

Systematic review and meta-analysis of school-based interventions to reduce body mass index

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ABSTRACT

Background Childhood obesity predisposes to adult obesity and increases the risk of many diseases. Schools provide a vehicle to deliver public health interventions to all children.

Methods Medline and Embase were used to undertake a systematic review of published studies of school-based interventions aimed at reducing the body mass index (BMI) of children ≤ 18 years. Preferred reporting items for systematic reviews and meta-analyses guidelines were followed, and eligible studies subjected to a random effects meta-analysis.

Results Between 1991 and 2010, 43 published studies provided 60 measurements of effect. The pooled effect was a 0.17 (95% CI: 0.08, 0.26, $P < 0.001$) reduction in BMI. Heterogeneity was high ($I^2 = 93.4\%$) but there was no significant small study bias (Egger's test, $P = 0.422$) nor significant variation by length of follow-up. The intervention comprised physical activity only in 11 (26%) studies, education only in three (7%), and combinations of these and improved nutrition in the remaining 29 (67%). On stratified analysis, physical activity used in isolation (-0.13 , 95% CI: -0.22 , -0.04 , $P = 0.001$) or combined with improved nutrition (-0.17 , 95% CI: -0.29 , -0.06 , $P < 0.001$) was associated with significant improvements in BMI. Interventions targeted at overweight/obese children reduced their BMI by 0.35 (95% CI: 0.12, 0.58, $P = 0.003$). Those delivered to all children reduced it by 0.16 (95% CI: 0.06, 0.25, $P = 0.002$).

Conclusions There is growing evidence that school-based interventions that contain a physical activity component may be effective in helping to reduce BMI in children.

Keywords children, health promotion, obesity

Introduction

The increasing prevalence of childhood obesity poses a major threat to public health. In the USA, the prevalence of severe [defined as body mass index (BMI) ≥ 99 th centile] childhood obesity has tripled in the last 25 years.¹ Obesity increases the risk of many conditions, including type II diabetes, hypertension, cardiovascular disease and musculoskeletal disease.² Lifestyle behaviours developed in childhood tend to perpetuate into adulthood. Hence, obese children are more likely to become obese adults.³ The WHO⁴ has acknowledged that childhood interventions are required to combat adult obesity effectively. In the UK, education is free to all children between 3 and 18 years of age. Therefore, schools provide an ideal vehicle for delivering public health interventions to all children,⁵ including those

from the most socio-economically deprived communities who are most at risk,^{6–8} and hardest to reach. According to the primary prevention strategy first mooted by Rose,⁹ small population shifts in BMI may be more effective at a population level than simply reducing the prevalence of obesity. The most recent meta-analysis of school-based interventions included studies published up to 2007.¹⁰ It demonstrated a significant reduction in the prevalence of obesity but, at that time, there was no evidence of a significant overall reduction in BMI. Because of the increasing public health importance

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of childhood obesity, many studies have been published more recently. Therefore, we conducted an up-to-date meta-analysis of published studies that evaluated the impact of school-based interventions on the body mass index (BMI) of pupils.

Methods

Systematic review

A literature review was conducted in parallel by H.V.L. and J.P.P. in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.¹¹ The search was undertaken using the Medline and Embase databases, applying the following search terms and Boolean connectors to titles, abstracts and subject headings: (child OR children OR childhood OR toddler* OR school-age* OR schoolage* OR infant* OR pediatric* OR paediatric*) AND (school* OR kindergarten* OR creche OR nursery OR nurseries OR afterschool) AND (prevent* OR intervention*) AND [(obes* OR overweight OR (weight adj1 gain)) OR ((increase* OR gain* OR change*) adj2 (BMI OR body mass index))]. The electronic search was limited to studies conducted on human subjects of 18 years of age or younger that were published in or translated into English. No restrictions were placed on publication date so as to include as many studies as possible. Duplicate articles were excluded. The last date on which the electronic search was run was 21 February 2011. The identified articles were reviewed manually and the following inclusion criteria applied:

- children aged 18 years of age or younger,
- any intervention delivered in a school setting and aimed at decreasing BMI or weight,
- effect reported as the mean change in BMI or this could be calculated from the pre- and post-intervention data provided and
- inclusion of a control group which received no intervention beyond normal school-based activities and for which change in BMI was also reported or able to be calculated.

Non-randomized intervention studies were not excluded. Where more than one article was found relating to the same study, the most recent publication was used. The reference lists of both review articles and eligible original articles were searched manually to identify any additional eligible articles not found as a result of the electronic search.

Meta-analysis

Study characteristics were extracted and recorded: publication year, country, age and sex of participants, study size and design, selection criteria, nature, timing and duration of the intervention, and length of follow-up. Where follow-up

results were recorded at different time points, the longest follow-up measure was used and, where available, sub-group results were used in favour of overall results. For studies that did not report the confidence interval or standard deviation (SD) for the mean change in BMI, this was imputed from the studies that did. Correlation coefficients were derived for the intervention and control groups using the formula: $\text{Corr} = (\text{SD}_{\text{baseline}}^2 + \text{SD}_{\text{final}}^2 - \text{SD}_{\text{change}}^2) / (2 \times \text{SD}_{\text{baseline}} \times \text{SD}_{\text{final}})$. The SD of the change in BMI was then calculated using the formula: $\sqrt{(\text{SD}_{\text{baseline}}^2 + \text{SD}_{\text{final}}^2 - (2 \times \text{Corr} \times \text{SD}_{\text{baseline}} \times \text{SD}_{\text{final}}))}$. A random effects meta-analysis was conducted on the full dataset and then repeated stratified by sex and then intervention type. I^2 was calculated as a measure of heterogeneity between studies. Bias was assessed both subjectively, using a funnel plot, and formally, using Egger's regression asymmetry test for small study bias. The influence of individual studies on the overall effect size was assessed using a meta-influence plot and a cumulative meta-analysis was performed to determine whether the pooled effect size changed over time as new studies were published. Univariate and multivariate meta-regression analyses were used to determine the effect of specific study characteristics on the overall effect size and, therefore, potential sources of between-study heterogeneity. Meta-regression analyses were subjected to 20 000 permutations to adjust for multiple testing, and therefore reduce the chance of type 1 errors. The adjusted R^2 and residual I^2 values were calculated in order to determine how much of the effect size was accounted for by the study characteristics recorded and how much heterogeneity remained after taking account of these. A bubble plot was produced to determine whether there was any relationship between length of follow-up and effect size. All analyses were performed using Stata version 11.1.

Results

Systematic review

The electronic search identified 1886 articles and the manual search of reference lists identified a further 195. Following exclusion of 466 duplicate articles, the remaining 1615 articles were reviewed manually. Of these, 1572 were excluded: 913 were irrelevant, 240 involved no intervention and, in 84, the interventions were not school-based, 183 evaluated effect using a measure other than BMI, 144 did not provide essential data, one study was not published in English and seven papers were rendered redundant by more recent publications based on the same study. Therefore, 43 studies met all of the inclusion criteria and were included in the meta-analysis.^{12–54}

The 43 studies were published between 1991 and 2010 and included a total of 36 579 pupils. Sixteen (37%) of the eligible studies were conducted in Europe,^{12–27} 19 (44%) in America,^{28–46} 5 (12%) in Asia,^{47–51} 2 (5%) in Australasia^{52,53} and 1 (2%) in Africa⁵⁴ (Table 1). Nine (21%) studies recruited more than 1000 pupils,^{24,27,28,31,37,41,45,47,48} and 38 (88%) were randomized or cluster-randomized-controlled

trials.^{12–23,25–34,36–38,40–43,46–54} Two (5%) studies were based in nursery or kindergarten (under 5 years of age),^{33,34} 26 (60%) in primary schools (5–11 years of age)^{12–17,19–21,24,25,28,29,31,36,37,39,41–49} and 15 (35%) in secondary schools (12–18 years of age).^{18,22,23,26,27,30,32,35,38,40,50–54} Thirty-seven (86%) studies included all pupils irrespective of baseline weight,^{12,14–28,30,31,33–37,39,41–49,52–54} but 6 (14%)

Table 1 Characteristics of studies examining the effect of school-based interventions on body mass index

Study	Year	Country	Study design	Sex	Weight criteria	School age	Timing	Intervention type	Intervention duration (months)
Angelopoulos <i>et al.</i> ¹²	2009	Greece	Cluster RCT	MF	None	Primary	School-time	PA, N	12
Barbeau ²⁹	2007	USA	RCT	F	Overweight	Primary	After school	PA	10
Bayne-Smith ³⁰	2004	USA	Cluster RCT	F	None	Secondary	School-time	PA, N	24
Caballero <i>et al.</i> ³¹	2003	USA	RCT	MF	None	Primary	School-time	PA, N	36
Carrel <i>et al.</i> ³²	2005	USA	RCT	MF	Overweight	Secondary	School-time	PA, N	9
Dennison <i>et al.</i> ³³	2004	USA	RCT	MF	None	Pre-school	School-time	SB	8
Donnelly <i>et al.</i> ²⁸	2009	USA	Cluster RCT	MF	None	Primary	School-time	PA	36
Duncan <i>et al.</i> ¹⁷	2009	UK	RCT	MF	None	Primary	After school	PA	15
El Ansari <i>et al.</i> ⁵⁴	2010	Egypt	RCT	M, F	None	Secondary	After school	PA	3
Fitzgibbon <i>et al.</i> ³⁴	2006	USA	Cluster RCT	MF	None	Pre-school	School-time	PA, N	3
Flores ³⁵	1995	USA	Efficacy trial	F	None	Secondary	School-time	PA, N	3
Foster <i>et al.</i> ³⁶	2008	USA	Cluster RCT	MF	None	Primary	School-time	N	24
Graf <i>et al.</i> ¹³	2006	Germany	Cluster RCT	MF	Overweight	Primary	After school	PA, N	9
Graf <i>et al.</i> ¹⁴	2008	Germany	Cluster RCT	MF	None	Primary	School-time	N	48
Haerens <i>et al.</i> ¹⁸	2006	Belgium	Cluster RCT	M, F	None	Secondary	School-time	PA, N	24
Harrell <i>et al.</i> ³⁷	1996	USA	RCT	MF	None	Primary	School-time	PA, N	2
Harrison <i>et al.</i> ¹⁹	2006	Ireland	Cluster RCT	MF	None	Primary	School-time	PA, SB	4
James <i>et al.</i> ¹⁵	2007	UK	Cluster RCT	MF	None	Primary	School-time	N	12
Jiang <i>et al.</i> ⁴⁷	2007	China	Cluster RCT	M, F	None	Primary	Both	PA, N, SB	36
Johnston <i>et al.</i> ³⁸	2008	USA	RCT	MF	Overweight	Secondary	School-time	PA, N	6
Kain <i>et al.</i> ⁴⁵	2008	Chile	Non RCT	M, F	None	Primary	School-time	PA, N	21
Kipping <i>et al.</i> ²⁰	2008	UK	Pilot cluster RCT	MF	None	Primary	School-time	PA, N, SB	5
Kriemler <i>et al.</i> ²¹	2009	Switzerland	Cluster RCT	MF	None	Primary	School-time	PA	10
Li <i>et al.</i> ⁴⁸	2010	China	Cluster RCT	MF	None	Primary	School-time	PA	12
Lionis <i>et al.</i> ²²	1991	Greece	Cluster RCT	MF	None	Secondary	School-time	PA, N	12
Manios <i>et al.</i> ¹⁶	2002	Greece	Cluster RCT	MF	None	Primary	School-time	PA, N	72
Matvienko and Ahrabi-Fard ³⁹	2010	USA	Quasi-experimental	MF	None	Primary	After school	PA	1
Melnyk <i>et al.</i> ⁴⁰	2007	USA	Pilot RCT	MF	Overweight	Secondary	After school	PA, N	2
Mihas <i>et al.</i> ²³	2009	Greece	RCT	MF	None	Secondary	School-time	PA, N	3
Mo-suwan <i>et al.</i> ⁴⁹	1998	Thailand	Cluster RCT	M, F	None	Primary	School-time	PA	7

Table 1 Continued

Study Year	Country	Study design	Sex	Weight criteria	School age	Timing	Intervention type	Intervention duration (months)
Nader <i>et al.</i> ⁴¹	1999 USA	Cluster RCT	MF	None	Primary	School-time	PA, N	36
Peralta <i>et al.</i> ⁵²	2009 Australia	Pilot RCT	M	None	Secondary	School-time	PA, N, SB	6
Plachta-Danielzik <i>et al.</i> ²⁴	2007 Germany	Quasi-RCT	MF	None	Primary	School-time	PA, SB	12
Robinson ⁴²	1999 USA	RCT	MF	None	Primary	School-time	SB	6
Salcedo Aguilar <i>et al.</i> ²⁵	2010 Spain	Cluster RCT	MF	None	Primary	After school	PA	6
Sichieri <i>et al.</i> ⁴⁶	2008 Brazil	Cluster RCT	MF	None	Primary	School-time	N	7
Simon <i>et al.</i> ²⁶	2008 France	RCT	MF	None	Secondary	Both	PA, SB	48
Singh <i>et al.</i> ²⁷	2009 Netherlands	RCT	MF	None	Secondary	School-time	PA, N, SB	8
Singhal <i>et al.</i> ⁵⁰	2010 India	Cluster RCT	MF	None	Secondary	School-time	PA, N	6
Stock <i>et al.</i> ⁴³	2007 Canada	Pilot prospective study	MF	None	Primary	School-time	PA, N	5
Vandongen <i>et al.</i> ⁵³	1995 Australia	Cluster RCT	M, F	None	Secondary	Both	PA, N	9
Wong <i>et al.</i> ⁵¹	2008 Singapore	RCT	M	Overweight	Secondary	School-time	PA	3
Yin <i>et al.</i> ⁴⁴	2005 USA	Cluster RCT	MF	None	Primary	After school	PA	8

USA, United States of America; UK, United Kingdom; RCT, randomized-controlled trial; M, male only; F, female only; MF, male and female reported together; M, F, male and female reported separately; PA, physical activity; N, nutrition; SB, sedentary behaviour.

restricted inclusion to overweight pupils.^{13,29,32,38,40,51} All of the interventions were conducted on school premises. Thirty-two (74%) took place during school-time,^{12,14–16,18–24,27,28,30–37,41–43,45–46,48–51,52} 8 (19%) were conducted after school hours,^{13,17,25,29,39,40,44,54} and 3 (7%) used a combination of these approaches.^{24,45,51} The duration of the intervention ranged from 1 month to 6 years, and the maximum length of follow-up was 6 years.

Fifteen (35%) studies used a single intervention (Table 2): 10 (23%) just physical activity and five (12%) just education. The remaining 28 (65%) used combinations of two or more interventions. In total, 34 (79%) interventions included a physical activity component (such as improved physical education lessons or extra games at break times), 12 (28%) included a behavioural component (such as teaching self-management, self-esteem and decision-making skills) and 6 (14%) included an environmental component (such as changes to school meals or installation of healthy vending machines). Thirty-two of the interventions included one or more educational

components (such as a change in the focus of regular lessons, additional lessons, newsletters or workbooks): 28 included education on nutrition, 22 education on physical activity and 9 education on sedentary behaviour. Three (7%) studies targeted only girls,^{29,30,31} and two (5%) targeted only boys.^{51,52} The remaining 38 (88%) included both girls and boys but 7 of these reported results separately by sex sub-group.^{18,25,45,47,49,53,54} Therefore, the 43 studies provided a total of 60 results for inclusion in the meta-analysis.

Meta-analysis

Of the 60 results, 40 suggested a reduction in BMI in the intervention group compared with the control group^{12,13,16–19,21–23,25,26,29–31,34–36,38,39,42–45,47–53} and 16 achieved statistical significance.^{12,16,18,21–23,29,32,33,45,47,48,54} In the overall random effects meta-analysis, the pooled estimate of BMI change was -0.17 kg/m^2 (95% CI: $-0.26, -0.08, P < 0.001$; Fig. 1). In the stratified

Table 2 Types of school-based intervention used in studies examining the effect on body mass index

Study	Educational			Environmental	Behavioural	Physical
	Physical activity	Nutrition	Sedentary behaviour			
Angelopoulos ¹²	•	•			•	•
Barbeau ²⁹						•
Bayne-Smith ³⁰	•	•			•	•
Caballero <i>et al.</i> ³¹	•	•		•		•
Carrel <i>et al.</i> ³²		•				•
Dennison <i>et al.</i> ³³			•			
Donnelly <i>et al.</i> ²⁸						•
Duncan <i>et al.</i> ¹⁷						•
El Ansari <i>et al.</i> ⁵⁴						•
Fitzgibbon <i>et al.</i> ³⁴	•	•				•
Flores ³⁵	•	•				•
Foster <i>et al.</i> ³⁶		•		•		
Graf <i>et al.</i> ¹³	•	•			•	•
Graf <i>et al.</i> ¹⁴		•			•	•
Haerens Group 1 ¹⁸	•	•		•		•
Haerens Group 2 ¹⁸	•	•		•		•
Harrell <i>et al.</i> ³⁷	•	•				•
Harrison <i>et al.</i> ¹⁹	•		•		•	
James <i>et al.</i> ¹⁵		•				
Jiang <i>et al.</i> ⁴⁷	•	•	•		•	•
Johnston <i>et al.</i> ³⁸		•				•
Kain <i>et al.</i> ⁴⁵		•				•
Kipping <i>et al.</i> ²⁰	•	•	•			•
Kriemler <i>et al.</i> ²¹		•				•
Li <i>et al.</i> ⁴⁸						•
Lionis <i>et al.</i> ²²	•	•				
Manios <i>et al.</i> ¹⁶	•	•			•	•
Matvienko and Ahrabi-Fard ³⁹	•					•
Melnyk <i>et al.</i> ⁴⁰					•	•
Mihas <i>et al.</i> ²³	•	•			•	
Mo-suwan <i>et al.</i> ⁴⁹						•
Nader <i>et al.</i> ⁴¹	•	•		•		•
Peralta <i>et al.</i> ⁵²		•	•		•	•
Plachta-Danielzik <i>et al.</i> ²⁴	•	•	•			•
Robinson ⁴²			•			
Salcedo Aguilar <i>et al.</i> ²⁵						•
Sichieri <i>et al.</i> ⁴⁶		•				
Simon <i>et al.</i> ²⁶	•		•			•
Singh <i>et al.</i> ²⁷	•	•	•	•		•
Singhal <i>et al.</i> ⁵⁰	•	•		•	•	
Stock <i>et al.</i> ⁴³	•	•			•	•
Vandongen Group 1 ⁵³	•					•
Vandongen Group 2 ⁵³	•	•				•
Vandongen Group 3 ⁵³		•				
Vandongen Group 4 ⁵³		•				
Vandongen Group 5 ⁵³		•				
Wong <i>et al.</i> ⁵¹						•
Yin <i>et al.</i> ⁴⁴						•

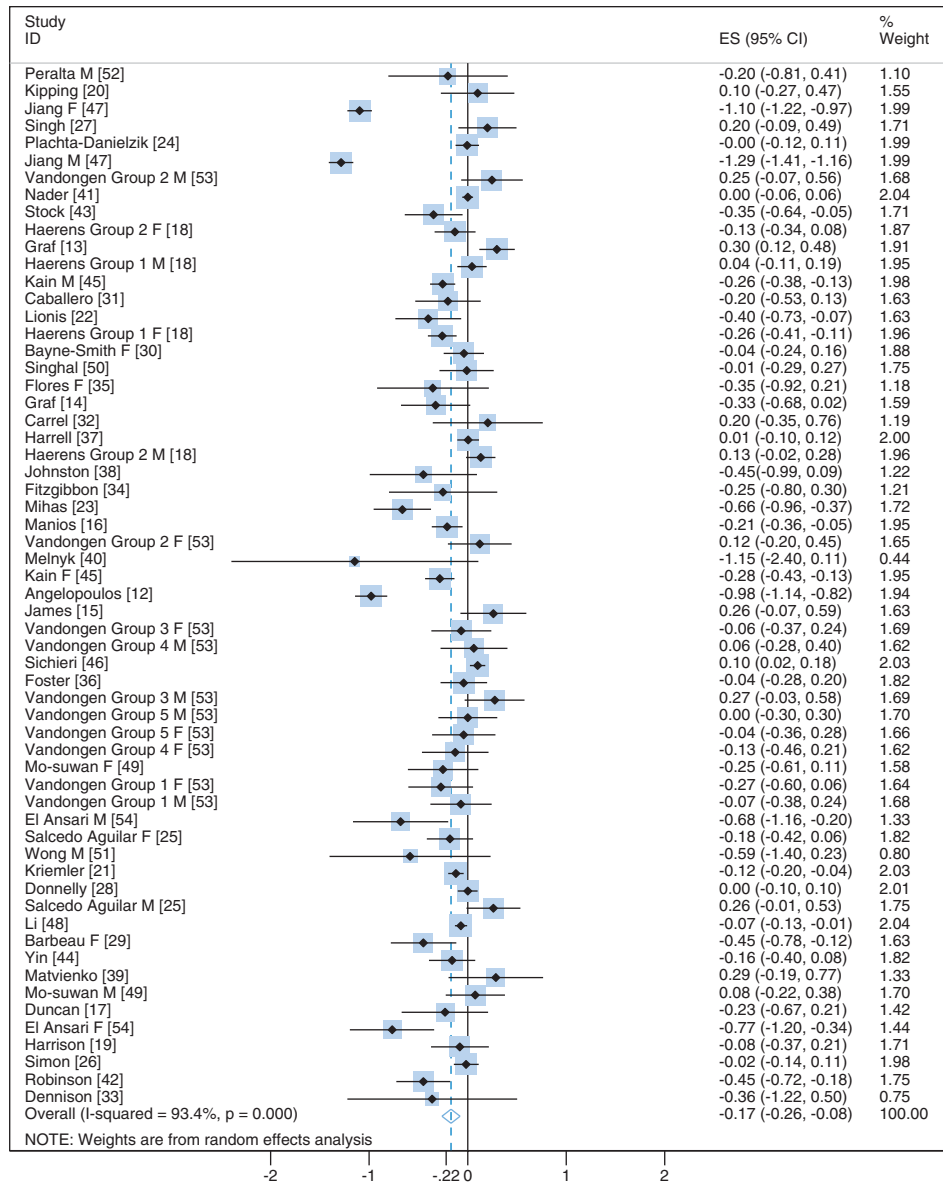


Fig. 1 Forest plot of randomized-effects meta-analysis of studies examining the effect of school-based interventions on body mass index. ES, effect size; CI, confidence interval; M, male; F, female.

analyses, the reduction reached statistical significance in girls (-0.28 , 95% CI: -0.50 , -0.06 , $P = 0.012$) but not boys (-0.17 , 95% CI: -0.26 , -0.08 , $P = 0.533$). Following stratification by intervention type, the reduction in BMI was statistically significant for physical activity used in isolation (-0.13 , 95% CI: -0.22 , -0.04), and in combination with improved nutrition (-0.17 , 95% CI: -0.29 , -0.06). Of the 60 results, six were derived from interventions targeted at overweight or obese children and the remaining 54 were delivered to all children. When the meta-analysis was re-run separately for these two sub-

groups, interventions delivered to just overweight and obese children produced a change in BMI of -0.35 (95% CI: -0.58 , -0.12 , $P = 0.003$) and interventions delivered to all children produced a change of -0.16 (95% CI: -0.25 , -0.06 , $P = 0.002$).

Overall, heterogeneity was high ($I^2 = 93.4\%$). In the multivariate meta-regression analysis, none of the study characteristics were significant predictors of effect size study. The adjusted R^2 for the multivariate meta-regression analysis was 9.74% and the residual I^2 value was 86.7%. The funnel plot showed no major asymmetry (Fig. 2), and

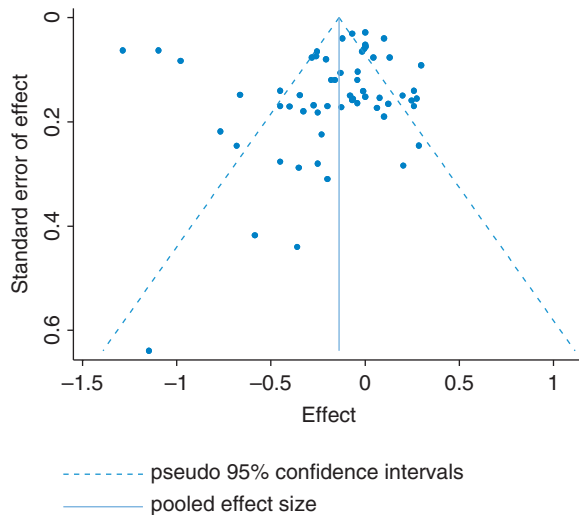


Fig. 2 Funnel plot of studies examining the effect of school-based interventions on body mass index.

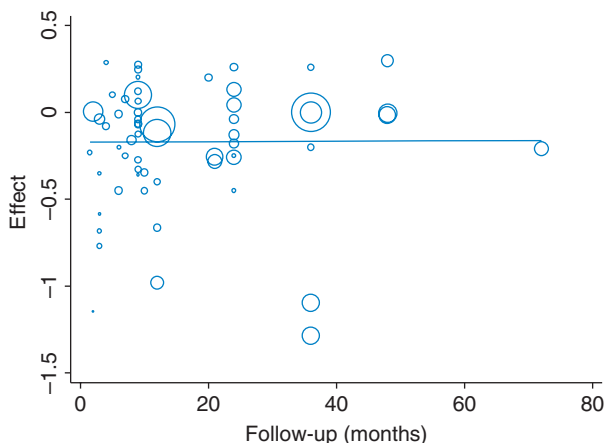


Fig. 3 Bubble plot of the univariate relationship between length of follow-up and reported effect size among studies examining the effect of school-based interventions on body mass index. The size of the bubble is proportional to the weight of studies in the meta-analysis.

Egger's test was non-significant (bias coefficient -0.692 , 95% CI: -2.407 , 1.022 , $P = 0.422$). The meta-influence plot showed that three results obtained from two studies had a large impact on the overall effect size.^{12,47} In the cumulative meta-analysis, the earliest studies showed a larger effect size but the pooled estimate has been stable and statistically significant since 2007. The bubble plot showed no relationship between the length of follow-up and effect size (Fig. 3).

Discussion

Main findings of the study

There is accumulating evidence that school-based interventions can significantly reduce children's BMI, especially if they include a physical exercise component. The evidence is reasonably consistent, in that a relatively large number of studies have now demonstrated a benefit. The effect size did not vary by length of follow-up suggesting that the benefits may be maintained over time, but only one study has followed-up participants for more than 4 years. Evidence of significant benefit is currently lacking for interventions that do not include a physical activity component. The absolute reduction in BMI was greater for interventions targeted at overweight and obese children, but studies delivered to all children nonetheless produced a significant reduction in overall BMI.

What is already known on this topic?

The prevalence of childhood obesity in developed countries is high and increasing, focusing attention on the urgent need to identify effective interventions.¹ Interventions can be targeted at individuals, families, the whole population or our obesogenic environment and all play a role. In a recent survey, 65% of American citizens believed that schools have a major role to play in tackling the obesity epidemic and only 7% believe that the school had no role to play at all.⁵⁵ The current NICE⁵ guidelines also recommend school-based interventions.

Earlier meta-analyses demonstrated conflicting results.^{10,56–58} The most recent, published in 2009, included 19 studies published up to 2007.¹⁰ Since then, an additional 21 eligible studies have been published. Therefore, an updated review is timely.

What this study adds?

Previous meta-analyses had already demonstrated the potential of school-based interventions to reduce the prevalence of obesity. Inclusion of more recent studies enabled us to demonstrate that a statistically significant reduction in overall BMI is also achievable. The absolute benefit was a 0.17 kg/m^2 reduction in BMI. This was statistically significant but is unlikely to be clinically significant at an individual level. It may, nonetheless, produce tangible health benefits at a population level. As first described by Rose, a small shift in population distribution can be an effective primary preventative strategy because more events occur among the large number of individuals at moderate risk than the small number at high risk.¹⁰

Strengths and limitations

Our study included data collected on 36 579 pupils, and was conducted in accordance with PRISMA guidelines. Random effects meta-analysis was chosen over fixed-effect because of differences in inclusion criteria and the nature of the intervention. Published studies have used a number of different anthropometric measures. By necessity, the meta-analysis needed to be based on studies using the same measure. Following a preliminary review, we chose BMI change as it was the most commonly used measure, enabling us to include the maximum number of studies. The need to exclude similar studies that used other measures, such as individual percentage fat mass or the overall percentage of pupils that were overweight, is an obvious limitation. Use of BMI z-score would have been preferable to the use of absolute BMI. However, only a minority of studies reported their results in terms of a change in z-score, therefore this was not possible. Furthermore, BMI may not be the best measure of childhood adiposity nor the best predictor of adult adiposity.⁵⁹ Where studies reported change in BMI adjusted for potential confounders, the adjusted result was used in the meta-analysis. However, some studies reported only unadjusted results which may be subject to bias. Some studies did not report SDs or confidence intervals for their results. In order to include as many studies as possible, we derived SDs for 16 studies that did not report this information. Since, the correlation coefficients for intervention and control groups were within one decimal place of each other (0.802 for intervention groups and 0.891 for control groups), this approach is unlikely to have introduced a large or systematic error and enabled us to include the maximum number of studies. Because of the small number of studies conducted in this area, we included non-randomized intervention studies. This is likely to have added to the heterogeneity of the results. In the future, as more studies become available, it would be useful to repeat the meta-analysis excluding non-randomized studies.

Conclusions

School-based interventions can reduce the BMI of pupils. The meta-analysis identified several areas where further research would be useful. The interventions examined to date appear to be less effective in boys than girls and further work is required to explore the reasons and whether they require modifications to the school-based interventions or an alternative approach. Existing studies suggest a benefit up to 6 years follow-up. Further research is required to determine whether it is maintained thereafter. Benefit has been

demonstrated for a number of different types of intervention. Further research is required to determine the ideal type of intervention, taking cognisance of cost-effectiveness as well as clinical effectiveness.

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Appendix: PRISMA flowchart of study selection in the systematic review

