Treatment of Obesity in Young People—a Systematic Review and Meta-analysis

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Abstract

Obesity in the young is increasingly prevalent. Early, effective intervention is paramount. Treatment options are lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery. However, the relative effectiveness of these treatments in young patients remains unclear. We systematically identify and meta-analyse studies evaluating weight loss treatments in young people (< 21 years) with obesity. From 16,372 identified studies, 83 were eligible for meta-analysis. Bariatric surgery resulted in high short/medium-term weight loss (pooled estimate 14.04 kg/m²). Lifestyle and pharmacological therapies impacted weight more moderately (pooled estimate 0.99 and 0.94 kg/m² respectively). Due to its high efficacy, bariatric surgery should be considered earlier when treating obesity in young people. However, due to the invasiveness and inherent risks of bariatric surgery, all other weight loss routes should be exhausted first.

Keywords Obesity · Young people · Bariatric surgery · Diet · Lifestyle · Metabolic surgery

Introduction

Obesity has a high and increasing prevalence in the young population [1]. The National Child Measurement Programme in England 2015–2016 found that 19.8% of children aged 10 to 11 years are currently obese [2]. Similarly, the National and Nutrition Examination Survey carried out in USA found that 20.5% of adolescents aged 12 to 19 are obese [3]. Importantly, childhood obesity is associated with a 16 times increased risk of adult obesity compared to normal-weight children [4]. Moreover, obesity results in an increased risk of type 2 diabetes, hypertension, dyslipidaemia, cardiovascular diseases, cancer, psychological conditions and

mortality [5]. Hence, there is a critical unmet need for innovative therapeutic strategies that address the treatment of obesity in young people. Early intervention in this cohort is likely to bring added benefits by preventing the cumulative deleterious health effects of obesity-related chronic disease and, in doing so, will reduce the associated cost burden [5].

Current treatment options for obesity include lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery [6]. Bariatric surgery is currently the gold standard treatment for long-term weight loss in adults [7]. However, the optimal treatment for young people is not known. The causes of obesity in young people as well as their biological and psychological response to interventions differ from those of adults. Younger patients are less habituated and may be more easily persuaded to undergo long-term lifestyle changes compared to their elder counterparts. Alternatively, children may be less compliant at taking weight loss medication on a daily basis.

The most recent review examining weight loss in young people dates from 2008 [6]. However, this review only evaluated lifestyle modifications and pharmacological therapies [6]. Since this, there have been a number of new trials that have added weight to this body of evidence.

The present systematic review and meta-analysis aims to be the first study to comprehensively summarise and quantify the comparative efficacy of body mass index (BMI)-reducing treatment options in the young population with obesity. It will

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help clinicians determine suitable courses of treatment in this cohort in order to more successfully achieve weight loss and, subsequently, improve associated comorbidities—an important issue in the ever-growing epidemic.

Methods

The systematic review and meta-analysis was conducted according to the principles endorsed in the PRISMA-P statement [8].

Literature Search Strategy

An extensive literature search of the MEDLINE and EMBASE databases from inception (last search May 2016) was conducted. Search terms were included to detect studies investigating lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery in the young population with obesity (Supplementary Appendix 1).

Eligibility Criteria

Studies were selected according to the following pre-defined eligibility criteria. *Type of participant:* We define young people as those aged 21 years or younger. Thus, included study participants were aged 21 years or younger with a BMI of 25 kg/m² or higher. Studies with pregnant females, neonates and patients with obesity-related genetic syndromes (e.g. Prader Willi syndrome) were excluded. *Type of intervention:* Four interventions were included: lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery. There was no restriction on who delivered the interventions, e.g. specialist doctors or teachers. The interventions could be community-, school- or clinic-based. *Type of comparison:* The highest level of available evidence was used in each group. Lifestyle and drug studies were all randomised control trials and had controls which had either no intervention, placebos or minimal interventions such as a single information session. Only a single randomised control trial (RCT) was retrieved assessing surgical management, so non-randomised studies were included for this sub-analysis. *Type of outcome measure:* Studies included one or more of the following outcomes: weight (kg), BMI (kg/m²), BMI standard deviation score (BMI-SDS or BMI-Z score), waist circumference (cm), fat mass (kg) or waist to hip ratio. These could either be reported as a primary or secondary outcome of the study.

Two independent reviewers (SS and NA) assessed the search strategy results. Study titles were examined for potential relevance and the abstract was then reviewed. Subsequently, the full text was retrieved to ensure eligibility. Review articles and studies with insufficient data for meta-analysis were excluded. No limits were applied for language

and foreign papers. This involved the translation of one Portuguese study [9]. The bibliographies of relevant articles were inspected for further eligible studies. In the case of any uncertainty regarding study inclusion, another investigator (NP) was consulted to assess eligibility.

Data Extraction

Eligible studies were sub-divided into four groups: lifestyle modifications, pharmacological therapies, endoscopic treatments and bariatric surgery. For the included studies, the following variables were obtained: study title, publication year, first author, type of intervention, number of participants, metric of measure for weight loss, baseline control and interventional group weight metrics, post-intervention control and interventional group weight metrics. Due to a sparsity of evidence using other weight metrics, BMI was utilised for the quantitative analysis.

Assessment of Methodological Quality

Methodological quality of RCTs was assessed using the Cochrane Collaboration Tool (Supplementary Appendix 2) [10]. This included assessment of random sequence generation, allocation concealment, blinding of participants and assessors, incomplete outcome data, selective reporting and other sources of bias [10].

Statistical Analysis

Any missing standard deviations were derived from other metrics provided, using standard formula found in the Cochrane handbook. The chi-squared test was completed to establish the degree of heterogeneity [11]. Higgins et al. suggest that 25, 50 and 75% indicate low, medium and high heterogeneity respectively [11]. As I^2 values were over 75%, the restricted maximum likelihood random-effects method was used to generate pooled mean BMI differences [11]. Publication bias was assessed using funnel plots (Supplementary Appendix 3). Statistical analyses were performed using the Metafor package in R (version 3.2.4).

Results

The comprehensive literature search identified 16,372 studies. After de-duplication and eligibility exclusions, 93 studies were included in the systematic review (Fig. 1). Eighty-three studies underwent quantitative analysis: 29 for lifestyle intervention (Fig. 2), 21 for pharmacological therapies (Fig. 3) and 33 for bariatric surgery (Fig. 4). Ten studies assessing endoscopic treatment were included for qualitative analysis. Study characteristics, patient characteristics, intervention

Fig. 1 PRISMA diagram illustrating the selection process for included studies

Fig. 2 Forest plot comparing BMI weighted mean difference in behavioural, exercise, diet and combined interventions

Fig. 3 Forest plot comparing BMI weighted mean difference in metformin, sibutramine, orlistat and corresponding control groups. AA African-American, C Caucasian

description, side effects/complications and adherence are described for lifestyle intervention, pharmacological therapies, endoscopic treatments and bariatric surgery (Table 1) respectively. A detailed description of the complications associated with bariatric surgery within the included studies is provided in Table 2. A list of the included studies is provided in Supplementary Appendix 4.

Lifestyle Modifications

Behaviour

Analysis revealed behavioural interventions decreased mean BMI by 0.18 kg/m² (95%CI - 0.52 to 0.15). One study continued for longer than 12 months [12]. Taylor et al. illustrated that monthly advice sessions and motivational interviews led to a statistically significant mean BMI reduction of 0.34 kg/m² in overweight/obese 4- to 8-year-old patients at 24 months [12].

Exercise

Pooled analysis demonstrated that mean BMI reduced by 0.89 kg/m² (95%CI - 2.20 to 0.42), compared to controls. One study continued for longer than 6 months [13].

Kokkvoll et al. found that over a 2-year intervention, patients continued to gain weight despite exercise [13].

Diet

Dietary interventions were trialled in three studies [14–16]. Pooled analysis revealed a reduction of mean BMI by 0.91 kg/m² (95%CI - 1.80 to -0.02) compared with comparison groups. Okeley et al. and Shalitin et al. found that diet was significantly better at reducing BMI than exercise at 12 months [14, 15]. However, Shalitin et al. discovered that patients regained any lost weight 9 months after suspension of intervention [14]. Ebbeling et al. found that a low glycaemic index diet caused a statistically significant reduction in BMI compared to a low-fat diet [16]. None of the studies were carried out for longer than 12 months.

Behaviour, Exercise and Diet

Pooled analysis revealed that combined lifestyle intervention reduced mean BMI by 1.34 kg/m² (95%CI - 2.19 to -0.50) at 6 months and by 1.52 kg/m² (95%CI - 2.97 to -0.07) at 12 months, revealing a non-significant difference between the two time intervals. A combined lifestyle approach illustrated an

Fig. 4 Forest plot comparing BMI weighted mean difference in laparoscopic adjustable gastric banding (LAGB), Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG)

overall reduction in mean BMI of 1.44 kg/m² (95%CI - 2.23 to - 0.65). This proved to be more effective than a single lifestyle intervention of either diet, exercise or behaviour. One study was carried out for longer than 12 months [17]. Kalarchian et al. found that the majority of 8- to 12-year-old patients regained their lost weight at 18 months [17].

The sub-group meta-analysis at 12 months of combined lifestyle interventions contains an outlier. Weigel et al. illustrated a much greater BMI reduction compared to other studies [18]. It consisted of intensive interventions with bi-weekly sessions for 12 months [18]. Other studies reduced their intervention frequency as the study progressed. However, after removing the outlier and re-conducting the meta-analysis, the results still remained statistically significant with a reduction of BMI by 1.06 kg/m² (95%CI - 1.78 to - 0.35) at 6 months and 0.86 kg/m² (95%CI - 1.61 to - 0.10) at 12 months.

Pharmacological Therapies

Metformin

Pooled analysis revealed metformin reduced mean BMI by 0.75 kg/m² (95%CI - 1.14 to - 0.35) compared with the placebo. There was a statistically insignificant difference

between studies that prescribed metformin at different time intervals. Two of the 14 studies were continued for longer than 6 months [19, 20]. Nwosu et al. found a statistically insignificant difference in BMI between baseline and study conclusion in the interventional group [19]. Wilson et al. illustrated that the treatment group had a higher BMI than the control group at 18 months due to rapid weight gain after metformin was withdrawn [20].

Sibutramine

Pooled analysis for sibutramine demonstrated a decrease in mean BMI of 1.66 kg/m² (95%CI - 2.48 to - 0.84) compared to the placebo. None of the studies evaluated BMI change maintenance.

Orlistat

Analysis revealed that orlistat decreased mean BMI by 0.87 kg/m² (95%CI - 1.19 to - 0.54) compared to the placebo. Two studies were longer than 6 months [21, 22]. Chanoine et al. illustrated a reduction in mean BMI of 0.55 kg/m² in the interventional group at 12 months [21]. Ozkan et al. found similar results after 11.7 months [22].

Table 1 Summary of included studies

Treatment option	Studies (n)	Study characteristics	Patient characteristics	Intervention description	Adverse effects	Adherence
Behaviour	8	<ul style="list-style-type: none"> • 3 multicentre studies • 4 studies in USA, remaining in Australia, Netherlands, Sweden or New Zealand • Study duration varied between 6 and 24 months 	<ul style="list-style-type: none"> • 2287 total patients • Mean age 4.8–13.23 years 	<ul style="list-style-type: none"> • 5 studies had family based interventions • Interventions included motivational interviews, internet interventions, lifestyle advice sessions • Controls were untreated or underwent minimal intervention 	<ul style="list-style-type: none"> • No adverse effects 	<ul style="list-style-type: none"> • 2 studies commented • 50% compliance for completing 2 out of 6 sessions
Exercise	6	<ul style="list-style-type: none"> • 2 studies in USA, remaining in Brazil, Canada, Norway or New Zealand • Study duration varied between 6 and 12 months 	<ul style="list-style-type: none"> • 738 total patients • Mean age 7.56–15.9 years 	<ul style="list-style-type: none"> • 3 studies were community based, 2 studies were school-based • Intervention varied from active video games to weekly aerobic sessions • Controls were untreated or given healthcare education 	<ul style="list-style-type: none"> • No adverse effects 	<ul style="list-style-type: none"> • Ranged between 58 and 62%
Diet	3	<ul style="list-style-type: none"> • All single centred • Study duration varied between 4 and 12 months 	<ul style="list-style-type: none"> • 111 total patients • Mean age 8.2–16.9 years 	<ul style="list-style-type: none"> • Interventions included low glycaemic index diet, low fat diet or reduction in calories. 	<ul style="list-style-type: none"> • No adverse effects 	<ul style="list-style-type: none"> • Compliance varied between 22.2–57.3% • Motivation and parental support were related to poor compliance
Behaviour, exercise and diet	10	<ul style="list-style-type: none"> • 2 in Germany, 2 in Mexico, 2 in USA, remaining in Finland, Australia, Netherlands and UK • 1 multicentre study • Study duration varied between 6 and 18 months 	<ul style="list-style-type: none"> • 1875 total patients • Mean age 7.4–12.4 years 	<ul style="list-style-type: none"> • 7 studies had family based interventions • All interventions contained behaviour, exercise and dietary aspects 	<ul style="list-style-type: none"> • No adverse effects 	<ul style="list-style-type: none"> • Varied adherence rates • Ranged from 53 to 94%
Metformin	14	<ul style="list-style-type: none"> • 3 multicentre studies • 7 studies in USA, 2 in Canada, remaining in Australia, Germany, Iran, Mexico or UK • Study duration varied between 3 and 22 months 	<ul style="list-style-type: none"> • 1145 (522 male) total patients • Mean age 10.1–15.7 years • Baseline mean BMI 25.4–41 kg/m² 	<ul style="list-style-type: none"> • 7 studies included lifestyle intervention in control and treatment groups • Metformin doses varied between 1000 and 2000 mg/day 	<ul style="list-style-type: none"> • No serious side effects reported • 11 studies mentioned gastrointestinal symptoms • 2 studies had drop-outs due to side effects • 3 studies reported fatigue as most common side effect 	<ul style="list-style-type: none"> • 60–94% adherence
Sibutramine	4	<ul style="list-style-type: none"> • All single centred • 2 studies in USA, remaining in Brazil or Mexico • Study duration varied between 3 and 6 months 	<ul style="list-style-type: none"> • 177 total patients • Mean age 13.9–16.7 years • Baseline mean BMI 30.1–38.5 kg/m² 	<ul style="list-style-type: none"> • Lifestyles intervention in all control and treatment groups • Sibutramine doses varied between 10 and 15 mg/day 	<ul style="list-style-type: none"> • No serious side effects reported • 2 studies reported changes in blood pressure and heart rate 	<ul style="list-style-type: none"> • No studies commented
Orlistat	3	<ul style="list-style-type: none"> • 1 multicentre study • Study duration varied between 3 and 12 months 	<ul style="list-style-type: none"> • 622 (228 male) total patients • Mean age 12.5–15.8 years • Baseline mean BMI 31.2–41.7 kg/m² 	<ul style="list-style-type: none"> • Lifestyles intervention in all control and treatment groups • All orlistat doses 120 mg, 3 times a day 	<ul style="list-style-type: none"> • 1 patient developed symptomatic cholelithiasis requiring a cholecystectomy 	<ul style="list-style-type: none"> • Poor adherence due to side effects

Table 1 (continued)

Treatment option	Studies (n)	Study characteristics	Patient characteristics	Intervention description	Adverse effects	Adherence
Intra-gastric balloon	7	<ul style="list-style-type: none"> • 3 studies from peer-reviewed journal, 4 conference abstracts • Study duration varied between 6 and 24 months 	<ul style="list-style-type: none"> • 104 (48 male) total patients • Mean age 13.89–18.5 years • Baseline BMI 30–55.4 kg/m² • 6 total patients • Mean age 18.2 years • Baseline mean BMI 44.7 kg/m² 	<ul style="list-style-type: none"> • All studies placed an intra-gastric balloon in the stomach endoscopically 	<ul style="list-style-type: none"> • Many gastrointestinal symptoms from oily stool to faecal incontinence reported • No major complications reported • Most common side effect was epigastric pain 	<ul style="list-style-type: none"> • No studies commented
Endobarrier	1	<ul style="list-style-type: none"> • 1 conference abstract • Study duration was 6 months 	<ul style="list-style-type: none"> • 824 (339 male) total patients • Mean age 15.8–18.5 years • Baseline mean BMI 42.5–50 kg/m² • All patients underwent psychological screening before enrolment 	<ul style="list-style-type: none"> • Duodenal–jejunal bypass liner was placed endoscopically 	<ul style="list-style-type: none"> • No major complications reported 	<ul style="list-style-type: none"> • No comment from study
LAGB	12	<ul style="list-style-type: none"> • 824 (339 male) total patients • Mean age 15.8–18.5 years • Baseline mean BMI 42.5–50 kg/m² • All patients underwent psychological screening before enrolment 	<ul style="list-style-type: none"> • 824 (339 male) total patients • Mean age 15.8–18.5 years • Baseline mean BMI 42.5–50 kg/m² • All patients underwent psychological screening before enrolment 	<ul style="list-style-type: none"> • 7 studies used LAP-BAND, 2 studies used only/mostly SAGB • 8 studies used pars flaccida approach • Mean operation time varied between 35 and 55.9 min 	<ul style="list-style-type: none"> • 1 intraoperative complication; laparotomy conversion after gastric perforation during band positioning • 1 post-operative death at 46 months; acute haemorrhage after band removal • Most common complication: asymptomatic iron deficiency (23%) 	<ul style="list-style-type: none"> • Good adherence to follow-up plans, 78% at 12 months • Finance and motivation were related to loss of follow-up
RYGB	12	<ul style="list-style-type: none"> • 630 total patients • Mean age 13–21 years • Baseline mean BMI 35–69 kg/m² • 9 studies screened patients for psychological issues 	<ul style="list-style-type: none"> • 630 total patients • Mean age 13–21 years • Baseline mean BMI 35–69 kg/m² • 9 studies screened patients for psychological issues 	<ul style="list-style-type: none"> • 6 studies used a laparoscopic approach • 2 studies contained a control group 	<ul style="list-style-type: none"> • No intraoperative complications • 2 post-operative deaths; 1 due to infectious colitis at 9 months, 1 due to cardiac failure at 5 months • Most common complication: hernia development (9%) 	<ul style="list-style-type: none"> • Mixed results, 1 study found 75% adherence • 1 study found adolescents are equally as likely to deviate from follow-up plans as adults
LSG	9	<ul style="list-style-type: none"> • 1099 total patients • Mean age 13.9–19 years • Baseline mean BMI 36–57 kg/m² • 5 studies needed psychological assessment before enrolment 	<ul style="list-style-type: none"> • 1099 total patients • Mean age 13.9–19 years • Baseline mean BMI 36–57 kg/m² • 5 studies needed psychological assessment before enrolment 	<ul style="list-style-type: none"> • 3 studies included a control group. These patients underwent lifestyle interventions 	<ul style="list-style-type: none"> • No intraoperative complications reported • No reported mortality • Most common complication: gastroesophageal reflux (28%) 	<ul style="list-style-type: none"> • 1 study commented • Adherence rate of over 70% to follow-up plans

Table 2 Complications after laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG) and roux-en-Y gastric bypass (RYGB) for the included studies in the surgical meta-analysis

Study	N	Complications (number of cases)
Laparoscopic adjustable banding		
Holterman, A. X. (2010)	20	Tube/port issues (3), band malfunction (1), hiatal hernia (1)
Khen-Dunlop, N. (2016)	49	Death (1), band slippage (1), psychological intolerance (1)
Nadler, E. P. (2009)	45	Band slippage (2), asymptomatic iron deficiency (19)
Nadler, E. P. (2007)	53	Band slippage (2), hiatal hernia (2), wound infection (1), reflux (1), mild hair loss (5), iron deficiency (4)
Nadler, E. P. (2008)	73	Band slippage (4), hiatal hernia (3), wound infection (1), port leak (1), mild hair loss (14), iron deficiency (13), vitamin D deficiency (4), gastroesophageal reflux (3), cholelithiasis (2), nephrolithiasis (1)
Silberhumer, G. R. (2011)	50	Dislocated port (1)
Silva, G. M. (2012)	14	Port Leakage (2), gallstone formation (1), micronephrolithiasis (1), gastroesophageal reflux (2), asymptomatic nutrient deficiency (2)
Angrisani, L. (2005)	58	Band slippage (1), gastric pouch dilation (2), intragastric migrations (3), psychological intolerance of band (2), conversion to gastric bypass (1)
Lanthaler, M. (2009)	41	Pouch dilations (11), band leakage (4), intragastric migration (2), port disconnection (2)
Dillard, B. E. (2007)	24	Pouch enlargement (6), port leak (1)
Laparoscopic sleeve gastrectomy		
Ahmed El-Matbouly, M (2017)	91	Endoscopic dilation due to stenosis (3)
Alqahtani, A. R. (2016)	274	Wound infection (2), nausea and vomiting (2), possible staple line leak (1), staple line bleed (1), gastroesophageal reflux (4), metabolic neuropathy (2)
Alqahtani, A. R. (2015)	291	Wound infection (2), nausea and vomiting (2), possible staple line leak (1), staple line bleed (1), gastroesophageal reflux (4), metabolic neuropathy (2)
Nadler, E. P. (2012)	23	Cholelithiasis (1), postviral gastroparesis (2)
Saleh M. Aldaqal (2013)	32	No complications occurred
Dargan, D. (2017)	208	No complications occurred
Dubnov-Raz, G. (2014)	25	Cholelithiasis (5), vitamin B ₁ , C, D and folic acid deficiency (1)
Alqahtani, A. R. (2012)	108	Wound infection (2), possible staple leak (1), gastroesophageal reflux (3)
Roux-en-Y gastric bypass		
Olbers, T. (2012)	81	Internal hernia (5), symptomatic gallstones (5), abdominal pain (5)
Messiah, S. E. (2013)	247	Nausea, vomiting, intestinal bleeding, diarrhoea or gallstones (29), hernia (6), small bowel obstruction (2), wound infection (1), vitamin A, B ₁₂ , D, folate, iron, magnesium, zinc, electrolytes deficiency (24), excess skin (3)
Inge, T. H. (2015)	22	Dehydration (1)
Inge, T. H. (2009)	11	Gastrointestinal leakage (1), small bowel obstruction (4), dehydration (1), gastrojejunal anastomotic stricture (1)
Inge, Y. H. (2017)	58	Upper endoscopy (13), cholecystectomy (12), repair of gastrointestinal perforation (7), blood and micronutrient infusion (6)
Teeple, E. A. (2012)	15	Ileus (1), port-site hernia (1), gastrojejunal anastomotic stricture bleed/leak (1)
DuCoin, C. (2015)	15	Pouch dilation (1)
Lawson, M. L. (2006)	31	Death (1), wound infection or anastomotic stricture, nausea, diarrhoea, dehydration, deep vein thrombosis or hypokalaemia (9), internal hernia (1), persistent iron deficiency or peripheral neuropathy secondary due to vitamin deficiency (6)
Brissman, M. (2016)	41	No complications reported
Cruz-Munoz, N. (2013)	71	Nausea and vomiting (2), iron deficiency (3)

Endoscopic Treatments

Intragastric Balloon

Only one study reported a statistically insignificant decrease in percentage change of BMI after 3 months ($p = 0.07$) [23]. At 6 months, these patients regained any lost weight and became more obese than before intragastric balloon (IGB) insertion [23]. Two studies mentioned weight loss maintenance [24, 25]. Adorisio et al. demonstrated that 24 months after balloon removal, 48.4% of patients maintained/continued weight loss in 11- to 21-year-old patients [25]. Curran et al. revealed that any weight loss achieved by lifestyle or IGB interventions was not maintained at 18 months [24].

Endobarrier

One conference abstract evaluated the Endobarrier [26]. At 6 months after insertion, all patients experienced significant weight loss with a mean weight reduction of 20.8% [26].

Bariatric Surgery

Laparoscopic Adjustable Banding

Pooled analysis revealed that laparoscopic adjustable banding (LAGB) decreased mean BMI by 9.74 kg/m^2 (95%CI – 11.61 to – 7.87) at 12 months post surgery. Nine studies were longer than 12 months [27–34]. All of these studies showed significant and sustained BMI reduction in young patients over a longer follow-up period [27–34]. These longer studies demonstrated an excess weight loss between 45 and 57.5% at study conclusion [27–34]. LAGB demonstrated a relatively good safety profile in the paediatric population with the most common complication being asymptomatic iron deficiency. However, one death was reported at 46 months following acute haemorrhage after band removal [35].

Roux-en-Y Gastric Bypass

Pooled analysis showed Roux-en-Y gastric bypass (RYGB) decreased BMI by 17.06 kg/m^2 (95%CI – 19.68 to – 14.45) at 12 months post surgery. Three trials continued for longer than 12 months [36–38]. Olbers et al. stated that there were a statistically insignificant change in BMI between 12 and 24 months in the surgical group [37]. Teeple et al. and Tsamis et al. revealed an excess weight loss of more than 50% at 24 months. Reduction in weight was maintained at 48 months [36, 38]. The most common complication following RYGB was vitamin and/or iron deficiency.

Laparoscopic Sleeve Gastrectomy

Pooled analysis revealed laparoscopic sleeve gastrectomy (LSG) decreased mean BMI by 16.13 kg/m^2 (95%CI – 17.92 to – 14.33). Four studies were carried out for longer than 12 months [39–42]. Patients maintained any weight loss achieved in the short term [39–42]. At study conclusion, which varied between 24 and 60 months across trials, all patients decreased their BMI by more than 18 kg/m^2 [39–42]. The most common complication following LSG was gastroesophageal reflux. Importantly, evidence regarding the long-term complications of bariatric surgery in young patients is still sparse and should not be underestimated.

Discussion

Key Statistics

Lifestyle BMI (kg/m^2) mean difference	– 0.99 (95%CI – 1.43 to – 0.53)
Drugs BMI (kg/m^2) mean difference	– 0.94 (95%CI – 1.30 to – 0.59)
Surgery BMI (kg/m^2) mean difference	– 14.04 (95%CI – 15.65 to – 12.43)

Principle Findings

This study investigated the comparative efficacy of BMI-reducing treatment options for obesity in the young population. It illustrates that as a single intervention, bariatric surgery is the most effective treatment for BMI reduction in the short and long terms. Furthermore, LSG and RYGB caused a statistically significant reduction in BMI compared to LAGB at 12 months.

Although this systematic review and meta-analysis is not designed to evaluate the relative risks between different treatment modalities for obesity in young patients, it is important that the risks that accompany surgery are well established. This study suggests that bariatric surgery has a good safety profile in the paediatric population. However, there are existing concerns over the long-term consequences of bariatric surgery on pre-pubertal children with severe obesity, including factors such as growth. Recently, Alqahtani et al. showed that, contrary to expectations, growth was improved after LSG, with approximately 1 extra millimetre of height gain per month compared with obese children who did not undergo surgery [41]. However, of the 2155 patients included that underwent surgical intervention, one death relating to the surgery was reported 48 months following LAGB [35]. The 19-year-old patient underwent emergency endoscopic evaluation 4 years post-gastric banding due to melena and

haematemesis. Gastric haemorrhage with band erosion was found. During gastric band removal, acute haemorrhage occurred and the patient subsequently died of uncontrolled bleeding [35]. This illustrates that although rare, severe post-operative complications are possible. Furthermore, evidence regarding the long-term complications associated with bariatric surgery on young patients is still sparse [43]. Therefore, it is important that the risks that accompany surgery are not underestimated and are well established in each individual case [44].

Moreover, evidence regarding the long-term efficacy of bariatric surgery in young patients is limited. However, recently, Olbers et al. conducted a prospective study analysing 5-year outcomes of adolescent patients after Roux-en-Y gastric bypass. It demonstrated a BMI reduction of 13.5 kg/m² compared to a control group undergoing lifestyle intervention that experienced an increase in BMI of 3.3 kg/m² [45]. Additionally, Inge et al. analysed 3-year outcomes of adolescent patients after Roux-en-Y gastric bypass and sleeve gastrectomy. The study found that patient BMI decreased by 15 and 13 kg/m², respectively [46]. Nevertheless, despite emerging studies that demonstrate the longer-term efficacy of bariatric surgery in adolescent patients, it is important to highlight that long-term data in this cohort is still limited and further studies are required.

Assessment of lifestyle interventions revealed that a combined approach of behaviour, exercise and dietary treatments resulted in a statistically significant greater BMI reduction compared to a solitary lifestyle intervention. Moreover, both lifestyle modifications and pharmacological therapies have similar impacts on BMI change in the short and medium terms.

Sibutramine appeared to be the most effective drug at achieving BMI loss in the short term. It facilitates weight loss by acting as a serotonin reuptake inhibitor causing activation of anorexigenic pathways to prevent cognitive sensations of hunger [47].

Metformin caused similar BMI changes over short- and medium-term administration periods. However, there is no clear benefit on BMI loss after long-term metformin administration compared with short- and medium-term. The mechanism by which metformin results in weight loss is unclear, but it is likely to be multifactorial [48]. Its effect on weight may be mediated by increasing glucagon-like peptide 1, reducing dipeptidyl peptidase-4 activity, modifying the gut microbiome, increasing lipid oxidation and promoting central satiety [48].

Orlistat inhibits gastric and pancreatic lipase and decreased absorption of triglycerides by approximately 30% [49]. It is the only weight-reducing drug approved for paediatric patients with obesity in USA [49]. However, it is imperative that more studies investigate the weight-reducing effects of orlistat in young adults to conclusively

determine whether it should be preferred to other available treatment options.

Endoscopic treatments appear to cause statistically significant weight loss in the short term. However, given the low number of studies included, it is vital that more studies are conducted to further assess its impact on weight loss. The mechanism behind the IGB includes the inflation of a balloon in the stomach of patients to fill its capacity, promoting satiety and decreasing calorie intake [50]. The Endobarrier leads to weight loss by creating a 60-cm-length barrier along the duodenal wall to reduce absorption of nutrients [51].

Strengths and Limitations

To our knowledge, this is the first comprehensive systematic review and meta-analysis to directly compare the efficacy of weight-reducing treatment options for obesity in the young population. Lifestyle modification and pharmacological therapy meta-analyses contain a large number of RCTs. The surgical meta-analysis contains five times the number of overall patients and double the number of LSG studies compared to the most recent topical paper [52].

This study includes sibutramine despite its withdrawal from the USA and UK market following the SCOUT study [53]. It was illustrated that sibutramine carries a relative risk of 1.16 for causing cardiac-related morbidity [54]. However, sibutramine can be found in small amounts within some diet pills and herbal remedies, which can be purchased online [55]. Therefore, it is important to know its possible impact on young people as well as using it as a historical benchmark to compare against current licenced medications.

Surprisingly, dietary interventions were rarely evaluated as a sole component of treatment in comparison with a minimal-intervention or no-treatment control group [56]. Therefore, many trials did not meet the inclusion criteria for statistical analysis in this study. Nevertheless, the available evidence demonstrates that dietary interventions do have the potential to cause a statistically significant decrease in BMI. Partsalaki et al. compared the efficacy of a ketogenic and a hypocaloric diet in obese children without the use of a control group [57]. At 6 months, both groups had a statistically significant decline in mean BMI of 3.7 and 3.3 kg/m², respectively. This illustrates a higher BMI reduction compared to RCTs included in this study. There is a clear need for well-designed RCTs that assess the long-term efficacy of alternative dietary interventions to allow conclusive determinations regarding its efficacy.

There is a lack of information from RCTs on sibutramine and its impact on BMI change after 6 months. A prospective observational study demonstrated that a large dropout rate was seen due to a slow rate of weight reduction after 6 months compared to the first 6 months of administration [47]. It was concluded that sibutramine has a limited effect on weight loss in the long term [47].

The surgical meta-analysis included non-randomised trials (Fig. 4) making it difficult to directly compare the efficacy of surgery to other interventions. The studies do not take into account the placebo effect and allow bias from potential confounding factors [58]. However, the lack of RCTs reflects the ethical concerns of randomising a vulnerable population, in this case children and adolescents with obesity [52]. Surgery includes a higher risk of complications and a greater cost, making it difficult to carry out RCTs in this area [59].

Another limitation includes the use of BMI to measure weight change in a paediatric population [59]. BMI can be inaccurate, as the calculation does not distinguish between lean and fat mass [59]. Moreover, variation in age, sex and maturation results in a large range of normal BMI scores in the paediatric population [59]. BMI-Z score would be a better measure of weight change as it considers age and gender [59]. However, studies most commonly reported BMI, and therefore, it was the used metric for this analysis.

The results from this meta-analysis apply to the general paediatric population of overweight and obese individuals below the age of 21 with a BMI of 25 kg/m² or more. In the included studies, mean age ranged from 4.8 to 19 years. As a whole, the patients undergoing bariatric surgery were older than those carrying out lifestyle modifications. This may have influenced findings. However, the limited number of studies prevented investigations through further stratification of results according to age groups.

Finally, a lack of studies with large sample sizes is a problem when evaluating the efficacy of orlistat and endoscopic treatment. It is important that more studies are carried out to further assess their impact on weight loss.

Comparison with Other Studies

McGovern et al. (2006) concluded that a combined lifestyle intervention is more effective than a single lifestyle intervention approach on BMI change and that pharmacological therapy (for example, sibutramine) can be beneficial in the short term [60]. Our study confirms this. We also extend this inference to note that overall lifestyle and pharmacological interventions have very similar impacts on BMI reduction, while metformin demonstrates similar effects on BMI reduction regardless of the time interval for which it is administered. Our results are also consistent with another review that found that metformin did not demonstrate any clear benefit on weight loss after long-term administration [61].

Our surgical meta-analysis contained solely non-randomised trials; however, its results mirrored the only published RCT in this area [62]. This RCT of 50 patients illustrated that the surgical arm reduced mean BMI by 12.7 kg/m² (95%CI – 11.3 to – 14.2), compared to a reduction of 1.3 kg/m² (95%CI – 0.4 to – 2.9) in the lifestyle modification control arm [62].

Conclusion

This meta-analysis conclusively determines the comparative efficacy of weight-reducing treatments in obese young patients. Currently, bariatric surgery is rarely considered in this cohort. However, this meta-analysis provides comprehensive evidence that compared with non-surgical obesity treatments, bariatric surgery leads to a greater BMI reduction in the short and long terms. Therefore, this data suggests that physicians and patients should have a lower threshold for considering bariatric surgery when lifestyle and pharmacological interventions have failed. Nevertheless, there should be a clear understanding of the risks this treatment option may entail for each individual young patient. Furthermore, future RCTs are required to enable a conclusive determination regarding long-term risks of bariatric surgery in young people. Due to the stigma and psychological impact of obesity, it is important that physicians approach this topic sensitively. There should be effective communication discussing the relative efficacy of all treatment options and their associated complications between those involved. The evidence for certain treatment options, in particular endoscopic treatments, remains unclear and calls for further research. This knowledge will assist physicians in determining a holistic, patient-centred treatment programme for young patients with obesity in order to achieve successful BMI reduction and subsequent improvement of associated comorbidities.

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Compliance with Ethical Standards

Competing Interests The authors declare that they have no conflicts of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Does not apply.

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