

Changes in Health-Related Quality of Life in children with obesity after participating in a lifestyle intervention: a meta-analysis

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Abstract

Context

The number of children with obesity increases, while having obesity as a child is associated with negative consequences for the Health-Related Quality of Life (HRQoL). HRQoL is a subjective measure, and the effect of obesity on the HRQoL could be assessed by using questionnaires. Nowadays, lifestyle interventions are used to change behaviour and to improve the weight status of children with obesity, which could also improve the HRQoL.

Research question

To assess the changes in HRQoL in children with obesity after participating in a lifestyle intervention. Hypothesized is that lifestyle interventions will improve the HRQoL through addressing diet, physical activity and behaviour change.

Methods

A systematic search was conducted in PubMed for studies involving lifestyle interventions for children with overweight/obesity. The primary outcome was the change in HRQoL measured by child-reported questionnaires, namely the PedsQL 4.0 and IWQOL-Kids. The PedsQL 4.0 comprises three scales: Total, Physical and Psychosocial. The results of the individual studies were collected, summarized and compared. The extent of heterogeneity of the reported results of the included articles was determined by using the Higgins I^2 . The overall effect test was used to determine whether studies offering lifestyle interventions significantly improved the HRQoL of children with overweight/obesity. The Cochrane Collaboration tool was used to assess the risk of bias.

Results

This meta-analysis included seven RCTs. All studies applied different lifestyle interventions, but all lifestyle interventions were composed of physical activity and eating behaviour components. These articles showed a homogeneous reported improvement in the Physical HRQoL measured by the PedsQL 4.0 after children with obesity participated in lifestyle interventions. Other homogeneous results were reported at follow-up in the Total and Physical scale and on all three the scales of the PedsQL 4.0 when only including articles which focused on children with obesity.

Conclusion

Current findings are limited by the small number of includable RCTs. Future studies should focus more on the effect of lifestyle interventions on the disease-specific HRQoL questionnaires and the long-term effect of lifestyle interventions on the HRQoL. Also, the findings of this study contribute to leads on how to improve the current Dutch treating practice for children with obesity.

Introduction

Worldwide problem

Worldwide, the trends of the number of children and adolescents with underweight, overweight or obesity are monitored. According to the Lancet, worldwide the number of children and adolescents, between 5-19 years old, that have obesity increased more than a ten-fold in the past four decades. Whereas in 1975, 11 million children with obesity were reported this increased to 124 million children with obesity in 2016 (1). To halt this increasing number of children with obesity, countries agreed to global targets set by the World Health Organization (WHO) by 2025. These comprise no increase in overweight among children under age 5, school-aged children and adolescents by 2025 compared to levels of 2010 (2). Nowadays, different countries have taken multiple actions to reach these targets, such as marketing restrictions, promotion of physical activity, monitoring prevention and treatment strategies. Alongside these national actions, governments should review their progress in order to meet the 2025 targets. A point for improvement of these national actions is to ensure access to obesity prevention and treatment that meets the individual's needs (2). This emphasizes the need for tailor-made care in the treatment of children with obesity.

In the Netherlands, the current treatment policy for children with obesity is based on a combined lifestyle-intervention approach. These treatment guidelines differed per age group and were established by Partnership Overweight Netherlands (PON) (3). The treatment is composed of simultaneous physical activity interventions, changing eating behaviour and behaviour change. Combining these interventions increases the effectiveness of the treatment compared to when these interventions are offered separately (4). The aim of the combined lifestyle-intervention is improvement of weight status as well as establishing health gains. The recommended duration of the intervention is at least one year, followed by long-term guidance aimed at weight maintenance. The guidelines also recommend improving the eating and living habits of the entire family (5).

What is already known

Having obesity as a child (aged 0-18 years old) is associated with negative consequences on physical and psychosocial health of the individual, both in the short and long term (6). The prevalence of psychosocial problems is primarily high for girls. Common psychosocial problems for children with obesity are eating disorders, low self-esteem and depressive symptoms (7).

Moreover, children with obesity also report a lower Health-Related Quality of Life (HRQoL) compared to children that have a healthy Body Mass Index (BMI) (8). HRQoL is a broad subjective measure, which assesses the impact of health and disease from a patient's perspective, on social, mental and physical well-being (9). This subjective aspect means that the effects of a chronic health condition, such as obesity, on aspects of a person's functioning, are variable. Some people with notable impairments in body functions are still able to participate in mundane activities and report a positive HRQoL. While others report a decreased HRQoL when one only has insignificant

impairments (10). The influence of a disease on the different aspects of an individual is usually described by the International Classification Framework for Disability and Functioning from the WHO (Figure 1). The HRQoL is not an explicit component of this Framework, but depends on several elements (11). HRQoL encompasses particularly elements related to participation and activity. The physiological body functions and contextual factors, such as personal and environmental factors, contribute to a lesser extent to the HRQoL.

Due to the aforementioned subjective character of HRQoL, it is measured by using questionnaires. The questionnaire addresses a section of the domains of well-being, namely the HRQoL (12). Whereas HRQoL focuses on the experienced limitations of disease on one's daily life, well-being focuses more on the positive evaluations of a person's life. Well-being has a broad definition which includes, among others, the presence of positive emotions in daily activities and overall life satisfaction (13).

These questionnaires that address the HRQoL are called Patient-Reported Outcome Measures (PROMs). These PROMs are used in the treatment of disease to assess the HRQoL. By including these Patient-Reported Outcomes (PROs) in the treatment, with the use of PROMs, this increases the understanding of the impact of an intervention or treatment on one's well-being (14). Nowadays, PROMs are advised to be used for three different purposes in the treatment of children with obesity in the Netherlands; as a diagnostic measure, as a tool for tailoring interventions and as an outcome measure (12).

Two types of PROMs can be distinguished. By using the 'generic' HRQoL PROMs, the effects of different diseases on the HRQoL can be compared. More knowledge about the specific effect of a disease-specific intervention on the daily functioning of people with a particular disease can be acquired by using 'disease-specific' HRQoL PROMs. Previous literature research conducted by Noordam *et al.* showed, that for Dutch treating practice for children with obesity, the most applicable and best available generic and disease-specific PROMs are PedsQL 4.0 and IWQOL-Kids, respectively. The disease-specific IWQOL-Kids is the most sensitive questionnaire to discern the effects of different lifestyle interventions on the HRQoL (12). While the PedsQL 4.0 is the most useful generic questionnaire to assess HRQoL for children with obesity (15).

What remains unknown and research question

A meta-analysis from UI-Haq *et al.* concluded that children with obesity have a significantly reduced overall, physical and psychosocial HRQoL. Moreover, a dose relationship was observed, implying that having obesity as a child has more detrimental effects on the HRQoL than having overweight (16). As the HRQoL of children with obesity is lower, information about the HRQoL of children with obesity could contribute to shaping lifestyle interventions to increase the HRQoL of these children (17).

A systematic review from Tsiros *et al.* and Griffiths *et al.* focused on the effects of both lifestyle and surgical interventions on the HRQoL of children with obesity (10, 18). The changes in HRQoL were measured by conducting a PROM measurement at baseline with a reassessment during the follow-up period. Tsiros *et al.* concluded that the overall HRQoL might be positively influenced by weight-loss. This study also stated that increasing physical activity through lifestyle interventions could have a positive effect on the HRQoL, which is independent of weight-loss (10). This finding is in accordance with another study from Hoedjes *et al.*, concluding that the degree of weight-loss during a combined lifestyle-intervention is not related to improvements in many psychosocial domains of the HRQoL. Even if weight-loss is not related to improvements in HRQoL, participating in a combined lifestyle-intervention does increase the HRQoL of children with obesity (19). Whether weight-loss is independently associated with improvements in HRQoL remains uncertain. Another remark on this systematic review from Tsiros *et al.* is that it only included 7 articles, among which two articles comprised of medication or surgical intervention (10). Griffiths *et al.* also concluded that children and adolescents with obesity that participated in interventions report improvements on the physical HRQoL (18). Since both Tsiros *et al.* and Griffiths *et al.* included lifestyle and surgical interventions, the effect of only lifestyle interventions on the HRQoL of children with obesity remains unknown.

A meta-analysis from Murray *et al.* assessed the changes in HRQoL after adolescents with overweight/obesity participated in lifestyle interventions. This meta-analysis concluded that after adolescents with overweight/obesity participated in these interventions significant improvements in the HRQoL was reported. However, the heterogeneity among the reported results of the individual studies was high. Another shortcoming of this meta-analysis was that it also included studies which assessed the effect of interventions on the HRQoL of children who were at risk of having overweight/obesity (20). Another meta-analysis from Ligthart *et al.* also focused on the effect of lifestyle interventions on the HRQoL of children with obesity (21). This meta-analysis showed conflicting findings with the meta-analysis of Murray *et al.* (20). Ligthart *et al.* concluded that there were no significant improvements in HRQoL, on the short- and long-term, between children with overweight/obesity that participated in lifestyle interventions compared to children with overweight/obesity that participated in control interventions. A limitation of both meta-analyses is that these included both child-reported and parent-proxy reported questionnaires (20, 21). Parents of children with obesity are more likely to report a higher degree of impairment on the HRQoL compared to the child's perspective (22). Whether these effects of lifestyle interventions might be found if only children with overweight/obesity will be included, and only child-reported HRQoL PROMs are used within these studies remains unknown.

Therefore, this meta-analysis aims to assess the changes in child-reported HRQoL in children with obesity after participating in a lifestyle intervention. It is hypothesized that lifestyle interventions will improve HRQoL significantly. Improvements of HRQoL are expected because interventions are aimed at losing weight and losing weight when one has obesity might be positively related to an

increase in the HRQoL (10). Moreover, other improvements in lifestyle behaviour, such as increasing the physical activity of children with obesity might improve the HRQoL independently (18). Lifestyle interventions can also decrease psychosocial problems of children with obesity participating in these interventions, such as an increase in the self-esteem of children with obesity. Therefore, a lifestyle intervention might contribute to an improvement of the HRQoL independent for weight-loss (19). If lifestyle interventions improve the HRQoL of children with obesity, this study can provide evidence to support the combined lifestyle-intervention approach that is applied in the treatment of children with obesity in the Netherlands.

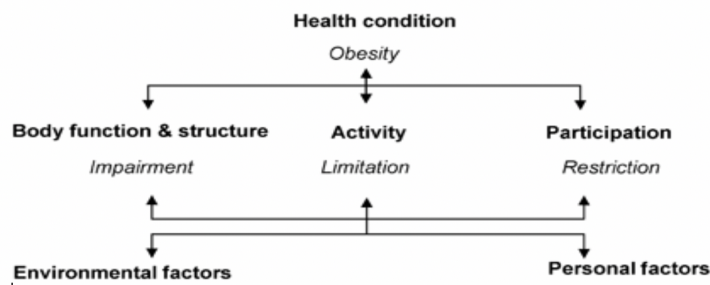


Figure 1: International Classification for Disability and Functioning (11)

Methods

Study protocol

This meta-analysis was based on the PRISMA statement. PRISMA statement comprises a 27-item checklist that is essential for ensuring transparency during reporting this meta-analysis (23).

Search strategy and selection procedure

For this meta-analysis an online search of relevant peer-reviewed literature published on PubMed was conducted, with restriction to Dutch and English articles. This online search in PubMed was performed on the 7th of April 2020. With an additional search for relevant articles that included the PedsQL 4.0 and/or the IWQOL-Kids on Google Scholar. Concerning background information, other sources, such as the WHO and information provided by the Care for Obesity project, were used as well.

Multiple researchers (AH, HK) performed the search and individually included articles by using the same search themes. The search strategy in PubMed comprised three search themes used in an AND-combination. Individual search themes were composed of multiple search terms in an OR-combination. The first search theme used comprised children and adolescents (e.g. child*, adolescen*, etc.), the second search theme used was obesity or overweight (e.g. obese, obesity, etc.) and the final search theme used were PROMs (e.g. pedsql, iwqol, etc.). All search terms used were MeSH-terms when available. However, when a search term was not available as MeSH-term, then articles were included if this search term was present in the title and/or abstract of the article (tiab). Detailed search themes and search terms that were applied can be found in Appendix 1.

Irrelevant articles were excluded by using the inclusion criteria. Applicable inclusion criteria can be found within the PICO (Population, Intervention, Comparison and Outcome). Firstly, when only including studies addressing children with obesity, the number of applicable studies for inclusion was insufficient. Therefore, studies were included if lifestyle interventions were offered to participants with overweight or obesity. Secondly, articles were included if they offered lifestyle interventions to children. An intervention was considered a lifestyle intervention if the three aspects of lifestyle were targeted: physical activity, eating behaviour and behaviour change. Thirdly, the control group was composed of children with obesity or overweight that only received usual care or were on a waiting-list during the intervention period. Fourthly, the articles were included if the PedsQL 4.0 and/or IWQOL-Kids was used to assess the HRQoL. The study design of the included articles was restricted to Randomized Controlled Trials (RCT).

Included PROMs

Paediatric Quality of Life Inventory 4.0 (PedsQL 4.0)

A study from Noordam *et al.* concluded that the PedsQL 4.0 is the best available questionnaire applicable to assess the generic HRQoL of children with obesity (12). Different questionnaires exist for ages 5 to 7, 8 to 12 and 13 to 18 years old (24). This questionnaire comprises 23 items divided into four scales: physical functioning, emotional functioning, social functioning and functioning at school. Each item is rated using a 5-point Likert-type scale, recalling last month HRQoL, ranging from 0 (never problems) to 4 (almost always problems). Three summary measures that are derived are Total scale score, Physical health summary score and Psychosocial health summary score (25). The internal consistency, Cronbach's alpha (α) ranges between 0.68 to 0.90, and the test-retest reliability, Interclass Correlation Coefficient (ICC) ranges between 0.67 to 0.82 (26). Moreover, also the reliability and validity of both the English and Dutch version of the PedsQL 4.0 have been reported as sufficient (12).

The Impact of Weight on Quality of Life-Kids (IWQOL-Kids)

The IWQOL-Kids is a disease-specific HRQoL questionnaire, which is the best available questionnaire applicable to assess the weight-specific HRQoL of children with obesity and is more sensitive to changes in HRQoL resulting from lifestyle interventions (12). This questionnaire is a validated tool for adolescents aged 11-19 years old (27). This questionnaire consists of 27 items, divided into 4 domains. These domains comprise: physical comfort, body esteem, social life and family relations. All items use phrasing in the context of their size, starting with the words 'Because of my weight...'. The questions have a recall period of one week, with five possible answers, ranging from 'always' [1] to 'never' [5]. Both the Total scale and subscales range from 0 to 100, with a higher score indicating a better HRQoL (28). The psychometric properties of the English version of the IWQOL-Kids were determined in the study of Kolotkin *et al.*, which concluded that the IWQOL-Kids is both a valid and responsive questionnaire to assess the HRQoL of children with obesity, with α ranging between 0.88 to 0.95. The ICC varies between 0.32 to 0.65 (28).

Synthesis of the results

Summary measure of interest was the change in child-reported Total, Physical and Psychosocial HRQoL, assessed by the PedsQL 4.0, after children with overweight/obesity participated in a lifestyle intervention compared to the control group. The HRQoL was reported by using means and standard deviations in the articles. If an article described the HRQoL by using median and interquartile intervals (IQI) then, if the data were reported as not skewed, median and means were

assumed as equal. Whereas the IQI were assumed as being approximately 1.35 standard deviations (29). This statistical analysis used Review Manager 5.3 to compute the results. The results were visualized by using a Forest plot. Effect sizes were computed as mean differences and expressed the difference in mean change between HRQoL of children after they participated in lifestyle interventions compared to the control group. To ensure that studies with larger samples were given higher weight, each effect size was weighted by the inverse of its variance. A random-effects model was applied to correct for variability in effect sizes caused by the difference in lifestyle intervention that was designed and used, differences between study populations and sampling error (30).

The extent of heterogeneity of results of the included articles was determined by using Higgins I^2 (31). This methodological measure was based on Cochrane's Q and degrees of freedom (df). Higgins I^2 represents the proportion of variability in an effect that is caused by heterogeneity instead of sampling error. The higher the Higgins I^2 , the higher the extent of heterogeneity between results of interest from the articles. The null hypothesis states that all studies are establishing the same effect (32). The attached value to Higgins I^2 depends on the magnitude and direction of effect (I) and the strength of the evidence for heterogeneity (p-value of Cochrane's Q and confidence interval of I^2) (31). For this meta-analysis the Higgins I^2 was interpreted as following, 0-40% heterogeneity might not be important, 30-60% may represent moderate heterogeneity, 50-90% may represent substantial heterogeneity and 75-100% considerable heterogeneity (31).

The test for overall effect (Z) addresses the weighted average effect size. For this meta-analysis this value represented, whether RCTs offering lifestyle interventions significantly improved the HRQoL of children with overweight/obesity. The null hypothesis states that there is on average no effect of lifestyle interventions on the HRQoL of children with overweight/obesity (33).

Study quality assessment

All included articles were evaluated for risk of bias. The Cochrane Collaboration tool was used to weigh the quality of articles in which an RCT study design was applied, and to determine the value of the reported results of that article. This tool was used to assess the occurrence of selection bias, performance bias, detection bias, attrition bias and reporting bias in the included articles (34). If the authors of the article had met a quality criterion in their research, the risk of bias was assumed to be 'low'. If authors had not met a quality criterion in their research, the risk of bias was assumed to be 'high'. In case a quality criterion was not clearly described in the article, the risk of bias was assumed to be 'unclear' (34).

Risk of bias of each article was determined by one researcher (AH). To prevent the occurrence of bias during the evaluation of a quality criterion, considerations for this assessment of the quality criterion were justified and discussed with another researcher (JH).

Results

Study selection

How the studies were selected can be found in figure 2 (for full-size image see Appendix 2). After the literature search in PubMed, 460 articles were found. Five extra articles were found through an additional search in Google Scholar and previously conducted searches in PubMed. First articles that were not written in English were excluded. The abstracts of the remaining 456 articles were reviewed. 27 studies were considered relevant, and subsequently, those complete articles were read. Of the 27 studies, 20 studies were excluded because of the following reasons: HRQoL was only used for establishing the cost-effectiveness and Quality Adjusted Life Years (QALYs), only focused on adults, used parent-proxy HRQoL questionnaires, lacked a measurement postintervention/follow-up, only focused on the caregivers, lacked information about the included population, only used descriptive improvement of the HRQoL or lacked a control group. Eventually, seven studies were included in this meta-analysis for qualitative and quantitative synthesis of results.

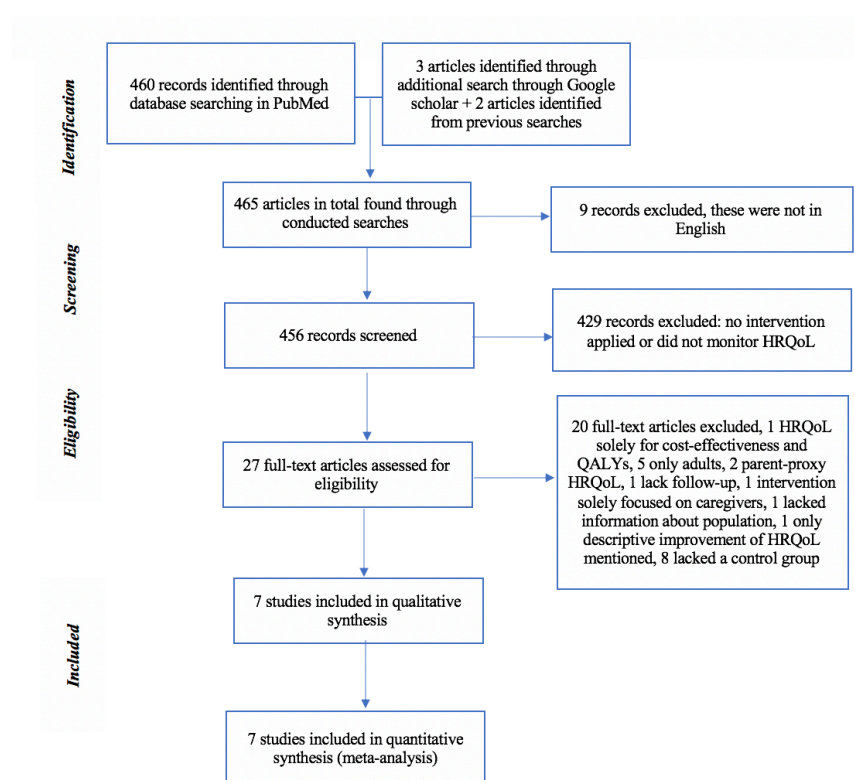


Figure 2. Flow of information through different phases of this meta-analysis

Study characteristics

The extracted data from these articles can be found in Table 1. For a summary of the components of the individual lifestyle interventions applied in the included studies, see Appendix 3. The final included studies were published between 2008 and 2019. Four studies (58%) were conducted in Europe (35-38), two studies (28%) were conducted in Middle East (39, 40), and one study (14%) was conducted in Australia (41). All studies included both boys and girls and the HRQoL was measured in all studies by using the PedsQL 4.0., except for Bonham *et al.*, which only applied the disease-specific IWQOL-Kids (41). In every study, the HRQoL was measured at baseline, with either a reassessment of the HRQoL directly after the intervention was completed and/or at follow-up. The follow-up periods varied between 6 months and 18 months. The number of included participants within the included RCTs varied between 40 and 130 participants. The age range of included participants with overweight/obesity varied between 5 and 18 years old, with a mean age varying between 9.1 years old and 16.2 years old. Three of the seven studies focused on both children having obesity and children with overweight (35, 38, 40). Of the remaining four studies, three studies only focused on children with obesity (36, 37, 39). Bonham *et al.* was the only article that included only children with overweight in their lifestyle intervention (41).

All articles except Hughes *et al.* described the HRQoL of children with obesity at baseline and post-intervention by using means and standard deviations. Hughes *et al.* described the HRQoL by using medians and interquartile intervals (IQI) (35).

Results of individual studies

All the included studies used a different lifestyle intervention to change behaviour, to improve the weight status and to increase the HRQoL in children with overweight/obesity. However, the aspects the lifestyle interventions are composed of comparable components. All the lifestyle interventions of the included articles aimed at improving diet and physical activity supported by behaviour change techniques. The lifestyle intervention of Hughes *et al.* also incorporated family aspects (35). Two studies included psychological aspects into the lifestyle intervention, namely Miri *et al.* and Yackobivitch-Gavan *et al.* (39, 40)

After lifestyle interventions were applied, significant improvements in Total HRQoL were reported by Miri *et al.* and Yackobovitch-Gavan *et al.* (39, 40). Other studies did not report significant improvements in Total HRQoL. However, in these studies significant improvements were observed in the physical/psychosocial scale or subdomains of the PedsQL 4.0, except for Wafa *et al.* and Hughes *et al.*, which were the only articles that did not report significant improvements in any of the subdomains or physical/psychosocial scale of the PedsQL 4.0 (35, 36). Hofsteenge *et al.* and Miri *et al.* both reported a significant improvement on the Physical summary scale during reassessment at follow-up (37, 40). Significant improvements in the Physical summary scale directly after completing

Table 1: Characteristics of the included articles

Author, publication year	Origin of population	Study design	Duration of intervention	Aspect of lifestyle intervention	Team	Follow-up period after completion of intervention	N	Overweight or obesity	Stratified sex	Age range (mean, sd)	PROM
Yackobovitch-Gavan M <i>et al.</i> 2008 (39)	Israel	RCT	12-week	Healthy dietary behaviour, PA	Dietitian, psychologist	Post-intervention	40	OB	No	12 – 18 (14.3; 1.7)	PedsQL 4.0
Hughes AR <i>et al.</i> 2008 (35)	Scotland	RCT	26 weeks	Healthy dietary behaviour, PA	Dietitian	Post-intervention	134	OW + OB	No	5 -11 (9.1; 1.7)	PedsQL 4.0
Wafa SW <i>et al.</i> 2010 (36)	UK	RCT	26-week	Healthy dietary behaviour, PA	Clinical psychologist, dietitian	6-month*	79	OB	No	7 – 11 (9.8; 1.5)	PedsQL 4.0
Hofsteenge G <i>et al.</i> 2013 (37)	The Netherlands	RCT	3 months	Healthy dietary behaviour, PA	Dietician, psychologist and paediatric endocrinologist	6-month, 18-month	95	OB	No	11 – 18 (14.5; 1.7)	PedsQL 4.0
Bonham MP <i>et al.</i> 2017 (41)	Australia	RCT	12 weeks	PA, healthy dietary behaviour	Dietitian at Jenny Craig	Post-intervention	130	OW	No	13 -17 (15.3; 1.3)	IWQOL-Kids
Freira S <i>et al.</i> 2018 (38)	Portugal	RCT	3 months	PA, healthy dietary behaviour	Pediatrician, dietitian and PA teachers	Post-intervention	97	OW + OB	No	(16.2; 1.49)	PedsQL 4.0
Miri SF <i>et al.</i> 2019 (40)	Iran	RCT	6 weeks	Healthy dietary behaviour, PA, CBT	2 therapists with 5-20 years' experience	6 months	110	OW + OB	No	13 -18 (14.64; 1.69)	PedsQL 4.0

*Physical activity (PA), Randomized Controlled Trial (RCT), *after intervention was completed*

a lifestyle intervention was reported by Yackobovitch-Gavan *et al.* (39). Freira *et al.*, in accordance with Yackobovitch-Gavan *et al.*, reported significant improvements in Psychosocial summary scale (38, 39). Hofsteenge *et al.* was the only article that reported significant improvements on the School functioning subdomain (37). Besides significant improvements in Total HRQoL, Miri *et al.* and Yackobovitch-Gavan *et al.*, both reported significant improvements on the Emotional subdomain (39, 40). None of the included articles reported significant improvements on the Social functioning subdomain of the PedsQL 4.0 after children with overweight and/or obesity participated in lifestyle interventions.

Synthesis of results

The seven RCTs provided 27 estimates of the effect of a lifestyle intervention on the self-reported HRQoL of children with overweight/obesity. Three of the seven included articles compared baseline HRQoL with the HRQoL of children with overweight/obesity directly after they had participated in a lifestyle intervention (35, 38, 39). Directly after the lifestyle intervention was completed there was no homogenous reported change in the Total, Physical and Psychosocial scale HRQoL, measured by the PedsQL 4.0, among the included articles ($p < 0.05$). Nor, there was a significant reported improvement in these HRQoL scales after children with overweight/obesity participated in lifestyle interventions (Table 2).

Three of the seven included articles reported the effect of a lifestyle intervention on the HRQoL, measured by the PedsQL 4.0, at baseline compared to a reassessment at follow-up period (36, 37, 40). There was no homogeneous result reported on the Psychosocial score HRQoL ($p < 0.05$), and moreover, there was no overall significant improvement at follow-up on this scale after children with overweight/obesity participated in lifestyle interventions. However, at follow-up after the children with overweight/obesity participated in lifestyle interventions, homogeneous results in the Total and Physical HRQoL PedsQL 4.0 scales were reported. However, there were no significant improvements in the HRQoL on these scales. Nevertheless, the 95% Confidence Intervals (CI) did report that there was a small improvement on the Total score and Physical score HRQoL after children with overweight/obesity participated in lifestyle interventions.

Subsequently, stratification between the post-intervention and the follow-up effect of lifestyle interventions on the HRQoL of children with overweight/obesity was disregarded. Thereafter, only the effect of lifestyle interventions on the HRQoL of children with obesity was analysed (36, 37, 39). Articles that reviewed children with obesity homogeneously reported results on all three the scales of the PedsQL 4.0. There was a significant improvement reported on the Physical scale of HRQoL PedsQL 4.0, whereas there were no significant improvements reported on the Psychosocial and Total HRQoL PedsQL 4.0 scales.

In the majority of the Forest plots, no individual study had a disproportionately large effect on the pooled estimates. In the Forest plot visualizing the effect of lifestyle interventions on the Physical

scale HRQoL of children with obesity after participating in lifestyle interventions, Hofsteenge *et al.* had a large effect (70.6%) on the Weighted Mean Difference (WMD). See Figure 3 for the visualization of the distribution around the WMD of the homogenous effect of lifestyle interventions on the HRQoL of children with overweight/obesity and the weight of the individual articles. The Forest plots of both the heterogeneous and homogeneous WMD are shown in Appendix 4.

One of the included articles also studied the effect of a lifestyle intervention on HRQoL assessed by IWQOL-Kids (41). Bonham *et al.* only concluded in the article that Total disease-specific HRQoL, measured by the IWQOL-Kids, significantly improved over time. In the article by Bonham *et al.* the effect of the lifestyle intervention on the weight-related HRQoL subdomains was not reported (41).

Table 2: Pooled estimates of the weighted mean difference (WMD) in Total, Physical, Psychosocial scale HRQoL (PedsQL 4.0) preintervention compared to post-intervention in children with obesity

Comparison	N	WMD	I ² (%)	P-value (I ²)	Z	P-value (Z)
Post-intervention						
Total score HRQoL	3	3.21 [-6.56, 12.98]	90%	<0.0001*	0.64	0.52
Physical score HRQoL	3	3.60 [-5.01, 12.21]	75%	0.02*	0.82	0.41
Psychosocial score HRQoL	3	2.99 [-6.60, 12.59]	89%	<0.001*	0.61	0.54
Follow-up						
Total score HRQoL	3	4.67 [0.01, 9.32]	62%	0.07	1.97	0.05
Physical score HRQoL	3	4.68 [0.01, 9.34]	62%	0.07	1.96	0.05
Psychosocial score HRQoL	3	4.11 [-1.25, 9.46]	71%	0.03*	1.50	0.13
Children or adolescents with obesity						
Total score HRQoL	3	2.34 [-1.17, 5.86]	11%	0.33	1.31	0.19
Physical score HRQoL	3	4.67 [0.58, 8.76]	0%	0.94	2.24	0.03*
Psychosocial score HRQoL	3	1.85 [-2.76, 6.46]	51%	0.13	0.79	0.43

*Significant ($P < 0.05$), WMD (Weighted Mean Difference), N (included articles)

Figure 3: Forest plots of homogeneous reported changes in HRQoL (PedsQL 4.0) of children with overweight/obesity after participating in a lifestyle intervention

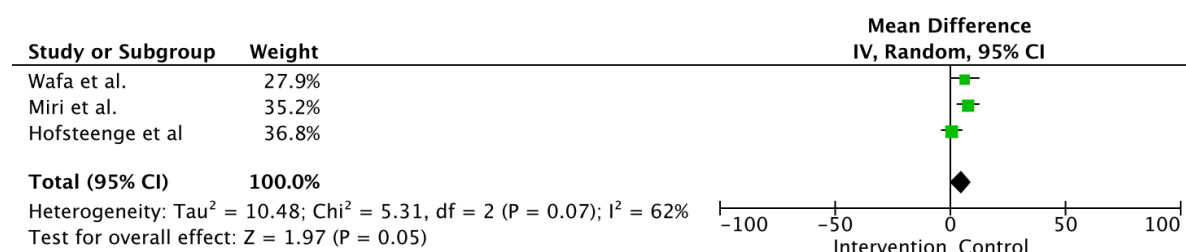


Figure 3A: Forest plot Total HRQoL at follow-up

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

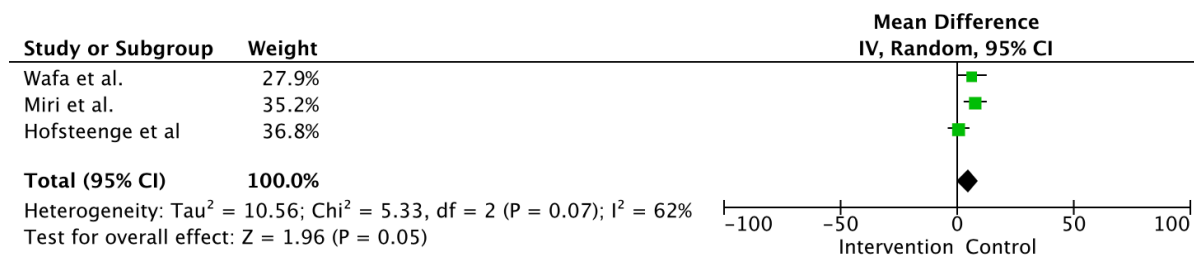


Figure 3B: Forest plot Physical scale HRQoL at follow-up

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

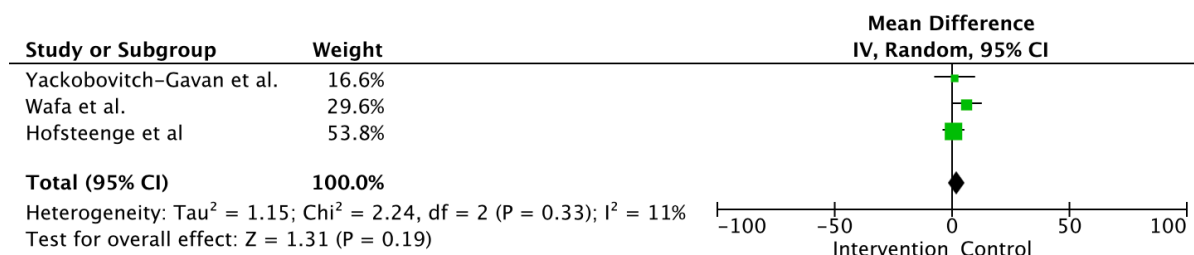


Figure 3C: Forest plot Total HRQoL children with obesity

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

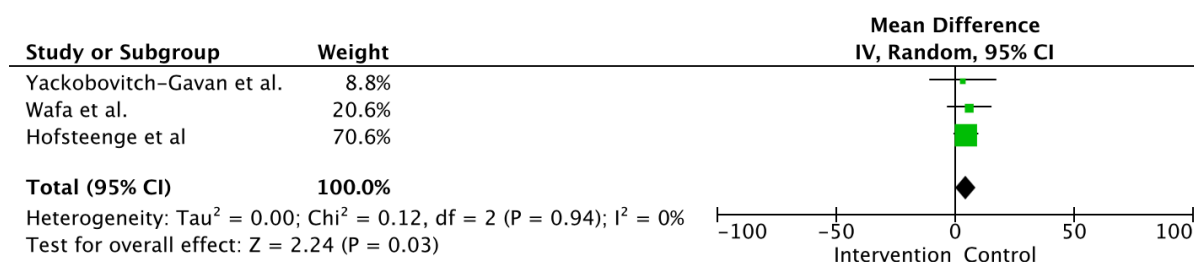


Figure 3D: Forest plot Physical scale HRQoL children with obesity

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

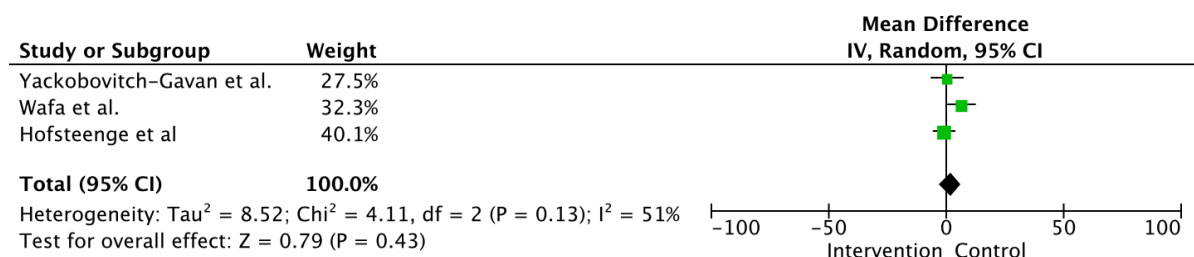


Figure 3E: Forest plot Psychosocial scale HRQoL children with obesity

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

Risk of bias within studies

This meta-analysis included articles which applied RCT as study design. The risk of bias of the included RCTs was established by using the Cochrane risk of bias tool, which is listed in table 3.

During the quality assessment, only Yackobovitch-Gavan *et al.* did not describe the method used to establish random sequence generation, which increased the risk of selection bias (39). The randomization of the groups in only Hofsteenge *et al.* was non-random, it was based on sex and age group, which increased the risk of selection bias (37). In all studies, the blinding of participants and personnel was unfeasible due to the use of lifestyle interventions. This accounts for a high risk of performance bias in all the included RCTs (35-41). For reporting bias, four of the seven included studies did not report all the results of the outcomes that were predefined (36, 38-40). Only Hofsteenge *et al.*, Hughes *et al.* and Bonham *et al.* reported and evaluated all the predefined primary and secondary outcomes (35, 37, 41). Considering other biases, four out of seven included studies were not clear about how the research was funded (36, 39-41). Hofsteenge *et al.* and Freira *et al.* were the only articles which had stated that the funding did not influence the interests of the study and personnel (37, 38). Hughes *et al.* also reported that procedures, such as peer review, were performed to prevent conflict of interest from occurring (35).

Table 3: The Cochrane Collaboration's tool for assessing risk of bias of Randomized Controlled Trials (RCTs)

Domain		Hofsteenge <i>et al.</i> 2013	Miri <i>et al.</i> 2019	Freira <i>et al.</i> 2018	Wafa <i>et al.</i> 2010	Yackobovitch- Gavan <i>et al.</i> 2008	Hughes <i>et al.</i> 2008	Bonham <i>et al.</i> 2017
Selection bias	Random sequence generation							
	Allocation concealment							
Performance bias								
Detection bias								
Attrition bias								
Reporting bias								
Other bias								

Green (Low risk of bias), Orange (Unclear risk of bias), Red (High risk of bias)

Discussion

Findings of this meta-analysis

Worldwide, there is an increase in the prevalence of children with obesity. Having obesity has a negative impact on both the physical and psychosocial health of children, and implicit a negative effect on the Health-Related Quality of Life (HRQoL). These effects of obesity on the HRQoL of these children can be measured by using PROMs. This meta-analysis assessed the effects of lifestyle interventions on the self-reported HRQoL of children with obesity. Due to a lack of includable articles, also articles were included which offered lifestyle interventions to children with overweight. Overall, there was a significant improvement in the Physical score HRQoL, measured by the PedsQL 4.0, when only articles in which children with obesity participated in lifestyle interventions were included. The 95% Confidence Intervals of the Total and Physical score HRQoL of children with overweight/obesity that participated in lifestyle interventions with reassessment at follow-up suggest that lifestyle interventions might improve these scales of the HRQoL on the long-term.

Comparison to other studies

The findings of this meta-analysis are in accordance with the findings from a systematic review by Tsiros *et al.*, which assumed that weight-loss established through interventions might have a positive influence on the HRQoL. An association was not definitive, as only 2 of the 7 included studies within this study from Tsiros *et al.* were RCTs (10).

Furthermore, findings from other studies suggest that after weight-loss is established through interventions, the Physical functioning scale improves more quickly, whereas, the improvements in the Psychosocial scale of the PedsQL 4.0 is hypothesized to be more resistive (42-44). According to Fullerton *et al.* physical functioning is more responsive to improvements from weight-loss, which is established through interventions compared to the psychosocial subdomains of the PedsQL 4.0 (42). These previous findings are in accordance with the findings of this study. As this meta-analysis reported a homogeneous significant improvement in the Physical score HRQoL of the PedsQL 4.0 when only studies which offered lifestyle interventions to children with obesity were included.

Reassessment of the HRQoL of children with overweight/obesity at follow-up almost showed a significant improvement in the Total and Physical HRQoL. This finding is in accordance with a meta-analysis from Ligthart *et al.* which also showed an almost significant long-term improvement of the HRQoL (21). According to Varni *et al.* improvement of 4.50 on the PedsQL 4.0 is considered clinically relevant (45). As this meta-analysis showed, at follow-up, an improvement of the Total and Physical HRQoL of 4.67 and 4.68, this can be viewed as clinically significant improvements.

All lifestyle interventions were composed of physical activity, eating behaviour and behaviour change aspects. Two RCTs also included psychological aspects in the lifestyle interventions, which were also the two RCTs that reported significant improvements in the Psychosocial quality of life after children with overweight/obesity participated in lifestyle interventions (39, 40). This finding is similar

with findings from Griffiths *et al.*, Murray *et al.* and Lowry *et al.*. These articles postulated that to improve Psychosocial scale of the HRQoL, lifestyle interventions should comprise psychological aspects (18, 20, 46). As the Psychosocial scale of the PedsQL 4.0 is part of the Total scale of the PedsQL 4.0, including psychological aspects in lifestyle interventions increases the likelihood of improving the HRQoL of children with overweight/obesity participating in lifestyle interventions.

Strength and limitations

This meta-analysis has several strengths. First, this article covered the effects of lifestyle interventions on both the generic and disease-specific reported HRQoL of children with overweight/obesity. The generic HRQoL PROMs are used to compare the HRQoL of children having different diseases. Both the generic and disease-specific HRQoL PROMs are used to assess the improvement of the HRQoL after participating in lifestyle interventions. The disease-specific HRQoL PROMs are more appropriate to measure the latter mentioned effect. Second, only studies were included when these addressed the best available and the most applicable generic and disease-specific HRQoL questionnaires which are used nowadays in the Dutch treating practice for children with obesity, namely the PedsQL 4.0 and the IWQOL-Kids. Therefore, the findings from this article contribute to more insights for leads to improve the Dutch treating practice for children with obesity, to eventually improve the combined lifestyle-intervention approach. Third, this meta-analysis included 7 RCTs with all the studies applying different lifestyle interventions. Nevertheless, most lifestyle interventions aimed at improving physical activity and diet supported by behaviour change techniques. Since the lifestyle interventions have similar aims, the effects of these lifestyle interventions on the HRQoL of children with overweight/obesity are comparable.

This meta-analysis has several limitations. Only one article was included that applied the disease-specific questionnaire (41). Therefore, in this meta-analysis, the effects of lifestyle interventions on the disease-specific measured HRQoL of children with obesity was under-analysed. Most included studies only used the generic PROM, PedsQL 4.0, to assess the effects of lifestyle interventions on the HRQoL. Due to having only seven includable RCTs and not all the RCTs reported changes in the subdomains of the PedsQL 4.0, the effects of lifestyle interventions on these subdomains of the HRQoL was not analysed. This meta-analysis only focused on the three scales of the HRQoL measured by the PedsQL 4.0, namely the Total, Physical and Psychosocial scales. Moreover, the amount of included RCTs in the statistic procedures was limited. Three of the seven studies included children with obesity in their lifestyle interventions, whereas the other four studies included children with obesity/overweight or solely children with overweight. When only the studies that included children with obesity were analysed the effects became more pronounced. Furthermore, three of the seven RCTs measured the HRQoL at baseline and directly after the lifestyle intervention was completed. The other three studies that addressed the PedsQL 4.0 used a follow-up period. By having a follow-up period, the long-term effect on the improvements of HRQoL established through

lifestyle interventions can be assessed. As only three articles had a follow-up reassessment, the long-term effect of lifestyle interventions on the HRQoL of children with obesity remains uncertain. Information about the long-term effects are of importance as one of the main goals of the Dutch treating practice for children with obesity is to establish health gains on the long-term (5). This meta-analysis only included RCTs in which child-reported HRQoL PROMs were applied. Parents tend to report, by using parent-proxy HRQoL PROMs, a more detrimental impact of their children being overweight/obese on the HRQoL of their children compared to child-reported impact (47). Multiple hypotheses are stated around these observed disparities. Having a child with overweight/obesity might evoke higher levels of stress and concerns, which could explain the underestimated HRQoL by the parents. This underestimation of the HRQoL by parents is higher among younger groups of overweight/obese children. As primarily young children are still developing their cognitive skills, a lack of understanding in younger children could be an explanation for the underestimated HRQoL. Suggestively, parent-reported HRQoL of their children with overweight/obesity might represent the impact of overweight/obesity better than children do themselves. Hence, it is recommended to assess the HRQoL of children with overweight/obesity both by using child-reported and parent-proxy HRQoL PROMs (47). Lastly, the findings of this meta-analysis should be interpreted with caution as the search for relevant and applicable articles was limited to PubMed with an additional limited search in Google Scholar.

Future research and Implications

Due to the lack of sufficient articles addressing the effects of lifestyle interventions on the self-reported HRQoL of children with obesity, more research should be conducted with the eventual aim to clarify the aforementioned association. Also, more knowledge should be acquired about the effect of lifestyle interventions on the subdomains of the HRQoL. Another aim is also to gain more understanding about the long-term effect of lifestyle interventions on the HRQoL of children with obesity. For future research, the searches should be performed through multiple databases. This will improve the number of relevant articles. Hence the findings will be more likely to represent the effect of lifestyle interventions on the HRQoL of children with obesity.

In contemporary research of PROMs in the treatment of children with obesity, PROMs are used as a measuring tool to assess the HRQoL. However, in future research, PROMs can also be used to tailor the treatment for children with obesity. The Care for Obesity project, housed at VU University in Amsterdam, aims to acquire more knowledge about the contribution of PROMs to measure the HRQoL of children with obesity. This project stresses the importance of conducting more research, with the eventual aim to tailor the treatment for the individual needs of children with obesity (12). In accordance with this goal, a systematic review conducted in 2018 concluded that researches that studied the use of PROMs to adjust and individualize the care for people with obesity are not yet performed. This review stated that an intervention which includes routinely measuring and

subsequently reviewing the HRQoL by using PROMs to treat cancer improves the effectiveness of the treatment and also improves the communication between the patient and the therapist. Therefore, it is hypothesized that routinely measuring the HRQoL can be used as a novel method to improve outcomes in the treatment of children with obesity (48). Research towards the effects of routinely measuring the HRQoL by using PROMs and subsequently tailoring the treatment for children with obesity should be performed. These researches should not only address the effects on the HRQoL directly after the treatment is completed but should also include the long-term effects on the HRQoL.

Nowadays, in the Dutch treating practice combined lifestyle interventions are used to improve among other the HRQoL of children with obesity. The findings of this meta-analysis and previous findings support the assumption that lifestyle interventions do only improve the physical HRQoL of children with obesity (10, 42-44). By improving the psychosocial aspects of lifestyle interventions, these improved lifestyle interventions might be able also to improve the psychosocial HRQoL of children with obesity in the near future. Since lifestyle interventions comprising psychological aspects did report significant improvements on the Total and Psychosocial scale of the HRQoL PedsQL 4.0 (39, 40).

Conclusion

This meta-analysis provides further evidence to support that lifestyle interventions have the potential to improve Physical functioning domain of the HRQoL in children with obesity. Further research is necessary to assess the effects of lifestyle interventions on the other (sub)domains of the PedsQL 4.0 of children with obesity. Future research is also needed to analyse further the long-term effects of lifestyle interventions on the HRQoL, as reassessment at follow-up showed an almost significant improvement in Total and Physical HRQoL after children with overweight/obesity participated in lifestyle interventions. This research can contribute to improving the current Dutch treating practice for children with obesity, with the eventual aim to improve all the scales/subdomains of the HRQoL measured by the PedsQL 4.0.

Words: 6460

Appendix 1: Search Strategy PubMed

Search strategy used in PubMed (performed on 22 March 2020, 598 articles found)

Population: Children (0-18 years old)/parents/carers/provided health care/adults

"Parents"[Mesh] OR "Health Personnel"[Mesh:NoExp] OR "Allied Health Personnel"[Mesh] OR "Nurses"[Mesh] OR "Physicians"[Mesh] OR "Nutritionists"[Mesh] OR "Caregivers"[Mesh] OR "Diet Therapy"[Mesh] OR "diet therapy" [Subheading] OR "Exercise"[Mesh] OR "Exercise Therapy"[Mesh] OR "Sports"[Mesh] OR "Healthy Lifestyle"[Mesh] OR "Psychotherapy"[Mesh] OR "Adult"[Mesh:NoExp] OR "Young Adult"[Mesh] OR child*[tw] OR adolescen*[tw] OR pediatric*[tw] OR paediatric*[tw] OR pube*[tw] OR juvenil*[tw] OR school*[tw] OR toddler*[tiab] OR youngster*[tiab] OR preschool*[tiab] OR kindergart*[tiab] OR kid[tiab] OR kids[tiab] OR playgroup*[tiab] OR playgroup*[tiab] OR playschool*[tiab] OR prepube*[tiab] OR preadolescenc*[tiab] OR junior high*[tiab] OR highschool*[tiab] OR senior high[tiab] OR young people*[tiab] OR minors[tiab] OR parent*[tiab] OR stepparent*[tiab] OR father*[tiab] OR mother*[tiab] OR health care provider*[tiab] OR healthcare provider*[tiab] OR healthcare worker*[tiab] OR health care worker*[tiab] OR health personnel*[tiab] OR health professional*[tiab] OR healthcare assistant*[tiab] OR healthcare support worker*[tiab] OR paramedic*[tiab] OR health worker*[tiab] OR caregiver*[tiab] OR carers[tiab] OR carer[tiab] OR care giver*[tiab] OR nurses[tiab] OR nurse[tiab] OR nursing*[tiab] OR nutritionist*[tiab] OR dietician*[tiab] OR dietitian*[tiab] OR physician*[tiab] OR general practitioner*[tiab] OR doctor[tiab] OR doctors[tiab] OR diet therap*[tiab] OR dietary modification*[tiab] OR diet modification*[tiab] OR exercis*[tiab] OR physical activit*[tiab] OR running[tiab] OR walking[tiab] OR swimming[tiab] OR jogging[tiab] OR sport[tiab] OR sports[tiab] OR healthy life style*[tiab] OR healthy lifestyle*[tiab] OR healthy diet*[tiab] OR healthy eating[tiab] OR healthy nutrition[tiab] OR prudent diet*[tiab] OR psychotherap*[tiab] OR conditioning therap*[tiab] OR behavior modification*[tiab] OR behaviour modification*[tiab] OR behavior therap*[tiab] OR behaviour therap*[tiab] OR behavioral therap*[tiab] OR behavioural therap*[tiab] OR cognitive therap*[tiab] OR cognitive psychotherap*[tiab] OR adult*[tiab] OR grown up*[tiab] OR grownup*[tiab]

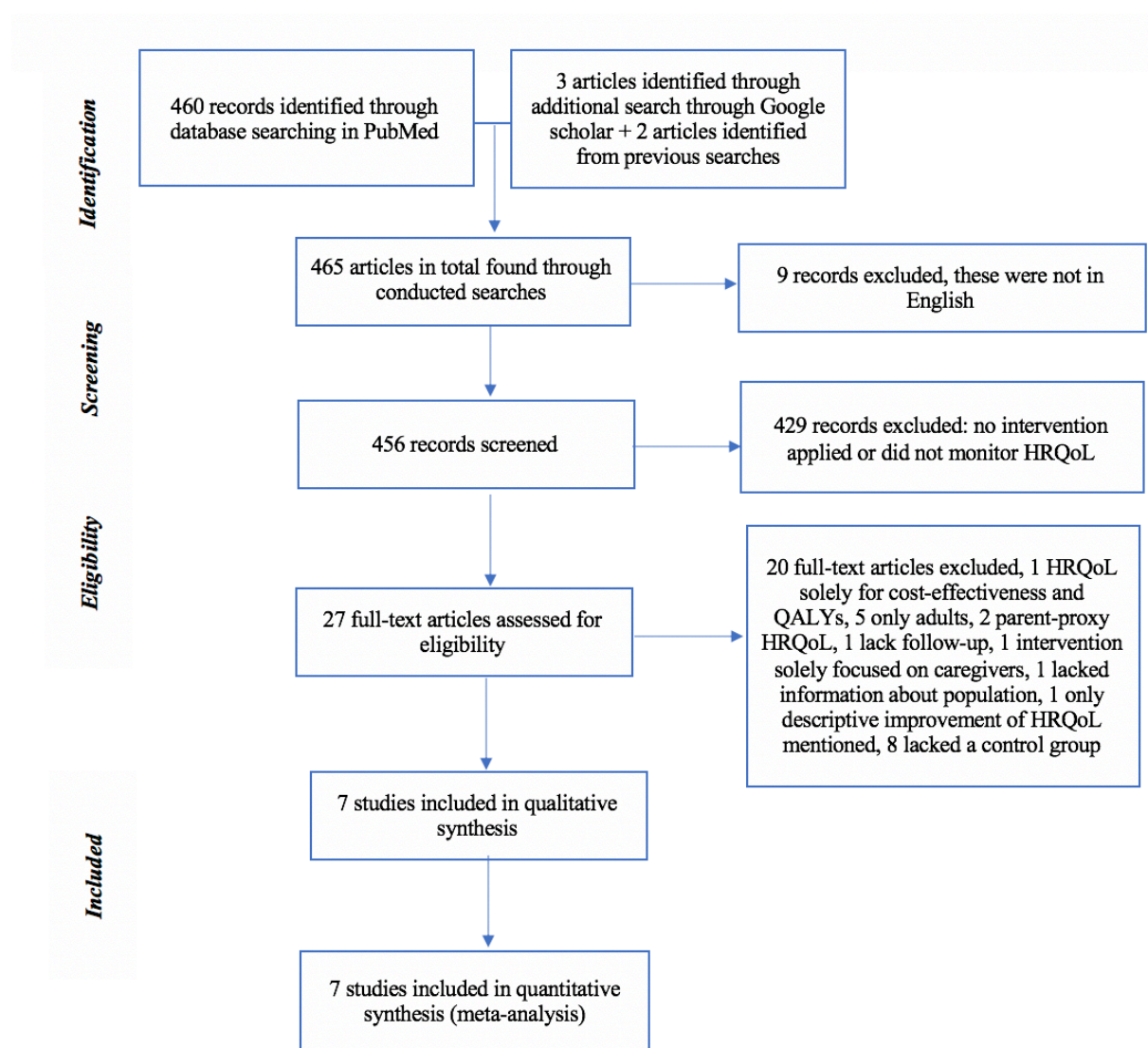
Problem: obesity/overweight

"Overweight"[Mesh] OR obese*[tiab] OR obesit*[tiab] OR overweight*[tiab]

Intervention: PROMs

"Patient Reported Outcome Measures"[Mesh] OR pediatric quality of life inventor*[tiab] OR paediatric quality of life inventor*[tiab] OR pedsq*[tiab] OR iwqol*[tiab] OR "impact of weight on quality of life lite iwqol lite"[tiab] OR "impact of weight on quality of life lite questionnaire"[tiab] OR "impact of weight on quality of life"[tiab] OR sizing them up[tiab] OR sizing me up[tiab] OR euroqol OR (euro[tiab] AND quality of life[tiab]) OR european quality of life[tiab] OR kidscreen*[tiab] OR kid screen*[tiab] OR patient reported outcome*[tiab] OR patient outcome assessment*[tiab] OR patient centered outcome*[tiab] OR patient centred outcome*[tiab] OR patient outcomes assessment*[tiab]

Appendix 2: Flow of information through different phases of this meta-analysis



Appendix 3: Characteristics of the applied lifestyle interventions of the included articles

Author, publication year	Name of lifestyle intervention	Intensity of intervention	Description of intervention	Aim of intervention
Yackobovitch-Gavan M <i>et al.</i> 2008 (39)	Weight-loss diets with different macronutrient compositions	3 months in which 3 different diets were given (depending on intervention group) combined with weekly sessions with dietitian and psychologist	3 different diets were given in order to increase compliance to the diet regiment. General recommendation to engage in regular physical activity.	To increase the HRQoL of the participants.
Quinlan NP <i>et al.</i> 2008 (49)	Weight-loss camp for overweight youth	Residential camp program ranging from 1 – 8 weeks	Nutritionally balanced 1800 kcal/day diet of three meals and two snacks. Nutrition classes were held 2 weekly and cooking classes 1 a week. Physical activities consisted of daily. Psychosocial component consisted of weekly 1-hour sessions (covering issues as self-esteem, body esteem, body image, emotional eating, teasing, family and peer support)	To establish weight reduction of overweight children and improve their HRQoL.
Hughes AR <i>et al.</i> 2008 (35)	Scottish Childhood Treatment Trial (SCOTT)	8 appointments, 5 hours over 6 months.	Modified traffic light diet approach, aim to increase physical activity to 1 hour/day, aims to reduce sedentary behaviour to less than 2 hours/day, to explore motivation, goals were set by the child and lifestyle self-monitoring was used throughout the program	Family-centred counselling and behavioural strategies to modify diet, physical activity and sedentary behaviour.
Wafa SW <i>et al.</i> 2010 (36)	Malaysian Childhood Obesity Treatment Trial (MASCOT)	Low intensity, 8 parent-centred group-sessions (8-hour contact time) delivered over a period of 26 weeks led by dietitian	Sessions of dietitian was supported by clinical psychologist who directly provided support to the parents.	Changing the behaviours of children with obesity, sedentary behaviour, diet and physical activity.
Cronk E <i>et al.</i> 2011 (50)	Sessions based on 'prevention plus' strategies	6 core sessions during 6 weeks to all families. With monthly coaching and supplemental activities offered through 12-month post-enrolment.	Sessions were family-centred and child-focused. Emphasis on healthy weight, family and/or self-selected goals and supplemental activities and education including cooking or shopping lessons and fitness activities.	To increase among others fruit and vegetable intake.
Hofsteenge G <i>et al.</i> 2013 (37)	Go4it multidisciplinary group treatment	7 sessions with 2-week interval, 2 parallel sessions for parents, 4 booster group sessions for adolescents 6, 14, 26 and 36 weeks after intervention	Education on healthy dietary behaviour, screen behaviour and physical activity	To encourage the adolescents to maintain and/or further improve their energy balance behaviour, discuss problems and answers.
Poeta LS <i>et al.</i> 2013 (51)	Interdisciplinary intervention	Counselling for 12-consecutive weeks. Nutritional guidelines were given 1 session/week, exercises performed 3 sessions/week. Each session was 60-minutes, totalling 36 sessions.	Physical exercises with recreational activities, and nutritional counselling to children and parents	Nutritional counselling aimed at adopting healthier eating habits.
Bock DE <i>et al.</i> 2014 (52)	HIP Kids	1-year intervention, initial 3-month intensive phase followed by a 9 month maintenance phase. Each of the 15 sessions was 90 minutes.	Intensive phase with bi-weekly individual counselling sessions. Maintenance phase with alternating monthly individual or group sessions. Session comprised 30 minutes educational blocks	To develop strategies for attaining short and long-term goals.

			focusing on nutrition, physical activity and psychosocial and behavioural aspects. Family involvement was central.	
Engebretsen S <i>et al.</i> 2016 (53)	ACT! (Actively Changing Together)	90 minutes classes for 12 weeks	Focuses on lifestyle modification, healthy eating, increased physical activity and behaviour modification. Classes consisted of a mixture of separate and combined activities for youth and the co-enrolled parents, 60 minutes together performing physical activity and learning healthy living topics, followed by 30 minutes spent apart.	Children learning physical activity and healthy living topics. Parents learned and improved their parenting skills, nutritional decision-making, troubleshooting barriers to healthy living and reducing sedentary time at home.
Morano M <i>et al.</i> 2016 (54)	Multicomponent, school-initiated obesity intervention	2 times 2-hour sessions per week of in- and outdoor activities. 1-week activity diary for adherence to recommended lifestyle changes, 7-day food diary	Incorporates school- and family-based components, nutritional education, fun-type skill-learning, physical activities and exercise training	To increase perceived physical competence which could lead to increased exercise adherence and promotion of the health benefits associated with it.
Bonham MP <i>et al.</i> 2017 (41)	JenMe program	12- week face-to-face program	One-on-one sessions with an in-house trained consultant that covers dietary and behavioural education as well as progress monitoring. Met with a consultant on a weekly basis for 13 consecutive sessions.	The effects of a structured short-term weight management program delivered by nonhealth professionals.
Freira S <i>et al.</i> 2018 (38)	IMAGINE study	30-minutes face-to-face counselling (motivational interviewing), physical exercise plan included 60 minutes daily of moderate to vigorous activity.	Individualized face-to-face counselling about lifestyle with paediatrician as interviewer. Conventional counselling comprised information, instruction, and advice without active elicitation of interactive discussion. Interviews were complemented with more specific dietetic and physical activity counselling.	To improve the motivation, hence, the physical activity and behaviour change of children with obesity/overweight
Hoedjes M <i>et al.</i> 2018 (19)	Helios	Exercise program 4 times/week and nutrition-education/behaviour modification sessions 1 time/week.	Focus on nutrition, physical activity and behaviour change of the participants and their parents. 3 groups; (A) 6 months intensive inpatient treatment program during weekdays, followed by 6-month return visits of 2 days; (B) 2-month intensive inpatient treatment program during weekdays, followed by biweekly return visits of 2-days/week; (C) usual care for 1-year, after which the participants will be randomly allocated to group A/B	To increase healthy lifestyle behaviour such as healthy nutritional behaviour, physical activity and behaviour change.
Miri SF <i>et al.</i> 2019 (40)	Cognitive-behavioural therapy (CBT)	6 face-to-face sessions. Record diet and PA for 2 days/week	CBT on nutrition improvement and weight. Sessions were based on treatment strategies which comprised nutritional recommendations and diet of adolescents and 2 sessions for parents. 30-45 minutes sessions which addressed motivation to reduce weight, behavioural strategies for changing eating habits, self-care and controlling external strategies.	To reduce the weight of obese and to improve their nutrition
Jebeile H <i>et al.</i> 2019 (55)	Intermittent Energy Restriction (IER)	Phase 1; 0-12 weeks Phase 2; 13-26 weeks	Phase 1; IER diet comprised of a VLED (very-low-energy-diet) 3 days/week and 4 days/week of healthy eating with support from a dietitian for 20-40 minutes individual face-to-service, or telephone call between visits.	To reduce BMI and cardiovascular disease risk and adapting a healthier lifestyle.

			Phase 2; choice between continue with VLED 3 days/week or reduce to 2,1 or VLED days/week in the context of a healthy eating plan for the next 14 weeks with the same support from a dietitian. No formal physical activity component to the intervention but participants were encouraged to increase physical activity and reduce recreational screen time	
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Appendix 4: Forest plots of reported changes in HRQoL (PedsQL 4.0) of children with obesity/overweight after participating in a lifestyle intervention

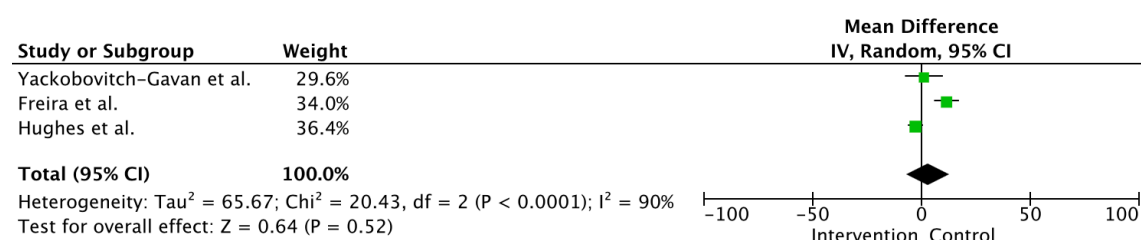


Figure 4A: Forest plot Total HRQoL at post-intervention
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

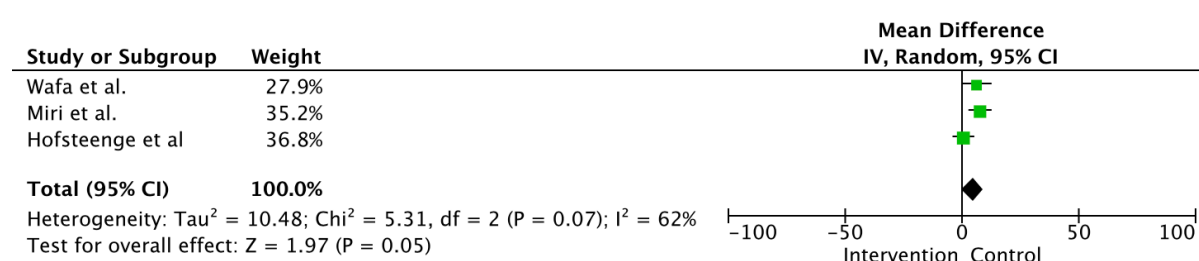


Figure 4B: Forest plot Total HRQoL at follow-up
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

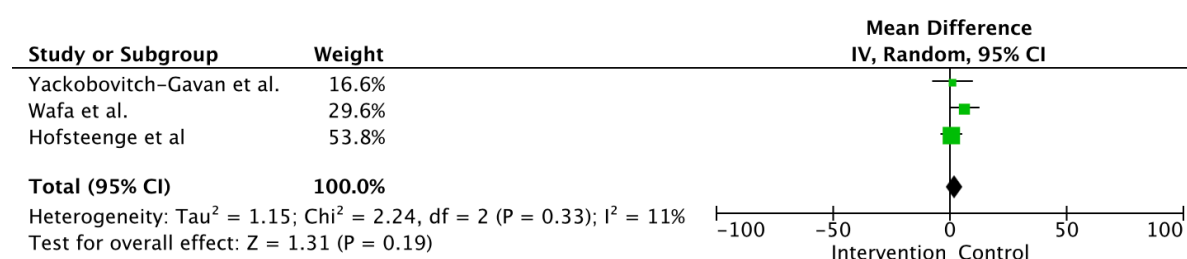


Figure 4C: Forest plot Total HRQoL children with obesity
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

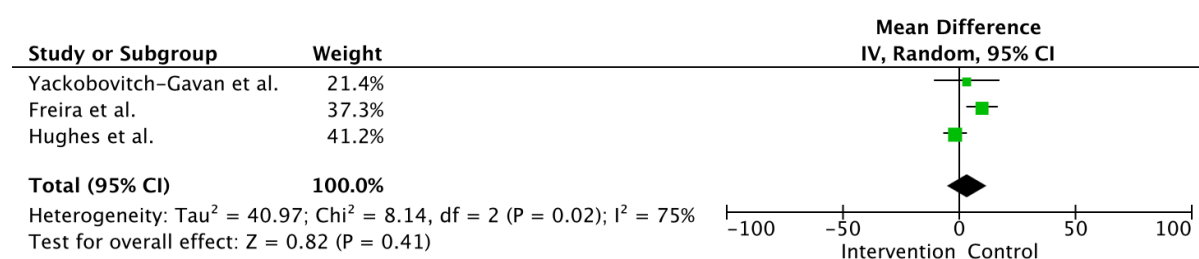


Figure 4D: Forest plot Physical scale HRQoL at post-intervention
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

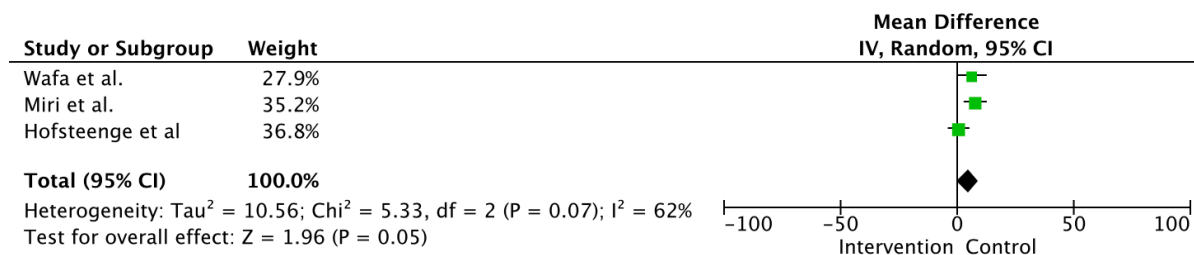


Figure 4E: Forest plot Physical scale HRQoL at follow-up

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

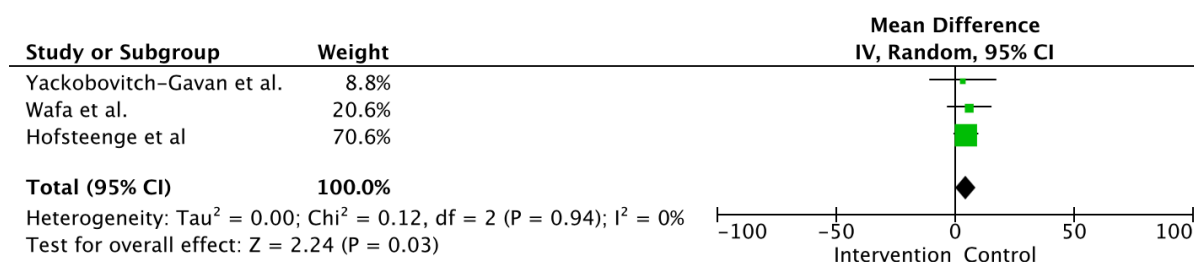


Figure 4F: Forest plot Physical scale HRQoL children with obesity

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

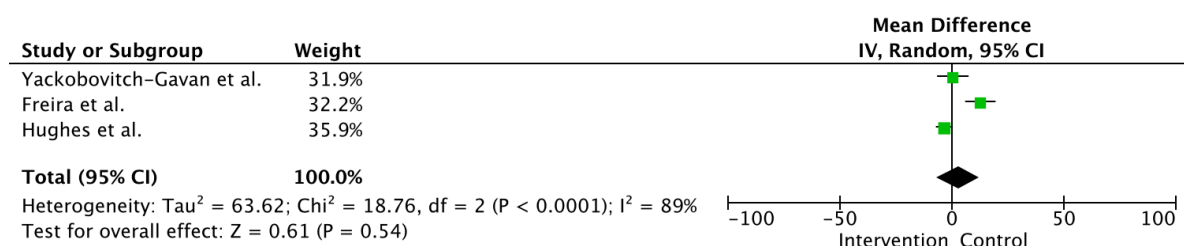


Figure 4G: Forest plot Psychosocial scale HRQoL at post-intervention

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

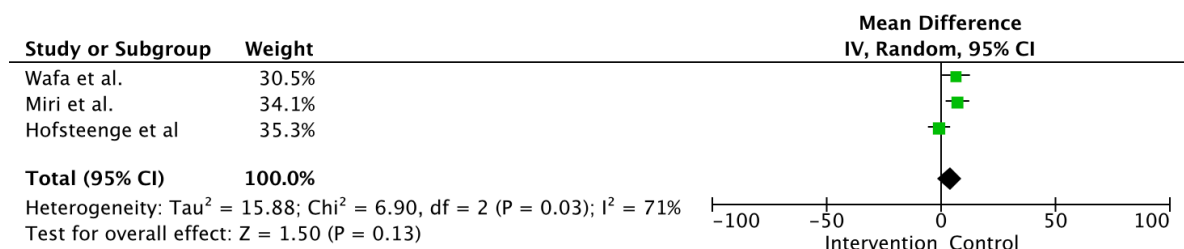


Figure 4H: Forest plot Psychosocial scale HRQoL at follow-up

Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

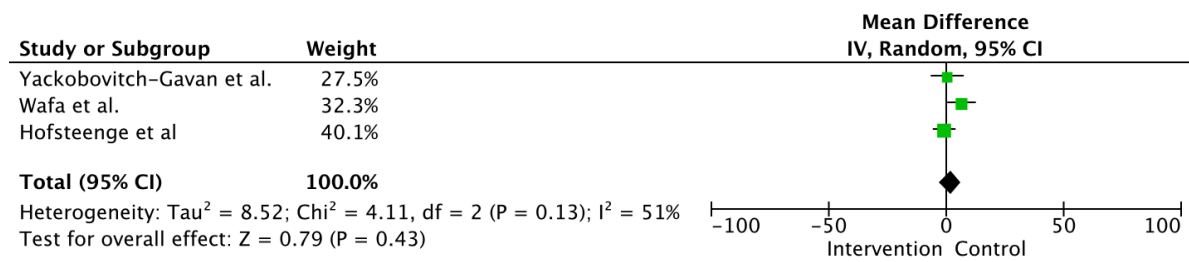


Figure 4I: Forest plot Psychosocial scale HRQoL children with obesity
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

Appendix 5: Findings when not only including RCTs

Methods of statistical analysis

By including other study designs rather than only RCTs, a more extensive representation of the effect of children with obesity/overweight that participated in lifestyle interventions was established. A Generic Inverse Variance Outcome type was used in RevMan 5.3, which made it possible to compare the results of articles with varying study designs (56). The mean difference (MD) and the Standard Error of the mean difference (SE(MD)) of the HRQoL at baseline and the HRQoL after the intervention was completed were used (57). These results were visualized by using a Forest plot. Effect sizes were computed as mean differences. Mean differences expressed the difference in mean change between the HRQoL of children after they participated in lifestyle interventions. To ensure that studies with larger samples were given a higher weight, each effect size was weighted by the inverse of its variance. A random-effects model was applied to correct for variability in effect sizes caused by the difference in lifestyle intervention that was designed and used, differences between study populations and sampling error (30).

The extent of heterogeneity of results of the included articles was determined by using Higgins I^2 (31). This methodological measure was based on Cochrane's Q and degrees of freedom (df). Higgins I^2 represents the proportion of variability in an effect that is caused by heterogeneity instead of sampling error. The higher the Higgins I^2 , the higher the extent of heterogeneity between results of interest from the articles. The null hypothesis states that all studies are establishing the same effect (32). The attached value to Higgins I^2 depends on the magnitude and direction of effect (I) and the strength of the evidence for heterogeneity (p-value of Cochrane's Q and confidence interval of I^2) (31). For this meta-analysis the Higgin's I^2 was interpreted as following, 0-40% heterogeneity might not be important, 30-60% may represent moderate heterogeneity, 50-90% may represent substantial heterogeneity and 75-100% considerable heterogeneity (31).

The test for overall effect (Z) addresses the weighted average effect size. For this meta-analysis this value represented, whether RCTs offering lifestyle interventions significantly improved the HRQoL of children with overweight/obesity. The null hypothesis states that there is on average no effect of lifestyle interventions on the HRQoL of children with overweight/obesity (33).

Study characteristics

The extracted data from these articles can be found in table 5. For a summary of the components of the individual lifestyle interventions applied in the included studies see Appendix 3. The final included studies were published between 2008 and 2019. Four studies (27%) were conducted in North America (49, 50, 52, 53), six studies (40%) were conducted in Europe (19, 35-38, 54), two studies (13%) were conducted in Middle East (39, 40), two study (13%) were conducted in Australia (41, 55), and one study (7%) was conducted in South America (51). All studies included both boys and girls and the HRQoL was measured in all studies by using the PedsQL 4.0., except in Bonham *et*

al., which only applied the disease-specific IWQOL-Kids (41). Together with Quinlan *et al.* and Hoedjes *et al.*, Bonham *et al.* were the only articles that applied the IWQOL-kids (19, 41, 49). In every study the HRQoL was measured at baseline, with either a reassessment of the HRQoL directly after the intervention was completed or at follow-up. The duration of the follow-up periods varied between 6 months and 18 months. The included articles had varying study sizes and included between the 16 and 130 participants in the studies. Between the included studies, the children with obesity/overweight that participated in lifestyle interventions had an age range that varied between 5 and 19 years old, with a mean age varying between 9.1 and 16.2 years old. Six of the 15 studies focused on both children having obesity or children with overweight (35, 38, 40, 50, 53, 54). Whereas of the remaining nine studies, eight studies only focused on children with obesity (19, 36, 37, 39, 50-52, 55). Quinlan *et al.* was the only article that included only children with overweight in their lifestyle intervention (49).

Seven of the 15 included articles were Randomized Controlled Trials (RCTs) (35-41). Four studies had a Nonrandomized trial study design (50, 51, 54, 55). Two studies applied a longitudinal study design (52, 53), and two of the included articles were prospective observational studies (19, 41).

All studies except Poeta *et al.* and Hughes *et al.* described the HRQoL of children with obesity at baseline and postintervention by using mean and standard deviations. Poeta *et al.* and Hughes *et al.* described the HRQoL by using median and interquartile intervals (IQI) (35, 51).

Results of individual studies

All the included studies used a different lifestyle intervention to achieve weight-loss and increase the HRQoL in children with obesity. However, the aspects of the lifestyle interventions are composed of comparable components. All the lifestyle intervention of the included articles comprised a physical activity and behaviour change aspect. Moreover, except for Cronk *et al.*, lifestyle interventions of all the included studies also focused on changing the eating behaviour of children with obesity/overweight (50). The lifestyle interventions of Morano *et al.*, Cronk *et al.*, Hughes *et al.* and Hoedjes *et al.* also incorporated family aspects in these interventions (19, 35, 50, 54). Three studies included psychological aspects into the lifestyle intervention, namely Miri *et al.*, Hoedjes *et al.* and Yackobovitch-Gavan *et al.* (19, 39, 40).

After the lifestyle intervention was applied significant improvements in Total HRQoL were reported by Miri *et al.*, Cronk *et al.*, Hoedjes *et al.*, Yackobovitch-Gavan *et al.*, Poeta *et al.*, Engebretsen *et al.* and Jebeile *et al.* (19, 39, 40, 50, 51, 53, 55). Other studies did not report significant improvements in Total HRQoL. The studies that did not found significant improvements in the Total HRQoL observed significant improvements in the Physical/Psychosocial scale or subdomains of the PedsQL 4.0. Wafa *et al.* and Hughes *et al.* were the only articles that did not report significant improvements in any of the scales and subdomains of the PedsQL 4.0 (35, 36).

Table 4: Characteristics of the included articles

Author, publication year	Origin of population	Study design	Duration of intervention	Aspect of lifestyle intervention	Team	Follow-up period after completion of intervention	N = (of intervention group)	Overweight or obesity	Stratified sex	Age range (mean, sd)	PROM
Yackobovitch-Gavan M <i>et al.</i> 2008 (39)	Israel	Randomized controlled trial	12-week	Healthy dietary behaviour, PA	Dietitian, psychologist	Postintervention	52	OB	No	12 – 18 (14.3; 1.7)	PedsQL 4.0
Quinlan NP <i>et al.</i> 2008 (49)	USA and UK	Observational design	1 – 8 weeks (most participants 3-5 weeks)	Healthy dietary behaviour, PA, psycho-educational support groups	Psychology staff, camp nursing and nutrition staff	Postintervention	130	OW	No	9 – 18 (12.8; 1.9)	PedsQL 4.0 IWQOL-Kids
Hughes AR <i>et al.</i> 2008 (35)	Scotland	Randomized controlled trial	26 weeks	Healthy dietary behaviour, PA	Dietitian	Postintervention	69	OW + OB	No	5 -11 (9.1; 1.7)	PedsQL 4.0
Wafa SW <i>et al.</i> 2010 (36)	UK	Randomized controlled trial	26-week		Clinical psychologist, dietitian	6-month	52	OB	No	7 – 11 (9.8; 1.5)	PedsQL 4.0
Cronk E <i>et al.</i> 2011 (50)	USA	Nonrandomized trial	Five waves of 6-week core sessions	Healthy dietary behaviour, PA	Clinical dietician	12-month	31	OW + OB	No	8 – 11 (9.4; 0.4)	PedsQL 4.0
Hofsteenge G <i>et al.</i> 2013 (37)	The Netherlands	Randomized controlled trial	3 months	Healthy dietary behaviour, PA	Dietician, psychologist and paediatric endocrinologist	6-month, 18-month	57	OB	No	11 – 18 (14.5; 1.7)	PedsQL 4.0
Poeta LS <i>et al.</i> 2013 (51)	Brazil	Nonrandomized Controlled clinical trial	12-week	PA, healthy dietary behaviour	Nutritionist, group of nutrition students	Postintervention	16	OB	No	8 – 11	PedsQL 4.0
Bock DE <i>et al.</i> 2014 (52)	Canada	Longitudinal design	12-month	PA, phealthy dietary behaviour, psychosocial aspects	dietitian, exercise specialist, social worker and pediatrician	Postintervention	42	OB	Yes	8 – 17 (12.8; 3.14)	PedsQL 4.0

Engebretsen S <i>et al.</i> 2016 (53)	USA	Longitudinal design	12-week	PA, healthy dietary behaviour	Health providers	Postintervention, 6-month, 12-month	65	OW + OB	Yes	8 -14 (10.8; 1.66)	PedsQL 4.0
Morano M <i>et al.</i> 2016 (54)	Italy	Nonrandomized trial	6 months	PA, healthy dietary behaviour	Specialist instructor, dietitian	Postintervention	18	OW + OB	Yes	10 -12	PedsQL 4.0
Bonham MP <i>et al.</i> 2017 (41)	Australia	Randomized controlled trial	12 weeks	PA, healthy dietary behaviour	Dietitian at Jenny Craig	Postintervention	42	OW	No	13 -17 (15.3; 1.3)	IWQOL-Kids
Freira S <i>et al.</i> 2018 (38)	Portugal	Randomized controlled trial	3 months	PA, healthy dietary behaviour	Paediatrician, dietitian and PA teachers	Postintervention	42	OW + OB	No	(16.2; 1.49)	PedsQL 4.0
Hoedjes M <i>et al.</i> 2018 (19)	The Netherlands	Prospective observational study	6 months	Healthy dietary behaviour, PA	Paediatricians, dietitians, psychologists, social workers, nurses, physiotherapists, general exercise therapists and exercise therapists Cesar	Postintervention, 12-months	120	OB	No	8 – 19 (14.8 ; 2.4)	PedsQL 4.0 IWQOL-Kids
Miri SF <i>et al.</i> 2019 (40)	Iran	Randomized controlled trial	6 weeks	Healthy dietary behaviour, PA, CBT	2 therapists with 5-20 years' experience	6 months	55	OW + OB	No	13 -18 (14.64; 1.69)	PedsQL 4.0
Jebeile H <i>et al.</i> 2019 (55)	Australia	Noncontrolled trial	26-week	Healthy dietary behaviour, PA encouragement	Dietitian	Postintervention	30	OB	No	12 – 17 (14.5; 1.4)	PedsQL 4.0

After reassessment at follow-up significant improvements on the Physical scale HRQoL were reported by Hofsteenge *et al.*, Miri *et al.* and Engebretsen *et al.* (37, 40, 53). Directly after completion of lifestyle interventions significant improvements on the Physical scale HRQoL were reported by Yackobovitch-Gavan *et al.*, Poeta *et al.* and Quinlan *et al.* (39, 49, 51). Improvements on the Psychosocial scale HRQoL were reported by 5 studies namely: Freira *et al.*, Morano *et al.*, Yackobovitch-Gavan *et al.*, Poeta *et al.*, Quinlan *et al.* and Engebretsen *et al.* (38, 39, 49, 51, 53, 54). Significant improvements in School functioning subdomain were reported by Miri *et al.*, Hofsteenge *et al.* and Yackobovitch-Gavan *et al.* (37, 39, 40). Freira *et al.*, Quinlan *et al.* and Bock *et al.* reported significant improvement in the Emotional subdomain, but not in Total HRQoL (38, 49, 52). Miri *et al.*, Quinlan *et al.* and Yackobovitch-Gavan *et al.* did report significant improvements in both Total HRQoL and Emotional subdomain (39, 40, 49). No significant improvements were reported on the Social functioning subdomain HRQoL measured by the PedsQL 4.0.

Synthesis of results

The 15 studies provided 60 estimates of the effect of a lifestyle intervention on the self-reported HRQoL of children with overweight/obesity. Ten of the 15 included articles compared baseline HRQoL with HRQoL of children with overweight/obesity directly after they had participated in a lifestyle intervention (35, 38, 39, 49, 51-55, 58). There was a heterogeneously significant improvement in both the Total and Physical HRQoL scores after these children participated in lifestyle interventions (Table 5). There was a homogeneous reported improvement on the Psychosocial scale of the HRQoL PedsQL 4.0 after children with obesity/overweight participated in lifestyle interventions ($p < 0.05$). The mean improvement on the Psychosocial HRQoL scale was 6.97 points.

Four of the 15 included articles assessed the effect of a lifestyle intervention on the HRQoL, measured by the PedsQL 4.0, at baseline compared to a reassessment at follow-up (37, 40, 53, 58). On all three scales of the HRQoL PedsQL 4.0 homogeneously significant improvements were reported in the articles after children with overweight/obesity participated in lifestyle interventions. With the most pronounced mean improvement in the Psychosocial scale (8.71 points) and the smallest improvement in the Physical scale (7.88 points).

Subsequently, stratification between the post-intervention and the follow-up effect of lifestyle interventions on the HRQoL of children with overweight/obesity was disregarded. Thereafter, only the effect of lifestyle interventions on the HRQoL of children with obesity was analysed (37, 39, 51, 52, 55, 58). Articles that only included children with obesity showed a homogeneously significant improvement in the Psychosocial scale HRQoL, measured by the PedsQL 4.0, after children with obesity participated in lifestyle interventions. Children with obesity on average reported improvements of 9.61 points on the Psychosocial scale of the HRQoL PedsQL 4.0. Whereas there was a heterogeneously significant improvement in both the Total and Physical scale HRQoL after children with obesity participated in lifestyle interventions.

In the majority of the Forest plots, no individual study had a disproportionately large effect on the pooled estimates. See Figure 5 for the visualization of the distribution around the WMD of the effect of lifestyle interventions on the HRQoL of children with overweight/obesity and the weight of the individual articles.

Three of the included studies also studied the effects of lifestyle interventions on HRQoL assessed by IWQOL-Kids (19, 41, 49). Hoedjes *et al.* and Quinlan *et al.* both reported that their lifestyle interventions significantly improved the disease-specific HRQoL in all domains except 'family relations'. Moreover, both articles reported that the most substantial improvements were observed in the domain of 'body esteem' (19, 49). Bonham *et al.* only concluded in the article that Total disease-specific HRQoL, measured by the IWQOL-Kids, significantly improved over time. In the article by Bonham *et al.*, the effect of the lifestyle intervention on the weight-related HRQoL was not reported (41).

Table 5: Pooled estimates of the weighted mean difference (WMD) in HRQoL (PedsQL 4.0) Pre- compared to post-intervention in children with obesity by using Generic Inverse Variance method

Comparison	N	WMD	I ² (%)	P-value (I ²)	Z	P-value (Z)
Post-intervention						
Total score HRQoL	10	6.28 [4.05, 8.51]	93%	<0.00001*	5.52	<0.00001*
Physical score HRQoL	10	6.50 [2.95, 10.06]	83%	<0.00001*	3.58	0.0003*
Psychosocial score HRQoL	10	6.97 [5.27, 8.67]	34%	0.14	8.06	<0.00001*
Follow-up						
Total score HRQoL	4	8.38 [6.50, 10.27]	0%	0.58	8.72	<0.00001*
Physical score HRQoL	4	7.88 [5.95, 9.81]	0%	0.43	8.00	<0.00001*
Psychosocial score HRQoL	4	8.71 [6.54, 10.88]	63%	0.05	7.87	<0.00001*
Children or adolescents with obesity						
Total score HRQoL	6	7.23 [2.29, 12.18]	92%	<0.00001*	2.87	0.004*
Physical score HRQoL	6	9.71 [4.77, 14.64]	77%	0.0007*	3.86	0.0001*
Psychosocial score HRQoL	6	8.52 [6.54, 10.49]	0%	0.66	8.45	<0.00001*

*Significant ($P < 0.05$), WMD (Weighted Mean Difference), N (included articles)

Figure 5: Forest plots of reported changes in HRQoL (PedsQL 4.0) of children with obesity/overweight after participating in a lifestyle intervention (using Generic Inverse Variance)

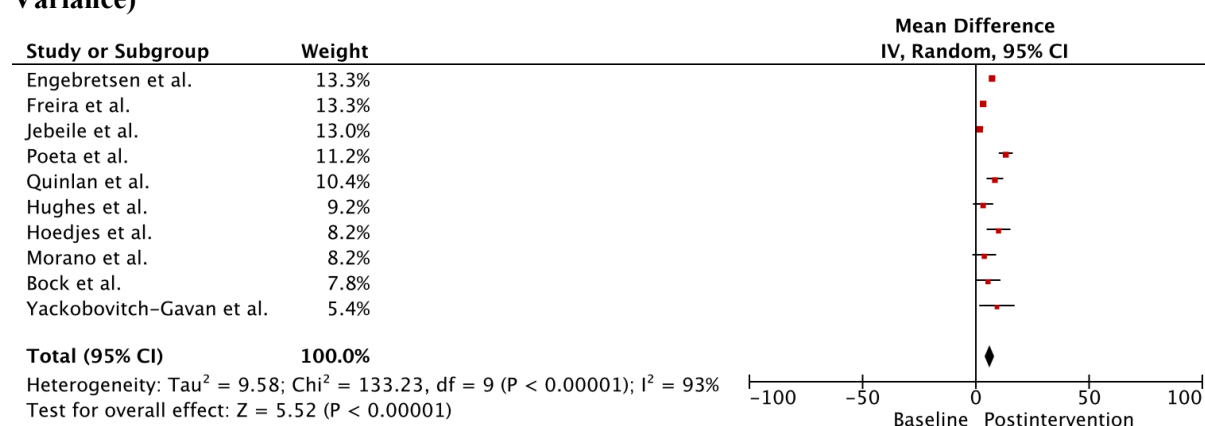


Figure 5A: Forest plot Total HRQoL at post-intervention
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

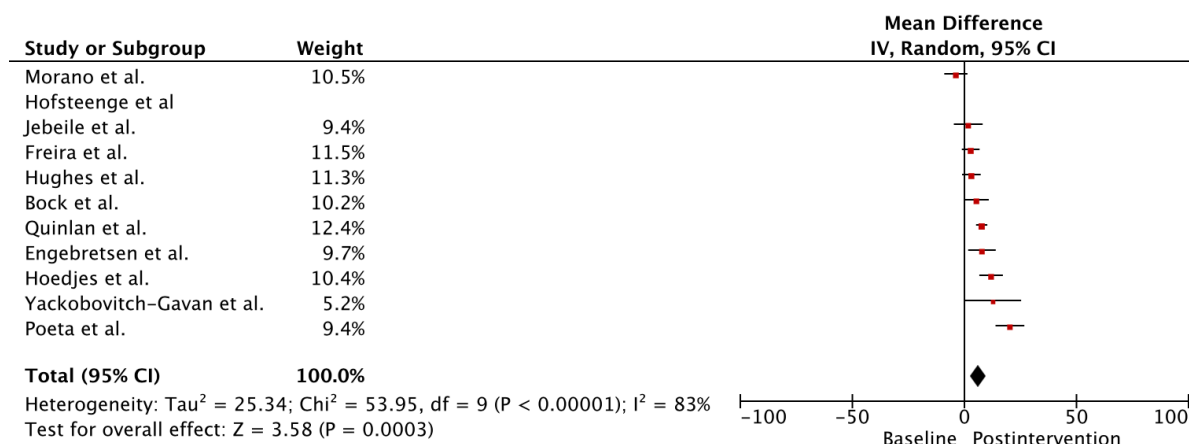


Figure 5B: Forest plot Physical scale HRQoL at post-intervention
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

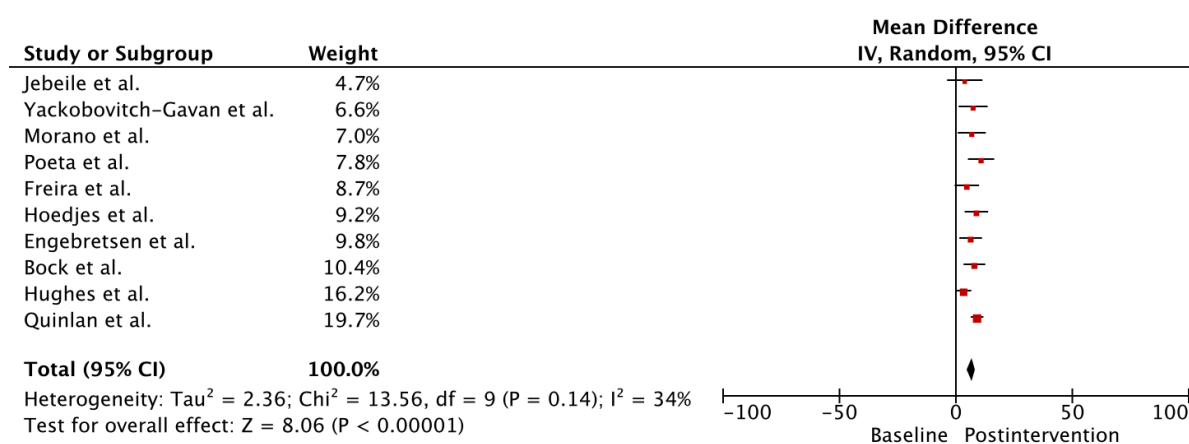


Figure 5C: Forest plot Psychosocial scale HRQoL at post-intervention
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

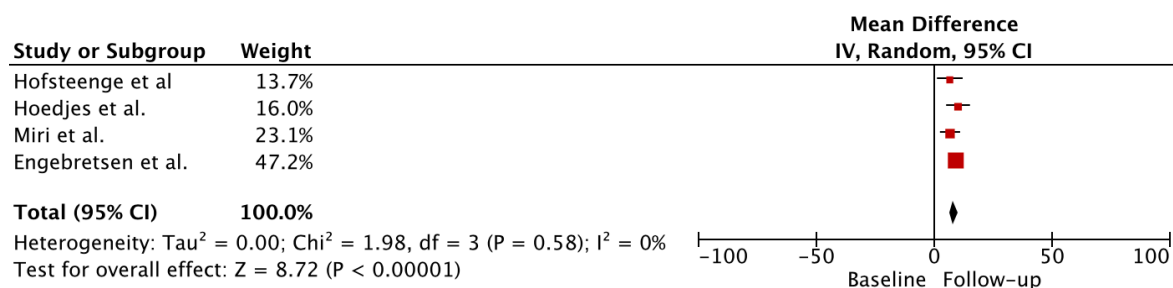


Figure 5D: Forest plot Total HRQoL at follow-up
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

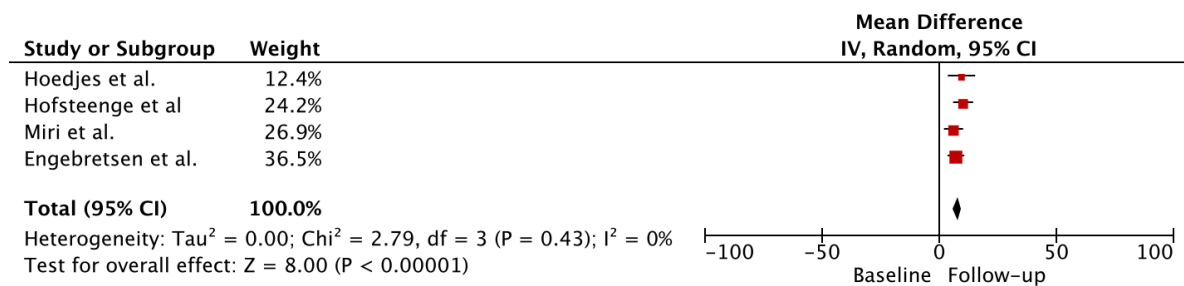


Figure 5E: Forest plot Physical scale HRQoL at follow-up
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

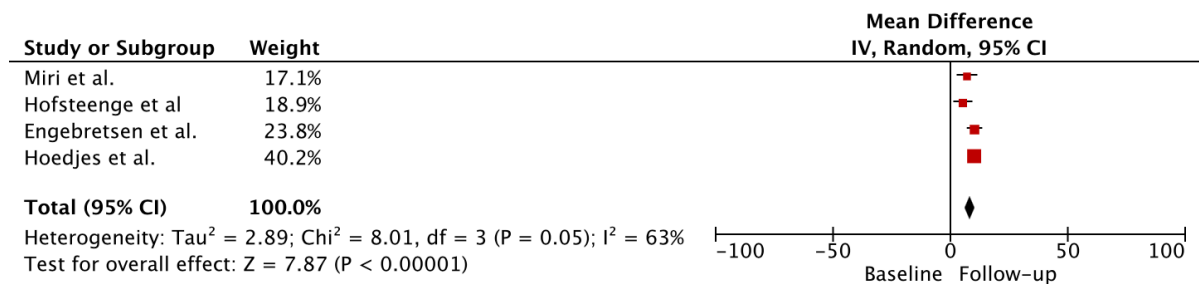


Figure 5F: Forest plot Psychosocial scale HRQoL at follow-up
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

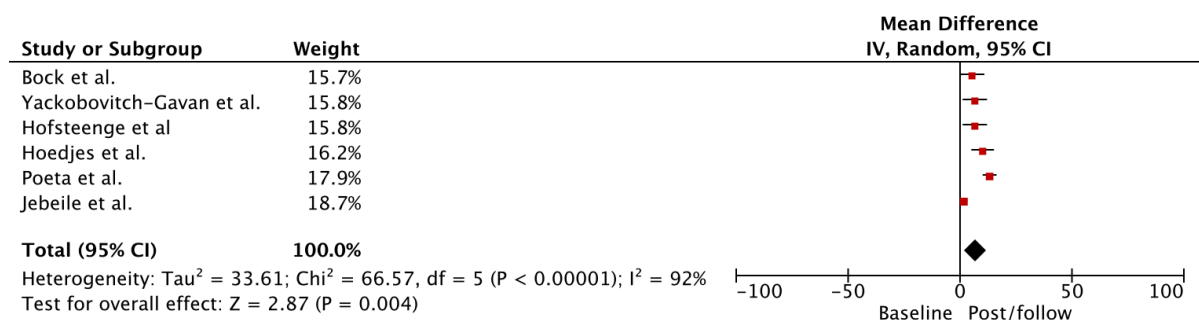


Figure 5G: Forest plot Total HRQoL children with obesity
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

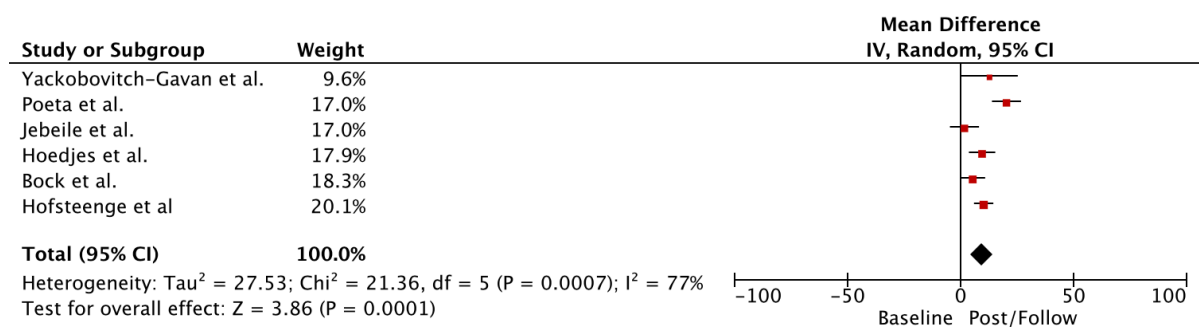


Figure 5H: Forest plot Physical scale HRQoL children with obesity
Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

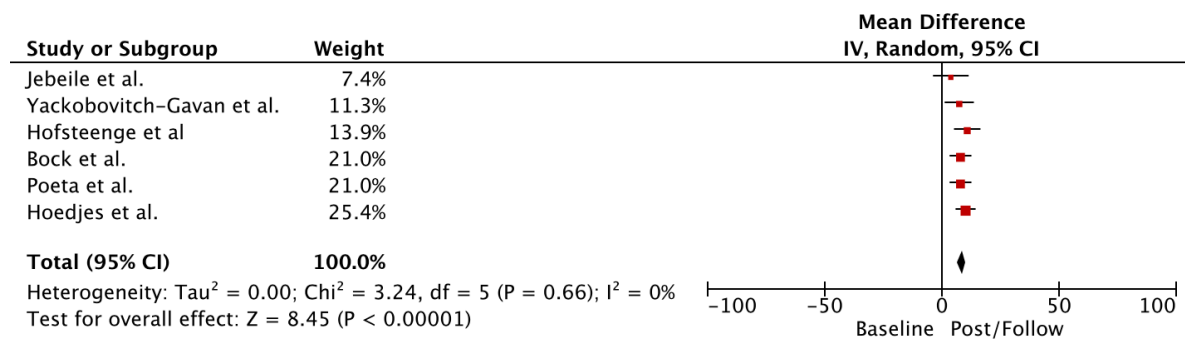


Figure 5I: Forest plot Psychosocial scale HRQoL children with obesity
 Inverse Variance (IV), Random effects model (Random), 95% Confidence Interval (95% CI)

References

1. NCD Risk Factor Collaboration N-R. Worldwide Trends in Body-Mass Index, Underweight, Overweight, and Obesity From 1975 to 2016: A Pooled Analysis of 2416 Population-Based Measurement Studies in 128.9 Million Children, Adolescents, and Adults. *Lancet* 2017 December;390(10113):2627-42.
2. World Health Organization. Taking action on childhood obesity. Geneva: WHO. 2018.
3. Seidell J, Halberstadt J, Noordam H, and Niemer S. An integrated health care standard for the management and prevention of obesity in The Netherlands. *Family practice*. 2012 April 1;29(suppl_1):i153-6.
4. Seidell J, Halberstadt J. *Zorgstandaard Obesitas*. Amsterdam: Partnerschap Overgewicht Nederland. 2010 November 25.
5. Seidell J, Beer A, and Kuijpers T. Richtlijn 'Diagnostiek en behandeling van obesitas bij volwassenen en kinderen'. *Nederlands tijdschrift voor geneeskunde*. 2008 September 20;152(38):2071-6.
6. Reilly JJ ME, McDowell ZC, Hacking B, Alexander D, Stewart L *et al*. Health consequences of obesity. *Archives of disease in childhood* 2003 September 1;88(9):748-52.
7. Gibson L, Allen K, Davis E, Blair E, Zubrick S, Byrne S. The psychosocial burden of childhood overweight and obesity: evidence for persisting difficulties in boys and girls. *European journal of pediatrics*. 2017 July 1;176(7):925 - 33.
8. Schwimmer J, Burwinkle T, and Varni J. Health-related quality of life of severely obese children and adolescents. . *JAMA* 2003 April 3;289(14):1813-9.
9. Testa M, Simonson D. Assessment of quality-of-life outcomes. *New England journal of medicine*. 1996 March 28;334(13):835 - 40.
10. Tsiros M, Olds T, Buckley J, Grimshaw P, Brennan L, Walkley J, et al. Health-related quality of life in obese children and adolescents. *International journal of obesity*. 2009 April 33(4):387
11. World Health Organization. International classification of functioning, disability and health: short version. Geneva: WHO; 2001.
12. Noordam H, Halberstadt J, Seidell J. Kwaliteit van leven als uitkomstmaat in de zorg voor kinderen (4-19 jaar) met obesitas. *Tijdschrift voor gezondheidswetenschappen*. 2016 December 1;94(8):300 - 4.
13. people H. Health-Related Quality of Life and Well-Being. *Foundation Health Measure Report* 2010 November.
14. Weldring T, Smith S. Article commentary: patient-reported outcomes (pros) and patient-reported outcome measures (PROMs). *Health Services Insights*. 2013 January 6:HSI-S11093.
15. Engelen V, Haentjens M, Detmar S, Koopman H, Grootenhuis M. Health related quality of life of Dutch children: psychometric properties of the PedsQL in the Netherlands. *BMC pediatrics*. 2009 December;1(68).
16. UI-Haq Z, Mackay D, Fenwick E, and Pell J. Meta-analysis of the association between body mass index and health-related quality of life among children and adolescents, assessed using the pediatric quality of life inventory index. *The Journal of pediatrics*. 2013 February 1;162(2):280 - 6.
17. Jalali-Farahani S, Alamdari S, Karimi M, and Amiri P. Is overweight associated with health-related quality of life (HRQoL) among Tehranian school children? *SpringerPlus*. 2016 December 1;5:313.
18. Griffiths L, Parsons T, and Hill A. Self-esteem and quality of life in obese children and adolescents: a systematic review. . *International journal of obesity*. 2010 Augustus 1;5(4):282-304.
19. Hoedjes M, Makkes S, Halberstadt J, Noordam H, Renders C, and Bosmans Jea. Health-related quality of life in children and adolescents with severe obesity after intensive lifestyle treatment and at 1-year follow-up. *Obesity facts*. 2018 April;11(2):116 - 28.
20. Murray M, Pearson J, Dordevic A, and Bonham M. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. . *Obesity reviews*. 2018 October 24;20(2):278-89.
21. Ligthart K, Paulis W, Djasmo D, Koes B, and van Middelkoop M. Effect of multidisciplinary interventions on quality of life in obese children: a systematic review and meta-analysis. *Quality of Life Research*. 2015 July;24(7):1635-43.

22. Hughes A, Farewell K, Harris D, and Reilly J. Quality of life in a clinical sample of obese children. *International journal of obesity*. 2007 January;31(1):39-44.
23. Liberati A, Altman D, Tetzlaff J, Mulrow C, Gøtzsche P, Ioannidis J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology*. 2009 October 1;62(10):e1-34.
24. Reinjfjell T, Diseth T, Veenstra M, Vikan A. Measuring health-related quality of life in young adolescents: Reliability and validity in the Norwegian version of the Pediatric Quality of Life Inventory™ 4.0 (PedsQL) generic core scales. *Health and quality of life outcomes*. 2006 December 1;4(1):61.
25. Varni J, Seid M, Kurtin P. PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. *Medical care*. 2001 August 1:800 - 12.
26. Lin C, Luh W, Yang A, Su C, Wang J, Ma H. Psychometric properties and gender invariance of the Chinese version of the self-report pediatric quality of life inventory version 4.0: short form is acceptable. *Quality of Life Research*. 2012 February 1;21(1):177 - 82.
27. Modi A, Zeller M. The IWQOL-Kids©: Establishing minimal clinically important difference scores and test-retest reliability. *International Journal of Pediatric Obesity*. *International journal of pediatric obesity*. 2011 June 1;6(sup3):e94-6.
28. Kolotkin R, Zeller M, Modi A, Samsa G, Quinlan N, Yanovski J, et al. Assessing weight-related quality of life in adolescents. *Obesity*. 2006 March 14(3):448 - 57.
29. Higgins J, and Thomas J. Medians and interquartile ranges. 2019. In: *Cochrane Handbook for Systematic Reviews of Interventions* [Internet]. Cochrane.
30. Higgins J, and Thomas J. Random-effects method. 2019. In: *Cochrane Handbook for Systematic Reviews of Interventions* [Internet]. Cochrane.
31. Higgins J, and Thomas J. Identifying and measuring heterogeneity 2019. In: *Cochrane Handbook for Systematic Reviews of Interventions* [Internet]. Cochrane.
32. Higgins J, Thompson S, Deeks J, and Altman D. Measuring inconsistency in meta-analyses. *BMJ*. 2003 September 4;327(7414):557-60.
33. Higgins J, and Thomas J. P values and statistical significance. 2019. In: *Handbook for systematic reviews of Interventions* [Internet]. Cochrane.
34. Higgins J, Altman D, Gøtzsche P, Jüni P, Moher D, Oxman A, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials *BMJ: British Medical Journal*. 2011 October 29;343:d5928.
35. Hughes A, Stewart L, Chapple J, McColl J, Donaldson M, Kelnar C, et al. Randomized, controlled trial of a best-practice individualized behavioral program for treatment of childhood overweight: Scottish Childhood Overweight Treatment Trial (SCOTT). *Pediatrics*. 2008 March 1;121(3):e539-46.
36. Wafa S, Talib R, Hamzaid N, McColl J, Rajikan R, Ng L, et al. Randomized controlled trial of a good practice approach to treatment of childhood obesity in Malaysia: Malaysian Childhood Obesity Treatment Trial (MASCOT). *International journal of pediatric obesity*. 2011 June 1;6(sup3):e62-9.
37. Hofsteenge G, Weijs P, Delemarre-van de Wall H, de Wit M, and Chinapaw M. Effect of the Go4it multidisciplinary group treatment for obese adolescents on health related quality of life: a randomised controlled trial. *BMC public health*. 2013 December;13(1):939.
38. Freira S, Fonseca H, Williams G, Ribeiro M, Pena F, do Céu Machado M, et al. Quality-of-life outcomes of a weight management program for adolescents based on motivational interviewing. Patient education and counseling. 2019 April 1;102(4):718-25.
39. Yackobovitch-Gavan M, Nagelberg N, Demol S, Phillip M, Shalitin S. Influence of weight-loss diets with different macronutrient compositions on health-related quality of life in obese youth. *Appetite*. 2008 November 1;51(3):697-703.
40. Miri S, Javadi M, Lin C, Griffiths M, Björk M, and Pakpour A. Effectiveness of cognitive-behavioral therapy on nutrition improvement and weight of overweight and obese adolescents: A randomized controlled trial. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2019 May 1;13(3):2190-7.

41. Bonham M, Dordevic A, Ware R, Brennan L, and Truby H. Evaluation of a commercially delivered weight management program for adolescents. . *The Journal of pediatrics* 2017 June 1;185:73-80.
42. Fullerton G, Tyler C, Johnston C, Vincent J, Harris G, and Foreyt J. Quality of life in Mexican–American children following a weight management program. *Obesity* 2007 November;15 (11):2553-6.
43. Ravens-Sieberer U, Redegeld M, Bullinger M. Quality of life after in-patient rehabilitation in children with obesity. *International Journal of Obesity*. 2001 May;25(Suppl 1):S63- S5.
44. Ravens-Sieberer U, Gosch A, Rajmil L, Erhart M, Bruil J, Power M, et al. The KIDSCREEN-52 Quality of Life Measure for Children and Adolescents: Psychometric Results from a Cross-Cultural Survey in 13 European Countries. *Value Health*. 2008 July - August;11(4):645 - 58.
45. Varni J, Burwinkle T, Seid M, Skarr D. The PedsQL™ 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambulatory pediatrics*. 2003 November 1;3(6):329 - 41.
46. Lowry K, Sallinen B, Janicke D. The effects of weight management programs on self-esteem in pediatric overweight populations. *Journal of Pediatric Psychology*. 2007 November 1;32(10):1179 - 95.
47. Bianchini J, da Silva D, Nardo C, Carolino I, Hernandez F, Junior N. Parent-proxy perception of overweight adolescents' health-related quality of life is different according to adolescent gender and age and parent gender. *European journal of pediatrics*. 2013 October 1;172(10):1371 - 7.
48. Hegland P, Aasprang A, Hjelle Øygard S, Nordberg S, Kolotkin R, Moltu C, et al. A review of systematic reviews on the effects of patient-reported outcome monitoring with clinical feedback systems on health-related quality of life – implications for a novel technology in obesity treatment. *Clinical obesity*. 2018 September 12;8(6):452 - 64
49. Quinlan N, Kolotkin R, Fuemmeler B, and Costanzo P. Psychosocial outcomes in a weight loss camp for overweight youth. . *International Journal of Pediatric Obesity*. 2009 January 1;4(3):134-42.
50. Cronk C, Hoffmann R, Mueller M, Zerpa-Urióna V, Dasgupta M, and Enriquez F. Effects of a culturally tailored intervention on changes in body mass index and health-related quality of life of Latino children and their parents. *American Journal of Health Promotion*. 2011 March;25(4):e1-.
51. Poeta L, Duarte M, de CB Giuliano I, and Mota J. Interdisciplinary intervention in obese children and impact on health and quality of life. *Jornal de pediatria*. 2013 September 1;89(5):499-504.
52. Bock D, Robinson T, Seabrook J, Rombeek M, Norozi K, Filler G, et al. The Health Initiative Program for Kids (HIP Kids): effects of a 1-year multidisciplinary lifestyle intervention on adiposity and quality of life in obese children and adolescents-a longitudinal pilot intervention study. *BMC pediatrics*. 2014 December 14(1):296.
53. Engebretsen S, Sorrells R, Yi-Frazie J, and Early K. Longitudinal quality of life improvement in underserved rural youth with obesity. *Obesity science & practice*. 2016 December 2;2(4):444-55.
54. Morano M, Rutigliano I, Rago A, Petteoello-Mantovani M, and Campanozzi A. A multicomponent, school-initiated obesity intervention to promote healthy lifestyles in children. *Nutrition*. 2016 October 1;32(10):1075-80.
55. Jebeile H, Gow M, Lister N, Mosalman Haghighi M, Ayer J, Cowell C, et al. Intermittent Energy Restriction Is a Feasible, Effective, and Acceptable Intervention to Treat Adolescents with Obesity. *The Journal of nutrition*. 2019 July 1;149(7):1189-97.
56. Higgins J, and Thomas J. The generic inverse variance outcome type in RevMan. 2019. In: *Handbook for systematic reviews of Interventions* [Internet]. Cochrane.
57. Higgins J, and Thomas J. Mean differences. 2019. In: *Handbook for systematic reviews of Interventions* [Internet]. Cochrane.
58. Hoedjes M MS, Halberstadt J, Noordam H, Renders CM, Bosmans JE *et al.* . Health-related quality of life in children and adolescents with severe obesity after intensive lifestyle treatment and at 1-year follow-up. *Obesity facts*. 2018 April;11(2):116 - 28.