

Exploring whether apparently effective primary preventive measures of childhood obesity may be effect-modified by the prevalence of overweight at baseline: Protocol for a systematic review of reviews and meta-regression analysis of published randomized trials

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ABSTRACT

Introduction:

The public sectors, public health, and the World Health Organization have within the last few decades been increasingly disposed to focus on prevention, particularly in preventing childhood onset of obesity. Several studies have targeted child obesity prevention programs, and subsequently a number of systematic reviews have questioned the effectiveness of these. Three levels of prevention (primary, secondary and tertiary) aim at minimizing the risk of obesity and subsequent consequences. According to systematic reviews, numerous trials have aimed at primary prevention of childhood obesity (i.e., unhealthy weight gain among children). However, we hypothesize that the apparently effective interventions for primary prevention are effect-modified by measuring a secondary preventive effect by baseline overweight/obesity status (i.e., weight reduction in overweight children). Our objective is to explore whether the effectiveness associated with primary prevention of childhood obesity is effect-modified by overweight at baseline, since this might be indicative of treatment of overweight rather than of prevention.

Methods and Analysis:

Systematic reviews will be located through a search of Medline, Embase and the Cochrane Database of Systematic Reviews, and duplicates will be excluded. Two reviewers will independently screen the titles and abstracts. Eligibility criteria include: Published trials included in previous systematic reviews. The relevance of the title and the abstract will determine the selection and exclusion process of the studies. Data will be extracted and a risk of bias (RoB) assessment performed. We will use meta-regression analysis to explore the association between the prevalence of overweight at baseline and the observed effect on body weight.

Ethics and Dissemination:

The characteristics of participants at baseline may determine the success or failure of childhood obesity prevention programs. Through a transparent approach, we will explore if childhood obesity can be prevented as assessed by trial evidence. Findings from this overview and meta-regression analyses of published systematic reviews will inform various stakeholders, via a peer-reviewed-journal and social media.

Protocol Registration: PROSPERO CRD42017071074

INTRODUCTION

Description of the condition

Globally, since 1980 and 2014, the prevalence of obesity has roughly doubled amongst children and adults (1). In 2013, 6.3% of children under the age of five were overweight (1;2). High-income countries have though recently documented a plateau in the prevalence rate of childhood obesity, while low- and middle-income countries continue seeing this rate rise (3). Evidence has also supported that having a higher BMI (> 25) during childhood increases the likelihood of becoming an obese adult; with nearly 50% of all obese children remaining so in adulthood (2;5).

There are numerous negative short- and long-term health effects associated with obesity, such as the development of diabetes, hypertension, and osteoarthritis (1;6;7). Mental health is also negatively impacted, since research has shown that overweight and obese children are more likely to have a poor self-image, depression, anxiety, and eating disorder symptoms (7;8). In addition to the negative physical and psychological consequences, lifetime educational attainment, labor market outcome, and financial attainment are all negatively impacted (2;9).

Description of the intervention

Over the last few decades, the term *prevention* has become a cornerstone of the public health and public sectors, especially in relation to childhood obesity. This is also the case in relation to research, as shown in the review conducted by Lobstein et al (3). According to this review, there was a significant increase in the yearly number of papers published about prevention of childhood obesity between 1980 and 2013 (3). Additionally, the World Health Organization's 2015 Sustainable Development Goals identified that the "*prevention* and control" of non-communicable diseases is of extreme importance and further emphasized the need for preventing childhood obesity (1;2).

Since then, numerous reviews investigating childhood obesity prevention programs have been conducted, such as the review by Summerbell et al (10). This and other reviews, investigating preventive practices has typically sought to determine effectiveness of the interventions, based on design features (diet, lifestyle, etc.) and outcome. In addition, the participants involved usually are mixed-weight, as pointed out by Peirson et al (11). Including a "mixed-weight population" thus makes it difficult to determine the effectiveness of primary prevention interventions. It is currently unclear whether this is a preventive effect occurring, or

it is a treatment effect amongst those overweight and or obese. This review will therefore focus on the baseline characteristics of primary prevention interventions to determine if a preventative effect was created.

The importance of conducting this review

Prevention is divided into three levels: primary, secondary, and tertiary. A primary prevention aims at controlling modifiable risk factors to help prevent the cause of disease, while a secondary prevention tries to detect disease prior to clinical symptoms develop (12). Lastly, the objective of carrying out a tertiary prevention is to control the existing disease and thereby preventing serious complications (12). Understanding prevention classification levels is an important aspect of this study, since primary prevention interventions will be the main focus.

Curbing and preventing childhood obesity remains a major focus in all industrial societies, as effective short- and long-term prevention strategies have yet to be created. Research concerning finding viable prevention methods continues, and the pressure on healthcare practitioners to deliver results has increased. However, there have been very few reviews, if any, that have focused on primary prevention interventions targeting at-risk, normal-weight children. Conducting this review enables us to examine if intervention for primary prevention of childhood obesity have, in fact, produced a preventative effect, or instead have been producing a treatment effect. The results from this study could then be used to develop a prevention proxy that could be applied for future primary prevention interventions.

Objective

The main objective of this study is to explore if the apparently effective prevention of childhood obesity interventions are truly measuring a preventative effect (i.e. primary prevention), or appears effective among those already obese at baseline (i.e. tertiary prevention). Further, a secondary objective will be to explore which type(s) of intervention will be recommendable for future preventative efforts.

METHODS

The recommendations from The Cochrane Handbook for Systematic Reviews of Interventions (13) will guide the search process of this meta-analysis, and the findings will be reported

according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (14). The protocol has been registered in PROSPERO (registration no. CRD42017071074.).

Eligibility criteria

Types of participants

Studies will be included if the participants are between 2 – 18 years of age. There will be no limitation based on gender or ethnicity.

Types of interventions

Any interventions aimed at childhood obesity prevention will be considered, as prevention modalities vary significantly.

Types of outcome measures and data extraction

The primary outcome for this study will be to investigate the effect of the interventions on weight, BMI or other anthropometric change indices and the corresponding prevalence of baseline overweight status. Secondary sources of information will be used as we will extract data from trials in existing systematic reviews with meta-analysis.

Information sources and search strategy

A search strategy, inspired from a previous Cochrane review from 2005, “*Interventions for preventing obesity in children,*” updated 2011 (10;15), will be conducted. Furthermore we will identify available literature reporting on randomized controlled trials through a more recent systematic review from 2015 (11). In addition, only trials included in published systematic reviews and meta-analyses investigating obesity prevention amongst children will be considered for inclusion. Additional manual searches of reference lists of identified systematic reviews will be performed, and authors of primary studies will be contacted if additional data is required.

Two researchers (KTF and JK) will search independently in Medline, Embase, and the Cochrane database of systematic reviews from inception for systematic reviews and meta-analyses investigating the association between childhood obesity at baseline and the effect of preventative

intervention, using the following search algorithm. The search will be restricted to abstract and title, only including studies of humans, without any language restrictions:

AND

| Overweight/Obesity | Prevention/Intervention | Design | Eligibility |
|---|---|--|--|
| obes* overweight weight gain* weight los* (BMI OR Body Mass Index) ((gain OR loss OR chang*) AND weight) weight chang* childhood obesity | behavior therapy social support psychotherapy therapy (lifestyle OR life style) (chang* OR intervention*) counsel* diet* (modif* OR strateg*) low calorie calorie control healthy eating (fasting OR modified fast*) (fruit OR vegetable) (high fat* OR low fat*) formula diet* exercis* (aerobic* OR physical therapy OR physical activit* OR physical inactivity) fitness (physical training OR physical educat*) (sedentary lifestyle OR sedentary behaviour OR sedentary behavior) (weightwatcher* OR weight watcher*) | meta-analys* metaanalys* (cochrane review) | child* toddle* adolesce* teenage* preteen* young people young person young adult (schoolchild* OR school child*) (preschoolchild* OR preschool child*) pediater* paediatr* Youth |

OR

| | | |
|--|---|--|
| | <p>(fat camp* OR diet* camp*) health promot* health educat*</p> <p>Intervent*</p> <p>(health polic* OR school polic* OR food polic* OR nutrition polic*)</p> <p>(primary prevent* OR secondary prevent* OR tertiary prevent*) (preventative measur* OR preventive measur*) (preventative care OR preventive care) (obesity prevent* OR obesity treat*)</p> | |
|--|---|--|

A manual review of references from eligible systematic or narrative reviews will also be performed. The titles, abstracts, and full texts of the resulting papers will be examined by two researchers (KTF & JK) in detail, and discrepancies will be resolved by consensus or a third reviewer. Limitations applied will be the participants' age (between 2 – 18 years of age). Furthermore, only published reviews will be included and only the latest version of each intervention will be selected, in instances where multiple versions exist. Reviews will be excluded after the title and abstract have been read and no relevance is found.

Study Selection

KTF & JK will perform the eligibility assessment. All relevant reviews will be screened by title and abstract, and managed through Reference Manager 12. We will exclude protocols and reviews that have been withdrawn, have no statistical synthesis on between group differences in body weight (or other obesity indices), and have no indication of the prevalence of overweight at baseline, unless the authors can provide this data. Only reviews including randomized and pseudorandomized trials will be considered for eligibility. Whenever a systematic review

contains two or more different pertinent intervention comparisons we will consider these separately. The studies that do not fulfill the eligibility assessment will be rejected, while the remaining studies will be read as full-text. If there are any doubts regarding a study's eligibility, discrepancies will be resolved by consensus or a third reviewer will be consulted (EMB or RC). Furthermore a matrix of included studies in SRs will be completed. Finally, a flow chart of the search and study selection according to PRISMA will be displayed.

Risk of bias in eligible trials

The risk of bias framework will be adapted from the *Cochrane Handbook for Systematic Reviews of Interventions* will be used to perform a quality assessment of all the included systematic reviews by two researchers (KTF & JK) (13). Discrepancies will be resolved by consensus or a third reviewer will be consulted. Each of the selected studies will subsequently receive a rating of low, high, or unclear risk of bias, based on each domain of the risk of bias tool. The additional sources of bias, including trial size and source of funding will also be rated. We will rely on the RoB judgements already assessed in the reviews included, or if none present, a RoB assessment will be performed.

Data collection process and data items

To guide the extraction process, a standardized template will be created, and performed by two researchers (KTF & JK). All of the information gathered will then be compiled into a table for further analysis. The primary outcome (body weight indices) will be extracted from the measures at the end of the trial, and the covariate (prevalence of overweight/obesity) will be extracted from the baseline characteristics tables of each trial. Additional information extracted will include authors of the study, year of publication, trial design, and demographic baseline variables of study characteristics, which include average age, sex, percentage normal weight, height, study duration, and participant completion. Authors of primary studies will be contacted in case of any missing data.

Statistical methods

The way in which weight and height is reported in each study varies, so we will need to recode these data into a uniform measure. There are various definitions for overweight and obesity among children. However, we will have to rely on the classifications at baseline provided in the original articles. If a proportion was not provided, we will attempt to estimate it before excluding it. Anticipating that there is no direct (meaningful) body weight measure common to all the studies, it may be possible to transform the study-specific summary to a standardized (scale-free) statistic denoted an effect size. One common estimator of effect size is the standardized mean difference which is calculated as the difference of means divided by the variability of the measures; i.e. a standardized mean difference (16).

We will conduct meta-analyses in Review Manager, version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration) and SAS software (version 9.4 for Windows). A restricted maximum likelihood (REML) method will be applied to estimate the between-study variance and the combined pooled analysis. In the overall model, heterogeneity will be evaluated between randomized comparisons, applying the standard Q statistic followed by the calculation of the I^2 value, an inconsistency index which can be interpreted as the percentage of total variation across several studies due to heterogeneity (17). Quantitatively, when various statistical models are evaluated and compared, the between-comparison variance in random-effects meta-analysis will be estimated as Tau-squared. For the stratified analysis, a fixed factor will be added to the model indexing subgroups across randomized comparisons. The stratified analysis is accompanied by interaction tests based on the Q statistics. REML-based (i.e. random-effects) meta-regression analysis (18) will be applied in order to answer the specific question – whether the prevalence of overweight at baseline is associated with the quantitative changes in body weight (obesity indices).

ETHICS AND DISSEMINATION

The study will evaluate and determine the impact of participants' baseline anthropometric characteristics on the effect of childhood obesity prevention interventions. The strength of this review is the use of a systematic and transparent approach, employing recommended and validated methods. The review will be inclusive and comprehensive by incorporating a wide range of interventions and outcomes relating to childhood obesity. The involvement of two

researchers at each stage of the literature screening, data extraction and quality appraisal will also increase the reliability of the conclusions drawn. This review is widely relevant to the general population and pertinent for obesity prevention strategies.

A limitation of the review will be the complex nature of extracting data from baseline on the prevalence of overweight/obesity, with inherent difficulties in defining terms and producing clear conclusions and recommendations. Also the anticipated (potential) findings from the meta-regression analyses will likely be criticized for being vulnerable to “ecological fallacy”.

The findings from this review will be shared with policy makers and practitioners through local stakeholder groups feeding into various stakeholder organizations. Written dissemination will be achieved through publication(s) for practitioner readership and submission to peer-reviewed journal(s). The results will be circulated to the general public using social media.

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Declaration of interests

The authors declare that they have no competing interests.

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