according to the study outcome which best matched the primary aim of the study.

Evidence from mainly uncontrolled studies showed a 'direction of travel' towards beneficial behaviour change and corroborative evidence provided insight into what types of modifications have the potential to produce behaviour change in South Asian pregnant women and infants. Promising modifications to obesity prevention interventions include home-based elements; the use of experienced, respected and trusted community linkworkers; and harnessing the role of 'significant others' such as grandmothers of South Asian children.

The review highlighted the limited evidence of obesity prevention interventions modified for South Asian pregnant women and children under six years. The inclusion criteria was less stringent than the criteria for the NICE obesity reviews[24] and so some evidence of direct relevance was identified but from weaker study designs.

This review will inform the design and content of a series of projects as part of the Born in Bradford NHS Research Programme, which will be field tested to determine possible components of a culturally appropriate obesity-prevention intervention[36;69].

O4 to assess how the evidence has informed national strategies and clinical practice.

The evidence contained within the submitted body of work underpins national guidance, informs government policy and influences clinical practice.

The NICE obesity guidance[37] is underpinned by evidence contained within the NICE reviews[24] of pre-school children; school-children; and black, minority ethnic groups, vulnerable groups and life stages. This evidence was also published as a short science review[45] which informed the report on tackling obesity produced by Foresight the Government Office for Science[18]. The UK government obesity strategy and advertising campaign[67] is in direct response to the NICE obesity guidance[37] and future predictions contained within the Foresight report[18].

The Foresight report[18] calls for a comprehensive, coherent and sustainable strategy to tackle obesity which requires a societal approach with partnership between government, science, business and civil society and intervention at multiple levels (individual, family, community and national). Any comprehensive long-term strategy to address obesity must include both prevention and treatment, with prevention being given priority.

Early childhood provides an opportunity to influence lifestyle behaviours[70] and promote a healthy lifestyle whilst simultaneously decreasing the risk of 'high risk' behaviours becoming embedded and tracking through the lifespan. Therefore it would seem intuitive that service provision be targeted at pre-school children with ethnic minority children and children from low-income families receiving extra support through targeted and tailored intervention.

There are proposals in recent media articles (Daily Mail, February 21st 2009) for children to be measured for weight at two years of age. This reflects the governments increasing focus on the early years as a crucial stage at which to combat obesity effectively. There is emerging evidence from ongoing trials in infants which will add to the evidence base in due course[71].

In response to the Foresight predictions and recommendations for change[18] is the Change4Life campaign[67]. It is a society-wide movement underpinned by social marketing theory and techniques which aims to encourage change towards a healthier diet and increased physical activity. A review of interventions to 'raise awareness' commissioned by NICE and conducted by the candidate demonstrated that public health media campaigns can raise awareness of what constitutes a healthy diet and the benefits of physical activity[24]. Dietary intake can improve, motivated subgroups can increase physical activity and food promotion has the potential to influence children's eating habits in a positive way.

Change4Life[67] targets pregnant women, parents of children aged 0-2 years, black and minority ethnic groups who have a higher than average BMI (starting with the Bangladeshi, Pakistani and Black African communities); and priority families that are at high risk of developing obesity and will require specific support.

The Change4Life marketing campaign is also based on qualitative research with families into attitudes and behaviours towards healthy eating and physical activity[72]. Change4Life[67] targets eight behaviours: reducing sugar intake ("Sugar Swaps"), increasing consumption of fruit and vegetables ("5 A Day"), having structured meals, especially breakfast ("Meal Time"), reducing unhealthy snacking ("Snack Check"), reducing portion size ("Me Size Meals"), reducing fat consumption ("Cut Back Fat"), 60 minutes of moderate intensity activity ("60 Active Minutes") and reducing sedentary behaviour ("Up & About").

Through the Change4Life campaign[67] the UK Department of Health is providing £30m to help nine towns to encourage healthy lifestyles[73]. The nine areas taking part in the 'Healthy Towns' Initiative are Manchester, Calderdale, Thetford, Portsmouth, Tower Hamlets, Dudley, Middlesbrough[74], Tewkesbury and Sheffield. All these local initiatives are underpinned by national guidance[37;37] which are based on the evidence from systematic reviews contained within this body of work.

The governments' obesity strategy is based on the 'best available' evidence and both the NICE obesity guidance[37] and Foresight obesity report[18] underpin evidence-based clinical practice for weight management in individuals and local obesity strategies. Tackling obesity is a priority for primary care trusts (PCTs) and there is a national goal to reduce the proportion of obese and overweight children to 2000 levels by 2020, as set out in Healthy Weight, Healthy Lives: A cross-government strategy for England[75].

The candidate has recently produced a rapid needs assessment of childhood healthy weight, commissioned by NHS Knowsley[76]. The approach was underpinned by best practice guidance in section C of Healthy Weight, Healthy Lives: A toolkit for developing local strategies[77]. The needs assessment examined local prevalence of overweight and applied national targets to the data in order to assess whether current service provision had adequate capacity to manage current and future levels of obesity.

It may be more difficult to produce change on a population-wide scale. The Foresight report[18] built on the evidence-base by modeling future levels of obesity to predict that by 2050, 60% of men, 50% of women and 25% of children will be obese, with obesity-related diseases costing an additional £45.5 billion per year. Modeling of the impact of various intervention scenarios demonstrated that significant changes in population BMI (a reduction of four BMI units across the whole population) will be required to produce significant changes in chronic disease levels, taking into account obesity across the lifespan and a considerable time-lag between reduction in BMI and improvement in obesity-related disease.

There are no rigorously tested population-wide interventions to prevent or treat obesity and strategies may have to rely more on the potential that interventions contained within this body of work have demonstrated. Population-wide interventions may suffer from a

perceived lack of need or motivation to change behaviour. From an individual perspective; the costs of positive energy balance are in the distant future and not as potent (and so not as readily amenable to change) as the immediate experienced 'benefit' of leading a sedentary lifestyle with an energy-dense diet that is currently supported by the immediate environment[78].

A comprehensive, systematic and sustainable public healthy obesity prevention strategy is beginning to come into force which is underpinned by the best available evidence contained within this submitted body of work. Whilst both prevention and treatment are necessary to manage obesity; the priority of any comprehensive strategy should be prevention by behavioural change; beginning at the stage of pre-conception. Population-wide recommendations may be effective in preventing a population increase in the prevalence of obesity only as part of a government strategy that includes environmental change and is coupled with targeted interventions to reduce the prevalence of obesity caused at least in part by social inequalities.

4.2 Practice recommendations

4.2.1 Recommendations for reviewers producing systematic reviews of obesity interventions

1. In cases where it is anticipated that limited evidence will be identified from high quality intervention studies; a 'stepped approach' using the 'best available evidence' is recommended. Rather than attempt to pre-specify which types of study design will be included it is more constructive to include a wide range of study designs (at least initially) and prioritize each identified intervention according to quality and relevance to the research question. Adopting this approach will influence each element of the process of producing a review including protocol, search strategy, inclusion criteria, data extraction and analysis.
2. The aims and objectives of a review should include clear and concise research questions to guide the reviewer when searching, extracting, synthesizing and analysing data. The results of the review should answer the research questions and describe the strength of the evidence underpinning the answers and, if necessary, give reasons why research questions cannot be answered.
3. It is important that the reviewer clearly states which outcomes will be used to determine whether an intervention is 'successful' (e.g. significant beneficial change in BMI or prevalence of overweight or both?)
4. The protocol needs to reflect the iterative nature of conducting a systematic review of complex public health interventions and allow for flexibility.
5. Inclusion criteria and search strategies need to be broad (because some evidence of direct relevance to the research question may be identified from

weaker study designs). A wide range of sources of evidence should be searched to identify the 'best available evidence'. These include but are not limited to:

- electronic databases (e.g. MEDLINE, EMBASE, Cochrane)
- systematic reviews
- websites (e.g. HTA, NICE, Medical Research Council, Food Standards Agency, Health Management Information Consortium, Evidence for Policy and Practice Information and Coordinating Centre)
- research registries (e.g. National Research Register)
- research networks
- databases of PhDs (e.g. British Library and Index to Theses)
- journals and conference proceedings
- reference lists of included interventions and systematic reviews
- experts (e.g. academics, dietitians, community linkworkers, key people active in local government and primary care trusts).

6. Outcome data should be extracted for mean BMI and prevalence of overweight. BMI is a useful measure to assess obesity from a public health perspective however prevalence data is equally important because it may be more sensitive to changes within individuals and vulnerable subgroups; which is useful information for policy-makers.
7. Process data should be extracted including data on appropriateness, implementation, feasibility, acceptability, sustainability and context. Evaluation of environmental change within which behaviour change occurs is vital. Both outcome and process data should be viewed as equally important elements of any intervention.
8. It is useful to map the intervention according to the spheres of influence that each intervention aims to influence (e.g. individual, family, school, supermarket, leisure facility). Mapping will produce a clear picture of where evidence is relatively 'strong', where there are gaps which require further research, and whether effectiveness varies according to the spheres of influence of the intervention.
9. The 'best available evidence' needs to be synthesized in order to make sense of the evidence. This can be done by grading the evidence according to quality and relevance to the research question. This provides the end-user with a certain level of confidence in the evidence which underpins the answers to the research questions.

4.2.2 Recommendations for researchers carrying out primary interventions in obesity research

Many practice recommendations for systematic reviewers (4.3.1) are useful to primary researchers when reporting their study. In addition, comprehensive and systematic

measurement of BMI during childhood throughout the UK using one universal method of classification of overweight would greatly enhance the work of these researchers.

1. Systematic reviews of the 'best available evidence' should be used to inform primary research. Primary studies should test interventions which show the greatest potential for health benefit (e.g. combined diet and physical activity interventions in schools) rather than interventions which evidence shows are unlikely to be effective (e.g. nutrition education alone). This will increase the likelihood of identifying an effective intervention and increase the evidence base.
2. Studies are needed which repeat interventions across the age range which have already shown potential for effectiveness in children, to evaluate whether it is the nature of the intervention or the age of the child which influences the effect.
3. More community-based interventions are required to reflect real life and recognition of the influence of an obesogenic environment. There is currently limited evidence of lifestyle interventions to prevent weight gain in healthy normal weight adults within the community. Many new policy interventions are community-based and we need to build an evidence-base of such interventions and develop new methods of evaluation.
4. Studies are required which are targeted and tailored for vulnerable groups at increased risk of obesity (e.g. minority ethnic groups, low-income groups and groups with limiting disabilities) and vulnerable life-stages (e.g. pregnancy and menopause).
5. Studies need to be sufficiently powered and of long enough duration to detect significant differences in outcome measures.
6. Study protocols should be registered to increase dissemination and reduce publication bias. Registration of protocols would also allow reviewers to assess whether outcomes that researchers aimed to measure were measured and reported (this is now recognised as an important element of quality assessment).
7. The aim of the study, the intervention and the primary outcomes of interest should be explicitly stated and justified. The intervention and the outcomes measured should match the aim (e.g. do interventions which increase fruit intake or provide a healthy breakfast at school 'fit' with an aim of preventing excessive obesity and is this best measured by behaviour change and/or weight change?)
8. A detailed description of the intervention including range, intensity, who when and how it was carried out should be reported.
9. Detailed reporting of demographic characteristics such as age, gender, socio-economic status and ethnicity is needed in order for reviewers to measure the impact of these variables on effectiveness and the impact of the intervention on health inequalities.

10. Change in mean BMI and prevalence of overweight should both be measured as it is useful to assess how change in prevalence and mean BMI has occurred (e.g. is prevalence change due to weight loss in the overweight population or is reduction in mean BMI due to reduced incidence in the normal weight population?)
11. The number of participants assessed at each time point in each group and the mean and standard deviation change for each outcome needs to be reported in order for systematic reviewers to carry out meta-analyses.
12. Process data should be measured and reported including data on appropriateness, implementation, feasibility, acceptability, sustainability and context.
13. Costs relating to carrying out the intervention should be measured and reported.

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Appendices