Towards optimal public health interventions for preventing obesity in children: protocol for a novel evidence synthesis

Higgins JPT[1,2,3], Caldwell DM[1], Moore THM[1,2,4], Breheny K[1], Nobles JD[1,2], Dawson S[1,2], Ijaz S[1,2,5], Bell M[2,3], Savović J[1,2], Gillison F[2,6], Hodder RK[7], Wolfenden L[7,8,9], Blackmore S[2,10,11], Jago R[2,12], Summerbell CD[13.14]

[1] Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK
[2] NIHR Applied Research Collaboration West (ARC West) at University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK
[3] NIHR Bristol Biomedical Research Centre at University Hospitals Bristol and Weston NHS Foundation Trust and the University of Bristol, Bristol, UK
[4] Methods Support Unit, Editorial Methods Department, Cochrane, London, UK
[5] Bristol City Council, Bristol, UK
[6] Centre for Motivation and Health Behaviour Change, Department for Health, University of Bath, Bath, UK
[7] Hunter New England Local Health District, Hunter New England Population Health, Wallsend, Australia
[8] University of Newcastle, School of Medicine and Public Health, Callaghan, Australia
[9] Hunter Medical Research Institute, New Lambton, Australia
[10] South Gloucestershire Council, Bristol, UK
[11] Centre for Public Health and Wellbeing, University of the West of England, Bristol, UK
[12] Centre for Exercise, Nutrition & Health Sciences, School for Policy Studies, University of Bristol, Bristol, UK
[13] Department of Sport and Exercise Sciences, Durham University, Durham, UK
[14] Fuse, The Centre for Translational Research in Public Health, Newcastle, UK

Document versions	
18 May 2021	Initial protocol
17 March 2023	Revision to (i) change collection of individual participant data to collection of subgroup summary data which will facilitate the same planned analyses (including a new sub-protocol in an Annex); and (ii) publish the analytic framework before coding the included studies.

Background and scientific rationale

Obesity is a risk factor for numerous chronic diseases including type 2 diabetes, hypertension, liver disease, osteoarthritis, stroke, mental health problems and some cancers. It has also become established as a predictor of high severity COVID-19 [1].

In 2020, 9.7% of children entering Reception class in England were obese, and the prevalence of obesity was more than double (20.2%) by Year 6 [2]. Rates vary with socio-economic background, with children from more deprived areas more likely to be overweight or obese. Obesity also often tracks from childhood into adulthood. Obesity is costly to society: it is estimated that the NHS spent £6.1 billion on overweight and obesity-related ill-health in 2014 to 2015, and the overall cost to wider society was estimated at £27 billion [3]. The UK Government recognizes the importance of addressing obesity. Its childhood obesity plan, started in 2016 [4], extended in 2018 [5] and updated most recently this July [6], emphases the need to prevent excessive weight gain across the population. These plans have included measures to address the environmental determinants of obesity (e.g. soft drinks

industry levy, advertising restrictions, front of pack labelling) and the individual determinants (e.g. Better Health campaign, weight management interventions).

The Government aims to halve childhood obesity, and significantly reduce the gap in obesity between children from the most and least deprived areas, by 2030 [5]. Local authorities have been encouraged to develop and implement interventions aimed at maintaining a healthy weight. These interventions are complex, since they are often comprised of many parts, and they intervene in systems that themselves are complex (e.g. schools, communities, online environments) [7]. As such, the interventions should be viewed as packages, and we need to recognize that their effects may depend strongly on the context [8].

Here we describe a novel, sophisticated synthesis of the robust evidence in this area, offering the potential to unearth intervention features of both upstream and downstream interventions that are more likely to be effective in public health practice.

Various sources of NICE Guidance make recommendations for future research [9-12]. Obesity prevention guidance recommends that schools should take whole-school approaches to improving diet and activity levels and recommends research on "the effectiveness of multicomponent interventions among key at-risk groups", and to identify "what elements make an intervention effective and sustainable". A guideline on working with local communities recommends research on "what factors are necessary for an effective and cost-effective approach". Guidance for preventing excess weight gain identifies a lack of systematic reviews "considering the complexity of a combination of dietary, physical activity and other lifestyle behaviours on weight outcome" and on "the effect of inequalities". There is a need to address these challenges.

Our project addresses many of the gaps identified by NICE, through interrogation of evidence from randomized controlled trials and other strong epidemiological designs. Randomized trials provide the most robust evidence on the effectiveness of interventions and offer the only possibility of removing the influence of participant or cluster characteristics on choice of intervention group. The large body of existing randomized trials of intervention to prevent obesity provides an invaluable resource whose potential has not been fully exploited. However, randomized trials address only a small selection of all possible intervention approaches and have limitations that others have articulated [13]. Some other study designs offer reasonably strong alternatives to randomized trials if performed well, and can provide good evidence on the effects of further interventions that target more upstream determinants of obesity (e.g. marketing & fiscal measures), particularly those aimed at community, regional or national level. The careful application of modern evidence synthesis methods to this evidence base has the potential to derive important new messages about what types of intervention work best, for whom and in what circumstances. In addition to the main synthesis, we will investigate differential effects of broad approaches according to aspects of inequity by collecting individual participant data from a substantial subset of the existing randomized trials; and examine economic issues.

Existing literature

There is a vast literature on prevention of childhood obesity, and there have been numerous systematic reviews and meta-analyses on the topic. In 2019, Psaltopoulou et al included 66 meta-analyses in an overview covering both prevention and treatment of childhood and adolescent obesity [14]. The year before, Kobes et al had included 51 meta-analyses in an overview covering a similar scope [15]. In 2016, Cauchi et al included 63 systematic reviews in their overview addressing environmental components of childhood obesity prevention interventions [16]. A very recent overview by Foldgren et al identified 13 systematic reviews of primary prevention interventions for overweight and obesity, in adolescents alone, published since 2008 [17].

A key systematic review is the Cochrane Review *Interventions for preventing obesity in children*. First published in 2001, it is one the most highly accessed of all Cochrane Reviews [18]. It was the only review out of 16 included that was assessed to be of high quality in a Flodgren et al's recent overview

[17], and was also judged to be of high quality by Cauchi et al [16]. In July 2019, our team published the latest update of the review. It includes 86 randomized trials of 89,936 children aged 6 to 12, and 29 randomized trials of 40,549 young people aged 13-18 [19]. It finds that physical activity interventions and combined diet and physical activity interventions have a small effect on average, but with notable variability of effects across studies. It is this variability, which must have some cause (including the possibility of differential biases) that makes us believe there is valuable unexplored information in the data.

None of the reviews we have identified takes a sophisticated approach to understanding variability across studies. One recent study investigated the role of intervention components in explaining variability, but undertook only rather naïve subgroup analyses and did not seek to isolate the effects of the individual components or their interactions [20]. Back in 2014, Kellou et al took a socio-ecologic approach to the evidence from 54 studies focussing on physical activity, considering dimensions such as how many levels are targeted by the intervention (e.g. individual, interpersonal, environmental, community), degree of interaction between dimensions and duration of follow-up, but did not use statistical methods to examine these. This represents a missed opportunity to exploit all the available information in order to understand what types of interventions, at which level and with which characteristics, might be most effective.

Obesity is inequitably distributed in the population. However, there is a risk that interventions may increase inequities (sometimes referred to as 'intervention-generated inequities') [21, 22]. Previous reviews have sought to understand the impact of interventions on inequity, although have been hampered by inconsistencies in methods and reporting across studies [23-26].

The Cochrane Review is restricted to randomized trials. Although robust in design, randomized trials are easier to conduct, and therefore most common, for interventions targeted at individuals or modestly sized groups of individuals. Many important interventions are difficult or infeasible to study using randomized trials, but should not be ignored, and may be evaluated using various types of non-randomized design. These include so-called 'natural experiments', in which interventions are assigned to individuals, groups or populations by factors outside the control of the investigator. Many systematic reviews have examined non-randomized studies of childhood obesity programmes. Bramante et al (2019) reviewed natural experiments for prevention or treatment of childhood obesity, including 33 studies that reported on BMI outcomes [27]. Most (24/33) of these were in school settings, and 7 were in community settings. Wang et al (2015) undertook a comprehensive review, funded by the US Agency for Healthcare Research and Quality (AHRQ) and the National Institutes of Health, of childhood obesity prevention programmes, including randomized and non-randomized studies [28]. They identified 139 studies, 10 of which were community-based or environmental-level interventions studies. In 2014, Wolfenden et al reviewed whole-of-community interventions in children or adults, finding 8 studies, all of which were in children [29]. We also identify relevant existing systematic reviews or review protocols addressing sugar-sweetened beverage taxes [30], food labelling [31], food product reformulation measures [32] and active school transport promotion interventions [33-35].

Our overriding aim in this research is to derive meaning from complexity in this large body of evidence. By synthesizing results across diverse randomized trials and non-randomized studies of interventions, we seek to identify effective means of preventing obesity in UK children that take account of individual and system level effects.

Specific objectives of the project are to:

1. update the evidence base through systematic reviews of randomized trials and robust non-randomized studies of interventions aimed at preventing obesity in children of school age (5-18);
2. synthesize the evidence, using modern, fit-for-purpose, evidence synthesis methods, informed by a novel analytic framework developed through engagement with stakeholders, to determine what types of public health intervention strategy are most promising;

3. explore the extent to which individual characteristics associated with inequity impact on intervention effectiveness, using individual participant data from a large subset of trials; and
4. collate evidence on the costs of childhood obesity preventative interventions and estimate the potential costs of intervention approaches emerging as effective.

Methods

Setting up

We will register the Cochrane Review updates with Cochrane and will submit two new review protocols to describe plans for the update. We will register the systematic review of non-randomized studies on PROSPERO (Centre for Reviews and Dissemination, University of York). The protocols and subsequent reports of the systematic review work will follow guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [36].

We will convene an advisory group, chaired by Prof Jeremy Grimshaw (University of Ottawa), to act as an independent steering group to oversee the project. The advisory group will include school attenders to ensure PPI is well represented on the committee and expertise to guide the project in relation to childhood obesity, public health practice, behavioural change and advanced evidence synthesis methodology.

Eligibility criteria

Participants: Children aged 5-18 in any setting, unless restricted to children with obesity (for randomized trials). For examination of community-level and population-level interventions (in non-randomized studies), studies must include at least 100 children aged 5-18 (in total), and at baseline must include a representative proportion of children without existing obesity.

Interventions: Interventions aimed at preventing obesity, including dietary and/or physical activity interventions involving nutrition, education, lifestyle change, social support and combinations of these, implemented in any setting. Comparators may be any active intervention or no intervention.

Study types: For interventions targeted at children: randomized trials (individually- or cluster-randomized). For interventions targeted at communities or populations: (i) interrupted time series studies; (ii) controlled before-after studies (including 'difference in difference' studies and controlled interrupted time series); or (iii) randomized trials and non-randomized 'experiments' in which interventions were assigned using non-random methods, involving at least three communities or populations in each group and at least 100 eligible children in total.

Outcomes of interest

We will focus on continuous outcome measures that underlie definitions of obesity, namely body mass index (BMI), unstandardized or standardized by age/sex. Where these are not reported we will seek dichotomized versions (e.g. proportion with obesity). For completeness, we will also collect data from randomized trials on other outcomes and process measures collected by the Cochrane Review, and measures of physical activity and dietary intake.

Search methods

To find randomized trials targeting children, we will follow procedures described in detail within the current existing Cochrane Review [18]. This includes searches of Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE (Ovid), Embase (Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (Ovid) and PsycINFO. The MEDLINE search strategy targets the intersection of four concepts: children; preventive interventions; BMI/obesity; and randomized trials (the last using a standard MEDLINE RCT filter).

To find non-randomized studies of community-level and population-level interventions, we will first search systematically for systematic reviews of community-level and population-level interventions that meet our eligibility criteria. We will examine those that: (i) provide a clear research question using the PICO framework; (ii) apply pre-specified eligibility criteria; (iii) take a systematic approach to the literature search, (iv) provide details of the databases searched (at least three), with at least one full search strategy presented (v) involve at least two reviewers performing study selection and key elements of data extraction (either done independently, or one independently checking the other's decisions); (vi) include primary studies that measured, or have a reasonable prospect of having measured, BMI in children; and (vii) provide sufficient information about the included studies to allow identification of those that meet the eligibility criteria for our review. For reviews that meet these criteria, we will select the most recent (or most comprehensive in scope) and use them as an initial source of studies. We will update the searches undertaken within the reviews to update the evidence base on each topic. For key interventions that have not been subject to systematic review, we will consider the feasibility of undertaking a full new systematic review, although we are mindful that our resources may not stretch to this.

We will also seek information about full economic evaluations undertaken for the included studies. We are aware that these are not always published, despite the data being collected alongside a trial. Furthermore, word count limits often restrict the amount of detail regarding economic analyses that can be reported in publications (e.g. only an ICER and total costs may be reported). Therefore we will examine trial registrations and protocols of studies identified for the review to identify where economic analysis was intended, and will use forward citation searching to locate published economic reports of full or partial economic evaluations.

Study selection, data extraction and risk of bias

Two reviewers will independently select newly eligible studies (using Rayyan; rayyan.qcri.org) and extract key data (e.g. outcome data) from these, with a single reviewer extracting less important, descriptive data. Two reviewers will perform risk-of-bias assessments independently on all randomized trials using the revised Cochrane risk-of-bias tool (RoB 2) [37]. We will draw on the risk-of-bias assessments in the current Cochrane Review to the extent that it is possible; for example, descriptions of, and judgements about, the randomization process carry forward directly from the original tool to the revised tool. Two reviewers will perform risk-of-bias assessments of all non-randomized studies using the risk of bias in non-randomized studies of interventions (ROBINS-I) tool [38].

Collection of subgroup data (updated March 2023)

We will request subgroup summary data from all included randomized trials to allow us to examine the impact of baseline factors associated with inequity. Provision of means and standard deviations of BMI or zBMI for each cell in the cross-classification of intervention group by baseline category of the PROGRESS variable will allow us to include the study in a meta-analysis of interaction estimates (see below under ‘Analysis methods’). Where investigators are unable or unwilling to derive these subgroup data, we will invite them to provide individual participant data for us to re-analyse (if resources allow). We do not propose to collect subgroup summary data from the non-randomized studies, since suitable data will not be available for many studies (e.g. for interrupted time series with repeated cross-sections), and the analyses of these studies will be highly diverse and complex.

Economic aspects

To explore the potential costs of interventions, we will look in detail for relevant information associated with the included studies, with attention paid to the intersectoral costs (costs incurred in sectors broader than healthcare, such as education and public health), equity issues and implementation costs. If reported, we will also document incremental cost-effectiveness ratios (ICERs),

which could contribute to later discussions regarding the cost-effectiveness of potential interventions. ICERs of interest would not be limited to BMI/zBMI but could also include QALYs and MET hours gained.

We will assess the methodological quality of any economic analyses identified (including partial analyses) using Drummond's checklist [39], as was done in the most recent review on the topic [40]. We will use cost data to estimate the potential cost of interventions identified as promising, for consideration alongside evidence on effectiveness.

Analytic framework for the synthesis

The main statistical synthesis will be informed by a novel analytic framework that will incorporate all of the key attributes of interventions, participants, contexts and systems that are likely to explain differential effects of attempts to prevent obesity in children. We will develop this framework as part of the project by drawing on existing frameworks and by working closely with key groups including young people and those in the public health and educational sectors.

Previous logic models have been proposed on this topic to represent how interventions are thought to produce outcomes, indicating dimensions that are likely to be important [41-43]. Since the interventions seek to change behaviour, an important consideration is the approach to behaviour change. Therefore, we will be guided by the COM-B model, and we will examine the included interventions against the intervention recommendations in the behaviour change wheel [44]. Consideration of the features of systems will also be important [45], since interventions – particularly upstream interventions – will create complex reactions with unintended consequences, feedback and adaptation. We have developed a preliminary logic model that embraces aspects of all of these existing frameworks (see Figure 1). The current objective focuses on refining this preliminary logic model, which is designed to feed directly into the strategy for synthesizing the evidence.

We will work with children, young people, parents, teachers and public health professionals to refine the set of core features of interventions and the systems into which they are introduced (including characteristics of the children themselves) that might have identifiable impacts on effectiveness. We will achieve this through a combination of (i) workshops with children, young people, parents and teachers; and (ii) an expert panel meeting involving the research team, public health professionals and representatives from the public (drawn from the workshops).

Coding of studies according to the analytic framework

Once an analytic framework is agreed, we will recode the primary studies according to each feature. The coded studies will be made available online and will be free to download and use. We will write a coding manual and pilot its implementation on at least 5 studies purposefully selected to provide a diverse collection. Two reviewers will independently code each study using the data extracted with recourse to the full study reports as necessary. This will be done in at least three waves. Ten studies will be randomly selected for the first wave, after which the reviewers will compare and discuss their findings. The second wave will include a further 20 studies. Modification to the coding scheme and/or coding manual will be made after each wave as necessary to achieve consistent and comprehensive capture of study features [46]. We will examine and report agreement for each wave using kappa statistics.

Protocol update: analytic framework coding manual (March 2023)

The coding manual for the analytic framework developed as of March 2023 is included as Appendix 1. This was informed by the early iterations of duplicate coding described above.

Data synthesis

Standard meta-analyses

We will first perform pairwise meta-analyses of similar studies, broadly following the strategy used in the current review. We will follow standard procedures for meta-analysis as described in the *Cochrane*

Handbook for Systematic Reviews of Interventions [47]. Of particular relevance to this review, we will adjust standard errors of results from cluster-randomized trials if these have not been computed appropriately, drawing on published intraclass correlation coefficients from studies of child-based outcomes in clusters of a similar nature to those we identify.

Complex synthesis

The heart of the project will be a state-of-the-art evidence synthesis [48] motivated and informed directly by the analytic framework. It will exploit the large, recoded study data set; and use novel synthesis methodology. The analytic framework will be turned into a prescriptive statistical analysis plan and lodged on an open science repository before analyses are undertaken. This will list the ways in which components will be defined, the variables to be investigated using meta-regression methods, any interactions among these factors that are believed to be important, and the specific statistical models and methods to be used.

Where individual participant data are available to us we will use results based on these rather than published data. The quantitative synthesis will include all the studies in one simultaneous analysis to maximize precision of estimating effects. We plan to perform separate analyses for the 5-11 and 12-18 age groups. We are aware that a mixture of BMIs and standardized BMIs (zBMIs) are reported. These are not directly comparable, but we aim to include both, appropriately, in the same model. In line with methods used to underpin NICE guidelines, we will focus on (proportional) changes from baseline, additionally accounting for the duration of follow up measured in each study. Adjustments will be made to account for intraclass correlation in cluster-randomized trials.

The synthesis model will focus on investigation of different components of either the interventions or the systems (or contexts) into which they are introduced [49]. For example, an intervention package may have an education component and an incentivization component, or just one of these, or neither; or a similar intervention may be implemented in a school or in a scout troop. Our approach has many features in common with the analysis by Michie et al, who applied meta-regression to examine 26 behavioural change techniques alongside various other study characteristics in 122 evaluations of cognitive or behavioural change strategies healthy eating and physical activity interventions in adults [50].

The features listed in green boxes in the analytic framework (see preliminary logic model in Figure 1) are the components that are included in the synthesis model. Specifically, each feature in our analytic framework represents a variable to be included in the data set, and the possible variants of each feature represent the possible values for that variable. This fully specified model will be subject to confirmatory (hypothesis testing) analysis as the primary investigation. We will assume additive effects wherever reasonable, though will include interaction effects where necessary, as driven by predictions from the expert panel about what features are thought to interact with others. An additive model will allow us to make predictions about what combinations of components or features will maximize the effectiveness of intervention (along with appropriate uncertainty about these effects), even if such combinations have not been implemented in any of the included studies.

The synthesis will also have exploratory (hypothesis-generating) aspects. This will include attempts to find reasons for unexplained heterogeneity of effects across studies, and secondary analyses investigating different model assumptions, which will be more explorative in nature. For example, we will explore the use of physical activity and/or dietary intake as moderator variables, examining whether the extent of change achieved in these behaviours predicts the magnitude of effect of intervention, having accounted for factors in our analytic framework. This follows the meta-regression approach taken by Thompson, who used the extent of cholesterol reduction achieved by various interventions to predict impact of cholesterol-lowering interventions on ischaemic heart disease [51].

The syntheses will allow for residual heterogeneity in intervention effects using a standard random-effects model. We will perform analyses within a Bayesian framework using WinBUGS or equivalent,

using uninformative prior distributions for effects of components and features, and data-based informative prior distributions for between-study heterogeneity parameters [52].

Subgroup data analysis (updated March 2023)

Subgroup summary data will be used to explore issues of inequity. Our main analyses will be two-stage meta-analyses, in which quantities are estimated separately within each study, then combined across studies using traditional meta-analysis methods. These two-stage approaches will focus on the differential effects of intervention according to each PROGRESS characteristic, dichotomized, in turn [53]. Statistically, we will estimate parameters that represent interaction between intervention and baseline covariate for each study and combine these across studies. We have argued in the past that this is the appropriate way to examine participant-level characteristics in IPD meta-analysis [54], and the approach was recently advocated as the 'deft' approach (in comparison with 'daft' and 'deluded' approaches) in a popular paper [55]. We will include important dimensions of interventions, participants and contexts in the analysis, based on important features emerging from the main synthesis, and it is likely that we will stratify analyses to maximize comparability of studies in the interaction analyses.

Two key challenges we will face are: first, that measures used to characterize variables associated with inequity (PROGRESS variables) will vary across studies; and second, that the underlying PROGRESS variables – and their relationships with intervention effectiveness – may vary markedly across contexts. The latter variation is particularly an issue across different countries. An advantage of our statistical approach is that harmonization of measures across studies is not required. However, strong assumptions are still necessary, and our aim will be to answer broad questions with high statistical power rather than to quantify associations in detail. We will ask trialists to make their own judgements when dividing the children into two subgroups, following guidance that we will provide.

Note: An addition to the original plan for examining interactions is that we will further seek to investigate interaction of intervention effect with baseline BMI, categorizing children as normal weight vs overweight/obese (main analysis) and as normal weight/overweight vs obese (secondary analysis, if feasible). A separate protocol for the interaction analyses addressing baseline BMI and features associated with inequity (PROGRESS items) was written in March 2023 (see Annex).

Funding

This project is funded by the National Institute for Health and Care Research (NIHR) Public Health Research programme (grant ref NIHR131572). The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

References

1. Foldi M, Farkas N, Kiss S, Zadori N, Vancsa S, Szako L et al. Obesity is a risk factor for developing critical condition in COVID-19 patients: A systematic review and meta-analysis. *Obes Rev* 2020.
2. NHS Digital. Statistics on Obesity, Physical Activity and Diet, England, 2020. 2020 [cited 2020; Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020.
3. Public Health England. Health matters: obesity and the food environment. 2017.
4. HM Government. Childhood obesity: a plan for action. 2016.
5. HM Government. Childhood obesity: a plan for action, chapter 2. 2018. https://www.gov.uk/government/publications/childhood-obesity-a-plan-for-action-chapter-2 [accessed 1 March 2020].
6. HM Government. Tackling obesity: empowering adults and children to live healthier lives. 2020; Available from: https://www.gov.uk/government/publications/tackling-obesity-

government-strategy/tackling-obesity-empowering-adults-and-children-to-live-healthier-lives.
7. Rutter H, Savona N, Glonti K, Bibby J, Cummins S, Finegood DT et al. The need for a complex systems model of evidence for public health. *Lancet* 2017;**390**:2602-2604.
8. Sniehotta FF, Araújo-Soares V, Brown J, Kelly MP, Michie S, West R. Complex systems and individual-level appraoches to population health: a false dichotomy? *Lancet Public Health* 2017;**2**:e396-e397.
9. National Institute for Health and Care Excellence. Obesity prevention (NICE Clinical Guideline CG43). 2006. https://www.nice.org.uk/guidance/cg43 [accessed 1 March 2020].
10. National Institute for Health and Care Excellence. Obesity: working with local communities (Nice Public Health Guideline PH42. 2012. https://www.nice.org.uk/guidance/ph42 [accessed 1 March 2020].
11. National Institute for Health and Care Excellence. Preventing excess weight gain (NICE Guideline NG7). 2015. https://www.nice.org.uk/guidance/ng7 [accessed 1 March 2020].
12. National Institute for Health and Care Excellence. Obesity in children and young people: prevention and lifestyle weight management programmes (NICE Quality Standard QS94). 2015. https://www.nice.org.uk/guidance/qs94 [accessed 1 March 2020].
13. Rutter H, Glonti K. Towards a new model of evidence for public health. *The Lancet* 2016;**388**:S7.
14. Psaltopoulou T, Tzanninis S, Ntanasis-Stathopoulos I, Panotopoulos G, Kostopoulou M, Tzanninis IG et al. Prevention and treatment of childhood and adolescent obesity: a systematic review of meta-analyses. *World J Pediatr* 2019;**15**:350-381.
15. Kobes A, Kretschmer T, Timmerman G, Schreuder P. Interventions aimed at preventing and reducing overweight/obesity among children and adolescents: a meta-synthesis. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2018;**19**:1065-1079.
16. Cauchi D, Glonti K, Petticrew M, Knai C. Environmental components of childhood obesity prevention interventions: an overview of systematic reviews. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2016;**17**:1116-1130.
17. Flodgren GM, Helleve A, Lobstein T, Rutter H, Klepp KI. Primary prevention of overweight and obesity in adolescents: An overview of systematic reviews. *Obes Rev* 2020.
18. Wiley. Cochrane Database of Systematic Reviews 2018 Impact Report. 2019. available from https://www.cochranelibrary.com/documents/20182/141048232/CDSR+-++2018+Journal+Impact+Report.pdf.
19. Brown T, Moore TH, Hooper L, Gao Y, Zayegh A, Ijaz S et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2019;**7**:CD001871.
20. Liu Z, Xu HM, Wen LM, Peng YZ, Lin LZ, Zhou S et al. A systematic review and meta-analysis of the overall effects of school-based obesity prevention interventions and effect differences by intervention components. *Int J Behav Nutr Phys Act* 2019;**16**:95.
21. Lorenc T, Petticrew M, Welch V, Tugwell P. What types of interventions generate inequalities? Evidence from systematic reviews. *J Epidemiol Community Health* 2013;**67**:190-3.
22. McGill R, Anwar E, Orton L, Bromley H, Lloyd-Williams F, O'Flaherty M et al. Are interventions to promote healthy eating equally effective for all? Systematic review of socioeconomic inequalities in impact. *BMC Public Health* 2015;**15**:457.
23. Bambra CL, Hillier FC, Cairns JM, Kasim A, Moore HJ, Summerbell CD. Public Health Research, in *How effective are interventions at reducing socioeconomic inequalities in obesity among children and adults? Two systematic reviews*. 2015, NIHR Journals Library: Southampton (UK).
24. Olstad DL, Teychenne M, Minaker LM, Taber DR, Raine KD, Nykiforuk CI et al. Can policy ameliorate socioeconomic inequities in obesity and obesity-related behaviours? A

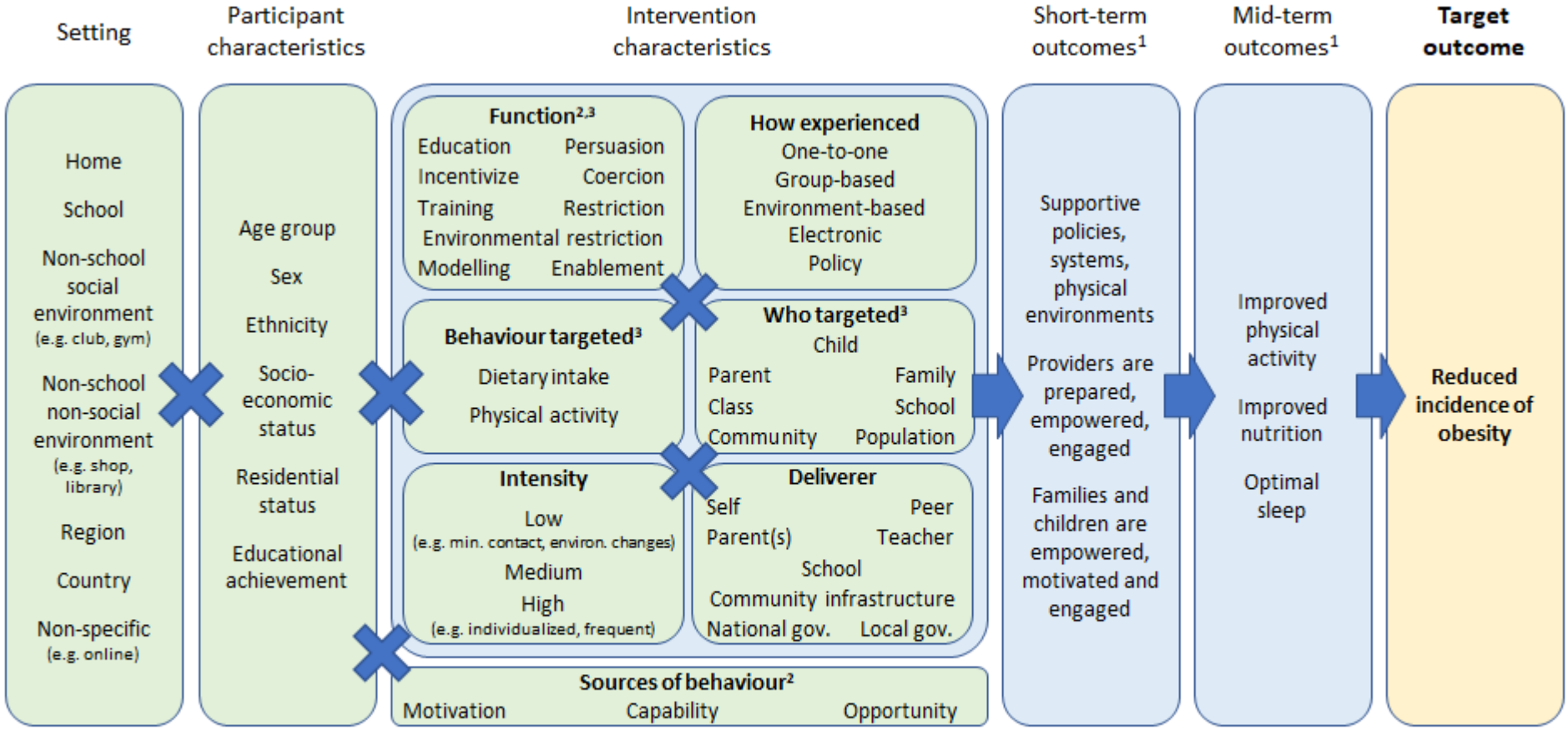
systematic review of the impact of universal policies on adults and children. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2016;**17**:1198-1217.

25. Venturelli F, Ferrari F, Broccoli S, Bonvicini L, Mancuso P, Bargellini A et al. The effect of Public Health/Pediatric Obesity interventions on socioeconomic inequalities in childhood obesity: A scoping review. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2019;**20**:1720-1739.
26. Hillier-Brown FC, Bambra CL, Cairns JM, Kasim A, Moore HJ, Summerbell CD. A systematic review of the effectiveness of individual, community and societal level interventions at reducing socioeconomic inequalities in obesity amongst children. *BMC public health* 2014;**14**:834.
27. Bramante CT, Thornton RLJ, Bennett WL, Zhang A, Wilson RF, Bass EB et al. Systematic Review of Natural Experiments for Childhood Obesity Prevention and Control. *American journal of preventive medicine* 2019;**56**:147-158.
28. Wang Y, Cai L, Wu Y, Wilson RF, Weston C, Fawole O et al. What childhood obesity prevention programmes work? A systematic review and meta-analysis. *Obesity reviews : an official journal of the International Association for the Study of Obesity* 2015;**16**:547-65.
29. Wolfenden L, Wyse R, Nichols M, Allender S, Millar L, McElduff P. A systematic review and meta-analysis of whole of community interventions to prevent excessive population weight gain. *Prev Med* 2014;**62**:193-200.
30. Teng AM, Jones AC, Mizdrak A, Signal L, Genc M, Wilson N. Impact of sugar-sweetened beverage taxes on purchases and dietary intake: Systematic review and meta-analysis. *Obes Rev* 2019;**20**:1187-1204.
31. Croker H, Packer J, Russell SJ, Stansfield C, Viner RM. Front of pack nutritional labelling schemes: a systematic review and meta-analysis of recent evidence relating to objectively measured consumption and purchasing. *J Hum Nutr Diet* 2020;**33**:518-537.
32. Hashem KM, He FJ, MacGregor GA. Systematic review of the literature on the effectiveness of product reformulation measures to reduce the sugar content of food and drink on the population's sugar consumption and health: a study protocol. *BMJ Open* 2016;**6**:e011052.
33. Villa-Gonzalez E, Barranco-Ruiz Y, Evenson KR, Chillon P. Systematic review of interventions for promoting active school transport. *Prev Med* 2018;**111**:115-134.
34. Jones RA, Blackburn NE, Woods C, Byrne M, van Nassau F, Tully MA. Interventions promoting active transport to school in children: A systematic review and meta-analysis. *Prev Med* 2019;**123**:232-241.
35. Martin A, Suhrcke M, Ogilvie D. Financial incentives to promote active travel: an evidence review and economic framework. *Am J Prev Med* 2012;**43**:e45-57.
36. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71.
37. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898.
38. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M et al. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. *BMJ* 2016;**355**:i4919.
39. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes*. 4th ed. 2015, Oxford: Oxford University Press.
40. Zanganeh M, Adab P, Li B, Frew E. A systematic review of methods, study quality, and results of economic evaluation for childhood and adolescent obesity intervention. *Int J Environ Res Public Health* 2019;**16**:485.
41. Leeman J, Sommers J, Vu M, Jernigan J, Payne G, Thompson D et al. An evaluation framework for obesity prevention policy interventions. *Prev Chronic Dis* 2012;**9**:E120.

42. Van Koperen TM, Jebb SA, Summerbell CD, Visscher TL, Romon M, Borys JM et al. Characterizing the EPODE logic model: unravelling the past and informing the future. *Obes Rev* 2013;**14**:162-70.
43. O'Connor DP, Lee RE, Mehta P, Thompson D, Bhargava A, Carlson C et al. Childhood Obesity Research Demonstration project: cross-site evaluation methods. *Child Obes* 2015;**11**:92-103.
44. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011;**6**:42.
45. Bagnall AM, Radley D, Jones R, Gately P, Nobles J, Van Dijk M et al. Whole systems approaches to obesity and other complex public health challenges: a systematic review. *BMC Public Health* 2019;**19**:8.
46. Sutcliffe K, Thomas J, Stokes G, Hinds K, Bangpan M. Intervention Component Analysis (ICA): a pragmatic approach for identifying the critical features of complex interventions. *Syst Rev* 2015;**4**:140.
47. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ et al., eds. *Cochrane Handbook for Systematic Reviews of Interventions*. 2nd ed. 2019, John Wiley & Sons: Chichester (UK).
48. Higgins JPT, López-López JA, Becker BJ, Davies SR, Dawson S, Grimshaw JM et al. Synthesising quantitative evidence in systematic reviews of complex health interventions. *BMJ Global Health* 2018;**4**:e000858.
49. Caldwell DM, Welton NJ. Approaches for synthesising complex mental health interventions in meta-analysis. *Evid Based Ment Health* 2016;**19**:16-21.
50. Michie S, Abraham C, Whittington C, McAteer J, Gupta S. Effective techniques in healthy eating and physical activity interventions: a meta-regression. *Health Psychol* 2009;**28**:690-701.
51. Thompson SG. Controversies in meta-analysis: the case of the trials of serum cholesterol reduction. *Statistical Methods in Medical Research* 1993;**2**:173-192.
52. Turner RM, Davey J, Clarke MJ, Thompson SG, Higgins JPT. Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of Systematic Reviews. *Int J Epidemiol* 2012;**41**:818-27.
53. Oliver S, Kavanagh J, Caird J, Lorenc T, Oliver K, Harden A et al. *Health promotion, inequalities and young people's health: a systematic review of research*. 2008, London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London.
54. Thompson SG, Higgins JPT. Treating individuals 4: can meta-analysis help target interventions at individuals most likely to benefit? *Lancet* 2005;**365**:341-6.
55. Fisher DJ, Carpenter JR, Morris TP, Freeman SC, Tierney JF. Meta-analytical methods to identify who benefits most from treatments: daft, deluded, or deft approach? *BMJ* 2017;**356**:j573.
56. Higgins JPT, Whitehead A, Turner RM, Omar RZ, Thompson SG. Meta-analysis of continuous outcome data from individual patients. *Statistics in Medicine* 2001;**20**:2219-2241.
57. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;**60**:7-12.
58. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 2). *J Epidemiol Community Health* 2006;**60**:95-101.
59. Howe LD, Galobardes B, Matijasevich A, Gordon D, Johnston D, Onwujekwe O et al. Measuring socio-economic position for epidemiological studies in low- and middle-income countries: a methods of measurement in epidemiology paper. *Int J Epidemiol* 2012;**41**:871-86.
60. Brion MJ, Lawlor DA, Matijasevich A, Horta B, Anselmi L, Araujo CL et al. What are the causal effects of breastfeeding on IQ, obesity and blood pressure? Evidence from comparing high-income with middle-income cohorts. *Int J Epidemiol* 2011;**40**:670-80.

Figure 1: Preliminary logic model

Aspects in green boxes form the analytic framework on which the main evidence synthesis will be based.



[1] Based on O'Connor et al, Childhood obesity research demonstration project: cross-site evaluation methods. *Childhood Obesity* 2015; 11: 92-103.
[2] From Michie et al, The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Science* 2011; 6: 42.
[3] More than one may apply.

Appendix 1: analytic Framework coding manual – updated 15 March 2023

Item	Explanation	Question	Answer
Setting	This characteristic is a measure of the setting where the intervention is delivered in the sense of school vs home vs community. School setting included after school programs based at school. Examples of community setting: club, gym, shop, library, health care centres. Note that if the intervention is conducted within school facilities but set in the community we will answer **No** to school and **Yes** to community. For example, an intervention in which families attend lessons and cooking classes, that uses the local schools facilities (that is not necessarily the school that the participating children attend to). It is possible to answer **Yes** to more than one of these questions. For example: an intervention that includes a school class on how to prepare healthy meals at home will be coded as **Yes** for school. If the intervention also includes delivery of a food box at home, we will also answer **Yes** to home. General information for parents (e.g., flyer or newsletter) received at home as part of a wider strategy set in school or community is **No** to home. An intervention that involves a significant component where the parent *receives instructions at home* to engage the child in behavioural changes (e.g. changes to meals or physical activities) is **Yes** to home. NB: If the instructions are delivered from the school (e.g. via the child) then this is Yes to school, No to home but Yes to 'home activity'. Examples of child **home activity**: homework (assigned according to the intervention protocol); cooking or games activities with parents. If an intervention is entirely electronic and the study *does not specify* where the children should engage with the electronic activity (e.g. 'children must log in to a website at school') then answer **No** to all. Otherwise answer **Yes** to the specified location.	Is the intervention delivered in a school (in full or in part)?	Yes/No
		Is the intervention delivered in the home (in full or in part)?	Yes/No
		Is the intervention delivered in the community or other non-school and non-home setting (in full or in part)?	Yes/No
		Does the intervention include a home activity for the child?	Yes/No

Mode of delivery to the child	This characteristic is a measure of how the child experiences the intervention. Although interventions may be delivered at various levels, the child will experience them in different ways, e.g. as an individualized intervention (e.g. a leaflet about healthy meals given to each student at school; a visit to an healthcare centre; homework with parents), through a group of children (e.g. school class or scout troop meeting), or otherwise. Note: if the child experiences the intervention with the parents, we will code it as individual. An electronic intervention is coded as **Exclusively or mainly individually**. If the intervention is delivered exclusively through electronic media (e.g. an app for exercising to use in the free time; a website to view at home) we will answer **Yes exclusively** to the second question.	How is the intervention delivered to the child?	Exclusively or mainly individually/ Both individually and as a group / Exclusively or mainly as a group
		Is the intervention delivered electronically?	Yes exclusively / Yes significantly / Yes as a minor component /No
Realm targeted	This characteristic is a measure of whether intervention seeks to change diet, activity (including increase in physical activity or decrease in sedentariness) or both. Examples of changes in diet include introduction or replacement of food beverages with healthier options; re-organization of food display in the school canteen or in shops; education on healthy diet; cooking classes; healthy meal box for the family. Examples of changes in activity includes intervention that increase physical activity (e.g. modified or additional physical activity classes at school) and interventions that reduce sedentary time at home (e.g. active video games). We will answer **Yes exclusively/substantially** if the dietary or activity is the only realm targeted or if it is substantial in case of both dietary and activity interventions. We will answer **Yes minimally** if the intervention is mainly one realm and there is a small component of the other realm (e.g. extension of the number of PA classes per week + a poster or leaflet about diet).	Does the intervention aim to change diet?	Yes exclusively or substantially/Yes minimally/No
		Does the intervention aim to change activity levels?	Yes exclusively or substantially/ Yes minimally/No

Multifactorness / Dimensionality	This characteristic is a measure of how non-simple/complex the intervention is. This includes how many ways the children are targeted, e.g., at multiple levels or in multiple phases. Interventions targeting the children at multiple levels are those that use different strategies at the same time. Examples of multiple strategies interventions are intervention that include school lectures, school workshops, leaflets and homework. Interventions targeting the children in multiple phases are interventions that use different strategies or settings at different time. A multi-phase intervention can also be an intervention with a more active phase followed by a less active "maintenance" phase or a "top-up" phase. Interventions applied for a continuous period are interventions without breaks between the beginning and the end of the intervention (although school holidays don't count as a break in continuity of school-based interventions). Interventions applied for a discontinuous period are these with a break during the intervention (e.g. lectures delivered for 12 weeks/year for two years). Examples of multiple strategy interventions delivered in multiple phases are interventions that include an initial series of school lectures at the end of which participants receive leaflets (phase 1) followed by a series of school workshops and homework (phase 2).	Does the intervention use multiple strategies (three or more)?	Yes/No
		Does the intervention applied have a single phase?	Yes/No
		Is the intervention applied continuously?	Yes/No

<table>
<tr>
<td rowspan="3">Peak intensity and duration</td>
<td rowspan="3">This characteristic is a measure of how intensely the intervention is experienced by the child. Ideally this would cover the duration and frequency of the intervention.

In the case of a multiphase intervention, we will add the duration of similarly intense periods.

The answer to the question “How many weeks does the intervention last?” will be the number of weeks of active intervention. For example, an intervention delivered for 12 weeks/year over two school years will be coded as 24 weeks.

The answer to the question “During how many weeks does the period of peak engagement with the intervention last?” we will consider the duration of the period of high engagement, if there is a clear distinction between a period of high engagement and a period of low engagement (e.g., an active period and a maintenance period). Often the total duration and peak engagement period will be the same (unless phases of intensity are explicitly stated).

To answer the question “What is the level of engagement with the children during the peak period?” we will use the number of sessions of engagement per week as guidance:
• High engagement is typically one or more sessions of engagement with the children per week.
• Low engagement is typically less than one session of engagement with the children per week.

NB: These cut-offs are for guidance only. Sometimes the number of sessions per week will not be specified. Coders should use their judgement as to whether the intervention seems high or low intensity.

For permanent and transient environmental changes (e.g. changes in the display of food at the school canteen) this will be coded as Low.</td>
<td>How many weeks does the intervention last (the period from baseline to end of intervention)?</td>
<td>Strictly numeric

We are calculating the duration in weeks based on 4.33 weeks/months . In case of range duration (e.g. 16 to 20 weeks, we will take the mean=18)</td>
</tr>
<tr>
<td>During how many weeks does the period of peak engagement with the intervention last?</td>
<td>Strictly numeric

See above</td>
</tr>
<tr>
<td>What is the level of engagement with the children during the peak period?</td>
<td>High/Low</td>
</tr>
</table>

Integration	This characteristic is a measure of the extent to which the intervention is 'normalized' within the curriculum or normal habits. This measure provides an indication of how much 'extra effort' (by the provider and/or the recipient) would be required for the intervention to be successful. Examples of **Yes** to intervention that is integrated: modification of physical activity classes; addition of, or replacement of regular school meals with, healthier options. Examples of **Partially** answer is an intervention with a combination of integrated activities and something extra (e.g. after school program or homework). Examples of **No** for an intervention that is not integrated at all): when the school needs to add something to an existing programme (e.g. an extra physical activity class extending school hours) or when the child needs to sign up for/agree to after-school classes. After school programs (ASP): in case of ASP, the intervention is integrated if it seeks to change the content of an existing ASP and we will answer **Yes**; otherwise, it is not integrated, and we will answer **No**. Electronic intervention: logging on to website is not integrated, receiving (and replying) to texts/messages/links is integrated.	Is the intervention integrated into the normal curriculum/ habits?	Yes/Partially (P)/No
Flexibility	This characteristic is a measure of the extent to which the intervention can be implemented flexibly, within the intervention protocol, e.g. an intervention is adapted to the particular classroom/household at teachers/parents' discretion. Example of **Yes**: an intervention consisting in the replacement of regular meals with healthy meals where the healthy meals are decided by each participating school kitchen staff. Also, an intervention that is tailored to the specific characteristics of the participant (e.g. a dietary intervention that take into consideration what food the child likes or not).	Is the intervention designed to be implemented in a flexible manner/tailored to specific participants?	Yes/No
Choice	This characteristic is a measure of the extent to which participants (children) are free to make the intervention work for them. Example of **Yes** is an intervention in which the child can choose which sport they do or which food to eat within the intervention.	Is choice of activity/diet designed into the intervention?	Yes/Partially (P)/No

Fun factor	This characteristic is a measure of the extent to which the intervention is designed with the intention to be fun and whether children in the intended age group would find this strategy fun. Examples of intervention that may look fun: game, song, play. Example of intervention that may not look fun to all children: sport activity, cooking with the parents. Example of intervention that may not look fun at all: a classroom lectures, replacement of sugar sweetened drinks with water. Examples of intervention that children aged 5-11 year (but not an adolescent) will find fun: a song about healthy eating. Similarly, a video game intervention designed for older children (12- 18 years old) may not be fun for a 5 year old child.	How enticing would you find this strategy? How enticing do you think children in the intended age group would find this strategy?	Boring / Worse than neutral / Neutral / Better than neutral / Fun Boring / Worse than neutral / Neutral / Better than neutral / Fun
Resonance	This characteristic is a measure of the extent to which the effectiveness of the intervention may depend on the degree of respect that young people have for the programme/deliverer, or on the credibility of the person delivering the intervention. An example of **Yes** answer is an intervention in which the children are encouraged to do PE with an external PE teacher or coach. Also, an intervention in which workshops on healthy nutrition are delivered by a dietician or a nurse. Other examples of role model are professional athletes (e.g. footballer), influencers, peers or older student. An example of **No** answer is an intervention in which the children are encouraged to do PA by a form teacher or a parent/career. It will be a **Yes** answer if the intervention is delivered primarily by schoolteachers and one session is delivered for example by a dietician or a professional PA coach.	Is the intervention experienced by children via someone external or unusual?	Yes/ No
Mechanism of action and recipient	This characteristic is a measure of who is the direct recipient of the intervention (e.g. child, the teacher(s), parent(s), the child's environment or others) and how does the intervention aim to achieve a change in the child's behaviour. Note that for complex interventions we may answer **Yes** to more than one question.	Does the intervention have an explicit component of modifying the child's behaviour?	Yes/No

	An example of an intervention that modifies the child's behaviour is a session of physical activity or a workshop on healthy nutrition in which the children are involved in cooking a meal. An example of an intervention that has a component of education or information is a provision of literature or lessons to *educate children* about the benefits of healthy eating/physical activity. An example of an intervention that has a component aiming to change the social environment of the child at school or home is an intervention in which teachers are instructed to encourage children to change their dietary or activity behaviours or parents are educated on healthy food. Training the teachers to deliver the intervention will normally be answered as **No.** Examples of interventions that have a component aiming to change the physical environment of the child (at school or home) include the placement of healthy foods in the school canteen, provision of exercise equipment at school or in the community; drawing running tracks in the playground; changing the school meal menu.	Does the intervention have an explicit component of education/information provision for the child?	Yes/No
		Does the intervention have an explicit component aiming to change the social environment of the child (e.g. at school or home)?	Yes/No
		Does the intervention have an explicit component aiming to change the physical environment of the child (e.g. at school or home)?	Yes/No
Commercial interests	This characteristic is a measure of whether commercial interests are involved in the intervention (e.g. industry involvement). An example of **Yes** answer is an intervention within a study that was funded by industry (e.g. food industry, manufacturer of sport equipment), even if the authors stated there were no conflict of interests.	Are commercial interests involved in the intervention?	Yes / No

Annex: Protocol for a meta-analysis of subgroup interactions to examine factors influencing effectiveness of interventions aimed at preventing obesity in childhood

Julian Higgins, Jennifer Palmer, Annabel Davies, Francesca Spiga, Eve Tomlinson, Deborah Caldwell, Russell Jago, Berit Lilienthal Heitmann, Carolyn Summerbell

17 March 2023

Rationale

Obesity is a risk factor for numerous chronic diseases including type 2 diabetes, hypertension, liver disease, osteoarthritis, stroke, mental health problems and some cancers. In 2020, 9.7% of children entering reception class in England were obese, and the prevalence of obesity was more than double (20.2%) by Year 6 [1]. Obesity also often tracks from childhood into adulthood. It is costly to society: it is estimated that the NHS spent £6.1 billion on overweight and obesity-related ill-health in 2014 to 2015 [2].

Evidence Synthesis for Components of Childhood Obesity Prevention Effectiveness (ESCCOPE) is an NIHR-funded research project led by Prof Julian Higgins at the University of Bristol, UK. Its overall aim is to understand the effectiveness of interventions to prevent obesity in 5 to 18-year old children. It will include a novel, sophisticated synthesis of the robust evidence in the area of obesity prevention in childhood, aiming to unearth intervention features of both upstream and downstream interventions that are more likely to be effective in public health practice. This analysis will be based on an updated version of a Cochrane review [3] including 200-250 randomized trials [4, 5]. This protocol relates to a sub-project of ESCCOPE examining factors around BMI and health equity. Specifically, we wish to explore whether the effectiveness of obesity prevention interventions on body mass index (BMI) varies according to baseline weight status (i.e. normal weight or overweight at baseline assessment), and on factors that contribute to health inequity. Health inequity refers to the unfair difference in disease burden between population groups.

Remaining at healthy weight throughout childhood and beyond is, by far, preferable to attempting to treat established obesity or to halt its progression. In addition, there is little evidence to suggest that treatment effects are lasting [6], so primary prevention of obesity is important not only to promote good long term physical and mental health but also to help children unleash their full life-time potential.

There is currently little evidence on how to prevent healthy weight children from becoming overweight, as most previous prevention initiatives were conducted among mixed-weight children [7]. Thus, it is currently unclear whether previous effective childhood obesity prevention interventions indeed prevented excessive weight gain among those with healthy weight. To this end, results from a recent subgroup analysis from the EU-IDEFICS intervention [8] found no primary preventive effects among the children with healthy weight at baseline but showed normalization of weight status among children who were initially overweight. Thus, further evidence from large meta-analyses of existing data is clearly needed.

Obesity rates vary with socio-economic background. In high income countries, children from more deprived areas are more likely to be overweight or obese (although in low-income countries, children from high socioeconomic backgrounds are more likely to be overweight or obese). It is important that attempts to prevent obesity recognize this and ensure, as best they can, that they do not lead to increased differences between those from different socio-economic backgrounds.

We aim to explore inequity factors identified in the framework PROGRESS [9]. The PROGRESS acronym describes sociodemographic characteristics that summarize social determinants of health and therefore contribute to health inequity [10]. It aims to ensure that there is explicit consideration for health inequity

when conducting research and adapting research evidence to inform the design of new interventions [11]. Recent work on race and religion in the UK suggests that consideration of these factors is critical to the design of new interventions [12].
The PROGRESS factors are:

- Place of residence,
- Race/ethnicity/culture/language,
- Occupation,
- Gender/sex,
- Religion,
- Education,
- Socio-economic status, and
- Social capital.

To investigate whether there are inequities in the effectiveness of obesity prevention interventions, we will seek trial results subgrouped according to baseline weight status and the relevant PROGRESS factors from those listed above. We anticipate that much relevant information has been collected by trial authors, but not reported. We will therefore contact researchers from the included randomized trials from the ESCCOPE review, in order to request these relevant data.

Objectives

We will use subgrouped data from multiple randomized trials to explore:

- whether the effects of interventions aimed at preventing obesity in children vary by baseline weight status: healthy weight (including underweight) vs overweight or obese;
- whether the effects of interventions aimed at preventing obesity in children vary by baseline PROGRESS characteristics; and
- whether any such variations tend to increase or decrease inequities in relation to obesity.

Eligibility criteria

Eligibility criteria will be identical to those in the updated Cochrane reviews, except that we are interested only in comparisons of active interventions against a control group. In brief, we will include studies that:

- were individually-randomized, or cluster-randomized with at least three clusters/groups of individuals per intervention arm (including the first period only of trials with a cross-over design, due to important concerns about carry-over);
- recruited children with a mean age >5 or <19 (or families that include such children);
- measured BMI or standardized BMI z-score (zBMI) (or weight and height from which BMI or zBMI could be calculated) assessed at baseline and at least 12 weeks after baseline (including collection of self-reported measurements);
- examined one or more interventions whose main aim is to change at least one from: diet, physical activity, sedentary behaviour, sleep, play or structured exercise to help prevent childhood obesity;
- the active intervention(s) are compared with a control intervention (as opposed to trials comparing active interventions only); and
- published primary results in 1990 or later.

Outcomes of interest

Our main outcomes of interest are zBMI and BMI. These should be measured from weight and height of the children at least 12 weeks after baseline and zBMI should be standardized to sex and age-specific local or national tables for BMI. We will request that trialists provide both zBMI and BMI data where available. zBMI is the preferred outcome for the analysis but we expect that more trials will be able to provide BMI. Collecting both outcomes where possible will allow us to perform a synthesis on either outcome using the maximum amount of available data. For studies that report outcomes at multiple follow up times we will request data only for the follow up time closest to 12 months.

Identification of trials

Trials will be identified through the update to the Cochrane systematic review *Interventions for preventing obesity in children* [4, 5]. Details of the methods for searching and trial selection are detailed in the Cochrane protocol for this update.

Data collection

We will extract relevant subgroup outcome data from publications where they are reported. Where relevant subgroup data have not been reported, we will email corresponding authors to request them. The email will include an invitation to read this protocol and access to a data collection table into which outcome data suitable for our analyses can be entered. Details of subgroup definitions and desired outcome data are described in the following two subsections.

In preparation for our investigation, we have collected information from the trials about what baseline weight status and PROGRESS related variables they have measured, and any relevant subgroup analyses they have reported. Based on this information, we will tailor each email to suit the specific trial. For example, we will not request data on a subgrouping factor if the trial reports homogeneity in this factor (e.g. the participants were all girls when the subgrouping factor is sex), or if the trial already reports the full data required for the subgroup analysis. Additionally, we will make specific reference to any weight status or PROGRESS variables that we believe they have collected. We will follow up on our initial email selectively with authors of trials likely to have most influence on our analyses. Specifically, we will focus on trials that (i) we know have collected data on baseline weight status and/or PROGRESS characteristics, (ii) were published within the last 15 years, and (iii) include at least 200 participants.

Subgroup definitions

We seek subgrouped data by baseline BMI and baseline measures of PROGRESS factors. We divide PROGRESS factors into primary factors (race/ethnicity/culture/language, gender/sex and socio-economic status, along with baseline BMI), secondary factors (place of residence, religion and social capital, (parental) occupation and (parental) education.

To increase the statistical power of the analysis, we aim to dichotomize each factor. For factors and dichotomies which are not reasonably precisely defined (such as sex), or where multiple proxies were measured for a factor, we will ask the trialists to use their judgement as to an appropriate measure of the factor and to define a dichotomization they deem to be meaningful or that leads to approximately equally sized subgroups. Since our primary interest is the direction of interactions, the precise cut off for dichotomization is not critical. Our preference is for inequity factors to be measured and dichotomized at the individual child level, but we will accept group-level categorizations for each child (e.g. at school-level) if that is how the factor was measured.

Primary factors

- Baseline weight status:
    1. Preferentially:

- Children who are a healthy weight at baseline (including underweight); vs
- Children who are overweight at baseline; vs
- Children who are obese at baseline.

2. Alternatively:
    - Children who are a healthy weight at baseline (including underweight); vs
    - Children who are overweight or obese at baseline.

We will ask trialists to use definitions of overweight and obesity based on BMI/zBMI/percentile cut offs that they deem appropriate for their population. Although we will ask for these three subgroups separately, our primary analysis will group overweight and obesity into a single category.

- Race/ethnicity/culture/language:

  We will ask trialists to select a demographic characteristic such as race, ethnicity or culture that best defines the group of people who are considered to be the most privileged or dominant within the wider population setting of the trial (for example, White British in the UK). We will request that participants are subgrouped based on whether they do or do not fall into that category, i.e.
  1. Most privileged or dominant race/ethnic/culture/language group in the population under study; vs
  2. Other race/ethnic/culture group.

- Gender/sex:
  1. Female; vs
  2. Male.

- Socio-economic status:
  1. High; vs
  2. Low.

  We will ask trialists to choose an appropriate measure (continuous or ordinal) of socio-economic status based on their trial population and the data collected. We will ask them to select a dichotomization that gives approximately equal numbers of participants in each subgroup, for example splitting the population at the median. This will ensure the maximum statistical power for the analysis.

Secondary subgroups

The following subgroups pertain to PROGRESS factors that are relevant to inequities among children but which we consider unlikely to have been measured or the type of measurement likely to be too heterogeneous across the trial populations to produce meaningful results. For completeness, we will invite trialists to contribute subgrouped results based on these factors if available, but do not anticipate receiving many and do not anticipate performing analyses.

- Place of residence:
  - Urban; vs
  - Rural and/or coastal.

  As most studies are school based, we expect a high level of homogeneity among participants within each study, particularly for secondary school-based studies, preventing a meaningful investigation of this factor.
- (Parental) occupation:

Occupation:
An example of an appropriate dichotomization in many contexts would be:
  - Professional and managerial occupation (e.g. International Standard Classification of Occupations groups 1-3); vs
  - Other occupation.

- Religion:
  - State religion or less oppressed religion in the population under study; vs
  - Other religion.

  Where appropriate this could refer to more than one religion, for example in the UK the first group might comprise 'Christian' and 'Non-religious'. The categorization will most likely refer to the child's parents' religion.
- (Parental) education:

  An example of an appropriate dichotomization in many contexts would be:
  - Higher education; vs
  - No higher education.
- Social capital:

  Social capital refers to support available through informal social networks. In young people, this is largely related to family structure and the form and quality of family relationships [10]. An example of an appropriate dichotomization would be:
  - Two parents living in the same residence as the child; vs
  - No parents or separated from parents (e.g. children in care or living with other family members), single parent or separated parents living in different locations.

Outcome data

We will seek the following data from each trial.

- Cluster information:
  1. Number of clusters and total number of participants, per intervention group or overall (at baseline and follow up where available)
  2. Intra-cluster correlation coefficient (where available)

We will request cluster information for each subgroup for each PROGRESS factor, and overall if not available at the subgroup level.

- Per subgroup: number of participants (N), mean value and standard deviation (SD) for zBMI and/or BMI measurements in each intervention group at the follow up time closest to 12 months. Our order of preference for measures is as follows:
  1. N, mean, SD for change from baseline;
  2. N, mean, SD for baseline and N, mean, SD after intervention, with correlation coefficient between baseline and post-intervention scores;
  3. N, mean, SD at baseline and N, mean, SD after intervention;
  4. N, mean, SD after intervention.

We will request results for both zBMI and BMI, indicating that zBMI is our preference. We will request raw means and SDs from each trial and will perform cluster adjustments ourselves.

Assessment of risk of bias

We will use the RoB 2 tool [13] to assess risk of bias in each result. The tool has five domains: bias arising from the randomization process, risk of bias due to deviations from the intended intervention, risk of bias due to missing data, risk of bias in measuring the outcome, and risk of bias in selection of the reported result. For the first three domains, we will use the assessments made for the Cochrane review. The last two domains will be reassessed based on the completeness of the data and the extent to which sought results are available. Risk-of-bias assessments will be undertaken by researchers at the University of Bristol who have not been involved in any of the trials. Clarifications will be sought from the trialists as needed to inform these assessments.

Data analysis

Our main analyses will be two-stage meta-analyses, in which quantities are estimated separately within each study, then combined across studies using traditional meta-analysis methods. These two-stage approaches will focus on the differential effects of intervention according to baseline weight status and each PROGRESS factor in turn.

Specifically, we will first estimate intervention effects separately for each subgroup as the mean difference between groups. In line with our outcome data collection, the mean difference will refer to (in order of preference) a mean difference in (i) change from baseline provided by the trialists, (ii) change from baseline calculated from baseline and follow up means and a correlation coefficient provided by the trialists, (iii) change from baseline calculated from baseline and follow up means and an imputed correlation coefficient, (iv) follow up means.

For cluster-randomized trials, we will adjust the standard error of the mean difference to account for clustering using the methods described in the Cochrane Handbook for Systematic Reviews of Interventions [14]. Where available, this adjustment will make use of the ICC reported by the trialists. If an ICC is not provided we will use an imputed value based on ICCs reported in other trials. We will perform a sensitivity analysis with ICC=0, 0.02, 0.04.

For each baseline factor of interest, we will then calculate the difference in intervention effects between the two subgroups. This estimates the interaction between the intervention and the factor defining the subgroup (i.e. either baseline weight status or one of the PROGRESS factors). Since the subgroups are independent, the variance on this parameter will be the sum of variances of the subgroup-specific intervention effect estimates. For baseline weight status, our primary analysis will group overweight and obesity into a single category and compare this group with the group of children at normal weight. In a sensitivity analysis we will group overweight children with normal weight children and compare this group with the group of children with obesity.

Next, we will combine the interaction parameters from each subgroup analysis across all studies using the standard procedures for meta-analysis [15]. The null hypothesis of each analysis is that the subgroup covariate has no impact on the intervention effect. In other words, the interaction parameter is zero. Using the summary estimate and confidence interval from the meta-analysis, we will perform a Z test of the null hypothesis. Based on this analysis we expect to have strong evidence for answering (confirmatory) questions such as “Is there a difference in effectiveness of interventions according to baseline weight status?”. We will perform a random effects meta-analysis to allow for heterogeneity in the estimated interaction parameters. Evidence of heterogeneity provides evidence that the impact of baseline weight status is importantly different in different contexts. We will take similar approaches for the PROGRESS stratification factors.

The summary estimate from the meta-analysis will provide an estimate of the average interaction effect for the covariate investigated by the subgroup analysis. This estimate will quantify the extent to which the intervention effect is impacted by the covariate. Compared with the test of the null hypothesis, practical interpretation of this result requires stronger assumptions about the similarity of relationships across studies.

Because the association of socioeconomic status with obesity is likely to differ between high- and lower-income settings (lower socioeconomic status is associated with higher obesity in high income countries but often with lower obesity in lower income countries) we will run a secondary analysis of the socioeconomic interaction effect, where trials are grouped according to whether they were carried out in high or lower-income countries. If there are insufficient data from lower-income countries for a meaningful analysis, we will run a sensitivity analysis by excluding trials from lower income countries and observing any changes in the interaction effect.

Publication

We aim to publish the findings under group authorship, and will invite a member from each trial team contributing new evidence to the analysis to be listed as a member of this group.

Discussion

Two key challenges we will face are: first, that measures used to characterize variables associated with inequity (PROGRESS variables) will vary across studies; and second, that the underlying PROGRESS variables – and their relationships with intervention effectiveness – may vary markedly across contexts. The latter variation is particularly an issue across different countries. An advantage of our statistical approach is that harmonization of measures across studies is not required. However, strong assumptions are still necessary, and our aim is to answer broad questions with maximum statistical power rather than to quantify associations in detail. Of the primary subgroups, socio-economic background is particularly challenging. We will ask trialists to use a measure they deem appropriate and for which they have available information. We therefore expect a high level of variation in the measures used.

Project team details

Central research team: Julian Higgins (University of Bristol), Jennifer Palmer (University of Bristol), Annabel Davies (University of Bristol), Berit Lilienthal Heitmann (University of Copenhagen), Francesca Spiga (University of Bristol), Deborah Caldwell (University of Bristol), Carolyn Summerbell (Durham University), Theresa Moore (University of Bristol), Eve Tomlinson (University of Bristol), Russ Jago (University of Bristol), Rona Campbell (University of Bristol), Jelena Savovic (University of Bristol), Katie Breheny (University of Bristol), Fiona Gillison (University of Bristol), James Nobles (University of Bristol), Sharea Ijaz (University of Bristol)

Project advisory group: Jeremy Grimshaw (University of Ottawa), Tom Trikalinos (Brown University), Miranda Pallan (University of Birmingham), Graham Moore (Cardiff University), Lesley Stewart (University of York), Elizabeth Sheldrick, Maddie Coleman.

Funders: National Institute for Health and Care Research Public Health Programme (NIHR131572)

References

1. NHS Digital. *Statistics on Obesity, Physical Activity and Diet, England, 2020*. 2020 [cited 2020; Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020.
2. Public Health England, *Health matters: obesity and the food environment.* 2017.
3. Brown, T., et al., *Interventions for preventing obesity in children.* Cochrane Database Syst Rev, 2019. **7**(7): p. CD001871.
4. Moore, T.H.M., et al., *Interventions to prevent obesity in children aged 5 to 11 years old.* Cochrane Database of Systematic Reviews, 2022(7).
5. Moore, T.H.M., et al., *Interventions to prevent obesity in children aged 12 to 18 years old.* Cochrane Database of Systematic Reviews, 2022(7).
6. van der Heijden, L.B., E.J.M. Feskens, and A.J. Janse, *Maintenance interventions for overweight or obesity in children: a systematic review and meta-analysis.* Obesity Reviews, 2018. **19**(6): p. 798-809.

7. Peirson, L., et al., *Prevention of overweight and obesity in children and youth: a systematic review and meta-analysis.* CMAJ Open, 2015. **3**(1): p. E23-E33.
8. Lissner, L., et al., *Differential outcome of the IDEFICS intervention in overweight versus non-overweight children: did we achieve 'primary' or 'secondary' prevention?* Obesity Reviews, 2015. **16**(S2): p. 119-126.
9. Evans, T. and H. Brown, *Road traffic crashes: operationalizing equity in the context of health sector reform.* Inj Control Saf Promot, 2003. **10**(1-2): p. 11-2.
10. Oliver, S., et al., *Health promotion, inequalities and young people's health*. 2008.
11. O'Neill, J., et al., *Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health.* J Clin Epidemiol, 2014. **67**(1): p. 56-64.
12. Rai, T., et al., *What would it take to meaningfully attend to ethnicity and race in health research? Learning from a trial intervention development study.* Sociology of Health & Illness, 2022. **44**(S1): p. 57-72.
13. Sterne, J.A.C., et al., *RoB 2: a revised tool for assessing risk of bias in randomised trials.* BMJ, 2019. **366**: p. l4898.
14. Higgins, J.P., S. Eldridge, and T. Li, *Including variants on randomized trials*, in *Cochrane Handbook for Systematic Reviews of Interventions*. 2019. p. 569-593.
15. Deeks, J.J., R.D. Riley, and J.P.T. Higgins, *Chapter 9: Combining results using meta-analysis*, in *Systematic Reviews in Health Research: Meta-analysis in Context (3rd Edition)*, M. Egger, J.P.T. Higgins, and G. Davey Smith, Editors. 2022, John Wiley & Sons: Chichester. p. 159-184.