

## AUTHORS' FINAL ACCEPTED COPY BEFORE PUBLISHER TYPESETTING

CHANGE IN HEALTH-RELATED QUALITY OF LIFE IN THE CONTEXT OF  
PEDIATRIC OBESITY INTERVENTIONS: A META-ANALYTIC REVIEW

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**ABSTRACT**

**Objective:** To quantitatively characterize change in health-related quality of life (HRQoL) in the context of behavioral (n= 16), surgical (n=5), and pharmacological (n=1) interventions for pediatric overweight and obesity. A secondary goal was to examine the relationship between change in HRQoL and change in weight status ( $\Delta$ BMI) by treatment type. The amount of weight loss necessary to observe a minimally clinically important difference (MCID) in HRQoL was determined. **Methods:** Data were gathered from studies reporting on weight change and  $\Delta$ HRQoL over the course of obesity interventions (N = 22) in youths (N=1,332) with average ages between 7.4 and 16.5 years (M = 12.2). An overall effect size was calculated for  $\Delta$ HRQoL. Moderation analyses were conducted using ANOVA and weighted regression. MCID analyses were conducted by converting HRQoL data to SEM units. **Results:** The overall effect size for  $\Delta$ HRQoL in the context of pediatric obesity interventions was medium ( $g = 0.51$ ). A significant linear relationship was detected between  $\Delta$ BMI and  $\Delta$ HRQoL ( $R^2 = 0.87$ ). This relationship was moderated by treatment type, with medical (i.e., surgical) interventions demonstrating a stronger relationship. Results indicated that it takes a change of 0.998 BMI units to detect true change in HRQoL. **Conclusions:** This study provides the first known quantitative examination of changes in HRQoL associated with weight loss in pediatric interventions. Medical interventions appear to offer a more substantial increase in HRQoL per unit of BMI change. These results offer a concrete weight loss goal for noticing positive effects in daily life activities.

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Pediatric obesity and overweight continue to be prevalent in the United States and abroad. Current estimates derived from national survey data suggest that approximately 32% of children in the United States (ages 2-19) are overweight, and that approximately 17% meet criteria for obesity (Ogden, Carroll, Kit, & Flegal, 2014). Worldwide, recent estimates suggest similar increases in overweight and obesity over the past three decades (e.g., Ng et al., 2014, Wang & Lim, 2012). Ng et al. estimate that in 2013 approximately 24% of boys and 23% of girls in developed countries were overweight or obese, and that approximately 13% of children (both boys and girls) in developing countries were overweight or obese. Both Ng et al. and Wang and Lim noted that, while increases seen in developed countries may be attenuating, further increases in pediatric obesity and

overweight are expected in developing countries in the coming years.

In addition to the significant physical health sequelae of overweight and obesity in children (see Ranzenhofer, Evans, McCullough, & Jelalian, *in press*), pediatric overweight and obesity have been associated with increased risk for a number of negative psychosocial outcomes (e.g., Eremis, Cetin, Tanar, Bukusoglu, Akdeniz, & Goksen, 2004; Griffiths, Parsons, & Hill, 2010; Pulgarón, 2013). For example, Morrison, Shin, Tarnopolsky, and Taylor (2015) reported that extent of obesity (% body fat) predicted elevated self-reported depressive symptoms and, importantly, lower health-related quality of life (HRQoL)<sup>1</sup> in a sample of treatment-seeking children and adolescents. Such results are consistent with a well-developed literature indicating that children with

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<sup>1</sup> HRQoL refers to a broad multidimensional concept that frequently includes subjective evaluations of both positive and negative aspects of life, and is usually considered in the

context of physical health (Centers for Disease Control and Prevention, 2011).

obesity are at particular risk for compromised HRQoL (e.g., Buttitta, Iliescu, Rousseau, & Guerrien, 2014; Griffiths et al., 2010; Schwimmer, Burwinkle, & Varni, 2003; Tsiros et al., 2009). Indeed, analyzing published data from a number of studies in the literature, Tsiros et al. reported an inverse linear relationship between body mass index (BMI) and HRQoL for both child self-reported ( $r=-0.70$ ,  $p<0.01$ ) and parent proxy-reported ( $r=-0.77$ ,  $p<0.01$ ) child HRQoL.

A range of interventions for pediatric obesity has been developed with the related goals of improving weight-related health and HRQoL. Indeed, several recent meta-analyses have documented the positive impact of behavioral interventions on weight-related outcomes in youths, with effect sizes (Cohen's  $d$ , or Hedge's  $g$ ) ranging from about .41 to about .75 (Janicke et al., 2014; Kitzmann et al., 2010; Wilfley et al., 2007). Further, a recent Cochrane Review of the literature on medical and behavioral interventions for pediatric obesity found significant favorable treatment effects for behavioral interventions delivered to both children (<12) and adolescents, and for medical interventions (i.e., orlistat and sibutramine) delivered to adolescents (Oude-Luttikhuis et al., 2009). More recently, Black, White, Viner, and Simmons (2013) reported relatively large effect sizes for a range of surgical interventions for pediatric/adolescent obesity, including Roux en Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and biliopancreatic diversion. Taken together, these meta-analyses suggest that both medical (i.e., surgical and pharmacological) and behavioral interventions for children and adolescents with obesity/overweight can be effective in terms of specific weight-related outcomes (e.g., change in  $z$ BMI).

In addition to improving weight-related health, interventions for have also been shown to be effective in terms of improving child and adolescent HRQoL among children and adolescents with obesity. For example, Tsiros et al. (2009) reviewed a number of treatment outcome studies and found that generally, weight loss in these interventions was associated with improved HRQoL, regardless of the nature of the intervention (e.g., surgical, pharmacological, behavioral or cognitive-behavioral). Similarly, in a systematic review of studies examining HRQoL and self-esteem in overweight and obese youths, Griffiths et al. (2010) found that the majority of intervention studies that resulted in weight loss also found improved HRQoL post-intervention. However, neither Tsiros et al. nor Griffiths et al. were able to quantify the association between weight loss and HRQoL because of limitations in the literature at that time.

While the literature has demonstrated that medical and behavioral interventions can have significant beneficial effects on both child/adolescent weight-related health and HRQoL, the literature has not yet quantified the degree to which changes in weight status are associated with changes in HRQoL. Based on the available literature, it is assumed and theorized that decreases in weight status are associated with improvements in HRQoL, likely in a linear fashion (e.g., Tsiros et al., 2009). However, there have been no systematic literature reviews (i.e., meta-analyses) examining this association. Thus, the primary purpose of this meta-analysis was to quantify change in HRQoL ( $\Delta$ HRQoL) in the context of both medical and behavioral interventions for pediatric overweight and obesity. Consistent with Tsiros et al.'s qualitative review, a significant association between  $\Delta$ BMI and  $\Delta$ HRQoL was hypothesized (i.e., greater reductions in BMI would be associated with greater increases in HRQoL).

However, because some studies have found differences in effect sizes of behavioral and medical interventions on weight loss ( $\Delta$ BMI; e.g., Oude-Luttikhuis et al. 2009), a secondary purpose of this study was to examine treatment type (i.e., behavioral, pharmacological, and surgical) as a moderator of the association between  $\Delta$ BMI and  $\Delta$ HRQoL. It was hypothesized that the association between  $\Delta$ BMI and  $\Delta$ HRQoL in behavioral interventions for pediatric obesity would be significantly stronger than the association between  $\Delta$ BMI and  $\Delta$ HRQoL in medical (i.e., surgical, pharmacological) interventions. This hypothesis was offered on the premise that most behavioral interventions rely exclusively on changes in physical activity or diet to effect change in BMI (see Altman & Wilfley, 2015), and changes to diet and physical activity have independently been associated with improvements in HRQoL (e.g., Herman, Seibston, Tremplay, & Paradis, 2014). It was surmised that behavioral interventions should produce change in HRQoL both as a result of the health behaviors themselves and as a result of change in BMI. Conversely, medical interventions (pharmacological or surgical) do not rely on behavioral changes to effect change in BMI to the same degree. Thus, it was anticipated that behavioral interventions would result in greater net changes in HRQoL *per unit of BMI change* than medical (pharmacological or surgical) interventions.

Finally, the association between  $\Delta$ BMI and  $\Delta$ HRQoL was examined in terms of minimally clinically important differences (MCIDs; Copay, Subach, Blassman, Polly, & Schuler, 2007). As noted by Copay et al., "[i]n the realm of healthcare, a difference may be *statistically significant*..., yet may

at the same time be of little or no importance to the health or quality of life of patients afflicted by a certain disease" (p. 541). An MCID represents the smallest change that would be considered "meaningful and worthwhile" to a patient (Copay et al., 2007, p. 542), and is frequently measured in terms of standard error of measurement (SEM; see Varni, Seid & Kurtin, 2001; Wyrwich, Tierney, & Wolinsky, 1999). As such, the amount of change in BMI that is required to observe a MCID in HRQoL was quantified. Tsiros et al. (2009) noted that it "is difficult to ascertain the change in weight status that is required before a positive influence on HRQoL is noted" (p. 396). Thus, the present study examined  $\Delta$ BMI in light of standardized MCID units to estimate the minimum change in BMI that should be associated with a MCID in HRQoL.

## METHOD

### *Literature Search*

A comprehensive literature search was conducted using PsycINFO, PubMed, and Dissertation Abstracts. Search terms included "weight", "quality of life", and "treatment OR intervention" across all three search engines. Filters were used in an attempt to restrict age to 0-18 years and articles published in English. Specifically, PsycINFO allowed use of childhood (birth-12 years of age) and adolescence (ages 13-17) filters and PubMed allowed use of a 0-18 year filter. Dissertation Abstracts did not have an age filter so studies including participants 19 years and older were excluded manually. All three search engines allowed use of an English filter.

### *Inclusion/Exclusion Criteria*

As indicated in **Figure 1**, a total of 1,553 records were screened for eligibility. To be considered for inclusion, articles must have (a) been written in English, (b) included participants 18 years of age or younger at Time 1, (c) included a sample of youth that are entirely overweight and/or obese (d) been a treatment or intervention study (i.e., not cross-sectional), (e) included both pre- and post- measures of weight (e.g., BMI, percentile scores, percent overweight, etc.) and HRQoL, (f) included weight loss as a primary study outcome (i.e., as opposed to diabetes management or metabolic control), and (g) included enough information to calculate an effect size for both weight change and HRQoL change. The full-texts of the abstracts that passed the initial screen (n=42) were further assessed for eligibility. Of these, 21 studies were included in the quantitative analyses. See **Figure 1** for the full PRISMA flow diagram of this study.

### *Coding of Studies*

Two authors coded each of the 21 articles separately, and any discrepancies were reconciled by the second author. Coders reached 90% reliability before review by the second author. To resolve discrepancies, the second author referred to the article in question and made the final decision on information to include in the analyses. Study characteristics that were coded included sample size, treatment type (behavioral, surgical, pharmacological), treatment duration, measures used, participant ethnicity, follow-up length, and child age.

### *Data Analysis*

Preliminary analyses included descriptive statistics regarding study characteristics, as well as analyses matched to specific objectives as described below.

*Change in HRQoL.* The primary purpose of this meta-analysis was to quantitatively characterize  $\Delta$ HRQoL in the context of interventions for pediatric overweight and obesity, and to relate  $\Delta$ HRQoL to  $\Delta$ BMI. As such, independent effect sizes were calculated for the change in adiposity (e.g., BMI, percent overweight) and  $\Delta$ HRQoL (child report and parent proxy report; any measure of this construct) in each identified treatment group. Multiple outcomes derived from the same sample were aggregated; each independent treatment group could contribute only one overall effect size for the primary outcome variables (see Card, 2012).

Hedges' *g* (Hedges & Olkin, 1985) was used as the index of standard mean difference between treatment conditions in the current meta-analysis. Hedges' *g* is preferred when studies in the sample of studies use relatively small sample sizes, with correspondingly greater standard errors (Card, 2012). Cohen's (1969) guidelines for interpreting effect sizes were used: small, 0.20; medium, 0.50; and large, 0.80. All effect sizes are expressed in terms of 95% confidence intervals, with confidence bands excluding zero considered statistically significant. Individual treatment group effect sizes were aggregated into an overall mean effect size using a weighted approach that assigns weight using the inverse of the squared standard error (Card, 2012).

To examine the homogeneity of effect sizes for the primary outcome variable, the *Q* statistic was utilized. A significant *Q* statistic indicates that within-group variability among effect sizes is greater than sampling error alone would predict, suggesting the presence of moderator variables (Card, 2012; Lipsey & Wilson, 2001). A random effects model was used for effect size calculations, which allows for between-study variation in accordance with the population

distribution, thus allowing for conclusions to be generalized to the broader literature.

*Moderator Analyses.* The second objective of this investigation was to examine treatment type (behavioral, surgical, pharmacological) as a moderator of the association between  $\Delta$ BMI and  $\Delta$ HRQoL. For the purposes of coding, behavioral treatments employed behavioral, dietary, and/or exercise approaches. First, ANOVA techniques were used to examine differences in HRQoL effect sizes between treatment types. Next, a regression analysis was conducted by treatment group to determine the  $R^2$  for the relationship between  $\Delta$ BMI and  $\Delta$ HRQoL by treatment category. Tests for moderation (i.e., whether treatment category significantly moderated this relationship) were conducted using the PROCESS Procedure for SPSS (release 2.12).

*Minimally Clinically Important Differences.* Finally, the amount of weight loss needed to achieve statistically significant improvements in HRQoL was quantified. To accomplish this objective, units of minimal clinically important difference (MCID) were calculated for each measure of HRQoL using the standard error of measurement (SEM) approach. The SEM approach assesses whether the change in scores is greater than the variation expected due to unreliability. A change greater than one SEM unit is considered likely to be due to true change rather than measurement error (Copay et al., 2007). In order to examine MCID units of HRQoL in light of weight loss, it was necessary to keep weight in its original units (i.e., not convert to an effect size). Because BMI was the most commonly calculated weight change metric across studies, this metric was selected as the unit of weight change for this objective. A weighted least-squares regression line was fitted to these two variables, such that studies with less error would contribute more weight to the regression equation. Once a regression line was fitted, that regression line equation was used to calculate BMI loss associated with a clinically significant change in HRQoL (i.e., a change of one SEM unit).

## RESULTS

The literature search returned 21 studies eligible for inclusion. Generally, studies were most often excluded due to age range, inclusion of healthy weight participants, and lack of both pre- and post- measures of both weight and HRQoL. Within these 21 studies,

29 independent treatment groups were included in study analyses. A single study contributed multiple groups to the analyses if both the intervention group and the control group met inclusion criteria (i.e., the control group was an active treatment). **Table 1** describes characteristics of included studies. Overall, group sample sizes ranged from 16 to 139. Five studies utilized surgical techniques (i.e., Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, and laparoscopic sleeve gastrectomy); one study utilized a pharmacological intervention (sibutramine). The remaining studies examined various combinations of behavior, exercise, and nutrition treatment components. Treatment duration varied considerably, with treatments ranging from a single episode of surgery to treatment sessions spanning weeks, months, and years (see **Table 1** for description of interventions and length of treatment). Data from the lone pharmacological study (Garcia-Morales et al., 2006) were retained for the calculation of the overall ES and for the calculation of the association between  $\Delta$ BMI and  $\Delta$ HRQoL, but were dropped for moderation analyses.<sup>2</sup>

### *Overall effect size $\Delta$ HRQoL*

The overall effect size for  $\Delta$ HRQoL in the context of pediatric weight-change interventions was statistically significant and falls in the medium range,  $g = 0.51$ , 95% CI (0.43-0.59), SE = 0.04. A forest plot of each study's effect size (on HRQoL) and confidence interval is depicted in **Figure 2**. Given the range of study characteristics included in this analysis, heterogeneity was assessed to determine whether moderator analyses were appropriate to conduct. Not surprisingly,  $Q$  was statistically significant ( $Q = 96.7$ ,  $p \leq .001$ ), indicating that more variability is present than would be expected due to chance alone.

In order to assess for potential publication bias, a fail-safe  $N$  calculation was conducted to determine the number of excluded studies averaging an effect size of zero that would have to be added to the current study to lower the total effect size to zero. The number of such null studies was calculated to be 1,216, suggesting that these findings are robust to publication bias.

### *Association between $\Delta$ BMI and $\Delta$ HRQoL*

The amount of weight change per study group is depicted in a forest plot in **Figure 3**. Weighted regression analyses were conducted to assess the linear

*and in the analyses of the relationship between  $\Delta$ BMI and  $\Delta$ HRQoL, but was not included in the examination of treatment type as a moderator of the relationship between  $\Delta$ BMI and  $\Delta$ HRQoL.*

<sup>2</sup> *The a priori intent of this paper was to quantify the change in HRQoL that could be expected from any intervention that impacted BMI. Interestingly, only one pharmacological intervention that reported on HRQoL as an outcome was identified. This study was included in the omnibus effect size*

relationship between  $\Delta$ BMI and  $\Delta$ HRQoL over the course of treatment. A significant linear relationship was detected with an  $R^2 = 0.87$ ,  $p < .0001$  (**Figure 4**).

#### *Moderator analyses*

Weighted moderator analyses were conducted to examine treatment effects due to surgical versus behavioral weight-loss approaches. While both intervention types yielded statistically significant changes to HRQoL (i.e., confidence interval of effect size did not include zero), a significant difference existed between these two treatment types, in line with the larger changes in BMI. Studies of surgical interventions yielded a large effect size for  $\Delta$ HRQoL,  $g = 1.27$ ; 95% CI (1.06-1.49),  $N = 5$  and large effect sizes for  $\Delta$ BMI,  $g = 2.26$ ; 95% CI (2.04, 2.49). Studies of behavioral interventions yielded a small effect size for  $\Delta$ HRQoL,  $g = 0.28$ ; 95% CI (0.19, 0.37),  $N = 23$  and  $\Delta$ BMI,  $g = 0.26$ ; 95% CI (0.17, 0.35).<sup>3</sup>

Regression analyses revealed that the moderated effect of  $\Delta$ BMI on  $\Delta$ HRQoL by treatment group was statistically significant, with surgical groups demonstrating a stronger relationship between these variables than behavioral interventions (see **Table 2**; **Figure 6**). Indeed, only the surgical intervention category demonstrated a significant association between  $\Delta$ BMI and  $\Delta$ HRQoL ( $R^2 = 0.94$ ,  $p < .05$ ).<sup>2</sup> Though behavioral interventions resulted in significant changes for both BMI and HRQoL, the degree of change in BMI was not significantly related to  $\Delta$ HRQoL ( $R^2 = 0.03$ , ns).

#### *Minimally Clinically Important Differences*

To determine the amount of weight loss needed to yield a clinically significant elevation in HRQoL, HRQoL data was converted to MCID units. Only BMI data were used for weight analyses. This weighted regression yielded a significant  $R^2 = 0.56$ . For the behavioral interventions, the regression coefficient  $R^2 = 0.49$ , and for the surgical interventions, the  $R^2 = 0.75$ . Overall, one unit of HRQoL MCID was associated with a change of 0.988 BMI units, indicating that it takes the loss of about a single BMI unit to detect a “true change” (Copoly et al., 2007, p. 544) in HRQoL (see **Figure 5**).

## DISCUSSION

Overweight and obesity continue to pose significant threats to the health and wellbeing of children and adolescents in the United States and

abroad (Ogden et al., 2014; Ng et al., 2013). Specific physical health risks experienced by children with overweight and obesity may include apnea, musculoskeletal problems, asthma, diabetes, and/or sleep problems (Ranzenhofer et al., *in press*). Psychosocial risks to children and adolescents with overweight and obesity may include internalizing and externalizing problems, self-esteem, peer-related problems, and/or diminished health-related quality of life (HRQoL; Eremis et al., 2004; Buttitta et al., 2014). Though previous studies and reviews have suggested that evidence-based interventions to reduce BMI can be associated with improved HRQoL (e.g., Tsiros et al. 2009), no studies were identified that quantitatively evaluated the associations between change in adiposity and change in HRQoL. Thus, the current study had three objectives: to quantify change in HRQoL in the context of interventions for pediatric overweight and obesity, to examine treatment type (medical, behavioral) as a moderator of the association between  $\Delta$ BMI and  $\Delta$ HRQoL, and to examine the association between  $\Delta$ BMI and  $\Delta$ HRQoL in terms of minimally clinically important differences (MCIDs; Copay et al., 2007; Wyrwich et al., 1999).

With regard to the first objective (i.e., to quantify  $\Delta$ HRQoL in the context of interventions for pediatric overweight and obesity), the results yielded a small-to-medium effect size for HRQoL change. Previous studies have demonstrated that HRQoL can increase as a result of weight loss and participation in obesity treatments (e.g., Griffiths et al., 2010; Tsiros et al., 2009), but the magnitude of  $\Delta$ HRQoL and the specific relationship between weight change and  $\Delta$ HRQoL was not known. Results from this meta-analysis suggest that participation in a weight-management intervention can be associated with significantly improved HRQoL. This is a particularly important finding, in that Tsiros et al. had noted that psychosocial functioning (i.e., HRQoL) might be more resistant to change than physical functioning or outcomes. The results reported here suggest that this may not be the case.

Further, and consistent with hypotheses, weight loss and  $\Delta$ HRQoL were significantly correlated and yielded a medium-large strength of correlation ( $R^2 = 0.87$ ). This finding is noteworthy as it suggests that across a range of interventions, weight loss was strongly and significantly associated with increases in HRQoL. In fact, further analyses on how much weight

<sup>3</sup> Due to its outlier status, analyses were also conducted without Aldaqual & Sehlo (2013). The overall correlation between  $\Delta$ HRQoL and  $\Delta$ BMI remained significant, but dropped in magnitude to 0.48. The correlation between  $\Delta$ HRQoL and  $\Delta$ BMI for surgical interventions became non-

significant. The effect size for surgical interventions dropped to 0.89 (0.67-1.1). This was the sole study to utilize the laparoscopic sleeve gastroscopy procedure, often considered a more complicated surgery than others, such as gastric banding.

loss is associated with clinically significant change in HRQoL (i.e., MCID) demonstrated that clinically significant changes in HRQoL can be detected after only a decrease of about one BMI unit (0.998 BMI; although the size of this relationship may differ by type of intervention). As noted by Copay et al., (2007), a potential use of MCID is as a benchmark for improvement of individual patients receiving specific treatments. At an aggregate level, these data provide a standard by which to evaluate future treatment outcome studies; in addition to tests of statistical significance, studies can be evaluated in light of the proportion of participants who achieve MCID (Copay et al., 2007). Of particular importance for future research in this area will be the inclusion of measures of HRQoL as new treatment outcome studies are designed and conducted.

Though caution must be exercised when considered at the individual level, the present data suggest that even relatively small changes in BMI may be associated with improvements in HRQoL. One BMI unit translates to roughly five pounds in 10-year-old children, and about three pounds in six-year-old children (Centers for Disease Control and Prevention, 2009). The amount of weight loss or height gain needed for a specific patient is easily calculable and offers a definable goal to begin noticing positive effects in daily life. Further, positive changes in HRQoL can be associated with subsequent positive health behavior change (e.g., increased physical activity; Breslin, Gossrau-Breen, McCay, Gilmore, MacDonald, & Hanna, 2012), perhaps predicting further decreases in adiposity and improvements in HRQoL.

An additional goal of the study was to examine the degree to which the type of intervention (i.e., behavioral, surgical, pharmacological) moderated the association between  $\Delta$ HRQoL and change in adiposity. It was supposed that—by virtue of their specific targeting of health behaviors that have been associated with improved HRQoL (e.g., Herman et al., 2014)—behavioral interventions would be associated with greater changes in HRQoL per unit of BMI change. However, contrary to predictions, surgical interventions yielded significantly greater increases in HRQoL (see **Table 2** and **Figure 6**) per unit of BMI change. While one might expect greater changes in HRQoL due to more substantial changes in BMI (i.e., main effects), the present finding of differential rate of change *per unit of BMI change* (i.e., moderation) is provocative, but complicated.

Surgical interventions are often recommended when behavioral treatments have failed or are implausible, or when very substantial weight loss is

necessary (see Pratt et al., 2009), whereas behavioral interventions are recommended for a greater proportion of children with overweight and/or obesity (Barlow et al., 2007). Further, surgical options are generally recommended for adolescents, whereas behavioral interventions can be recommended for children of most ages. It may be that the increased rate of change in HRQoL per unit change in BMI observed in the surgical interventions is an artifact of participant age or initial weight status. However, the differential association between  $\Delta$ HRQoL and  $\Delta$ BMI may be due to specific salutary effects of bariatric surgery. Black, White, Viner, and Simmons (2013) have noted that the specific mechanisms of action of bariatric surgery are not as clear as once believed. It is possible that there are additive benefits to surgery beyond weight loss, including those that might impact HRQoL. Although the present analyses do not suggest that surgery is the preferred method of weight loss intervention for all youth, they do indicate that when surgery is considered appropriate, providers and patients can expect clinically meaningful improvements in both adiposity and in HRQoL. Because the relationship between  $\Delta$ HRQoL and  $\Delta$ BMI in surgical studies was influenced by one study with very large treatment effects (Aldaqual & Sehlo, 2013), additional study of this association is warranted.

Building on the reviews by Oude-Luttikhuis et al. (2009) and Tsiros et al. (2009), this meta-analysis reflects the growing quantity and diversity of interventions for pediatric obesity, and provides a unique examination of HRQoL-related outcomes associated with this range of treatment options. However, only one pharmacological intervention was located that assessed HRQoL in children, limiting the degree to which the associations between  $\Delta$ HRQoL and  $\Delta$ BMI across all three intervention types (behavioral, surgical, and pharmacological) could be examined. Given the importance of HRQoL as an outcome in its own right (see Tsiros et al., 2009), future investigations of pharmacological interventions for pediatric obesity should routinely include measures of HRQoL as an outcome variable. Future meta-analyses should endeavor to refine intervention groups (e.g., educational, behavioral, pharmacological, different types of surgical procedures) and intervention characteristics (e.g., treatment duration, session length, provider background), and examine specific HRQoL outcomes associated with each. Furthermore, given the discrepancy between samples on participant characteristics such as age and baseline weight status, future studies should examine these factors.

An additional limitation of the current study was that the broad level of analyses did not allow



examination of the degree to which weight change was associated with specific components or subdomains of HRQoL (e.g., physical function, emotional function). In the current sample of studies, only a handful reported on HRQoL subscale scores rather than total scores, limiting potential analyses at this level. Relatedly, the present investigation did not allow independent assessments of the associations between weight loss and changes in generic vs. weight-specific measures of HRQoL. All studies included in this analysis used generic measures of HRQoL. As noted by Dalton, Smith, Dalton, and Slawson (*in press*), condition-specific measures (e.g., *Sizing Me Up*; Zeller & Modi, 2009) may be more likely to identify changes in HRQoL than generic measures (e.g., *PedsQL*; Varni, Seid & Kurtin, 2001). As more investigations utilize condition-specific measures of HRQoL, future analyses may suggest greater treatment-related gains in HRQoL using such measures.

Also important to note is that the present analyses examined HRQoL effects collapsed across child and parent report. Some studies (e.g., Ul-Haq, Mackay, Fenwick, & Pell, 2013) have suggested that parents may overestimate the impact of obesity on HRQoL. Future work should examine the degree to which child weight loss is associated with parent- vs. child-reported HRQoL. Comparisons between treatment types and—in particular—the question of treatment type as a moderator of the relationship between HRQoL and BMI, can only be addressed definitively through studies that use random assignment to treatment group (i.e., medical vs. behavioral). In the current sample of studies, only one study was designed in this manner (i.e., O'Brian et al., 2010). Finally, and as noted above, future studies might also examine the mechanisms by which weight loss is associated with increased HRQoL by tracking changes in potentially mediating variables such as physical activity.

Although the CDC (2009) notes that BMI-SDS and BMI percentile (BMI%) are preferred when measuring adiposity as a treatment outcome in children, studies

included in this analysis reported on change in adiposity using a variety of metrics, including BMI-SDS, BMI%, change in percent overweight, and unstandardized BMI. The current analysis used standardized (i.e., unitless) effects sizes to characterize pre-post change within each study and to examine the relationships among variables of interest. Correspondingly, the results of the meta-analyses are robust to different measurement strategies of children's adiposity. However, since this examination of minimally clinically important differences (MCID) used only studies with a common adiposity metric (BMI), it is possible that this analysis was subject to selection bias, and that the relationship between MCID and change in adiposity would have been attenuated with the use of BMI% or BMI-SDS. MCID analyses are presented to provide general expectations for the relationship between weight change and HRQoL. Clinical decision-making about how much weight a child should lose should be discussed on an individual basis relative to age, sex, and other specific health-related risk factors and circumstances.

Overall, the present study contributes to the literature by providing the first known quantitative examination of changes in HRQoL associated with pediatric weight loss interventions and of the association between weight loss (i.e.,  $\Delta$ BMI) and  $\Delta$ HRQoL. Results suggest a small to medium effect of weight loss interventions on HRQoL and a moderate association between change in weight and  $\Delta$ HRQoL. Importantly, the present results suggest that a decrease of about one BMI unit can be associated with minimally important clinical differences (MCID) in total HRQoL, with greater changes possible from medical (i.e., surgical) vs. behavioral interventions. Future work is needed to refine these initial results, with particular emphasis on measurement issues (e.g., parent- vs. child-report measures; condition-specific vs. generic measures of HRQoL) and on examination of changes in HRQoL in the context of more specific treatment categories.

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<sup>4</sup>Studies marked by an asterisk were included in the meta-analysis.



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TABLE 1. STUDY CHARACTERISTICS

First author, year	Treatment Group	Baseline Sample Size (N)	Weight Change Effect size, 95% CI	HRQoL Effect Size, 95% CI	Treatment Duration	HRQOL Measure	HRQOL Reporter	Mean Age (SD)	Weight Metric	Baseline Weight Status (SD)
Aldaqual, 2013**	Laparoscopic sleeve gastrectomy	32	6.12 (4.55, 7.70)	3.49 (2.44, 4.54)	Medical pre-surgery evaluation + surgery	Peds QL	Child and Parent/Care giver	15.16 (1.2)	BMIz	2.79 (0.22)
Croker, 2012**	Behavioral therapy	37	0.05 (-1.10, 1.2)	0.11 (-0.74, 0.95)	15 sessions, 6 months	Peds QL	Child and Parent/Care giver	10.3 (1.6)	BMI	30.6 (5.1)
Cronk, 2011	Behavioral therapy	59	0.36 (-0.16, 0.88)	0.95 (0.08, 1.83)	6 sessions, 6 weeks	Ped QL	Child	10 (0.9)	BMIz	2.04 (0.37)
de Niet, 2012	A) Behavioral therapy + text messages	73	1.25 (0.12, 2.37)	0.30 (-0.47, 1.07)	14 sessions, 3 months + weekly text messages, 9 months	Child Health Questionnaire	Parent/Care giver	9.9 (1.3)*	BMI-SDS	2.63 (0.45)
	B) Behavioral therapy	68	0.35 (-0.75, 1.45)	0.25 (-0.53, 0.25)	14 sessions, 3 months	Child Health Questionnaire	Parent/Care giver	9.9 (1.3)*	BMI-SDS	2.54 (0.44)
Dove, 2008**	A) Diet, exercise, and behavioral modification	22	0.40 (-0.86, 1.67)	0.09 (-0.89, 1.06)	30 sessions, 10 weeks	Peds QL	Child	Not reported	BMI	31.7 (6.2)
	B) Exercise Only	20	0.17 (-1.07, 1.41)	0.23 (-0.73, 1.19)	50 PE classes, 10 weeks	Peds QL	Child	Not reported	BMI	31.7 (6.2)
Garcia-Morales, 2006**	Pharmacology (Sibutramine)	23	0.50 (-0.71, 0.50)	0.60 (-0.33, 1.52)	6 sessions, 6 months	SF-36	Not reported	14.95 (1.2)*	BMI	35.1 (5.3)

Holterman, 2010**	Laparoscopic adjustable gastric banding	20	0.96 (-0.27, 2.20)	1.33 (0.43, 2.23)	4-6 months treatment pre-surgery + surgery	Peds QL	Child and Parent/Care giver	16 (1)	BMI	50 (10)
Kalarchian, 2009**	Behavioral therapy	97	0.03 -1.06, 1.12)	0.24 (-0.53, 1.00)	20 sessions, 6 months	Child Health Questionnaire	Parent/Care giver	10.2 (1.2)*	BMI	31.71 (5.21)
McCallum, 2007	Behavioral therapy	82	0.03 (-1.06, 1.13)	0.26 (-0.52, 1.03)	4 sessions, 12 weeks	Peds QL	Parent/Care giver	7.4 (1.6)	BMIz	2.00 (0.50)
O'Brian, 2010**	A) Laparoscopic adjustable gastric banding	25	2.01 (0.76, 3.26)	0.65 (-0.26, 1.56)	2 month pre-randomization treatment, surgery	Child Health Questionnaire	Child	16.55 (1.3)*	BMI	42.3 (6.1)
	B) Behavioral therapy	25	0.32 (-0.89, 1.53)	0.19 (-0.74, 1.11)	2 month pre-randomization treatment support, 4 sessions, 24 months	Child Health Questionnaire	Child	16.55 (1.3)*	BMI	40.4 (3.1)
Pinard, 2012	Behavioral therapy	26	0.03 (-1.16, 1.23)	0.56 (-0.35, 1.46)	6 sessions, 3 months	Peds QL	Child	10.5 (1.2)	% body fat	38.2 (6.3)
Robertson, 2011**	Behavioral therapy	27	0.05 (-1.18, 1.28)	0.60 (-0.24, 1.43)	12 sessions, 12 weeks	Peds QL	Child	9.3 (1.9)	BMIz	2.7 (0.64)
Shoemaker, 2011**	Behavioral therapy	26	0.05 (-1.17, 1.27)	0.28 (-0.69, 1.25)	12 sessions, 12 weeks	Peds QL	Child	11 (2.1)	BMI	30.4 (7.8)
Steele, 2012	A) Behavioral therapy	47	0.41 (-0.73, 1.55)	0.55 (-0.28, 1.39)	10 sessions, 10 weeks	Peds QL	Child and Parent/Care giver	11.57 (2.64)*	BMIz	2.2 (0.34)

	B) Diet only	46	0.25 (-0.90, 1.40)	0.19 (-0.65, 1.03)	3 sessions, 10 weeks	Peds QL	Child and Parent/Care giver	11.57 (2.64)*	BMIz	2.24 (0.36)
Sysko, 2012**	Laparoscopic adjustable gastric banding	101	0.18 (-0.91, 1.26)	0.11 (-0.64, 0.86)	Surgery, 15 routine follow-up appointments, 15 months	Peds QL	Child	15.8 (1.1)	BMI	47.23 (8.84)
Vos, 2012	Behavioral therapy	36	0.34 (-0.80, 1.48)	0.30 (-0.52, 1.12)	15 sessions + booster sessions, 2 years	DisabKids	Child and Parent/Care giver	13.2 (2)	BMI-SDS	4.2 (0.7)
Wafa, 2011**	Behavioral therapy	52	0.00 (-1.13, 1.13)	0.22 (-0.52, 0.96)	8 sessions, 26 weeks	Peds QL	Child and Parent/Care giver	9.8 (1.5)	BMIz	2.9 (0.49)
Wake, 2009**	Behavioral therapy	139	-0.18 (-1.25, 0.90)	0.69 (-0.31, 1.68)	4 sessions, 12 weeks	PedsQL	Parent/Care giver	Not reported	BMI	20.2 (2.3)
Yakovitch-Gavan, 2008**	A) Diet only (low carb, low protein)	18	0.43 (-1.50, 2.35)	0.50 (-0.53, 1.52)	12 sessions, 12 weeks	Peds QL	Child	14.3 (1.7)*	BMI	36 (7.7)
	B) Diet only (low carb, high protein)	17	0.37 (-1.74, 2.48)	0.56(-0.31, 1.43)	12 sessions, 12 weeks	Peds QL	Child	14.3 (1.7)*	BMI	33.6 (5.5)
	C) Diet only (high carb, low protein)	36	0.30 (-1.82, 2.42)	0.39 (-0.43, 1.20)	12 sessions, 12 weeks	Peds QL	Child	14.3 (1.7)*	BMI	34.4 (6.2)
Yakovitch-Gavan, 2009**	A) Exercise	52	0.27 (-1.92, 2.46)	0.55 (-0.27, 1.37)	36 sessions, 12 weeks	Peds QL	Parent/Care giver	8.3 (1.6)*	BMI	25.5 (3.53)

	B) Diet	55	0.62 (-0.82, 2.06)	0.43 (-0.37, 1.24)	12 sessions, 12 weeks	Peds QL	Parent/Care giver	8.3 (1.6)*	BMI	26.5 (3.56)
	C) Diet and exercise	55	0.54 (-0.98, 2.07)	1.53 (0.46, 2.61)	48 sessions, 12 weeks	Peds QL	Parent/Care giver	8.3 (1.6)*	BMI	25.9 (3.56)
Zeller, 2011**	Roux-en-Y gastric bypass	16	2.63 (1.19, 4.07)	0.47 (-0.37, 1.31)	Surgery + clinical visits	Peds QL	Child	16.2 (1.4)	BMI	59.91 (8.71)

\*The mean and standard deviation represents average age across the study groups.

\*\*Studies included in MCID calculations.



**TABLE 2. REGRESSION TABLE FOR TESTING THE INTERACTION BETWEEN BMI AND HRQOL ACROSS TREATMENT**

TYPE .  $R^2$  INCREASE DUE TO INTERACTION: 0.02,  $F = 4.71$ ,  $p < 0.05$ .

<b>R</b>	<b>R<sup>2</sup></b>	<b>MSE</b>	<b>F</b>	<b>df1</b>	<b>df2</b>	<b>p</b>
0.94	0.89	0.06	63.31	3	24	<0.05

<b>Variable</b>	<b>Coefficient</b>	<b>SE</b>	<b>t</b>	<b>p</b>
Constant	0.44	0.21	2.14	>0.05
Treatment Type	-0.09	0.17	-0.55	ns
BMI	-0.26	0.35	-0.74	ns
BMI x Type	0.39	0.18	2.17	<0.05

FIGURE 1. PRISMA 2009 FLOW DIAGRAM

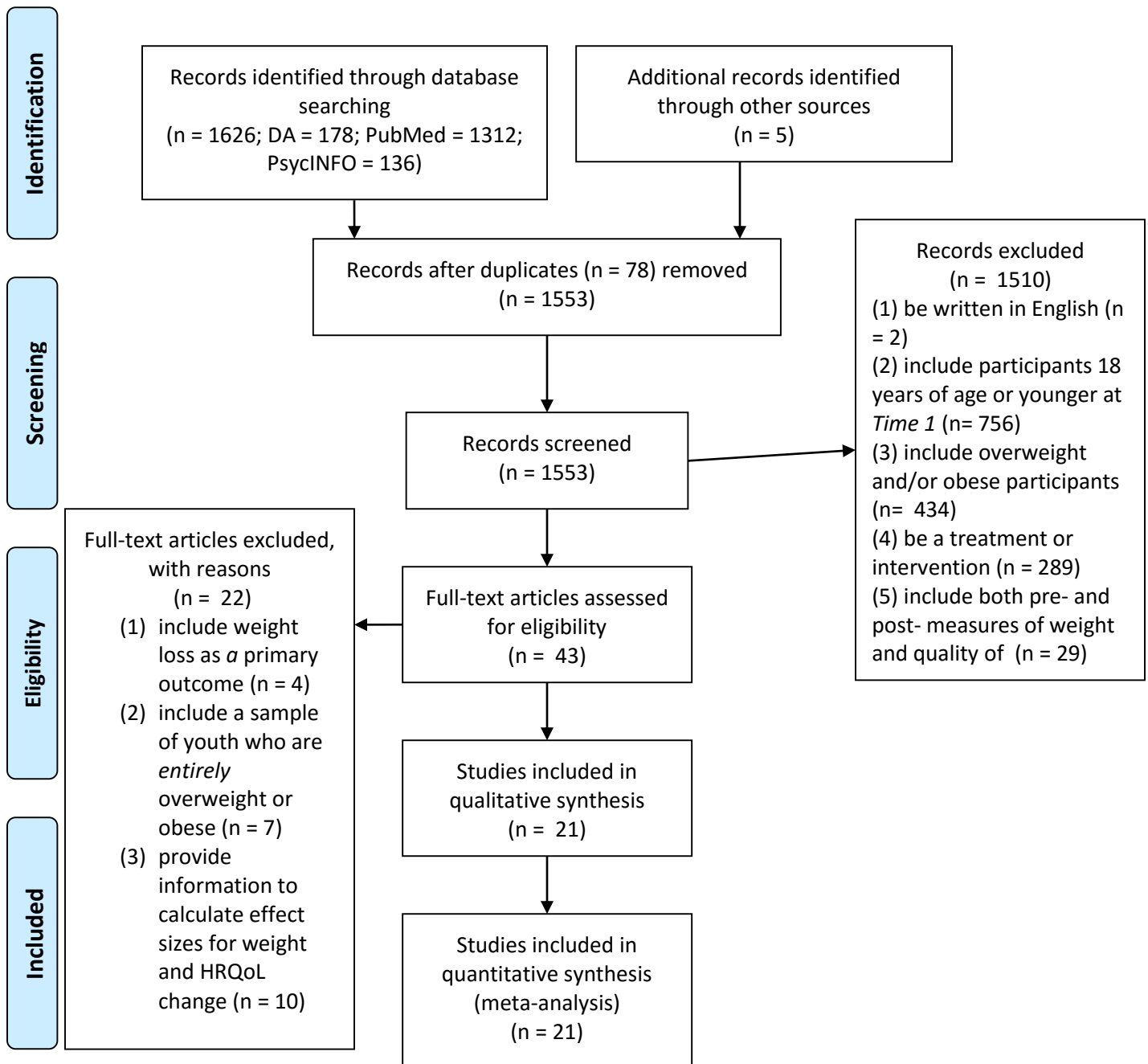


FIGURE 2. FOREST PLOT OF HRQOL CHANGE EFFECT SIZE

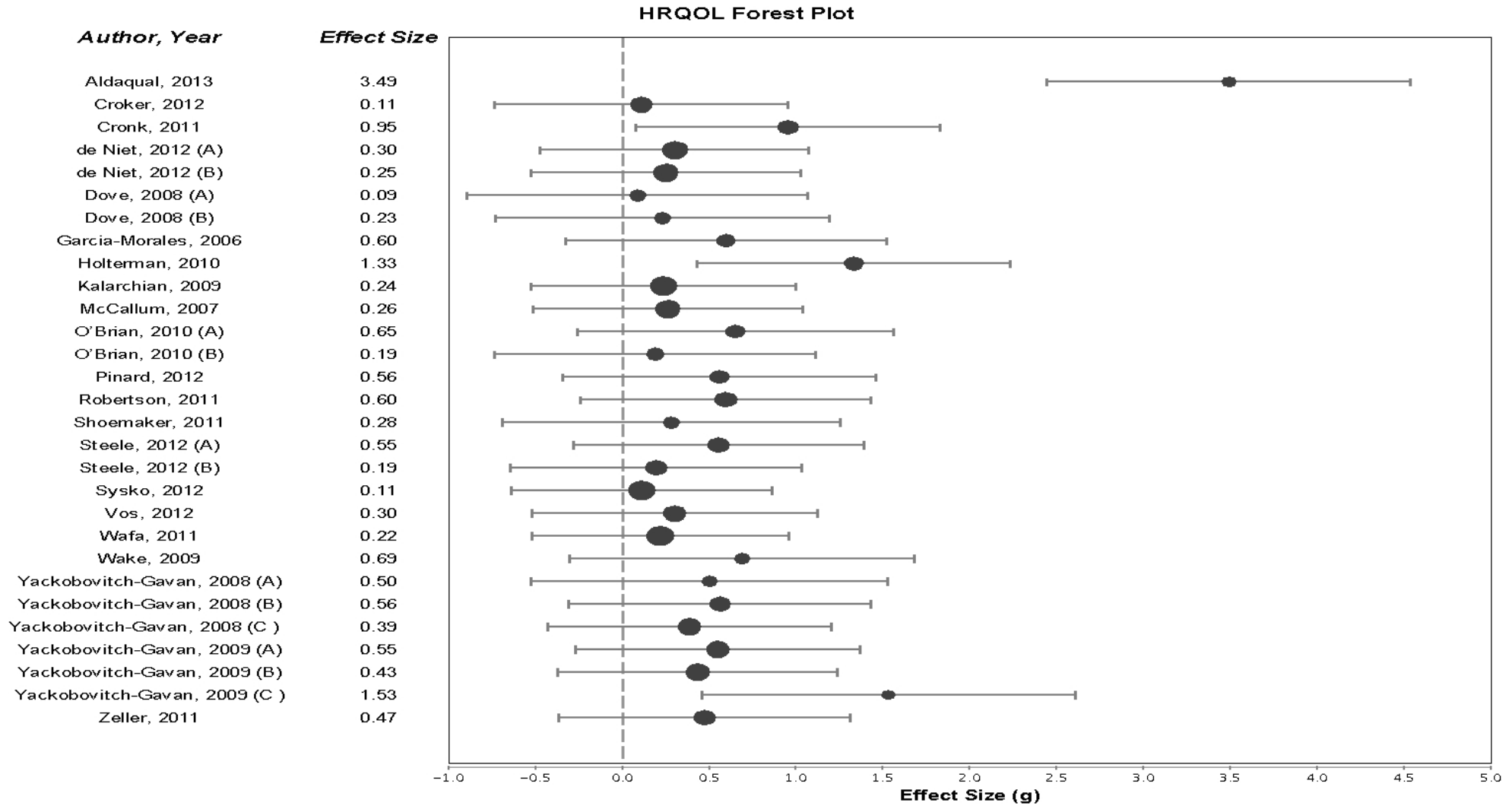
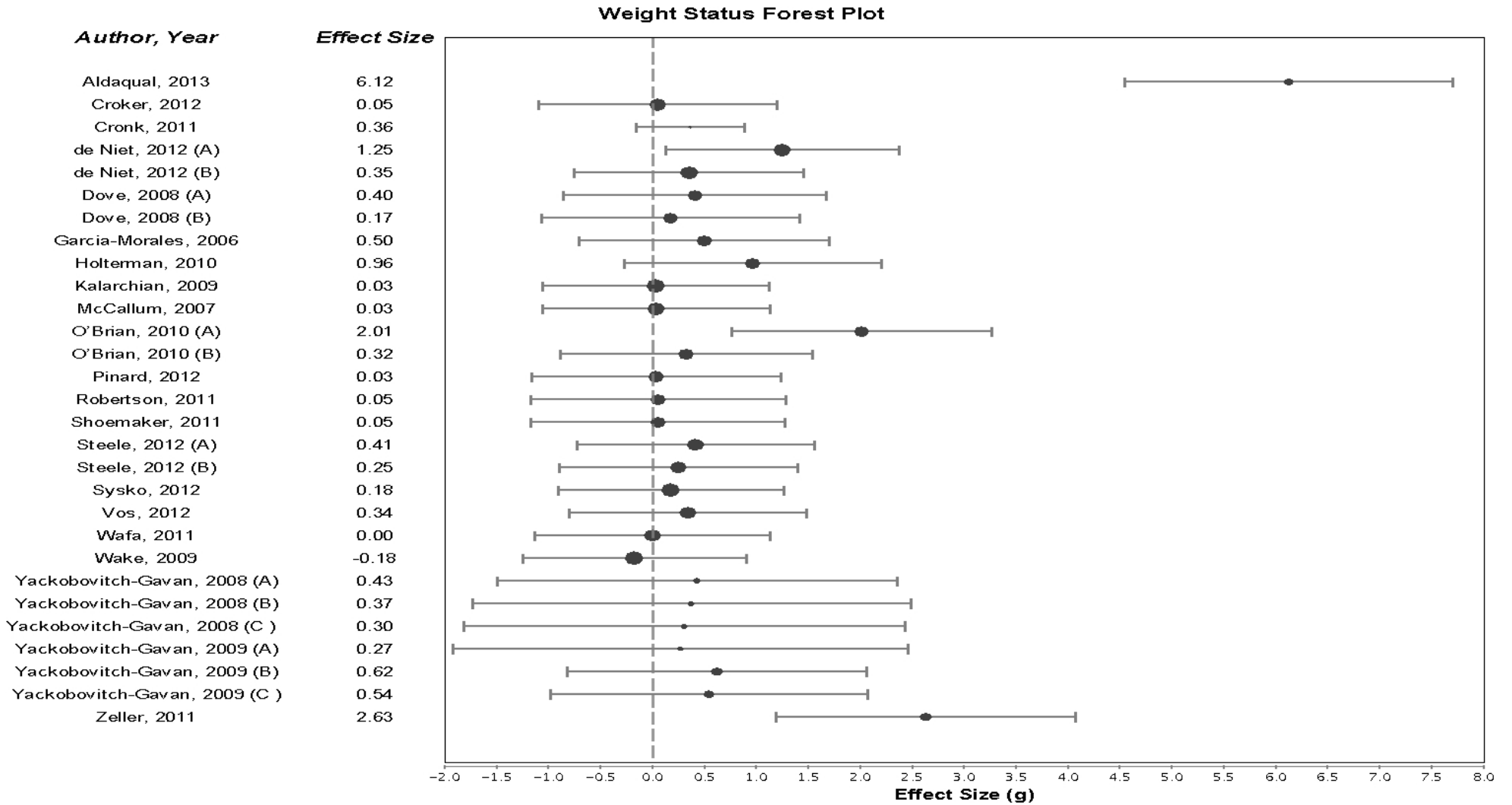
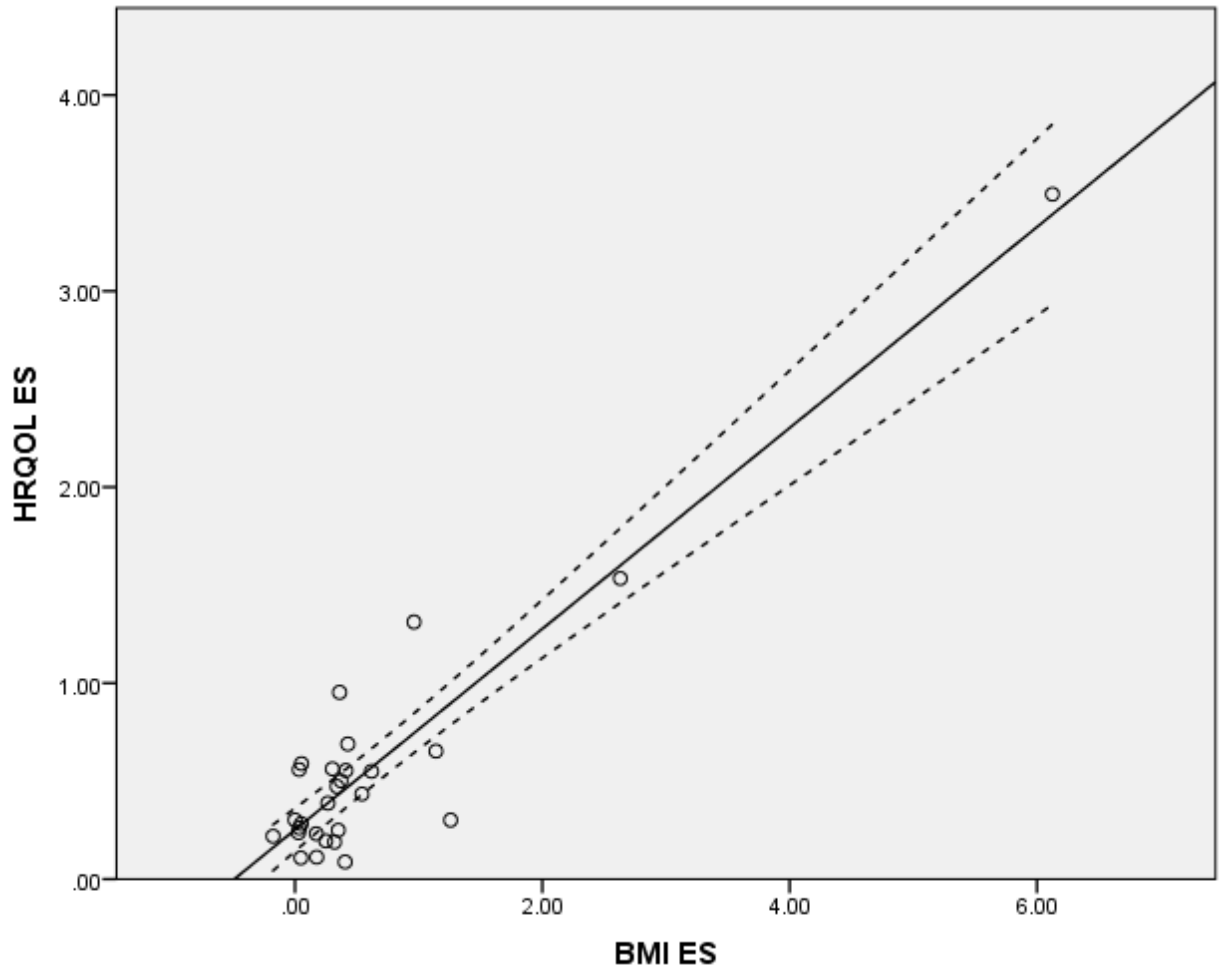


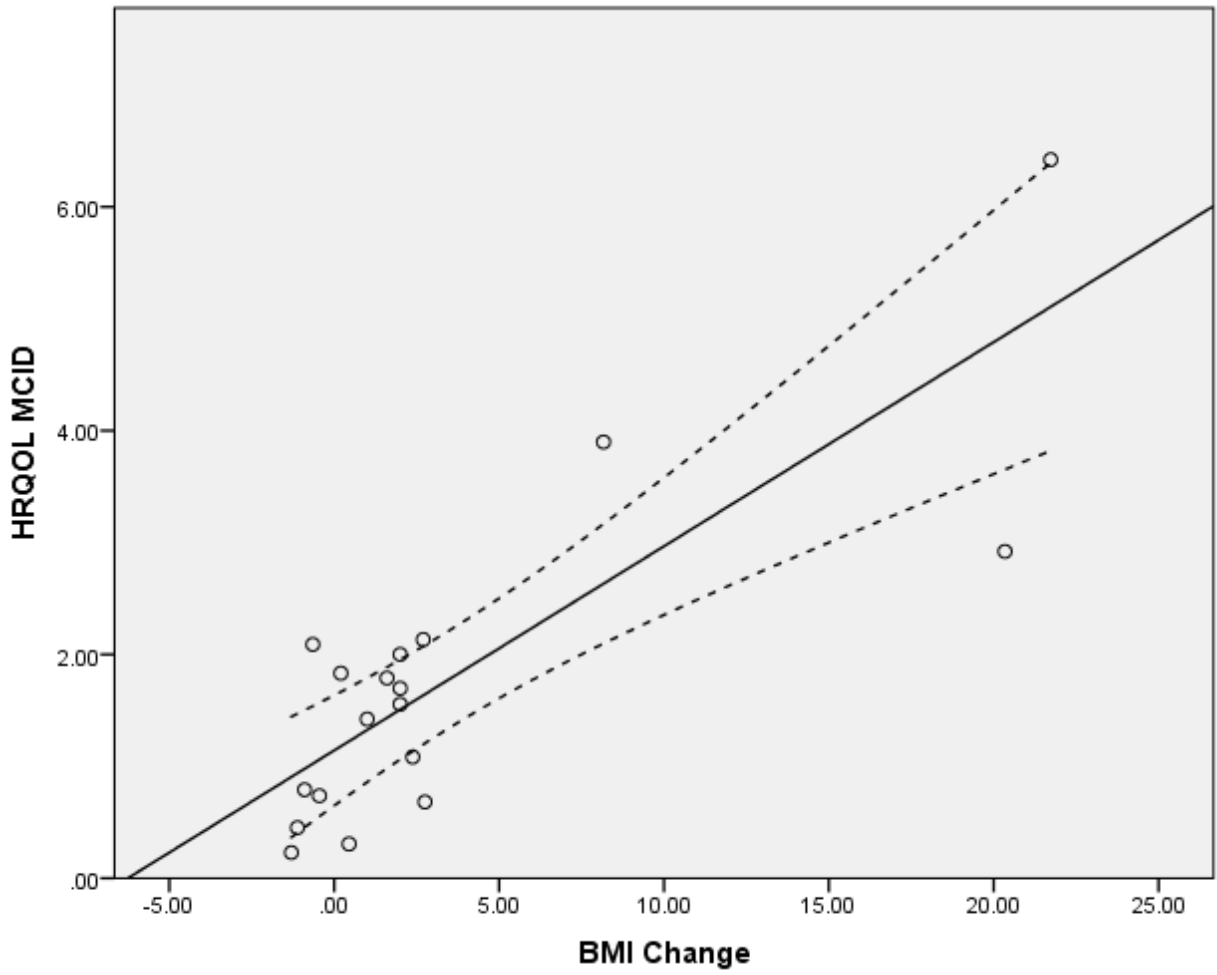
FIGURE 3. FOREST PLOT OF WEIGHT CHANGE EFFECT SIZE



**FIGURE 4. SCATTERPLOT AND REGRESSION LINE DEPICTING RELATIONSHIP BETWEEN BMI EFFECT SIZE (BMIES) AND HRQOL EFFECT SIZE (QOLES) FOR EACH STUDY. NOTE: EACH CIRCLE REPRESENTS AN INTERVENTION GROUP. DASHED LINES REPRESENT 95% CONFIDENCE INTERVAL.**



**FIGURE 5. SCATTERPLOT AND REGRESSION LINE DEPICTING THE MCID ANALYSES, SPECIFICALLY THE RELATIONSHIP BETWEEN BMI CHANGE AND HRQOL SEM UNITS.**





**FIGURE 6. SCATTERPLOT AND REGRESSION LINES OF THE RELATIONSHIP BETWEEN HRQOL EFFECT SIZE AND BMI EFFECT SIZE BY TREATMENT GROUP.**

