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1. Title

The use of measures of obesity in childhood for predicting obesity and the development of obesity-related diseases in adulthood.

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3. Plain English Summary

Obesity is an accumulation of excess body fat to the extent that it may impact adversely on a person's health. Determining if a child is obese or not is difficult, as natural age-related variations in body composition needs to be taken into consideration. To be useful in practice, the methods also have to be acceptable to healthcare workers, children and their guardians. Currently used methods include measures such as body mass index (BMI), waist-to-hip ratio, and skinfold thickness, with various pre-specified cut-off points. Obesity in childhood and adolescence is thought to increase the risk of adult illnesses such as type II diabetes, cardiovascular disease and cancer, possibly through increasing the chance that they will become obese adults, or possibly through a direct cause. To date most research into this has been based on childhood obesity identified using the BMI measure. It is therefore currently unclear which simple measures of obesity best determine if a child is obese, and to predict if a child is at risk of obesity and obesity-related health problems in adulthood.

This project will assess how well the various simple measures predict the risk of childhood obesity for subsequent adulthood obesity and obesity-related diseases such as cardiovascular disease, diabetes and cancer. It will also investigate how accurate each of the simple measures is for measuring body

fat in children and how acceptable these measures are in practice to children, guardians and healthcare professionals.

4. Background

4.1. Obesity

Adiposity, or obesity, is defined as an accumulation of excess body fat to the extent that it may have an adverse effect on health.[1] Adult obesity in England has increased from approximately 16% in 1995 to approximately 26% in 2010, with the increase seemingly continuing. Obesity in adults has been linked to increased mortality and morbidity.[1] A meta-analysis of 26 cohort studies reported 60,374 deaths, 17,708 deaths from coronary heart disease, and 27,099 deaths from cardiovascular disease (CVD) among 388,622 adults recruited in the studies. When the normal weight people were compared to those who were obese (using BMI) the risk of mortality was significantly increased for the obese group. The pooled relative risks (95% confidence intervals) reported were: 1.20 (1.12 to 1.29) for men and 1.28 (1.18 to 1.37) for women, for overall mortality; 1.51 (1.36 to 1.67) for men and 1.62 (1.46 to 1.81) for women, for death from coronary heart disease; and 1.45 (1.33 to 1.59) for men and 1.53 (1.38 to 1.69) for women, for death from CVD.[2]

4.2. Childhood obesity

According to the figures reported by the National Obesity Observatory (NOO), the proportion of children aged 11 to 15 years old in England who were obese was similar to adults (16 years and over) up to 2004. Just under 15% were obese in 1995, rising to just over 25% in 2004, but unlike adults, there has been a decrease since, with the proportion obese plateauing in 2010 at approximately 18%. In children aged 2 to 10 years, the proportion who were obese was less, 10% obese in 1995 which rose to a peak of approximately 17% in 2005, followed by a decrease to just under 15% in 2010.[3] More recently, data for younger children has been provided by the National Child Measurement Programme (NCMP) which has been in progress for six years. The prevalence of obesity has been measured using BMI (using the 85th centile for overweight and 95th for obese) at two time points (aged 4/5 and 10 years) using a cross-sectional study design. In England in the 2011/2 school year the NCMP recorded 1,056,780 measurements in children (participation rate of 93%).[4] At reception (aged 4 to 5 years), 22.6% of children were either overweight or obese and 9.5% were obese. These figures increased in Year 6 (aged 10 years by 1st September (start of school year)) to 33.9% of children being either overweight or obese and 19.2% being obese.[4, 5] From these figures, it seems that the prevalence of overweight and obesity, and changes over time, varies for different age groups of children. It has been projected that by 2050, the prevalence of obesity in children will increase in boys to over 35% in those ages 6 to 10 years and 23% in those aged 11 to 15 years, and in girls to 20% in those ages 6 to 10 years and 35% in those aged 11 to 15 years.[6]

The prevalence of childhood obesity varies depending upon ethnicity.[7] The NCMP reported that the rate of obesity was significantly higher in children of black or Asian descent;[8] a recent cross-sectional survey conducted in London, Birmingham and Leicester primary schools also reported higher adiposity levels in South-Asian children, but similar or lower adiposity in black African-Caribbean children compared to white Europeans.[9] Another review that specifically evaluated the impact of ethnicity on the prevalence of obesity in the UK reported that prevalence was inconsistent across studies in South Asian and black African and Caribbean populations: the risk of obesity was shown to be higher than whites in South Asian boys but lower in girls, with the reverse being the case for black African and Caribbean.[10] The authors stated that certain obesity metrics may bias obesity prevalence among particular ethnic groups relative to white populations.[10] There are currently no ethnicity-specific classifications for any measure of obesity other than those tested for bioelectrical impedance analysis (BIA) in a recent study, which demonstrated that ethnic- and gender-specific equations for predicting fat free mass (FFM) from BIA can provide better estimates of ethnic differences in FFM and fat mass in children, while generic equations can misrepresent these ethnic differences. [11]

4.3. Relationship between childhood obesity and adulthood obesity and morbidity

It is generally accepted that adult obesity increases the risk of some morbidities, particularly CVD, type 2 diabetes and some types of cancer.[7, 12-14] It may also be associated with other chronic conditions such as rheumatologic disorders, asthma, psychological illness, sleep disorders, and reduced fertility.[7] However, the link between childhood obesity and adult morbidity is less clear, with uncertainty as to whether it is the tracking of obesity from childhood into adulthood that is the key factor, or whether childhood obesity is an independent risk factor for adult morbidity,[15] particularly when measured in children under 7 years of age.[16] A recent systematic review of 25 studies stated that all the studies consistently reported that overweight and obese children were at an increased risk of becoming overweight or obese adults; the risk of tracking into adulthood obesity increasing as the level of overweight/obesity in childhood increased.[17] The findings from that review suggested a moderate likelihood of persistence of overweight into adulthood for children who were overweight or obese, but there were considerable variations in the predictive values across studies. Regarding the link between childhood obesity and adult morbidity, recent systematic reviews support the opinion that it is adult obesity,[18] or the continued overweight/obesity from childhood into adulthood,[1, 19, 20] that increases the risk of adult morbidity, rather than obesity in childhood being an independent risk factor for adult morbidities,but there is some uncertainty and it may vary across the morbidities.

4.4. Measuring obesity

4.4.1.Simple measures of obesity

There are a range of simple, anthropometric, indirect measures of adiposity.[21, 22] The simplest measure is weight, however, on its own, this provides little useful information as confounding variables such

as a person's height and body composition are not taken into consideration. Waist circumference is a useful single measure, as it gives an indication as to the distribution of excess body fat, however, in isolation it provides insufficient information regarding overall adiposity. BMI is the most commonly used simple measure of obesity, and is also the only measure recommended for use in children in the UK. It is calculated by dividing weight in kilograms by height in metres squared (Kg/m^2). BMI increases sharply in infancy, peaking at around 9 months, and then falls to its lowest at around 6 years.[23] BMI (adjusted for age and gender) is recommended by NICE (CG43) as a practical estimate of overweight in children and young people, but the guidance warns that the result needs to be interpreted with caution because BMI is not a direct measure of adiposity.[24] The main limitation of BMI is that it measures excess weight, rather than excess fat which is what determines whether someone is obese or not. Therefore, those with strong bones and/or well-developed muscularity but little fat will have a high BMI and could be categorised as obese, as bone and muscle are more dense than fat.[25] Also BMI is not consistent across the normal height range, with shorter heights producing higher BMI values. [26] BMI also does not give any indication as to the distribution of fat in the body: in adults, central adiposity is more closely associated with health risks than general adiposity,[27, 28] and the use of BMI and waist circumference is recommended in adults in the UK. Other simple measures include:

- *Neck circumference*: This is thought to be correlated with cardiovascular disease in adults; a neck circumference of over 35.5 cm in men and 32 cm in women has been suggested as the cut off values for obesity in adults aged 18 to 20 years.[29, 30] The use of the measure has been investigated in children, and is thought to reliable for identifying children with high adiposity.[31-33] Thresholds for obesity being suggested as: 29 cm in prepubertal boys, 28 cm in prepubertal girls, 32.5 cm in pubertal boys, and 31 cm in pubertal girls.[33]
- *Rohrer's Ponderal Index (Rohrer's Index, Ponderal Index or Corpulence Index)*: Similar to the BMI, but is calculated by dividing weight in kilograms by height in metre-cubed (Kg/m3) , rather than height in metre-squared.[25] Normal values for a 12 month old infant are suggested as between 10.3 and 13.9 kg/m^3.
- *Benn's Index*: Calculated by dividing weight in kilograms by $height^p$ (Kg/m^p); ^{p} is a power index derived from the weight to height ratio (p=bH0/W0) making the index independent of height.[25, 34] Benn's index is rarely used as p is neither constant, nor necessarily a whole number, which means the calculations are complicated.[25] A study in boys from four countries showed that the power of p required to produce a correlation of zero between the index and height varied with age and ethnicity; for US, Japanese, and Singaporean boys, the p value was <2.8 at age 6, increased to <3.5 at age 9 to 10, and decreased to <2.0 by age 16. For UK boys, p started at <2.3, increased to <2.6 then decreased to <2.0.[35]

- *Waist-to-height ratio*: As with waist-to-hip ratio, waist-to-height ratio is a measure of fat distribution, and primarily identifies those with abdominal obesity. A person is considered obese if their waist circumference is over half their height (threshold of 0.5).
- *Waist-to-hip ratio*: A measure of regional fat distribution used as marker for intra-abdominal fat in adults; whether there is a similar correlation in children is unclear.[21] A waist-to-hip ratio of 0.85 or over in females, and 1.0 or over in males, is considered to be indicative of a high risk of health problems. One of the limitations with ratios using waist measurement is the potential for measurement error, as there is inconsistency as to the actual site of the waist measurement.
- *Body adiposity index (BAI)*: This was suggested by Bergman *et al*. (2011) as reflecting the percentage body fat in adults regardless of gender or ethnicity without numerical correction, and therefore was considered an improvement on BMI.[36] BAI is calculated by the equation (hip circumference/(height)^{x})-18, with x being a unitless power term. The highest correlation between BAI and percentage adiposity was highest when x was between 1.47 and 1.5, therefore the use of 1.5 as the power term in adults was suggested.[36] The measure has not been validated in children, and a power term for children has not been specified.
- *Skinfold thickness*: A direct anthropometric measure of adiposity. Skin fold measurements are considered as good indicators as they are a direct measure of the fat layer, but the measurements are site and gender-specific.[23] The most common sites are the subscapular and the triceps;[21] other potential sites include the chest, axilla, abdomen, suprailium and thigh.[22] Scores can be presented adjusted for age and gender. There are also a large number of equations available that can be used to obtain an estimate of percentage subcutaneous fat from skinfold thickness measurements,[21, 22] though these may introduce biases and have not been standardised for children over the age of six.[37] In adults, women with 32% or higher, and men with 26% or higher, body fat are classified as obese. One of the limitations of skinfold thickness is that visceral fat (fat in the abdominal cavity) is not measured. As with waist measurements, measurement error is a particular limitation of this method. There can be considerable variability across practitioners, leading to the requirement for specific training.
- *Bioelectrical impedance analysis (BIA)*: Measures the opposition to the flow of an electric current applied to extremities of the body (usually the wrists or ankles; in children, foot to foot currents are used as this requires the child only to stand barefoot on scales), using a low-level (below the threshold of human perception usually a single frequency of 50 kHz) alternating electrical current passing through the body; this is used to estimate total body water. As fat contains little water compared to other body tissues, impedance can be used as a proxy measure for fat-free body mass. Body fat can then be calculated from the difference between fat-free body mass and overall weight. BIA has several limitations. Firstly, the body is a number of cylinders of different length and diameter (legs, torso, arms), rather than a single cylinder, and given that resistance decreases

as the cross section of a cylinder increases, the arms and legs contribute more to resistance than the torso. The limbs represents 50% of body weight but 90% of the body's impedance; this means that impedance is more closely related to changes in the muscle mass of the limbs. In addition, as there is an assumption that fat free mass is 73% water,[22] factors such as dehydration, exercise, diuretics or a full bladder will affect the results.[38] Furthermore, equations based on height and weight are used to determine overall adiposity and these vary across manufacturers. The equations used by some instruments may be unknown, and results may vary across different instruments and populations.[39] Given these limitations, BIA is currently not recommended for use in the UK.

- *Fat mass index (FMI)*: Calculated from fat mass as determined by BIA (Kg) divided by height squared. FMI plus the fat free mass index (FFMI; fat-free mass/height squared) = BMI.[40]
- *Near-infrared interactance (NIR)*: A beam of infrared light is transmitted into the biceps; the light is reflected by underlying muscle and absorbed by fat, therefore the proportion of reflected light will indicate the proportion of fat. The NIR light penetrates the tissues to a depth of 4 cm and is reflected back to the detector, which measures the optical density at wavelengths of 940 nm (optical density 1) and 950 nm (optical density 2). The underlying principle is that optical densities are linearly and inversely related to percent body fat, and thus, the smaller the optical density, the greater the absorption of NIR light and the higher the fat composition.[22]

4.4.2. More complex measures of obesity

Apart from skinfold thickness, the anthropometric measures listed above are indirect measures of adiposity. There are a number of more direct measures of adiposity available; these are not routinely available and need to be conducted by those who have been specifically trained, and are therefore not useful as population measures. Such measures include:

- *Densitometry (hydrostatic weighing)*: This method measures underwater weight. This distinguishes fat mass and fat-free mass, assuming specific densities of these two tissues, and therefore requires measurement of total body density (body mass/body volume).[41] While the density of fat is relatively constant, that of fat-free mass varies according to its composition. This variability is partly explained by the process of chemical maturation that occurs before adulthood, but inter-individual variability is also significant, even in healthy children.
- *Densitometry (air displacement plethysmography; PEA POD)*: A new system that uses the displacement of air rather than water. This is thought to have better precision than hydrodensitometry in children, and is acceptable in children as young as 4 years.[42] An infant plethysmograph has become available allowing the measurement of body volume during the first 6 months of life. In general, densitometry is unsuitable for application as a two-component technique in patients where the composition of lean mass may be abnormal, such as excess fluid

retention and under-mineralisation, as these decrease the density of lean mass and lead to an overestimation of fatness.[42, 43]

- *Multicomponent models*: These models combine the results of three, four or five different measures. The three-component models divides body weight into fat, water, and fat-free dry tissue, and requires measurements of body weight, body water by hydrometry, and body volume by densitometry. The four component model further divides fat-free dry tissue into protein and mineral, and requires the measurement of bone mineral by DXA. Its advantages are that it is most accurate approach, with all the component measurements being acceptable. It has the disadvantage of being expensive and thus generally limited to specialist research.[41] Body volume index (BVI) is a new multicomponent measure that uses BMI, waist circumference, and waist-hip ratio along with other volumetric and body composition analyses. The method requires a 3D full body scanner.[44]
- *Dual-energy X-ray absorptiometry (DXA)*:[41] DXA is a three compartment model as it measures bone mineral, bone-free lean mass and fat mass. For accurate estimation of body fat, the hydration of lean body mass needs to be established; often a constant for hydration of lean body mass (0.73 mL/g) is assumed, which is based on non-elderly, healthy, adult measurements. The use of this assumption can lead to an error in the amount of lean tissue, particularly in children, the elderly, and the sick; DXA is likely to be more reliable in healthy adults with a constant tissue hydration.[45, 46] DXA may therefore have difficulty accurately assessing body mass in infants, with increasing accuracy as body size increases. DXA also has difficulty distinguishing between bone and non-bone lean mass in high bony areas (thorax, forearm).[45] In a review comparing DXA to four-compartment models, DXA tended to underestimate body fat in most studies, with this underestimation usually being greater in leaner people. Some studies did find DXA overestimated body fat, and some no difference; there seemed to be differences in accuracy with different DXA technology.[47]
- *Deuterium dilution method*: Deuterated water ($^2H_20$) is currently the most accurate way of measuring total body water. The difference in secreted markers (urine, saliva) between baseline and post ingestion is used in an algorithm to calculate total body water and fat free mass. The difference then between total body mass and fat free mass gives fat mass, so you can work out body comp, but the method is most effective for total body water when used in a multi-(four)-component model with body density (hydrostatic weighing or bodpod), BIA and DXA. The method is safe and has been validated in wide range of populations but does have disadvantages; it is expensive, time consuming (requires sample collections and analyses) and rather invasive because it requires participants to ingest a dose of deuterium-enriched water.[48]

4.5. Challenges when measuring obesity in children

To monitor the trend in, and to reduce the prevalence of, overweight and obesity, several initiatives have been introduced in the UK. Programmes that target obesity in general include the Department of Health's 'Call to Action',[49] the National Obesity Observatory,[50] and the International Obesity Task Force.[51] Programmes aimed specifically at children include the National Child Measurement Programme, which measures the weight and height of children in reception class (aged 4 to 5 years) and year 6 (aged 10 to 11 years) in order to assess overweight and obesity levels within primary schools.[8] In order for such programmes to succeed, the measure of obesity needs to be accurate and simple to implement. It is therefore important to investigate whether BMI, the most commonly used simple measure, is the best measure for wide-ranging screening programmes, and if not, which measure (or combination of measures) should replace it in order to ensure that children at risk of obesity-related morbidity are identified.

The assessment of childhood obesity using BMI, and other anthropometric measures, is more complicated than that of adults.[52] The major limitation of anthropometric measures to determine obesity in children is that most are confounded by natural age-related physiological variations in body composition.[23, 53] As a result, actual measurements are compared to reference data to determine whether a child is overweight or obese. However, for BMI, the most commonly used anthropometric measure in children, there are several reference datasets available, including the centiles of the UK 1990 Growth Reference, International Obesity Taskforce thresholds, and the World Health Organisation (WHO) Growth Reference; the advantages and disadvantages of each have been summarised elsewhere.[54] This results in different thresholds being used for defining overweight and obesity across organisations and countries, which makes the comparability of data and the determination of the accuracy of these measures difficult.[55] In the UK, BMI is related to the UK90 BMI growth reference charts to determine whether a child is obese. For clinical purposes, overweight is defined as a BMI $\geq 91^{st}$ centile and obesity $\geq 98^{th}$ centile, however, much of the data available has been collected within a research context, and for research purposes the 85^{th} and 95^{th} centiles are recommended to classify overweight and obesity, respectively.[1] The associated standardised scores based on UK90 reference data are: 1.04 for the 85^{th} centile; 1.34 for the 91^{st} centile; 1.64 for the 95^{th} centile; and 2.0 for the 98^{th} centile. Most of the anthropometric measures being investigated in this review will be affected by a child's age, gender and ethnicity and will therefore require standardisation . Neck circumference, NIR and waist-to-height ratio are measures not subjected to standardisation. It is unclear whether this is because these measures are suitable for use in children without standardisation, or merely that such standards have not yet been established. A lack of requirement of standardisation for age and gender for a measure would afford that measure some advantage over anthropometric measures that do require standardisation; whether this would be at the cost of accuracy would need to be established.

A further challenge arises when an association needs to be made between childhood obesity and adult morbidity, as very long-term studies are required. One study followed 1000 families from Newcastle (UK), involving 1142 children recruited at birth in 1947; 412 were followed to the age 50.[56] The study concluded that there was little tracking of obesity from childhood to adulthood, there was no excess adult health risk from childhood or teenage overweight, and being thin as a child offered no protection against obesity in adulthood.[56] This contrasts with the results of other studies and reviews;[15-18] although this may be related to population differences due to the age of the cohort, it may also be a result of the study being underpowered. A comparison of two British birth cohorts, one of children born in 1946 and the other born in 1958, showed that girls in the 1958 cohort had a higher average BMI during seven years in childhood, and that both boys and girls in the 1958 had a greater rate of increase in BMI during adulthood.[57] These studies illustrate that potential determinants and levels of adiposity in childhood differ between these birth cohorts, and are likely to differ for the present day child population. However, the long-term relationships between childhood obesity and adult morbidity may not change as a result of these differences and standardisation of obesity scores is thought to mitigate some of the changes observed over time.

4.6. Summary

It is generally accepted that adult obesity is associated with an increased risk of morbidity (type II diabetes, CVD and cancer) and premature mortality in adults. However, the link between childhood obesity and adult morbidity and obesity is less clear; this could be due to the persistence of childhood obesity into adulthood, or childhood obesity may be an independent predictor of obesity-related diseases in adulthood. Recent systematic reviews have indicated that childhood obesity is predictive of adult obesity, but that childhood obesity is not an independent predictor of obesity-related diseases in adulthood. However, these reviews have primarily been based on studies that used BMI to determine the presence and level of obesity. BMI is the most commonly used measure, but there are concerns regarding it's suitability in determining obesity in children, particularly in relation to the need for standardisation. The question remains whether another simple measure, either used alone or in combination with BMI or some other simple measure, would be better for gauging the association between childhood obesity and adult obesity and (separately) adult morbidity. It is therefore important to determine the diagnostic and predictive accuracy of the simple measures that are available in order to inform the decision as to which should be used for screening children to identify those at risk of developing obesity and serious obesity-related morbidities as adults.

5. Decision problem

The decision problem to be addressed is: "What is the best simple measure, or combination of simple measures, of obesity in children for predicting the development of obesity-related health problems

such as type II diabetes, CVDs and cancer in adolescence and/or adulthood?". Given the relationship between adult obesity and morbidity, the ability of these simple measures to predict the persistence of obesity from childhood into adolescence and adulthood will be investigated. Acceptability and ease of use of the measures are also important when considering whether any one of these measures should be introduced as the standard method for the assessment of childhood obesity; this will also be addressed within the review.

6. Objectives

The objective of our research will be to address through systematic reviews the questions raised in the decision problem.

1. To what degree do simple measures of obesity in children accurately predict the tracking of obesity into adolescence and adulthood?
2. Is obesity in children an independent risk factor for CVD, type II diabetes and/or cancer in adolescents and adults, and do the results vary according to the simple measure of obesity employed?

In order to fully evaluate the predictive value of the simple measures of obesity, and therefore the relationship between the measures and subsequent adult obesity and morbidity, the relationship between the measure and actual adiposity needs to be established. Therefore, a third question will be addressed:

3. How accurately do simple measures of obesity reflect actual adiposity in children?

Once the most promising measure(s) has been determined in terms of diagnostic and predictive accuracy, a fourth question will be addressed for that measure(s):

4. How acceptable are these measures of adiposity to children and their carers, and how easy is it for health professionals to implement them?

7. Methods of synthesising evidence of clinical effectiveness

Systematic reviews of primary studies will be conducted for the first three review questions above: These systematic reviews will be conducted following the general principles recommended in CRD guidance for undertaking reviews in health care,[58] and the reporting guidance of the PRISMA statement.[59] However, existing systematic reviews have already been identified for questions 1 and 2.[60-63] Therefore prior to conducting full systematic reviews of primary studies, the literature will be checked for further directly relevant, recent, and good quality systematic reviews. The systematic reviews identified will be used as the basis for the current reviews, thereby avoiding duplication of effort. A commentary on the findings of these reviews will be included in our report. A re-synthesis of

the data will be undertaken to address questions 1 and 2 only if additional primary studies are identified or if flaws or limitations in the existing analyses are identified.

A systematic review will also be conducted for question 4, to determine the acceptability and ease of use of the measures, including BMI (as this is the most commonly used measure in clinical practice and is the comparator for the other measures being evaluated) and other measures shown to be the most promising in terms of diagnostic and/or predictive accuracy.

7.1. Search Strategy

Published and unpublished literature will be identified from systematic searches of electronic databases, grey literature resources, reference checking, citation searching, and consultation with experts in the field. For this project we will undertake three separate searches of the literature about: (i) tracking of obesity from childhood into adulthood; (ii) systematic reviews about measures of childhood obesity predicting CVD, type II diabetes and cancer in adolescents and adults; and (iii) diagnostic accuracy of the simple measures of obesity in children. The search strategies will be structured using the following concepts:

- Question 1, tracking: Obesity AND Children AND Index test terms AND Tracking
- Question 2, prediction of adult morbidities: Systematic reviews search filter AND Obesity AND Children AND Index test terms AND (CVD OR Diabetes OR Cancer).
- Question 3, diagnostic accuracy: Obesity AND Children AND Index test terms AND Reference test terms

Search terms will be identified through discussion between the review team, by scanning background literature, and by browsing database thesauri. The searches will not be restricted by date or language.

The following databases and resources will be searched: MEDLINE, EMBASE, PsycINFO, CINAHL, the Cochrane Library including Cochrane Database of Systematic Reviews (CDSR), Cochrane Controlled Trials Register (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), and Health Technology Assessment (HTA) database, EPPI-Centre databases, Science Citation Index, Conference Proceedings Citation Index-Science, and Health Management Information Consortium (HMIC), as well as grey literature resources, such as OAIster, SIGLE, and related organisation websites and conference proceedings.

The three draft search strategies are available in Appendix 1; a strategy will be developed along similar lines for question 4 once the most promising measures have been identified.

7.2. Inclusion/exclusion criteria

Reviews have already been conducted for questions 1 and 2, therefore, initially systematic reviews that meet the criteria in Sections 7.2.1 and 7.2.2 will be sought for these questions, respectively. When recent, relevant good quality reviews have been identified these will be used as a source of primary studies for the current systematic reviews. The quality of the systematic reviews, and therefore selection for inclusion, will be based on the criteria used to determine inclusion on the DARE database. Systematic reviews that pass this assessment and are selected for inclusion will be subject to a more rigorous critical appraisal based on pre-specified criteria (see Section 7.4). Primary studies that meet the criteria in Sections 7.2.1 and 7.2.2 will be included for questions 1 and 2, respectively. Given the nature of the data required for meta-analysis, many of the studies included for these questions may be cohorts recruited when influences in childhood were most likely different to those of the present day child population. However, the long-term relationships between childhood obesity and adult morbidity may not change as a result of these differences, and these older cohort studies can still provide useful information. Therefore, reviews where such older cohorts are included will not be excluded from the review. In terms of the anthropometric measures, we will include studies regardless of the equation used to derive the measure, or to convert the measure into an estimate of body fat. The details of these equations will be extracted and the impact of variations will be investigated.

7.2.1. To what degree do simple measures of childhood obesity predict the tracking of obesity into adolescence and/or adulthood?

- *Population*: Studies recruiting children and/or adolescents (up to the age of 18 years) will be eligible for inclusion. Studies recruiting a mixture of adults and children/adolescents will be included if the results for children/adolescents are reported separately. Studies have to recruit either population based samples of children, or overweight/obese children; studies conducted only in children who were not overweight or obese will be excluded. We will accept the definition of obesity/adiposity used in the study, and investigate and discuss the impact of any variability observed for each measure.
- *Interventions*: The following simple measures will be evaluated: BMI, neck circumference, waist circumference, waist-to-hip ratio, waist-to-height ratio, BAI, Rohrer's Ponderal Index, Benn's Index, FMI, skinfold thickness, BIA and NIR. Studies will be included for each of these measures, regardless of how the measurement was conducted (i.e. any BMI equation or level at which the waist is measured, will be eligible).
- *Outcomes*: The study will have to report relative risks, odds ratios, hazard ratios (including measures of variance), or sensitivity and specificity, or sufficient data from which these can be derived, for the association between the estimate of adiposity in childhood and/or adolescence and the incidence of obesity in adulthood.

- *Study design*: Prospective, longitudinal studies that evaluate any one of the interventions of interest, will be eligible; case-control studies and retrospective studies will be excluded. We will initially restrict inclusion to studies that recruit at least 100 children. Smaller studies will be included; however, small studies will have to be free of serious methodological bias to be included. Inclusion will be restricted to those studies where predictive accuracy of the anthropometric measure can be established; studies that report only correlations between the childhood and adult measures will be excluded. We will not exclude any study based on the measures used to establish adiposity at the various time-points; if these differ across time-points within a study, the potential impact of this will be investigated and discussed.

7.2.2. Is obesity in children an independent risk factor for CVD, type II diabetes and cancer in adolescence and/or adulthood?

- *Outcomes*: The study will have to report relative risks, odds ratios, hazard ratios, or summary estimates of predictive accuracy, or sufficient data from which these can be derived, for the association between childhood obesity and adult CVD, type II diabetes or cancer. For the purposes of this review CVD will incorporate major cardiovascular events such as cardiovascular death, myocardial infarction, stroke, and heart failure, as well as the development of the two major cardiovascular risk factors, including hypertension and hypercholesterolaemia.
- *Study design*: Prospective, longitudinal studies that are sufficiently powered that evaluate any one of the interventions of interest used in childhood for the prediction of a morbidity of interest in adolescence or adulthood, will be eligible; case-control studies and retrospective studies will be excluded.

7.2.3. How accurately do simple measures of obesity reflect actual adiposity in children?

- *Population*: Studies recruiting children and/or adolescents (up to the age of 18 years as defined in the NICE CG43 obesity guidelines) will be eligible for inclusion. Studies recruiting a mixture of adults and children/adolescents will be included if the results for children/adolescents are reported separately. Studies have to recruit either a population based sample of children, or overweight/obese children; studies conducted only in children who were not overweight or obese will be excluded.
- *Interventions*: The following simple measures will be evaluated: BMI, neck circumference, waist circumference, waist-to-hip ratio, waist-to-height ratio, BAI, Rohrer's Ponderal Index, Benn's Index, FMI, Skinfold thickness, BIA and NIR.
- *Reference standard*: Multicomponent models that measure four or five compartments will be considered the gold standard in this project for assessing the accuracy of simple anthropometric measures of adiposity in children, because the precision of these models is considered to be higher

than other complex measures. The other complex measures such as DXA, deuterium dilution, and densitometry (water or air displacement) will be used as reference standards, as they are more commonly used in research studies; these will be considered imperfect reference standards, and the potential impact of their limitations on the estimates of diagnostic accuracy will investigated and discussed.

- *Outcomes*: The study will have to report either summary estimates of diagnostic accuracy, or sufficient data from which these can be derived.
- *Study design*: Prospective single-gate (diagnostic cohort) studies that evaluate any one of the interventions of interest in comparison to any one of the reference standards will be eligible for inclusion. For measures for which these are not available, prospective two-gate (diagnostic case-control) studies will be included; these must match cases and controls on at least age and gender, or provide estimates of sensitivity and specificity that have been adjusted for these variables.

7.2.4. How acceptable to children and their carers, and easy to implement for health professionals, is the most accurate simple measure(s) of obesity in children?

Once the most promising measure(s) in terms of diagnostic and predictive accuracy have been identified, primary studies that undertake a robust evaluation (such as the use of questionnaires or interviews) of the acceptability and ease of use of BMI and these comparator measures in children (from the perspective of the child, parent or health professional) will be included in the systematic review of acceptability of the simple measures. Studies that discuss these issues with no direct measurement of acceptability or ease of implementation will not be included. Given the recent changes in the distribution across the population, the emphasis placed on education and intervention for obesity, and general attitudes towards obesity, the inclusion of primary studies will be restricted to those conducted within the prior five years (search start date 2008); this will ensure the population assessed as representative of the current overweight and obese population as possible.

As we expect the number of studies to have addressed this issue to be very small or even zero, we plan to conduct a simple elicitation exercise (survey) to obtain some indication of the attitudes of children, school nurses and parents to the measures being evaluated. The conduct of this exercise will be subject to ethical approval by the Carnegie Faculty Committee, Leeds Metropolitan University, UK. If approval is granted, children (including overweight, obese and healthy weight), school nurses, and parents will be asked to complete structured questionnaires, developed specifically for the project, and suitable for their age group. We anticipate a sample of around 200 children and parents and at least 10 school nurses. We plan to elicit opinions for four of the measures being evaluated in the review: BMI, skinfold thickness, waist-to-hip ratio and waist-to-height ratio. These were chosen as they are the most commonly used in clinical practice.

7.3. Data extraction strategy

Data extraction will be conducted by one reviewer using standardised data extraction forms and independently checked by a second reviewer; separate forms will be developed for the different review questions as required. Discrepancies will be resolved by discussion, with involvement of a third reviewer when necessary. Attempts will be made to contact authors for missing data. Data from multiple publications of the same study will be extracted and reported as a single study. Where applicable and available, extraction will include data on: study details (e.g. study identifier/EndNote ID, author, year, country, setting, number of participants), patient characteristics (e.g. age, gender, ethnicity), details of intervention (measure used; classification and reference data used; timing of measurement; threshold used for diagnosis of overweight and obesity; variations in the method used when undertaking the measurement (e.g. BMI equation used, level at which waist measurement was taken, and where applicable, whether measurements were taken with or without clothing or whether adjustments were made for clothing), study quality, and reported outcomes as specified above.

7.4. Quality assessment strategy

The quality of the individual studies will be assessed by one reviewer, and independently checked by a second reviewer. No study will be excluded based on the result of the quality assessment but sensitivity analyses will be undertaken where appropriate. Any disagreements will be resolved by consensus and if necessary a third reviewer will be consulted. The quality of included studies will be assessed using standard checklists suitable for the study design: QUADAS will be used for studies of diagnostic accuracy and the criteria proposed by Haden will form the basis of the assessment of the studies of predictive value.[64-67] These tools will be adapted as necessary to be review question-specific and incorporate topic-specific quality issues; the most important of these adaptations will be an assessment of measurement bias. The quality of the recent and relevant systematic reviews under consideration for inclusion in the current review will be assessed using the criteria used by CRD for inclusion on the DARE database. Those that pass those criteria, and are deemed to be relevant (i.e. in terms of population and currency of technology used), will be assessed in terms of the strategy used to identify studies, the clarity of the review question and reproducibility of the inclusion criteria, the use of methods to reduce error and bias during the review process, the appropriateness of the quality assessment tool used to assess primary studies and the reporting of the results, the analyses undertaken and the interpretation of the results, and the appropriateness of the conclusions drawn; whether the patient population representative will also be assessed. The primary predictive accuracy studies within these reviews will be assessed using the Hayden criteria.[64, 65] Primary qualitative studies will be assessed using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist.[68]

7.5. Methods of synthesis for individual sections of the review

Key study characteristics, patient outcomes and study quality will be summarised in tables and a narrative. Data synthesis methods are described in the following sections.

7.5.1. Predictive (tracking and comorbidity) and diagnostic accuracy

For objectives 1, 2 and 3 we will synthesise studies using established meta-analysis methods for diagnostic accuracy studies. Where sufficient data are available, summary estimates of sensitivity and specificity, with 95% confidence intervals and predictive regions, will be derived using a bivariate random effects model. These estimates will be used to calculate the positive and negative likelihood ratios (LR+/-). To examine diagnostic accuracy across various obesity thresholds, and to compare different tests hierarchical summary receiver operating characteristic (HSROC) curves will be produced. Where raw data are available that has not been adjusted using the reference data, analyses will be performed to determine diagnostic accuracy both at specific ages in childhood/adolescence and for accuracy of predicting adolescent/adult obesity from childhood measurements. Where possible, we will evaluate the accuracy of the simple measures to predict tracking of obesity into adolescence (aged 13 to 18 years) and adulthood (aged over 18 years) separately. Where predictive studies provide only overall odds ratios, these will be converted into measures of predictive accuracy using appropriate assumptions.[69]

7.5.1.1. Potential sources of heterogeneity

Several potential confounders and sources of heterogeneity have been identified *a priori*. These will be investigated using subgroup/sensitivity analyses, and where appropriate meta-regression, if sufficient data are available. The following variables are relevant for all anthropometric measures:

- Gender
- Ethnicity
- Socioeconomic status/deprivation
- Age at which tests were conducted
- Height
- Pubertal status
- Unselected vs. overweight/obese populations
- Degree of overweight
- Overweight/obese vs. non-overweight/obese parents
- Study quality

Measure-specific variables include:

- Difference in equations used to calculate BMI (or other ratios)

- Site and number of skin fold measurements
- Site of the waist circumference measurement (for example at the midpoint or the smallest circumference between the ribs and iliac crest)
- Where applicable, variations in the equations used to calculate measures
- Frequency of pulse used in BIA
- Location of the surface electrodes for BIA (hand/foot, foot/foot, hand/hand).

Question-specific variables include:

- Reference standard used - sensitivity analyses will be conducted based on the reference standard used for both the review of diagnostic accuracy (restricted to those studies using the gold standard), and the prediction of tracking into adolescence and obesity (restricting studies using a reference standard of BMI, DXA, densitometry or a four- or five-component model in adulthood).
- Cut off/thresholds for determining overweight/obesity.

7.5.2. Acceptability and ease of use

Study details and results will be summarised in tables, and studies combined in a narrative. The results of the elicitation exercise will also be summarised in a narrative; tabulated results from the exercise will be provided.

7.5.3. Meta-analysis combining the results of the reviews of diagnostic and predictive accuracy

Given the complexity of the research question, and the interplay between childhood obesity, the tracking of obesity into adulthood, and morbidity and mortality in adulthood, separate meta-analyses would not provide a full assessment of the utility of the simple measures being evaluated. Therefore, in order to adequately address the review question, the results of the systematic reviews of the tracking of obesity into adulthood, and subsequent adult morbidity and mortality, would need to be combined in a single meta-analysis. In Appendix 13.2 we present the method by which this could be achieved.

8. Methods of synthesising evidence of cost-effectiveness

There will be no assessment of the cost-effectiveness of the measures used to assess childhood obesity.

9. The TAR team

9.1. TAR centre

The Technology Assessment Review team at the University of York is drawn from two specialist centres: the Centre for Reviews and Dissemination (CRD) and the Centre for Health Economics (CHE). This Technology Assessment will be conducted by CRD only. CRD undertakes reviews of research about the effects of interventions used in health and social care (www.york.ac.uk/inst/crd). The centre maintains various databases, provides an enquiry service and disseminates results of research to NHS decision makers.

CRD/CHE conducted a systematic review, published in 2007, investigating whether primary school children should be routinely screened for obesity. Other recent TARs undertaken by CRD/CHE at York relate to the identification of the seizure focus in patients with refractory epilepsy being considered for surgery, the use of bone turnover markers to monitor osteoporosis treatments, and the clinical effectiveness of interventions for adult Eustachian tube dysfunction.

9.2. *Expertise in the TAR team*

Jane Burch, Research Fellow (jane.burch@york.ac.uk). Ten years of experience in health technology assessment, systematic reviews and systematic review methodology. Jane has worked on systematic reviews for NICE and the NIHR HTA Programme. Jane will contribute to all aspects of the review and be responsible for co-ordinating the production of the protocol and final report.

Huiqin Yang, Research Fellow (huiqin.yang@york.ac.uk). Eight years of experience in Health Services Research. Huiqin has undertaken a number of health technology assessment projects for NICE and the NIHR HTA Programme. Huiqin will contribute to all aspects of the review.

Mark Simmonds, Research Fellow (mark.simmonds@york.ac.uk). Eight years of experience as a medical statistician, with particular experience in meta-analysis. Mark has particular expertise in the meta-analysis of diagnostic and predictive tests and in medical screening and prevention of cardiovascular disease. Mark will take primary responsibility for the statistical analyses.

Alexis Llewellyn, Research Fellow (alexis.llewellyn @york.ac.uk). Four years of experience as a systematic reviewer. Alexis has worked on several systematic reviews, including for NICE and the NIHR HTA Programme. Alexis will contribute to all aspects of the review.

Steven Duffy, Information Specialist (steven.duffy@york.ac.uk). A qualified librarian with several years of experience working as a member of different teams conducting systematic reviews. Steven

will be responsible for designing and running the search strategies, maintaining the Endnote library and writing the searching sections of the protocol and report.

Nerys Woolacott, Senior Research Fellow, Centre for Reviews and Dissemination (nerys.woolacott@york.ac.uk). Nerys is TAR project manager at CRD and has twelve years of experience in health technology assessment, systematic reviews and review methodology. Nerys has produced and managed a large number of technology assessments and systematic reviews for HTA, NICE, Department of Health and others. Nerys will provide input at all stages of the project and take overall responsibility.

9.3. Advisory group

Claire Griffiths, Senior Lecturer in Physical Activity, Exercise & Health, Leeds Metropolitan University, LS6 3QS (C.Griffiths@leedsmet.ac.uk).

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10. Competing interests of authors

None.

11. Timetable

Submission of:	
Draft protocol to HTA	28th March 2013
Expected date for HTA to send comments on draft protocol	12th April 2013
Commence project	6th June 2013
Team submit assessment report to HTA	31st January 2014

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13. Appendices

13.1. Draft search strategies

Draft search strategy 1: Diagnostic accuracy. MEDLINE (OvidSP).

1 exp Obesity/ (125479)
2 Overweight/ (9310)
3 Weight Gain/ (20691)
4 Weight Loss/ (21524)
5 obes$.ti,ab. (141940)
6 (overweight or over weight).ti,ab. (29584)
7 (weight gain or weight loss).ti,ab. (77760)
8 or/1-7 (251872)
9 exp child/ (1467433)
10 exp Infant/ (892666)
11 Adolescent/ (1515388)
12 Young Adult/ (269705)
13 (child$ or infant$ or pediat$ or paediat$ or schoolchild$ or school age$ or schoolage$).ti,ab. (1161330)
14 (adolescen$ or juvenile$ or youth$ or teenage$ or youngster$).ti,ab. (225029)
15 (girl or girls or boy or boys or kid or kids).ti,ab. (149758)
16 (young people or young person or young persons or young adult$).ti,ab. (63490)
17 or/9-16 (3088663)
18 body mass index/ (69679)
19 Skinfold Thickness/ (5371)
20 Waist Circumference/ (3278)
21 Waist-Hip Ratio/ (2512)
22 Electric Impedance/ (10645)
23 (body mass index or body mass indices or bmi or Quetelet$).ti,ab. (104067)
24 (fat mass index or fat mass indices or FMI or fat free mass index or fat free mass indices or FFMI).ti,ab. (447)
25 (body adiposity index or body adiposity indices).ti,ab. (12)
26 body fat percentage$.ti,ab. (1021)
27 ((skin fold or skinfold) adj3 thickness$).ti,ab. (3906)
28 ((waist or hip or neck) adj3 circumference$).ti,ab. (11829)
29 ((waist-to-hip or waist-hip) adj2 ratio$).ti,ab. (5854)
30 ((waist-to-height or waist-height) adj2 ratio$).ti,ab. (442)
31 (((bioelectric$ or bio electric$) adj2 impedance) or bia).ti,ab. (3553)
32 (near infrared interactance or NIR).ti,ab. (4260)
33 ((benn$ or rohrer$ or ponderal or corpulence) adj2 (index or indices)).ti,ab. (926)
34 sagittal abdominal diameter.ti,ab. (97)
35 or/18-34 (152031)
36 exp Densitometry/ (27024)
37 exp Plethysmography/ (18050)
38 Neutron Activation Analysis/ (1669)
39 (body volume index or body volume indices).ti,ab. (0)
40 (densitometr$ or hydrostatic weighing or underwater weighing or (hydrostatic adj2 analys$) or hydrodensitometry).ti,ab. (13561)
41 (absorptiometry or DXA or DEXA).ti,ab. (17695)
42 ((water or air) adj2 displacement).ti,ab. (859)
43 (air displacement plethysmograph$ or pea pod or peapod or infant body composition system$ or bodpod).ti,ab. (303)
44 neutron activation.ti,ab. (2439)
45 ((multicomponent or multi component or multimodal or multi modal or composite or multicompartment) adj2 model$).ti,ab. (827)
46 or/36-45 (65452)

47 8 and 17 and 35 and 46 (1053)
48 Animals/ not Humans/ (3692018)
49 47 not 48 (1052)

Draft search strategy 2: Tracking. MEDLINE (OvidSP).
1 exp Obesity/ (125479)
2 Overweight/ (9310)
3 Weight Gain/ (20691)
4 Weight Loss/ (21524)
5 obes$.ti,ab. (141940)
6 (overweight or over weight).ti,ab. (29584)
7 (weight gain or weight loss).ti,ab. (77760)
8 or/1-7 (251872)
9 exp child/ (1467433)
10 exp Infant/ (892666)
11 Adolescent/ (1515388)
12 Young Adult/ (269705)
13 (child$ or infant$ or pediat$ or paediat$ or schoolchild$ or school age$ or schoolage$).ti,ab. (1161330)
14 (adolescen$ or juvenile$ or youth$ or teenage$ or youngster$).ti,ab. (225029)
15 (girl or girls or boy or boys or kid or kids).ti,ab. (149758)
16 (young people or young person or young persons or young adult$).ti,ab. (63490)
17 or/9-16 (3088663)
18 body mass index/ (69679)
19 Skinfold Thickness/ (5371)
20 Waist Circumference/ (3278)
21 Waist-Hip Ratio/ (2512)
22 Electric Impedance/ (10645)
23 (body mass index or body mass indices or bmi or Quetelet$).ti,ab. (104067)
24 (fat mass index or fat mass indices or FMI or fat free mass index or fat free mass indices or FFMI).ti,ab. (447)
25 (body adiposity index or body adiposity indices).ti,ab. (12)
26 body fat percentage$.ti,ab. (1021)
27 ((skin fold or skinfold) adj3 thickness$).ti,ab. (3906)
28 ((waist or hip or neck) adj3 circumference$).ti,ab. (11829)
29 ((waist-to-hip or waist-hip) adj2 ratio$).ti,ab. (5854)
30 ((waist-to-height or waist-height) adj2 ratio$).ti,ab. (442)
31 (((bioelectric$ or bio electric$) adj2 impedance) or bia).ti,ab. (3553)
32 (near infrared interactance or NIR).ti,ab. (4260)
33 ((benn$ or rohrer$ or ponderal or corpulence) adj2 (index or indices)).ti,ab. (926)
34 sagittal abdominal diameter.ti,ab. (97)
35 or/18-34 (152031)
36 track$.ti,ab. (60445)
37 traject$.ti,ab. (23990)
38 (persistence or persistent$).ti,ab. (188014)
39 (observ$ adj3 (repeat$ or regular$ or continu$ or frequent$ or period$ or recurr$ or perenn$ or prolong$ or perpetu$ or long term)).ti,ab. (69530)
40 (monitor$ adj3 (repeat$ or regular$ or continu$ or frequent$ or period$ or recurr$ or perenn$ or prolong$ or perpetu$ or long term)).ti,ab. (32995)
41 (surveil$ adj3 (repeat$ or regular$ or continu$ or frequent$ or period$ or recurr$ or perenn$ or prolong$ or perpetu$ or long term)).ti,ab. (5923)
42 ((annual$ or regular$ or recurr$) adj3 interview$).ti,ab. (556)
43 or/36-42 (373499)
44 Adiposity/ or Adipose Tissue/ (60806)
45 exp Body Composition/ (33511)

46 (adiposity or adipose).ti,ab. (52785)
47 body composition.ti,ab. (18173)
48 (fatness or weight).ti,ab. (509130)
49 or/44-48 (592833)
50 43 and (8 or 49) (17899)
51 17 and 35 and 50 (1193)

Draft search strategy 3. Systematic reviews of adult disease prediction. MEDLINE (OvidSP).
1 review.ab. (595481)
2 review.pt. (1756296)
3 meta-analysis as topic/ (12514)
4 meta-analysis.ab. (30843)
5 meta-analysis.pt. (38252)
6 meta-analysis.ti. (20998)
7 or/1-6 (1989514)
8 (letter or editorial or comment).pt. (1163634)
9 animals/ not humans/ (3692018)
10 7 not (8 or 9) (1828194)
11 exp Obesity/ (125479)
12 Overweight/ (9310)
13 Weight Gain/ (20691)
14 Weight Loss/ (21524)
15 obes$.ti,ab. (141940)
16 (overweight or over weight).ti,ab. (29584)
17 (weight gain or weight loss).ti,ab. (77760)
18 or/11-17 (251872)
19 exp child/ (1467433)
20 exp Infant/ (892666)
21 Adolescent/ (1515388)
22 Young Adult/ (269705)
23 (child$ or infant$ or pediat$ or paediat$ or schoolchild$ or school age$ or schoolage$).ti,ab. (1161330)
24 (adolescen$ or juvenile$ or youth$ or teenage$ or youngster$).ti,ab. (225029)
25 (girl or girls or boy or boys or kid or kids).ti,ab. (149758)
26 (young people or young person or young persons or young adult$).ti,ab. (63490)
27 or/19-26 (3088663)
28 body mass index/ (69679)
29 Skinfold Thickness/ (5371)
30 Waist Circumference/ (3278)
31 Waist-Hip Ratio/ (2512)
32 Electric Impedance/ (10645)
33 (body mass index or body mass indices or bmi or Quetelet$).ti,ab. (104067)
34 (fat mass index or fat mass indices or FMI or fat free mass index or fat free mass indices or FFMI).ti,ab. (447)
35 (body adiposity index or body adiposity indices).ti,ab. (12)
36 body fat percentage$.ti,ab. (1021)
37 ((skin fold or skinfold) adj3 thickness$).ti,ab. (3906)
38 ((waist or hip or neck) adj3 circumference$).ti,ab. (11829)
39 ((waist-to-hip or waist-hip) adj2 ratio$).ti,ab. (5854)
40 ((waist-to-height or waist-height) adj2 ratio$).ti,ab. (442)
41 (((bioelectric$ or bio electric$) adj2 impedance) or bia).ti,ab. (3553)
42 (near infrared interactance or NIR).ti,ab. (4260)
43 ((benn$ or rohrer$ or ponderal or corpulence) adj2 (index or indices)).ti,ab. (926)
44 sagittal abdominal diameter.ti,ab. (97)
45 or/28-44 (152031)

46 exp Cardiovascular Diseases/ (1765537)
47 (cardiovascular adj3 (disease$ or disorder$ or failure$)).ti,ab. (89418)
48 (cardio vascular adj3 (disease$ or disorder$ or failure$)).ti,ab. (468)
49 (heart adj3 (disease$ or disorder$ or failure$)).ti,ab. (199887)
50 (coronary adj3 (disease$ or disorder$ or failure$)).ti,ab. (99403)
51 (circulatory adj3 (disease$ or disorder$)).ti,ab. (4080)
52 (CVD or CHD).ti,ab. (26227)
53 or/46-52 (1829829)
54 Diabetes Mellitus, Type 2/ (76040)
55 (diabetes adj2 type 2).ti,ab. (51124)
56 (diabetes adj2 type II).ti,ab. (5478)
57 (diabetes adj2 (non insulin or noninsulin)).ti,ab. (9311)
58 (NIDDM or T2DM or metabolic syndrome).ti,ab. (10576)
59 or/54-58 (94072)
60 exp Neoplasms/ (2406630)
61 cancer$.ti,ab. (920205)
62 neoplas$.ti,ab. (177961)
63 or/60-62 (2551925)
64 53 or 59 or 63 (4296608)
65 10 and 18 and 27 and 45 and 64 (474)

13.2. Synthesis of the results of the reviews (simulation exercise)

This review has covered three main questions:

1. Which simple measures of obesity in children accurately predicts the tracking of obesity into adolescence and adulthood?
2. Is obesity in children an independent risk factor for CVD, type II diabetes and/or cancer in adolescents and adults?
3. How accurately do simple measures of obesity reflect actual adiposity in children?

These questions, individually, do not completely address the overall review question, namely: 'How well do the simple measures of obesity in children predict the development of obesity-related health problems in adults'. To answer this question a suitable method to meta-analyse the findings from across all three reviews would be required. To aid this synthesis a statistical simulation exercise is proposed. This is outlined below. This simulation is not an integral part of this protocol; it will not be undertaken unless and until it, or a similar exercise, is commissioned by NIHR HTA as an addition to the present study.

A simulated sample of 100,000 children at age 11 would be generated by Monte Carlo simulation, designed to have the same adiposity profile as children in the general UK population. This simulation will be informed by data from a UK cross-sectional database (see below). This sample size would be necessary to ensure sufficient numbers of adult morbidity events were simulated. Using results from the analysis of tracking obesity into adolescence and adulthood (question 1), levels of adiposity and measurements of obesity would be similarly simulated through adolescence and into adulthood. Adult morbidity would then be simulated, based on quantitative evidence identified in the review of the association between childhood obesity and adult morbidity (question 2), and by using existing validated prediction tools for morbidity (namely the QRISK2 tool for predicting CVD). Measurements of obesity (e.g. BMI, waist-to-hip ratio) would be simulated in childhood and adolescence, using the associations between measurements and adiposity calculated in the diagnostic accuracy review (question 3), or, where available, from the UK database or other reliable UK sources. This would generate a simulated population with obesity and morbidity profiles that represent both the best findings from the reviews and the UK population. To ensure consistency multiple simulations would be conducted and compared.

This simulated population would be used to address the main research question by analysing the predictive accuracy of obesity measurements in childhood for the prediction of later obesity-related morbidity, in terms of sensitivity, specificity and other relevant accuracy measures. The methods for conducting such a simulation study to assess predictive accuracy have been described elsewhere for the prediction of cardiovascular risk in adults.[70, 71]

In order to create a simulated population that reasonably represents the UK population the analysis would make use of an existing cross-sectional database, which contains assessments of obesity. One such data set which includes measurement made using BMI, waist circumference and waist-to-height ratio at the age of 11 for around 13,000 children in Leeds, West Yorkshire. This Leeds dataset was collected by one of the members of the systematic review team (Claire Griffiths), therefore the review team would have full access to the individual patient data; such data is a valuable resource for the proposed statistical model. The data were subject to validity checks. Each of the three obesity measurements was conducted twice in the same day in a subset of children, resulting in coefficients of variation well within the acceptable level of variation for a good quality dataset. In addition, Leeds City Council conducted independent validity checks of the data across the three years of the study.[52] This database also has longitudinal follow-up data for around 800 children. One of our clinical advisors has also indicated that longitudinal data could be available to us from the Avon Longitudinal Study of Parents and Children, University of Bristol; the researchers have not been approached by the review team to investigate the possibility of such collaboration, and will only do so if it is agreed that the modeling is to be undertaken. The use of other nationally representative data sets could be explored. These data would be used to generate the adiposity data and obesity measurements at age 11 in the simulation, so that the simulated population resembles this representative UK cohort.

Some further analyses could be applied to the simulated population. It would be compared to the longitudinal follow-up of the children to determine whether the simulated data, and hence the findings of the review, match an actual UK population. The potential impact of childhood and adolescent obesity on future adult morbidity, the possible impact of increasing childhood obesity in the future, and the effect of successful programmes to reduce obesity in childhood and adolescence, would also be investigated. As the simulation study would make a number of assumptions based on the review findings its results would be indented to be indicative of how the UK population might evolve, rather than definitive. The robustness of the model would be tested in a range of sensitivity analyses and in other data sets.