PATIENT REPORTED OUTCOMES

Patient-Reported Pediatric Quality of Life Inventory™
4.0 Generic Core Scales in Pediatric Patients with
Attention-Deficit/Hyperactivity Disorder and Comorbid Psychiatric Disorders: Feasibility, Reliability, and Validity

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ABSTRACT

Objectives: The primary objective of the study was to evaluate the feasibility, reliability, and validity of the Pediatric Quality of Life Inventory™ (PedsQL) 4.0 Generic Core Scales as a patient self-reported health-related quality of life measurement instrument in pediatric patients with attention-deficit/hyperactivity disorder (ADHD) and physician-diagnosed comorbid psychiatric disorders being seen in a pediatric psychiatric clinic. The secondary objective was to evaluate parent proxy-reported PedsQL in this population. Methods: One hundred seventy-nine children with ADHD and comorbid psychiatric disorders ages 5 to 18 years and 181 parents completed the PedsQL 4.0 Generic Core Scales and parents also completed the Vanderbilt ADHD Diagnostic Rating Scales. Known-groups discriminant validity comparisons were made between the sample of pediatric patients with ADHD and comorbid psychiatric disorders and healthy, cancer, and type 1 diabetes samples. Results: The PedsQL evidenced minimal missing responses for patient self-report and parent proxy-report (0.2% and 0.5%, respectively), demonstrated no significant floor or ceiling effects, and achieved excellent reliability for the Total Scale Score (α = 0.85 patient self-report, 0.92 parent proxy-report). Pediatric patients with ADHD and comorbid psychiatric disorders and their parents reported statistically significantly worse PedsQL scores than healthy children, with large effect sizes across all domains, supporting known-groups discriminant validity. Pediatric patients with ADHD and comorbid psychiatric disorders and their parents reported worse PedsQL scores compared to pediatric patients with cancer and diabetes with the exception of physical health, in which pediatric cancer patients manifested lower physical health, indicating the relative severe impact of ADHD and comorbid psychiatric disorders. More severe ADHD symptoms were generally associated with more impaired PedsQL scores, supporting construct validity. Conclusions: These data demonstrate the feasibility, reliability, and validity of patient self-reported PedsQL 4.0 Generic Core Scales in this high risk population of pediatric patients and highlight the profound negative impact of ADHD and comorbid psychiatric disorders on generic health-related quality of life, comparable to or worse than serious pediatric chronic physical diseases.

Keywords: ADHD, PedsQL, attention-deficit/hyperactivity disorder, children, comorbidity, health-related quality of life, patient reported outcomes.

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent childhood chronic disorders, affecting an estimated 3% to 7% of school-aged children [1]. Symptoms of ADHD include impulsivity, a developmentally inappropriate activity level, low frustration tolerance, poor organization of behavior, distractibility, and an inability to sustain attention and concentration [2,3].

The past 10 years have witnessed a significant increase in the utilization of health-related quality of life (HRQOL) instruments in pediatric patients with ADHD [4]. HRQOL is a multidimensional construct, consisting at the minimum of the physical, psychological (including emotional and cognitive), and social health dimensions delineated by the World Health Organization [5,6]. A number of authors have argued that improving HRQOL is the ultimate goal of health care [7].

Competing interests: Dr. Varni holds the copyright and the trademark for the PedsQL and receives financial compensation from the Mapi Research Trust, which is a nonprofit research institute that charges distribution fees to for-profit companies that use the PedsQL. The PedsQL is available at: http://www.pedsql.org.

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Legislative changes during the past several years, including the Pediatric Exclusivity Provision of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act, have established voluntary and mandatory guidelines for drug studies in children that have resulted in a significant growth in clinical trials for pediatric patients. Despite the above-mentioned pediatric initiatives, which have created the opportunity for children to be included in clinical trials, when evaluating the health outcomes of treatments in the vast majority of pediatric clinical trials to date, pediatric patients have not been provided the right to self-report on matters pertaining to their health and well-being [8].

In clinical trials for pediatric patients with ADHD, treatment response often centers on symptom reduction measured through behavioral rating scales completed by a child’s parents and teachers [9]. These behavior rating scales, such as the Conners’ Rating Scales, are restricted in their ability to evaluate a child’s functioning broadly since they are specific for behavioral characteristics of ADHD (e.g., inattention, hyperactivity, cognitive problems, oppositional behavior, anxiety, and social problems). In addition, many of these behavior rating scales are not able to evaluate a young child’s perspective regarding his/her functioning because they only provide parent and teacher reports for young children.

This practice stands in sharp contrast to the recent Food and Drug Administration guidance for industry for evaluating patient-reported outcome (PRO) instruments as health outcomes in clinical trials for pediatric patients [8]. The emerging paradigm shift toward PROs in clinical trials has provided the opportunity to underscore the importance and essential need for pediatric patient self-reported health outcomes as efficacy outcomes in pediatric ADHD clinical trials. Pediatric patient self-reported generic HRQOL measurement can complement ADHD behavior rating scales and provide a more thorough understanding of the patient’s perspective on the impact of ADHD and its treatment on their health and well-being [4].

Measurement of HRQOL in ADHD is complicated by the fact that there is a high frequency of comorbid (coexisting) psychiatric disorders in children with ADHD [10,11]. Comorbid psychiatric disorders often associated with ADHD include oppositional defiant disorder, conduct disorder, depression, bipolar disorder, anxiety, tic disorders, obsessive compulsive disorder, learning disabilities, and mental retardation [2]. ADHD symptoms are associated with impairments across multiple domains, including emotional, social, and school functioning [12]; the coexistence of ADHD with other psychiatric disorders in children has been associated with greater severity of ADHD symptoms and behavioral problems, and more substantial impairments in psychosocial functioning [10].

Estimates of comorbid oppositional defiant disorder/conduct disorder range from 30% to 50% of cases; lifetime rates of comorbid depression in children with ADHD range from 29% to 45%; children with ADHD with comorbid psychiatric disorders have been found to require increased psychiatric treatment [12]. Thus, the high incidence of comorbid psychiatric disorders in pediatric patients with ADHD further increases the significant at risk status for impaired HRQOL in this population of children. To our knowledge, no study has ever investigated patient self-reported HRQOL in pediatric patients with ADHD and physician-diagnosed comorbid psychiatric disorders.

Furthermore, studies that have evaluated HRQOL in children with ADHD provide an incomplete picture since HRQOL was assessed only through parent proxy-report for all but one of the studies [13–24]. Although these studies demonstrated the significant negative effect of ADHD on HRQOL from the perspective of parent proxy-report, particularly in terms of psychosocial functioning, only the study by Varni and Burwinkle [13] assessed pediatric patient self-reported HRQOL in children with ADHD. However, this study was a population-based study so children were identified by their parents as having ADHD, not by a physician. In addition, information on comorbid psychiatric disorders was unavailable as was information on ADHD symptom severity.

Given the far-reaching psychosocial difficulties associated with ADHD and comorbid psychiatric disorders, and the documented discrepancies between child and parent reports in the pediatric literature [25,26], documenting the measurement properties of pediatric patient self-reported HRQOL in patients with ADHD and comorbid psychiatric disorders addresses an important gap in the empirical literature. As noted in a recent review [4], “Unfortunately the majority of studies in relation to child mental health in general and ADHD in specific have used only parent/carers as informants and not asked the child themselves about their Qol.” Thus, pediatric patient self-reported HRQOL in ADHD continues to be underinvestigated, notably in pediatric patients with ADHD and comorbid psychiatric disorders. In fact, in the recent review by Edmund et al. [4], no study was found in the extant empirical literature that included patient self-reported HRQOL in pediatric patients with ADHD and comorbid psychiatric disorders.

The Pediatric Quality of Life Inventory™ (PedsQL) 4.0 Generic Core Scales [27] has emerged as a widely used generic HRQOL measure in pediatric chronic health conditions that has resulted from an extensive iterative process involving numerous patient and parent focus groups and individual focus interviews, item generation, cognitive interviewing, pretesting, and subsequent field testing, with more than 500 peer-reviewed journal publications and 70 international translations [28]. The PedsQL 4.0 Generic Core Scales has been increasingly used in pediatric psychiatric disorders, demonstrating significant impairments in HRQOL [13,29] and significant intercorrelations with the Child Behavior Checklist [30–32] and measures of emotional distress including the Children’s Depression Inventory [33], the State-Trait Anxiety Inventory for Children [32], the Revised Children’s Manifest Anxiety Survey [33], and the Social Phobia and Anxiety Inventory for Children and Short Mood and Feeling Questionnaire [34]. However, the measurement properties of the PedsQL 4.0 Generic Core Scales as a patient self-reported measurement instrument in pediatric patients with ADHD and comorbid psychiatric disorders has not been previously investigated.

Consequently, the primary objective of this study was to evaluate the feasibility, reliability, and validity of the PedsQL 4.0 Generic Core Scales as a patient self-reported generic HRQOL measurement instrument in pediatric patients with ADHD and physician-diagnosed comorbid psychiatric disorders being seen in a Pediatric Psychiatric Clinic. The secondary objective was to evaluate the measurement properties of the PedsQL parent proxy-report version in this population since previous PedsQL studies did not include pediatric patients with ADHD and comorbid psychiatric disorders. This population of pediatric patients with ADHD treated at a Pediatric Psychiatric Clinic was specifically selected given that patients being seen in a psychiatric clinic manifest a high prevalence of comorbid psychiatric disorders [35,36].

Based on previous findings [14,20], we hypothesized that children and adolescents with ADHD and comorbid psychiatric disorders would demonstrate significantly lower PedsQL scale scores (effect sizes in the medium to large range) than a matched sample of healthy children, with the greatest differences evidenced on psychosocial functioning. We anticipated that more impaired PedsQL scale scores would be associated with more severe ADHD symptoms, consistent with previous findings using parent proxy-report [14,18,20,21]. We also compared the sample of pediatric patients with ADHD and comorbid...
psychiatric disorders to two groups of pediatric patients with serious chronic physical diseases; that is, cancer and diabetes, to determine the relative impact of ADHD and comorbid psychiatric disorders on patient reported PedsQL scores. Finally, based on the general pediatric HRQOL literature [25], we hypothesized that children and their parents would demonstrate moderate agreement regarding the child’s PedsQL scores, and that parents would report lower mean PedsQL scores than their children.

Method

Participants

Participants in this cross-sectional study were 179 children with a physician diagnosis of ADHD and comorbid psychiatric disorders ages 5 to 18 years and 181 parents of children with a physician diagnosis of ADHD and comorbid psychiatric disorders ages 5 to 18 years being seen in a pediatric psychiatric clinic. One hundred seventy-seven participants had both patient self-report and parent proxy-report PedsQL data; two participants only had patient self-report and four participants only had parent proxy-report PedsQL data, which accounts for the differences in sample size presented in the sociodemographic description of the sample below.

Measures

PedsQL 4.0 Generic Core Scales

The 23-item PedsQL 4.0 Generic Core Scales encompass 1) physical functioning (eight items); 2) emotional functioning (five items); 3) social functioning (five items); and 4) school functioning (five items). The Physical Health Summary Score (eight items) is the same as the Physical Functioning Scale. To create the Psychosocial Health Summary Score (15 items), the mean is computed as the sum of the items divided by the number of items answered in the Emotional, Social, and School Functioning Scales. The PedsQL 4.0 Generic Core Scales are comprised of parallel child self-report and parent proxy-report formats. Child self-report includes ages 5 to 7 years, 8 to 12 years, and 13 to 18 years. The items for each of the forms are essentially identical, differing in developmentally appropriate language. This scale construct consistency facilitates the evaluation of differences in HRQOL across and between age groups, as well as the tracking of HRQOL longitudinally. The instructions ask how much of a problem each item has been during the past 1 month. A five-point categorical response scale is utilized across child self-report for ages 8 to 18 years (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Items are reverse-scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered. To further increase the ease of use for the young child self-report (ages 5 to 7 years), the response scale is reworded and simplified to a three-point scale (0 = not at all a problem; 2 = sometimes a problem; 4 = a lot of a problem), with each response choice anchored to a happy-to-sad faces scale. The instrument takes approximately 5 minutes to complete [27]. In this study, only children ages 5 to 18 years and their parents completed the PedsQL given the low prevalence of children with ADHD ages 2 to 4 years seen in the pediatric psychiatric clinic in which data were collected.

Vanderbilt ADHD Diagnostic Rating Scales

Parents completed the parent version of the Vanderbilt ADHD Diagnostic Rating Scales. Content of the Vanderbilt ADHD Diagnostic Rating Scales Parent Version has been shown to be consistent with the Diagnostic and Statistical Manual for Mental Disorders, 4th Edition diagnosis of ADHD in school-aged children [37], and a single parent rater has been successfully used to identify children with ADHD in a nationally representative sample [38]. The Vanderbilt includes a nine-item Inattentive Scale and nine-item Hyperactive/Impulsive Scale. The Total ADHD Symptom Score (18 items) is a summary score of the Inattentive Scale and Hyperactive/Impulsive Scale. The Vanderbilt scales use a four-point Likert rating, in which the parent notes whether over the past 6 months the behavior symptoms have occurred rarely, sometimes, often, or very often. Higher scores indicate more severe ADHD symptomatology.

PedsQL Family Information Form

Parents completed the PedsQL Family Information Form [27], which contains demographic information such as the child’s date of birth, sex, race/ethnicity, and parental education and occupation information required to calculate the Hollingshead Socioeconomic Status (SES) Index [39]. Mean Hollingshead Index scores between 66 and 55 indicates upper class, 54 to 40 indicates upper-middle class, 39 to 30 indicates middle class, 29 to 20 indicates lower-middle class, and 19 to 8 indicates lower class.

Disease-specific indicators

The following information was retrieved from the child’s medical chart by a research nurse: number of months since ADHD diagnosis, number of psychiatric diagnoses, category of comorbid diagnoses, number of daily psychiatric medications, and number of months on psychiatric medications.

Procedures

Data collection for the ADHD and comorbid psychiatric disorders sample took place over a 3-year period between 2005 and 2008. ADHD and comorbid psychiatric diagnoses were made after an extensive clinical interview by a child psychiatrist before the child was enrolled in the study based on signs and symptoms presented and history, including in some cases diagnostic scales completed by parents and teachers. Children ages 5 to 18 years and their parents were given a specific PedsQL 4.0 Generic Core Scales age-appropriate form depending on the child’s age (5 to 7 years, 8 to 12 years, and 13 to 18 years). Younger children (5 to 7 years) were assisted by a research assistant in completing the measure. The research assistant was also available to assist children in the older groups and parents as needed. All research assistants were trained using a detailed protocol to ensure administration of the questionnaires was standardized across the sample. After completing the PedsQL 4.0 Generic Core Scales, parents completed the Vanderbilt ADHD Diagnostic Rating Scales Parent Version and the PedsQL Family Information Form, in that order. Participants completed instruments in a patient examination room in the Pediatric Psychiatric Clinic, either while waiting for the physician or after the child’s appointment with the physician. Each child/parent pair was provided a $10 gift certificate for their participation in the study. Written parental informed consent and child assent for children ages 7 years and older were obtained. This research protocol was approved by the institutional review board at Scott and White Memorial Hospital and Clinics. The healthy children sample was derived from the previously conducted PedsQL 4.0 Generic Core Scales initial field test [27] and a statewide State Children’s Health Insurance Program evaluation [40]. Children were assessed either in physicians’ offices during
well-child visits, by telephone, or via a statewide mailing. The pediatric cancer sample was derived from the PedsQL 3.0 Cancer Module field test [41]. Children and their parents were assessed in-person by a research assistant at two pediatric cancer centers. The type 1 diabetes sample was derived from the PedsQL 3.0 Diabetes Module field test [42] and a subsequent study in a hospital-based pediatric endocrinology clinic [43]. Children and their parents were assessed in-person by a research assistant at the pediatric endocrinology clinic or via telephone. Across the healthy, cancer, and diabetes samples, both child self-report and parent proxy-report versions of the PedsQL 4.0 Generic Core Scales were utilized. These research protocols were approved by the appropriate local institutional review boards.

Statistical analyses

Feasibility of the PedsQL 4.0 Generic Core Scales as a PRO measure for pediatric patients with ADHD and comorbid psychiatric disorders was determined from the percentage of missing values for each item [44]. To determine scale internal consistency reliability, Cronbach’s coefficient alphas were calculated [45]. Scales with reliabilities of 0.70 or greater are recommended for comparing patient groups, while a reliability criterion of 0.90 is recommended for analyzing individual patient scale scores [46,47]. Range of measurement was based on the percentage of scores at the extremes of the scaling range, that is, the maximum possible score (ceiling effect) and the minimum possible score (floor effect) [44]. Surveys with small floor or ceiling effects (1–15%) are considered to meet acceptable measurement standards, whereas surveys with moderate floor or ceiling effects (more than 15%) are considered less precise in measuring latent constructs at the extremes of the scale [48].

Discriminant validity for the PedsQL 4.0 Generic Core Scales was determined utilizing the known-groups method [49]. The known-groups method compares scale scores across groups known to differ in the health construct being investigated. Independent samples t tests were used to compare pediatric patients with ADHD and comorbid psychiatric disorders to a matched sample of healthy children on the PedsQL 4.0 Generic Core Scales. The healthy children sample was randomly matched by age, sex, and race/ethnicity to the ADHD and comorbid psychiatric disorders sample utilizing the SPSS version 16.0 statistical software random sample case selection command. This command allows the percentage of children in the healthy sample to be matched to the ADHD sample on the targeted demographic characteristics. Effect sizes were calculated in order to determine the magnitude of the differences between pediatric patients with ADHD and healthy children [50]. Effect size as utilized in these analyses was calculated by taking the difference between the healthy sample mean and the ADHD sample mean, divided by the pooled standard deviation. Effect sizes for differences in means are designated as small (0.20), medium (0.50), and large (0.80) in magnitude [50]. Surveys with small floor or ceiling effects (1–15%) are considered to meet acceptable measurement standards, whereas surveys with moderate floor or ceiling effects (more than 15%) are considered less precise in measuring latent constructs at the extremes of the scale [48].

Intraclass correlation coefficients (ICCs) were utilized to determine the magnitude of the differences between pediatric patients with ADHD and their parents, effect sizes were calculated [50]. Effect size as utilized in these analyses was calculated by taking the difference between the child mean and the parent sample mean, divided by the pooled SD. As previously noted, effect sizes for differences in means are designated as small (0.20), medium (0.50), and large (0.80) in magnitude [50]. Statistical analyses were conducted using SPSS version 16.0 for Windows [55].

Results

Sociodemographic characteristics

ADHD and comorbid psychiatric disorders sample

The mean age of the 57 girls (31.1%) and 124 boys (67.8%; missing, n = 2, 1.1%) was 11.08 ± 3.70 years. In terms of race/ethnicity, the sample contained 147 (80.3%) white non-Hispanic, 8 (4.4%) Hispanic, 20 (10.9%) black non-Hispanic, 5 (2.7%) other, and 3 (1.6%) missing. Mean SES was 40.62 ± 11.71, indicating on average a middle to upper middle class sample based on the Hollingshead Index [39]. The comorbid diagnoses included mood disorders (n = 82), disruptive behavior disorders (n = 99), anxiety disorders (n = 52), psychotic disorders (n = 7), substance use disorders (n = 1), learning disability/mental retardation (n = 28), and other (n = 13). The median number of daily psychiatric medications children in the sample were taking was 1 ± 0.57; range 0–3. Mean number of months children had been on psychiatric medications was 42.09 ± 31.71; range 1–153. More than 98% of patients in the sample were taking at least one daily psychiatric medication (44.8% of the sample were taking two daily psychiatric medications, 3.8% of the sample were taking three daily psychiatric medications).

Healthy sample

The mean age of the 957 boys (65.9%) and 496 girls (34.1%) was 9.21 ± 4.46 years. In terms of race/ethnicity, the sample contained 1170 (80.5%) white non-Hispanic, 112 (7.7%) Hispanic, 131 (9.0%) black non-Hispanic, 26 (1.8%) other, and 14 (1.0%) missing. Mean SES was unavailable for this sample, although the statewide Child Health Insurance Program. The sample was representative of low-income families (less than 250% of the federal poverty level).

Pediatric cancer sample

The sample included pediatric cancer patients on cancer treatment (chemotherapy and radiation) with acute lymphocytic leukemia (n = 118, 64.5%), brain tumors (n = 8, 4.4%) non-Hodgkin’s lymphoma (n = 9, 4.9%), Hodgkin’s lymphoma (n = 6, 3.3%), Wilms’ tumor (n = 7, 3.8%), and other cancers (n = 35, 19.1%). For all forms combined, the average age of the 107 boys (58.5%) and 75 girls (41.0%; missing = 1, 0.5%) was 8.22 ± 4.83 years. The sample was heterogeneous with
respect to race/ethnicity, with 57 (31.3%) white non-Hispanic, 91 (49.7%) Hispanic, 8 (4.4%) black non-Hispanic, 10 (5.5%) Asian/Pacific Islander, 1 (0.5%) American Indian or Alaskan Native, and 2 (1.1%) missing.

**Pediatric type 1 diabetes sample**
For all participants combined, the mean age of the 172 girls (53.8%) and 148 boys (46.3%) was 12.34 ± 3.94 years. With regard to race/ethnicity, the sample contained 193 (60.3%) white non-Hispanic, 62 (19.4%) Hispanic, 25 (7.8%) black non-Hispanic, 12 (3.8%) Asian/Pacific Islander, and 28 (8.8%) other or missing.

**Measurement properties**
Feasibility
For patient self-report and parent proxy-report, the percentage of missing item responses for the ADHD and comorbid psychiatric disorders sample on the PedsQL 4.0 Generic Core Scales was 0.2% and 0.5%, respectively.

Range of measurement
Table 1 contains the percentage of scores at the extremes of the scaling range (floor and ceiling effects). There was no significant floor or ceiling effects for any of the summary or scale scores for patient self-report and parent proxy-report.

**Internal consistency reliability**
Table 1 presents the internal consistency reliability alpha coefficients for the ADHD and comorbid psychiatric disorders sample on the PedsQL 4.0 Generic Core Scales. All patient self-report scales and parent proxy-report scales on the Generic Core Scales, with the exception of the School Functioning Scale for patient self-report (α = 0.65), met or exceeded the minimum reliability standard of 0.70 required for group comparisons. The total score for both patient self-report and parent proxy-report met or approached the reliability criterion of 0.90 recommended for analyzing individual patient scale scores.

**Discriminant validity**
Mean comparison to matched healthy sample
Means and SDs of the PedsQL 4.0 Generic Core Scale Scores for patient self-report and parent proxy-report are presented in Table 1. For all PedsQL 4.0 Generic Core Scales, pediatric patients with ADHD and comorbid psychiatric disorders and their parents reported statistically significant worse PedsQL scores than healthy children. All effect sizes were in the large range, with the greatest effects for both patients self-report and parent proxy-report found on the Psychosocial Health Summary Score. It should be noted that the large effect sizes reported between our sample and healthy children on the Physical Health Summary Score was not an anticipated finding. A post-hoc analysis of responses to individual items on the PedsQL Physical Health Summary Score in the current sample revealed that 11.7% of the patients self-reported “often” or “almost always” having low energy, whereas 14.5% of the patients self-reported “often” or “almost always” having hurts or aches; 19.9% of parents reported their child “often” or “almost always” had low energy, whereas 14.5% of parents reported their child “often” or “almost always” had hurts or aches.

**Mean comparisons to pediatric cancer and diabetes**
Table 2 presents PedsQL 4.0 Generic Core Scales Scores for pediatric patients with cancer and type 1 diabetes. Pediatric patients with ADHD and comorbid psychiatric disorders self-reported significantly lower PedsQL scale scores than pediatric patients with type 1 diabetes across all PedsQL 4.0 Generic Core Scales, with the greatest effect sizes demonstrated on psycho-
Table 2 – Pediatric Quality of Life Inventory™ (PedsQL) 4.0 Generic Core Scales for pediatric patients with attention-deficit/hyperactivity disorder (ADHD) and comorbid psychiatric disorders sample and comparisons with pediatric cancer patients on treatment and pediatric patients with type 1 diabetes.

<table>
<thead>
<tr>
<th>PedsQL Scales</th>
<th>ADHD/ comorbid psychiatric disorders**</th>
<th>Cancer (on treatment)**</th>
<th>Type 1 diabetes**</th>
<th>Mean differences</th>
<th>Effect size a vs. b**</th>
<th>Effect size a vs. c**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 179)</td>
<td>(n = 105)</td>
<td>(n = 292)</td>
<td></td>
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<tr>
<td>Patient self-report</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Total score</td>
<td>67.00  15.80</td>
<td>68.92  15.97</td>
<td>80.79  12.78</td>
<td>a &lt; c**</td>
<td>0.12</td>
<td>0.98</td>
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<tr>
<td>Physical Health</td>
<td>76.59  17.60</td>
<td>65.54  23.14</td>
<td>85.80  13.16</td>
<td>a &lt; c**; a &gt; b**</td>
<td>0.56</td>
<td>0.61</td>
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<tr>
<td>Psychosocial Health</td>
<td>61.89  17.57</td>
<td>71.04  15.17</td>
<td>78.06  14.55</td>
<td>a &lt; b, c**</td>
<td>0.55</td>
<td>1.03</td>
</tr>
<tr>
<td>Emotional Functioning</td>
<td>59.16  23.41</td>
<td>68.81  21.24</td>
<td>74.16  19.77</td>
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<td>0.43</td>
<td>0.71</td>
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<td>66.73  24.86</td>
<td>77.19  18.29</td>
<td>85.93  16.42</td>
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<td>0.46</td>
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<td>School Functioning</td>
<td>59.99  20.55</td>
<td>66.22  19.60</td>
<td>74.27  18.16</td>
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<td>0.31</td>
<td>0.75</td>
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<td>Parent proxy-report</td>
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<tr>
<td>Total score</td>
<td>58.38  18.04</td>
<td>66.95  19.85</td>
<td>77.48  14.33</td>
<td>a &lt; b, c**</td>
<td>0.45</td>
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<tr>
<td>Physical Health</td>
<td>70.77  24.44</td>
<td>65.00  26.26</td>
<td>82.19  17.97</td>
<td>b &lt; a; a &lt; c**</td>
<td>0.23</td>
<td>0.55</td>
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<tr>
<td>Psychosocial Health</td>
<td>51.76  17.87</td>
<td>68.19  18.25</td>
<td>74.91  15.12</td>
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<td>0.91</td>
<td>1.43</td>
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<td>71.35  19.04</td>
<td>a &lt; b, c**</td>
<td>0.72</td>
<td>1.22</td>
</tr>
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</table>

* P < 0.05, ** P < 0.01, *** P < 0.001 based on independent samples t tests (with a Bonferroni correction only values significant at P < 0.008 should be considered statistically significant).

** Effect sizes are designated as small (0.20), medium (0.50), and large (0.80).

social health. Pediatric patients with ADHD and comorbid psychiatric disorders self-reported significantly lower PedsQL scale scores than pediatric patients with cancer on treatment on psychosocial health, emotional functioning, social functioning, and school functioning; they self-reported a comparable Total Score and significantly higher Physical Health Summary Score than pediatric cancer patients. Parents of pediatric patients with ADHD and comorbid psychiatric disorders reported significantly lower PedsQL scale scores for their children than parents of pediatric patients with cancer and type 1 diabetes across all PedsQL 4.0 Generic Core Scales, with the exception of physical health in which parents of pediatric patients with cancer reported significantly lower physical health for their children.

Associations with disease indicators

Table 3 shows the intercorrelations among the PedsQL 4.0 Generic Core Scales, the Vanderbilt Scales, and disease-specific indicators for the ADHD and comorbid psychiatric disorders sample. Intercorrelations between patients self-reported PedsQL 4.0 Generic Core Scales and the parent proxy-reported Vanderbilt Total ADHD Symptom Score were generally not statistically significant. The only intercorrelation that was significant between the patient self-reported PedsQL 4.0 Generic Core Scales and parent proxy-reported Vanderbilt Total ADHD Symptom Score was evidenced on the School Functioning Scale (r = −0.16, P < 0.05). The patient self-reported PedsQL School Functioning Scale was also significantly negatively correlated with number of diagnoses (r = −0.27, P < 0.001), number of months on medicines (r = −0.21, P < 0.01), and number of months since diagnosis (r = −0.20, P < 0.01). The patient self-reported PedsQL Psychosocial Health Summary Score was significantly negatively correlated with number of diagnoses (r = −0.18, P < 0.05). All of the patient self-report intercorrelations were in the small effect size range (r < 0.30).

All parent proxy-reported PedsQL 4.0 Generic Scales were significantly correlated with the parent proxy-reported Vanderbilt Total ADHD Symptom Score, with the largest intercorrelations demonstrated on psychosocial health (r = −0.56, P < 0.001) and school functioning (r = −0.52, P < 0.001). Pearson’s product moment correlations between the parent proxy-reported PedsQL 4.0 Generic Core Scales and parent proxy-reported Vanderbilt Total ADHD Symptom Score were all in the medium to large effect size range. Number of diagnoses was also significantly correlated with all parent proxy-reported PedsQL 4.0 Generic Core Scales, with the largest intercorrelation found on psychosocial health (r = −0.33, P < 0.001). Parent proxy-reported PedsQL psychosocial health and school functioning were significantly correlated with number of daily medicines (r = −0.17, P < 0.05; r = −0.17, P < 0.05), number of months on medicines (r = −0.19, P < 0.05; r = −0.19, P < 0.05), and number of months since diagnosis (r = −0.19, P < 0.05; r = −0.18, P < 0.05).

Parent/child agreement

ICCs between pediatric patient self-report and parent proxy-report for the ADHD and comorbid psychiatric disorders sample across the PedsQL 4.0 Generic Core Scales are presented in Table 4. These ICCs are in the poor to fair agreement range. The greatest agreement was found between children and parents on school functioning, whereas the lowest agreement was demonstrated between children and their parents on physical health. Mean scores for the 177 children with ADHD and comorbid psychiatric disorders and their parents who both completed the PedsQL 4.0 Generic Core Scales are presented in Table 5. Across all PedsQL scales, children self-reported significantly higher HRQOL than their parents, with the greatest differences evidenced on school functioning (effect size 0.61) and psychosocial health (effect size 0.57).
Table 3 – Intercorrelations among Pediatric Quality of Life Inventory™ (PedsQL) 4.0 Generic Core Scales and disease-specific indicators for pediatric patients with attention-deficit/hyperactivity disorder (ADHD) and comorbid psychiatric disorders.

<table>
<thead>
<tr>
<th>PedsQL Scales</th>
<th>Vanderbilt ADHD symptom score</th>
<th>Vanderbilt inattentive scale</th>
<th>Vanderbilt hyperactive-impulsive scale</th>
<th>Number of diagnoses</th>
<th>Number of daily medicines</th>
<th>Number of months on medicines</th>
<th>Number of months since diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient self-report</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>−0.12</td>
<td>−0.16*</td>
<td>−0.09</td>
<td>−0.12</td>
<td>−0.02</td>
<td>−0.05</td>
<td>−0.05</td>
</tr>
<tr>
<td>Physical Health</td>
<td>−0.04</td>
<td>−0.06</td>
<td>−0.01</td>
<td>0.03</td>
<td>0.05</td>
<td>0.07</td>
<td>0.08</td>
</tr>
<tr>
<td>Psychosocial Health</td>
<td>−0.15</td>
<td>−0.19*</td>
<td>−0.13</td>
<td>−0.18*</td>
<td>−0.06</td>
<td>−0.11</td>
<td>−0.10</td>
</tr>
<tr>
<td>Emotional Functioning</td>
<td>−0.04</td>
<td>−0.07</td>
<td>−0.04</td>
<td>−0.07</td>
<td>−0.03</td>
<td>−0.06</td>
<td>−0.07</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>−0.13</td>
<td>−0.09</td>
<td>−0.16*</td>
<td>−0.12</td>
<td>−0.03</td>
<td>−0.02</td>
<td>0.00</td>
</tr>
<tr>
<td>School Functioning</td>
<td>−0.16*</td>
<td>−0.29***</td>
<td>−0.07</td>
<td>−0.27***</td>
<td>−0.08</td>
<td>−0.21**</td>
<td>−0.20**</td>
</tr>
<tr>
<td>Parent proxy-report</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>−0.51***</td>
<td>−0.55***</td>
<td>−0.37***</td>
<td>−0.31***</td>
<td>−0.09</td>
<td>−0.19*</td>
<td>−0.19*</td>
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<tr>
<td>Physical Health</td>
<td>−0.33***</td>
<td>−0.37***</td>
<td>−0.24**</td>
<td>−0.21**</td>
<td>0.04</td>
<td>−0.13</td>
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<tr>
<td>Psychosocial Health</td>
<td>−0.56***</td>
<td>−0.59***</td>
<td>−0.40***</td>
<td>−0.33***</td>
<td>−0.17*</td>
<td>−0.19*</td>
<td>−0.19*</td>
</tr>
<tr>
<td>Emotional Functioning</td>
<td>−0.48***</td>
<td>−0.47***</td>
<td>−0.39***</td>
<td>−0.27***</td>
<td>−0.20**</td>
<td>−0.10</td>
<td>−0.12</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>−0.44***</td>
<td>−0.45***</td>
<td>−0.34***</td>
<td>−0.29***</td>
<td>−0.06</td>
<td>−0.20**</td>
<td>−0.19*</td>
</tr>
<tr>
<td>School Functioning</td>
<td>−0.52***</td>
<td>−0.61***</td>
<td>−0.31***</td>
<td>−0.28***</td>
<td>−0.17*</td>
<td>−0.19*</td>
<td>−0.18*</td>
</tr>
</tbody>
</table>

Effect sizes are designated as small (0.10), medium (0.30), and large (0.50) for Pearson’s product moment correlations.

* P < 0.05, ** P < 0.01, *** P < 0.001.

Discussion

The primary objective of this study was to evaluate the measurement properties of patient self-reported PedsQL 4.0 Generic Core Scales scores in pediatric patients with ADHD and physician-diagnosed comorbid psychiatric disorders being seen in a pediatric psychiatric clinic. These findings support the feasibility, reliability, and validity of the pediatric patient self-reported PedsQL 4.0 Generic Core Scales in this population of pediatric patients at risk for significantly impaired HRQOL. The PedsQL 4.0 Generic Core Scales evidenced minimal missing responses for patient self-report, demonstrating that pediatric patients with ADHD and comorbid psychiatric disorders are willing and able to provide good quality data regarding their generic HRQOL. Range of measurement was demonstrated, with no significant floor or ceiling effects across the PedsQL summary or scales scores. Internal consistency reliabilities exceeded the minimum standard of 0.70 for group comparisons for all scales except school functioning for patient self-report. The PedsQL Total Scale Score met or approached an α of 0.90 recommended for individual patient analysis for patient self-report, making the Total Scale Score suitable as a summary score for the primary analysis of generic HRQOL in clinical trials for pediatric patients with ADHD and comorbid psychiatric disorders.

As anticipated, pediatric patients with ADHD and comorbid psychiatric disorders demonstrated significantly lower psychosocial health than a matched sample of healthy children, with large effect sizes supporting discriminant validity. However, we also found large effects between pediatric patients with ADHD and healthy children on physical health in contrast to previous studies of pediatric patients with ADHD on this dimension [13,20]. Our findings may in part be attributed to differences in symptom severity between our sample and the previous samples. Our sample consisted of children with ADHD and comorbid psychiatric disorders being treated at a psychiatric clinic (98.4% of children were taking at least one daily medication to treat symptoms). Children with ADHD in the Varni and Burwinkle study [13] were from a population-based sample (comorbidity diagnoses and medication use were unknown). Children from the Klassen et al. study [20] were from an ADHD clinic; however, according to the authors, one-third of the sample was newly identified by family doctors and not necessarily complex (only 27.5% of children in the sample were taking ADHD medications).

There is empirical literature that has shown that after adjusting for measures of global disadvantage (i.e., poverty, caretaker’s education, parental marital status, number of diagnoses other than ADHD) the correlation between ADHD and physical health problems was significant for children with ADHD seen in treatment facilities [56]. This may in part be attributed to the fact that children with ADHD seen in treatment facilities are often treated with stimulant medications which can have side effects that affect physical functioning (i.e., loss of appetite, headaches, and stomachaches). Furthermore, children with ADHD seen in treatment facilities are more likely to have comorbid psychiatric disorders such as depression and anxiety that have known physical effects, including fatigue and pain [57]. Thus, our finding that children with ADHD and healthy...
children evidenced large effect sizes on physical health from the perspective of both pediatric patients and parents may in part be a function of the more severe nature of our sample and accompanying comorbid psychiatric disorders. Previously we demonstrated that children with ADHD treated in a general pediatric clinic manifested better PedsQL 4.0 Generic Core Scales scores than pediatric patients with ADHD with physician-diagnosed psychiatric comorbid psychiatric disorders treated in a pediatric psychiatric clinic [58]. The additional comparisons in the present study between patients with ADHD and comorbid psychiatric disorders with pediatric patients with cancer on-treatment and those children with type 1 diabetes are important in further understanding the profound negative impact of ADHD and comorbid psychiatric disorders on patient reported PedsQL 4.0 Generic Core Scales scores.

The finding that only one patient self-reported PedsQL Scale (school functioning) was significantly correlated with the Vanderbilt Total ADHD Symptom Score (compared to all parent proxy-reported PedsQL Scales) may in part be a function of shared method variance for parent proxy-report, and is consistent with the general pediatric HRQOL literature that pediatric patient and parent perspectives provide different, but equally important, sources of information regarding patient functioning [25].

This study has a number of potential limitations. Data were pooled across age forms given that sample sizes for each age form were not large enough to conduct separate analyses. Furthermore, there was variability within our sample with regard to disease-specific indicators such as time since diagnosis and time on medications. There was no standardized protocol for diagnosing a child with ADHD or comorbid psychiatric disorders in our study. However, ADHD and comorbid psychiatric diagnoses were made by a child psychiatrist before the child was enrolled in the study based on signs and symptoms presented and history, including in some cases diagnostic scales completed by parents and teachers. We did not have information on the exact comorbid psychiatric disorders patients in our sample had, but rather the diagnostic category. Our sample was predominantly white males, which may further limit the generalizability of the findings. However, it should be noted that in terms of sociodemographics, our sample was representative of the underlying population of children with ADHD in the United States, which is more likely to be white males [59]. The cancer and type 1 diabetes samples came from an existing database and consequently we were not able to match these samples to the ADHD sample on sociodemographic characteristics given sample size limitations. This was a cross-sectional study, thus it provided only a snapshot of PedsQL scale scores at one time point. Finally, ADHD symptom severity was measured only from the perspective of parents in our study.

### Implications for research, policy, and practice

These findings have several implications for future research and clinical practice with pediatric patients with ADHD and comorbid psychiatric disorders. First, given the large effect sizes reported between our sample and healthy children on physical health, it is important that interventions designed for children with ADHD and comorbid psychiatric disorders not only address psychosocial difficulties, but also the physical impairments that may result from medications and/or comorbid psychiatric disorders such as anxiety or depression. The findings suggest that the constructs of fatigue and pain may be important to address in future interventions with this population. It will be beneficial for future research to elucidate the relationship between fatigue, pain, and generic PedsQL scale scores so that more efficacious interventions can be developed. Given the growing body of literature that suggests children with ADHD experience chronic sleep difficulties [60], future research should also investigate the relationship between sleep deficits and physical health in children with ADHD and comorbid psychiatric disorders.

The finding that pediatric patients and their parents demonstrated poor to fair agreement regarding the child’s PedsQL scale scores underscores the importance of evaluating both children’s and parents’ perspectives regarding generic HRQOL in routine assessment in clinical practice and clinical trials for children with ADHD and comorbid psychiatric disorders because their different perspectives potentially provide unique information. Discrepancies between patient and parent reports of the child’s PedsQL scale scores can be used clinically to facilitate communication between parents and children. For example, if a child reports that “almost always” other kids tease him/her and his mother reports that the child “never” gets teased by other children, this would be an opportunity for the child’s health-care provider to intervene and discuss these differences in perspective with the child and parent. A number of studies with children with chronic health conditions have reported greater agreement between parents and children on physical functioning because this is a more observable construct [61].

The finding that agreement was lowest between parents and

### Table 5 – Comparisons between Pediatric Quality of Life Inventory™ (PedsQL) 4.0 Generic Core Scales for pediatric patient self-report and parent proxy-report for the attention-deficit/hyperactivity disorder and comorbid psychiatric disorders sample.

<table>
<thead>
<tr>
<th>PedsQL Scales</th>
<th>Pediatric patient self-report</th>
<th>Parent proxy-report</th>
<th>Mean differences</th>
<th>Effect size†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>66.99 15.88</td>
<td>58.42 18.19</td>
<td>8.57***</td>
<td>0.50</td>
</tr>
<tr>
<td>Physical health</td>
<td>76.45 17.65</td>
<td>70.90 24.61</td>
<td>5.55</td>
<td>0.26</td>
</tr>
<tr>
<td>Psychosocial health</td>
<td>61.94 17.66</td>
<td>51.76 18.02</td>
<td>10.18***</td>
<td>0.57</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>59.27 23.52</td>
<td>48.35 20.61</td>
<td>10.92***</td>
<td>0.49</td>
</tr>
<tr>
<td>Social functioning</td>
<td>66.61 24.96</td>
<td>58.79 22.99</td>
<td>7.82***</td>
<td>0.33</td>
</tr>
<tr>
<td>School functioning</td>
<td>60.16 20.59</td>
<td>48.10 19.23</td>
<td>12.06***</td>
<td>0.61</td>
</tr>
</tbody>
</table>

SD, standard deviation.

* P < 0.05, ** P < 0.01, *** P < 0.001 based on paired sample t tests (with a Bonferroni correction only values significant at P < 0.008 should be considered statistically significant).

† Effect sizes are designated as small (0.20), medium (0.50), and large (0.80).
children on physical health in our sample further demonstrates the need for future research to investigate the construct of physical health in pediatric patients with ADHD and comorbid psychiatric disorders. Future studies should also evaluate the factors that influence parent–child discordance in this population of patients with severely impaired PedsQL scale scores.

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REFERENCES


