Physical Activity and Health-Related Quality of Life in Children and Adolescents: A Systematic Review and Meta-Analysis

By

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Abstract

Physical activity is associated with broad physical and psychological benefits in children and adolescents. One construct which may universally characterize functioning across various pediatric populations is health-related quality of life (HRQOL). A number of studies have found positive associations between physical activity and HRQOL; however, to date no systematic review and meta-analysis of physical activity and HRQOL has successfully quantified effects in children and adolescents. A systematic search of PubMed, PsycINFO, and ProQuest Dissertation Abstracts identified 1081 relevant, non-duplicate articles. Out of these possible articles, 33 studies, including both descriptive and pre-post intervention designs, met inclusion criteria and were included in effect size analyses. In descriptive studies, there was a small, positive effect of physical activity on HRQOL based on child-reports (Hedge's $g = .302$, $p < .001$) and a negligible effect based on parent-proxy reports (Hedge's $g = .115$, $p = .101$). In intervention studies, there was a small, positive effect of physical activity intervention on HRQOL based on child-reports (Hedge's $g = .279$, $p = .014$) and a medium, positive effect based on parent-proxy reports (Hedge's $g = .522$, $p = .012$). However, effects are attenuated by removal of a single intervention study. Overall, these findings supported the primary hypothesis that increased levels of physical activity would be related to better HRQOL in youth, although the magnitude of these effects did not represent a minimal clinically important difference (MCID) in most studies. Hypothesized moderators, including chronic disease status, weight status, sex, and study rigor, did not significantly moderate the relationship between physical activity and HRQOL. Exploratory analyses did not find intervention contact hours or age to moderate the effect of exercise on HRQOL. Future studies are needed to assess HRQOL in youth before and after high-quality exercise interventions to quantify the type, frequency,

duration, and intensity of physical activity needed to change HRQOL to a clinically meaningful level. Although effects were small and analyses were limited, this study represents the first meta-analysis of physical activity and HRQOL across pediatric populations and may serve as a guide for future studies.

Keywords: *physical activity, health-related quality of life, child, adolescent*

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Physical activity and health-related quality of life in children and adolescents: A systematic review and meta-analysis

The U.S. Department of Health and Human Services (2008) and the World Health Organization (2010) recommend that children and adolescents achieve 60 minutes of moderate-to-vigorous physical activity (MVPA) each day to optimize health benefits. Unfortunately, only a quarter of all U.S. children and adolescents currently meet these guidelines (Dentro et al., 2014). Physical activity is associated with a number of positive physical health outcomes, such as maintaining a healthy weight (Janssen et al., 2005), developing strong bones (Boreham & McKay, 2011), and reducing the risk of chronic diseases and some cancers (US Department of Health and Human Services, 2008; Ekelund et al., 2012; Centers for Disease Control, 2015). For example, a recent meta-analysis of objectively measured physical activity found higher levels of child MVPA to be associated with significant reductions in risk factors for cardiometabolic disease, including waist circumference, systolic blood pressure, triglycerides, high-density lipoprotein cholesterol, and insulin levels (Ekelund et al., 2012). Mirroring the literature on physical health, physical activity in children and adolescents is also linked to improved mental health functioning, including reduced depressive and anxiety symptoms (Larun et al., 2006; Brown et al., 2013), improved cognitive function, and increased self-esteem (Biddle & Asare, 2011).

Beyond these specific health associations, a number of studies indicate an association between physical activity and health-related quality of life (HRQOL). HRQOL is a description of holistic health that takes into account an individual's perceptions of physical, mental, and social functioning (Centers for Disease Control, 2011; Office of Disease Prevention and Health Promotion, 2015). HRQOL is a patient-reported outcome that measures global health across

disorders and disciplines, mirroring the Patient-Reported Outcomes Measurement Information System (PROMIS) initiative developed by the National Institutes of Health to improve patient-provider communication and disease management (National Institutes of Health, 2017). HRQOL is a "unique indicator" of the impact of disease on individuals, which can be used to improve treatment effectiveness, patient-provider communication, clinical decision-making, and patient satisfaction (Acquadro et al., 2003, p. 524; Varni et al., 2005). HRQOL provides interdisciplinary researchers and clinicians with a conceptual understanding of the subjective burdens associated with individual patient health (Centers for Disease Control, 2011).

Importantly, HRQOL helps to quantify individual perceptions about functioning, in addition to objective functional ability (Tsiros et al., 2009). One may assume that a pediatric cancer patient currently undergoing chemotherapy would report poorer HRQOL than a child struggling with excess weight that limits his or her mobility. However, this assumption does not take into account the individual's subjective experiences and how these experiences impact overall functioning. According to Tsiros et al. (2009):

> A health condition may cause significant impairments in body functions, although the individual may still be able to participate fully in community life and report positive HRQOL. In contrast, others with minor physical impairments may report significant participation restrictions and impaired HRQOL (p. 388).

In fact, severely obese children report levels of HRQOL similar to pediatric cancer patients (Schwimmer et al., 2003), illustrating the importance of assessing subjective perceptions of quality of life as a measure of global functioning.

Notably, HRQOL can be used as a universal construct to describe global functioning across disorders and disciplines, allowing the comparison of functioning across diverse

populations. A number of HRQOL measures exist that are salient and easy to use in a variety of settings (Palermo et al., 2008b). For instance, a single-item measure of HRQOL (i.e. "In general, how would you rate your health?") can differentiate a two-fold increase in mortality risk in adults (DeSalvo et al., 2006), demonstrating how a simple HRQOL measure can provide invaluable information for research and clinical applications.

Physical Activity and HRQOL

As a measure of perceived health, HRQOL should be highly related to the physical and psychosocial health outcomes that are positively impacted by physical activity and described above. At least one team of researchers have proposed a model for how physical activity may act through neurobiological, psychosocial, and/or behavioral pathways to affect global well-being (Lubans et al., 2016). Lubans and colleagues (2016) suggested that being physically active releases neurotransmitters, improves mood, builds social connectedness, and increases sleep quality (as well as a variety of other mechanistic pathways), which interact to result in positive downstream effects on mental health and subjective well-being.

Several studies have assessed the associations between HRQOL and physical activity in children and adolescents, using both cross-sectional and longitudinal approaches. For example, one large cross-sectional study of primary and high school students found an association between greater self-reported physical activity in the past week and increased self-reported HRQOL (Chen et al., 2014). Similarly, Dalton et al. (2011) reported a positive association between recalled physical activity in the past week and global HRQOL among a sample of children in middle school. Consistent with these examples, the literature generally indicates that higher levels of physical activity are positively associated with higher HRQOL ratings in children and adolescents (Granger et al., 2017; Herman et al., 2014; Kantor et al., 2015; Lacy et al., 2012;

Lubans et al., 2016; Poitras et al., 2016; Wong et al., 2017). There may even be a dose-response relationship between physical activity and HRQOL in children, with 12 year-olds reporting 1.5-2.6 unit increases in physical functioning HRQOL for each increased hour spent being physically active (Gopinath et al., 2012).

Positive relationships between physical activity and HRQOL in youth appear to be replicated in longitudinal studies as well. For example, a longitudinal study of adolescents found those who maintained the highest levels of total physical activity over 5 years had significantly higher total, physical, and social HRQOL scores (Gopinath et al., 2012). Higher baseline levels of HRQOL also predicted future engagement in physical activity, up to 1 year later, for preadolescent children (Jensen et al., 2014). These positive associations have been replicated across ethnic groups, with at least one study finding associations between greater physical activity and higher HRQOL in Hispanic elementary school children (Kantor et al., 2015).

Although a quantitative meta-analysis was not located, several related reviews have examined associations between physical activity and mental health, subjective health, or psychosocial well-being in healthy youth and adolescents (Granger et al., 2017; Gu, 2017; Lubans et al., 2016; Poitras et al., 2016; Wong et al., 2017). Consistent with the literature summarized above, these reviews suggest that physical activity is generally related to higher self-reported health and psychological well-being (Granger et al., 2017; Poitras et al., 2016; Wong et al., 2017). Notably, Granger et al. (2017) found that physical activity was positively related to self-reported health status in nine out of eleven studies. However, only three of the studies reviewed by Granger et al. (2017) used validated measures of HRQOL, while the rest used visual analog scales or single-item ratings of perceived health. Wong et al. (2017) also found that more time spent in MVPA was associated with higher HRQOL ratings in adolescents in 13 out of 15

studies. However, the reviews described above were limited by a dearth of studies, a lack of objectively measured physical activity, high study heterogeneity, and inconsistent use of HRQOL and physical activity measures that restricted authors from determining aggregate effects (Granger et al., 2017; Lubans et al., 2016; Poitras et al., 2016; Wong et al., 2017). An additional review was severely limited because it did not systematically review the literature (Gu, 2017).

The primary aim of this meta-analytic study was to systematically review the literature and summarize the magnitude and direction of associations between physical activity and HRQOL in youth. Meta-analyses contribute to the advancement of the scientific literature by combining all published evidence on a topic, including contradictory and difficult-to-interpret evidence, into a single, comprehensive analysis (Card, 2012; Chan & Arvey, 2012; Haidich, 2010). Meta-analyses provide researchers and clinicians with organized, evidence-backed recommendations for direct clinical applications and benchmarks for evaluating future research (Card, 2012). A meta-analysis was especially needed to combine findings about physical activity and HRQOL in youth because research in this area has focused on diverse, specific pediatric populations, such as pediatric cancer survivors and obese youth. To date, findings have not been synthesized across these specialty populations, making it difficult to compare the differential effects of physical activity in specific pediatric populations and to generalize the effects of physical activity on HRQOL across youth. This meta-analysis is especially timely because HRQOL is becoming more widely used as a universal outcome measure of individual functioning across disorders (National Institutes of Health, 2017). Quantifying the magnitude of associations between physical activity and HRQOL across diverse populations of children and adolescents will inform universal interpretations of pediatric functioning in relation to exercise.

It was hypothesized that youth who were more physically active would report significantly higher HRQOL across domains (i.e. HRQOL total score or global rating).

Moderators

The secondary aim of this review was to identify moderators of the relationship between HRQOL and physical activity. Moderator analyses investigate disparate outcomes across studies by identifying predictors of relationship complexity that cannot be explained by a simple summary of overall effects (Card, 2012). Previous reviews cited high between-study heterogeneity as a limitation, which could indicate the presence of moderators that accounted for study differences (Granger et al., 2017; Poitras et al., 2016; Wong et al., 2017). Specifically, this review examined four *a priori* moderators, which were hypothesized to affect the association between physical activity and HRQOL including chronic disease status, weight status, sex, and study rigor.

Chronic Disease Status. On first glance, it appears that a positive relationship exists between physical activity and HRQOL for children with chronic conditions. Previous studies with specific disease populations have found generally positive associations between physical activity and HRQOL in pediatric cancer patients (Paxton et al., 2010) and children suffering from chronic pain (Lim et al., 2014; Palermo et al., 2008a), mirroring associations seen in healthy youth. Exercise interventions have been shown to be effective for improving HRQOL in children and adolescents with cerebral palsy (Verschuren et al., 2007), asthma (Flapper et al., 2008), obesity (Knopfli et al., 2008), and depression (Daley et al., 2006; Hughes et al., 2013). However, a dearth of studies simultaneously investigated associations between HRQOL, physical activity, and health status in both chronically disordered and healthy youth. Children with chronic health disorders typically report lower HRQOL than healthy controls (Varni et al.,

2007); however, the impact of chronic illness on the relationship between physical activity and HRQOL in youth remains unclear. This review aimed to be the first to examine the differential impact of physical activity on HRQOL across various chronic illness populations. Children with physically impairing chronic disorders were predicted to display greater improvements in HRQOL after relatively minor increases in physical activity, while healthy children would require greater amounts of physical activity to achieve similar changes in HRQOL. This prediction was built on the assumption that children suffering from serious, chronic impairments would be more positively impacted by minor returns to normalcy, such as engaging in small increases in physical activity (Speyer et al., 2010); whereas healthy children would need to engage in higher levels of physical activity (i.e. the recommended amount of 60 minutes of daily MVPA; U.S. Department of Health and Human Services, 2008; World Health Organization, 2010) to achieve similar benefits.

Weight Status. Weight status was proposed as a separate moderator due to the large proportion of the literature pertaining to HRQOL and physical activity in youth who are overweight or obese. Similar to other chronic disease populations, youth with overweight/obesity consistently report lower global levels of HRQOL than healthy-weight peers (Dalton et al., 2015; Herman et al., 2014; Lacy et al., 2012; Morales et al., 2013; Swallen et al., 2005; Tsiros et al., 2009) and significant improvements in HRQOL following physical activity interventions (Finne et al., 2013; Knopfli et al., 2008). However, children with overweight/obesity may experience additional stressors (e.g. teasing) that can further reduce HRQOL scores at all levels of activity (Jensen et al., 2014). An evaluation of weight status as an independent moderator was needed because many physical activity interventions in youth with overweight/obesity use control groups of only youth who are overweight/obese, thus failing to

show whether children of healthy weight would experience a similar rate and magnitude of change in HRQOL. One study which did compare youth with overweight/obesity and healthy controls found that weight status explained up to a third of the variance in HRQOL, thus highlighting the importance of including this moderator (de Beer et al., 2007). It was hypothesized that children with overweight/obesity would experience significantly greater changes in HRQOL from smaller alterations in physical activity than children of healthy weight.

Sex. Based on conflicting research about the impact of gender on both physical activity and HRQOL (Dalton et al., 2015; Ekelund et al., 2012; Herman et al., 2014; Lacy et al., 2012; Swallen et al., 2005; Kantor et al., 2015), sex was proposed as another potential moderator. Typical patterns of physical activity may vary across sex, with boys engaging in significantly more MVPA than girls (Ekelund et al., 2012). Differences in amount of physical activity may relate to findings that both obese and healthy weight girls reported poorer health outcomes and lower HRQOL than boys in some studies (Dalton et al., 2015; Lacy et al., 2012; Swallen et al., 2005). However, girls reported higher general, physical, emotional, and social HRQOL in at least one study (Kantor et al., 2015). In addition, some evidence suggests that boys may be more sensitive to changes in physical activity (Granger et al., 2017). In one study by Herman and colleagues (2014), school-aged boys who did not meet physical activity guidelines or who fell in the lowest tertile of reported activity were 2 and 6 times more likely, respectively, to report lower HRQOL scores; this effect was not found for girls. Unfortunately, these studies did not clarify how HRQOL may vary by sex, and how the relationship between physical activity and HRQOL is affected by sex. Therefore, sex was included as an exploratory moderator, but no explicit hypotheses were proposed for the magnitude or direction of sex as a moderator between physical activity and HRQOL.

Study Rigor. The final moderator evaluated was study rigor. Child and adolescent self-reported physical activity shows only low-to-moderate correlations (r = 0.3-0.4) with objective measures of physical activity (i.e. direct observation, accelerometry) and self-reporters often overestimate the duration and intensity of exercise (Ekelund et al., 2011), indicating that studies comparing HRQOL with self-reported physical activity may report artificially inflated results. Conversely, randomized controlled designs were expected to have lower between-study variability in outcomes than less tightly controlled designs (i.e. cross-sectional, matched groups). To account for the effect of these aspects of study design, rigor was assessed using a version of the 18-item rigor assessment created by Lundahl and colleagues (2010) and adapted by Mitchell, Amaro, and Steele (2016). This measure assigns points to studies based on design strengths, with higher scores indicating better study quality (Lundahl et al., 2010). A composite score of study rigor was used to encompass expected differences based on self-reported versus objective physical activity measures and other aspects of study design. Studies of higher quality, including objectively measured physical activity and more rigorous designs, were hypothesized to show smaller associations between physical activity and HRQOL, due to the greater homogeneity of findings expected in tightly controlled, rigorous studies and smaller expected effects of objective measures.

Summary

The present study aimed to synthesize the current literature on physical activity and HRQOL in children and adolescents. Effect sizes were calculated to quantify the overall effect of physical activity on HRQOL in youth. It was hypothesized that children who engaged in greater amounts of physical activity would report significantly higher levels of HRQOL. Further, it was predicted that this relationship would be attenuated by moderator variables,

including chronic disease status, weight status, sex, and study rigor. Chronic disease populations and youth with overweight/obesity were predicted to exhibit greater HRQOL reactivity to relatively small changes in physical activity (i.e. larger effect sizes), versus children free from chronic illness and children of healthy weight. In contrast, studies with more rigorous design quality (e.g. objectively measured physical activity) were expected to exhibit smaller effect sizes for HRQOL. Based on previous literature, the authors expected changes in physical activity to produce disparate effects on HRQOL for boys versus girls, but did not include an *a priori* hypothesis for the direction of this effect due to limited prior evidence.

Methods

Literature Search

The databases PubMed, PsycINFO, and ProQuest Dissertations were searched to conduct a comprehensive literature review of both published and unpublished articles about physical activity and HRQOL in youth. Search terms included the keywords *physical activ** OR *exercise* AND *health related qualify of life* AND *child* OR *adolescent* OR *youth* OR *pediatric*. For PsycINFO, the age filter was used to select articles pertaining to childhood (birth-12 years) and adolescence (13-17 years), in place of the keywords *child* OR *adolescent* OR *youth* OR *pediatric*. Forward and backward-searching, based on the reference sections of included articles and relevant reviews, was used to identify additional articles not yielded in the preliminary database search. The initial literature search was conducted on March 26, 2016 and the search was finalized on July 26, 2017.

Inclusion/Exclusion Criteria

To be included in the analysis, articles must have (a) been written in English, (b) available in full text, (c) included participants with a mean age <18 years at the time of study

participation, (d) measured target outcomes of both physical activity and health-related quality of life or included a physical activity intervention with HRQOL outcomes, and (e) provided enough information to calculate effect sizes. Articles that measured physical activity in continuous units (e.g. minutes, steps, metabolic equivalents [METs]) or included an exercise intervention and reported a total/global measure of HRQOL were included. Articles that measured physical activity categorically (e.g. Likert scale, met/did not meet physical activity recommendations), articles that measured physical fitness but not physical activity, and articles that reported only specific domains of HRQOL (e.g. psychosocial, physical, emotional) were excluded. Duplicate articles from the same study were also excluded. Authors were contacted in an effort to include articles that appeared to measure target outcomes but did not initially provide enough information to calculate effect sizes.

Two types of studies were included in this meta-analysis: descriptive studies and intervention studies. Descriptive studies included non-intervention studies (e.g. cross-sectional surveys, observational studies, baseline characteristics only) that directly measured associations between physical activity and HRQOL (e.g. Pearson or Spearman correlation, regression). Outcomes were aggregated for longitudinal studies that reported direct associations between physical activity and HRQOL at multiple time points. Descriptive studies that did not measure the direct association between physical activity and HRQOL (e.g. baseline means and standard deviations only, complex models that included other covariates) were excluded. Intervention studies had to include an exercise intervention (e.g. resistance training, aerobic fitness, physical activity education) and measure HRQOL values pre- and post-intervention against a comparison group. Case studies and interventions that lacked a control group were excluded.

Coding of Studies

Two trained reviewers (e.g. research assistants and graduate students) independently reviewed article abstracts for inclusion/exclusion criteria. Included articles were then reviewed in their full-text format by two trained reviewers and discrepancies were resolved by consensus. The first author coded all articles selected for inclusion, and 20% of the final selected articles were coded by a second reviewer to establish coding reliability. Each study was coded for sample size, mean participant age, participant demographic characteristics (e.g. sex, ethnicity, weight status, health status), study method (e.g. cross-sectional, longitudinal, intervention), study duration, assessment time points, measures used, physical activity measurement method (e.g. self-report, pedometer, accelerometer), mean physical activity, and total HRQOL. EndNote version X7 (Clarivate Analytics, Philadelphia, PA) was used to facilitate the organization and coding of relevant articles.

Study Rigor

An 18-point measure of study rigor, initially developed by Lundahl et al. (2010) and later adapted by Gayes and Steele (2014) and Mitchell, Amaro, and Steele (2016), was used to assess study quality. Points were assigned for each aspect of study quality that was explicitly reported, such as describing three or more demographic indicators of the sample, including multiple sites, reporting study drop-outs, using objective measurement tools, and using randomization to condition (for intervention studies). Points were summed and total scores ranged from 0-18, where higher scores indicated greater study rigor. A copy of this measure is included in **Appendix A**. Twenty percent of articles were coded independently by two reviewers and the intra-class correlation coefficient for reliability across coders for this instrument was .95 (ICC; 95% confidence interval = .64-.99).

Data Analysis

Effect sizes were calculated using Hedge's *g* to quantify the magnitude and direction of the associations between physical activity and HRQOL in youth (Durlak, 2009; Card, 2012). Hedge's *g* was selected to best describe effect sizes while correcting for study sample sizes, which varied from less than 20 participants per group to over 1000 participants (Durlak, 2009; Hedges & Olkin, 1985). Effect sizes for descriptive studies were calculated from measures that directly associated physical activity and HRQOL, including bivariate Pearson correlations, t-tests, and F-tests. Effect sizes for intervention studies were calculated using pre-post means, standard deviations, and sample sizes for the intervention versus control group. In select cases where pre-post standard deviations were not provided in the article, standard deviations were calculated from 95% confidence intervals.

Four separate random effects models were used to compute effect sizes in descriptive and intervention studies, as well as child- and parent-proxy-report of HRQOL. For instance, if a single study included both child- and parent-report of HRQOL measures, two effect sizes were calculated for this study to represent these quantifiably different outcome types. If a single study included multiple outcomes from a single reporter (e.g. multiple child-reported HRQOL measures), these data were averaged and aggregated for one overall effect size per study (Durlak, 2009). The Q statistic was calculated for all models to test for significant within-group variability (Card, 2012). For models with a significant Q statistic, analyses were conducted to examine the impact of hypothesized moderator variables on the relationship between physical activity and HRQOL, including chronic disease status, weight status, sex, and study rigor. Chronic disease status was categorized dichotomously as 1 (youth with chronic disease) or 0 (typically developing youth). Weight status and sex were tested as continuous moderators using

percent of the sample that was overweight/obese and percent of the sample that was female. Study rigor was also tested as a continuous moderator using study rigor scores from the modified Lundahl assessment.

Finally, the fail-safe *N* statistic was calculated to determine the number of non-significant, excluded studies needed to reduce overall effect sizes to non-significance, as a measure of potential publication bias. The fail-safe N statistic was calculated using the formula $N = k(M_{ES} - ES_{min}) / (ES_{min} - ES_{excluded})$ where k was the number of studies, M_{ES} was the mean effect size, ES_{min} was the minimally significant effect size of 0.1, and $ES_{excluded}$ was zero (Card, 2012). Forest and funnel plots were created to graphically represent effect sizes and visualize publication bias. Analyses were completed using Comprehensive Meta-Analysis software version 3 (Biostat, Englewood, NJ). Effect sizes were interpreted using Cohen's guidelines: 0.20 (small), 0.50 (medium), and 0.70 (large; Cohen, 1988; Durlak, 2009). Results were evaluated at the $p = .05$ level, unless otherwise stated.

Results

Search Strategy

The initial key terms literature search identified 1202 articles from PubMed, PsycINFO, and ProQuest. After duplicates and non-articles (e.g. book chapters) were removed, 1081 unique articles remained. Abstracts for each of these articles were screened for study inclusion/exclusion criteria. Abstract screeners had 62.9% agreement and interrater reliability was fair (Cohen's $k = .232$; Sim & Wright, 2005; Viera & Garrett, 2005). Discrepant abstract screens were reconciled to 100% agreement by consensus, leaving, 473 articles identified as potentially meeting inclusion criteria. Of these, 471 were reviewed in their full text format because two were not available in full text. Percent agreement on reviewing full texts was 91.5%

and interrater reliability was moderate (Cohen's k = .519). Again, discrepancies for full text reviews were reconciled to 100% agreement by consensus. Forward and backward searches identified an additional five articles that met full criteria. Thirty-three total studies met inclusion criteria, provided enough information to calculate effect sizes, and were included in analyses. These included 14 descriptive studies and 19 intervention studies. A PRISMA of all articles assessed during the review process and detailed reasons for study exclusion is provided in **Figure 1**.

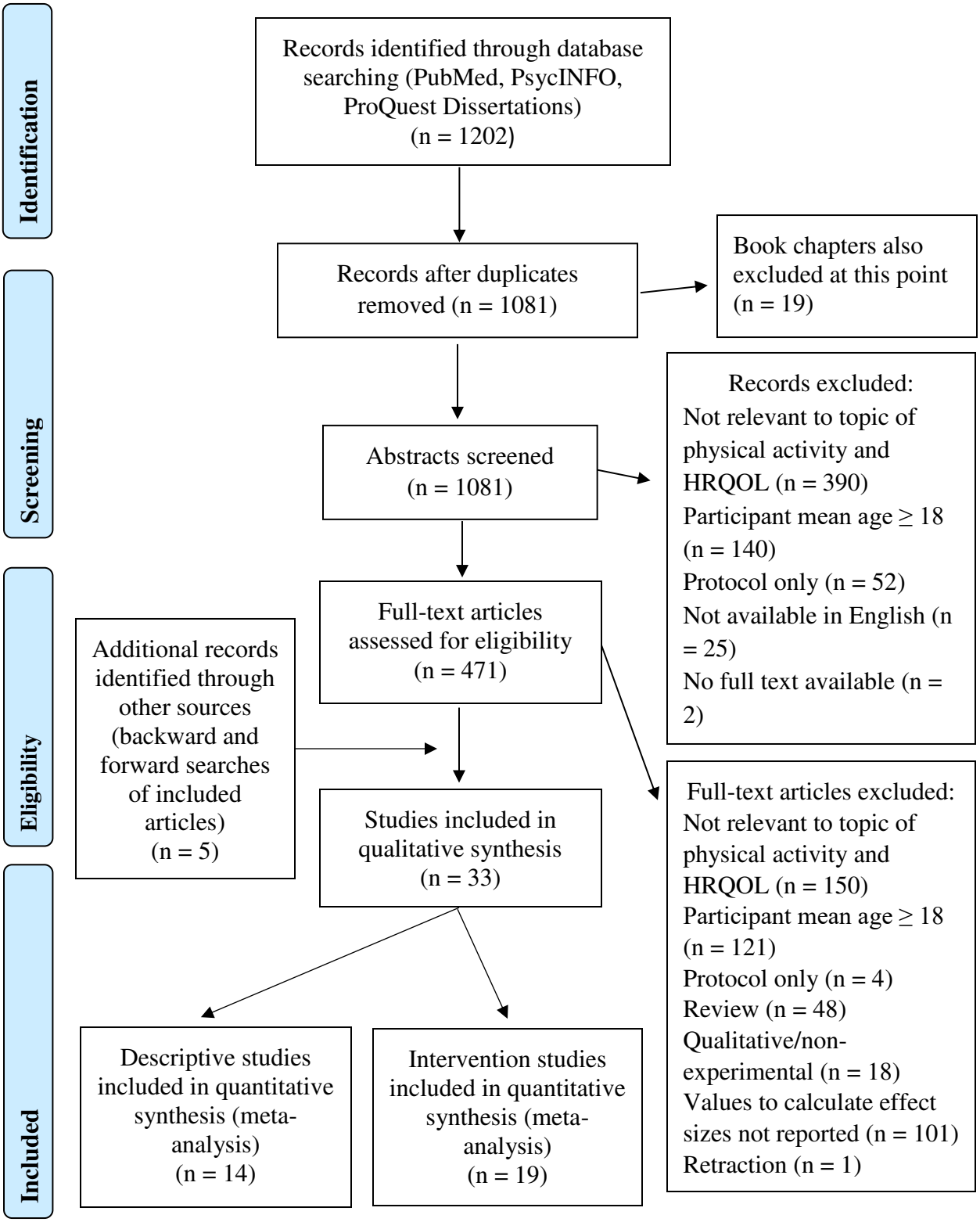

Figure 1. PRISMA flow diagram of literature search screening process.

Description of Included Studies

Descriptive studies are summarized in **Table 1** and intervention studies are summarized in **Table 2**. Descriptive studies included youth ranging in age from 3-18 years and all studies included a near-equal split of males and females. About half of the studies focused on children with a specific chronic disease, including overweight/obesity, cancer, epilepsy, cystic fibrosis, and those who required a kidney transplant. Seven of the studies used samples of typically developing youth and one included both typically developing and overweight/obese youth. The majority of descriptive studies were cross-sectional, either collecting data over less than a week or administering surveys at a single time point. One study included baseline data from a larger intervention, one described longitudinal data from the control group only of an intervention, and one study described an intervention with no control group. Over half of the studies quantified physical activity using subjective self-report measures, such as the Godin Leisure-Time Exercise Questionnaire (Godin & Shephard, 1997; Godin, 2011) and 7-day Physical Activity Recall (Sallis et al., 1993). Seven studies used objective physical activity measures, including five studies that used pedometers and three studies that used ActiGraph accelerometers (ActiGraph, LLC, Pensacola, FL). For HRQOL, the majority of studies used the Pediatric Quality of Life Questionnaire (PedsQL; Varni et al., 2003), although two studies used the KIDSCREEN-27 (Ravens-Sieberer et al., 2005; The KIDSCREEN Group Europe, 2006), one used the KINDL-R-Kiddo (Ravens-Sieberer & Bullinger, 1998), and one used the Cystic Fibrosis Questionnaire (CFQ-R; Quittner et al., 2005). The majority of HRQOL measures were completed by children, although four studies also included parent-proxy report and one study relied on parent-proxy report alone. Study rigor scores for both descriptive and intervention studies are listed in **Table 3**.

Table 1. *Descriptive studies between physical activity and health-related quality of life included in meta-analysis.*

Reference	Population	N	Participant Age	Sex	Weight Status	Study Design	Physical Activity Measure	PA Informant	HRQOL Measure	HRQOL Informant	Direct Association Statistic(s)
Boyle, 2010	Healthy youth	1770	11-15 years; Mean age = 13.2 (1.2)	48.3 % female	23.5 % overweight/obese	Cross-sectional survey	Western Australian Child and Adolescent Physical Activity and Nutrition Survey (CAPANS)	Child	PedsQL	Child	r=.01, p=.626
									EQ	Child	r=.004, p=.076
Groenveld, 2012	Cystic fibrosis	28	6-17 years; Mean age = 11.6 (3.1)	50.0 % female	--	Cross-sectional study (5 days)	Actigraph accelerometer (model 7164)	Child	Cystic Fibrosis Questionnaire (CFQ-R) spanish version*	Child	"no sig. association"
										Parent proxy	***Not reported; used to calculate parent-child agreement only***
Gu, 2015	Healthy youth	336	9-12 years; Mean age = 9.87 (0.04)	53.3% female	--	Correlational study (3 days)	ACCUSPLIT pedometer (steps/min)	Child	PedsQL 4.0	Child	r=.24, p<.01

Ha, 2015	Healthy youth	115	Mean age = 11.6 (1.76)	55.7 % female	--	Cross-sectional study (10 days)	Actigraph GT3X+	Child	KIDSCREEN-27	Child	r=.26, p<.05
Hamiwka, 2009	Kidney transplant	53	6-18 years; Mean age = 14.3 (3.2) transplant, 14.0 (1.6) no transplant	58.5 % female	24.5 % overweight/obese	Cross-sectional study (7 days)	Pedometer ***also administered PAQ 7-day recall but no test statistic reported***	Child	PedsQL 4.0	Child (with parent assistance)	r=.309, p<.034
Jalali-Farahani, 2016	Healthy youth	465	14-17 years; Mean age = 15.56 (0.93)	48.8 % female	38.5 % overweight/obese	Cross-sectional survey	Quantification de l'Activite Physique en Altitude Chez les Enfants (QAPACE)	Child	PedsQL 4.0	Child	r=.12, p>.05 (girls); r=.14, p<.05 (boys)
										Parent proxy	r=.07, p>.05 (girls); r=.03, p>.05 (boys)
Lim, 2014	Overweight/obesity	270	8-12 years; Mean age = 10.36 (1.38)	54.4 % female	100 % overweight/obese	Pre-treatment assessment	Block Kids Physical Activity Screener	Child (with parent assistance)	PedsQL 4.0	Child	r=.06, p>.05 (moderate PA); r=.09, p>.05 (vigorous PA)
										Parent proxy	r=.01, p>.05 (moderate PA); r=.05, p>.05

											(vigorous PA)
Michels, 2016	Healthy youth	210	3.9-7.1 years; Mean age = 5.0 baseline, 5.9 follow-up	53.0 % female	13.3 % overweight/obese	Data from control group only of 1-year longitudinal intervention	Actigraph MTI/CSA	Child	PedsQL 4.0	Parent proxy	r=.139, p=.044 (baseline); r=.015, p=.838 (follow-up)
Norris, 2010	Cancer	17	10-17 years; Mean age = 13.5 (2.2)	52.9 % female	20.3 % overweight/obese	Cross-sectional survey	Godin Leisure Time Exercise Questionnaire	Child	PedsQL 4.0	Child	"no sig. association"
										Parent proxy	r=.48 (mom-report); r=.55 (dad-report)
Paxton, 2010	Cancer	94 (adolescent data only included)	11-33 years; Mean age of adolescents = 14.3 (1.8)	48.9 % female	51.1 % overweight/obese	Cross-sectional survey	Godin Leisure Time Exercise Questionnaire	Child	PedsQL	Child	r=.29, p=.007 (Leisure-time PA)
Spengler & Woll, 2013	Healthy youth	1828	11-17 years; Mean age = 14.2 (1.9)	48.7 % female	--	Cross-sectional survey	MoMo PAQ	Child	KINDL-R-Kiddo	Child	t=6.538, p<.001 (total activity time)

Standage, 2012	Healthy youth	494	Mean age = 12.58 (0.74)	58.9 % female	--	Cross-sectional survey	Yamax Digiwalker SW-31 pedometer	Child	PedsQL 4.0	Child	r=.12, p<.01 (total 4-day step count)
Whitney, 2013	Epilepsy	8	8-14 years; Mean age = 12.1 (1.7)	50.0 % female	--	Cross-sectional study	Digi-Walker SW-200 pedometer	Child	KIDSCREEN-27	Child	"no sig. association"
Woods, 2015 (Thesis)	Healthy and overweight/obese youth	25	5-11 years; Mean age = 7.8 (2.17)	52.0 % female	--	Non-randomized intervention	PAR 7-day recall	Child (with parent assistance)	PedsQL 4.0	Child	r(18)=.56, p<.01 (baseline); r=.49, p>.05 (post-intervention); r(3)=-.99, p<.01 (3 month follow-up)

Table 2. *Physical activity intervention studies included in meta-analysis.*

Reference	Population	N	Age Range	Sex	Weight Status	Study Design	Intervention Group	Comparison Group	HRQOL Measure	HRQOL Informant
Azevedo, 2014	Healthy youth	497	11-12 years; Mean age = 11.25 (0.4)	64.2 % female	--	Natural intervention	School-wide implementation of dance mats	Schools without dance mats	KIDSCREEN-27	Child
Bocca, 2014	Obesity	75	3-5 years; Mean age = 4.7 (0.8)	72.0 % female	100% overweight /obese	Intervention	Group physical activity in 12, 60 min sessions over 16 weeks; plus 6 psychological counseling and 6 dietary advice sessions	3, 90-minute sessions on general healthy lifestyle advice	DUX-25	Parent proxy
Casey, 2014	Healthy youth	621	12-15 years; Mean age = 13.4 (0.9)	100 % female	--	Cluster RCT	PE plus 2 sport units with local YMCA per week; implemented at school level	Usual PE	PedsQL 4.0	Child
Demuth, 2012	Cerebral palsy	58	7-18 years; Mean age = 10.95 years	53.2 % female	--	Multisite RCT	30 , 60-min. stationary cycling sessions over 12 weeks between 70-80% max Karvonen HR	Usual care	PedsQL	Child
									PODCI*	Parent proxy
Finkelstein, 2013	Healthy youth	285	6-12 years; Mean age = 8.21 (1.5)	45.96% female	--	Cluster RCT	Pedometer step program with rewards based on achievement of 8000 steps/day for at least half the days in a month plus 2 outdoor sessions per month; 3 month duration	Usual daily activities	PedsQL 4.0	Parent proxy

Flapper, 2008	Asthma	36	7-12 years; Mean age = 10.0 (1.0)	47.0 % female	--	RCT	Group exercise; 1.5 hrs education plus 1 hr exercise each week for 10 weeks; plus 5 bi-weekly parent sessions	Usual care	DUX-25	Child & Parent proxy
									TACQOL	Child & Parent proxy
									TACQOL asthma*	Child & Parent proxy
Hofsteenge et al., 2013	Overweight/obesity	95	11-18 years; Mean age = 14.6 (1.6) intervention, 14.5 (1.7) control	55.8% female	100% overweight /obese	RCT	Multidisciplinary group obesity intervention; 7 educational sessions over 14 weeks plus 4 long-term booster sessions	Usual care	PedsQL 4.0	Child
Mendonca, 2013	Juvenile idiopathic arthritis	50	8-18 years; Mean age = 11.8 (3.4) intervention, 11.0 (3.9) control	64.0 % female	--	Randomized prospective single blind trial	Pilates group; 50 min pilates 2x per week for 48 sessions total	Conventional exercise group; resistance training plus stretching	PedsQL 4.0	Child & Parent proxy
Mendoza, 2017	Cancer survivors	60	14-18 years; Mean age = 16.6 (1.5)	59.3% female	--	Pilot RCT (unblinded)	Weekly increasing step goals via phone/text for 10-weeks using Fitbit Flex/mHealth app; achievement tracked via Facebook group badges; text message reminders of goals and encouragement	Usual care	PedsQL 4.0; PedsQL Cancer Module*	Child

Quaresma, 2014	Healthy youth	1042	10-16 years; Mean age = 10.42 (1.09)	47.3% female	--	Group randomized design (by school)	90 min/week sessions on health and weight education and physical activities; 2 school years in duration	General information about eating and physical activity	KIDSCREEN-10	Child
Takken, 2003	Juvenile idiopathic arthritis	54	5-13 years; Mean age = 8.66 (2.29) intervention, 8.88 (1.86) control	74.1 % female	--	RCT	Aquatic exercise 1 hr/week; mix of high and low intensity increased stepwise throughout program	Usual care	JAQQ*	Child
									CHQ	Parent proxy
Taracki, 2012	Juvenile idiopathic arthritis	81	5-17 years; Mean age = 10.02 (3.44) intervention, 10.82 (4.0) control	54.3% female	--	RCT	Individual exercise sessions for 12 weeks (20-45 min per session; range of motion, strengthening, stretching, posture exercises) 1 day/week with physical therapist and 3 days/week with parent supervision at home	Wait list	PedsQL 4.0	Child & parent proxy
van Dijk-Lokkart, 2015	Cancer	68	8-18 years; Mean age = 13.0 (3.0) intervention, 12.6 (3.1) control	47.0 % female	--	RCT	Intensive cardiorespiratory + muscle strength training; 2 sessions/week for 45 min each for 12 weeks, plus 8 psychosocial education sessions	Usual care	PedsQL	Child & Parent proxy

Vos et al., 2012	Obesity	81	8-17 years; Mean age = 13.3 (2.0) intervention, 13.1 (1.9) control	53.2% female	100% overweight /obese	RCT	Multidisciplinary obesity intervention; 4.5 contact hours over 3-month screening phase plus 7 child and 5 parent meetings, each 2.5 hrs long; educational with CBT framework	General recommendations on physical activity and nutrition	DISABKIDS	Child & Parent proxy
Wafa, 2011	Obesity	107	7-11 years; Mean age = 9.8 (1.5)	50.0 % female	100% obese	RCT	8 1-hr sessions over 26 weeks (multicomponent obesity program adapted from SCOT and Bright Bodies; parent educational sessions while children exercised)	No treatment control	PedsQL 4.0	Child & Parent proxy
Wake, 2009	Overweight/obesity	258	5-10 years; Mean age = 7.4 (1.4) intervention, 7.6 (1.4) control	60.5 % female	100% overweight /obese	RCT	4 visits over 12 weeks; focus on sedentary time, physical activity, water consumption, family eating habits, low fat food options	No treatment control	PedsQL 4.0	Child & Parent proxy
Wang, 2006 (Thesis)	Cerebral palsy	64	7-18 years; Mean age = 10.9 (3.0) intervention, 11.3 (2.7) control	51.7% female	--	RCT	Cycling intervention; 25 min sessions 3x per week for 12 weeks; resistance progressively increased	No cycling control	PedsQL	Child
									PODCI	Child & Parent proxy

Wilson, 2010 (Thesis)	Healthy and obese youth	40	8-11 years; Mean age = 9.55 (0.99)	45.0 % female	57.5% obese	Randomized pilot intervention	Small group and individual exercise/sport activities for 1 hrs, 3 days per week, for 16 weeks; Target HR 140 bpm (approximately 70% max HR based on age)	No treatment control	PedsQL 4.0	Child
Yackobovitch-Gavan, 2009	Obesity	162	6-11 years; Mean age = 8.3 (1.6)	50.0 % female	100% obese	Intervention	Exercise + diet group (12-week exercise intervention 3 days/week 90-min training session [45 min aerobic, 45 min resistance])	Diet only group (12 weekly general nutrition meetings; children and parents)	PedsQL	Parent proxy

Abbreviations: *bpm beats per minute; HR heart rate; hrs hours; HRQOL health-related quality of life; min minutes; MVPA moderate-to-vigorous physical activity; PA physical activity; PE physical education; RCT randomized controlled trail; Children's Health Questionnaire (CHQ); Cystic Fibrosis Questionnaire (CFQ-R); DISABKIDS; Dutch Children Quality of Life Questionnaire (DUX-25); Juvenile Arthritis Quality of Life Questionnaire (JAQQ); Pediatric Quality of Life Questionnaire (PedsQL); Pediatric Outcomes Data Collection Instrument (PODCI); TNO-AZL Children quality of life questionnaire (TACQOL)*

**disease-specific HRQOL measure*

Table 3. *Study rigor coding by study based on modified Lundahl assessment.*

Study	Study Rigor Score	Study	Study Rigor Score
Descriptive Studies		***Intervention Studies***	
Boyle, 2010	7	Azevedo, 2014	10
Groenveld, 2012	8	Bocca, 2014	12
Gu, 2015	6	Casey, 2014	9
Ha, 2015	9	Demuth, 2012	14
Hamiwka, 2009	7	Finkelstein, 2013	12
Jalali-Farahani, 2016	11	Flapper, 2008	14
Lim, 2014	6	Hofsteenge et al., 2013	11
Michels, 2016	11	Mendonca, 2013	13
Norris, 2010	6	Mendoza, 2017	7
Paxton, 2010	8	Quaresma, 2014	11
Spengler & Woll, 2013	7	Takken, 2003	15
Standage, 2012	6	Taracki, 2012	14
Whitney, 2013	4	van Dijk-Lokkart, 2015	14
Woods, 2015 (Thesis)	7	Vos, 2012	13
Mean (SD) =	7.36 (1.95)	Wafa, 2011	14
		Wake, 2009	16
		Wang, 2006 (Thesis)	13
		Wilson, 2010 (Thesis)	8
		Yackobovitch-Gavan, 2009	12
		Mean (SD) =	12.21 (2.39)

Intervention studies included youth ranging in age from 3 to 18 years. Most intervention studies included both males and females, although one study included females only. The majority of intervention studies included chronic disease populations, including six studies in youth with overweight/obesity, three with juvenile idiopathic arthritis, two with cerebral palsy, two with cancer, and one asthma. Four studies used samples of typically developing youth and

one included both typically developing and overweight/obese youth. The majority of intervention studies were randomized controlled trials, three were randomized pilot trials, two were non-randomized interventions, and one was a natural experiment that studied existing differences in physical activity resources across schools. Six studies included traditional group-based exercise interventions (i.e. cardiorespiratory and/or resistance training) and five were multicomponent obesity interventions which included exercise, diet, and education components. The remaining interventions tested specific types of exercise, including dance exergaming, physical education/YMCA activities, stationary cycling, Pilates, aquatic exercises, and technology-based physical activity promotion. Exercise interventions ranged from ten weeks to two academic years in length with visits occurring <1-3 days per week and each visit lasting 25-90 minutes. The most common intervention length was 12 weeks and intervention contact hours ranged from 1.5-54 total hours (Mean = 24.58 ± 15.31; six studies did not report detailed information to determine total contact hours). Four interventions were administered at the school level, while all other interventions enrolled participants individually. Fifteen studies compared a treatment group against a no treatment control group, usual care, or wait list; four studies compared treatment to an active control group that included education only or a different kind of exercise intervention.

The majority of studies did not directly measure physical activity. For HRQOL, thirteen studies used the PedsQL (Varni et al., 2003) and one also administered the PedsQL Cancer module. Two studies each used the Dutch Children Quality of Life Questionnaire (DUX-25; Koopman et al., 1998), the Pediatric Outcomes Data Collection Instrument (PODCI; Daltroy et al., 1998), the KIDSCREEN (Ravens-Sieberer et al., 2005; The KIDSCREEN Group Europe, 2006), and the Child Health Questionnaire (CHQ; Landgraf et al., 1996). One study each used

the DISABKIDS (The DISABKIDS Group Europe, 2006), the TNO-AZL Children's Quality of Life questionnaire (TACQOL; Verrips et al., 1998; Vogels et al., 1998), and the Juvenile Arthritis Quality of Life Questionnaire (JAQQ; Duffy et al., 1997). Six studies assessed HRQOL using two or more measures. The majority of intervention studies collected both child and parent-proxy report of HRQOL measures, while six studies included child self-report only and three studies included parent-proxy report only.

Effect Sizes

Overall, descriptive studies demonstrated a small, positive association between physical activity and HRQOL based on child-reports (Hedge's $g = .302$, $p < .001$; **Figure 2**) and a negligible (non-significant) association based on parent-proxy reports (Hedge's $g = .115$, $p = .101$; **Figure 3**). Across studies, there was wide variation in child-reported effects. One study found a large effect of physical activity on HRQOL (Woods, 2015), four found medium effects (Gu et al., 2015; Ha et al., 2015; Hamiwka et al., 2009; Paxton et al., 2010), three studies found small effects (Jalali-Farahani et al., 2016; Spengler & Woll, 2013; Standage et al., 2012), and an additional five studies found negligible effects (Boyle et al., 2010; Groenveld et al., 2012; Lim et al., 2014; Norris et al., 2010; Whitney et al., 2013). Importantly, three of these studies did not report exact statistics, but merely stated that there was no significant association between physical activity and HRQOL (Groenveld et al., 2012; Norris et al., 2010; Whitney et al., 2013). In an effort to include these null findings in the analyses, correlations of zero were imputed for the three studies with missing values.[1]

[1] Studies with imputed zero correlations include standard error and variance estimates calculated from a Pearson correlation of zero and the study sample size.

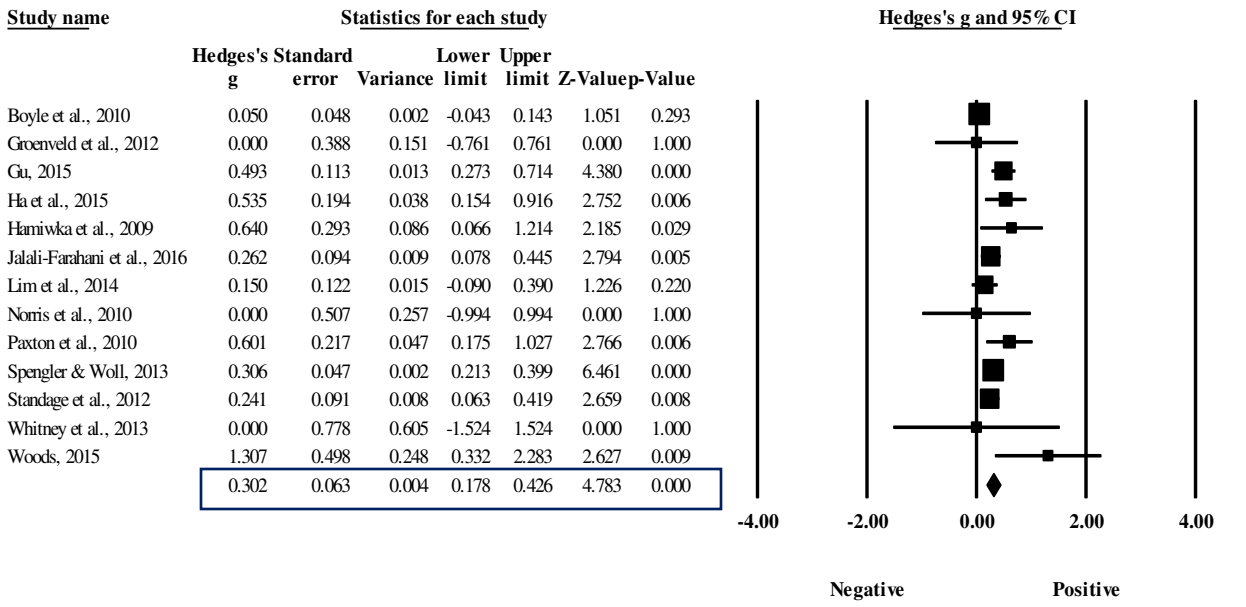

Figure 2. Forest plot of random effects model for descriptive studies: Child-reported HRQOL.

Effect sizes from parent-proxy reports in descriptive studies were variable. Although one study found a large association between physical activity and HRQOL (Norris et al., 2010), the remaining studies found non-significant associations (Lim et al., 2014; Jalali-Farahani et al., 2016; Michels et al., 2016). Interestingly, Norris et al. (2010) found a large association based on parent-proxy reports but no association between child-reported physical activity and HRQOL.

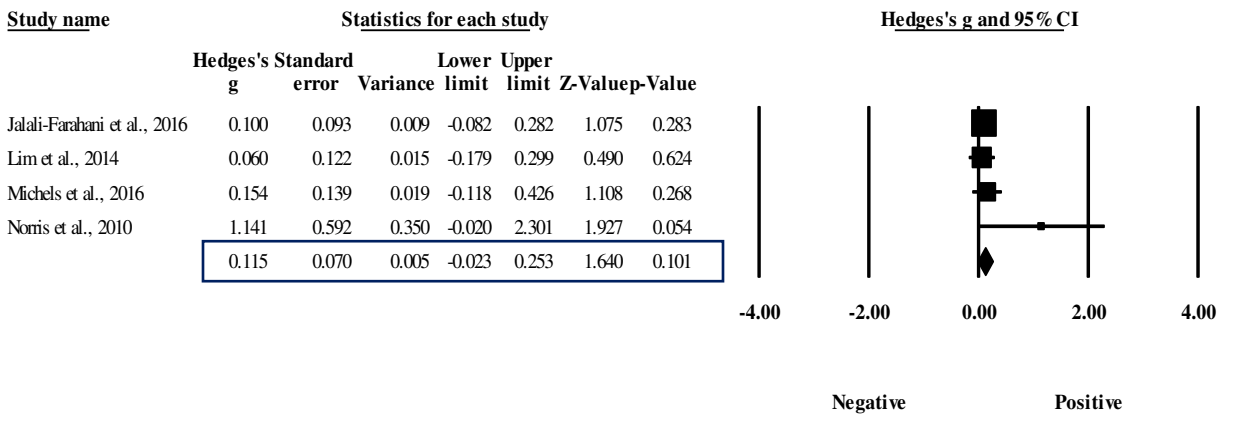

Figure 3. Forest plot of random effects model for descriptive studies: Parent-reported HRQOL.

Intervention studies yielded a small, positive effect of physical activity interventions on HRQOL based on child-reports (Hedge's g = .279, p = .014; **Figure 4**) and a medium, positive effect of physical activity interventions on HRQOL based on parent-proxy reports (Hedge's g = .522, p = .012; **Figure 5**).[2] Based on child-reported HRQOL, three studies found large, positive effects for their exercise interventions improving HRQOL (Mendonca et al., 2013; Flapper et al., 2008; Taracki et al., 2012), four studies found small effects (Casey et al., 2014; Finkelstein et al., 2013; Vos et al., 2012; Wafa et al., 2011), six studies found negligible effects (Demuth et al., 2012; Hofsteenge et al., 2013; Quaresma et al., 2014; van Dijk-Lokkart et al., 2015; Wang, 2006; Wilson, 2010), and three studies found small, negative effects (Azevedo et al., 2014; Mendoza et al., 2017; Takken et al., 2003).

[2] Mendonca et al. (2013) reported findings over three standard deviations larger than the average effect in both child and parent-proxy reported intervention models. If this study is removed from analyses, the overall effect size for intervention studies based on child reported HRQOL is reduced to marginal significance (Hedge's g = .169, p = .052) and the overall effect for intervention studies based on parent-proxy reported HRQOL is reduced to a small, significant effect (Hedge's g = .261, p = .016).

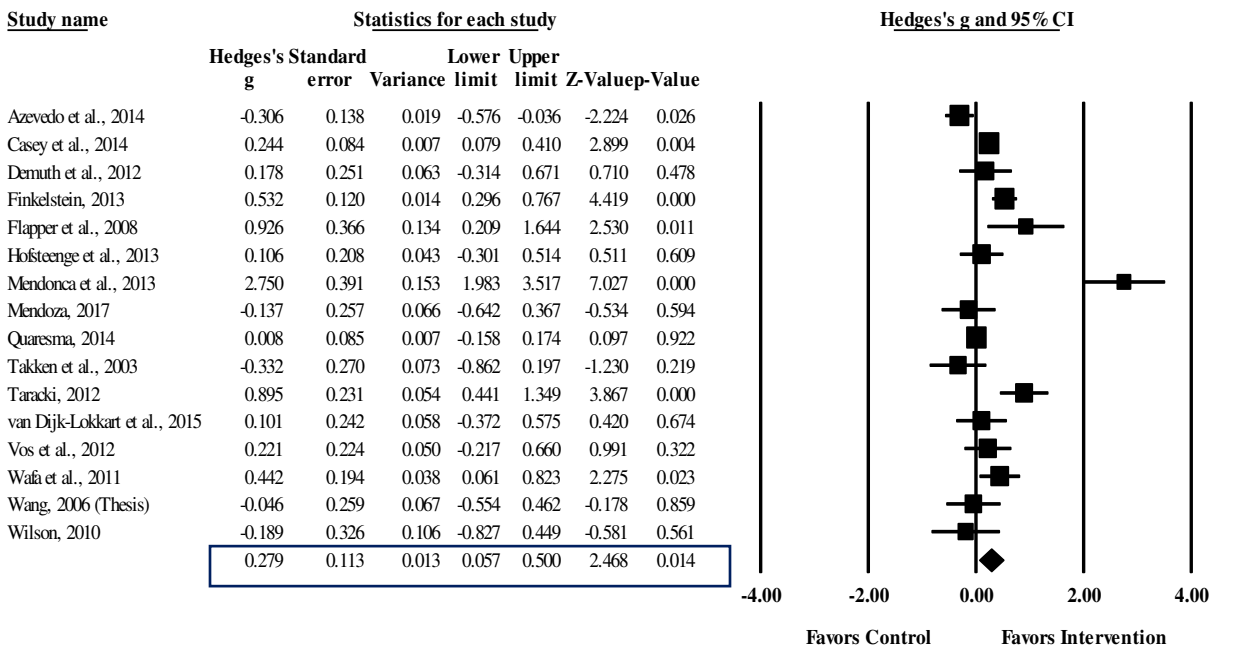

Figure 4. Forest plot of random effects model for intervention studies: Child-reported HRQOL.

Again, effect sizes based on parent-proxy reports of HRQOL following an exercise intervention were variable. Two studies found large effects of physical activity interventions for children on parent-proxy reported HRQOL (Mendonca et al., 2013; Taracki et al., 2012), one study found a medium effect (Flapper et al., 2008), four studies found small effects (Bocca et al., 2014; Vos et al., 2012; Wafa et al., 2011; Wake et al., 2009), and three studies found negligible effects (van Dijk-Lokkart et al., 2015; Wang, 2006; Yackobovitch-Gavan, 2009).

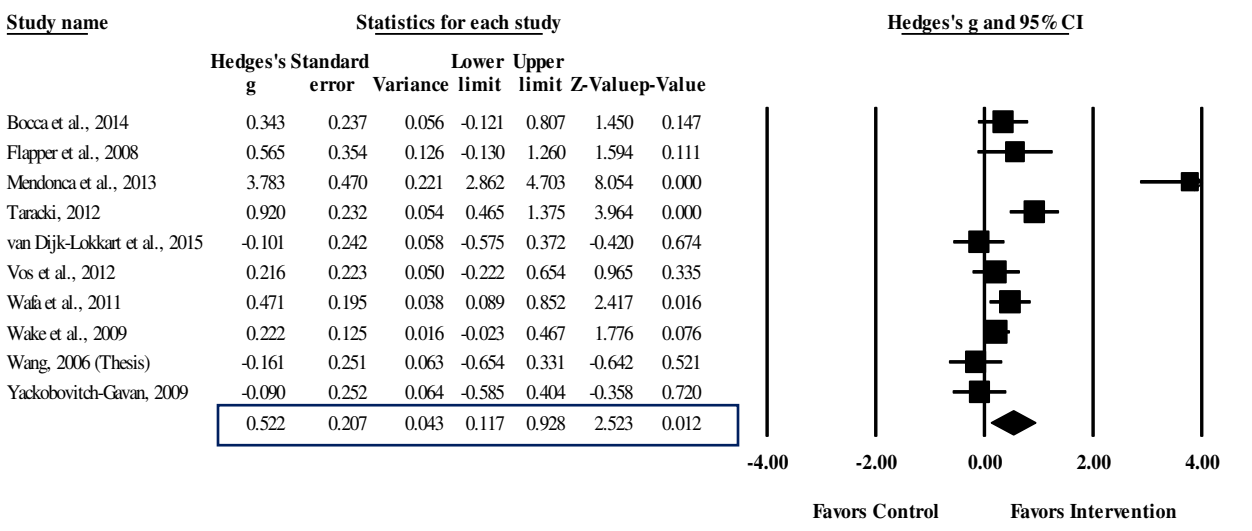

Figure 5. Forest plot of random effects model for intervention studies: Parent-reported HRQOL.

Hypothesized Moderators

The Q-statistic was calculated for all four models (i.e. descriptive versus intervention; child report versus parent-proxy report) to test for significant sample heterogeneity, indicating the presence of between and within-study variability that could be explained by potential moderating variables. Significant Q-statistics were found for the overall effect of physical activity on HRQOL in three of the four models: descriptive studies using child-report [$Q(12) = 35.568$, $p < .001$], intervention studies using child-report [$Q(11) = 91.747$, $p < .001$], and intervention studies using parent-report [$Q(6) = 72.254$, $p < .001$]. A non-significant Q-statistic was found for the parent-reported descriptive model [$Q(3) = 3.310$, $p = .346$], so this model was not included in moderator analyses.

For the models with significant Q-statistics, chronic disease status, weight status, sex, and study rigor were examined as potential moderators. Weight status was entered in a separate model because it was reported for only about half of the studies, and thus would exclude half of

the studies from meta-regression analyses if it was included in the overall moderation model. Chronic disease status and weight status were unable to be tested as moderators in parent-reported intervention studies because all of these studies were conducted in chronic disease samples and only studies conducted in entirely overweight/obese samples reported on youth weight status.

None of the tested moderators explained a significant portion of between or within-study heterogeneity (all *p*s>.12; **Table 4**). For descriptive studies based on child-reported HRQOL, visual inspection of non-significant trends suggested that studies with higher study rigor scores, studies in chronic disease samples, and studies with more females frequently had larger effect sizes. For intervention studies with child-reported HRQOL, non-significant trends were observed for larger effect sizes in studies that included chronic disease samples, a larger number of overweight/obese youth, and more females. A similar trend was seen for sex in the same intervention studies that utilized parent-proxy reported HRQOL. However, these observations of non-significant moderators should be interpreted with caution, as these trends were likely skewed by the low number of studies in each comparison. No detectable trend was observed between study rigor and effect size the parent-proxy model.

Table 4. *Random effects meta-regression models for hypothesized moderators.*

Moderator	Coefficient	Standard Error	95% Confidence Interval	Z-value	p-value
Descriptive Studies - Child Report Model 1					
Chronic Disease Status	0.088	0.161	-0.228 – 0.405	0.55	0.584
Sex	0.018	0.020	-0.021 – 0.057	0.89	0.372
Study Rigor	0.036	0.048	-0.059 – 0.131	0.74	0.457
Descriptive Studies - Child Report Model 2					
Weight Status	-0.0002	0.004	-0.007 – 0.007	-0.05	0.958
Intervention Studies - Child Report Model 1					
Chronic Disease Status	0.105	0.317	-0.517 – 0.727	0.33	0.741
Sex	0.003	0.010	-0.015 – 0.023	0.38	0.701
Study Rigor	0.084	0.062	-0.038 – 0.205	1.35	0.176
Intervention Studies - Child Report Model 2					
Weight Status	0.011	0.008	-0.005 – 0.027	1.32	0.189
Intervention Studies - Parent Report Model					
Sex	0.051	0.033	-0.014 – 0.115	1.54	0.124
Study Rigor	0.016	0.220	-0.415 – 0.447	0.07	0.941

Exploratory Analyses

While the initial aim of this study was to characterize the association between physical activity and HRQOL in descriptive studies, exercise interventions were added to increase the number of included studies and reach of this meta-analysis. Although not hypothesized *a priori*, previous reviews have cited heterogeneity in exercise intervention duration, intensity, and frequency as possible confounders of intervention effectiveness (Granger et al., 2017; Lubans et al., 2016; Poitras et al., 2016; Wong et al., 2017). Therefore, *post hoc* analyses were conducted

to examine intervention contact hours as a proxy for exercise duration and frequency. Thirteen out of 19 studies reported detailed information to calculate total intervention contact hours, which was tested in two models based on child- or parent-proxy reported HRQOL. In both models, contact hours did not significantly moderate the effect of physical activity intervention on HRQOL (*ps* > .22; **Table 5**).

Due to the broad range of child ages in included studies (3-18 years), age was also examined as an exploratory *post hoc* moderator. All studies reported adequate information to include age as a moderator, so it was tested in all models with significant Q statistics. In all models, age was not a significant predictor of the association between physical activity and HRQOL (*ps* > .43; **Table 5**).

Table 5. *Random effects meta-regression models for exploratory moderators.*

Moderator	**Coefficient**	**Standard Error**	**95% Confidence Interval**	**Z-value**	**p-value**
Descriptive Studies - Child Report Model					
Age	-0.027	0.035	-0.096 – 0.041	-0.78	0.436
Intervention Studies - Child Report Model					
Intervention Contact Hours	0.024	0.022	-0.083 – 0.066	1.12	0.264
Age	0.108	0.178	-0.242 – 0.458	0.60	0.546
Intervention Studies - Parent Report Model					
Intervention Contact Hours	0.020	0.017	-0.012 – 0.053	1.22	0.224
Age	0.032	0.099	-0.163 – 0.226	0.32	0.749

Publication Bias

Funnel plots for visual inspection of publication bias displayed notable gaps, particularly for descriptive studies (**see Figures 6-7**). Without imputed zero correlations for the three studies that found no significant association between physical activity and HRQOL but did not report exact values, there would be no studies in the lower left quadrant of the funnel plots, where highly non-significant studies would be expected. However, these plots should be interpreted with caution as gaps in models with less than ten studies may be due to a lack of studies, rather than true publication bias (Sterne et al., 2011).

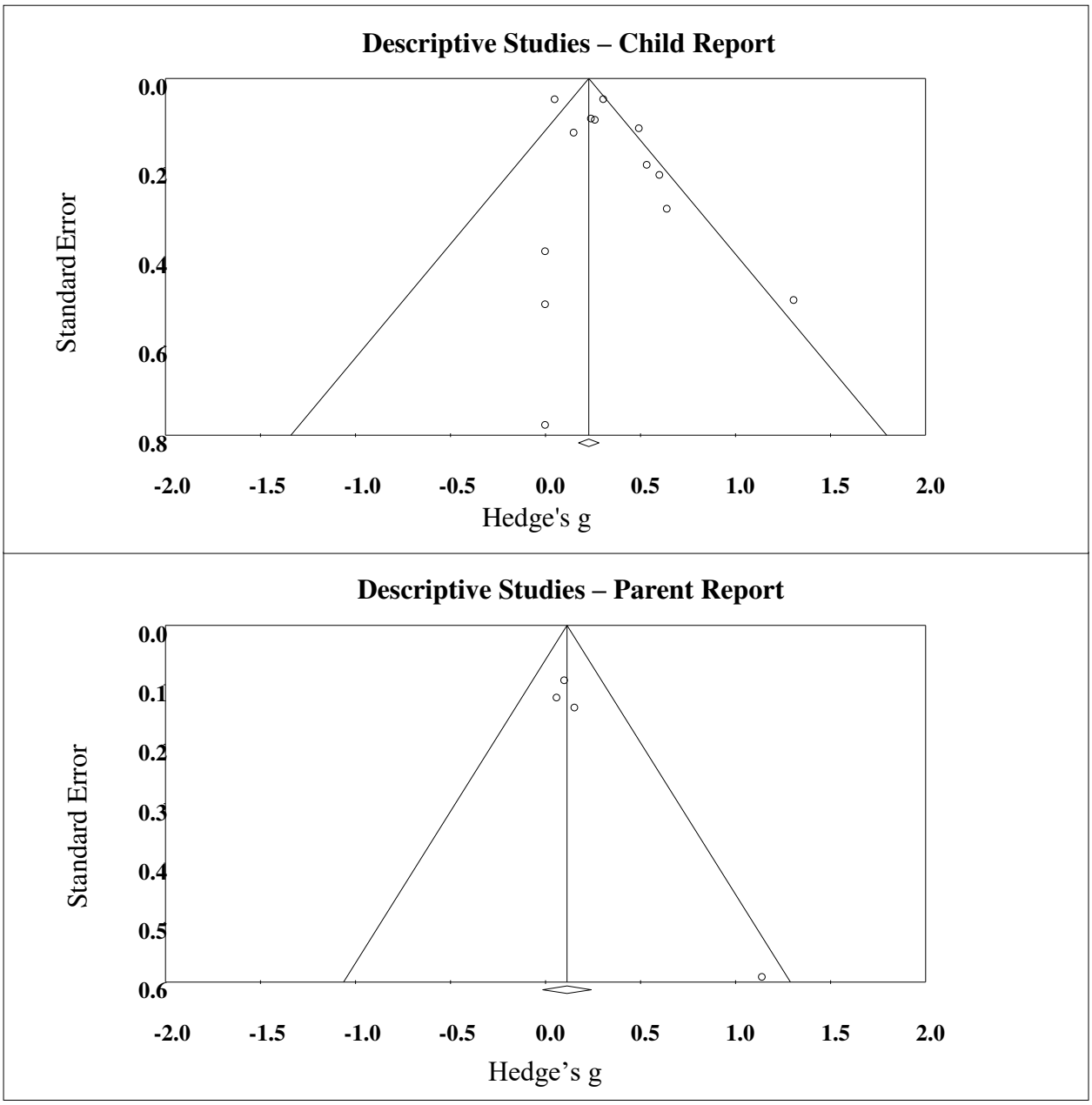

Figure 6. Funnel plots of asymmetry as tests of publication bias (standard error by Hedge's g) in descriptive studies.

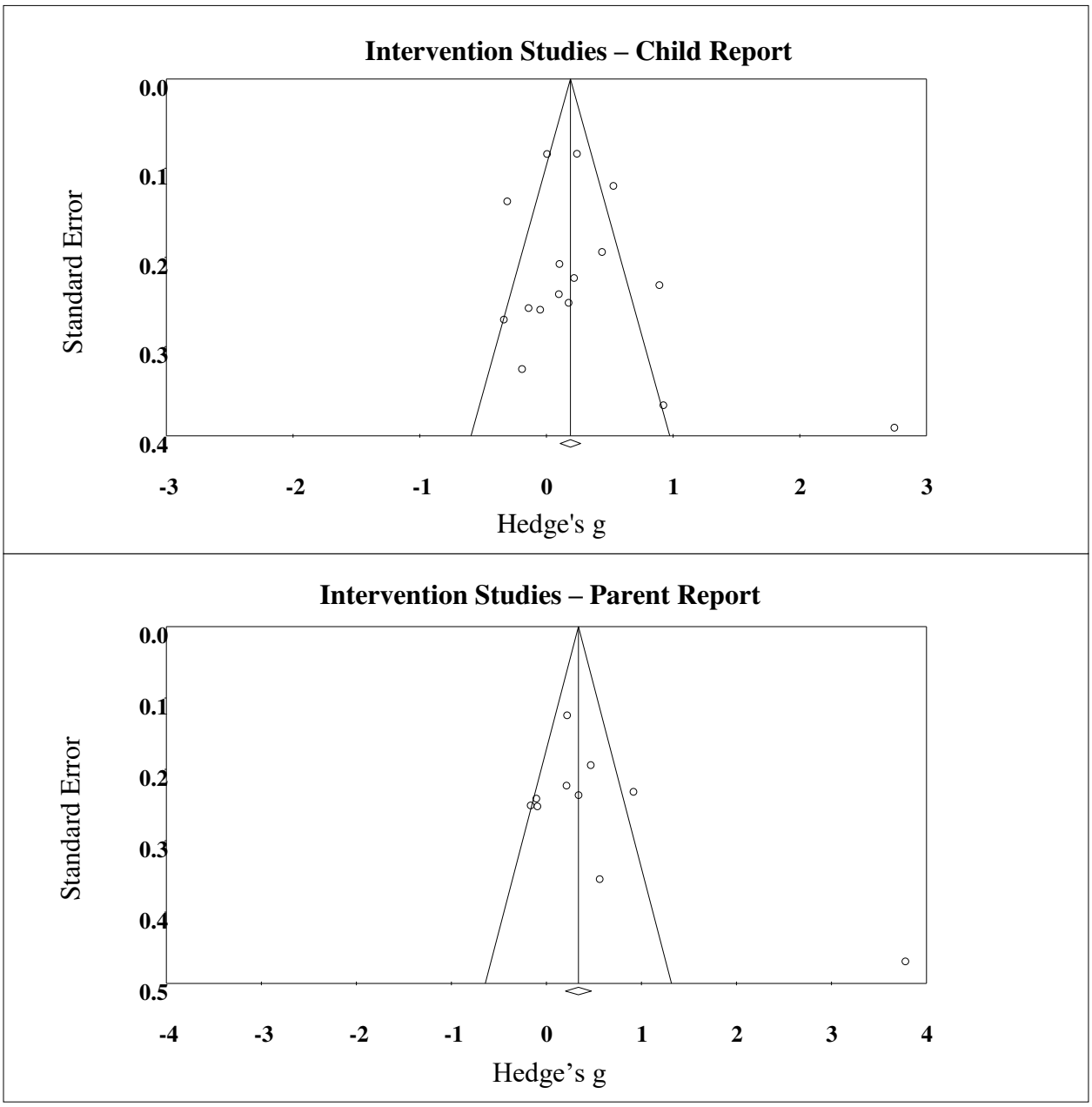

Figure 7. Funnel plots of asymmetry as tests of publication bias (standard error by Hedge's g) in intervention studies.

A fail-safe *N* statistic of 26.26 was obtained for descriptive studies using child report, 0.60 for descriptive studies using parent report, 28.64 for intervention studies using child report, and 42.20 for intervention studies using parent report. These statistics indicate that between 26 and 42 additional non-significant studies would be needed to reduce the overall effect sizes to a negligible effect of 0.1 for three out of four models. However, for descriptive studies that utilized parent-reported HRQOL, less than one additional non-significant study would be needed to reduce this effect size to 0.1, consistent with the already negligible effect size found for this model. Removing the impact of the outlying study (Mendonca et al., 2013) from analyses, failsafe *N* values drop to 10.35 for intervention studies using child report and 14.49 for intervention studies using parent report.

Discussion

The primary aim of this study was to quantify the magnitude of the association between physical activity and HRQOL in children and adolescents. Physical activity is linked to both physical and mental health outcomes in youth (Ekelund et al., 2012; Larun et al., 2006; Brown et al., 2013) and recent initiatives recommend the use of HRQOL as a cross-disciplinary measure of subjective health outcomes (NIH, 2017; CDC, 2011). This systematic review and meta-analysis aimed to be the first comprehensive examination of the relationship between physical activity and HRQOL across pediatric populations.

Aggregate data demonstrated a small, positive effect of physical activity on HRQOL. More specifically, a small to negligible association between physical activity and HRQOL was found across 14 descriptive studies, while a small to medium effect of exercise interventions on pre-post changes in HRQOL was found across 19 intervention studies. However, among the intervention studies, a large portion of this effect was driven by a single study (Mendonca et al.,

2013). When removed, the aggregate effect size across intervention studies was reduced to a small to marginal effect. Generally, findings supported the primary hypothesis that increased levels of physical activity would be related to better HRQOL in a limited way. This finding matches previous systematic reviews of physical activity, health and, well-being outcomes in both adults (Bize et al., 2007) and youth (Granger et al., 2017; Poitras et al., 2016; Wong et al., 2017). In adults, Bize and colleagues (2007) identified significant positive associations between level of physical activity and HRQOL in five out of seven cross-sectional studies, and positive effects of physical activity on HRQOL in four RCTs. In adolescents, Granger et al. (2017) found positive associations between physical activity and self-reported health status in nine studies and Wong et al. (2017) found that more time spent in MVPA was related to higher HRQOL in thirteen out of fifteen studies. However, previous reviews in children and adolescents included highly heterogeneous studies and were unable to calculate overall effect sizes; thus, this review extends the literature by quantifying the overall size of this effect in youth. The small to marginal positive effect found in this meta-analysis indicates that increasing physical activity may result in positive, but limited increases in self-perceived health in children and adolescents.

To better understand these results, the small overall effect was interpreted in light of the minimal clinically significant difference (MCID), which is the smallest change in a target domain that is needed for a patient to perceive a change as clinically beneficial (Copay et al., 2007). A change above the MCID threshold would indicate a level of improvement in the target outcome that, in the absence of adverse side effects or unsustainable costs, would recommend a change in care, such as participation in a physical activity intervention to improve HRQOL.

Recommended levels for the MCID based on changes in HRQOL were developed by Varni et al. (2003) for the Pediatric Quality of Life Inventory (PedsQL), the most commonly

used measure of HRQOL in this review. The PedsQL MCID was calculated using the standard error of measurement (SEM), where one SEM represents the MCID for clinical responsiveness to change in HRQOL (Copay et al., 2007; Varni et al., 2003). The recommended MCID for the PedsQL equates to a pre-post change in HRQOL total score of 4.4 based on child report or 4.5 based on parent-proxy report (Varni et al., 2003). Of intervention studies included in this review, only three treatment groups saw improvements in HRQOL as measured by the PedsQL that would meet these MCID criteria based on child-report (Wafa et al., 2011), parent-proxy report (Yackobovitch-Gavan et al., 2009), or both (Mendonca et al., 2013). In addition, at least one of these studies showed greater improvement in the control group than the treatment group, although a clinically significant improvement was seen for the intervention group (Yackobovitch-Gavan et al., 2009). Importantly, findings by Mendonca et al. (2013) represent an outlier that found larger effects of physical activity on HRQOL than other interventions. Therefore, in most cases, the small effect sizes seen following exercise interventions did not indicate a clinically meaningful improvement in HRQOL. These findings suggest that existing physical activity interventions may have positive, but limited effects on HRQOL.

An additional way to interpret these results is using the number needed to treat (NNT), or the average number of participants needed to complete an intervention in order to have one successful outcome (Kraemer & Kupfer, 2006). NNT can also be operationalized as the number of patients that would need to be treated (versus an untreated or alternative treatment comparison group) to see a difference in outcome (Citrome, 2008). The NNT calculated from effect sizes for intervention studies based on child report (Hedge's g = .279) indicates that 14 patients would need to be treated with an exercise intervention to achieve a clinically significant improvement in one patient above and beyond that of a no-treatment or alternative intervention control group.

For intervention studies based on parent report (Hedge's g = .522), 6 patients would need to be treated to achieve one participant with a significantly better outcome in HRQOL beyond that of the control group. This metric can help researchers and practitioners further understand the generally small effect found in this meta-analytic review. Overall, 6 to 14 patients may need to be treated with existing exercise interventions for one patient to achieve a meaningful improvement in HRQOL. If one outlying study is removed (Mendonca et al., 2013), these NNT numbers would increase to 13 to 22 patients who would need to receive an exercise intervention for one patient to show a clinically relevant improvement in HRQOL. As discussed more fully below, this indicates that existing physical activity interventions are not sufficiently effective to improve HRQOL for the majority of youth.

The secondary aim of this review was to explore the impact of moderators on the relationship between physical activity and HRQOL. None of the *a priori* moderators, including chronic disease status, weight status, sex, and study rigor, were found to significantly moderate the relationship between physical activity and HRQOL. Additional *post hoc* examinations of age and total intervention contact hours (as a proxy measure of exercise duration and frequency) also did not significantly moderate the effect of physical activity on HRQOL in intervention studies.

Based on previous estimations, it was not surprising that these analyses failed to identify significant moderators, given the limited number of studies identified by this review that could be included in moderator analyses and differential study types (i.e. child versus parent-reported HRQOL, descriptive versus intervention study designs) which required analyses to be conducted in four separate models. For example, Groenveld et al. (2012, p.1841) estimated that "the sample size needed to detect a small effect size [for sex on HRQOL] would be N ~780," while the median sample size for included studies was approximately 87. Limited variability in *a*

priori moderators across included studies, particularly for chronic disease status and weight status, further limited these analyses. The majority of included studies were conducted in youth with a chronic disease, indicating the need for high quality studies in healthy youth that report all data necessary to calculate effect sizes. Weight status was also not adequately reported in studies whose primary aims did not include assessing youth with overweight/obesity or it was reported in a variety of formats that could not be directly compared (e.g. body weight, body mass index [BMI], BMI percentile, percent overweight/obese). Weight status may be an important demographic indicator to report systematically in future pediatric studies. Previous reviews were unable to calculate even overall effect sizes in children and adolescents due to high heterogeneity between studies (Granger et al., 2017; Poitras et al., 2016; Wong et al., 2017), indicating that additional moderators not assessed in this analysis could explain variability between studies.

Although *a priori* moderators were not significant, effect sizes did qualitatively vary across study type and HRQOL reporter. In general, larger effect sizes (Hedges g = .279-.522) were observed for intervention studies, indicating that HRQOL is a construct that can be positively altered by physical activity education and structured exercise involvement. Effect sizes were typically smaller in descriptive studies (Hedges g = .115-.302) where physical activity and HRQOL levels were measured concurrently without intervention. Aggregate effect sizes were more consistent across studies that used child-report of HRQOL (Hedges g = .279-.302), while effect sizes based on parent-proxy reports of youth HRQOL were more variable (Hedges g = .115-.522). The variability in effects based on parent-proxy reports of youth HRQOL could be due to the more limited number of studies that included parent-proxy reports in this review. Unfortunately, these qualitative variations were unable to be tested as quantitative moderators because these differences existed across meta-analytic models, which would be inappropriate to

directly compare (i.e. parent versus child-report; intervention versus cross-sectional study design).

One possible explanation for the limited effect sizes observed in this study requires a closer look at exercise interventions for youth. Two previous reviews of exercise interventions in childhood found that physical activity interventions displayed small to negligible improvements in objectively measured physical activity immediately following or six months after an intervention (Metcalf et al., 2012; Sims et al., 2015). Average increases in activity level following an active intervention were only 4.47 minutes per day of total activity or 1.47 minutes per day of MVPA (Sims et al., 2015). With such small changes in physical activity, it is not surprising that downstream effects on psychosocial outcomes like HRQOL would also be small. Some evidence suggests a dose-response relationship between physical activity and HRQOL, with 1.5-2.6 unit increases in physical functioning HRQOL reported for each increased hour of physical activity (Gopinath et al., 2012). However, this implies that adolescents would have to increase physical activity levels by over two hours per day to achieve a change in HRQOL commensurate with estimates for a clinically meaningful change (HRQOL total score difference of 4.4-4.5; Varni et al., 2003). In contrast, physical activity guidelines recommend youth above six years to engage in only one hour of MVPA to achieve health-related benefits (U.S. Department of Health and Human Services, 2008; World Health Organization, 2010). This disconnect between physical activity guidelines and amount of change in activity following an exercise intervention will be an important area for future research.

Importantly, twelve out of 19 intervention studies failed to objectively measure physical activity to determine whether interventions resulted in significant changes in physical activity. Ten of the studies did not measure physical activity at all. Without direct measures of pre-post

physical activity, small observed effects on HRQOL could be due to intervention failure (i.e. physical activity level did not actually increase), compensatory decreases in naturally occurring physical activity (e.g. Melanson et al., 2013), or low-level changes in physical activity that were not large enough to achieve significant subjective health-related benefits. As described in Sims et al., (2015), at least one study has successfully increased child physical activity by almost 60 minutes (Araujo-Soares et al., 2009), indicating that it may be possible for exercise interventions to increase activity to a level that could facilitate clinically meaningful downstream effects on psychosocial outcomes. However, as demonstrated by the lack of physical activity measurement in this meta-analysis, there is a need for exercise interventions that objectively assess changes in physical activity and concurrent changes in HRQOL. Subjective measures are not an acceptable alternative as it is well-documented that subjective measures of physical activity often overestimate duration and intensity (Ekelund et al., 2011). Promisingly, research suggests that objective physical activity devices are used in pediatric research, acceptable for youth wear, and increasingly affordable (Bjornson, 2005; Cain et al., 2013; Van Coevering et al., 2005). The increased use of objectively measured physical activity bodes well for a growing number of studies that will have the capacity to relate objective changes in physical activity level to HRQOL outcomes.

Further complicating a more in-depth analysis of why physical activity interventions did not affect HRQOL in a clinically meaningful way, exercise interventions included in this review were highly heterogeneous. Included studies ranged from conventional cardiorespiratory and resistance training (e.g. Taracki et al., 2012; Van Dijk-Lokkart et al., 2015) to educational multidisciplinary treatments (e.g. Vos et al., 2012; Wake et al., 2009) to specific, alternative exercise types, such as Pilates and aquatic training (e.g. Mendonca et al., 2013; Takken et al.,

2003). Differences in these types of exercise may help to explain differential effects of physical activity on HRQOL between studies. For instance, interventions in this analysis with individual sessions including both cardiorespiratory and strength-training exercises (Taracki et al., 2012) or 48 sessions of Pilates exercises (Mendonca et al., 2013) displayed the largest effect sizes. While implementation of dance mats across schools and aquatic exercise once a week displayed small negative effects (Azevedo et al., 2014; Takken et al., 2003). Consistent with the model proposed by Lubans et al. (2016), this may indicate that factors such as type of exercise, number of training sessions, and how the intervention was administered had a large impact on the effectiveness of these interventions.

To further assess why some exercise interventions resulted in larger effects on HRQOL than others, intervention contact hours were included as a proxy for intervention duration and frequency in this meta-analysis *post-hoc*. Although intervention contact hours did not significantly moderate the relationship between physical activity and HRQOL, analyses were limited by six out of 19 studies that failed to report detailed information on intervention frequency and duration. This may indicate disciplinary differences in the development, implementation, and reporting of exercise interventions for youth. Studies that objectively assessed changes in physical activity, had detailed descriptions of intervention methods, and provided scientific rationales for the intensity of training may have been less likely to include psychosocial measures like HRQOL and thus were not included in this review; whereas, psychologically-minded researchers who included patient-reported outcomes like HRQOL may have been less likely to include rigorous exercise designs, true exercise interventions, or objective measures of physical activity. A more in-depth examination of aspects of exercise interventions that could influence their effectiveness for changing HRQOL was beyond the scope

of this study, but should be a focus of future meta-analytic reviews. Future researchers may benefit from using the Lubans et al. (2016) mechanistic model to develop structured exercise interventions in youth that are of adequate frequency, intensity, time, type, and context to facilitate meaningful changes in subjective psychological well-being and quality of life. Future researchers may also benefit from developing cross-discipline collaborations to overcome potential disciplinary gaps in intervention design and implementation.

Finally, aspects of study rigor and systematic limitations in the existing literature should be considered when interpreting these results. Some aspects of study rigor were generally good across studies. For example, almost all studies reported at least three demographic variables and most studies reported on intervention drop-outs or study completion rates. Over half of the studies included multi-informant reports of HRQOL (i.e. child self-report and parent-proxy report), although these had to be analyzed in separate analyses. A fair number of studies included a minimum sample size of at least 40 participants (or 20 participants per group) and most of the intervention studies used randomized controlled designs.

However, studies were less likely to collect data from multiple sites, report use of a standardized treatment manual, or use blinded assessors. No included study measured treatment fidelity. Lower study rigor scores were observed across descriptive studies, generally, because some aspects of the study rigor coding were not present and automatically scored zero for studies that did not include an intervention. In addition, some studies may have included additional aspects of study rigor but failed to adequately report each aspect in the published work, resulting in artificially lower scores. For future studies, larger sample sizes and more consistent inclusion of both child and parent-proxy reported outcomes should continue to be a focus. The main areas for improvement in study rigor are a need for the use of standardized intervention manuals and

intervention fidelity checks, as well as better inclusion of blinding to reduce the potential for biased outcomes by assessors who know the participant's treatment allocation.

Finally, although the initial search returned a high number of studies that included both physical activity and HRQOL, HRQOL was rarely compared directly to physical activity outcomes and was even more rarely a primary outcome. For studies that did directly compare physical activity and HRQOL outcomes, many studies failed to report total HRQOL scores (e.g. reported subscale scores only) or reported test statistics that were unable to be converted into an effect size (e.g. median, interquartile range). Future research should aim to include validated HRQOL measures as a primary outcome, report on both sub-domain and total HRQOL scores, and report test statistics that are readily usable to calculate effect sizes.

Strengths and Limitations

Beyond the specific limitations of the literature noted above, this study had a number of limitations. As with any meta-analysis, there was a risk that the literature search did not capture all of the relevant literature. However, the authors tested and reviewed search terms with colleagues prior to conducting the final database search, conducted forward- and backward-searches to identify additional relevant articles, and contacted authors for missing information to help ensure that the search returned the most complete literature possible. This study was also at risk for finding skewed (larger) effect sizes because it did not include unpublished works. To counteract this risk, the ProQuest Dissertations database was used to find relevant, unpublished dissertations and theses and the fail-safe *N* was calculated. Based on the number of studies in this meta-analytic review, it is unlikely that an additional 10-42 unpublished, non-significant studies exist that could reduce the small, positive effect found in this analysis to a negligible effect for three out of four models.

Effect sizes may also have been impacted by the search criteria, which excluded interventions without control groups and limited the types of HRQOL and physical activity measures that could be included (e.g. validated HRQOL measures with total scores, no single-item measures, physical activity in minutes or METs). However, these decisions were made in an effort to include higher quality studies that were directly comparable. Importantly, overall effect sizes in intervention studies changed from small to marginal, and medium to small when a single study was removed from analyses (Mendonca et al., 2013). Several factors, including the nature of the sample (children with juvenile rheumatoid arthritis), the nature of the intervention (Pilates), and the number of exercise sessions may have individually or in combination resulted in larger than expected results in this study.

Not all of the *a priori* moderators could be tested in each model due to a limited number of studies that provided information on the proposed moderators (i.e. weight status) and the limited sample variability across some studies (i.e. all studies in a model conducted in chronic disease populations). Finally, the conclusions of this meta-analysis are only as accurate as the previously published literature. Existing gaps in the literature, including a limited number of studies that directly measured physical activity and HRQOL, published studies that included these variables but did not report usable test statistics, and limited research on physical activity and HRQOL in young children, were unable to be rectified by this meta-analysis.

In spite of these limitations, this meta-analysis had a number of strengths. One strength was the broad sample of children and adolescents included in this review. Previous investigations of physical activity and HRQOL have focused on disorder-specific pediatric sub-populations or healthy youth only. This analysis provided the first integration of previous research that cuts across pediatric populations for a broader understanding of the relationship

between physical activity and HRQOL in youth. Another strength of this systematic review was the breadth of the literature search, which included 1801 non-duplicate articles from multiple databases, unpublished dissertations and theses, and forward- and backward-searches to identify the most relevant literature possible. In addition, this review incorporated a systematic coding scheme to assess study rigor and statistical techniques, including a Q statistic and fail-safe *N* statistic, to evaluate the quality of the literature from which conclusions were drawn. The authors accounted for variations in study sample sizes and their potential impact on effect sizes by calculating Hedges *g*, rather than Cohen's *d*, to reduce bias due to small sample sizes and overweighting due to large sample sizes. Findings were also related to MCID and NNT standards, to provide clinically relevant interpretation of the effects from intervention studies.

Conclusion

This synthesis of the differential effects of physical activity on HRQOL across pediatric populations revealed a small to negligible positive association between physical activity and HRQOL in descriptive studies, and a small to medium positive effect of physical activity on HRQOL in intervention studies. For intervention studies, overall effect sizes were largely impacted by a single intervention, and effects were attenuated if this study was removed. Overall, physical activity did not appear to have a clinically meaningful effect on HRQOL, implying that existing structured exercise interventions may not be of adequate intensity, frequency, duration, or type to significantly improve HRQOL in youth. Although this analysis was limited by wide variation in effects across individual studies and limited ability to detect moderators of this variability, this meta-analysis was the first to quantify aggregate effects of pediatric HRQOL in relation to exercise. As the use of patient-reported outcomes and HRQOL measures continues to increase across disciplines in response to national health organization

initiatives, additional research is needed to consistently replicate findings for the relationship between physical activity and HRQOL in youth. Additional research is needed to determine the level of physical activity that would be required to improve HRQOL in a clinically meaningful way across both healthy and chronically ill pediatric populations. Researchers should be mindful that the dose of physical activity needed to significantly improve psychosocial outcomes like HRQOL may not correspond exactly with current physical activity guidelines for youth. Most importantly, additional research is needed that objectively measures the impact of exercise type, duration, frequency, and intensity on HRQOL in children and adolescents.

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Appendix A. Coding criteria for assessment of study rigor.

Authors: _____ *Year:*_____

I. The study…

Reported on three or more demographic indicators of the sample [1] Y N

Collected data at a follow-up period beyond immediate completion of the study [1] Y N

Included more than one site [1] Y N

Reported data from all dependent variables they assed [1] Y N

Utilized coders who were "blind" to participants' group assignment [1] Y N

Utilized objective measurement tools instead of relying solely on client self-report [1] Y N

Utilized a manual to direct training or standardized delivery [1] Y N

Reported on dropouts [1] Y N

Included more than 20 participants in the intervention and comparison groups [1] Y N

Total points for this section: _____

II. Choose one:

The data used to calculate effect sizes came from means, standard deviations, and/or numbers of participants (percentages) [2] Y N

An exact statistic was used (e.g., *t* test) [1] Y N

Effect sizes were derived from *p*-values [0] Y N

Total points for this section: _____

III. Choose one:

Measurement of outcomes came from at least two sources (e.g., participant and collateral source) [2] Y N

Collateral only [1] Y N

Participant only [0] Y N

Total points for this section: _____

IV. Choose one:

Fidelity was assessed and considered high [2]	Y	N
Fidelity was assessed by not scored [1]	Y	N
Fidelity was not measured [0]	Y	N

Total points for this section: _____

V. Choose one:

True randomization was used [3]	Y	N
Matched groups were used [2]	Y	N
Groups were tested for pretreatment equivalence [1]	Y	N
Groups were not equivalent or equivalence could not be determined [0]	Y	N

Total points for this section: _____

POINTS

Section I: _____

Section II: _____

Section III: _____

Section IV: _____

Section V: _____

TOTAL: _____