

BMJ Open What change in body mass index is associated with improvement in percentage body fat in childhood obesity? A meta-regression

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ABSTRACT

Objective Using meta-regression this paper sets out the minimum change in body mass index-SD score (BMI-SDS) required to improve adiposity as percentage body fat for children and adolescents with obesity.

Design Meta-regression.

Setting Studies were identified as part of a large-scale systematic review of the following electronic databases: AMED, Embase, MEDLINE via OVID, Web of Science and CENTRAL via Cochrane library.

Participants Individuals aged 4–19 years with a diagnosis of obesity according to defined BMI thresholds.

Interventions Studies of lifestyle treatment interventions that included dietary, physical activity and/or behavioural components with the objective of reducing obesity were included. Interventions of <2 weeks duration and those that involved surgical and/or pharmacological components (eg, bariatric surgery, drug therapy) were excluded.

Primary and secondary outcome measures To be included in the review, studies had to report baseline and post-intervention BMI-SDS or change measurements (primary outcome measures) plus one or more of the following markers of metabolic health (secondary outcome measures): adiposity measures other than BMI; blood pressure; glucose; inflammation; insulin sensitivity/resistance; lipid profile; liver function. This paper focuses on adiposity measures only. Further papers in this series will report on other outcome measures.

Results This paper explores the potential impact of BMI-SDS reduction in terms of change in percentage body fat. Thirty-nine studies reporting change in mean percentage body fat were analysed. Meta-regression demonstrated that reduction of at least 0.6 in mean BMI-SDS ensured a mean reduction of percentage body fat mass, in the sense that the associated 95% prediction interval for change in mean percentage body fat was wholly negative.

Conclusions Interventions demonstrating reductions of 0.6 BMI-SDS might be termed successful in reducing adiposity, a key purpose of weight management interventions.

Trial registration number CRD42016025317.

INTRODUCTION

Childhood obesity is one of the most serious global public health challenges of the 21st century.¹ In England, the latest figures

Strengths and limitations of this study

- We believe that this is the first paper to attempt to bring together all studies that have reported both a change in body mass index-SD score and changes in a marker of adiposity in the paediatric population with obesity.
- The systematic methods employed to identify the included studies were stringent, but it is possible that some relevant studies might have been missed.
- There was some variation in the reporting of results where there were multiple publications of the same study; in these cases, the results from the most comprehensive paper have been used.
- Studies that did not report change in mean percentage body fat could not be included in this meta-regression.

from the National Child Measurement Programme, which measures the height and weight of around 1 million school children every year, showed that 9.5% of children aged 4–5 years and 20.1% of those aged 10–11 years were obese.^{2 3} Childhood obesity has adverse health consequences in both the short-term and long-term, including an increased risk of developing metabolic disturbances, like hypertension, dyslipidaemia and insulin resistance, and becoming obese adults.⁴ The presence of adverse changes in cardiac and vascular function and type 2 diabetes, which were previously considered adult morbidities, now being identified in children and adolescents with obesity^{5–11} illustrates the urgent need for effective weight management treatment interventions to reduce adiposity and improve the metabolic health status of the paediatric population.

Moderate weight loss has been shown to have a positive impact on many metabolic and cardiovascular risk factors.^{12 13} Weight management interventions for adults with

obesity that result in a 5–10% decrease in body weight are associated with significant improvements in blood pressure, serum lipid levels and glucose tolerance¹⁴ and reduction in the prevalence of hypertension and diabetes.¹⁵ Minimum weight management targets can therefore be set to improve metabolic health in this population.¹⁶

During childhood, all measurements over time are complicated by the influence of growth, meaning that cut-offs routinely used in the adult population cannot be used in children and adolescents. However, measured values of body mass index (BMI) can be standardised into SD scores (SDS) with respect to reference populations.¹⁷ These standardised scores, referred to as BMI-SDS throughout this paper, provide a normalised measurement for the degree of obesity in children and young people, indicating to what degree an individual BMI lies above or below the median BMI value.

A meta-analysis by Ho *et al*¹⁸ concluded that lifestyle interventions can lead to improvements in weight and cardiometabolic outcomes in child obesity. However, while numerous lifestyle intervention programmes to tackle childhood obesity are conducted across the UK, and many describe statistically significant reductions in BMI-SDS,¹⁹ these results do not necessarily translate into clinical benefit for the individual. How reducing BMI-SDS in a trial translates to a reduction in adiposity is uncertain.

Paediatric weight management guidelines exist in many countries to promote best practice, but at present many of these recommendations are based on low-grade scientific evidence.²⁰ Understanding how much BMI must be reduced to positively affect body composition and metabolic health is important to ensure that treatment interventions are appropriately designed and evaluated.²¹

Given the scale of the obesity problem and the significant and sustained adverse effects on health, clinically effective paediatric weight management treatment options are vital. A meta-analysis of cardiovascular disease risk in healthy children and its association with BMI has been conducted,²² but there is yet to be a systematic quantification of the reduction in BMI required to improve adiposity in the paediatric population with obesity.

It is important to highlight that when assessing interventions designed to manage overweight and obesity in children and adolescents, it is essential to recognise that measures such as BMI and derived SDS are surrogates of the real purpose: reduction of adiposity, fat being the key organ involved in metabolic complications.²³ To rigorously assess the clinical and cost-effectiveness of weight management interventions in young people, it is first necessary to understand what BMI-SDS change means in terms of key outcomes such as effects on adiposity. This paper is designed to put BMI-SDS changes in context when considering improvement in adiposity (fatness). Through meta-regression analysis, we explore the potential impact of BMI-SDS reduction in terms of change in percentage body fat. The outcome of which will both inform clinical guidelines for paediatric weight

management interventions and guide outcome measures in future clinical trials.

Objective

This paper aims to establish the minimum change in BMI-SDS needed to effect improvements in adiposity markers of children and adolescents with obesity. This is the first of a series of three papers reporting on the findings from studies identified in a large systematic review (n=90 studies; searched up to May 2017) and focuses on the evidence in relation to adiposity (percentage body fat); the others relating to metabolic and cardiovascular health.

METHODS

The studies included in this paper were identified as part of large-scale systematic review (PROSPERO CRD42016025317). The protocol for this systematic review is available: <https://doi.org/10.1186/s13643-016-0299-0>. The final search was conducted in May 2017, the review was completed in January 2018 and the results are still being evaluated.

Participants

Studies with participants aged 4–19 years with a diagnosis of obesity using defined BMI thresholds were considered for inclusion. BMI-SDS was calculated as a function of the degree of obesity of the subjects when compared with BMI references. BMI standards included, but were not limited to, the 98th percentile on the UK 1990 growth reference chart,²⁴ 95th percentile on the US Centre for Disease Control and Prevention growth chart,²⁵ the International Obesity Task Force (IOTF) BMI for age cut-points²⁶ and the WHO growth references,^{27 28} in addition to country-specific obesity thresholds using BMI reference data from their paediatric populations. Studies that included overweight, as opposed to obese, individuals, pregnant females or those with a critical illness, endocrine disorders or syndromic obesity were excluded from this review.

Interventions

Studies of lifestyle treatment interventions that included dietary, physical activity and/or behavioural components with the objective of reducing obesity were included. Interventions of <2 weeks duration and those that involved surgical and/or pharmacological components (eg, bariatric surgery, drug therapy) were excluded. Studies focused on obesity prevention were also excluded. No restrictions were imposed regarding the setting or delivery of the interventions.

Outcome measures

To meet the inclusion criteria of the full systematic review, interventions had to report baseline (preintervention) and postintervention BMI-SDS or change measurements of BMI-SDS plus one or more markers of metabolic health (please refer to the published protocol paper for a complete list of the metabolic health markers of interest; <https://doi.org/10.1186/s13643-016-0299-0>).

This paper focuses on change in BMI-SDS and adiposity measures other than BMI, including waist circumference and percentage body fat.

Study design

Completed, published, randomised controlled trials (RCTs) and non-randomised studies (cohort studies) of lifestyle treatment interventions for children and adolescents with obesity, with or without follow-up.

Ethics

Ethical approval was not required as this paper reviewed published studies only.

Patient and public involvement

There was no patient or public involvement in this review of published studies.

Information sources and search methods

Studies were identified by searching five electronic databases from inception to May 2017 (AMED, Embase, MEDLINE via OVID, Web of Science and CENTRAL via Cochrane library), alongside scanning reference lists of included articles and through consultation with experts in the field. The search strategy for MEDLINE database is presented in online supplementary appendix 1.

Study selection and data extraction

Titles and abstracts were assessed for eligibility and the data outcome measures described previously were extracted by two independent reviewers from the review team using a standardised data extraction template, which was piloted by both reviewers before starting the review to ensure consistency.

Quality assessment

The focus of this study is the relationship between change in BMI-SDS and change in metabolic health parameters, rather than the specific treatment interventions that effect those changes. Therefore, risk of bias tools, such as the Cochrane Risk of Bias tool,²⁹ were not considered appropriate. The included studies were assessed for methodological quality by two members of the review team during the data extraction process using the Quality Assessment tool used in the 2004 Health Technology Assessment (HTA) systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement.³⁰ This Quality Assessment tool comprises 20 questions which are added together to give a final score and a percentage rating, from which a level of quality is assigned. Any discrepancies in Quality Assessment scoring were resolved through discussion.

Analysis

We carried out random-effects meta-regression as implemented in Stata³¹ to try to quantify the relationship between mean change in BMI-SDS (independent, predictor variable) and mean change in percentage body fat (target variable), where these were either reported, or

were able to be calculated from reported data. Further details are given below. We were not trying to assess the relative effects of the various interventions, but rather to examine the relationship between these two outcomes. Meta-regression allows for residual heterogeneity in the target variable not explained by the predictor. Subsets from the same study (eg, intervention vs control, boys vs girls, see below) were regarded as independent observations provided there was no data duplication.

RESULTS

Search results

In total, 98 published articles relating to 90 different studies met the inclusion criteria for the entire systematic review. See figure 1 for a flow diagram illustrating the number of papers excluded at each stage of the review. For studies reported in multiple publications, the reference that provided the most comprehensive information has been used (see footnote of table 1 for details).

The Venn diagram (figure 2) illustrates how many studies were identified for the various markers of metabolic health. Seventy-three studies assessed and reported adiposity measures. The adiposity measures reported included percentage body fat, body fat-SDS, body mass, fat mass, fat-free mass, waist circumference and waist circumference-SDS. The 68 studies that examined diabetes/inflammation measures (HOMA-IR, insulin, glucose, C reactive protein, interleukin-6, alanine transaminase and the 71 studies examining cardiac measures (eg, lipids, cholesterol, blood pressure) will be reported separately.

Studies for inclusion in meta-regression analysis

Seventy-three studies assessed and reported adiposity measures. Of the different adiposity measures that were reported in these studies (percentage body fat, body fat-SDS, body mass, fat mass, fat-free mass, waist circumference and waist circumference-SDS), we elected to examine percentage body fat as it was far more frequently reported across studies. Therefore, of the 73 adiposity studies, we conducted our meta-regression on 39 studies which reported percentage body fat values. These studies are presented in table 1 with the corresponding changes in BMI-SDS.

The results of five studies were duplicated in multiple papers, thus the reference that reported the most comprehensive information was used in the analysis; see table 1 footnote for details. Thirty-four studies were excluded from the meta-analysis; the characteristics of the excluded studies, along with the reason for exclusion, are summarised in online supplementary appendix 2.

Narrative description of studies that reported BMI-SDS and percentage body fat

Of the 39 studies that reported percentage body fat included in our analysis, 7 were conducted in both Germany and the USA, 4 in Italy, followed by Australia (n=2), Denmark (n=2), the Netherlands (n=2), Poland

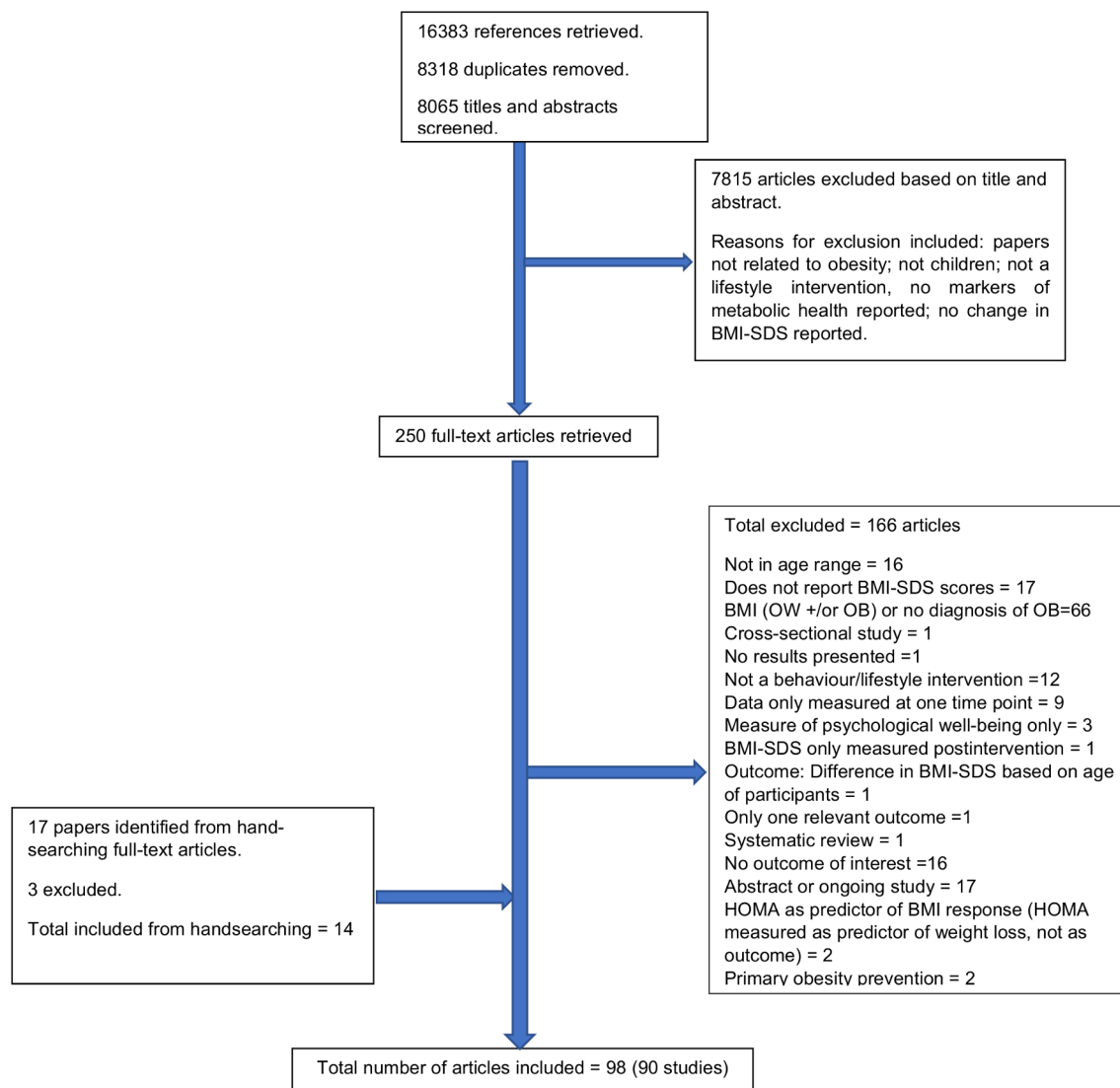


Figure 1 Flow diagram from the systematic review that identified the included studies. BMI-SDS: body mass index-SD score; HOMA, homeostatic model assessment (method of assessing insulin resistance); OB: obese; OW: overweight.

(n=2), Switzerland (n=2), Tunisia (n=2) and one each in Belgium, Brazil, Canada, Chile, France, Portugal, Spain, Thailand and the UK. There were country-specific variations in the definition of obesity, with most studies defining obesity by participants having a BMI-SDS >2, or a BMI percentile of at least >90th percentile. Most of studies used a cohort design (n=27), 11 were RCTs, of which 1 included results from a cohort of the original RCT. There was also one study which adopted a quasi-randomised design.

Most studies (n=20) conducted their intervention in the hospital clinic setting. Eight studies conducted the intervention in the community setting and 10 in academic institutions. One conducted the intervention in a mixed setting, reporting use of both a community setting and academic institution.

Twenty-eight studies conducted interventions that comprised both diet and exercise components. The remaining studies (n=11) used interventions that focused either on exercise or diet only. The duration

of the interventions ranged from 15 days to 24 months. The majority of studies (n=29; 74%) did not report any follow-up after the lifestyle treatment intervention. The duration of follow-up in the studies where it was conducted and reported, ranged from 6 months to 2 years.

The sample sizes of the included studies ranged from 8 to 203 participants. The age of the participants ranged from 4 to 19 years. Studies predominantly had a mix of males and females (95%) with only three studies specifically focused on either only girls^{32 33} or boys.³⁴ Seventeen studies (44%) measured pubertal development of participants according to Marshall and Tanner staging, with pubertal status categorised into three groups: prepubertal, pubertal and late/postpubertal.³⁵ Four studies (10%) reported that pubertal development was measured but the methodology was not defined. Eighteen studies (46%) did not report any measures of pubertal development.

Table 1 Characteristics of studies reporting adiposity outcomes with results of mean change in BMI-SDS and percentage body fat

Author, Country, (Intervention name)	Study design: Sample size (n) Analysed (An)	Obesity definition	Age range (inclusion): Mean $\pm$ (SD) Sex (% F)	Pubertal status measured	Diet D/ Exercise (E)/ D+E: Setting	Format & content	Duration (months): Follow up (months)	Method of % body fat measurement	Δ BMI SDS/ z-score by subgroup when reported	Δ % body fat score by subgroup when reported
1 Bell <i>et al</i> ⁶² Australia	Cohort: Total = 14 (14)	BMI $\geq 95^{\text{th}}$ %ile	Age range: 9-16 12.7(0.32); F=43%	Yes—Tanner	E: community	8 weeks structured circuits exercise training: 3 x 1hr sessions/week. No standard dietary modifications.	2: 0	DXA	All: -0.03	All: -0.57
2 Bock <i>et al</i> ⁶³ Canada HIP KIDS	Cohort: Total = 42 (41)	BMI $\geq 95^{\text{th}}$ %ile (CDC)	Age range: 8-17 12.8 $\pm$ 3.14; F=50%	Yes—Tanner	D+E: Clinic (Hospital)	Intensive phase (3 months): bi-weekly 90 min counselling. Maintenance phase (9 months): alternating mthly GP or individual sessions (90 mins). Sessions focus on exercise/psychosocial/behavioural aspects.	12: 0	B/A	All: -0.04	All: -1.39
3 Bruyndonckx <i>et al</i> ⁶⁴ Belgium	Quasi-RCT: Total = 61 IG = 33 (27) CG = 28 (21)	BMI $\geq 97^{\text{th}}$ %ile adolescents <16 years; BMI $\geq 95^{\text{th}}$ %ile adolescents ≥ 16 years	Age range: 12-18 IG: 15.4 $\pm$ 1.5; F = 79% CG: 15.1 $\pm$ 1.2; F=73%	NR	D+E: Clinic (Hospital)	Intervention: Dietary restriction 1500-1800 kcal/day + 2 hrs/day supervised play/lifestyle activities + 2hrs/wk PE + 3 x 40min/wk supervised training session. Control: Usual care.	10: 0	Subsample also measured using DXA	IG: -1.21 CG: 0.13	IG: -11.30 CG: 0.4
4 Bustos <i>et al</i> ⁶⁴ Chile	Cohort: Total = 50 (28 completed)	CDC	Age range: 9.5 $\pm$ 1.9; F=48%	NR	D+E: Academic Institution	Nutrition/behavioural modification session 40 min/wk + PA 50 min x2/wk+ Family support every 15 days for first 2 months, then monthly.	8: 0	DXA	All: -0.3	All: -3.00
5 Calcatera <i>et al</i> ⁶⁵ Italy	Cohort: Total = 22 (22)	BMI > 95th %ile	Age range: 9-16 13.23 $\pm$ 1.76; F=41%	Yes - Tanner	E: Academic Institution	2 x 90 mins exercise training sessions/ wk	3: 0	B/A	All: -0.15	All: -3.30
6 Dobe <i>et al</i> ⁶⁶ Germany OBELDICKS - mini	Cohort: Total = 103 (103)	>97th to 99.5 percentile	Age range: 4-8 6.1 $\pm$ 1 F=56%	NR	D+E: Academic Institution	Obeldicks mini: focus on training parents (22.5 hrs for parents, 4.5 hrs for children). Group sessions. Parents+children classes every 4th session. Children's classes: 9 x monthly sessions (30 mins); 1 x introduction; 3 x diet; 5 x eating habits Parenting classes: 13 x monthly sessions (1.5 hrs); 1x introduction 1x medicine 3x nutrition 5x eating habits + education tips 3x discussion circle Individual consultation: every 2 months (30 mins) Exercise: 50 x weekly sessions (1.5 hrs)	12: 0	B/A	Obeldicks-mini: -0.46	Obeldicks mini: -3.00
7 Farpour-Lambert <i>et al</i> ⁶⁶ Switzerland	RCT: Total = 44 IG= 22 (22) OC = 22 (22)	BMI >97th %ile	Age range: 6-11 8.9 $\pm$ 1.5 IG: F=59% OC: F= 68%	Yes	E Clinic (Hospital)	180 min/wk PA + 135 min/wk PE	3: 0	Skinfold measurements	IG: -0.1 CG: 0	IG: -1.50 CG: 0.80
8 Ford <i>et al</i> ^{48, 57} UK	RCT: Total = 106 (91) Gp1 SC = 52 (46) Gp2 Mandometer = 54 (45)	BMI $\geq 95^{\text{th}}$ %ile (CDC)	Mandometer: 9.0-16.9 SC: 9.1-17.5 Mandometer: 12.7 $\pm$ 2.2 SC: 12.5 $\pm$ 2.3 overall F=56%	Yes	D Clinic (Hospital)	Mandometer device to regulate rate of eating and total intake vs SC	12: 0	DXA	IG: -0.36 CG: -0.14	IG: -4.60 CG: -1.30

Continued

Table 1 Continued

Author, Country, (Intervention name)	Study design: Sample size (n) Analysed (An)	Obesity definition	Age range (Inclusion): Mean $\pm$ (SD) Sex (% F)	Pubertal status measured	Diet D/ Exercise D+E: Setting	Format & content	Duration (months): Follow up (months)	Method of % body fat measurement	Δ BMI SDS/ z-score by subgroup when reported	Δ % body fat score by subgroup when reported
9 Gajewska <i>et al</i> ⁶⁷ Poland	Cohort: Total = 100 (76) With WL = 71 (56) Without WL = 29 (20)	BMI SDS >2	Age range: 5–10 with WL: 8.1 (6.8–9.2); F = 51% without WL: 8.8 (7.3–9.6); F = 59% overall F = 53%	Reported with Tanner stage, any with pubertal development excluded.	D+E: Community & Academic institution	3-month intervention, low energy diet (1200–1400kcal), 3–5 meals every day, instructions concerning PA, 10–14 food day diary, 3-day food diary.	3: 0	B/A	WL: –0.98 No WL: –0.2	WL: –2.90 No WL: 0.30
10 Garant-Bogacka <i>et al</i> ⁶⁸ Poland	Cohort: Total = 50 (50)	BMI >97 th %ile (Polish ref pop.)	Age range: 8–18 14.2 $\pm$ 2.6; F = 58%	Yes	D+E: Clinic (Hospital)	Exercise therapy (Instructions in PA + reducing sedentary behaviour) + reduction in fat and sugar intake.	6: 0	Skinfold measurements & Lohman's formula	All: –1	All: –4.70
11 Gronbaek <i>et al</i> ⁶⁹ & Kazankov <i>et al</i> ⁶⁰ Denmark Julemaerket Hjemmet Hobro (same cohort)	Cohort: Total = 117 (117) (n=71 attended 12 mth FU)	NR. Obese. BL BMI-SDS: 2.93 $\pm$ 0.52	Age range: NR 12.1 $\pm$ 1.3 F = 56%	NR	D+E: Community	Individually designed healthy diet + moderately strenuous PA program (at least 1hr/day).	2.5 months/10 weeks: 12	B/A	All: –0.63	All: –4.30
12 Hvidt <i>et al</i> ⁶¹ Denmark	Cohort: Total = 61 (61)	Children's Obesity Clinic; BMI >90 th %ile (Danish ref pop.) = z-score 1.28. BL BMI-SDS: 2.73 $\pm$ 0.60	Age range: 10–18 Median: 12.5 F = 54%	NR	D+E: Clinic (Hospital)	Family-centred approach involving behaviour changing techniques (90 advice and advice strategies on low-calorie diet + activity for example, 10–20 items aimed to reduce obesity).	12: 0	B/A	All: –0.21	All: –3.40
13 Kirk <i>et al</i> ⁴⁷ USA	Cohort: Total = 177 (177) Children (6–10yrs) = 85 Adolescents (11–19yrs) = 92	BMI >95 th %ile	Age range: 5–19 9.0 $\pm$ 1.5 Overall F = 61% Children: F = 24% Adolescents: F = 59%	NR	D+E: Clinic (Hospital)	Behavioural intervention with individualised behavioural goals for nutrition, PA & family support.	5: 6	DXA	GP1: –0.18 GP2: –0.13 All: –0.15	GP1: –2.10 GP2: –2.40 All: –2.20
14 Klijn <i>et al</i> ⁶² The Netherlands	Cohort: Total = 15 (15)	BMI >30	Age range: 10–18 14.7 (2.1); F = NR	NR	E: Community	Aerobic exercise training programme – 12 weeks: 3 x 30–60 min aerobic group sessions/week (2x gym/outdoors, 1 x swimming pool). PE teacher led. Diverse indoor, outdoor and swimming activities.	3: 0	% body fat calculated by "dividing fat mass by total body mass"	All: –0.4	All: –3.80
15 Lazzar <i>et al</i> ⁶³ Italy	Cohort: Total = 19 Boys = 7 (7) Girls = 12 (12)	BMI >97 th %ile	Age range: 8–12 Boys: 9.9 $\pm$ 1.6 Girls: 11.2 $\pm$ 1.5 Overall F = 63%	Yes – Tanner	D+E: Community	2 x 50min/wk endurance training + 2hr/ wk PE lessons + 1 x wk child & parent dietetic class + 1 x wk psychological group class.	8: 12	DXA	Boys: –0.4 Girls: –0.2	Boys: –4.00 Girls: –2.20
16 Meyer <i>et al</i> ⁶⁴ Germany	RCT: Total = 67 IG = 33 (63) OC = 34 (34)	BMI >97 th %ile (German paediatric population)	Age range: 11–16 IG: 13.7 $\pm$ 2.1; F = 48% OC: 14.1 $\pm$ 2.4; F = 50%	Yes – Tanner	E: Clinic (Hospital)	3 x exercise sessions (Monday: swimming and aqua aerobic training 60 min + Wednesday sports games 90 min + Friday walking 60 min/ wk; Control: Maintain current level of PA	6: 0	B/A	IG: –0.43 CG: –0.14	IG: –1.00 CG: 0.00
17 Miraglia <i>et al</i> ⁶⁵ Brazil	Cohort: Total = 27 (27)	BMI z-score >2	Age range: 6–13 Median 10.3; F = 48%	NR	D+E: Clinic (Hospital)	AmO: Outpatient Ambulatory. Obesity outpatient clinic - lifestyle change based on goals agreed relative to feeding habits & physical exercise, followed mthly. 12 months: Subjects assessed at inclusion & after 12 months of FU to obtain anthropometric & adipokine measurements.	12: 0	B/A	All: –0.4	All: –0.10

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Table 1 Continued										
Author, Country, (Intervention name)	Study design: Sample size (n) Analysed (An)	Obesity definition	Age range (inclusion): Mean $\pm$ (SD) Sex (% F)	Pubertal status measured	Diet D/ Exercise (E)/ D+E: Setting	Format & content	Duration (months): Follow up (months)	Method of % body fat measurement	Δ BMI SDS/ z-score by subgroup when reported	Δ % body fat score by subgroup when reported
18 Morell-Azanza <i>et al</i> ⁶⁶ & Rendo-Urteaga <i>et al</i> ⁶⁷ Spain (same cohort)	Cohort: Total = 54 (40) high responders =21 low responders = 19	OW/OB as per Cole <i>et al</i> 2000	Age range: 7–15 Mean =11 F=53% (of N analysed)	Yes – Tanner	D: Clinic (Hospital)	Moderate energy-restricted diet + nutritional education sessions with dietitian + family involvement.	2.5: 0	BIA	HR: –0.79 LR: –0.18 HR: –0.64 LR: –0.07	HR: –3.10 LR: –0.60 HR: –2.49 LR: –0.37
19 Murer <i>et al</i> ⁶⁸ & Aeberli <i>et al</i> ⁶⁹ Switzerland (same cohort)	Cohort: Total = 206 (203)	BMI >98th %ile	Age range: 10–18 14.1 $\pm$ 1.9; F=44%	NR	D+E: Clinic, hospital	Moderate caloric restriction.2 x 60–90 min/day endurance exercise + 4–5 hr/wk. exercise session + behaviour modification.	2: 0	BIA	All: –0.42	All: –5.50
20 Murbolo <i>et al</i> ⁷⁰ Italy	Cohort: Total = 53(53) Responders = 44 Non-responders = 9	NR	Age range: 5–13 Responders: 9.0 $\pm$ 1.1; F=50% Non-responders: 2.09 $\pm$ 0.32; F=33%	Yes – Tanner	D+E: Community	Educational Wt Excess Reduction Program	24: >6	BIA	Responders: –0.44 Non-responders: 0.11	Responders:–2.90 Non-responders: –2.00
21 Ning <i>et al</i> ⁷¹ & BEAN <i>et al</i> ⁷² USA TEENS (same cohort)	Cohort: Total = 145*(145)	BMI $\geq$ 95th %ile (CDC)	Age range: 11–18 13.1 F=65%	NR	D+E: Academic Institution	12 x 30 min nutritional session with adolescent and parent/s + Education/behavioural support sessions once every 2 wks, or alternating wks + PA 3 x 60 min/wk during initial 12 wks, then minimum of twice/wk.	6: 0	DXA	All: –0.1	All: –2.40
22 Pacifico <i>et al</i> ⁷³ Italy	Cohort: Total = 120 (120)	BMI >95th %ile	Age range: (11.5–12.2) 11.9; F=35%	Yes (method ND)	D+E: Clinic (Hospital)	Hypocaloric diet (25–30 Kcal/kg/day) + 60 min/day ~ 5 days/wk moderate exercise + Reduce sedentary behaviour.	12: 0	NR	All: –0.32	All: –2.10
23 Racil <i>et al</i> ⁸² Tunisia	RCT: Total = 34 HIT = 11 (11) MIT = 11 (11) OC = 12 (12)	BMI >97th %ile (French standards)	Age range: NR HIT: 15.6 $\pm$ 0.7 MIT: 16.3 $\pm$ 0.52 OC: 15.9 $\pm$ 1.2 Overall F=100%	Yes –Tanner	D+E: Community	4-day diet records + HIIT or MIT. Interval training program 3 x /wk on non-consecutive days.	3: 0	BIA	HIT: –0.4 MIT: –0.3 OC: 0	HIT: –2.90 MIT: –2.00 OC: –0.40
24 Racil <i>et al</i> ⁸³ Tunisia	RCT: Total = 47 HIT = 17 (17) MIT = 16 (16) OC = 14	BMI $\geq$ 97th %ile (French standards)	Age range: NR 14.2 $\pm$ 1.2; F=100%	NR	E: Academic Institution	HIIT (Warm up + Interval training at 100%/50% MAS + Cooling down); MIT (Warm up + Interval training 80%/50% MAS + Cooling down)	3: 0	BIA	HIT: –0.3 MIT: –0.3 OC: 0	HIT: –3.90 MIT: –3.40 OC: –0.50
25 Reinehr <i>et al</i> ⁸⁸ Germany OBELDICKS	Cohort: Total = 42 (42)	BMI $\geq$ 97th %ile	Age range: 6.1–15.1 10.2; F=57%	Yes – Tanner	D+E: Clinic (Hospital)	Obeldicks: Intensive phase 3 months (Parents' course 2x/month + Behaviour therapy 2x/month + Nutritional course 2x/month + Exercise therapy 1x/ wk) + Establishing phase 3 months (Talk rounds for parents 1x/month + Psychological therapy + Exercise therapy 1x/wk) + Establishing phase 2 for 3 months (Psychological therapy + Exercise therapy 1x/wk) + Establishing phase 3 for 3 months (Exercise therapy 1x/wk).	12: 0	% body fat skinfold thickness	Sig. WL: –0.9 NS WL: –0.2	Sig. WL: –7.50 NS WL: –3.00
26 Reinehr <i>et al</i> ^{74,75} Germany OBELDICKS	Cohort: Ob + Sub. WL = 25 Ob + no change = 18 Normal control = 19 (BL data only)	IOTF using pop. –specific data	Ob: 10.8 $\pm$ 2.6; F=61% Lean C: 10.3 $\pm$ 2.9; F=58% Ob + Sub. WL: F= 68% Ob + no change: F = 50%	Yes –Tanner	D+E: Clinic (Hospital)	Obeldicks	12: 0	% body fat skinfold thickness	WL: –0.6 No WL: –0.1	WL: –8.00 No WL: 0.00

Continued

Table 1 Continued

Author, Country, (Intervention name)	Study design: Sample size (n) Analysed (An)	Obesity definition	Age range (Inclusion): Mean $\pm$ (SD) Sex (% F)	Pubertal status measured	Diet D/E Exercise (E)/ D+E: Setting	Format & content	Duration (months): Follow up (months)	Method of % body fat measurement	Δ BMI SDS/ z-score by subgroup when reported	Δ % body fat score by subgroup when reported
27 Rohrer <i>et al</i> ⁷⁸ Germany Fit Kids	Cohort: Total = 22 (22) Unchanged BMI = 12 Reduced BMI = 10	BMI >99.5th %ile (German standard values) or BMI >97th %ile with obesity-associated risk factors or BMI >90th %ile with obesity-associated disease	Age range: 7-15 Median: 11.9 F=27% Unchanged BMI: F = 33% Reduced BMI: F=20%	NR	D+E: Community	Physical exercise (2 x wk, 100 hrs in total) + Nutritional/health education and psychological care for the child (x wk, 43.5 hrs total) and parent/s (2 x wk, 12 hrs total).	12: 0	B/A	Increased BMI: 0.12 Reduced BMI: -0.35	Increased BMI: 1.05 Reduced BMI: -0.05
28 Rolland-Cachera <i>et al</i> ⁷⁷ France	RCT: Total = 99 PROT- = 61 (53) PROT+ = 60 (46)	BMI > 97th %ile (French reference values)	Age range: 11-16 PROT- = 14.1 $\pm$ 1.2; F = 74% PROT+ = 14.4 $\pm$ 1.3; F = 72%	NR	D+E: Academic Institution	Wt reducing diet; 7hr/wk vigorous sports + 7hr/wk outdoor activities; advice on nutrition & PA during weekends/holidays.	9: 12+24	B/A	PROT-: -2.6 PROT+: -2.5	PROT-: -12.40 PROT+: -12.10
29 Roth <i>et al</i> ⁷⁹ Germany OBELEDICKS	Cohort: Total = 69 OB + WL = 32 OB + with WL = 37	OB as per IOTF criteria	NR - (see Obeldicks age range) Ob with WL: 11.8 $\pm$ 2.0; F=50% Ob without WL: 12.1 $\pm$ 2.1; F=51% Normal wt: 12.3 $\pm$ 3.0; F=45%	Yes - Tanner	D+E: Clinic (Hospital)	Obeldicks	12: 0	% body fat skinfold thickness	WL: -0.69 No WL: 0.03	WL: -9.60 No WL: -4.30
30 Savoye <i>et al</i> ⁷⁹ USA Bright Bodies	Cohort: Total = 33 (25) SMP = 10 (8) BFC = 23 (17)	BMI $\geq$ 95th %ile (CDC)	Age range: 11-16 13.5 $\pm$ 0.3; SMP: 13.3 $\pm$ 0.6; F=75% BFC: 13.6 $\pm$ 0.3; F=65%	NR	D+E: Academic Institution	Bright Bodies Weight Management Program: nutrition education, exercise, behavioural modification. 2 x 30 min exercise sessions + 1 x 45 min nutrition/behaviour medication group session per week. 4 levels: Beginner, Intermediate I, Intermediate II, Advanced. All levels 12 weeks duration. Monthly maintenance classes after 1 yr (support-group style)	12: 12	B/A	SMP: -0.36 BFC: -0.12	SMP: -6.50 BFC: -4.20
31 Savoye <i>et al</i> ^{80, 81} USA Bright Bodies (data taken from 2011 paper)	RCT+ Long term FU results (cohort) RCT Total = 174 BB = 105 CC = 69 1 YR ANALYSIS BB = 75 CC = 44	BMI $\geq$ 95th %ile (CDC)	Age range: 8-16 BB: 12.0 $\pm$ 2.5; F=56% CC: 12.5 $\pm$ 2.3; F=68%	NR	D+E: Academic Institution (local school).	Bright Bodies Weight Management Program: nutrition education, exercise, behavioural modification. 2 x sessions/ wk for 6 months, then biweekly for next 6 months. BB: 2x50 min exercise + 1x40 min nutrition/behaviour modification per wk + 12 months no active intervention. Control group: standard care - paed. obesity clinic (biannual clinic appt; diet + exercise counseling). Structured tx & teaching program (28 x 45 min therapeutic sessions for example, PA, nutrition, healthy cooking)	12: 12 FU 1.5: 24	B/A	IG: -0.21 CG: 0.01	IG: -3.90 CG: 2.10
32 Savoye <i>et al</i> ⁸² USA Bright Bodies	RCT Total = 75 BB = 38 (31) CC = 37 (27)	BMI $\geq$ 95th %ile	Age range: 10-16 BB: 12.7 (1.9); F=68% CC: 13.2 (1.8); F=62%	Yes-Tanner	D+E: Academic Institution	Bright Bodies Weight Management Program: nutrition education, exercise, behavioural modification. 2 x 30 min exercise sessions + 1 x 45 min nutrition/behaviour medication group session per week. 4 levels: Beginner, Intermediate I, Intermediate II, Advanced. All levels 12 weeks duration. Monthly maintenance classes after 1 yr (support-group style)	6: 0	B/A	BB: -0.05 CC: 0.04	BB: -3.30 CC: 0.40

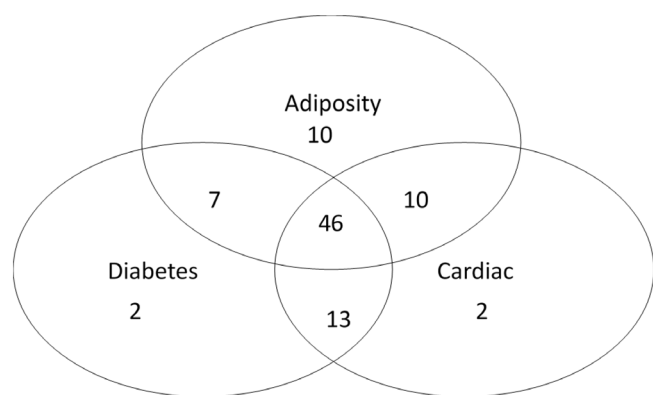
Table 1 Continued

Author, Country, (Intervention name)	Study design: Sample size (n) Analysed (An)	Obesity definition	Age range (inclusion): Mean $\pm$ (SD) Sex (% F)	Pubertal status measured	Diet D/ Exercise (E)/ D+E: Setting	Format & content	Duration (months): Follow up (months)	Method of % body fat measurement	Δ BMI SDS/ z-score by subgroup when reported	Δ % body fat score by subgroup when reported
33 Schiel <i>et al</i> ⁶⁵ Germany	Cohort: Total = 143 (143)	BMI-SDS ≥ 97 th %ile	Age range: NR 13.9 $\pm$ 2.4; F=62%	NR	D+E: Clinic (Hospital)	Structured Tx & Teaching Program (STTP): 28 x 45 min therapeutic sessions for example, PA, nutrition, healthy cooking	1.5: 24	NR	All: -0.26	All: -3.40
34 Seabra <i>et al</i> ⁶⁴ Portugal	Cohort: Total = 88 soccer = 29 (29) Trad. Act. = 29 (29) OC = 30 (30)	BMI-SDS > 2	Age range: 8-12 Soccer: 10.6 $\pm$ 1.5 Trad. act.: 11.0 $\pm$ 1.6 OC=10.0 $\pm$ 1.3 Overall F=0%	Yes - Tanner	E: Community	Soccer & trad. activity programmes (3 x 60-90min/wk) + 2 x 1hr at BL & 3 months later energy balance session.	6: 0	DXA	Soccer: -0.2 Trad.: -0.2 CG: -0.1	Soccer: -2.20 Trad.: -4.10 CG: 3.10
35 Truby <i>et al</i> ⁶⁴ Australia	RCT: Total = 87 SMC = 37 (33) SLF = 36 (32) WLlist OC = 14 (14)	BMI >90th %ile (CDC)	Age range: 10-17 SMC: 13.2 $\pm$ 1.9; F=73% SLF: 13.2 $\pm$ 2.1; F=72% WLlist OC: 13.6 $\pm$ 1.9; F=71%	Yes -Tanner	D: Clinic (Hospital)	Structured modified CHO diet (35% CHO; 30% protein; 35% fat), structured low-fat diet (55% CHO; 20% protein; 25% fat), Control (no dietary advice).	3: 0	B/A	SLF: -0.09 SMC: -0.15 CG: 0.02	SLF: -0.13 SMC: -0.40 CG: 2.62
36 Van der Bant-Slootweg <i>et al</i> ⁶⁵ The Netherlands	RCT: Total = 90 Inpt. = 45 (37) AmO = 45 (36)	BMI z score $\geq$ 3.0 or > 2.3 with OB-related health problems	Age range: 8-18 Inpt: 13.8 $\pm$ 2.3; F=58% AmO: 13.9 $\pm$ 2.5; F=58%	NR	D+E: Clinic (Hospital)	Inpt. (Hospitalised 26 wks on working days - 4 days/wk 30-60min exercise + nutrition/BM once/wk + parents/caregivers 3 x 1hr lesson on nutrition/BM); Ambulatory (12 visits at increasing time intervals - 1 hr exercise session + encouraged 3 x exercise/wk + 1 hr educational programme + 30 min nutrition education).	6: 24	B/A	Inpt: -0.6 AmO: -0.35	InP: -3.34 AmO: -7.87
37 Visutranukul <i>et al</i> ⁶⁶ Thailand	RCT: Total = 70 (52) I = 35(25) OC = 35 (27)	ND. BL BMI z-score: I = 3.7 $\pm$ 0.9 C = 3.6 $\pm$ 1.6	Age range: 9-16 I = 11.9 $\pm$ 1.9; F=36% C = 12.0 $\pm$ 2.1; F=30%	Yes -Tanner	D: Clinic (Hospital)	I (Low GI diet + Energy restriction 1400-1500 kcal/day + Increased exercise); OC (Energy restriction 1200-1300 kcal/day + Low fat/high fibre diet + Increased exercise).	6: 0	B/A	IG: -0.3 CG: -0.3	IG: 0.10 CG: 0.10
38 Vitola <i>et al</i> ⁶⁷ USA	Cohort: Total = 8(7)	BMI ≥ 95 th %ile	Age range: NR 15.3 $\pm$ 0.6; F=12.8%	Yes -Tanner	D+E: Clinic (Hospital)	Individual behavioural therapy sessions with psychologist. Parents involvement encouraged. Self-monitoring of PA & food intake. Gradual reduction of caloric intake to $\approx$ 1200-1500 kcal/day. Ongoing therapy - wt loss therapy repeated when 5% body wt lost & wt stable for at least 4 wks	NR	DXA	All: -0.3	All: -5.30
39 Wickham <i>et al</i> ⁶⁸ & Evans <i>et al</i> ⁶⁹ USA	Cohort: Total = 168 (64)** Completers only = 57	BMI ≥ 95 th %ile (CDC)	Age range: 11-18 13.9 $\pm$ 1.9; F=62%	NR	D+E: Academic Institution	Exercise 1 day/wk at facility + 2 additional exercise days at facility of ppis' choice + 30 min/wk nutrition education/behavioural support sessions.	6: 0	B/A	Completers: -0.07	Completers: -1.30

For studies reported in multiple publications, the reference that provided the most comprehensive information has been used (thus Ning *et al*⁷¹ includes data from Bean *et al*⁷²; Evans *et al*⁶⁹; Aeberli *et al*⁶⁸ is reported under Murer *et al*⁶⁶; Rendo-Ortega *et al*⁶⁷ is reported under Morell-Azanza *et al*⁶⁸ and Kazankov *et al*⁶⁸ is reported under Gronbaek *et al*⁶⁹).

**Minor discrepancies in reporting of data in papers.

KEY: %ile, percentile; AmO, outpatient ambulatory; An., analysed; apt., appointment; BB, Bright Bodies; BIA, bioelectrical impedance analysis; BFC, better food choices; BL, baseline; BMI, body mass index; C, control; CBT, cognitive behavioural therapy; CDC, Centre for Disease Control; CG, control group; CHO, carbohydrate; D, diet; DXA, Dual-energy X-ray absorption; E, exercise; FBBT, family-based behavioural treatment; F, female; FU, follow up; GI, glycaemic index; GT, group therapy; HGI, high glycaemic index; HLT, high intensity interval training; hr, hour; HZ, heterozygous; HO, homozygous; ht, height; I, intervention; IG, International Obesity Task Force; Inpt., inpatient; LGI, low glycaemic index; LMS, least-mean-squares; LS, long stay; MAS, maximal aerobic speed; MIT, moderate intensity interval training; min, minute; MO, morbidly obese; norm, normal; n, number; NAFED, Non-alcoholic fatty liver disease; ND, not described; NR, not reported; OB, obese; OC, obese control; OW, overweight; paed., paediatric; PA, physical activity; PE, physical activity; PROT, protein; RCT, randomised controlled trial; SD, standard deviation; SDS, standard deviation score; SMP, structured meal plan; SS, short stay; Sub., substantial; SMC, structured modified carbohydrate diet; trad., traditional; tx, treatment; wk, week; WLlist OC, wait list obese control; WL, weight loss; wt, weight; X-over, crossover; yr, year.



TOTAL NUMBER OF STUDIES = 90

Figure 2 Venn diagram illustrating the markers of metabolic health measured.

Quality assessment

The quality of the conduct of each study was assessed using the same criteria as the HTA systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement.³⁰ The results of the quality assessment can be found in table 2. In summary, none of the 39 studies that reported percentage body fat were considered to be of poor quality, 21 studies (54%) were rated as being of moderate quality and 18 studies (46%) achieved a score over 81% indicating high quality.

Quantitative analysis

From the 39 studies we identified all data subsets that reported a mean change in BMI-SDS, an associated mean change in percentage body fat (or pre-study and post-study values from which these could be calculated) and the number of cases analysed. A few studies yielded only aggregated data for the whole study. For the others, typical data subsets included intervention versus control, male versus female or good versus poor responders (table 1), and these were used in preference to aggregated results if both were available. In all, there were 66 subsets, with numbers analysed totalling 2618.

SEs were required for the mean changes in percentage body fat and, if not given explicitly, were calculated, from either the SDs or the 95% CIs of the mean changes. In total, 22 data sets had SEs. For the remainder, the SEs were estimated from the SDs associated with the baseline and the postintervention percentage body fat values, making an assumption about the degree of correlation between them. The median and IQR of the correlation coefficients estimated from the nine data sets where both the SEs of mean change and the SDs for baseline and postintervention percentage body fat values were available was 0.81 (IQR 0.59–0.82) and 0.81 has been used in the following analysis.

A small number of data sets (n=6)^{36–38} only had medians and IQRs (or range) reported for the baseline

and postintervention results; the mean and SDs were estimated from them.³⁹

The meta-regression line was fitted and plotted together with the 95% prediction intervals for the change in percentage body fat across the study data sets. The smallest reduction of mean BMI-SDS associated with a reduction in mean percentage body fat was determined as the smallest reduction in mean BMI-SDS with an associated 95% prediction interval wholly below zero.

A series of sensitivity analyses were conducted. Sensitivity analysis 5A: using the 22 cases where the SEs of the mean change in percentage body fat were actually known, sensitivity analysis 5B: omission of two extreme values and sensitivity analysis 5C: assuming a correlation of 0.50 instead of 0.81. In further exploratory analyses, the percentage of girls and the length of the study (baseline to end of intervention) were added to see if these affected the prediction of mean change in percentage body fat.

Results from the quantitative analysis

Figure 3 shows the results of the analysis and the fitted regression line. The circles represent the study results (ie, the mean changes in percentage body fat and mean changes in BMI-SDS) analysed for each study, with the size of the circles representing the precision of the mean change in percentage body fat, that is, the reciprocal of the SE squared.

The fitted regression line shown in figure 3 is:

Mean change in percentage body fat = $5.179 \times \text{mean change in BMI-SDS} - 0.767$.

The regression slope was statistically significant ($p < 0.001$), confirming a relationship between the mean loss of percentage body fat and the mean change in BMI-SDS across the data subsets; the proportion of the between-subset variance explained by the mean change in BMI-SDS (ie, 'a type of adjusted R-squared') was 68%. There was, however, significant between-subset heterogeneity with 89% of the percentage of the total residual variance attributable to this (ie, I^2).² It was further noted that when added to the model, neither the percentage girls in the study sets nor the durations of the interventions significantly improved the prediction of mean change in percentage body fat from the mean change in BMI-SDS ($p = 0.36$, $p = 0.89$, respectively).

Figure 3 also shows the 95% prediction intervals for the mean change in percentage body fat. The upper limit of the prediction interval was below 0 only when the mean reduction in BMI-SDS was > 0.6 , suggesting that any new study should aim to reduce the BMI-SDS by at least this amount to be confident of achieving a mean reduction of percentage body fat.

A normal plot for the standardised predicted random effects is shown in figure 4. Most were within ± 2 , although the data sets themselves were not wholly independent (as some came from the same studies).

None of the sensitivity analyses conducted (figure 5) significantly altered the findings, namely that a mean change of 0.6 or more in BMI-SDS was associated with a

Continued

Table 2 Quality assessment of included studies																						
Study	Sample				Conduct of study				Follow-up				Analysis			Interpretation				Total (x/40)	Overall rating	
	1. Aims clearly stated	2. Sample size justified	3. Age of participant defined	4. Measurements at start clearly stated?	5. Measurements likely to be valid and reliable?	6. Risk factors recorded clearly?	7. Was the intervention before follow-up defined?	8. Setting of the study clear?	9. Is mode of assessment described?	10. Did untoward events occur during the study?	11. Was there a follow-up?	12. Was follow-up necessary?	13. Are losses to follow-up defined?	14. Was basic data adequately described?	15. Do numbers add up?	16. Did analysts allow for passage of time?	17. Was statistical significance assessed?	18. Were the main findings interpreted adequately?	19. Were null/negative findings interpreted?			20. Are important effects overlooked?
1	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	35	87.5
2	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	36	90
3	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	36	90
4	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	30	75
5	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	?	No	31	77.5
6	?	No	Yes	?	?	No	Yes	?	?	No	No	Yes	No	Yes	Yes	Yes	Yes	?	?	No	26	65
7	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	37	92.5
8	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	?	?	35	87.5
9	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	?	No	31	77.5
10	Yes	No	Yes	Yes	Yes	?	?	?	Yes	?	No	?	No	Yes	?	Yes	Yes	Yes	?	No	26	65
11	Yes	?	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	37	92.5
12	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	?	?	34	85
13	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	?	No	Yes	?	Yes	Yes	Yes	Yes	Yes	?	?	29	72.5
14	Yes	No	Yes	Yes	Yes	No	Yes	?	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	27	67.5
15	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	32	80
16	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	30	75
17	Yes	No	No	Yes	Yes	No	Yes	?	Yes	No	No	Yes	No	?	Yes	Yes	Yes	?	Yes	Yes	25	62.5
18	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	32	80
Morell-Azanza et al. ⁶⁵ Rendo-Urtaaga et al. ⁶⁷																						
19	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	?	31	77.5
Murer et al. ⁶⁸ Aeberli et al. ⁶⁹																						
20	Yes	No	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	28	70
21	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	34	85
Ning et al. ⁷¹ Bean et al. ⁷²																						
22	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	?	31	77.5
Pacifico et al. ⁷³																						
23	Yes	No	Yes	Yes	Yes	No	Yes	?	Yes	No	No	?	No	Yes	Yes	Yes	Yes	Yes	?	?	29	72.5
Racil et al. ⁷²																						
24	Yes	No	?	Yes	Yes	No	Yes	?	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	28	70
Racil et al. ⁷³																						
25	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	?	29	72.5
Reinehr et al. ⁷⁴																						
26	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	32	80
Reinehr et al. ^{74, 75}																						
27	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	?	?	No	33	82.5
Rohrer et al. ⁷⁶																						
28	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	No	No	33	82.5
Rolland-Cachera et al. ⁷⁷																						
29	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	28	70

Table 2 Continued

Study	Sample			Conduct of study			Follow-up		Analysis		Interpretation			Total (x/40)	Overall rating								
	1. Aims clearly stated	2. Sample size justified	3. Age of participant defined	4. Measurements at start clearly stated?	5. Measurements likely to be valid and reliable?	6. Risk factors recorded clearly?	7. Was the intervention before follow-up defined?	8. Setting of the study clear?	9. Is mode of assessment described?	10. Did untoward events occur during the study?	11. Was there a follow-up?	12. Was follow-up necessary?	13. Are losses to follow-up defined?			14. Was basic data adequately described?	15. Do numbers add up?	16. Did analysis allow for passage of time?	17. Was statistical significance assessed?	18. Were the main findings interpreted adequately?	19. Were null/negative findings interpreted?	20. Are important effects overlooked?	
30	Savoye <i>et al</i> ⁸³	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	34	85
31	Savoye <i>et al</i> ^{80,81}	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	36	90
32	Savoye <i>et al</i> ⁸²	Yes	Yes	Yes	Yes	No	Yes	?	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	35	87.5
33	Schiel <i>et al</i> ⁸³	Yes	No	?	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	?	Yes	No	?	Yes	Yes	29	72.5
34	Seabra <i>et al</i> ⁸⁴	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	34	85
35	Truby <i>et al</i> ⁸⁴	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	38	95
36	van der Baan-Slootweg <i>et al</i> ⁸⁵	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	36	90
37	Visuthranukul <i>et al</i> ⁸⁶	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	38	95
38	Vitola <i>et al</i> ⁸⁷	Yes	No	Yes	Yes	No	?	?	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	28	70
39	Wickham <i>et al</i> ⁸⁸ Evans <i>et al</i> ⁸⁹	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	?	Yes	Yes	Yes	Yes	No	Yes	?	?	30	75

For Q6, Were risk factors clearly recorded? We said 'no', rather than 'unclear', to all the studies that did not record risk factors.

For Q10, Did untoward events occur during the study? We said 'no', rather than 'unclear' if not mentioned.

Rating: not satisfactory 1%–50%; moderate quality=51%–80%; high quality=81%.

?, unclear.

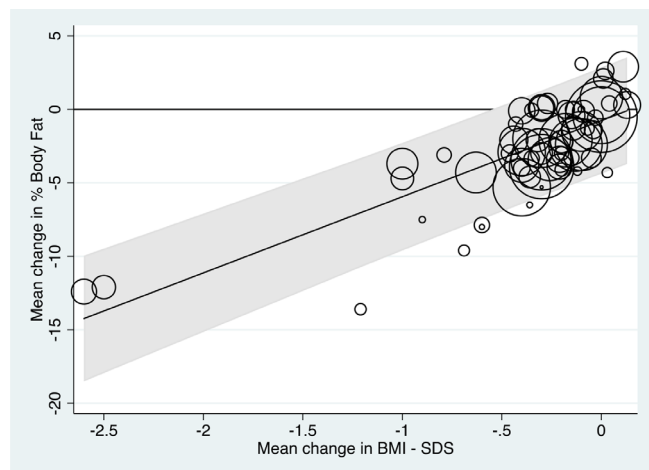


Figure 3 Meta-regression line showing the relationship between mean change in percentage body fat and body mass index-SD score (BMI-SDS) across the 39 studies (66 subsets) analysed.

definitive mean loss in percentage body fat. In [figure 5B](#), with the exclusion of the two extreme data points, the linear trend can be seen more clearly across the range of mean BMI-SDS losses.

DISCUSSION

Summary of main results

This is the first of a series of papers that report on studies identified in a large systematic review. The objective of this paper was to attempt to establish the minimum change in BMI-SDS needed to achieve improvements in body fat in children and adolescents with obesity; BMI-SDS being by far the most frequently reported outcome in terms of weight management trial interventions in childhood. Seventy-three of the 90 included studies reported adiposity measures, but in our meta-regression only percentage body fat can be used as a reliable, comparable marker of change of adiposity. Thus, the analyses presented in this paper were conducted using data from 39 studies. All of

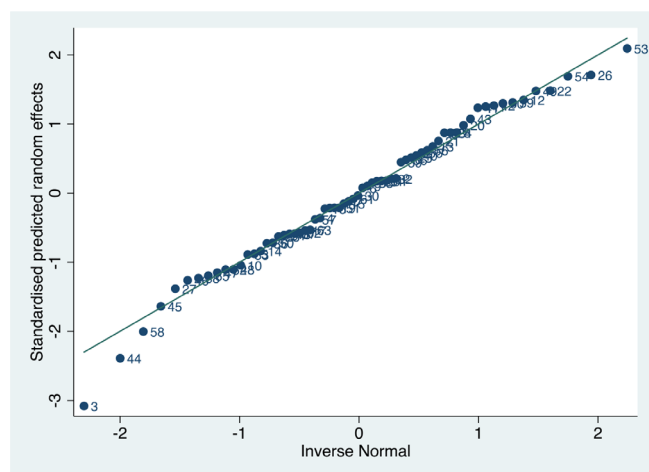


Figure 4 Normal plot for the standardised predicted random effects from the meta-regression.

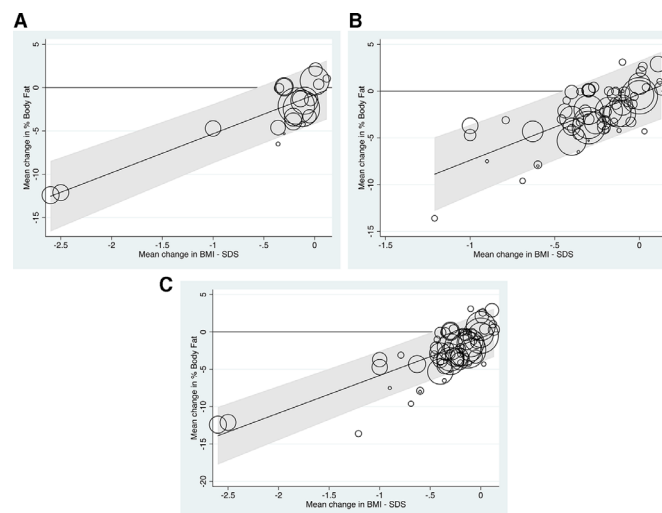


Figure 5 Sensitivity analysis. BMI-SDS, body mass index-SD score. (A) Analyses based on the 22 subsets where the SEs of the mean changes in percentage Body Fat were known (Fitted meta-regression line: Mean change in % body fat = $4.502 \times \text{Mean change in BMI-SDS} - 0.810$). (B) Analysis using all data subsets but excluding two extreme values (reduction of mean BMI-SDS of more than 1.5), leaving 64 subsets (Fitted meta-regression line: Mean change in % body fat = $7.078 \times \text{Mean change in BMI-SDS} - 0.318$). (C) Analysis using all 66 data subsets but using a correlation coefficient of 0.50, rather than 0.81, to estimate the SE of the mean change in % Body Fat for the $66 - 22 = 44$ subsets where this was not available (Fitted regression line: Mean change in % body fat = $5.039 \times \text{Mean change in BMI-SDS} - 0.783$).

the included studies were considered to be of moderate to high quality according to the HTA quality assessment tool.³⁰ Despite there being a positive relationship between mean change in percentage body fat and mean change in BMI-SDS, our modelling suggested that, in order to be confident of effecting a mean loss in percentage body fat, any future study should aim to reduce the BMI-SDS by at least 0.6.

Strengths and limitations

We believe that this is the first paper to attempt to bring together all studies that have reported both a change in BMI-SDS and changes in a marker of adiposity in the paediatric population with obesity. The systematic methods employed to identify the included studies were stringent, but it is possible that some relevant studies might have been missed. In addition, there was some variation in the reporting of results where there were multiple publications of the same study; in these cases, the results from the most comprehensive paper have been used. An important limitation to address in the broader context going forward is whether BMI-SDS is the best way to represent changes in BMI at extremes of body weight. The US Center for Disease Control cautioned the use of BMI-SDS in weight extremes in 2009.⁴⁰ Freedman *et al* have suggested that there are better measures of adiposity in severe obesity, such as percentage of 95th percentile BMI ($\% \text{BMI}^{95}$) or distance in kg/m^2 from the 95th

percentile (ΔBMI^{p95}).⁴¹ Other groups have identified alternate methods when dealing with extremes of obesity such as BMI%⁴² or percentage above IOTF-25.⁴³ Vanderwell *et al* have also suggested that BMI-SDS is only a weak to moderate predictor of percentage body fat in children, especially under 9 years of age.⁴⁴ Notwithstanding these cautions, we based this analysis on the data available to us which was almost entirely reported in terms of BMI-SDS and continues to be the case in most recent publications to date.

It has been suggested that the relationship between change in percentage body fat and change in BMI-SDS may differ between very young and older children.⁴⁵ Our inclusion criteria stipulated ages from 4 to 19 years. Most of the studies spanned a wide range of ages (table 1) and we did not have access to individual child data to facilitate stratification by age. Data from four subsets of children up to 10 years,^{37 46 47} however, did not suggest a different relationship from the whole cohort (see online supplementary appendix 3).

Agreements and disagreements with other research

Previous research has shown that an improvement in body composition and cardiometabolic risk can be achieved with a BMI-SDS reduction of ≥ 0.25 in adolescents with obesity, with greater benefits achieved when losing at least 0.5 BMI-SDS.⁴⁸

In clinical practice, the degree of weight loss with lifestyle intervention is moderate and the success rate 2 years after onset of an intervention is low ($<20\%$ with a decrease in BMI-SDS <0.25).⁴⁹ There have been numerous reports of lifestyle-based weight management interventions for children with obesity, many documenting changes in BMI-SDS, but a recent meta-analysis has documented that while such changes may be statistically significant, they are unlikely to lead to clinical improvements in metabolic health.^{50 51} To our knowledge, this is the first paper to establish the minimum change in BMI-SDS required to be certain of improving adiposity as percentage body fat for children and adolescents with obesity in clinical trials.

Clinical implications

If reducing fat mass is the aim of weight management interventions, our analysis in this review demonstrates that BMI-SDS changes must be of an order seldom achieved in trials worldwide. From our model, to be confident about ensuring an improvement in mean body fat, one should aim to reduce mean BMI-SDS by at least 0.6. Figure 3 and sensitivity analysis 5B (figure 5) suggest that to reduce body fat by 5% requires a much larger BMI-SDS reduction, of the order of 1.3–1.5, although there was a paucity of data in this region.

Recommendations for future research

While we are undertaking further analyses looking at key cardiovascular and metabolic outcomes in childhood obesity that may demonstrate improvements at lesser levels of BMI-SDS reduction, the evidence suggests that

very few childhood weight management trials to date are likely to have improved percentage body fat and calls in to question their overall efficacy in terms of health improvement. That said, any trial demonstrating an improvement of the magnitude of 0.6 BMI-SDS might be termed successful with a likely reduction in fat mass. However, given the mounting evidence that BMI-SDS may not accurately reflect adiposity at extremes of obesity, it seems prudent for future trials to report additional indices of derived BMI values which may better reflect changes in actual adiposity. Which of the many measures suggested eventually establishes itself as the 'optimal' determinant at extremes of body mass is yet to be determined?

CONCLUSIONS

Using our model, to predict any fat mass improvement when reporting a weight management trial outcome requires a BMI-SDS decrease of 0.6. When evaluating key outcomes for future weight management trials and services, this figure needs to be borne in mind by researchers, healthcare professionals and commissioners when assessing apparent success.

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