

Effects of lifestyle interventions on mental health in children and adolescents with overweight or obesity: a systematic review and meta-analysis



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Summary

Background Childhood obesity and mental health disorders are increasingly prevalent. While lifestyle interventions are widely recognized as effective for managing obesity in children and adolescents, their effects on mental health remain unclear. This study aimed to systematically evaluate the effects of lifestyle interventions on mental health outcomes among children and adolescents with overweight or obesity.

Methods In this systematic review and meta-analysis, we searched five databases (PubMed, Embase, MEDLINE, CENTRAL and CINAHL) for relevant randomised controlled trials (RCTs) or non-randomised studies of interventions (NRSIs) published from database inception to December 7, 2024, without language restrictions. Lifestyle interventions are defined as structured programs that promote health-related behavioural changes across diverse domains, such as physical activity, dietary adjustments, cognitive training, and psychosocial support. We included studies that assessed the effects of lifestyle interventions on mental health outcomes among children and adolescents with overweight or obesity. Two reviewers independently screened records for eligibility, extracted study-level data and assessed risk of bias of RCTs and NRSIs via the revised Cochrane Risk of Bias Tool for randomised controlled trials (RoB 2) and the Risk of Bias in Non-randomised Studies-of Interventions (ROBINS-I), and certainty of the evidence by the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. RCTs were prioritized as the primary source of evidence, while NRSIs served as supplementary evidence. A random-effects meta-analysis model was performed to calculate pooled standardized mean differences (SMDs) and 95% confidence intervals (CIs). Subgroup analyses stratified by age, body mass index (BMI) category, intervention type, theoretical framework, duration, and World Bank income region, were further conducted to identify potential sources of heterogeneity. The review protocol was registered in PROSPERO, CRD42024571061.

Findings We identified 20,359 records, of which 26 studies (17 RCTs and nine NRSIs) involving 3511 children and adolescents with overweight or obesity were included. Mental health outcomes assessed included depression, anxiety, self-concept, self-efficacy, negative affect, quality of life, and emotional functioning. Lifestyle interventions evaluated encompassed physical activity, health education, emotion regulation, diet, and multicomponent approaches. Among RCTs, reductions in depression (SMD = -0.24, 95% CI: -0.39 to -0.10, *I-square* [I^2] = 0.0%) and improvements in quality of life (SMD = 0.24, 95% CI: 0.04–0.44, I^2 = 44.0%) were observed, with moderate certainty. Subgroup analyses revealed greater reductions in depression among adolescents and participants with obesity, in programs that involving multicomponent approaches, lasting below three months, using behavioural and cognitive theory, or being conducted in high-income countries (HICs). For quality of life, greater improvements were observed among participants with overweight or obesity, in programs based on behavioural and cognitive theory, or in those conducted in low- and middle-income countries (LMICs). Meanwhile, among NRSIs, reductions in depression (SMD = -0.22, 95% CI: -0.33 to -0.11, I^2 = 11.5%), as well as enhancements in self-concept (SMD = 0.19, 95% CI: 0.09–0.29, I^2 = 0.0%), quality of life (SMD = 0.52, 95% CI: 0.23–0.81, I^2 = 86.2%), and emotional functioning (SMD = 0.40, 95% CI: 0.21–0.60, I^2 = 0.0%) were noted. However, the effects on other mental health outcomes, including anxiety, negative affect, and self-efficacy, remain inconclusive.

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Interpretation Lifestyle interventions modestly improve depressive symptoms and quality of life in children and adolescents with overweight or obesity, with additional benefits for self-concept and emotional functioning observed in NRSIs. These findings underscore the potential of lifestyle interventions to address both physical and mental health. Future research should focus on evaluating long-term psychological outcomes and developing cost-effective, culturally tailored interventions.

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Keywords: Mental health; Lifestyle intervention; Obesity; Children; Adolescents

Research in context

Evidence before this study

We searched PubMed, Embase, and MEDLINE for studies evaluating the effects of lifestyle interventions on mental health outcomes in children and adolescents with overweight or obesity, covering publications from database inception to December 7, 2024, using a search strategy that included terms related to lifestyle interventions, overweight or obesity, children and adolescents, and mental health. Many randomised trials have examined the effects of various lifestyle interventions on mental health outcomes in this population, but only a few systematic reviews have synthesised these findings, typically focusing on specific interventions, like physical activity, or isolated outcomes, such as depression or anxiety. To date, no systematic review has comprehensively examined the effects of a broad range of lifestyle interventions on diverse mental health outcomes in children and adolescents with overweight or obesity.

Added value of this study

To the best of our knowledge, this study is the first systematic review and meta-analysis to comprehensively evaluate the impact of lifestyle interventions on mental health outcomes

among children and adolescents with overweight or obesity. Our findings demonstrated that lifestyle interventions can bring out temporary improvements in several mental health outcomes, including depression, self-concept, quality of life, and emotional functioning, among children and adolescents with overweight or obesity. These findings underscore the potential for lifestyle interventions to address both the physical and psychological challenges associated with childhood obesity, which offers a holistic solution to this growing public health concern.

Implications of all the available evidence

As obesity interventions are increasingly developed and implemented worldwide, it is essential for policymakers, healthcare providers, and public health practitioners to identify the most effective components and consider the dual benefits of these programs. Our findings provide important implications for global health strategies, offering a solid evidence foundation for promoting lifestyle interventions as part of integrated approaches to address both the physical and psychological needs of this vulnerable population.

Introduction

Overweight and obesity, characterized by an excessive accumulation of body fat, have emerged as considerable global health concerns, particularly among children and adolescents.¹ Recent estimates from the World Health Organization (WHO) indicate that over 340 million children and adolescents with overweight or obesity were identified in 2022.² This alarming trend is observed across diverse geographical and socioeconomic contexts, with significant implications for both individual health and public health systems.³ The health consequences of childhood obesity are extensive, including an increased risk of chronic diseases such as diabetes, cardiovascular diseases, and metabolic disorders.² Furthermore, these health challenges can lead to long-term economic burdens on healthcare systems and decreased quality of life for affected individuals.⁴

Childhood represents a critical period for physiological, psychological, and social development, and in addition to the physical risks associated with obesity, mental health disorders among children and adolescents have emerged as a global crisis.⁵ According to the WHO, one in seven individuals aged 10–19 years is affected by a mental health disorder, underscoring the urgent need to prioritize mental health in public health agendas.⁶ The impact of poor mental health extends beyond individual well-being, placing substantial pressure on healthcare systems, educational institutions, and broader societal structures.⁵ Moreover, rising social and environmental stressors have exacerbated inequalities and driven a rise in mental health challenges among young people.⁵ Given that mental illnesses are conceptualised as chronic disorders of young people, addressing these issues during early developmental stages has emerged as a global health priority.⁷

The relationship between physical and mental health in children is well-documented,^{8–11} revealing a complex interplay that warrants further exploration. Studies have demonstrated that children with obesity face a heightened risk of mental health challenges, including anxiety and depression, conduct problems (e.g., aggression, rule-breaking, lying, and defiance), and difficulties in peer relationships and emotional regulation.^{8–11} Simultaneously, children experiencing mental health issues are more likely to experience obesity.¹² Given this bidirectional relationship and the shared aetiology, interventions targeting obesity may also have significant implications for mental health. Lifestyle interventions have been shown to improve weight management and cardiometabolic health in children with obesity.^{13–16} However, an important question arises: can these widely implemented lifestyle interventions also confer additional mental health benefits beyond physical health? While previous systematic reviews have primarily focused on specific interventions or limited mental health outcomes, a comprehensive analysis encompassing diverse outcomes across various lifestyle interventions is lacking.^{17,18} Given the widespread development and implementation of these interventions for children and adolescents with overweight or obesity across different settings and countries, a holistic evaluation of their potential mental health benefits is urgently needed.^{19,20}

To the best of our knowledge, this study provides the first comprehensive evaluation of the impacts of lifestyle interventions on mental health outcomes among children and adolescents with overweight or obesity. By analysing existing literature, we seek to elucidate the extent to which these interventions can improve not only physical health but also emotional and psychological well-being. Our findings will have the potential to provide valuable insights for global health initiatives, informing policymakers and healthcare practitioners about the dual benefits of lifestyle interventions. Ultimately, this research aims to support the development of integrated strategies that address both physical and mental health in children, promoting comprehensive approaches to childhood obesity that can enhance overall well-being and foster healthier future generations.

Methods

Search strategy

This systematic review and meta-analysis was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines²¹ and the Cochrane Handbook of Systematic Reviews of Interventions for systematic reviews.²² This review protocol was registered with the PROSPERO international database (protocol number: CRD 42024571061).

We conducted a comprehensive search of five major English electronic bibliographic databases, namely

PubMed, Embase, MEDLINE, CENTRAL and CINAHL, from inception to December 7, 2024. This search aimed to identify all eligible studies investigating the effects of lifestyle interventions on mental health outcomes in children and adolescents with overweight or obesity. Our search strategy combined medical subject headings and free-text terms related to *lifestyle interventions* (e.g., *exercise, diet, health education*), *overweight or obesity, children and adolescents, and mental health* (e.g., *depression, anxiety, bipolar disorder*). No restrictions on language were applied during the searches. Detailed search strategies for each database are provided in the [Appendix](#) pp 3–5. Additionally, we manually scanned the reference lists of eligible publications and relevant reviews to supplement the electronic database searches.

Selection criteria

All titles and abstracts were independently screened by two investigators (YS and CZ). Following the removal of duplicate records and irrelevant titles and abstracts, full-text articles were obtained and further assessed by the same two investigators for final inclusion. The limited abstract thinking, shorter attention spans, and reliance on concrete experiences characteristics of preschool children make self-reported mental health assessments challenging. Consequently, studies included in this review focused on children and adolescents aged 7–19 years with overweight or obesity. Studies were eligible if: (1) the intervention group received at least one type of lifestyle intervention; (2) the outcomes measured were changes in mental health from baseline to the end of the lifestyle intervention programs; (3) the designs were randomised controlled trials (RCTs) or quasi-experimental/non-randomised studies of interventions (NRSIs); and (4) the full texts were available in English or Chinese. Studies were excluded if: (1) they were observational (e.g., cross-sectional, case-control, and cohort); or (2) they involved children with other conditions, such as diabetes, coronary artery disease, or pre-existing diagnosed mental health disorders; or (3) they focused on other types of interventions; or (4) they had inconsistent or insufficient data.

Data extraction

Data extraction was independently conducted by two investigators (YS and CZ), with a secondary review for completeness and accuracy by two additional investigators (JZ and LZ). The extracted information encompassed: (1) study characteristics: title, first author's name, publication year, country, and setting; (2) population characteristics: sample size, proportion of girls, age, and body mass index (BMI) category; (3) intervention features: type, program duration, frequency, and session time; and (4) the means and standard deviations (SDs) of pre- and post-intervention mental health outcomes for both the intervention group and control group.

Any disagreements during the review and data extraction stages were resolved through discussion among the investigators until consensus was achieved.

Outcomes

RCTs were prioritized as the primary source of evidence, given their higher methodological rigor and predominance in the dataset. NRSIs were included as supplementary evidence to complement the findings from RCTs. To increase the statistical power of the NRSIs analysis, intervention arms from RCTs were incorporated into the NRSIs dataset.

Included studies are required to have measures of one or more of the following outcomes: depression, anxiety, self-esteem, self-worth, self-concept, self-efficacy, negative affect, quality of life, and emotional functioning. These outcomes were pre-defined based on their relevance and frequent use in prior literature. We combined the closely related components of self-esteem, self-worth, and self-concept into a single construct, namely self-concept, given their interrelated nature and the limited number of individual outcomes. Finally, seven mental health outcomes were included in our studies.

Statistics

The methodological quality of all included RCTs and NRSIs was independently assessed by two investigators (YS and CZ), using the revised Cochrane Risk of Bias Tool for randomised controlled trials (RoB 2) and the Risk of Bias in Non-randomised Studies-of Interventions (ROBINS-I), respectively. The RoB 2 tool was used to assess the risk of bias across five domains: (1) bias arising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result.²³ The tool assessed the risk of bias in each domain and the overall quality could be evaluated as low risk, some concerns, and high risk. In addition, the ROBINS-I tool included two extra domains, namely bias due to confounding and bias in classification of interventions, which yields an overall risk rating of low risk, moderate risk, serious risk, or critical risk. Furthermore, two investigators (JZ and LZ) independently evaluated the certainty of evidence for each outcome using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach in following domains: study limitations (risk of bias), inconsistency, indirectness, imprecision, publication bias, with the quality of evidence classified as very low, low, moderate, or high.^{22,24} Detailed quality assessment scales are presented in the [Appendix](#) pp 6–8.

Among various mental health outcomes, the continuous indicators were employed and were assessed in different scales, therefore the standardized mean difference (SMD) was appropriate to be a measure of

pooled effect size for each outcome. Three of these outcomes—depression, anxiety, and negative affect—were negatively scaled, where higher scores denoted greater severity. Accordingly, a negative SMD reflected the desired impact of the lifestyle intervention. In contrast, self-concept, self-efficacy, quality of life, and emotional functioning were all positively scaled, with higher scores indicating improvements. Therefore, a positive SMD represented a favourable intervention effect.

In the context of RCTs, the SMDs were computed by dividing the difference in mean change from baseline to post-intervention in either the intervention group or control group by the pooled SD. This calculation is performed as follows:

$$d = \frac{(\text{mean}_{\text{intervention group}} - \text{mean}_{\text{control group}})}{SD_{\text{pooled}}}$$

For NRSIs, we used the mean and SD of post-intervention data as outcomes for the intervention group, and pre-intervention values for the control group, according to the expression:

$$d = \frac{(\text{mean}_{\text{post-intervention}} - \text{mean}_{\text{pre-intervention}})}{SD}$$

Heterogeneity among the effect sizes in the included studies was assessed using *I*-squared (*I*²) statistic, with values of 50% or higher indicating significant heterogeneity.²⁵ To address variability in participant characteristics, intervention types, and instruments used to measure mental health outcomes, the random-effects model (DerSimonian and Laird) was applied to obtain more conservative estimates.²⁶ The quantitative synthesis of specific mental health outcomes was visualized using separate forest plots for RCTs and NRSIs, which illustrates the effects of lifestyle interventions on these outcomes within the target population clearly.

Subgroup analyses, stratified by age group (children or adolescents), BMI category (overweight or obesity), intervention type (e.g., physical activity, emotion regulation, health education), intervention theory (e.g., behavioural, cognitive, behavioural and cognitive), intervention duration, and World Bank income levels (high-income countries [HICs], or low- and middle-income countries [LMICs]) were further conducted to identify potential sources of heterogeneity.

Sensitivity analyses were performed using a leave-one-out approach, identifying a study as influential if its exclusion caused the pooled estimate to fall outside the 95% confidence intervals (CIs) of the overall pooled estimate.²⁶ To assess the potential presence of publication bias, we constructed funnel plots for all outcomes. Formal statistical tests for publication bias, such as Egger's and Begg's tests, were performed for outcomes with ten or more studies.

All analyses were performed using the “metafor” package in R, version 4.3.3. A two-sided probability value (P) < 0.05 was indicative of statistical significance.

Ethics

Ethics approval is not required for systematic review and meta-analysis.

Role of the funding source

This study was supported by National Natural Science Foundation of China (72474196). The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Search selection and study characteristics

As outlined in Fig. 1, a total of 20,359 records were retrieved from the database searching, and 35 from searching reference lists of other relevant systematic reviews. After removing duplicates, 11,814 records were identified through database searching, along with 14 additional records from reference lists. Following the exclusion of the 11,729 irrelevant records based on title and abstract review, 99 records were selected for full-text assessment. Finally, a total of 26 studies (17 RCTs and nine NRSIs) were included (Table 1, Appendix pp 9–11, 48–49).

The study characteristics of the included 26 studies are presented in Table 1 and Appendix pp 9–11. In total, they covered 3511 children and adolescents with overweight or obesity, with 1913 in the intervention groups and 1598 in the control groups. More than half of the

studies were published after 2010 ($N = 20$). Among the included studies, three (two RCTs and one NRSI) included only boys, two RCTs included only girls, and the remaining 21 studies had a percentage of girls ranging from 38.7% to 67.0%. The number of children in each study ranged from 8 to 948 with mean age ranged from 8.1 years ($SD = 1.2$) to 16.13 years ($SD = 0.74$). Most studies were originally from HICs ($N = 20$) (Appendix p 12). Studies were implemented in a diverse range of settings including school ($N = 12$), community ($N = 4$), laboratory ($N = 2$), hospital ($N = 4$), clinic ($N = 5$), healthcare centres ($N = 1$), lifestyle camps ($N = 1$), and family settings ($N = 1$). Lifestyle interventions ranging in duration from one week to 24 months were mainly classified into four categories: physical activity, health education, emotion regulation, diet, and multicomponent approaches. Overall, mental health outcomes assessed covered depression ($N = 12$), anxiety ($N = 6$), self-concept ($N = 13$), self-efficacy ($N = 3$), negative affect ($N = 2$), quality of life ($N = 8$) and emotional functioning ($N = 3$). Since five RCTs were consisted of two intervention groups and one RCT was consisted of three intervention groups, a total of 33 NRSI groups were obtained. The questionnaires used to assess these mental health outcomes, along with details on their internal consistency, are provided in the Appendix p 47, while raw data from RCTs and NRSIs are available in the Appendix pp 13–17.

Effects of lifestyle intervention on mental health outcomes

The detailed results of the overall and subgroup analyses for effects of lifestyle intervention on each mental health outcome, as well as their certainty of evidence are shown in Fig. 2, Table 2, and in the Appendix pp 18–35, 40.

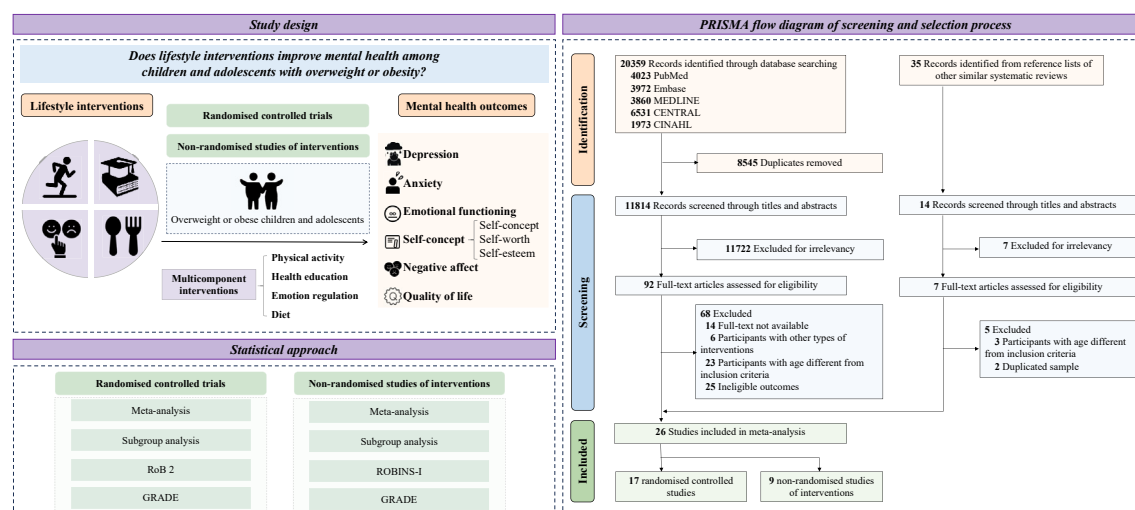


Fig. 1: PRISMA flow diagram of screening and selection process. Note: RoB 2, the revised Cochrane Risk of Bias Tool for randomised controlled trials; ROBINS-I, the Risk of Bias in Non-randomised Studies-of Interventions; GRADE, the Grading of Recommendations, Assessment, Development and Evaluations.

Source	Design	Setting	Sample size	Percentage of girls, %	Age (SD)	BMI category	Intervention strategy	Mental health outcome
DeBar et al., 2011 (America)	RCT	Hospital	195 (IG = 100, CG = 95)	100.0	14.1 (1.4)	Overweight	5 months of multicomponent interventions: (1) change in dietary intake and eating patterns; (2) increasing physical activity; (3) addressing issues associated with obesity; and (4) training participants' primary care providers to support behavioural weight management goals collaboratively	Self-concept; quality of life
Nguyen et al., 2012 (Australia)	RCT	School, hospital, and community	151 (IG = 78, CG = 73)	51.7	14.1 (0.9)	Overweight or obesity	24 months of multicomponent interventions: in the first 2 months, received lifestyle modification; from 2 to 24 months, attended booster sessions	Self-concept
Ding et al., 2021 (China)	NRSI	School	26	61.0	10.15 (0.82)	Obesity	2 months of physical activity interventions: (1) flexibility exercises; (2) aerobic movements; (3) resistance exercises; (4) relaxation.	Depression; self-concept; negative affect; quality of life; emotional functioning
Latino et al., 2021 (Italy)	RCT	School	60 (IG = 30, CG = 30)	100.0	16.13 (0.74)	Overweight	3 months of moderate to vigorous aerobic exercises	Self-efficacy
Romero-Pérez et al., 2020 (Mexico)	RCT	School	105 (IG = 54, CG = 51)	57.1	10.02 (0.79)	Obesity	5 months of physical activity interventions	Depression; anxiety
Fidelix et al., 2019 (Brazil)	RCT	Laboratory	28 (IG = 14, CG = 14)	0.0	15 (1.5)	Obesity	6 months of physical activity interventions	Depression; anxiety; self-concept
Williams et al., 2019 (America)	RCT	Laboratory	175 (IG = 90, CG = 85)	61.1	9.7 (0.9)	Overweight	8 months of aerobic exercise interventions	Depression; self-concept
Fenner et al., 2016 (Australia)	NRSI	School, hospital, and community	56	NA	13.9 (1.5)	Obesity	2 months of physical activity interventions	Depression; anxiety; quality of life
Schranz et al., 2013 (Australia)	RCT	School and community	56 (IG = 30, CG = 26)	0.0	IG:14.9 (1.4); CG:15.1 (1.6)	Overweight or obesity	6 months of physical activity interventions	Self-concept; self-efficacy
Staiano et al., 2013 (America)	RCT	School	54 (IG = 38, CG = 16)	55.6	15–19	Overweight or obesity	5 months of physical activity interventions	Self-concept; self-efficacy
Poeta et al., 2013 (Brazil)	NRSI	School	32	50.0	9.5	Obesity	4 months of multicomponent lifestyle programs: physical exercises with recreational activities, and nutritional counselling to children and parents	Quality of life; emotional functioning
Lofrano-Prado et al., 2012 (Brazil)	NRSI	Clinic	8	0.0	15.44 (2.06)	Obesity	1 week of physical activity interventions	Depression; anxiety
Wagener et al., 2012 (America)	RCT	Clinic	40 (IG = 20, CG = 20)	67.0	14 (1.66)	Obesity	2.5 months of dance-based exergame exercise	Depression; anxiety; self-concept
Goldfield et al., 2012 (Canada)	NRSI	Clinic	26	46.2	14.5 (1.6)	Overweight or obesity	2.5 months of physical activity interventions	Self-concept
Sacher et al., 2013 (England)	RCT	Community	116 (IG = 60, CG = 56)	56.6	IG: 10.3 (1.3); CG: 10.2 (1.3)	Obesity	6 months of multicomponent lifestyle programs: (1) education; (2) skills training; and (3) motivational enhancement	Self-concept
Shalitin et al., 2009 (Israel)	NRSI	Clinic	162	50.0	Exercise: 8.21 (1.78); Diet: 8.51 (1.52) Diet and exercise: 8.2 (1.56)	Obesity	3 months of interventions with a 9-month follow-up period: (1) exercise; (2) diet, and (3) diet and exercise.	Emotional functioning
Petty et al., 2009 (America)	RCT	School	207 (IG = 139, CG = 68)	57.5	9.35 (1.05)	Overweight	4 months of physical activity interventions: (1) high dose aerobic exercise; (2) low dose aerobic exercise	Depression; self-concept
Daley et al., 2006 (England)	RCT	Unclear	81 (IG = 28, CG = 53)	55.6	13.1	Obesity	2 months of physical activity interventions	Depression; negative affect

(Table 1 continues on next page)

Source	Design	Setting	Sample size	Percentage of girls, %	Age (SD)	BMI category	Intervention strategy	Mental health outcome
(Continued from previous page)								
Moon et al., 2004 (Korea)	RCT	School	62 (IG = 34, CG = 28)	38.7	10–12	Obesity	2 months of health education interventions	Depression
Dreimane et al., 2007 (America)	NRSI	Family	264	51.9	11.5 (2.1)	Overweight	3 months of multicomponent lifestyle programs: the program comprised interactive nutrition and exercise sessions with behaviour modification.	Self-concept
Fullerton et al., 2007 (America)	RCT	School	80 (IG = 40, CG = 40)	NA	12.1	Overweight	6 months of multicomponent lifestyle programs: received 1 nutrition class and 4 physical activity classes weekly for 12 weeks with English-speaking interventionists; learned behavioural strategies to increase healthy behaviours	Quality of life
Diao et al., 2020 (China)	RCT	School	948 (IG = 518, CG = 430)	49.5	11.39 (1.81)	Overweight or obesity	12 months of multicomponent lifestyle programs: health education, diet, and physical activity.	Quality of life
Sepulveda et al., 2024 (Spain)	RCT	Healthcare centres	113 (IG = 62, CG = 51)	42	10.3 (1.4)	Obesity	3 months of multi-component, family system-based interventions, addressing lifestyle changes, children's emotional and social development and the family system	Depression; anxiety; self-concept
Kleppang et al., 2024 (Norway)	NRSI	Clinic	166 (IG = 89, CG = 77)	60	IG: 8.5 (2.1); CG: 8.1 (1.2)	Overweight or obesity	6 months of family-based multicomponent lifestyle interventions: Individual family counselling. Participation in physical activity groups and nutrition courses. A combination of theoretical and practical learning sessions to improve dietary habits.	Quality of life
Jakobsen et al., 2024 (Denmark)	NRSI	Lifestyle camps	185	58	12.3 (1.3)	Overweight or obesity	2.5 months of multicomponent lifestyle camps: six meals daily, physical activity daily, and attend school at camp daily	Quality of life
Debeuf et al., 2024 (Belgium)	RCT	Hospital	115 (IG = 65, CG = 50)	52	12.6 (1.64)	Obesity	3 months of emotion regulation training interventions	Depression
RCT, randomised controlled trial; NRSI, non-randomised studies of interventions; SD, standard deviation; BMI, body mass index; IG, intervention group; CG, control group; NA, not available. N indicated the number of the included studies.								
Table 1: A summary of the studies that met the criteria of the systematic review on lifestyle interventions in children and adolescent with overweight or obesity (N = 26).								

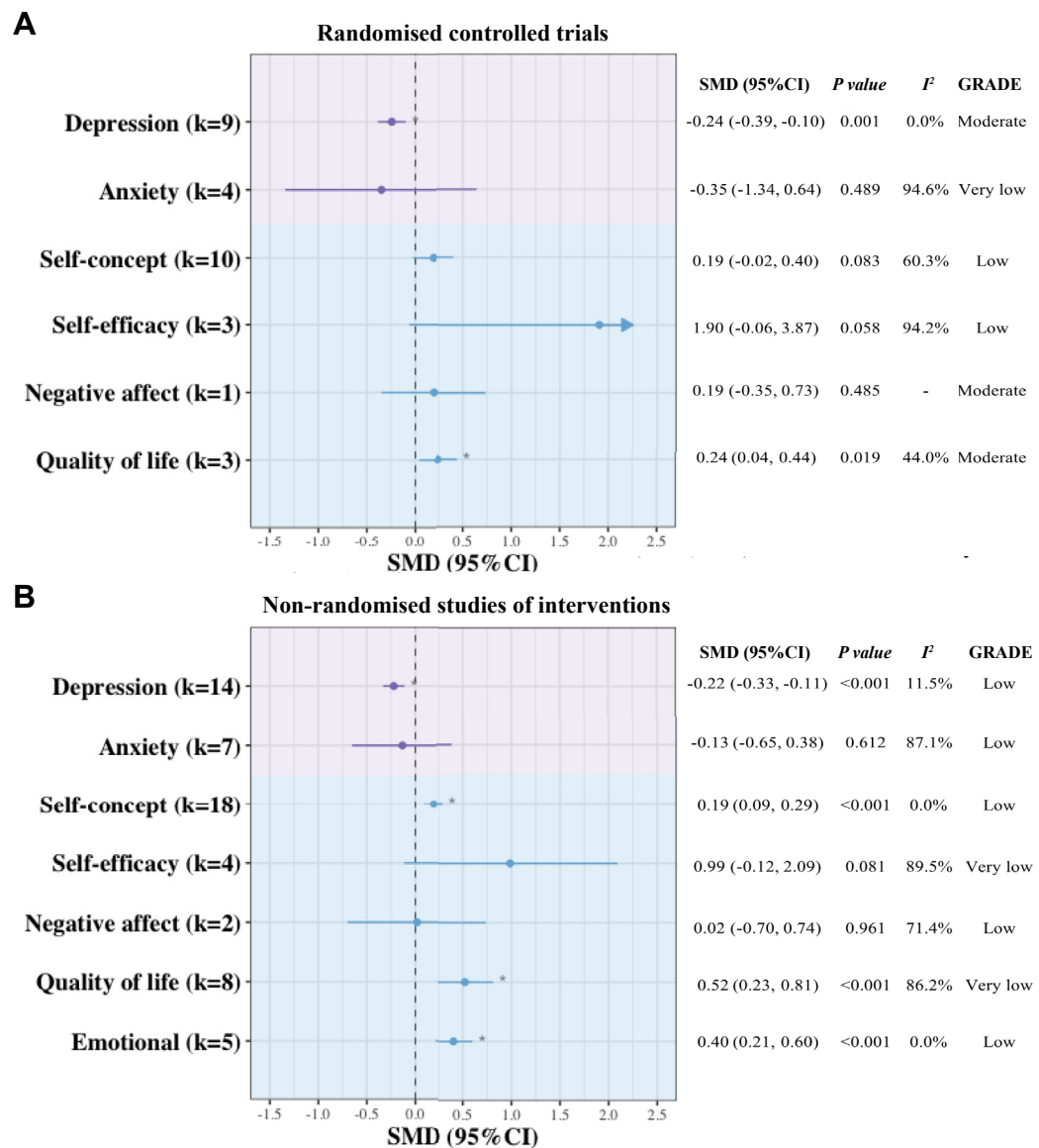


Fig. 2: Forest plot of the SMD for all specific mental health outcomes, grouped by RCTs (N = 17) and NRSIs (N = 26). **Note:** Panel A. Summary of the SMD on each mental health outcome from RCTs (N = 17); **Panel B.** Summary of the SMD on each mental health outcome from NRSIs (N = 26). RCT, randomised controlled trial; NRSI, non-randomised studies of interventions; SMD, standardized mean difference; CI, confidence interval; I², I-square; P-value, probability value. SMDs are represented by points, with error bars indicating the corresponding 95% CIs. N indicated the number of the included studies while k indicated the number of intervention groups incorporated into the meta-analysis.

Depression

Based on nine RCTs comprising 898 participants, life-style interventions resulted in a significant reduction in depression (SMD = -0.24, 95% CI: -0.39 to -0.10), with no significant heterogeneity (I² = 0.0%, P = 0.512). The certainty of this evidence was rated as moderate. Sub-group analyses revealed greater reductions in depression among adolescents (SMD = -0.37, 95% CI: -0.73 to -0.01) and participants with obesity (SMD = -0.29,

95% CI: -0.46 to -0.11). Notably, more significant improvements were observed in programs that involving multicomponent approaches (SMD = -0.54, 95% CI: -0.91 to -0.16), using behavioural and cognitive theory (SMD = -0.54, 95% CI: -0.91 to -0.16), lasting below three months (SMD = -0.32, 95% CI: -0.52 to -0.12), or being conducted in HICs (SMD = -0.25, 95% CI: -0.42 to -0.09). Similarly, evidence from NRSIs showed comparable reductions in depression

Mental health outcomes	k	SMD (95%CI)	I ²	P-value of Q test	Subgroup Difference
Depression					
Intervention type					
Health education interventions	1	-0.26 (-0.77, 0.24)	/	/	0.429
Physical activity interventions	6	-0.20 (-0.38, -0.03)	0.0%	0.494	
Emotion regulation interventions	1	-0.15 (-0.52, 0.22)	/	/	
Multicomponent lifestyle programs	1	-0.54 (-0.91, -0.16)	/	/	
Intervention duration					
Below three months	5	-0.32 (-0.52, -0.12)	0.0%	0.611	0.339
Greater than or equal to three months	4	-0.18 (-0.39, 0.02)	12.7%	0.329	
BMI category					
Overweight	2	-0.17 (-0.50, 0.16)	59.7%	0.115	0.523
Obesity	7	-0.29 (-0.46, -0.11)	0.0%	0.675	
Age group					
Children	6	-0.22 (-0.39, -0.06)	15.0%	0.318	0.461
Adolescents	3	-0.37 (-0.73, -0.01)	0.0%	0.682	
Theory					
Behavioural	8	-0.20 (-0.34, -0.05)	0.0%	0.717	0.100
Behavioural and cognitive	1	-0.54 (-0.91, -0.16)	/	/	
World Bank income region					
HICs	7	-0.25 (-0.42, -0.09)	3.5%	0.399	0.771
LMICs	2	-0.20 (-0.54, 0.15)	0.0%	0.332	
Anxiety					
Intervention type					
Physical activity interventions	3	0.21 (-0.09, 0.51)	0.0%	0.513	<0.01
Multicomponent lifestyle programs	1	-1.78 (-2.22, -1.34)	/	/	
Intervention duration					
Below three months	2	-0.74 (-2.80, 1.33)	96.6%	<0.01	0.403
Greater than or equal to three months	2	0.16 (-0.23, 0.55)	14.1%	0.281	
BMI category					
Obesity	4	-0.35 (-1.34, 0.64)	94.6%	<0.01	/
Age group					
Children	2	-0.75 (-2.76, 1.26)	97.9%	<0.01	0.416
Adolescents	2	0.11 (-0.38, 0.61)	6.7%	0.301	
Theory					
Behavioural	3	0.21 (-0.09, 0.51)	0.0%	0.513	<0.01
Behavioural and cognitive	1	-1.78 (-2.22, -1.34)	/	/	
World Bank income region					
HICs	2	-0.74 (-2.80, 1.33)	96.6%	<0.01	0.403
LMICs	2	0.16 (-0.23, 0.55)	14.1%	0.281	
Self-concept					
Intervention type					
Physical activity interventions	6	0.29 (0.03, 0.55)	46.3%	0.097	0.356
Multicomponent lifestyle programs	4	0.09 (-0.25, 0.42)	68.7%	0.022	
Intervention duration					
Below three months	2	-0.08 (-0.40, 0.24)	0.0%	0.587	0.104
Greater than or equal to three months	8	0.26 (0.01, 0.50)	63.5%	<0.01	
BMI category					
Overweight	3	0.28 (0.07, 0.48)	32.0%	0.230	0.639
Overweight or obesity	3	0.28 (-0.38, 0.93)	81.3%	<0.01	
Obesity	4	0.06 (-0.33, 0.46)	56.4%	0.076	
Age group					
Children	4	0.30 (0.05, 0.55)	53.0%	0.095	0.313
Adolescents	6	0.09 (-0.24, 0.42)	60.5%	0.027	

(Table 2 continues on next page)

Mental health outcomes	k	SMD (95%CI)	I ²	P-value of Q test	Subgroup Difference
(Continued from previous page)					
Theory					
Behavioural	6	0.24 (0.02, 0.45)	47.2%	0.092	0.516
Cognitive	1	0.59 (−0.14, 1.33)	/	/	
Behavioural and cognitive	3	0.07 (−0.42, 0.57)	78.0%	0.011	
World Bank income region					
HICs	9	0.22 (0.00, 0.44)	62.1%	0.007	0.218
LMICs	1	−0.27 (−1.02, 0.47)	/	/	
Self-efficacy					
Intervention type					
Physical activity interventions	3	1.90 (−0.06, 3.87)	94.2%	<0.01	/
Intervention duration					
Below three months	1	3.93 (3.04, 4.81)	/	/	<0.01
Greater than or equal to three months	2	0.97 (0.43, 1.52)	27.4%	0.241	
BMI category					
Overweight	1	3.93 (3.04, 4.81)	/	/	<0.01
Overweight or obesity	2	0.97 (0.43, 1.52)	27.4%	0.241	
Age group					
Adolescents	3	1.90 (−0.06, 3.87)	94.2%	<0.01	/
Theory					
Behavioural	2	2.54 (−0.13, 5.21)	96.1%	<0.01	0.178
Cognitive	1	0.64 (−0.11, 1.39)	/	/	
World Bank region					
HICs	3	1.90 (−0.06, 3.87)	94.2%	<0.01	/
Quality of life					
Intervention type					
Multicomponent lifestyle programs	3	0.24 (0.04, 0.44)	44.0%	0.167	/
Intervention duration					
Greater than or equal to three months	3	0.24 (0.04, 0.44)	44.0%	0.167	/
BMI category					
Overweight	2	0.11 (−0.13, 0.34)	0.0%	0.860	0.060
Overweight or obesity	1	0.36 (0.23, 0.49)	/	/	
Age group					
Children	1	0.07 (−0.37, 0.51)	/	/	0.860
Adolescents	1	0.12 (−0.15, 0.39)	/	/	
Theory					
Behavioural	1	0.12 (−0.15, 0.39)	/	/	0.335
Behavioural and cognitive	2	0.29 (0.06, 0.53)	34.3%	0.217	
World Bank income region					
HICs	2	0.11 (−0.13, 0.34)	0.0%	0.860	0.060
LMICs	1	0.36 (0.23, 0.49)	/	/	
RCT, randomised controlled trial; SMD, standardized mean difference; CI, confidence interval; I ² , I-square; P-value, probability value; HICs, high-income countries; LMICs, low- and middle-income countries. N indicated the number of the included studies while k indicated the number of intervention groups incorporated into the meta-analysis.					
Table 2: Subgroup analyses of lifestyle interventions on mental health outcomes in children and adolescent with overweight or obesity from RCTs (N = 17).					

(SMD = −0.22, 95% CI: −0.33 to −0.11), with minimal heterogeneity ($I^2 = 11.5\%$, $P = 0.328$) but was rated as low certainty.

Anxiety

Among four RCTs with 286 participants, lifestyle interventions did not significantly reduce anxiety scores

(SMD = −0.35, 95% CI: −1.34 to 0.64), with significant heterogeneity ($I^2 = 94.6\%$, $P < 0.010$). Subgroup analyses revealed greater reductions in anxiety among programs employing multicomponent approaches and those grounded in behavioural and cognitive theories (SMD = −1.78, 95% CI: −2.22 to −1.34). The certainty of this evidence was rated as very low. Meanwhile, results

from NRSIs also exhibited no significant impact on anxiety symptoms (SMD = -0.13, 95% CI: -0.65 to 0.38), with significant heterogeneity ($I^2 = 87.1\%$, $P < 0.010$) and low-certainty evidence.

Self-concept

According to ten RCTs with 1052 participants, lifestyle interventions showed no significant effect on self-concept (SMD = 0.19, 95% CI: -0.02 to 0.40), with low-certainty evidence and significant heterogeneity ($I^2 = 60.3\%$, $P < 0.010$). Subgroup analyses, however, revealed greater improvements in self-concept among children (SMD = 0.30, 95% CI: 0.05–0.55), participants with overweight (SMD = 0.28, 95% CI: 0.07–0.48), and those engaged in physical activity interventions (SMD = 0.29, 95% CI: 0.03–0.55). Notably, interventions lasting longer than or equal to three months (SMD = 0.26, 95% CI: 0.01–0.50), based on behavioural theory (SMD = 0.24, 95% CI: 0.02–0.45), or conducted in HICs (SMD = 0.22, 95% CI: 0.00–0.44) were also associated with significant improvements. Similarly, findings from NRSIs demonstrated a modest but significant improvement in self-concept (SMD = 0.19, 95% CI: 0.09–0.29), with no significant heterogeneity ($I^2 = 0.0\%$, $P = 0.528$) but were also rated as low-certainty evidence.

Self-efficacy

Among three RCTs comprising 151 participants, low-certainty evidence indicated that lifestyle interventions did not significantly improve self-efficacy (SMD = 1.90, 95% CI: -0.06 to 3.87), with a substantial heterogeneity ($I^2 = 94.2\%$, $P < 0.010$). Subgroup analyses revealed greater improvements in self-efficacy among participants with overweight (SMD = 3.93, 95% CI: 3.04–4.81), or when the program was with the intervention duration below three months (SMD = 3.93, 95% CI: 3.04–4.81). Similarly, evidence from NRSI showed no significant effect of lifestyle interventions on self-efficacy (SMD = 0.99, 95% CI: -0.12 to 2.09), based on very low-certainty evidence and characterized by significant heterogeneity ($I^2 = 89.5\%$, $P < 0.010$).

Negative affect

Regarding the effects of lifestyle interventions on negative affect in children and adolescents with overweight or obesity, no significant impact was observed in either the RCT groups ($N = 1$, SMD = 0.19, 95% CI: -0.35 to 0.73; moderate-certainty evidence) or the NRSI groups ($N = 2$, SMD = 0.02, 95% CI: -0.70 to 0.74; low-certainty evidence).

Quality of life

Among three RCTs comprising 1236 participants, lifestyle interventions significantly improved quality of life (SMD = 0.24, 95% CI: 0.04–0.44), with moderate-certainty evidence and no significant heterogeneity

($I^2 = 44.0\%$, $P = 0.167$). Subgroup analyses revealed greater improvements in quality of life among participants with overweight or obesity (SMD = 0.36, 95% CI: 0.23–0.49), in program based on behavioural and cognitive theory (SMD = 0.29, 95% CI: 0.06–0.53), or in those conducted in LMICs (SMD = 0.36, 95% CI: 0.23–0.49). Similarly, NRSI results showed a significant enhancement in quality of life (SMD = 0.52, 95% CI: 0.23–0.81), based on very low-certainty evidence and significant heterogeneity ($I^2 = 86.2\%$, $P < 0.010$).

Emotional functioning

Due to data limitations, only five NRSI groups, involving 204 participants, assessed the overall effect of lifestyle interventions on emotional functioning. These interventions significantly improved emotional functioning, yielding a SMD of 0.40 (95% CI: 0.21–0.60). The evidence, although of low certainty, showed no significant heterogeneity ($I^2 = 0.0\%$, $P = 0.842$).

Risk of bias

In the assessment of the overall risk of bias of the 17 RCTs, three (17.6%) were judged to be at low risk of bias, and 12 studies (70.6%) had some concerns of bias. By domain, five included studies (29.4%) incurred bias due to the process of randomization; six studies (35.3%) had bias resulting from deviations from the intended intervention; three studies (17.6%) had bias in missing data; 12 studies (70.6%) had bias arising from the outcome measurement; and three (17.6%) generated bias in selection of reported result (Appendix pp 36–37). Regarding NRSIs, the detailed results of the assessment of risk of bias are presented in the Appendix pp 38–39.

Sensitive analysis and publication bias

Sensitivity analysis, conducted by systematically omitting one study at a time, demonstrated that no single study significantly influenced the pooled effect size (Appendix pp 43–46). Funnel plots for RCTs and NRSIs, used to visually depict publication bias, are presented in the Appendix pp 41–42.

Discussion

This systematic review and meta-analysis of 26 studies involving 3511 participants demonstrated that lifestyle interventions can bring out temporary improvements in several mental health outcomes among children and adolescents with overweight or obesity. Specifically, reductions in depressive symptoms and improvements in quality of life were observed in both RCTs and NRSIs. Additionally, enhancements in self-concept (including self-esteem and physical self-perception) and emotional functioning were noted in NRSIs. However, evidence for other mental health outcomes, such as anxiety, self-efficacy, and negative affect remains inconclusive. These findings emphasize the potential for lifestyle

interventions to address both the physical and psychological challenges associated with childhood obesity, offering a holistic solution to this growing public health issue.

While the physical health benefits of lifestyle interventions, such as weight reduction and metabolic improvements, are well-established, this study broadens the scope by systematically examining their mental health impacts.^{27,28} Our findings are consistent with prior research in adult populations. For example, a recent meta-analysis conducted in women of reproductive age with overweight or obesity found that lifestyle interventions significantly reduce depressive symptoms.²⁷ Similarly, a RCT in Chinese adults with metabolic syndrome showed that lifestyle changes effectively reduced body weight and depression.²⁸ By extending this evidence to children and adolescents, this study highlights the importance of early intervention during this critical developmental stage. Adolescents are particularly vulnerable to psychological challenges, such as body dissatisfaction and social stigma, which are often associated with obesity.²⁹ Addressing these issues early not only improves mental health during childhood but may also mitigate the risk of long-term psychological and physical health consequences. These findings align with global public health priorities, such as the United Nations Sustainable Development Goal 3, which emphasizes promoting healthy lifestyles and mental well-being for all ages.³⁰

Our findings regarding the reduction in depressive symptoms are particularly notable. Previous studies in adults have consistently shown that lifestyle interventions, particularly those involving physical activity, can reduce depressive symptoms.²⁷ A meta-analysis focusing on children and adolescents similarly has shown that exercise-only interventions can significantly reduce depressive symptoms.³¹ Our results confirm and extend these findings by demonstrating that lifestyle interventions are effective in reducing depressive symptoms specifically in children and adolescents with overweight or obesity. Additionally, we observed improvements in quality of life, a finding consistent with earlier studies indicating that interventions combining physical activity with nutrition education can enhance overall well-being.³² Notably, interventions involving parents were particularly effective in achieving sustained improvements in quality of life. This highlights the critical role of family-based approaches in promoting long-term behavioural changes and mental well-being in children.³²

Enhancements in self-concept, including self-esteem and physical self-perception, as well as improvements in emotional functioning, were noted exclusively in NRSIs. These findings are consistent with previous research demonstrating that higher levels of physical activity are associated with improved self-esteem and body image in children and adolescents.³³ Lifestyle interventions that

focus on physical activity and dietary habits appear to play a crucial role in addressing body dissatisfaction, a prevalent challenge among children with obesity, thereby promoting healthier self-perception and self-worth.³⁴ Such improvements are particularly significant, as body dissatisfaction and low self-esteem are key psychological challenges faced by this population. Moreover, addressing these issues can lead to broader benefits in emotional functioning, such as reducing emotional distress and enhancing overall well-being. These findings highlight the potential of lifestyle interventions to not only improve physical health but also support positive self-concept and emotional well-being, thereby addressing key psychological dimensions of childhood obesity.

The effects of lifestyle interventions on other mental health outcomes, such as anxiety, self-efficacy, and negative affect, were less conclusive in our study. While point estimates from both RCT and NRSI analytical scenarios suggested reductions in anxiety and improvements in self-efficacy and negative affect, these effects did not reach statistical significance. This is likely due to insufficient statistical power, driven by the small number of included studies and their relatively small sample sizes. Additionally, the heterogeneity across studies, stemming from variations in measurement tools, study designs, and intervention characteristics, may have further complicated the ability to detect robust effects. Despite the lack of statistical significance, the consistent directional trends observed across studies suggest that lifestyle interventions may hold promise for improving these dimensions of mental health. These findings underscore the need for larger, well-designed studies with standardized methodologies to better clarify the impact of lifestyle interventions on anxiety, self-efficacy, and negative affect, particularly in children with overweight or obesity.

The mechanisms underlying the mental health benefits of lifestyle interventions in children and adolescents with overweight or obesity are likely to be multifactorial and interrelated, involving both physiological and psychological processes. Physical activity, a core component of most lifestyle interventions, has been shown to enhance mood and emotional regulation through the release of neurochemicals such as endorphins, while also improving cognitive function and reducing systemic inflammation.^{29,35} Additionally, physical activity promotes neuroplasticity via increased levels of brain-derived neurotrophic factor, supporting both cognitive and emotional well-being.^{29,35} Psychologically, lifestyle interventions often improve body image and physical fitness, which can enhance self-esteem and self-worth, particularly in children and adolescents who may face body dissatisfaction and social stigma related to their weight.²⁹ The achievement of fitness or weight-related goals further fosters a sense of accomplishment, boosting self-confidence and overall mental

well-being.^{29,35} These psychological benefits are further reinforced by the social support and peer interaction often found in group-based interventions, which can reduce isolation and promote a sense of belonging.³⁶ Importantly, these mechanisms do not operate in isolation. Improvements in one dimension of mental health, such as self-esteem, can lead to positive changes in others, such as depression and quality of life, creating a reinforcing cycle of benefits across physical, psychological, and social dimensions.

To our knowledge, this study provides the most comprehensive and up-to-date evaluation of the mental health benefits of lifestyle interventions for children and adolescents with overweight or obesity. This review adhered to rigorous research standards, including a preregistered protocol, transparent reporting, and compliance with the PRISMA guidelines, ensuring the validity and reliability of our findings. A key strength of this study lies in its broad scope, encompassing diverse mental health outcomes such as depression, self-concept, and quality of life—domains that are often overlooked in obesity-related interventions. By including both RCTs and NRSIs, this study balances methodological rigor with real-world applicability. While RCTs, as the gold standard for intervention efficacy, formed the majority of included studies, NRSIs were incorporated to supplement areas where RCT data were limited, particularly to capture real-world complexities. Intervention arms from RCTs were also included in the NRSI analysis to strengthen statistical power, a common but cautious approach due to the potential for overestimating the NRSI evidence base.³⁷ Our study provides valuable insights into the mental health benefits of lifestyle interventions targeting children and adolescents with overweight or obesity, with significant implications for public health policy. While the physical benefits, such as weight reduction and metabolic improvements, are well established, our findings highlight the additional psychological benefits—particularly reductions in depressive symptoms, improvements in self-concept, and enhanced quality of life. These dual benefits make lifestyle interventions a holistic and valuable approach for addressing childhood obesity. As many countries and policymakers are already promoting lifestyle interventions, recognizing their psychological benefits could be pivotal in convincing policymakers and stakeholders to support, implement, and sustain these programs when their broader impact is considered.³⁸ Given that obesity and related psychological challenges often extend into adulthood, these findings have far-reaching implications for reducing long-term health and economic burdens on healthcare systems, further justifying the prioritization of lifestyle interventions in public health strategies.

A key limitation of this systematic review and meta-analysis is the various quality of the included studies. While RCTs are considered the gold standard for

evaluating intervention efficacy, many had high or unclear risks of bias, particularly in allocation concealment and blinding, which may have impacted the reliability of their findings. NRSIs, included to complement RCTs, were prone to biases like confounding and selection bias despite rigorous screening. The certainty of evidence, assessed using the GRADE framework, was frequently rated as moderate or low due to issues such as imprecision, inconsistency, and potential publication bias. For example, evidence for the effects of lifestyle interventions on depressive symptoms was of moderate certainty in RCTs but low certainty in NRSIs. Besides, the substantial heterogeneity in intervention characteristics, such as duration, intensity, and delivery methods, may have influenced the overall findings. As the duration of interventions in the included studies ranged from several weeks to two years, and follow-up assessments after the intervention were rarely conducted, further evidence is needed to substantiate the long-term effects of lifestyle interventions on mental health in this target population. Variability in the criteria used to define overweight and obesity, influenced by population characteristics, cultural norms, and health guidelines, may have further contributed to heterogeneity across studies. Another critical limitation was the geographic distribution of the studies; most were conducted in HICs, with limited representation from LMICs. While our findings are robust for HIC contexts, caution is needed when generalizing to LMICs, where healthcare systems, cultural contexts, and economic conditions differ substantially.³⁹ Finally, while no language restrictions were applied during the search, only studies with full texts available in English or Chinese were included in the final analysis due to the research team's linguistic capabilities. All of these highlight the need for additional high-quality, well-conducted studies, particularly in LMICs, to strengthen the evidence base and provide more definitive conclusions.

The global childhood obesity pandemic demands solutions that are effective, accessible, and scalable. From a public health perspective, lifestyle interventions, encompassing dietary modifications, physical activity, and behavioural strategies, are widely recognized as the cornerstone of obesity management due to their safety, affordability, and adaptability across diverse socioeconomic and cultural settings.⁴⁰ These attributes make lifestyle interventions particularly suitable for population-level implementation, especially in LMICs, where healthcare systems are often constrained by limited resources.³⁹ In contrast, pharmacological treatments and bariatric surgery, while highly effective for certain individuals, require substantial healthcare infrastructure, financial investment, and specialized expertise, limiting their feasibility for widespread implementation in many LMICs settings. Childhood is a critical period for establishing healthy behaviours that can yield lifelong benefits, including reduced healthcare

costs, improved quality of life, and mitigation of obesity-related comorbidities.^{13–16} However, research on lifestyle interventions has disproportionately focused on economically developed regions, leaving a significant gap in knowledge regarding their applicability in resource-limited settings. This underscores the urgent need to adapt and implement evidence-based interventions in LMICs, where the dual burden of obesity and mental health disorders is growing rapidly. Future studies should aim to unravel the mechanisms underlying the mental health benefits of lifestyle interventions, identify the most effective components of these programs, and tailor their design to address the unique challenges faced by LMICs.

In conclusion, this systematic review and meta-analysis demonstrates that lifestyle interventions can bring out temporary improvements in several mental health outcomes, such as depression, self-concept, quality of life and emotional well-being, among children and adolescents with overweight or obesity. However, their effects on outcomes such as anxiety, self-efficacy, and negative affect remain inconclusive, underscoring the need for further high-quality studies to clarify these effects. Future studies should also evaluate the long-term sustainability of the observed benefits and identify the most effective components. Additionally, considerations of cost-effectiveness and scalability are critical, particularly in resource-limited settings where the dual challenges of obesity and mental health disorders are increasingly prevalent. These findings have important implications for global health strategies, providing a strong foundation for policymakers and healthcare practitioners to promote lifestyle interventions as part of integrated approaches to tackling childhood obesity and its associated mental health burdens.

Contributors

PS designed the study. YS, CZ, and LZ extracted and checked the data. JZ prepared the first draft. JZ managed and analysed the data, while YS and JY reviewed the analyses and validated the results. YS, JY, CZ, JW, SS, JZ, LZ and WX revised the paper. All authors read and approved the final manuscript.

Data sharing statement

All data generated or analysed during this study are included in this article and [Appendix](#).

Declaration of interests

The authors declare that the research was conducted in the absence of conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.eclinm.2025.103121>.

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