Author/s:
Jonsson, U;Alaie, I;Löfgren Wilteus, A;Zander, E;Marschik, PB;Coghill, D;Bölte, S

Title:
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Date:
2017-04-01

Citation:
Jonsson, U., Alaie, I., Löfgren Wilteus, A., Zander, E., Marschik, P. B., Coghill, D. & Bölte, S. (2017). Annual Research Review: Quality of life and childhood mental and behavioural disorders – a critical review of the research. Journal of Child Psychology and Psychiatry and Allied Disciplines, 58 (4), pp.439-469. https://doi.org/10.1111/jcpp.12645.

Persistent Link:
https://hdl.handle.net/11343/291822

Received Date : 29-Feb-2016
Revised Date : 11-Aug-2016
Accepted Date : 12-Aug-2016
Article type : Annual Research Review

Short title: ***Quality of life and childhood mental and behavioural disorders***

Annual Research Review: Quality of life and childhood mental and behavioural disorders – a critical review of the research

Ulf Jonsson[1,2,3,*], Iman Alaie[1,3,*], Anna Löfgren Wilteus[1,2],
Eric Zander[1,2], Peter Marschik[1,4], David Coghill[5,6], and Sven Bölte[1,2]

[1] Neuropsychiatry Unit, Dept. of Women's and Children's Health, Center of Neurodevelopmental Disorders (KIND), Karolinska Institutet, Stockholm, Sweden
[2] Child and Adolescent Psychiatry, Center of Psychiatry Research, Stockholm County Council, Sweden
[3] Dept. of Neuroscience, Child and Adolescent Psychiatry, Uppsala University, Uppsala, Sweden
[4] iDN – Interdisciplinary Developmental Neuroscience, Institute of Physiology, Medical University of Graz, Austria
[5] Depts. of Paediatrics and Psychiatry, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Australia
[6] Child and Adolescent Psychiatry, University of Dundee, Scotland

Conflict of interest statement: No conflicts declared.

*Contributed equally**Background:** An individual's subjective perception of well-being is increasingly recognized as an essential complement to clinical symptomatology and functional impairment in children's mental health. Measurement of quality of life (QoL) has the potential to give due weight to the child's perspective. **Scope and methodology:** Our aim was to critically review the current evidence on how childhood mental disorders affect QoL. First, the major challenges in this research field are outlined. Then we present a systematic review of QoL in children and adolescents aged 0 to 18 years formally diagnosed with a mental and behavioural disorder, as compared to healthy or typically developing children or children with other health conditions. Finally, we discuss limitations of the current evidence base and future directions based on the results of the systematic review and other relevant literature. **Findings and conclusion:** The systematic review identified forty-one eligible studies. All were published after the year 2000 and twenty-one originated in Europe. The majority examined QoL in neurodevelopmental disorders, including attention-deficit hyperactivity disorder (*k*=17), autism spectrum disorder (*k*=6), motor disorders (*k*=5), and intellectual disability (*k*=4). Despite substantial heterogeneity, studies demonstrate that self-reported global QoL is significantly reduced compared to typical/healthy controls across several disorders and QoL dimensions. Parents' ratings were on average substantially lower, casting doubt on the validity of proxy-report. Studies for large diagnostic groups such as depressive disorders, anxiety disorders, (early onset) schizophrenia and eating disorders are largely lacking. We conclude that representative, well-characterized normative and clinical samples as well as longitudinal and qualitative designs are needed to further clarify the construct of QoL, to derive measures of high ecological validity, and to examine how QoL fluctuates over time and is attributable to specific conditions or contextual factors.

Keywords: Quality of life; psychopathology; mental health; adolescence.

Introduction

A recent meta-analysis of 41 studies from 27 countries (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015) estimates that the worldwide prevalence of mental disorders in children and adolescents is 13.4%. Some conditions, most prominently autism spectrum disorder (ASD) (Idring et al., 2015), attention-deficit hyperactivity disorder (ADHD) (Visser et al., 2014) and bipolar disorder (Medici, Videbech, Gustafsson, & Munk-Jorgensen, 2015), are currently diagnosed far more frequently in clinical practice than just a decade ago. Paralleling these trends, novel ways of conceptualizing behavioural problems have been suggested (Insel, 2014), and a broader view on well-being in youth and its impact on health care systems has gained more attention (Whiteford et al., 2013). For instance, there is an increasing consensus today that mental health should be described along at least three dimensions: First, by psychopathology or clinical symptomatology. Second, by the impact on adaptive functioning and impairment in everyday life as observed or evaluated from the outside (“objective reality”). Third, through the self-assessed impact on the individual’s quality of life (QoL), or more specifically health-related quality of life (“subjective reality”) (Coghill, Danckaerts, Sonuga-Barke, & Sergeant, 2009). At present, however, mental disorders are predominantly operationalized by prototypic clinical symptomatology. Whilst it is necessary for a clinical diagnosis that symptoms cause impairment in adaptive functioning (American Psychiatric Association, 2013), the nature of the required impairment is rather unspecified. The current definitions of mental and behavioural disorders do not properly take the more subjective and personally experienced concept of QoL into consideration. This is surprising, as several influential authors and researchers for many years have stressed its importance. For instance, Spitzer and colleagues (Spitzer et al., 1995) recommended that the primary objective of healthcare ultimately should be to improve individuals’ perceptions of their health and the degree to which disease interferes with their QoL, rather than their psychopathology or impairment.

Compared to adult mental health (Alonso et al., 2004; Ritsner et al., 2000) and a multitude of somatic diseases of childhood (Solans et al., 2008), where low QoL has been consistently reported, subjective well-being in mental and behavioural disorders with childhood onset is much less established. Still, data from a national survey from Australia suggest that children with mental disorders have worse parent-reported QoL in many domains of life than children with physical disorders (Sawyer et al., 2002). A systematic review by Dey, Landolt, and Mohler-Kuo (2012) also suggests reduced QoL across multiple domains in childhood mental disorders, especially within psychosocial and family-related areas of life. However, only 16 studies were identified, the majority of which focused on ADHD. The authors also noted several limitations of the literature, including a focus on clinical samples of a restricted age range and a reliance on parental proxy ratings of QoL. The literature search for the review by Dey and colleagues was conducted in 2011, indicating that an update is now warranted.

Our aim was to take stock on the current research and developments regarding QoL in mental and behavioural disorders of childhood. The text is divided into three main sections: First, we introduce the concept of QoL and the challenges raised by its measurement in childhood mental and behavioural disorders. Theoretical issues in this research field have previously been expounded in detail by Coghill and colleagues (2009). Here, we elaborate and update their article for the particular age group and conditions that are the focus of the present review. Second, we systematically review the empirical evidence on QoL in children and adolescents aged 0 to 18 years formally diagnosed with a mental or behavioural disorder. We limit this review to comparative studies that include a control group comprising healthy/typically developing children or those with other health conditions. Third, we discuss limitations of the current concept of QoL, its evidence base and future directions in the light of our systematic review and other pertinent literature.

Section one: Concepts and challenges

Quality of life and mental health in childhood

Even more than some other clinical entities in mental health, QoL is a latent construct, not directly observable or measurable. Indeed, an integral aspect of the concept is the subjectivity of experienced being. While there is no standard definition of QoL, it is generally accepted that it should be considered a multidimensional concept that requires the integration of several domains, such as emotional and physical well-being and self-esteem (Meyer, Oberhoffer, Hock, Giegerich & Müller, 2016). The most basic contemplation of QoL is consistent with Maslow's (1943) hierarchy of safety, belonging, happiness, and a sense of community and economic security. An extended definition by Eiser and Morse (2001) includes five areas of QoL: philosophical, economic, sociological, psychological/cognitive and medical/physical. Leidy, Revicki, and Geneste (1999) describe QoL as "an individual's subjective perception of the impact of health status, including disease and treatment, on physical, psychological, and social functioning". Similarly, the World Health Organization's (WHO) QoL group describes QoL as "the individual's perception of their position in life, in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns" (1993). This description is consistent with the WHO's (1946) general operationalization of health, which emphasises that health is not merely the absence of disease. The Mental Health Division of the WHO (1994) demands QoL measures to be age-appropriate and child-centred, take into account self-reports, be independent of the health status and culture and assess both positive and negative aspects of the family/social relations, physical function, and social and material environment.

A range of instruments has been generated to assess QoL in childhood from different rater perspectives, using generic and disorder-specific approaches with single or multidimensional concepts and scoring. Generic measures are designed to be more comprehensive in their coverage, but may, as a consequence, be less sensitive to certain health conditions and treatment-related change. Disorder-specific measures or modules focus on areas of particular concern, but do not readily allow comparisons across health conditions. While it is generally accepted that QoL is a multidimensional concept and that the core domains tap into physical, psychological, cognitive and social aspects of functioning, measures define these domains in different ways. As a consequence, there is a considerable degree of inter-instrument non-overlap and one cannot assume equal coverage by different QoL measures. The variety of instruments contributes to the variability of operationalisations and limits comparability between studies. In an overview on QoL instruments, Eiser and Morse (2001) previously identified 19 generic and 24 disorder specific tools to measure QoL in childhood. Seventeen were collecting children's perspectives, 7 were collecting parents' perspectives, and 16 used both self- and proxy versions. A set of different response formats such as graphic, facial expression or visual analogue scales and presentation styles, including pictorial and computerized and the use of props, are used in QoL measures (Cremeens, Eiser, & Blades, 2006). Nevertheless, classical Likert scales are the most frequently used. A comprehensive review of these instruments is beyond the scope of this review. Summaries of psychometric properties for these scales are reported elsewhere (Brazier et al., 2014; Cremeens et al., 2006; Janssens, Rogers, et al., 2015; Janssens, Thompson Coon, et al., 2015).

The added value of the QoL concept for clinical mental health practice depends on whether it can be operationalized adequately, that is if it demonstrates sufficient stand-alone characteristics in addition to psychopathology and adaptive functioning, and if it can be translated into instruments with good psychometric properties. Compared to somatic medicine – where the distinction between symptoms of disease, impairment and QoL is often much more clear-cut – disentangling and delineating psychopathology, functional impairment, and QoL is particularly challenging in psychiatry. For instance, it is possible to suffer from a severe general medical condition (e.g., diabetes) without major day-to-day impairment, while impairment or distress is a mandatory criterion for most psychiatric diagnoses. While the three dimensions might be relatively distinct in single individual cases and certain mental disorders (Bastiaansen, Koot, & Ferdinand, 2005), overall and ideally, the operationalisation of psychopathology, impairment, and QoL should overlap to a moderate degree in order to signal both their relatedness, but also their independent contributions to mental health status.

Despite overlaps, there are several apparent differences between the three fundamental mental health concepts (Sawyer et al., 2001). First, impairment and psychopathology are ultimately judged by an observer and often by an expert, while QoL is by definition, based on the patient's own experience. Second, impairment is integral of mental disorders, while psychopathology interacts more variably with QoL. The content and construction of scales to assess QoL is key to maximising the utility of QoL measures and to ensuring that one avoids both a theoretical and a practical confusion of mental health concepts. It is particularly important to ensure that adequate item validation is obtained, and that the effects of the precise item wording on informants are sufficiently examined and understood (Coghill et al., 2009). For instance, items that might intend to measure different constructs (e.g. "I am happy", "I am as happy as I wish", "I could do better if I was happier") perhaps appear similar to respondents. Studies that examined change of QoL and psychopathology over time and their associations, mostly in the field of neurodevelopmental disorders reported moderate correlations (Coghill & Hodgkins, 2015; Kuhlthau et al., 2013; Rentz, Matza, Secnik, Swensen, & Revicki, 2005). These findings suggest that despite overlap of general mental health concepts, there are independent aspects assessed when adding QoL measures, which will yield additional information on overall well-being.

Apparently the overlap of mental health related constructs differ substantially between disorders. A close examination of diagnostic criteria reveals that mental and behavioural disorders – in stark contrast to somatic diseases – are characterized by both observable symptoms and subjective experiences. Here, logically, subjective experiencing is highly weighted in the diagnostic criteria for internalizing disorders, while the evaluation of third parties is crucial for externalizing disorders. In particular, the definition of depressive disorders is closely linked to the concept of QoL. Therefore, Katschnig (2006) strongly recommends researchers to control for the presence of psychopathology items within Qol instruments, and to especially assess depressive and anxiety symptoms when studying QoL in medical and other psychiatric conditions.

Challenges related to age and development

Even though different domains of physical, psychological and social QoL are universal and lifelong, what constitutes each domain is age-specific. This needs to be taken into account in order to reach an appropriate level of abstraction and authentic information on relevant QoL domains (Carona et al., 2013; Matza, Swensen, Flood, Secnik, & Leidy, 2004). According to Schor (1998), QoL domains are less distinguishable in childhood compared to adulthood. Therefore, while it is mostly meaningful to inquire about the same symptoms of psychopathology across age and developmental ranges, a simple transfer of adult to child domains or vice versa is misleading in QoL assessment (World Health Organization, 1993). Still, for longitudinal studies the utilization of some developmentally overlapping QoL domains is recommended to ensure comparisons of follow-up assessments.

One of the most frequently discussed methodological issues in QoL research in children is the usage of self- or proxy-reporting. As subjectivity is an essential aspect of QoL, it is always preferable to obtain the child’s own report of QoL. However, in early and middle childhood, a certain degree of parental involvement is almost inevitable. Coghill and Hodgkins (2015) found associations across most domains for children’s own and their parents’ ratings of their QoL, but these were low to moderate in strength. It has been reported that also teachers sometimes are acceptable proxies for certain domains of QoL (Glaser, Abdul Rashid, U, & Walker, 1997; Glaser, Davies, Walker, & Brazier, 1997). Children, however, tend to rate their QoL lower than their teachers do. The latter, and the findings of other studies on parent proxies for child QoL (Danckaerts, et al., 2010) suggest that parent-ratings can be understood as approximations of the child’s own experience of QoL, but are definitely not well suited to replace them. If self-reported QoL is set as gold standard, parents of children with chronic conditions tend to underestimate their children’s QoL (White-Koning et al., 2007), while the opposite is true for community samples (Upton, Lawford, & Eiser, 2008). For some disorders and domains, the level of disagreement might be large, as in the social domain in ASD where parents often desire social integration of their children, while the children themselves might not be interested and may not want to be forced into it (Ikeda, 2013). Agreement is usually higher in observable domains and physical domains compared to psychosocial domains (White-Koning et al., 2007). Surprisingly, despite the limitation of proxy-report, studies on QoL in childhood mental health frequently rely on parental ratings (Ikeda et al., 2014). Understandable reasons for this are that collecting children's own perception is complicated not only by the disorders per se, but also by age-related limitations and the child's general development or maturation status (Bell, 2007; Varni, Burwinkle, & Lane, 2005). Young children (e.g., under 7 or 8 years of age) may lack the understanding, insight or communication skills to provide valid self-ratings of QoL (Bibace & Walsh, 1980). Therefore, proxy-ratings can provide important additional perspective and may be useful to identify potential areas of conflict or concern, even where they do not agree with a child's view and therefore might not represent core QoL. Nevertheless, an overreliance on parental report may hinder the implementation of an empowering, strength-based approach to children and adolescents with mental disorders by neglecting their resiliency and their abilities to fulfil their potential (Patel, Flisher, Hetrick, & McGorry, 2007). Parents are not objective judges, but have their own perspective, which can serve as an additional source of information. Clearly, a proxy rating will allow only a partial sense of the overall impact of a condition on QoL, which may place important constraints on the validity of such measurements. An alternative view, which has received little attention, is the extent to which parent proxy measures of QoL are aligned with the concept of functional impairment and not QoL. According to clinical impression, it might well be that parents rather evaluate their children's impairment when inquired about their QoL.

Relevance

Despite the challenges outlined above, there are good reasons to continue the effort to clarify how mental health conditions affect QoL in childhood. First, valid estimates of subjective QoL are needed to make the true impact of mental disorders visible and enable comparisons across the full range of health conditions. If accepted by regulatory authorities as a valid building block for reimbursement, QoL can function as a complementary way to calculate health related service costs and allocation of resources (Dolan, 2000), as it reflects the individual's experience of the problem as a whole and the related need for improvement. Different European regional and national guidelines for childhood mental disorders now stress the importance of QoL as an indicator for the quality of service delivery and treatment outcome (e.g., National Institute for Health and Clinical Excellence, 2008). Moreover, in several countries (e.g., UK, Germany) mandatory parameters for evidence based benefit assessments of a medicine or other form of intervention – which constitute the basis for reimbursement by sickness funds – include improvement in QoL, in addition to improvement of the state of health and reduction in the duration of illness (Bekkering & Kleijnen, 2008; National Institute for Health and Clinical Excellence, 2004). Second, the concept of QoL might be less controversial and more accessible to laymen than expert concepts such as psychopathology, leading to less stigmatization and greater understanding among the general public. Third, QoL is likely to be perceived as more important, meaningful and understandable by the patient than psychopathology, as it is based on one's own experience. Fourth, for the same reasons, QoL facilitates the communication between patients, their social environment, and experts. Fifth, QoL can function as a guide for the development of novel treatments based on self-perception, as well as for treatment planning, in terms of both aims and hierarchy of intervention actions, derived from the priorities and perceptions of the patient. For this approach the term "QoL therapy" has been coined (Frisch, 2000). Sixth, as reduction of clinical symptoms and even decreased impairment does not necessarily indicate improved QoL, it is an important complement in assessing treatment success (Lack et al., 2009). Finally, seventh, from an ethical point of view, an increased involvement and consideration of the patient's voice, thoughts, and feelings is indispensable (Singh, 2013) and a top concern of many self-advocacy organizations.

Section two: A systematic review of comparative studies on QoL in children with mental and behavioural disorders

While overviews have been published on QoL in single childhood disorders, such as ADHD (Danckaerts et al., 2010) and ASD (Ikeda, Hinckson, & Krageloh, 2014), few attempts have been made previously to systematically search and synthesize the evidence across a broader range of mental and behavioural disorders. In addition to the review by Dey and colleagues (2012) mentioned earlier, there is also a more recent overview included 66 clinical studies with and without control groups (Carona, Silva, & Moreira, 2015). However, the authors examined to what extent a developmental approach to QoL assessment was applied in the selected articles, but did not investigate the results of the included studies in detail.

In the present review we addressed the following question: to what extent do childhood mental and behavioural disorders affect QoL? We limited the review to comparative studies of children and adolescents formally diagnosed with a mental or behavioural disorder and a well-defined control group comprising healthy/typically developing children or children with other health conditions. We required that data on the clinical group and the control group were collected within approximately the same time frame and community, thereby excluding several studies relying only on comparisons with normative data collected in other contexts (e.g. standardization of QoL scales). These restrictions were used to enable conclusions about the effect of the specific mental disorders on QoL by keeping constant contextual factors (e.g., secular events, cultural and value systems). We included both self- and proxy-reported QoL, but kept these separate in the analyses. Due to the large variety of instruments (and subdomains) used, we primarily focused on global measures of QoL. However, syntheses across diagnostic groups were conducted for each subdomain when this was feasible.

It should be noted that other designs – including qualitative studies, longitudinal studies, and clinical trials – were not within the scope of the present systematic review. While such designs can certainly give valuable insight (e.g., increased understanding of the concept of QoL, how QoL fluctuate over time and how QoL responds to treatment) they do not address the principal question of to what extent mental and behavioural disorders affect QoL. We discuss all the above study designs and their importance for the research field in section three.

Method

This is a brief summary of the review method. The full description reported in accordance with the PRISMA statement can be found in Appendix S1 (available online).

Eligibility criteria

Study population: All included participants were aged 0 to 18 years. If the age range was not reported, the participants' mean age plus two standard deviations should fall within the 0 to 18 years of age range.

Exposure. A confirmed diagnosis of a mental or behavioural disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fourth (DSM-IV) or fifth edition (DSM-5), or International Classification of Diseases, tenth edition (ICD-10).

Comparator. Children serving as healthy/normative controls, sometimes referred to as typically developing, or having a specific diagnosed medical condition or mental disorder.

Data on comparator(s) had to be collected with the same procedure as data on the study population, within the same five-year period, and with subjects recruited from the same community.

Outcome. Standardized measures of self-, parent-, clinician- or teacher-reported QoL (with psychometric data reported in the same or a separate publication).

Design. Comparative studies of children with one or more of the eligible mental or behavioural disorders (population) and children serving as healthy controls or having another health condition (comparator).

Language. Studies published in English.

Publication type. Studies published in peer-reviewed journals.

Search strategy

The electronic databases Medline (Ovid), PubMed, EMBASE (Elsevier), Cochrane Library (Wiley), and PsycINFO (Ovid) were searched for relevant publications between 1990 up to January 8, 2016. For detailed information about the search strategies, see Appendix S1 (available online).

Study selection

Two researchers independently screened the titles and abstracts for eligibility. All publications of potential relevance according to the inclusion criteria were obtained in full text. One researcher assessed the relevance of the full text articles, while the other controlled the accuracy of the assessment. Disagreements were resolved by consensus. Reference lists were screened for additional relevant studies.

Risk of bias in individual studies

To ascertain the validity of included studies, four key quality criteria for observational studies were considered (Guyatt et al., 2011):

1. Failure to develop and apply appropriate eligibility criteria (inclusion of control population): In order for a study to be eligible, data on the control population(s) had to be contemporaneous and from the same community as the study population. Socio-demographic characteristics of the control group(s) were extracted and compared to the characteristics of the study population.

2. Flawed measurement of both exposure and outcome: Eligible studies had to use a validated measure of QoL and include a study population with a confirmed diagnosis of a specific mental or behavioural disorder. Any differences in outcome measurement between the study population and the control group(s) were recorded. 3. Failure to adequately control confounding: Any attempts to measure factors known to be associated with QoL and to adjust for such factors were recorded.

4. Incomplete follow-up: Given that eligible studies typically are cross-sectional, information about the number of approached children refusing participation was recorded.

Planned methods of analysis

The principal summary measure for each study was standardized mean difference (Hedge's *g*) and 95% confidence interval for global QoL calculated with Review Manager (RevMan) Version 5.3.4. Effect sizes were calculated if data was reported in a way that made this possible. If not, we report whether there was a significant difference as reported by the authors. Effect sizes were reported as small (0.2), medium (0.5), or large (0.8) in accordance with the definition by Cohen (1988). Studies of the same condition and with similar comparison groups were synthesized in meta-analyses as long as the necessary data was available.

Secondary analyses of domain specific results were conducted for instruments used in two or more studies within two or more diagnostic categories. A meta-analysis was carried out for each domain, with all eligible studies entered into the same meta-analysis regardless of diagnosis.

Results

Study selection

A total of 41 studies were identified for inclusion in the review. The search provided a total of 6155 citations. Of these, 5666 were discarded after reviewing the abstracts. The remaining 489 citations were examined in full text. Out of these, 448 did not meet the eligibility criteria and were excluded (see Appendix S2 available online for reasons). Checking the references of published systematic reviews identified no additional studies that met the criteria for inclusion. See PRISMA flow diagram (Fig. 1).

About here Figure 1

Overview of the included studies

A total of 30 studies of QoL in children with neurodevelopmental disorders were included. Of these, 14 focused specifically on ADHD (Coghill & Hodgkins, 2015; Escobar et al., 2005; Göker, Aktepe, & Kandil, 2011; Hakkaart-van Roijen et al., 2007; Jafari, Ghanizadeh, Akhondzadeh, & Mohammadi, 2011; Kandemir, Kiliç, Ekinci, & Yüce, 2014; Marques et al., 2013; Patrick, Edwards, & Topolski, 2002; Pongwilairat, Louthrenoo, Charnsil, & Witoonchart, 2005; Thaulow & Jozefiak, 2012; Topolski et al., 2004; Varni & Burwinkle, 2006; Yang, Hsu, Chiou, & Chao, 2007; Zambrano-Sanchez, Martinez-Cortes, del Rio-Carlos, Dehesa-Moreno, & Poblano, 2012), five on motor disorders (Eddy et al., 2011; Hao, Tian, Lu, Chai, & Rao, 2010; Liu et al., 2014; O'Hare et al., 2015; Wuang, Wang, & Mao-Hsiung, 2012), four on ASD (Bastiaansen, Koot, Ferdinand, & Verhulst, 2004; de Vries & Geurts, 2015; Domellöf, Hedlund, & Ödman, 2014; Potvin, Snider, Prelock, Wood-Dauphinee, & Kehayia, 2015), and four on intellectual disability (Basgul, Uneri, & Cakin-Memik, 2011; Brantley, Huebner, & Nagle, 2002; Elbasan, Duzgun, & Oskay, 2013; Golubovic & Skrbic, 2013). Two additional studies included data on both children with ADHD and ASD (Petrou et al., 2010; Petrou & Kupek, 2009), while another compared children with conduct disorder (CD) or oppositional defiant disorder (ODD) with children with ADHD (Chavez et al., 2014). Children with disorders other than those classified as neurodevelopmental were the focus of additional 11 studies: five on elimination disorders (Al-Zaben & Sehlo, 2015; Ertan et al., 2009; Kilicoglu et al., 2014; Natale, Kuhn, Siemer, Stockle, & von Gontard, 2009; Ucer & Gumus, 2014), four on sleep-wake disorders (Crabtree, Varni, & Gozal, 2004; Furudate, Komada, Kobayashi, Nakajima, & Inoue, 2014; Inocente et al., 2014; Tran, Nguyen, Weedon, & Goldstein, 2005), one on major depressive disorder (MDD; Kiss, Kapornai, Baji, Mayer, & Vetro, 2009), and one on obsessive-compulsive disorder (OCD; Vivan Ade, Rodrigues, Wendt, Bicca, & Cordioli, 2013).

No included study was published before year 2001. Thereafter a steady increase of published studies was evidenced, with seven studies published in the time period from 2001 to 2005, 10 from 2006 to 2010, and 24 from 2011 to 2015. More than half of the included studies (*k*=21) were conducted in Europe, including seven from Turkey. Eight studies were conducted in different parts of Asia, eight in North America, three in South/Central America, and one in Australia. A total of 14 different instruments were used across studies (Table 1). While the majority were generic QoL measures, utility-based approaches and conditions-specific measures were also included in some studies.

About here Table 1

ADHD

Study characteristics

A total of 14 studies focusing on ADHD. The studies were conducted in 12 different countries distributed in Europe (*k*=6), North America (*k*=3), Asia (*k*=3) and South/Central America (*k*=2). An additional three studies that compared ADHD with other mental disorders are described under heading below. Children within the age range 6 to 18 years were included across studies. The number of participants with ADHD was within the range of 40 to 80 in most studies, with a few studies including a larger sample. A minority of the participants were female (0-37%). The study populations were recruited from clinical settings, with the exception of one study in which a mail survey was utilized (Varni & Burwinkle, 2006). Typically developing children were included as a comparison group in all of the studies. Some of the studies included additional comparators of children with specific health conditions: type 1 diabetes, asthma, mobility disability, cancer, and cerebral palsy (Table 2).

About here Table 2

Results of individual studies

A total of 11 studies included a measure of self-reported QoL. The Pediatric Quality of Life Inventory (PedsQL; Varni, Seid, & Kurtin, 2001; Varni, Seid, & Rode, 1999) was used in seven of these studies, of which six indicated large and significant effects, and one indicated a small to medium effect, all suggesting better QoL in typical controls. Youth Quality of Life

Instrument-Research Version (YQLI-R; Edwards, Huebner, Connell, & Patrick, 2002; Patrick et al., 2002) was used as a self-report measure in two studies. One of these studies reported a medium effect for significantly better QoL in typical controls. The other reported a similar mean difference, but no measure of dispersion was reported. One study measuring self-reported QoL with the Inventory for the Assessment of Life Quality in Children and Adolescents (ILK; Mattejat et al., 2003) reported a medium effect for significantly higher QoL in typical controls, while one study using the AutoQuestionnaire Qualité de Vie-Enfant-Imagé (AUQUEI; Assumpcao, Kuczynski, Sprovieri, & Aranha, 2000) found a significant difference but failed to report a measure of dispersion.

Parent-reported QoL was included in 11 of the studies. The PedsQL was used in seven of these studies, and indicated a medium to large effect size for significantly poorer QoL in ADHD. The Child Health Questionnaire (CHQ-PF50; Landgraf, Abetz, & Ware, 1996, 1999) was used in three and ILK in one of the studies, all suggesting a large effect size for significantly poorer QoL in ADHD.

Children with ADHD had significantly lower self-reported QoL (PedsQL) than children with diabetes (Coghill & Hodgkins, 2015) and significantly lower parent-reported QoL (CHQ-PF50) than children with asthma (Escobar, et al., 2005). Children with ADHD did not differ significantly from children with cancer and cerebral palsy on self-reported PedsQL, but had significantly higher ratings than these two groups on parent-reported PedsQL (Varni & Burwinkle, 2006). Two studies using the YQOL-R did not find a significant difference between children with ADHD and children with mobility impairments (Patrick, et al., 2002; Topolski, et al., 2004; Table 3).

About here Table 3

Synthesis

Nine studies with a total of 665 children with ADHD and 3909 typical controls could be included in a meta-analysis of self-reported QoL (Fig 2). Despite diminished confidence owing to significant heterogeneity, overall effects were large with significantly poorer QoL in the children with ADHD with the exception of one study with a small and non-significant effect. The studies taken together indicate that children with ADHD rate their QoL significantly lower than typical controls, but our confidence in the pooled estimate is somewhat limited due to the heterogeneous effect sizes of the individual studies.

About here Figure 2

Ten studies with a total of 865 children with ADHD and 4041 typical controls could be included in a meta-analysis of parent-reported QoL (Fig 3). Also this meta-analysis indicated significant heterogeneity, with effects spanning from medium to large effect sizes across studies showing significantly poorer QoL in children with ADHD. The heterogeneity diminishes our confidence in the pooled estimate.

About here Figure 3

Autism spectrum disorder

Study characteristics

The six included studies with participants with ASD were conducted in The Netherlands (Bastiaansen, et al., 2004; de Vries & Geurts, 2015), UK (Petrou, et al., 2010; Petrou & Kupek, 2009), Sweden (Domellöf, et al., 2014), and USA (Potvin, et al., 2015). The diagnosis had been established with structured instruments, clinical consensus, or medical records. Children in the age range of 6 to 18 years were included. The number of participants with ASD ranged from 28 to 120 across studies. A minority of the participants were female (10-18%). The study populations were recruited from specialist clinics, a survey of young people with disabilities, through organizations, and advertisement. Typically developing children were included as a comparison group in three of the studies (Bastiaansen et al., 2004; de Vries & Geurts, 2015; Potvin et al., 2015). One study compared ASD, intellectual disability, movement disorders and hearing disabilities, but did not include a typical control group (Domellöf et al., 2014). Two studies compared a range of mental and general medical conditions, including ASD and hyperactivity disorders (Petrou et al., 2010; Petrou & Kupek, 2009; Table 4)

About here Table 4

Results of individual studies

The three studies with a typical control comparator measured QoL using the PedsQL. The results in all three studies indicated large to medium effect sizes for significantly poorer QoL in ASD on parent-reported QoL. One study found no significant difference on self-reported QoL (Bastiaansen et al., 2004), while one study indicated a large effect size for significantly poorer self-reported QoL in the children with ASD (Potvin et al., 2015). The comparisons of ASD with intellectual disability (Domellöf, et al., 2014) and hyperactivity disorders/ADHD

(Petrou et al., 2010; Petrou & Kupek, 2009) did not show a significant difference as measured with the utility-based measures EuroQol Five Dimensions Health Questionnaire, Youth version (EQ-5D-Y; Wille et al., 2010) and Health Utilities Index Mark 3 (HUI3; Horsman, Furlong, Feeny, & Torrance, 2003), respectively (Table 5).

About here Table 5

Synthesis

Due to heterogeneity of the comparators and differences in how the results were reported (i.e., one study reported the raw score on PedsQL), no synthesis in form of a meta-analysis was conducted.

Intellectual disability

Study characteristics

The four included studies focusing on intellectual disability were conducted in Turkey (Basgul et al., 2011; Elbasan et al., 2013), Serbia (Golubovic & Skrbic, 2013), and the USA (Brantley et al., 2002). Children in the age range of 5 to 18 years were included across studies, with one study focusing only on children age 5 to 7 years old, and one only on adolescents. The number of participants with intellectual disability ranged from 41 to 221 across studies. The proportion of females ranged from 36 to 59%. The study population was recruited from specialist clinics in one study and from schools in the remaining studies. Their level of intellectual disability was reported as mild to moderate, with the exception of one study in which 5% had severe level of impairment (Basgul et al., 2011). Typically developing children or healthy controls were included as comparators in all of the studies. One study included additional comparison groups comprising children with cerebral palsy and hearing loss (Elbasan et al., 2013; Table 4).

Results of individual studies

Self-reported PedsQL indicated a medium and significant effect size in favour of the typically developed in one study (Golubovic & Skrbic, 2013). However, no significant difference in self-reported QoL was reported in a study using Multidimensional Student's Life Satisfaction Scale (MSLSS; Huebner, Laughlin, Ash, & Gilman, 1998). Parent-reported

QoL (PedsQL in two studies and the CHQ-PF50 in one study) indicated large effect sizes for significantly poorer QoL in children with intellectual disability. No significant difference was observed compared to the clinical comparison groups included in one study (Table 5).

Synthesis

A meta-analysis of the three studies measuring parent-reported QoL of children with intellectual disability compared with typically developing children was conducted. The synthesis included 329 children with intellectual disability and 367 typically developing children, and indicated large but heterogeneous effects for better QoL in typically developing (Fig 4). Confidence in the pooled estimates is again limited by the heterogeneity.

About here Figure 4

Motor disorders

Study characteristics

The four studies included children with Tourette's disorder were conducted in China (Hao et al., 2010; Liu et al., 2014), Australia (O'Hare et al., 2015), and UK/Italy (Eddy et al., 2011). The age range of the study population was 7 to 17 years across studies, and the number of participant with Tourette's disorder ranged from 50 to 424. A minority of participants were females (12 to 31%). The study populations were recruited from clinical settings, schools and Tourette's disorder associations. Typical controls of similar ages were included as comparator in all of these four studies. The proportion of females ranged from 27 to 52% in the control groups. One study included an additional comparison group comprising children with epilepsy (Eddy et al., 2011), while another had three additional comparators: children with leukemia, migraine, and epilepsy (Hao et al., 2010).

An additional study focused on children with developmental coordination disorder (Wuang et al., 2012). The study was conducted in Taiwan and included 369 children between 7 and 15 years of age. They were compared to a group of typically developing children within a similar age range and gender distribution (Table 5).

Results of individual studies

Standardized mean differences in self-reported QoL between children with Tourette's disorder and healthy controls ranged from small and non-significant effect sizes (Eddy et al.,

2011) measured with YQOL-R to medium or large significant effect sizes (Hao et al., 2010; Liu et al., 2014) measured with PedsQL and the Inventory of Subjective Life Quality for Children and Adolescents (ISLQ; Zaohuo, Beiling, & Jian, 1998). Children with Tourette's disorder, epilepsy, or migraine had comparable scores on PedsQL, while children with leukemia rated their QoL substantially lower (Hao et al., 2010). Also, the study using YQOL-R found that children with Tourette's disorder and children with epilepsy rated their QoL similarly (Eddy et al., 2011). Parent-reported QoL rendered large effect sizes for significantly poorer QoL in Tourette's disorder compared to typically developing children (O'Hare et al., 2015) and developmental coordination disorder (Wuang et al., 2012), measured with PedsQL and the psychosocial summary score of CHQ-PF50, respectively.

Synthesis

A meta-analysis of the three studies including measures of parent-reported QoL of children with Tourette's disorder compared to healthy controls was conducted. The synthesis included 581 children with Tourette's disorder and 1683 healthy controls. The results revealed highly heterogeneous effects spanning from a small and non-significant effect to a large effect for significantly poorer QoL in children with Tourette's. Our confidence in the pooled analysis is therefore limited (Fig 5).

About here Figure 5

Elimination disorders

Study characteristics

Four studies focused on nocturnal enuresis, as compared to healthy controls. Three of these studies were from Turkey (Ertan et al., 2009; Kilicoglu et al., 2014; Ucer & Gumus, 2014), and one from Saudi Arabia (Al-Zaben & Sehlo, 2015). The study populations were recruited from clinics. The participants were aged between 7-16 years, with the number of participants with enuresis ranging from 43 to 101 and the proportion of females spanning from 26 to 71% across studies. The fifth study in this diagnostic category compared 49 children with urinary incontinence with age- and gender-matched healthy controls (Natale et al., 2009).

About here Table 6

Results of individual studies

Self-reported QoL in the children with nocturnal enuresis was measured with PedsQL in three studies and KINDL (Bullinger, Brutt, Erhart, & Ravens-Sieberer, 2008; Ravens-Sieberer & Bullinger, 1998) in one study. The studies using PedsQL indicated a medium to large effect size for significantly better QoL in healthy controls, while the study using KINDL reported a small and non-significant effect. Parent-reported QoL with PedsQL included in one study showed a large effect size for significantly better QoL in healthy controls. The study of urinary incontinence did not find a significant effect for self- and parent-reported QoL measured with KINDL.

About here Table 7

Synthesis

A meta-analysis of the four studies of self-reported QoL in children with nocturnal enuresis compared to healthy controls was conducted. The synthesis included 270 children with enuresis and 198 healthy children. The results (Hedges' g) revealed significant heterogeneity, with effects spanning from small and non-significant to large indicating significantly poorer QoL in children with enuresis (Fig 6). Our confidence in the pooled analysis is limited.

About here Figure 6

Other disorders

Study characteristics

Two studies compared samples with CD/ODD and ADHD: one from UK including 17 children around age 11 in each group (Petrou et al., 2010) and one from Puerto Rico including 35 children with CD/ODD and 53 with ADHD in the age range 12 to 18 years (Chavez et al., 2014). Gender-ratio was not reported. No other disorder was represented in more than one study. The only study on depressive disorders was conducted in Hungary and included 248 children and adolescents with MDD (Kiss et al., 2009). A study from Brazil included 75 adolescents with OCD (Vivan Ade et al., 2013). Four studies compared children with different sleep-wake disorders (obstructive sleep apnea, sleep-disordered breathing, restless legs syndrome, and narcolepsy) with healthy controls (Table 6).

Results of individual studies

One of the studies of CD/ODD versus ADHD measured self-reported QoL with the

Adolescent Quality of Life Mental Health Scale (AQOL-MHS) and found a large effect size for significantly better QoL in ADHD (Chavez et al., 2014). The other used the utility-based measure HUI3 (parent-report) and found a small and non-significant effect size for better QoL in CD compared to ADHD (Petrou et al., 2010). The study focusing on MDD and OCD suggested significantly poorer QoL in these groups than in healthy controls, as measured with ILK and the World Health Organization Quality of Life Assessment (WHOQOL-BREF; The WHOQOL Group, 1998), respectively. All studies on sleep-wake disorders showed a significant effect for better QoL of healthy controls, using PedsQL, Vécu et Santé Perçue de l'Adolescent (VSP-A; Serra-Sutton et al., 2009; Simeoni, Auquier, Antoniotti, Sapin, & San Marco, 2000; Simeoni, Sapin, Antoniotti, & Auquier, 2001), and Obstructive Sleep Apnea 18 (OSA-18; Franco, Rosenfeld, & Rao, 2000; Table 7).

Synthesis

No synthesis was feasible due to the heterogeneity of the disorders represented in the studies.

Generalizability and risk of bias

The studies on ADHD were dispersed over a wide range of cultural and geographical regions, while only a limited number of regions were represented within the other diagnostic groups. With a few exceptions, the instruments used were validated in the cultural setting where the study was conducted. Across all diagnostic categories, mainly clinical samples were recruited. While the severity of the included participant conditions or level of symptoms was usually reported, few studies included information about psychiatric comorbidity. Overall, the information about clinical and socio-demographic characteristics of included participants was limited in most studies.

Several studies on ADHD, ASD, and motor disorders included a substantially larger proportion of females in the control group, which might threaten the internal validity of the results. However, it should be noted that Coghill and Hodgkins (2015) reported that there were no significant differences in any domain of any scale for any of the groups with respect to gender in their study of QoL in children with ADHD. In a few studies, parental education was reported to be higher in the control group. Matching or adjustment for variables such as age, gender, and socioeconomic status were used in several of the ADHD studies and some of the other studies. Comorbidity was usually not reported.

Domain specific results across diagnostic categories

In a series of secondary analyses, we looked at the scores on the four dimensions of the self-report version of PedsQL (physical functioning; emotional functioning; social functioning; school functioning) across diagnostic categories. A meta-analysis was carried out for each dimension, with all eligible studies entered into the same meta-analysis regardless of diagnosis. PedsQL was the only instrument used in several studies across several different diagnostic groups. Thus, syntheses of domain specific results for the other instruments were not meaningful.

A total of 12 studies (three of which only reported data on physical functioning) were included, spanning across the diagnoses ADHD, ASD, intellectual disability, Tourette's disorder, enuresis, and sleep-disordered breathing. The overall pattern of results suggests poorer QoL in the study populations than in healthy controls in all four dimensions. This pattern was more consistent for the psychosocial dimensions than for the physical dimension, although substantial heterogeneity across studies was indicated for all dimensions. Differential patterns for the represented diagnoses cannot be discerned from the few studies included (Fig 7 to 10).

About here Figure 7 to 10

Section three: Limitations of the current evidence base and future directions

The systematic review presented in this article summarises the current evidence on how childhood mental and behavioural disorders affect QoL. A total of 41 case-control studies were identified. Several studies examined QoL in ADHD, ASD, intellectual disability, Tourette's disorders, and enuresis, but no eligible studies were detected for a multitude of other large diagnostic groups, such as anxiety disorders, (early onset) schizophrenia, and eating disorders. Studies mainly examined samples of small to medium size. No less than 14 different instruments were used to measure QoL. Both self- and proxy-ratings indicated medium to large effect sizes for diminished global QoL compared to typical or healthy controls in the large majority of included studies. Proxy-ratings mostly indicated poorer QoL than the children's own ratings, which is consistent with prior reports (Coghill & Hodgkins, 2015; White-Koning et al., 2007). The PedsQL was the only instrument used in several studies across several diagnostic groups. All four dimensions measured by this instrument (physical functioning; emotional functioning; social functioning; school functioning) suggested poorer self-rated QoL for the clinical cases than for typical/healthy controls. However, no clear QoL domain profiles distinguishing different diagnoses were discerned.

Studies aggregated in the meta-analyses indicate substantial variability of findings. This could stem from heterogeneous samples (of both the study population and the comparator), which itself might be explained by sampling effects owing to limited sample size (in several studies), differences in age and developmental ranges, and socio-demographic differences across settings and geographical regions. Indeed, the variability of the results could simply and appositely reflect the clinical heterogeneity in most childhood mental disorders. Diversity is particularly pronounced in neurodevelopmental disorders where comorbidity is rather the rule than the exception, generating complex and variable phenotypes (Angold, Costello, & Erkanli, 1999; Simonoff et al., 2008).

Aside from heterogeneity, a couple of encouraging trends and characteristics of the current state of research should be mentioned. First, it is apparent that QoL evidence is accumulating at a relatively high pace. All included studies were published after the year 2000 with an accelerating publication rate during the past 15 years. Second, we found a number of ambitious QoL studies, in particular on ADHD, which were based on relatively large samples of well-characterized children (e.g., Coghill & Hodgkins, 2015; Escobar et al., 2005). Third, self-report QoL instruments were included in most studies. Fourth, the identified studies reveal that this line of research is conducted across a wide range of cultural and geographical regions.

This being said, our main conclusion still is that the practical usefulness of the accumulated QoL evidence to date is limited. More precisely, we see four overarching challenges that undermine conclusions about how different childhood mental and behavioural disorders affect QoL: 1) There are still major gaps in the literature in terms of non- and under investigated childhood disorders and their QoL profiles; 2) There is a non-trivial risk of bias in available studies; 3) The generalizability of the results across contexts and heterogeneous diagnostic groups is unclear; and 4) There are several threats to the validity of the measurements of QoL. Below, we address these issues one by one. We then round off this research review on QoL with a discussion of two additional pivotal issues: changes in QoL over time – spontaneous or brought on by treatment – and future directions for this research field.

Gaps

The QoL evidence base is clearly skewed towards neurodevelopmental disorders, with a notable lack of studies on diagnostic groups such as depressive disorders, anxiety disorders, and eating disorders. Even if we had applied less stringent eligibility criteria, few studies on these disorders would have been available. It is also striking that most studies focus on single disorders, while there is a lack of studies comparing disorders head-to-head to establish specificity or universality of QoL findings. A population-based study from Australia compared parent-reported scores on the Child Health Questionnaire for children aged 6 to 17 years with ADHD, conduct disorder, or depressive disorder is a notable exception (Sawyer et al., 2002). This study was not eligible for our synthesis, due to the fact that results on the overarching domains were not reported. Children with depressive disorder were reported to have more emotional problems, pain and discomfort, while children with ADHD or conduct disorder exhibited more behavioural problems. Although these profiles indicate distinguishable QoL structures for the examined diagnoses, they are clearly aligned with the diagnostic criteria for the respective disorders. Thus, the findings might be viewed as circular, providing only moderate added information. The lack of more informative QoL domain profile research is disappointing, as QoL is a multidimensional construct, which theoretically seems illogical to be expressed in form of a single score (Eisen, Ware, Donald, & Brook, 1979). Clinically, particularly in the context of treatment planning (Katschnig, 2006), a single QoL score might camouflage patterns of strengths and weaknesses, hampering targeted therapeutic strategies. More research is needed to determine what extent diagnostic groups show specific patterns of QoL challenges. Among the barriers for overcoming these gaps is the usage of a large number of measures with varying domains.

Risk of bias

In order to estimate the magnitude to which child mental and behavioural disorders affect QoL, a range of contextual factors must be considered. We required that data on comparator(s) should be collected with the same procedure as data on the study population, within the same five-year period, and that samples were recruited from the same community. While these demands are likely to eliminate differences between the groups related to the procedure, cultural systems and secular events, other dissimilarities (measured or unmeasured) could still account for an important part of the variance. First, female participants constituted a substantially larger proportion of the control groups in several studies. While Coghill and Hodgkins (2015) did not identify any significant sex differences in their study of ADHD compared with typical controls, thorough matching for gender or adjusting for this factor appears mandatory. Second, in most studies, information about socio-demographic variables has often been sparse and thus remains largely unknown in QoL research in the area as a whole. Nevertheless, the impact of such factors may not be negligible and deserves to be controlled for. For example, ADHD research on QoL indicates that factors such as health status of the caregivers, maternal smoking, living with a single parent, parental separation/divorce, moves, and conflict with siblings or peers, all have a negative impact on QoL (Preuss et al., 2006; Newcorn et al., 2005), while living with both parents is associated with higher QoL (Riley et al., 2006). Third, comorbid conditions were seldom reported. Similarly, psychiatric symptoms that often are present across diagnostic categories (e.g., depressive symptoms or anxiety) were not measured and adjusted for in the analyses. Most reports either excluded children with comorbidity or did not measure comorbidity. Obviously, additional mental health problems or disorders would be expected to increase a negative impact on QoL. Indeed, studies of QoL in childhood ADHD do suggest that having an additional co-occurring diagnosis, such as oppositional defiant disorder (Newcorn, Spencer, Biederman, Milton, & Michelson, 2005) or other common comorbidities is associated with a greater reduction in QoL (Klassen, Miller, & Fine, 2004). Oppositional defiant disorder and conduct disorder – in combination with tic disorder, depression and anxiety disorder – has also been reported to yield lower QoL-ratings (Klassen et al., 2004). We therefore concur with the recommendation by Katschnig (2006) that comorbidity and symptoms of depression and anxiety should always be accounted for in QoL research.

Generalizability

Judgements about generalizability across populations are restricted by the gaps in the literature outlined above, but also by how studies are reported and how data is analysed.

Obstacles included limited information about the examined samples, reliance on clinical samples, exclusion of age groups, restricted coverage of geographical and cultural regions, and few female participants in many studies. Gender-specific results are of increasing interest in child psychology and psychiatry, especially for neurodevelopmental disorders (Nussbaum, 2012; Werling & Geschwind, 2013). The female-to-male-ratio within the examined samples varied considerably. While it was overall relatively balanced in intellectual disability, sleep disorders, elimination disorders, and depression, it was consistently skewed towards including more males than females in ASD, ADHD, and motor disorders. While some of these proportions may be representative for the disorders, the low number of included females precludes sub-analyses.

The majority of studies used clinical rather than epidemiological samples, and they were of small to medium size. Clinical samples may not be representative of full range of children meeting the diagnostic criteria for the specific disorder. While some information about the severity of the conditions usually was reported, the association of symptom severity and impairment with the levels of QoL was generally not analysed. Moreover, the samples mainly comprised school aged children and adolescents. This is understandable given that many conditions either typically have an onset at this age or are detected and diagnosed when the children enter school. On the other hand, this presumably also reflect the difficulties in obtaining valid reports of how younger children perceive their position in life.

Half of the studies originated in Europe and only a minority in North America, whereas the distribution of research quantities is often inverse between Europe and North America in other childhood mental health research fields (Bölte et al., 2016; Bramness, Henriksen, Person, & Mann, 2014). Some disorders were extensively studied in a specific country, with for instance three out of the four studies on enuresis originating in Turkey. Only ADHD had been examined over a large number of geographical and cultural regions. Extrapolation of the results across geographical regions could be risky given large differences in attitudes towards mental and behavioural disorders in healthcare and society at large. Such attitudes might shape the individual’s self-perceived well-being, expectations, and goals.

Measurement

Even if the accumulated research covered the major diagnostic groups, the population characteristics were meticulously reported, and the risk of bias in the individual studies were low, the estimates would tell us little unless we knew what exactly QoL instruments actually measure. This is especially true, as the number of different scales used is substantial. We identified 14 instruments and other widely used QoL scales not represented in this review are KIDSCREEN, DISABKIDS (Bullinger, Schmidt, & Petersen, 2002; Ravens-Sieberer et al., 2001) and Child Health Illness Profile – Child Edition (CHIP-CE; Riley et al., 2001). These tools' theoretical underpinnings, operationalised QoL domains, and items vary largely, casting justified doubts on the assumption they assess comparable constructs. The usage of self- and proxy report adds further to the confusion.

Let us first consider the definition of QoL by WHO's QoL group (1993) in the context of childhood mental and behavioural disorders. The definition stresses the "individual's perception of their position in life" in the "context of culture and value systems" and in relation to the individuals "goals, expectations, standards and concerns" (1993). Both psychopathology per se and the related functional impairment would be expected to decrease an individual's subjective well-being. However, altered expectations on QoL and changed states of mind in children with mental and behavioural disorders must also be considered. First, it is possible that individuals adjust their standards to their level of impairment in some domain and instead prioritize other aspects of life. Similarly, attitudes toward mental and behavioural disorders within the cultural system could alter the individuals' expectations and goals. While such subjective adjustments of standards and expectations could apply also to general medical conditions, altered perception due to the individual's state of mind is more clearly related to psychopathology (Katschnig, 2006). Individuals with depressive symptoms, for instance, are likely to have a bleak outlook on life due to their current state of mind. Consequently, they would be expected to rate their QoL lower than their objective situation would suggest.

The PedsQL was the by far most frequently used instrument in the studies included in our systematic review. The instrument has shown good psychometric properties and combines several attractive characteristics, including short administration time, a limited number of dimensions (physical functioning, emotional functioning, social functioning, and school functioning), parallel versions for parent proxy and child-report, and age-adapted versions that can be completed by children as young as 5 years (Varni, Limbers, & Burwinkle, 2007a, 2007b). In the following discussion, we consider some of the prominent features of PedsQL, and the implications of these features for measurement of QoL in childhood mental and behavioural disorders. To begin, close inspection of the PedsQL items reveals substantial overlap between the emotional functioning dimension and the ICD/DSM criteria for depressive disorders and anxiety disorders. It has been assumed that reported subjective well-being often tends to simply reflect altered psychological states, while analyses of QoL should adjust for items clearly overlapping with other psychological constructs (Katschnig, 2006). Nevertheless, while adjustment for depressive and anxiety symptoms seems reasonable for conditions which are not defined by such psychopathology, such a procedure is likely to result in severe underestimation of the QoL impact of disorders that are defined by these symptoms (i.e., depressive and anxiety disorders). An alternate implementation of QoL could be to recognize that some mental and behavioural disorders partly are defined by subjective experiences closely related to the concept of QoL. Anyhow, it is paramount importance to enhance our understanding of how self-ratings of QoL are affected by mental states (e.g., depression and anxiety) and traits (e.g., neuroticism).

A closely related issue is how measurements should account for fluctuations in self-perceived QoL over time. The PedsQL asks the rater to recall the past month. Apart from the obvious risk of recall bias, there is a risk that the rating for the whole period reflects the individual's current state of mind. In particular, this threatens to undermine the validity of ratings in conditions where the mood can shift from day to day, or from one hour to the next. In order to increase ecological validity, we suggest that traditional questionnaires such as PedsQL be combined with other types of data collection. Experience sampling methodology (ESM), which requires that the participants report their experiences at random points throughout the day, could be a valuable complement. This methodology has, for instance, recently been reported to be helpful in identifying the nature and quality of social experiences in children with ASD (Cordier, Brown, Chen, Wilkes-Gillan, & Falkmer, 2016).

Finally, the PedsQL does not explicitly take the child's own goals and expectations into consideration. In contrast to some other measures, such as the Quality of Life Inventory (QOLI; Frisch, 1994), each item is not weighted based on how important it is for the individual. Entering the child's own priorities into the equation is essential to amplify the subjective element, which is viewed the core of QoL. If this is refrained from, there is an apparent risk that the results will reflect functional impairment observed or experienced by others. The subjective nature of priorities, goals, and expectations is a potential source of variance between self and proxy-report. Some children with ASD might for instance not regard social contact as an important aspect of their life, while their parents supposedly do. Given the many situations when self-report is not a viable option, it would be worthwhile to investigate if the quality of proxy-report can be improved by explicitly guiding a rater to take the child's perspective. In conclusion, we recommend that measurement of QoL in children with mental and behavioural disorders better accounts for fluctuations over time and put the child's own views and priorities first.

Treatment response and stability

The cross-sectional studies included in our systematic review are designed to estimate the general impact of mental and behavioural disorders on QoL for certain age groups. However, it is equally important how QoL responds to treatment and changes over time. Although some intervention studies have addressed this question (Coghill, 2010; Corona et al., 2015; Perwien et al., 2004), QoL has not been routinely measured in clinical trials. In trials on pharmacological treatment for children with ADHD, however, the effect on QoL has recently been more regularly reported (e.g., Banaschewski et al., 2013; Escobar et al, 2009; Newcorn et al., 2008; Svanborg et al, 2009). Most available trials suggest significant effects on one or more QoL domains. CHIP-CE:PRF and CHQ-PF50 are by far the most frequently used QoL instruments in these trials, indicating reliance on parent proxy ratings. Although there might be concerns that the use of self-rated instruments will result in higher rates of missing data, mandatory inclusion of self-report would better account for the children's perspective. QoL is now also increasingly recognized in psychological treatment research (e.g., Vigerland et al., 2016; Weidle, Ivarsson, Thomsen, Lydersen, & Jozefiak, 2015), indicating a general trend towards increased consideration of the children's subjective experience of well-being following intervention.

Less attention has so far been given to the question of how childhood mental and behavioural disorders influence the individuals' QoL over time. Indeed, there is a general lack of prospective longitudinal studies following affected children into adulthood. Available research indicates that about half of the children affected by childhood psychopathology will not fulfil diagnostic criteria for the same or a different disorder as young adults, although a substantial proportion will still have impairments in important areas of life (Costello & Maughan, 2016). Obviously, the level of QoL in adulthood might not depend solely on current clinical symptoms and psychosocial outcomes. A range of potential mediating factors should be considered, including formal and informal social support systems, coping strategies, acceptance, and the individual’s view of life.

Future directions

Several approaches would be useful to further increase our knowledge on QoL in childhood mental and behavioural disorders, which we will briefly sketch in form of hypothetical ideal studies that address caveats of the current evidence base. In line with what is recommended for psychopathology and functional impairment research, such ideal studies would need to be conducted across cultures using a global perspective, as for instance low and middle-income countries or other low-resource environments might strongly influence the relation between psychopathology, impairment and QoL (De Vries & Bölte, 2016). First, a large sample of children across ages, diagnosed according to current best clinical practice, and treated for mental and behavioural disorders with a variety of evidence-based interventions, would allow for head-to-head comparison between the major diagnostic categories. Depending on how mental health services are organised, sampling from both specialized services (e.g., child and adolescent psychiatric, paediatric, neuropediatric, clinical genetic, speech and language services) and primary care might be required. Second, population-based samples from the same communities would ideally constitute reference groups of typically developing children as well as affected but undiagnosed and untreated children and children with intermediate/subclinical phenotypes. Information on symptom severity, psychiatric and somatic comorbidity, symptoms cutting across diagnostic categories (e.g., depressive symptoms), functional impairment, and socio-demographic characteristics should be collected in order to ascertain internal validity and enable judgement about external validity. As a complement to questionnaires, methods such as ESM could give insight into the immediate effect of treatment and how self-perceived QoL fluctuate over time. Finally, the children’s expectations and goals, and how these affect their ratings of QoL, should be investigated with both qualitative and quantitative approaches.

Supporting Information

Additional Supporting Information may be found on the online version of this article.

Appendix S1: Methods

Appendix S2: Excluded publications with reasons

Acknowledgements

This review was invited by the Editors of this journal, who offered a small honorarium to cover expenses to the first author. S.B. declares no conflict of interest related to this work. He has in the last 3 years acted as a consultant or lecturer for Shire, Roche, Eli Lilly, Prima Psychiatry, Kompetento, Expo Medica, System Analytic and Prophase, and receives royalties from Kohlhammer and Hogrefe/Huber publishers. D.C. has within the last 3 years served in an advisory or consultancy role and/or received speakers' fees from Flynn Pharma, Lilly, Janssen, Medice, Novartis, Shire and Vifor. He has received research funding from Shire and Vifor. He receives royalties from Oxford University Press. I.A. was supported by the Pediatric Research Foundation at Astrid Lindgren Children's Hospital. S.B. was supported by the Swedish Research Council. The present work is unrelated to the above grants and relationships. The remaining authors have no potential conflicts of interest to declare.

The authors would like to thank Carl Gornitzki and Klas Moberg for their assistance with the literature search.

Correspondence

Sven Bölte, Center of Neurodevelopmental Disorders (KIND), CAP Research Center, Gävlegatan 22, 11330 Stockholm, Sweden; e-mail: sven.bolte@ki.se

Key points

- In addition to psychopathology and impairment, quality of life (QoL) is a significant aspect of children's mental health.
- Existing case-control studies have mainly focused on neurodevelopmental disorders, including attention-deficit hyperactivity disorder, autism spectrum disorder, motor disorders and intellectual disability.

- Self- and parent-rated QoL is significantly reduced in the studied diagnostic groups, as compared to typical/healthy controls.
- QoL research is largely lacking for children and adolescents with depressive disorders, anxiety disorders, (early onset) schizophrenia or eating disorders.
- To estimate the extent to which the reduction in QoL is attributable to the specific disorders, future studies need to account for potential confounders.

References

Al-Zaben, F.N., & Sehlo, M.G. (2015). Punishment for bedwetting is associated with child depression and reduced quality of life. *Child Abuse & Neglect, 43,* 22-29.

Alonso, J., Angermeyer, M.C., Bernert, S., Bruffaerts, R., Brugha, T.S., Bryson, H., . . . & Vollebergh, W.A. (2004). Disability and quality of life impact of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica. Supplementum,* 38-46.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th edn.). Arlington, VA: American Psychiatric Association.

Angold, A., Costello, E.J., & Erkanli, A. (1999). Comorbidity. *Journal of Child Psychology and Psychiatry, 40,* 57-87.

Assumpcao, F.B., Jr., Kuczynski, E., Sprovieri, M.H., & Aranha, E.M. (2000). [Quality of life evaluation scale (AUQEI--Autoquestionnaire Qualite de Vie Enfant Image). Validity and reliability of a quality of life scale for children 4 to 12 years-old]. *Arquivos de Neuro-Psiquiatria, 58,* 119-127.

Banaschewski, T., Soutullo, C., Lecendreux, M., Johnson, M., Zuddas, A., Hodgkins. P,, Adeyi, B., Squires, L.A., Coghill, D. (2013). Health-related quality of life and functional outcomes from a randomized, controlled study of lisdexamfetamine dimesylate in children and adolescents with attention deficit hyperactivity disorder. *CNS Drugs, 27,* 829-840.

Basgul, S.S., Uneri, O.S., & Cakin-Memik, N. (2011). Parents' perception of the quality of life of children with intellectual disabilities. *Turkish Journal of Pediatrics, 53,* 541-546.

Bastiaansen, D., Koot, H.M., & Ferdinand, R.F. (2005). Psychopathology in children: improvement of quality of life without psychiatric symptom reduction? *European Child & Adolescent Psychiatry, 14,* 364-370.

Bastiaansen, D., Koot, H.M., Ferdinand, R.F., & Verhulst, F.C. (2004). Quality of life in children with psychiatric disorders: self-, parent, and clinician report. *Journal of the American Academy of Child & Adolescent Psychiatry, 43,* 221-230.

Bell, A. (2007). Designing and testing questionnaires for children. *Journal of Research in Nursing, 12,* 461–469.

Bibace, R., & Walsh, M.E. (1980). Development of children's concepts of illness. *Pediatrics, 66,* 912-917.

Bölte, S., Bartl-Pokorny, K.D., Jonsson, U., Berggren, S., Zhang, D., Kostrzewa, E., . . . & Marschik, P.B. (2016). How can clinicians detect and treat autism early? Methodological trends of technology use in research. *Acta Paediatrica, 105*, 137-144.

Bramness, J.G., Henriksen, B., Person, O., & Mann, K. (2014). A bibliometric analysis of European versus USA research in the field of addiction. Research on alcohol, narcotics, prescription drug abuse, tobacco and steroids 2001-2011. *European Addiction Research, 20*, 16-22.

Brantley, A., Huebner, E.S., & Nagle, R.J. (2002). Multidimensional life satisfaction reports of adolescents with mild mental disabilities. *Mental Retardation, 40*, 321-329.

Brazier, J., Connell, J., Papaioannou, D., Mukuria, C., Mulhern, B., Peasgood, T., . . . & Parry, G. (2014). A systematic review, psychometric analysis and qualitative assessment of generic preference-based measures of health in mental health populations and the estimation of mapping functions from widely used specific measures. *Health Technology Assessment, 18*, vii-viii, xiii-xxv, 1-188.

Bullinger, M., Brutt, A.L., Erhart, M., & Ravens-Sieberer, U. (2008). Psychometric properties of the KINDL-R questionnaire: results of the BELLA study. *European Child and Adolescent Psychiatry, 17 Suppl 1*, 125-132.

Bullinger, M., Schmidt, S., & Petersen, C. (2002). Assessing quality of life of children with chronic health conditions and disabilities: a European approach. *International Journal of Rehabilitation Research. Internationale Zeitschrift fur Rehabilitationsforschung. Revue Internationale de Recherches de Readaptation, 25*, 197-206.

Carona, C., Crespo, C., Silva, N., Lopesa, A.F., Canavarroa, M.C., & Bullingerb, M. (2013). Examining a developmental approach to health-related quality of life assessment: psychometric analysis of DISABKIDS generic module in a Portuguese sample. *Vulnerable Children and Youth Studies, 8*, 243-257.

Carona, C., Silva, N., & Moreira, H. (2015). Applying a developmental approach to quality of life assessment in children and adolescents with psychological disorders: challenges and guidelines. *Expert Review of Pharmacoeconomics & Outcomes Research, 15*, 47-70.

Chavez, L.M., Ramirez, R., Garcia, P., Canino, G., Mir, K., Ortiz, N., & Morales, L.S. (2014). Measurement properties of the Adolescent Quality of Life Mental Health Scale (AQOL-MHS). *Quality of Life Research, 23*, 1327-1335.

Coghill, D. (2010). The impact of medications on quality of life in attention-deficit hyperactivity disorder: a systematic review. *CNS Drugs, 24*, 843-866.

Coghill, D., Danckaerts, M., Sonuga-Barke, E., & Sergeant, J. (2009). Practitioner review: Quality of life in child mental health--conceptual challenges and practical choices. *Journal of Child Psychology and Psychiatry, 50*, 544-561.

Coghill, D., & Hodgkins, P. (2016). Health-related quality of life of children with attention-deficit/hyperactivity disorder versus children with diabetes and healthy controls. *European Child and Adolescent Psychiatry, 25,* 261-271.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd edn.). Hillsdale, NJ: Lawrence Earlbaum Associates.

Cordier, R., Brown, N., Chen, Y.W., Wilkes-Gillan S., & Falkmer T. (2016). Piloting the use of experience sampling method to investigate the everyday social experiences of children with asperger syndrome/high functioning autism. *Developmental Neurorehabilitation, 19,* 103-108.

Costello, E.J., & Maughan, B. (2015). Annual Research Review: Optimal outcomes of child and adolescent mental illness. *Journal of Child Psychology and Psychiatry, 56,* 324–341

Crabtree, V.M., Varni, J.W., & Gozal, D. (2004). Health-related quality of life and depressive symptoms in children with suspected sleep-disordered breathing. *Sleep, 27*, 1131-1138.

Cremeens, J., Eiser, C., & Blades, M. (2006). Characteristics of health-related self-report measures for children aged three to eight years: a review of the literature. *Quality of Life Research, 15*, 739-754.

Danckaerts, M., Sonuga-Barke, E.J., Banaschewski, T., Buitelaar, J., Dopfner, M., Hollis, C., . . . Coghill, D. (2010). The quality of life of children with attention deficit/hyperactivity disorder: a systematic review. *European Child and Adolescent Psychiatry, 19,* 83-105.

De Vries, P., & Bölte, S. (in press). Measuring functional ability of autism spectrum disorder in a global context. *Developmental Medicine & Child Neurology.*

de Vries, M., & Geurts, H. (2015). Influence of Autism Traits and Executive Functioning on Quality of Life in Children with an Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders, 45*, 2734-2743.

Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. (1998). *Psychological Medicine, 28*, 551-558.

Dey, M., Landolt, M.A., & Mohler-Kuo, M. (2012). Health-related quality of life among children with mental disorders: a systematic review. *Quality of Life Research, 21*, 1797-1814.

Dolan, P. (2000). The measurement of health-related quality of life for use in resource allocation decisions in health care. In A.J. Culyer & J.P. Newhouse (Eds.), *Handbook of Health Economics* (pp. 1723–1760). North-Holland: Elsevier.

Domellöf, E., Hedlund, L., & Ödman, P. (2014). Health-related quality of life of children and adolescents with functional disabilities in a northern Swedish county. *Quality of Life Research, 23*, 1877-1882.

Eddy, C.M., Rizzo, R., Gulisano, M., Agodi, A., Barchitta, M., Cali, P., . . . & Cavanna, A.E. (2011). Quality of life in young people with Tourette syndrome: a controlled study. *Journal of Neurology, 258*, 291-301.

Edwards, T.C., Huebner, C.E., Connell, F.A., & Patrick, D.L. (2002). Adolescent quality of life, part I: conceptual and measurement model. *Journal of Adolescence, 25*, 275-286.

Eisen, M., Ware, J.E., Jr., Donald, C.A., & Brook, R.H. (1979). Measuring components of children's health status. *Medical Care, 17*, 902-921.

Eiser, C., & Morse, R. (2001). A review of measures of quality of life for children with chronic illness. *Archives of Disease in Childhood, 84*, 205-211.

Elbasan, B., Duzgun, I., & Oskay, D. (2013). Is There any Difference in Health Related

Quality of Life, Self Care and Social Function in Children with Different Disabilities Living in Turkey? *Iranian Journal of Pediatrics, 23,* 281-288.

Ertan, P., Yilmaz, O., Caglayan, M., Sogut, A., Aslan, S., & Yuksel, H. (2009). Relationship of sleep quality and quality of life in children with monosymptomatic enuresis. *Child: Care, Health & Development, 35,* 469-474.

Escobar, R., Montoya, A., Polavieja, P., Cardo, E., Artigas, J., Hervas, A., & Fuentes, J. (2009). Evaluation of patients' and parents' quality of life in a randomized placebo-controlled atomoxetine study in attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology, 19,* 253-263.

Escobar, R., Soutullo, C.A., Hervas, A., Gastaminza, X., Polavieja, P., & Gilaberte, I. (2005). Worse quality of life for children with newly diagnosed attention-deficit/hyperactivity disorder, compared with asthmatic and healthy children.[Erratum appears in Pediatrics. 2005 Nov;116(5):1266]. *Pediatrics, 116,* e364-369.

Franco, R.A., Jr., Rosenfeld, R.M., & Rao, M. (2000). First place--resident clinical science award 1999. Quality of life for children with obstructive sleep apnea. *Otolaryngology--Head and Neck Surgery, 123,* 9-16.

Frisch, M. B. (1994). *Test manual and treatment guide for the QOLI (Quality of Life Inventory).* Minneapolis, MN: Pearson Assessments.

Frisch, M.B. (2000). Improving mental and physical health care through quality of life therapy and assessment. In E. Diener & D.R. Rahtz (Eds.), *Advances in quality of life theory and research.* (pp. 207-241). Dordrecht: Kluwer.

Furudate, N., Komada, Y., Kobayashi, M., Nakajima, S., & Inoue, Y. (2014). Daytime dysfunction in children with restless legs syndrome. *Journal of the Neurological Sciences, 336,* 232-236.

Glaser, A.W., Abdul Rashid, N.F., U, C.L., & Walker, D.A. (1997). School behaviour and health status after central nervous system tumours in childhood. *British Journal of*

Cancer, 76, 643-650.

Glaser, A.W., Davies, K., Walker, D., & Brazier, D. (1997). Influence of proxy respondents and mode of administration on health status assessment following central nervous system tumours in childhood. *Quality of Life Research, 6*, 43-53.

Golubovic, S., & Skrbic, R. (2013). Agreement in quality of life assessment between adolescents with intellectual disability and their parents. *Research in Developmental Disabilities, 34*, 1863-1869.

Guyatt, G.H., Oxman, A.D., Vist, G., Kunz, R., Brozek, J., Alonso-Coello, P., . . . & Schunemann, H.J. (2011). GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). *Journal of Clinical Epidemiology, 64*, 407-415.

Göker, Z., Aktepe, E., & Kandil, S. (2011). Self-esteem and quality of life in children and adolescents with attention deficit hyperactivity disorder. *Yeni Symposium, 49*, 209-216.

Hakkaart-van Roijen, L., Zwirs, B.W., Bouwmans, C., Tan, S.S., Schulpen, T.W., Vlasveld, L., & Buitelaar, J.K. (2007). Societal costs and quality of life of children suffering from attention deficient hyperactivity disorder (ADHD). *European Child and Adolescent Psychiatry, 16*, 316-326.

Hao, Y., Tian, Q., Lu, Y., Chai, Y., & Rao, S. (2010). Psychometric properties of the Chinese version of the Pediatric Quality of Life Inventory 4.0 generic core scales. *Quality of Life Research, 19*, 1229-1233.

Horsman, J., Furlong, W., Feeny, D., & Torrance, G. (2003). The Health Utilities Index (HUI): concepts, measurement properties and applications. *Health and Quality of Life Outcomes, 1*, 54.

Huebner, E.S., Laughlin, J.E., Ash, C., & Gilman, R. (1998). Further validation of the Multidimensional Students' Life Satisfaction Scale. *Journal of Psychological Assessment, 16*, 118-134.

Idring, S., Lundberg, M., Sturm, H., Dalman, C., Gumpert, C., Rai, D., . . . & Magnusson, C. (2015). Changes in prevalence of autism spectrum disorders in 2001-2011: findings from the Stockholm youth cohort. *Journal of Autism and Developmental Disorders, 45*, 1766-1773.

Ikeda, E. (2013). *Quality of life and self-report in children and adolescents with cognitive disability*. Auckland University of Technology, Auckland.

Ikeda, E., Hinckson, E., & Krageloh, C. (2014). Assessment of quality of life in children and youth with autism spectrum disorder: a critical review. *Quality of Life Research, 23*, 1069-1085.

Inocente, C.O., Gustin, M.P., Lavault, S., Guignard-Perret, A., Raoux, A., Christol, N., . . . & Franco, P. (2014). Quality of life in children with narcolepsy. *CNS Neuroscience & Therapeutics, 20*, 763-771.

Insel, T.R. (2014). Mental disorders in childhood: shifting the focus from behavioral symptoms to neurodevelopmental trajectories. *JAMA, 311*, 1727-1728.

Jafari, P., Ghanizadeh, A., Akhondzadeh, S., & Mohammadi, M.R. (2011). Health-related quality of life of Iranian children with attention deficit/hyperactivity disorder. *Quality of Life Research, 20*, 31-36.

Janssens, A., Rogers, M., Thompson Coon, J., Allen, K., Green, C., Jenkinson, C., . . . & Morris, C. (2015). A systematic review of generic multidimensional patient-reported outcome measures for children, part II: evaluation of psychometric performance of English-language versions in a general population. *Value in Health, 18*, 334-345.

Janssens, A., Thompson Coon, J., Rogers, M., Allen, K., Green, C., Jenkinson, C., . . . & Morris, C. (2015). A systematic review of generic multidimensional patient-reported outcome measures for children, part I: descriptive characteristics. *Value in Health, 18*, 315-333.

Kandemir, H., Kiliç, B.G., Ekinci, S., & Yüce, M. (2014). An evaluation of the quality of life of children with ADHD and their families. *Anadolu Psikiyatri Dergisi, 15*, 265-271.

Katschnig, H. (2006). Quality of life in mental disorders: challenges for research and clinical practice. *World Psychiatry, 5*, 139-145.

Kilicoglu, A.G., Mutlu, C., Bahali, M.K., Adaletli, H., Gunes, H., Duman, H.M., . . . Uneri, O.S. (2014). Impact of enuresis nocturna on health-related quality of life in children and their mothers. *Journal of Pediatric Urology, 10,* 1261-1266.

Kiss, E., Kapornai, K., Baji, I., Mayer, L., & Vetro, A. (2009). Assessing quality of life: mother-child agreement in depressed and non-depressed Hungarian. *European Child and Adolescent Psychiatry, 18*, 265-273.

Klassen, A.F., Miller, A., & Fine, S. (2004). Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics, 114,* e541-547.

Kuhlthau, K., Kovacs, E., Hall, T., Clemmons, T., Orlich, F., Delahaye, J., & Sikora, D. (2013). Health-related quality of life forchildren with ASD: Associations with behavioral characteristics. *Research in Autism Spectrum Disorders, 7*, 1035-1042.

Lack, C.W., Storch, E.A., Keeley, M.L., Geffken, G.R., Ricketts, E.D., Murphy, T.K., & Goodman, W.K. (2009). Quality of life in children and adolescents with obsessive-compulsive disorder: base rates, parent-child agreement, and clinical correlates. *Social Psychiatry and Psychiatric Epidemiology, 44*, 935-942.

Landgraf, J.M., Abetz, L., & Ware, J.E. (1996). *The Child Health Questionnaire (CHQ): A User's Manual*. Boston, MA: Health Institute, New England Medical Center.

Landgraf, J.M., Abetz, L., & Ware, J.E. (1999). *The Child Health Questionnaire (CHQ): A User's Manual* (2nd edn.). Boston, MA: Health Institute, New England Medical Center.

Leidy, N.K., Revicki, D.A., & Geneste, B. (1999). Recommendations for evaluating the validity of quality of life claims for labeling and promotion. *Value in Health, 2*, 113-

127.

Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gotzsche, P.C., Ioannidis, J.P., . . . & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ, 339,* b2700.

Liu, S., Zheng, L., Zheng, X., Zhang, X., Yi, M., & Ma, X. (2014). The Subjective Quality of Life in Young People With Tourette Syndrome in China. *Journal of Attention Disorders*. Advance online publication. doi: 10.1177/1087054713518822

Marques, J.C., Oliveira, J.A., Goulardins, J.B., Nascimento, R.O., Lima, A.M., & Casella, E.B. (2013). Comparison of child self-reports and parent proxy-reports on quality of life of children with attention deficit hyperactivity disorder. *Health & Quality of Life Outcomes, 11*, 186.

Maslow, A.H. (1943). A theory of human motivation. *Psychological Review, 50*, 370-396.

Mattejat, F., Simeon, B., König, U., Quaschner, K., Barchewitz, C., Felbel, D., . . . & Remschmidt, H. (2003). Lebensqualität bei psychisch kranken Kindern und Jugendlichen – Ergebnisse der ersten multizentrischen Studie mit dem Inventar zur Erfassung der Lebensqualität bei Kindern und Jugendlichen (ILK). *Zeitschrift für Kinder und Jugendpsychiatrie und Psychotherapie, 31*, 293-303.

Matza, L.S., Swensen, A.R., Flood, E.M., Secnik, K., & Leidy, N.K. (2004). Assessment of health-related quality of life in children: a review of conceptual, methodological, and regulatory issues. *Value in Health, 7,* 79-92.

Medici, C.R., Videbech, P., Gustafsson, L.N., & Munk-Jorgensen, P. (2015). Mortality and secular trend in the incidence of bipolar disorder. *Journal of Affective Disorders, 183,* 39-44.

Meyer, M., Oberhoffer, R., Hock, J., Giegerich, T., Müller, J. (2016). Health-related quality of life in children and adolescents: Current normative data, determinants and reliability on proxy-report. *Journal of Paediatrics and Child Health.* Advance online publication. doi: 10.3109/17518423.2014.915244

Natale, N., Kuhn, S., Siemer, S., Stockle, M., & von Gontard, A. (2009). Quality of life and self-esteem for children with urinary urge incontinence and voiding postponement. *Journal of Urology, 182*, 692-698.

National Institute for Health and Clinical Excellence. (2004). Guide to the methods of technology appraisal. NICE, London.

National Institute for Health and Clinical Excellence (2008). *Attention deficit hyperactivity disorder: diagnosis and management of ADHD in children, young people and adults.* (Clinical guideline 72.) www.nice.org.uk/CG72

Newcorn, J.H., Kratochvil, C.J., Allen, A.J., Casat, C.D., Ruff, D.D., Moore, R.J., Michelson, D., & Atomoxetine/Methylphenidate Comparative Study Group (2008). Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. *American Journal of Psychiatry, 165,* 721-730.

Newcorn, J.H., Spencer, T.J., Biederman, J., Milton, D.R., & Michelson, D. (2005). Atomoxetine treatment in children and adolescents with attention-deficit/hyperactivity disorder and comorbid oppositional defiant disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*, 240-248.

Nussbaum, N.L. (2012). ADHD and female specific concerns: a review of the literature and clinical implications. *Journal of Attention Disorders, 16,* 87-100.

O'Hare, D., Helmes, E., Eapen, V., Grove, R., McBain, K., & Reece, J. (2016). The Impact of Tic Severity, Comorbidity and Peer Attachment on Quality of Life Outcomes and Functioning in Tourette's Syndrome: Parental Perspectives. *Child Psychiatry and Human Development, 47,* 563-573.

Patel, V., Flisher, A.J., Hetrick, S., & McGorry, P. (2007). Mental health of young people: a global public-health challenge. *Lancet, 369,* 1302-1313.

Patrick, D.L., Edwards, T.C., & Topolski, T.D. (2002). Adolescent quality of life, part II: initial validation of a new instrument. *Journal of Adolescence, 25*, 287-300.

Perwien, A.R., Faries, D.E., Kratochvil, C.J., Sumner, C.R., Kelsey, D.K., & Allen, A.J. (2004). Improvement in health-related quality of life in children with ADHD: an analysis of placebo controlled studies of atomoxetine. *Journal of Developmental and Behavioral Pediatrics, 25*, 264-271.

Petrou, S., Johnson, S., Wolke, D., Hollis, C., Kochhar, P., & Marlow, N. (2010). Economic costs and preference-based health-related quality of life outcomes associated with childhood psychiatric disorders. *British Journal of Psychiatry, 197*, 395-404.

Petrou, S., & Kupek, E. (2009). Estimating preference-based health utilities index mark 3 utility scores for childhood conditions in England and Scotland. *Medical Decision Making, 29*, 291-303.

Polanczyk, G.V., Salum, G.A., Sugaya, L.S., Caye, A., & Rohde, L.A. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry, 56*, 345-365.

Pongwilairat, K., Louthrenoo, O., Charnsil, C., & Witoonchart, C. (2005). Quality of life of children with attention-deficit/hyper activity disorder. *Journal of the Medical Association of Thailand, 88*, 1062-1066.

Potvin, M.C., Snider, L., Prelock, P.A., Wood-Dauphinee, S., & Kehayia, E. (2015). Health-related quality of life in children with high-functioning autism. *Autism, 19*, 14-19.

Preuss, U., Ralston, S.J., Baldursson, G., Falissard, B., Lorenzo, M.J., Rodrigues Pereira, R., . . . Coghill, D. (2006). Study design, baseline patient characteristics and intervention in a cross-cultural framework: results from the ADORE study. *European Child and Adolescent Psychiatry, 15 Suppl 1*, I4-14.

Ravens-Sieberer, U., & Bullinger, M. (1998). Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. *Quality of Life Research, 7*, 399-407.

Ravens-Sieberer, U., Gosch, A., Abel, T., Auquier, P., Bellach, B.M., Bruil, J., . . . Rajmil, L. (2001). Quality of life in children and adolescents: a European public health perspective. *Sozial- und Praventivmedizin, 46*, 294-302.

Rentz, A.M., Matza, L.S., Secnik, K., Swensen, A., & Revicki, D.A. (2005). Psychometric validation of the child health questionnaire (CHQ) in a sample of children and adolescents with attention-deficit/hyperactivity disorder. *Quality of Life Research, 14*, 719-734.

Riley, A.W., Robertson, J.A., Forrest, C.B., Green, B.F., Rebok, G., & Starfield, B. (2001). *Technical manual for the Child Health and Illness Profile – Child Edition (CHIP-CE) Parent and Child Report Forms* (1st edn.). Baltimore, MD: Johns Hopkins University.

Riley, A.W., Spiel, G., Coghill, D., Dopfner, M., Falissard, B., Lorenzo, M.J., . . . Ralston, S.J. (2006). Factors related to health-related quality of life (HRQoL) among children with ADHD in Europe at entry into treatment. *European Child and Adolescent Psychiatry, 15 Suppl 1*, I38-45.

Ritsner, M., Modai, I., Endicott, J., Rivkin, O., Nechamkin, Y., Barak, P., . . . & Ponizovsky, A. (2000). Differences in quality of life domains and psychopathologic and psychosocial factors in psychiatric patients. *The Journal of Clinical Psychiatry, 61*, 880-889; quiz 890.

Sawyer, M.G., Arney, F.M., Baghurst, P.A., Clark, J.J., Graetz, B.W., Kosky, R.J., . . .& Zubrick, S.R. (2001). The mental health of young people in Australia: key findings from the child and adolescent component of the national survey of mental health and well-being. *The Australian and New Zealand Journal of Psychiatry, 35*, 806-814.

Sawyer, M.G., Whaites, L., Rey, J.M., Hazell, P.L., Graetz, B.W., & Baghurst, P. (2002). Health-related quality of life of children and adolescents with mental disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 41*, 530-537.

Schor, E.L. (1998). Children’s health and the assessment of health-related quality of life. In D. Drotar (Ed.), *Measuring Health-Related Quality of Life In Children And Adolescents* (pp. 25-39). Hillsdale, New Jersey: Lawrence Hillbaum.

Serra-Sutton, V., Ferrer, M., Rajmil, L., Tebe, C., Simeoni, M.C., & Ravens-Sieberer, U. (2009). Population norms and cut-off-points for suboptimal health related quality of life in two generic measures for adolescents: the Spanish VSP-A and KINDL-R. *Health and Quality of Life Outcomes, 7*, 35.

Simeoni, M.C., Auquier, P., Antoniotti, S., Sapin, C., & San Marco, J.L. (2000). Validation of a French health-related quality of life instrument for adolescents: the VSP-A. *Quality of Life Research, 9,* 393-403.

Simeoni, M.C., Sapin, C., Antoniotti, S., & Auquier, P. (2001). Health-related quality of life reported by French adolescents: a predictive approach of health status? *The Journal of Adolescent Health, 28*, 288-294.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*, 921-929.

Singh, I. (2013). Brain talk: power and negotiation in children's discourse about self, brain and behaviour. *Sociology of Health & Illness, 35*, 813-827.

Solans, M., Pane, S., Estrada, M.D., Serra-Sutton, V., Berra, S., Herdman, M., . . . & Rajmil, L. (2008). Health-related quality of life measurement in children and adolescents: a systematic review of generic and disease-specific instruments. *Value in Health, 11,* 742-764.

Spitzer, R.L., Kroenke, K., Linzer, M., Hahn, S.R., Williams, J.B., deGruy, F.V., 3rd, . . . Davies, M. (1995). Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. *JAMA, 274,* 1511-1517.

Svanborg, P., Thernlund, G., Gustafsson, P.A., Hägglöf, B., Schacht, A., & Kadesjö, B. (2009). Atomoxetine improves patient and family coping in attention deficit/hyperactivity disorder: a randomized, double-blind, placebo-controlled study in Swedish children and adolescents. *European Child and Adolescent Psychiatry,18,* 725-735.

Thaulow, C.M., & Jozefiak, T. (2012). A comparison between child psychiatric outpatients with AD/HD and anxiety/depression. *Nordic Journal of Psychiatry, 66*, 396-402.

The WHOQOL Group. (1993). Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). *Quality of Life Research, 2*, 153-159.

Topolski, T.D., Edwards, T.C., Patrick, D.L., Varley, P., Way, M.E., & Buesching, D.P. (2004). Quality of life of adolescent males with attention-deficit hyperactivity disorder. *Journal of Attention Disorders, 7*, 163-173.

Tran, K.D., Nguyen, C.D., Weedon, J., & Goldstein, N.A. (2005). Child behavior and quality of life in pediatric obstructive sleep apnea. *Archives of Otolaryngology -- Head & Neck Surgery, 131*, 52-57.

Ucer, O., & Gumus, B. (2014). Quantifying subjective assessment of sleep quality, quality of life and depressed mood in children with enuresis. *World Journal of Urology, 32*, 239-243.

Upton, P., Lawford, J., & Eiser, C. (2008). Parent-child agreement across child health-related quality of life instruments: a review of the literature. *Quality of Life Research, 17*, 895-913.

Varni, J.W., & Burwinkle, T.M. (2006). The PedsQL as a patient-reported outcome in children and adolescents with Attention-Deficit/Hyperactivity Disorder: a population-based study. *Health & Quality of Life Outcomes, 4*, 26.

Varni, J.W., Burwinkle, T.M., & Lane, M.M. (2005). Health-related quality of life measurement in pediatric clinical practice: an appraisal and precept for future research and application. *Health & Quality of Life Outcomes, 3*, 34.

Varni, J.W., Limbers, C.A., & Burwinkle, T.M. (2007a). How young can children reliably and validly self-report their health-related quality of life?: an analysis of 8,591 children across age subgroups with the PedsQL 4.0 Generic Core Scales. *Health & Quality of Life Outcomes, 5*, 1.

Varni, J.W., Limbers, C.A., & Burwinkle, T.M. (2007b). Parent proxy-report of their children's health-related quality of life: an analysis of 13,878 parents' reliability and validity across age subgroups using the PedsQL 4.0 Generic Core Scales. *Health & Quality of Life Outcomes, 5*, 2.

Varni, J.W., Seid, M., & Kurtin, P.S. (2001). PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Medical Care, 39*, 800-812.

Varni, J.W., Seid, M., & Rode, C.A. (1999). The PedsQL: measurement model for the pediatric quality of life inventory. *Medical Care, 37*, 126-139.

Vigerland, S., Ljotsson, B., Thulin, U., Ost, L.G., Andersson, G., & Serlachius, E. (2016). Internet-delivered cognitive behavioural therapy for children with anxiety disorders: A randomised controlled trial. *Behaviour Research and Therapy, 76*, 47-56.

Visser, S.N., Danielson, M.L., Bitsko, R.H., Holbrook, J.R., Kogan, M.D., Ghandour, R.M., . . . & Blumberg, S.J. (2014). Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *Journal of the American Academy of Child and Adolescent Psychiatry, 53*, 34-46 e32.

Vivan Ade, S., Rodrigues, L., Wendt, G., Bicca, M.G., & Cordioli, A.V. (2013). Quality of life in adolescents with obsessive-compulsive disorder. *Revista Brasileira de Psiquiatria, 35*, 369-374.

Weidle, B., Ivarsson, T., Thomsen, P.H., Lydersen, S., & Jozefiak, T. (2015). Quality of life in children with OCD before and after treatment. *European Child and Adolescent Psychiatry*, *24*, 1061-1074.

Werling, D.M., & Geschwind, D.H. (2013). Sex differences in autism spectrum disorders. *Current Opinion in Neurology, 26*, 146-153.

White-Koning, M., Arnaud, C., Dickinson, H.O., Thyen, U., Beckung, E., Fauconnier, J., . . & Colver, A. (2007). Determinants of child-parent agreement in quality-of-life reports: a European study of children with cerebral palsy. *Pediatrics, 120,* e804-814.

Whiteford, H.A., Degenhardt, L., Rehm, J., Baxter, A.J., Ferrari, A.J., Erskine, H.E., . . . Vos, T. (2013). Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet*, *382*, 1575-1586.

Wille, N., Badia, X., Bonsel, G., Burstrom, K., Cavrini, G., Devlin, N., . . .& Ravens-Sieberer, U. (2010). Development of the EQ-5D-Y: a child-friendly version of the EQ-5D. *Quality of Life Research, 19,* 875-886.

World Health Organization. (1946). Constitution of the World Health Organization. *American Journal of Public Health and the Nation's Health*, *36*, 1315-1323.

World Health Organization. (1993). *Measurement of quality of life in children: report of WHO/IACAPAP working party.* London, UK: WHO.

World Health Organization - Division of Mental Health. (1994). *Measurement of Quality of Life in Children. MNH/PSF/94.5.* Geneva: WHO.

Wuang, Y.-P., Wang, C.-C., & Mao-Hsiung, H. (2012). Health-related quality of life in children with developmental coordination disorder and their parents. *OTJR: Occupation, Participation and Health, 32*, 142-150.

Yang, P., Hsu, H.Y., Chiou, S.S., & Chao, M.C. (2007). Health-related quality of life in methylphenidate-treated children with attention-deficit-hyperactivity disorder: results from a Taiwanese sample. *Australian and New Zealand Journal of Psychiatry*, *41*, 998-1004.

Zambrano-Sanchez, E., Martinez-Cortes, J.A., del Rio-Carlos, Y., Dehesa-Moreno, M., & Poblano, A. (2012). Low quality of life scores in school children with attention deficit-hyperactivity disorder related to anxiety. *Arquivos de Neuro-Psiquiatria, 70*, 180-184.

Zaohuo, C., Beiling, G., & Jian, P. (1998). The Inventory of Subjective Life Quality for Child and adolescent: Development, Reliability, and Validity. *Chinese Journal of Clinical Psychology*, *6,* 11-16.

Table 1. Measure of quality of life used in the included studies

Instrument	**Reference**	**Subscales/domains**	**Age range**	**Used in *k* included studies**
Pediatric Quality of Life Inventory (PedsQL)	Varni et al., 1999, 2001	Physical; emotional; social; school functioning	5-13 years	*k*=19
Child Health Questionnaire – Parent Form 50 (CHQ-PF50)	Landgraf et al., 1996, 1999	General health, physical and psychosocial health and associated disabilities	5 years and older	*k*=5
Youth Quality of Life Instrument-Research Version (YQOL-R)	Edwards et al. 2002; Patrick et al., 2002	Self; relationships; environment; general QoL	Adolescents	*k*=3
Health Utilities Index Mark 3 (HUI3)	Horsman et al., 2003	Vision; hearing; speech; ambulation; dexterity; emotion; cognition; pain	Children/adolescents	*k*=2
Inventory for the Assessment of Life Quality in Children and Adolescents (ILK)	Mattejat et al., 2003	School; family; peers; interests and leisure; physical health; psychological health; global QoL	6-18 years	*k*=2
KINDL	Ravens-Sieberer & Bullinger, 1998; Bullinger et al., 2008	Physical wellbeing; emotional wellbeing; self-esteem; family; friends; school	4 years and older	*k*=2
Adolescent Quality of Life Mental Health Scale (AQOL-MHS)	Chavez et al., 2014	Self; peers; family; school; environment	12-18 years	*k*=1

AutoQuestionnaire Qualité de Vie-Enfant-Imagé (AUQUEI)	Assumpção et al., 2000	Autonomy; leisure; functioning; family	4-12 years	*k*=1
EuroQol Five Dimensions Health Questionnaire, Youth version (EQ-5D-Y)	Wille et al., 2010	Mobility; self-care; general activity; pain/physical symptoms; anxiety/depression	8 years and older	*k*=1
Inventory of Subjective Life Quality for Children and Adolescents (ISLQ)	Zaocho et al., 1998	Depression; anxiety; somatic symptoms; family life; peer intercourse; school life; living environment; self-awareness	Children/adolescents	*k*=1
Multidimensional Student’s Life Satisfaction Scale (MSLSS)	Huebner et al., 1998	Family; friends; school; living environment; self	8-18 years	*k*=1
Obstructive Sleep Apnea 18 (OSA-18)	Franco et al., 2000	Sleep disturbance; physical distress; emotional distress; daytime problems; caretakers' concerns	Children	*k*=1
Vécu et Santé Perçue de l’Adolescent (VSP-A)	Simeoni et al., 2000	Psychological and physical well-being; body image; vitality; friends; parents; teachers; medical staff; leisure; school performance; global QoL	11-18 years (adopted for 8-10 years)	*k*=1
World Health Organization Quality of Life Assessment (WHOQOL-BREF)	The WHOQOL Group, 1998	Physical health; psychological health; social relationships; environment	18 years and older	*k*=1

Table 2. Characteristics related to the study population and the control population in controlled studies of quality of life in children with attention-deficit hyperactivity disorder

Author, year	**Study population**				**Control population**			**Country**	**Additional eligible comparator(s)**	**Recruitment**	**Matching/ adjustment**
	Condition	**Diagnostic assessment**	**N (% females)**	**Age M (SD); range**	**Comparator**	**N (% females)**	**Age M (SD); range**				
Attention-Deficit/Hyperactivity Disorder											
Coghill & Hodgkins, 2015	ADHD	Structured instrument	213 (11%)	12.2 (2.7); 6-16	Healthy controls	117 (59%)	10.1 (2.8); 6-16	UK	Type 1 Diabetes Mellitus (n=58)	Outpatient clinics (ADHD, diabetes, and dental)	Adjustments for age and socioeconomic status
Escobar et al., 2005	ADHD	Structured instrument	120 (22%)	9.0 (1.9); 6-12	Healthy controls	120 (22%)	9.3 (1.8); 6-12	Spain	Asthmatic (n=93)	Specialist and pediatric clinics	Age-, gender- and healthcare area-matched comparison groups
Göker et al., 2011	ADHD	Clinical consensus	50 (20%)	10.3 (2.0); 7-15	Healthy controls	30 (27%)	10.2 (NR); 7-15	Turkey	N/A	Specialist clinic and schools	Age- and gender-matched healthy school children from the same country

Hakkaart-van Roijen et al., 2007	ADHD	Clinical consensus	65 (20%)	10.5 (2.7); NR	Children with no behaviour problems	47 (64%)	7.8 (1.0); NR	Netherlands	N/A	Patients being treated for ADHD by paediatricians, and non-matched groups of children from a large school population-based study on the detection of ADHD	N/A
Jafari et al., 2011	ADHD	Structured instrument	72 (20%)	11.4 (2.0); 8-18	School children	140 (NR)	NR	Iran	N/A	Specialist clinic	Age- and gender-matched school children from the same community
Kandemir et al., 2014	ADHD	Clinical consensus	76 (29%)	NR (NR); 7-16	Healthy controls	59 (37%)	NR (NR); 7-16	Turkey	N/A	Specialist clinic	Age-, gender-, family income level-, and family type-matched healthy children
Marques et al., 2013	ADHD	Clinical consensus	45 (22%)	9.8 (NR); 8-12	Typically developing	43 (19%)	9.2 (NR); 8-12	Brazil	N/A	Specialist clinic	School children similar in terms of age, gender,

											family income, parents' marital status, and parental education
Patrick et al., 2002	ADHD	Medical report document	68 (0%)	NR (NR); 12-18	No chronic condition	116 (41%)	NR (NR); 12-18	USA	Mobility disability (n=52)	Hospital, community and health clinics, and ads in local newspapers	N/A
Pongwilairat et al., 2005	ADHD	NR	46 (15%)	10.1 (1.5); 8-12	No chronic condition	94 (49%)	10.1 (1.3); 8-12	Thailand	N/A	Pediatric clinic	Children of the same age without chronic illnesses from the same hospital or a primary school in the same area
Thaulow & Jozefiak, 2012	ADHD	Clinical consensus	62 (37%)	NR (NR); 8-15.5	Healthy controls	65 (39%)	NR (NR); 8-16	Norway	N/A	Specialist clinic	Age- and gender-matched comparison groups from the same county
Topolski et	ADHD	Clinical consensus	55 (0%)	13.9 (1.6);	No chronic	107 (40%)	14.8 (1.6);	USA	Mobility	Specialist and	N/A

al., 2004		+ questionnaires		11-18	condition		NR		impairment (n=52)	health clinics, and ads in local newspapers	
Varni & Burwinkle 2006	ADHD	Parental report	72 (17%)	10.9 (3.1); 5-16	Healthy controls	3260 (48%)	10.7 (3.1); NR	USA	Cancer (=65); Cerebral palsy (n=57)	Statewide mail survey	Comparisons to samples randomly matched by age group
Yang et al., 2007	ADHD	Clinical consensus + questionnaires	119 (19%)	9.6 (1.8); 6-15	Healthy controls	129 (26%)	10.1 (2.2); 6-15	Taiwan	N/A	Specialist clinic; ADHD sample receiving methylphenidate treatment	Age-matched healthy controls recruited from the same community
Zambrano-Sánchez et al., 2012	ADHD	Clinical consensus	120 (27%)	9.0 (2.1); 7-12	School children	98 (23%)	9.4 (2.3); 7-12	Mexico	N/A	Specialist clinic	Age-, school grade-, and socioeconomic status-matched controls from the same school

Key: M, Mean; N/A, Not applicable; NR, Not reported; SD, Standard deviation

Table 3. Results of controlled studies of quality of life in children with attention-deficit hyperactivity disorder

Author, year	**Study population**		**Control population**			**QoL measure**	**Hedges’ *g* (95% CI) favouring the comparator**
	Self-reported M (SD)	**Parent-reported M (SD)**	**Comparator**	**Self-reported M (SD)**	**Parent-reported M (SD)**		
Attention-Deficit/Hyperactivity Disorder							
Coghill & Hodgkins, 2015	71.5 (SE=1.2)	61.8 (SE=1.2)	Healthy controls	88.0 (SE=1.7)	88.2 (SE=1.8)	PedsQL 4.0	Self: 0.92 (0.67; 1.18) Parent: 1.48 (1.22; 1.74)
Escobar et al., 2005	N/A	38.3 (7.5)	Healthy controls	N/A	53.2 (5.7)	CHQ-PF50 (QoL index reported using PSS)	2.23 (1.91; 2.55)
Göker et al., 2011	75.1 (15.8)	56.7 (15.6)	Healthy controls	79.6 (10.5)	76.9 (16.3)	PedsQL 4.0	Self: 0.32 (0.14; 0.77) Parent: 1.26 (0.77; 1.76)
Hakkaart-van Roijen et al., 2007	N/A	38.9 (NR)	Children with no behavior problems	N/A	52.9 (NR)	CHQ-PF50 (QoL index reported using PSS)	Significant difference
Jafari et al., 2011	62.39 (17.2)	57.06 (14.67)	School children	78.5 (12.8)	73.47 (17.1)	PedsQL 4.0	Self: 1.11 (0.81; 1.42) Parent: 1.00 (0.70; 1.30)

Kandemir et al., 2014	72.13 (15.02)	69.06 (14.32)	Healthy controls	83.35 (13.10)	81.92 (13.15)	PedsQL 4.0	Self: 0.78 (0.43; 1.14) Parent: 0.93 (0.57; 1.28)
Marques et al., 2013	69.15 (15.90)	67.10 (14.83)	Typically developing	79.28 (8.46)	88.64 (8.46)	PedsQL 4.0	Self: 0.77 (0.33; 1.20) Parent: 1.76 (1.26; 2.25)
Patrick et al., 2002	75.19 (SE=1.48)	N/A	No chronic condition	82.20 (SE=1.14)	N/A	YQOL-R	0.57 (0.26; 0.87)
Pongwilairat et al., 2005	1508.69 (312.25)	1362.50 (296.26)	No chronic condition	1779.25 (322.61)	1609.04 (362.43)	PedsQL 4.0	Self: 0.78 (0.43; 1.14) Parent: 0.72 (0.35; 1.08)
Thaulow & Jozefiak, 2012	73.6 (14.9)	62.5 (13.8)	Healthy controls	82.0 (13.5)	89.7 (9.4)	ILC/ILK	Self: 0.59 (0.23; 0.94) Parent: 2.30 (1.85; 2.75)
Topolski et al., 2004	73.95 (NR)	N/A	No chronic condition	81.74 (NR)	N/A	YQOL-R	Significant difference
Varni & Burwinkle, 2006	70.17 (18.28)	69.5 (16.17)	Healthy controls	84.29 (12.56)	79.87 (16.24)	PedsQL 4.0	Self: 1.11 (0.88; 1.35) Parent: 0.64 (0.40; 0.88)

Yang et al., 2007	N/A	34.48 (10.26)	Healthy controls	N/A	49.87 (7.56)	CHQ-PF50 (QoL index reported using PSS)	1.71 (1.42; 2.00)
Zambrano-Sánchez et al., 2012	45.2 (NR)	N/A	School children	54.3 (NR)	N/A	AUQUEI	Significant difference

Key: AUQUEI, AutoQuestionnaire Qualité de Vie-Enfant-Imagé; CHQ-PF50, Child Health Questionnaire – Parent Form 50; CI, Confidence Interval; ILC = The Inventory of Life Quality in Children and Adolescents; IQR, Inter Quartile Rage; M, Mean; N/A, Not applicable; NR, Not reported; PedsQL 4.0, Pediatric Quality of Life Inventory; PSS, Psychosocial Summary Score; QoL, Quality of Life; SD, Standard deviation; YQOL-R, Youth Quality of Life Instrument-Research Version

Table 4. Characteristics related to the study population and the control population in controlled studies of quality of life in children with neurodevelopmental disorders other than attention-deficit hyperactivity disorder

Author, year	**Study population**				**Control population**			**Country**	**Additional eligible comparator(s)**	**Recruitment**	**Matching/ adjustment**
	Condition	**Diagnostic assessment**	**N (% females)**	**Age M (SD); range**	**Comparator**	**N (% females)**	**Age M (SD); range**				
Autism spectrum disorder											
Bastiaansen et al., 2004	Pervasive developmental disorders	Structured instrument + questionnaires	28 (18%)	9.7 (2.4); 6-18	Children with no DSM-IV diagnosis	67 (43%)	12.6 (3.2); 6-18	Netherlands	N/A	Specialist clinics	N/A
de Vries & Geurts, 2015	Autism spectrum	Structured instrument +	119 (10%)	10.2 (1.3); 7.3-12.6	Typically developing	73 (43%)	10.1 (1.2); 8.0-12.9	Netherlands	N/A	Mental health care institutions,	School children aged 7-12 years

	disorder	clinical consensus								and Internet advertisements	with IQ above 80, and with absence of a seizure disorder
Domellöf et al., 2014	Autism spectrum disorders	Medical report document	61 (13%)	12 (3); 7-16	Intellectual disabilities	43 (40%)	12.3 (3.2); 7-17	Sweden	Movement disorders (n=38); hearing disabilities (n=33)	Specialist clinic	N/A
Petrou et al., 2010*	Any autistic disorder in children born preterm or normal term	Structured instrument + clinical consensus	11 (NR)	approximately 11 years	Any ADHD-diagnosis in children born preterm or term	17 (NR)	approximately 11 years	UK	Any conduct disorder (n=17)	Data from the EPICure study, a whole-population longitudinal study of all infants born at 20 to 25 completed weeks of gestation in the UK and Ireland	N/A
Petrou & Kupek, 2009	Autism spectrum disorders	Clinical consensus	105 (NR)	11.0 (NR); 5-16	Hyperactivity disorders	50 (NR)	10.9 (NR); 5-16	UK	Several health conditions	Data from the ‘‘Disability Survey 2000: Survey of Young People With a	Analyses were adjusted for age, gender, presence of siblings in the household,

										Disability and Sport''	family type, ethnicity, and housing tenure
Potvin et al., 2015	High-functioning autism	Medical report document + questionnaires	30 (13%)	9.2 (1.6); 7-13	Typically developing	31 (13%)	9.9 (1.9); 7-13	USA	N/A	Organizations for support and service, professional email lists, ASD-specific parent support groups	N/A
Intellectual disability											
Basgul et al., 2011	Intellectual disability	Reviewing children's files	221 (36%)	NR; 5-18	Healthy controls	217 (41%)	NR; 5-18	Turkey	N/A	Special education and an elementary school for disabled children	Age- and gender-matched healthy children from database
Brantley et al., 2002	Mental disability	Multidisciplinary team	80 (59%)	15.8 (1.1)	Typically developing	80 (59%)	16.5 (1.8)	USA	N/A	Schools	Race- and gender-matched students from regular schools

Elbasan et al., 2013	Mental retardation	Medical record	41 (NR)	6.6 (0.7); 5-7	Healthy controls	28 (NR)	5.9 (0.8); 5-7	Turkey	Cerebral palsy (n=34); hearing loss (n=27)	Specialist clinic	Age-matched school children
Golubovic & Skrbic, 2013	Intellectual disability	School records	67 (48%)	15.8 (14.7); 13-18	Typically developing	122 (49%)	15.5 (15.7); 13-18	Serbia	N/A	Schools	School children from same area/country
Motor disorders											
Eddy et al., 2011	Tourette’s disorder	Structured instrument + clinical consensus	50 (12%)	13.3 (2.3); 10-17	Healthy controls	102 (33%)	13.1 (1.7); 10-17	Italy/UK	Epilepsy (n=50)	Tertiary referral centre and local schools	N/A
Hao et al., 2010	Tourette’s disorder	NR	424 (31%)	NR; 8-12	Healthy controls	1583 (52%)	NR; 5-12	China	Leukemia (n=43); migraine (n=618); epilepsy (n=250)	Kindergarten, primary schools, and hospitals	N/A
Liu et al., 2014	Tourette’s disorder	Clinical consensus	107 (14%)	10.1 (1.1); NR	Healthy controls	107 (45%)	9.9 (1.0)	China	N/A	Pediatric clinic	N/A
O’Hare et al., 2015	Tourette’s disorder	Parental report	86 (15%)	11.4 (2.8); 7-16	Healthy controls	108 (27%)	11.3 (2.6); 7-16	Australia	N/A	Tourette Syndrome Associations	Parents of age- and gender-matched peers with no known

											psychiatric or medical diagnosis
Wuang et al., 2012	Developmental coordination disorder	Structured instrument	369 (39%)	11.2 (3.7); 7-15	Typically developing	360 (41%)	11.4 (4.1); 7-15	Taiwan	N/A	Medical centers, private clinics, and schools	Age-, gender, and SES-matched healthy controls from the same community

Key: M, Mean; N/A, Not applicable; NR, Not reported; SD, Standard deviation

*Also included in Tables 6 and 7 with a comparison between conduct disorder and ADHD

Table 5 Results of controlled studies of quality of life in children with neurodevelopmental disorders other than attention-deficit hyperactivity disorder

Author, year	**Study population**		**Control population**			**QoL measure**	**Hedges' *g* (95% CI) favouring the comparator**
	Self-reported M (SD)	**Parent-reported M (SD)**	**Comparator**	**Self-reported M (SD)**	**Parent-reported M (SD)**		
Autism spectrum disorder							

Bastiaansen et al., 2004	69.6 (14.0)	61.5 (13.1)	Children with no DSM-IV diagnosis	73.5 (13.2)	70.1 (14.7)	PedsQL 4.0	Self: 0.29 (-0.16; 0.73) Parent: 0.60 (0.15; 1.05)
de Vries & Geurts, 2015	N/A	32.9 (11.6)	Typically developing	N/A	9.2 (7.1)	PedsQL 4.0 (raw scores)	2.33 (1.96, 2.70)
Domellöf et al., 2014	80.7 (18.8)	N/A	Intellectual disabilities	79.4 (19.8)	N/A	EQ-5D-Y	-0.07 (-0.46; 0.32)
Petrou et al., 2010*	N/A	0.609 (0.257)	Any ADHD-diagnosis	N/A	0.629 (0.271)	HUI3	0.07 (-0.69; 0.83)
Petrou & Kupek, 2009	N/A	Median: 0.41 (IQR: 0.239-0.695)	Hyperactivity disorders	N/A	Median: 0.41 (IQR: 0.266-0.669)	HUI3	NS
Potvin et al., 2015	64.14 (13.24)	56.10 (13.58)	Typically developing	81.28 (10.79)	85.54 (8.75)	PedsQL 4.0	Self: 1.40 (0.84; 1.97) Parent: 2.55 (1.87; 3.24)
Intellectual disability							
Basgul et al 2011	N/A	60.41 (17.05)	Healthy controls	N/A	81.78 (11.81)	PedsQL 4.0	1.45 (1.24; 1.66)

Brantley et al 2002	2.99 (0.39)	N/A	Typically developing	3.05 (0.42)	N/A	MSLSS	0.15 (-0.16; 0.46)
Elbasan et al 2013	N/A	36.9 (25.3)	Healthy controls	N/A	85.7 (15.8)	CHQ-PF50 (QoL index reported using PSS)	2.20 (1.59; 2.81)
Golubovic & Skrbic 2013	76.78 (15.27)	66.99 (15.52)	Typically developing	84.14 (8.51)	82.12 (9.48)	PedsQL 4.0	Self: 0.64 (0.34; 0.95) Parent: 1.26 (0.93; 1.58)
Motor disorders							
Eddy et al 2011	307.12 (59.99)	N/A	Healthy controls	320.0 (47.74)	N/A	YQOL-R	0.25 (-0.09; 0.59)
Hao et al 2010	79.18 (11.45)	N//A	Healthy controls	86.52 (9.8)	N/A	PedsQL 4.0	0.72 (0.61; 0.83)
Liu et al 2014	57.32	N/A	Healthy controls	65.97	N/A	ISLQ	0.58 (0.31; 0.86)

	(15.45)			(14.07)			
O’Hare et al 2015	N/A	59.58 (18.06)	Healthy controls	N/A	82.84 (11.37)	PedsQL 4.0	1.57 (1.25; 1.90)
Wuang et al., 2012	N/A	40.6 (10.1)	Typically developing	N/A	49.1 (10.1)	CHQ-PF50 (QoL index reported using PSS)	0.84 (0.69; 0.99)

Key: CHQ-PF50, Child Health Questionnaire – Parent Form 50; CI, Confidence Interval; EQ-5D-Y, EuroQol Five Dimensions Health Questionnaire, Youth version; HUI3, Health Utilities Index Mark 3; ISLQ, Inventory of Subjective Life Quality for Children and Adolescents; IQR, Inter Quartile Rage; M, Mean; MSLSS, Multidimensional Student’s Life Satisfaction Scale; N/A, Not applicable; NS, Not significant; PedsQL 4.0, Pediatric Quality of Life Inventory; PSS, Psychosocial Summary Score; QoL, Quality of Life; SD, Standard deviation; YQOL-R, Youth Quality of Life Instrument-Research Version

*Also included in table 6 and 7 with a comparison between conduct disorder and ADHD

Table 6 Characteristics related to the study population and the control population in controlled studies of quality of life in children with mental disorders other than neurodevelopmental disorders

Author, year	**Study population**				**Control population**			**Country**	**Additional comparator(s)**	**Recruitment**	**Matching/ adjustment**
	Condition	**Diagnostic assessment**	**N (% females)**	**Age M (SD); range**	**Comparator**	**N (% females)**	**Age M (SD); range**				

Depressive disorders											
Kiss et al., 2009	Major depressive disorder	Structured instrument and clinical consensus	248 (48%)	11.5 (2.0); 7-15	Non-depressed controls	1695 (56%)	10.3 (2.2); 7-15	Hungary	N/A	Specialist clinic	N/A
Obsessive-compulsive and related disorders											
Vivan Ade et al., 2013	OCD	Structured instrument	75 (79%)	16.2 (1.1); 14-18	Healthy controls	150 (60%)	16.0 (1.0); 14-18	Brazil	N/A	Population based epidemiological study; high school students	N/A
Sleep-wake disorders											
Tran et al., 2005	Obstructive sleep apnea	Clinical consensus and polysomnography	42 (40%)	5.8 (2.5); 2-11.5	Children without a history of snoring, scheduled for unrelated elective surgery	41 (29%)	7.3 (3.8); 2,1-14	USA	N/A	Specialist clinic (pediatric otolaryngology)	N/A
Crabtree et al., 2004	Sleep-disordered breathing	Clinical consensus and polysomnography	41(49%)	10.2 (1.4); NR	Non-snoring healthy controls	31 (58%)	9.6 (0.9); 8-10	USA	Obese children with sleep disordered breathing (n=44)	Referral to hospital sleep medicine center	Age- and sex-matched control group
Furudate et al., 2014	Restless legs syndrome	Clinical consensus	25 (76%)	12.3 (3.8); 7-18	Siblings with no symptoms of RLS	28 (64%)	13.2 (NR); NR	Japan	N/A	Specialist clinic	Family

Inocente et al., 2014	Narcolepsy	Clinical consensus and polysomnography	117 (45%)	11.6 (3.1); 5-17.5	Healthy controls	69 (58%)	13.5 (3.2); 7-17	France	N/A	Hospitals	N/A
Elimination disorders											
Al-Zaben and Sehlo, 2015	Monosymptomatic nocturnal enuresis	Clinical consensus	43 (26%)	9.9 (1.8); 7-13	Healthy controls	40 (23%)	8.9 (1.7); 7-14	Saudi Arabia	Children punished for nocturnal enuresis (n=22)	Specialist clinic	Age- and gender-matched
Ertan et al., 2009	Monosymptomatic nocturnal enuresis	Clinical consensus	44 (71%)	9.9 (2.9); 6-15	Healthy controls	27 (63%)	11.1 (3.0); 6-15	Turkey	N/A	Paediatric nephrology outpatient department	N/A
Kilicoglu et al., 2014	Nocturnal enuresis	Clinical consensus	82 (40%)	9.6 (1.3); 8-12	Healthy controls	93 (45%)	9.5 (1.2); 8-12	Turkey	N/A	Specialist clinic	Age-, gender-, parental education level-, and SES-matched
Ucer and Gumus, 2014	Monosymptomatic nocturnal enuresis	Clinical consensus	101 (39%)	10.9 (2.1); 8-16	Healthy controls (children of hospital staff)	38 (37 %)	11.1 (1.9); 8-14	Turkey	N/A	Specialist clinic	N/A
Natale et al., 2009	Urinary incontinence	Structured instrument +	49 (42%)	7.3 (2.1); 5-13	Healthy controls	32 (41%)	7.3 (NR);	Germany		Specialist clinic	Age- and gender-matched

		clinical consensus					NR				
Disruptive, Impulse-Control, and Conduct Disorders											
Petrou et al., 2010*	Any conduct disorder in children born preterm or normal term	Structured instrument + clinical consensus	17 (NR)	Approximately 11 years	Any ADHD-diagnosis in children born preterm or normal term	17 (NR)	Approximately 11 years	UK	Any autistic disorder (n=11)	Data from the EPICure study, a whole-population longitudinal study of all infants born at 20 to 25 completed weeks of gestation in the UK and Ireland	N/A
Chavez et al., 2014	ODD/CD	Structured instrument	30 (NR)	NR; 12-18	ADHD	53 (NR)	NR; 12-18	Puerto Rico	N/A	Specialist clinics, and through the use of electronic media and posters	N/A

Key: M, Mean; N/A, Not applicable; NR, Not reported; SD, Standard deviation

*Also included in table 4 and 5 with a comparison between ASD and ADHD

Table 7 Results of controlled studies of quality of life in children with mental disorders other than neurodevelopmental disorders

Author, year	**Study population**			**Control population**			**QoL measure**	**Hedges' *g* (95% CI) favouring the comparator**
	Condition	**Self-reported M (SD)**	**Parent-reported M (SD)**	**Comparator**	**Self-reported M (SD)**	**Parent-reported M (SD)**		
Depressive disorders								
Kiss et al., 2009	Major depressive disorder	17.85 (NR)	16.5 (NR)	Non-depressed controls	23.44 (NR)	24.04 (NR)	ILK	Significant difference
Obsessive-compulsive and related disorders								
Vivan Ade et al., 2013	OCD	63 (18.1)	N/A	Healthy controls	71.4 (18.1)	N/A	WHOQOL-BREF	0.46 (0.18; 0.74)
Sleep-wake disorders								
Crabtree et al., 2004	Sleep disordered breathing	66 (18.1)	63.62 (19.1)	Non-snoring healthy controls	84.47 (15.5)	86.43 (11.2)	PedsQL 4.0	Self: 1.07 (0.57; 1.57) Parent: 1.39 (0.87; 1.92)
Furudate et al., 2014	Restless legs syndrome	70.7 (8.9)	N/A	Siblings with no symptoms of restless legs	87.2 (1.1)	N/A	PedsQL	2.64 (1.89; 3.39)
Inocente et al., 2014	Narcolepsy	Children (n=31): 58.8 (NR)	Parents (n= 83): 61.7 (NR)	Healthy controls	Children (n=23): 75.8 (NR)	Parents (n=60): 73.7 (NR)	VSP-A, VSP-P, VSP-E	Significant difference

		Adolescents (n=52): 60.4 (NR)			Adolescents (n=43): 69.5 (NR)			
Tran et al., 2005	Obstructive sleep apnea	N/A	4.0 (1.2)	Children without a history of snoring and scheduled for unrelated elective surgery	N/A	1.5 (0.5)	OSA-18	2.68 (2.08; 3.28)
Elimination disorders								
Al-Zaben and Sehlo, 2015	Monosymptomatic nocturnal enuresis	74.23 (4.11)	N/A	Healthy controls	82.21 (2.66)	N/A	PedsQL 4.0 (Psychosocial health summary score)	2.27 (1.71; 2.82)
Ertan et al., 2009	Monosymptomatic nocturnal enuresis	65.1 (11.0)	N/A	Healthy controls	67.4 (13.7)	N/A	KINDL-R	0.19 (-0.29; 0.67)
Kilicoglu et al., 2014	Nocturnal enuresis	68.74 (15.89)	65.47 (15.52)	Healthy controls	80.98 (11.16)	78.23 (12.22)	PedsQL 4.0	Self: 0.90 (0.59; 1.21) Parent: 0.92 (0.60; 1.23)
Ucer and Gumus, 2014	Monosymptomatic nocturnal enuresis	1659.9 (296.01)	N/A	Healthy controls (children of hospital staff)	1818.42 (227.92)	N/A	PedsQL 4.0	0.56 (0.19; 0.94)

Natale et al., 2009	Urinary incontinence	77 (13.1)	74 (9.8)	Healthy controls	76 (12.0)	78 (7.6)	KINDL-R	Self: -0.08 (-0.52; 0.37) Parent: 0.44 (-0.01; 0.89)
Disruptive, Impulse-Control, and Conduct Disorders								
Petrou et al., 2010*	Any conduct disorder in children born preterm or normal term	N/A	0.727 (0.260)	Any ADHD-diagnosis	N/A	0.629 (0.271)	HUI3	-0.36 (-1.04; 0.32)
Chavez et al., 2014	ODD/CD	59.47 (12.77)	N/A	ADHD	75.44 (12.74)	N/A	AQOL-MHS	1.24 (0.75; 1.73)

Key: AQOL-MHS, Adolescent Quality of Life Mental Health Scale; CI, Confidence Interval; HUI3, Health Utilities Index Mark 3; ILK, Inventory for the Assessment of Life Quality in Children and Adolescents; M, Mean; N/A, Not applicable; NR, Not reported; OSA-18, Obstructive Sleep Apnea 18; PedsQL 4.0, Pediatric Quality of Life Inventory; QoL, Quality of Life; SD, Standard deviation; VSP-A, Vécu et Santé Perçue de l'Adolescent; VSP-E, Vécu et Santé Perçue par l'Enfant; WHOQOL-BREF, World Health Organization Quality of Life Assessment

*Also included in table 4 and 5 with a comparison between ASD and ADHD

FIGURE LEGENDS

Figure 1 PRISMA flow-chart of review process and study selection

Figure 2 Self-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls

Figure 3 Parent-reported quality of life in children with attention-deficit hyperactivity disorder, as compared to healthy controls

Figure 4 Parent-reported quality of life in children with intellectual disability, as compared to typically developing children

Figure 5 Self-reported quality of life in children with Tourette's disorder, as compared to typically developing children

Figure 6 Self-reported quality of life in children with nocturnal enuresis, as compared to healthy controls

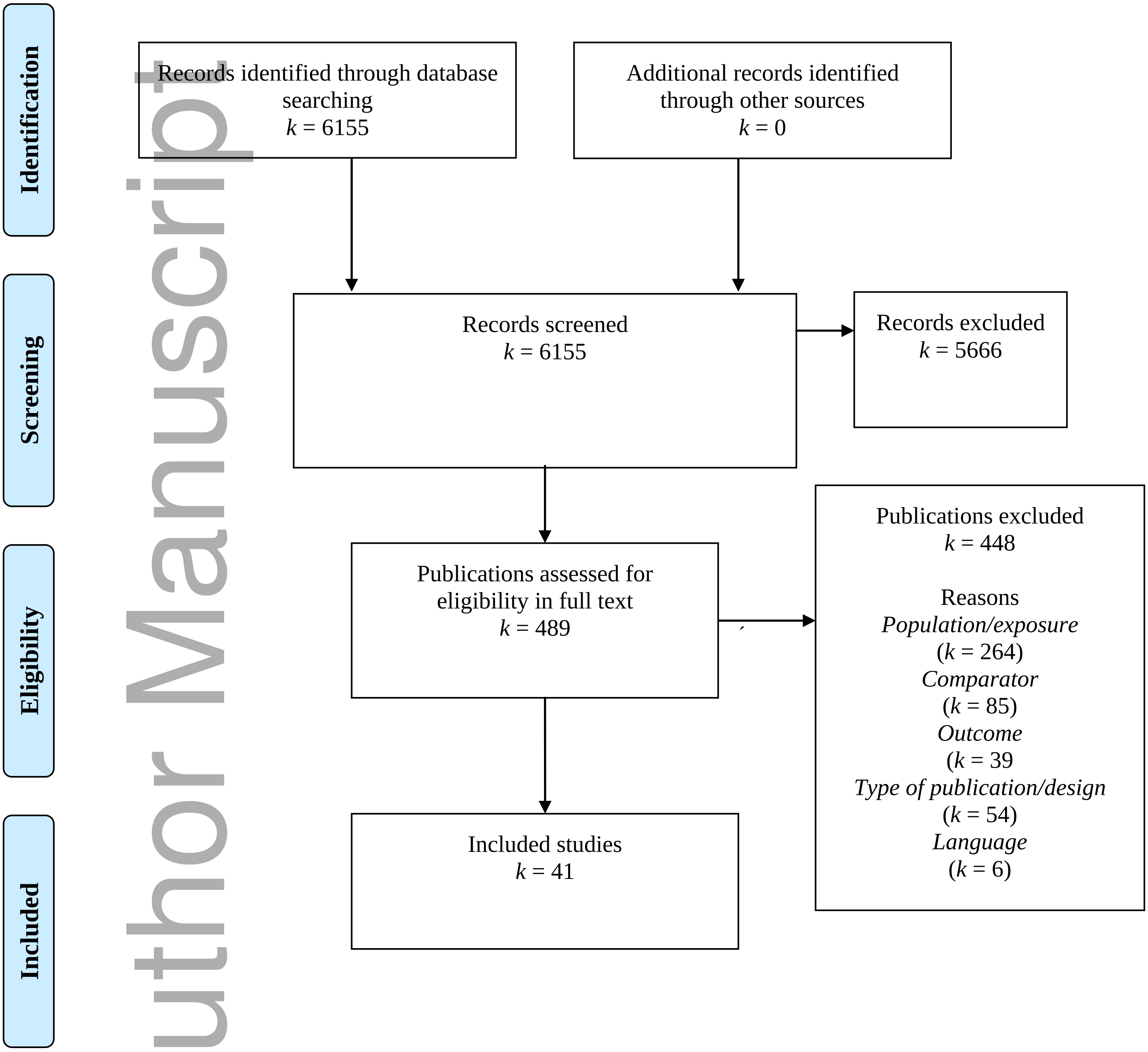
Figure 7 Self-reported results on the Physical Functioning dimension of the PedsQL across childhood mental disorders, as compared to healthy controls

Figure 8 Self-reported results on the Emotional Functioning dimension of the PedsQL across childhood mental disorders, as compared to healthy controls

Figure 9 Self-reported results on the Social Functioning dimension of the PedsQL across childhood mental disorders, as compared to healthy controls

Figure 10 Self-reported results on the School Functioning dimension of the PedsQL across childhood mental disorders, as compared to healthy controls

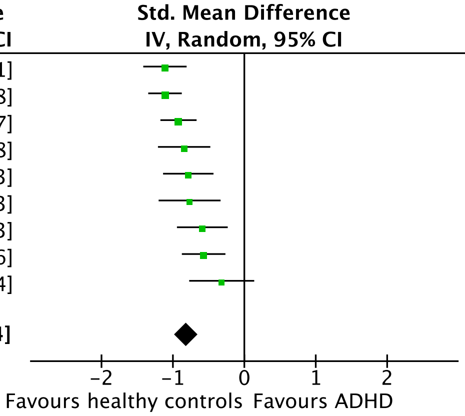
Figure 1 PRISMA flow-chart of review process and study selection



Study or Subgroup	ADHD Mean	ADHD SD	ADHD Total	Healthy controls Mean	Healthy controls SD	Healthy controls Total	Weight	Std. Mean Difference IV, Random, 95% CI
Jafari 2011	62.39	17.2	72	78.5	12.8	140	12.1%	−1.11 [−1.42, −0.81]
Varni and Burwinkle 2006	70.17	18.28	72	84.29	12.56	3256	14.3%	−1.11 [−1.35, −0.88]
Coghill and Hodgkins 2015	71.5	17.5134	174	88	18.3883	106	13.7%	−0.92 [−1.18, −0.67]
Pongwilairat 2005	1,508.69	312.25	46	1,779.25	322.61	94	10.2%	−0.84 [−1.21, −0.48]
Kandemir 2014	72.13	15.02	76	83.35	13.1	59	10.6%	−0.78 [−1.14, −0.43]
Marques 2013	69.15	15.8984	45	79.28	9.3116	43	8.5%	−0.77 [−1.20, −0.33]
Thaulow and Jozefiak 2012	73.6	14.9	62	82	13.5	65	10.5%	−0.59 [−0.94, −0.23]
Patrick 2002	75.19	12.2044	68	82.2	12.2782	116	12.0%	−0.57 [−0.87, −0.26]
Göker 2011	75.1	15.8	50	79.6	10.5	30	8.1%	−0.32 [−0.77, 0.14]
Total (95% CI)			**665**			**3909**	**100.0%**	**−0.81 [−0.98, −0.64]**

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 18.76$, df = 8 ($P = 0.02$); $I^2 = 57\%$

Test for overall effect: $Z = 9.50$ ($P < 0.00001$)



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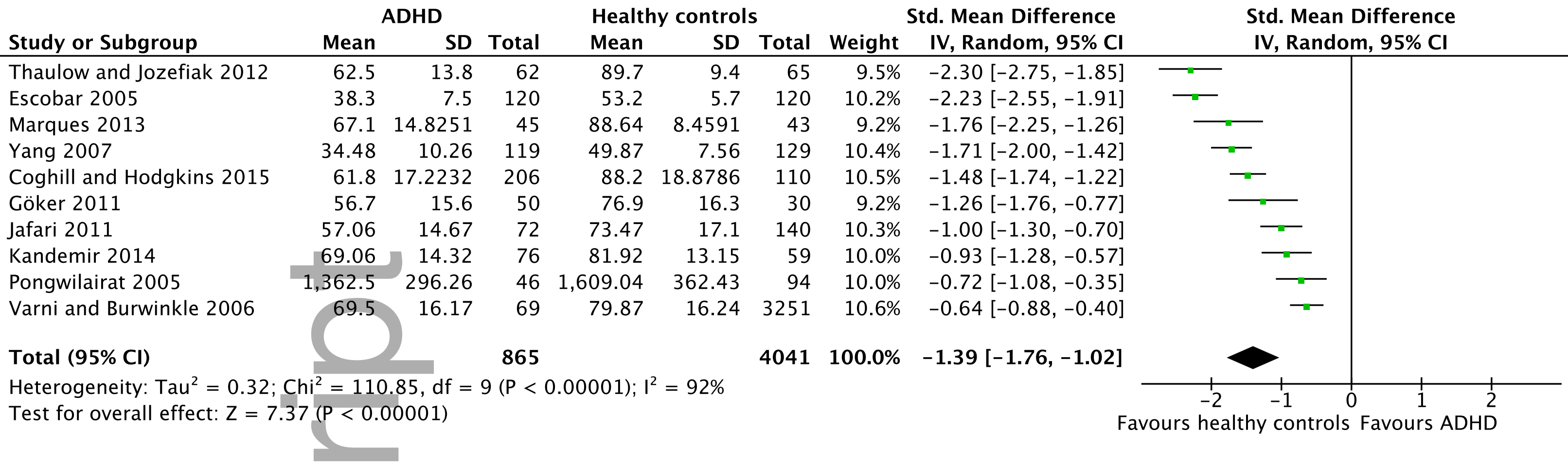

Study or Subgroup	ADHD Mean	ADHD SD	ADHD Total	Healthy controls Mean	Healthy controls SD	Healthy controls Total	Weight	Std. Mean Difference IV, Random, 95% CI
Thaulow and Jozefiak 2012	62.5	13.8	62	89.7	9.4	65	9.5%	−2.30 [−2.75, −1.85]
Escobar 2005	38.3	7.5	120	53.2	5.7	120	10.2%	−2.23 [−2.55, −1.91]
Marques 2013	67.1	14.8251	45	88.64	8.4591	43	9.2%	−1.76 [−2.25, −1.26]
Yang 2007	34.48	10.26	119	49.87	7.56	129	10.4%	−1.71 [−2.00, −1.42]
Coghill and Hodgkins 2015	61.8	17.2232	206	88.2	18.8786	110	10.5%	−1.48 [−1.74, −1.22]
Göker 2011	56.7	15.6	50	76.9	16.3	30	9.2%	−1.26 [−1.76, −0.77]
Jafari 2011	57.06	14.67	72	73.47	17.1	140	10.3%	−1.00 [−1.30, −0.70]
Kandemir 2014	69.06	14.32	76	81.92	13.15	59	10.0%	−0.93 [−1.28, −0.57]
Pongwilairat 2005	1,362.5	296.26	46	1,609.04	362.43	94	10.0%	−0.72 [−1.08, −0.35]
Varni and Burwinkle 2006	69.5	16.17	69	79.87	16.24	3251	10.6%	−0.64 [−0.88, −0.40]
Total (95% CI)			**865**			**4041**	**100.0%**	**−1.39 [−1.76, −1.02]**

Heterogeneity: $Tau^2 = 0.32$; $Chi^2 = 110.85$, df = 9 ($P < 0.00001$); $I^2 = 92\%$

Test for overall effect: $Z = 7.37$ ($P < 0.00001$)

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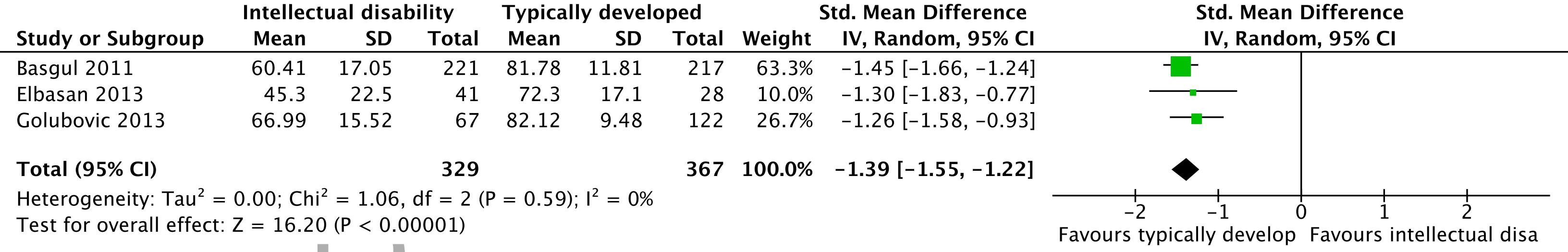

	Intellectual disability			Typically developed				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Basgul 2011	60.41	17.05	221	81.78	11.81	217	63.3%	−1.45 [−1.66, −1.24]
Elbasan 2013	45.3	22.5	41	72.3	17.1	28	10.0%	−1.30 [−1.83, −0.77]
Golubovic 2013	66.99	15.52	67	82.12	9.48	122	26.7%	−1.26 [−1.58, −0.93]
Total (95% CI)			**329**			**367**	**100.0%**	**−1.39 [−1.55, −1.22]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.06$, df = 2 ($P = 0.59$); $I^2 = 0\%$

Test for overall effect: $Z = 16.20$ ($P < 0.00001$)

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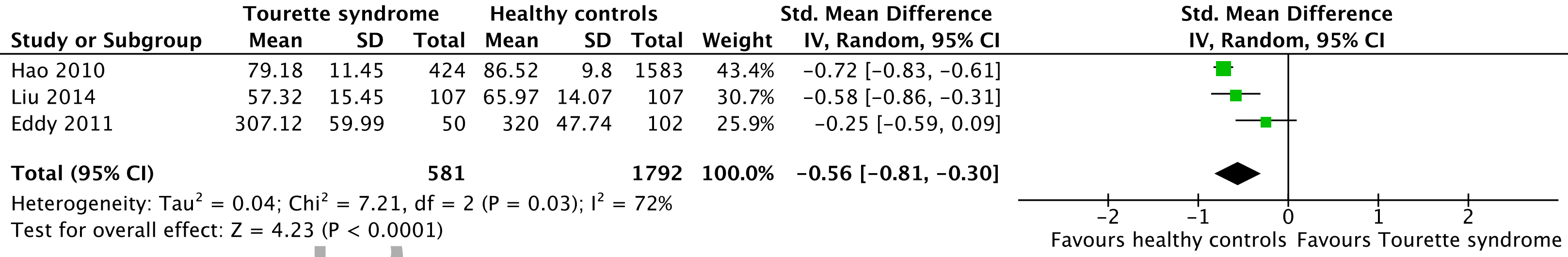

Study or Subgroup	Tourette syndrome Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Hao 2010	79.18	11.45	424	86.52	9.8	1583	43.4%	−0.72 [−0.83, −0.61]
Liu 2014	57.32	15.45	107	65.97	14.07	107	30.7%	−0.58 [−0.86, −0.31]
Eddy 2011	307.12	59.99	50	320	47.74	102	25.9%	−0.25 [−0.59, 0.09]
Total (95% CI)			**581**			**1792**	**100.0%**	**−0.56 [−0.81, −0.30]**

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 7.21$, df = 2 (P = 0.03); $I^2 = 72\%$
Test for overall effect: Z = 4.23 (P < 0.0001)

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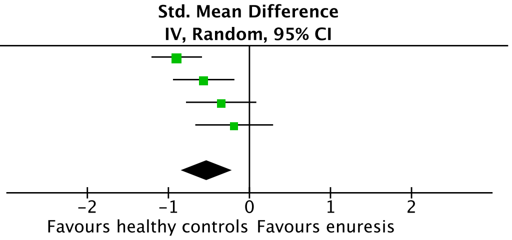
Study or Subgroup	Enuresis Mean	Enuresis SD	Enuresis Total	Healthy controls Mean	Healthy controls SD	Healthy controls Total	Weight	Std. Mean Difference IV, Random, 95% CI
Kilicoglu 2014	68.74	15.89	82	80.98	11.16	93	29.6%	−0.90 [−1.21, −0.59]
Ucer and Gumus 2014	1,659.9	296.01	101	1,818.42	227.92	38	26.0%	−0.56 [−0.94, −0.19]
Al-Zaben and Sehlo 2015	74.23	26.9511	43	82.21	16.8233	40	23.3%	−0.35 [−0.78, 0.08]
Ertan 2009	65.1	11	44	67.4	13.7	27	21.2%	−0.19 [−0.67, 0.29]
Total (95% CI)			**270**			**198**	**100.0%**	**−0.53 [−0.85, −0.22]**

Heterogeneity: Tau^2 = 0.06; Chi^2 = 7.62, df = 3 (P = 0.05); I^2 = 61%
Test for overall effect: Z = 3.32 (P = 0.0009)



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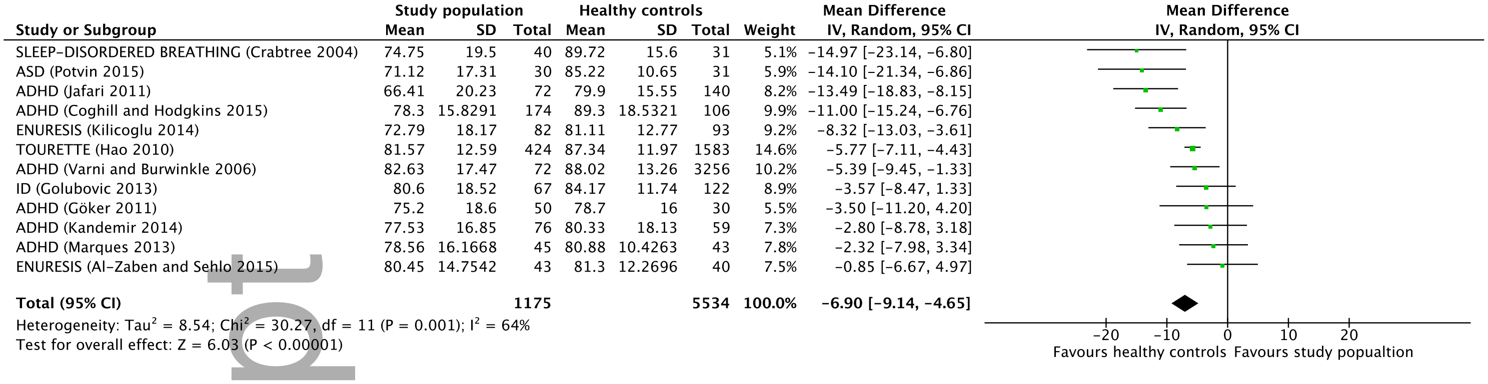

Study or Subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
SLEEP–DISORDERED BREATHING (Crabtree 2004)	74.75	19.5	40	89.72	15.6	31	5.1%	−14.97 [−23.14, −6.80]
ASD (Potvin 2015)	71.12	17.31	30	85.22	10.65	31	5.9%	−14.10 [−21.34, −6.86]
ADHD (Jafari 2011)	66.41	20.23	72	79.9	15.55	140	8.2%	−13.49 [−18.83, −8.15]
ADHD (Coghill and Hodgkins 2015)	78.3	15.8291	174	89.3	18.5321	106	9.9%	−11.00 [−15.24, −6.76]
ENURESIS (Kilicoglu 2014)	72.79	18.17	82	81.11	12.77	93	9.2%	−8.32 [−13.03, −3.61]
TOURETTE (Hao 2010)	81.57	12.59	424	87.34	11.97	1583	14.6%	−5.77 [−7.11, −4.43]
ADHD (Varni and Burwinkle 2006)	82.63	17.47	72	88.02	13.26	3256	10.2%	−5.39 [−9.45, −1.33]
ID (Golubovic 2013)	80.6	18.52	67	84.17	11.74	122	8.9%	−3.57 [−8.47, 1.33]
ADHD (Göker 2011)	75.2	18.6	50	78.7	16	30	5.5%	−3.50 [−11.20, 4.20]
ADHD (Kandemir 2014)	77.53	16.85	76	80.33	18.13	59	7.3%	−2.80 [−8.78, 3.18]
ADHD (Marques 2013)	78.56	16.1668	45	80.88	10.4263	43	7.8%	−2.32 [−7.98, 3.34]
ENURESIS (Al–Zaben and Sehlo 2015)	80.45	14.7542	43	81.3	12.2696	40	7.5%	−0.85 [−6.67, 4.97]
Total (95% CI)			**1175**			**5534**	**100.0%**	**−6.90 [−9.14, −4.65]**

Heterogeneity: $Tau^2 = 8.54$; $Chi^2 = 30.27$, df = 11 (P = 0.001); $I^2 = 64\%$

Test for overall effect: Z = 6.03 (P < 0.00001)

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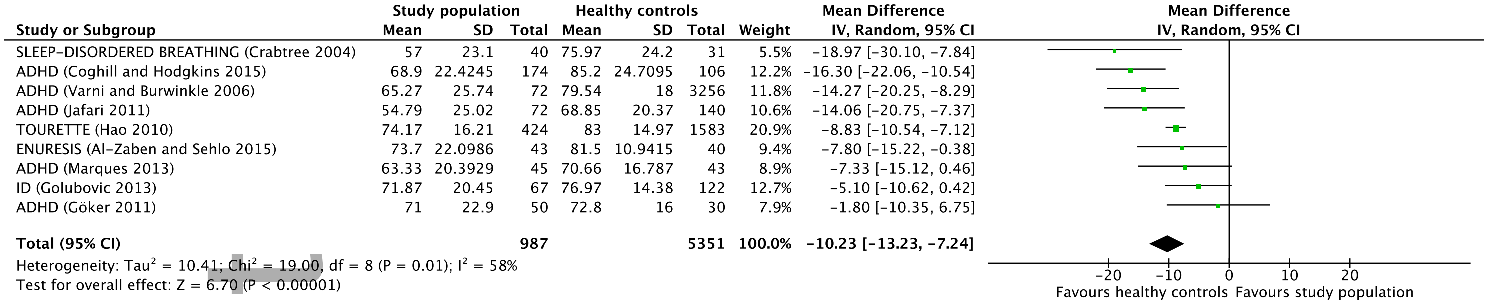

Study or Subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
SLEEP–DISORDERED BREATHING (Crabtree 2004)	57	23.1	40	75.97	24.2	31	5.5%	−18.97 [−30.10, −7.84]
ADHD (Coghill and Hodgkins 2015)	68.9	22.4245	174	85.2	24.7095	106	12.2%	−16.30 [−22.06, −10.54]
ADHD (Varni and Burwinkle 2006)	65.27	25.74	72	79.54	18	3256	11.8%	−14.27 [−20.25, −8.29]
ADHD (Jafari 2011)	54.79	25.02	72	68.85	20.37	140	10.6%	−14.06 [−20.75, −7.37]
TOURETTE (Hao 2010)	74.17	16.21	424	83	14.97	1583	20.9%	−8.83 [−10.54, −7.12]
ENURESIS (Al–Zaben and Sehlo 2015)	73.7	22.0986	43	81.5	10.9415	40	9.4%	−7.80 [−15.22, −0.38]
ADHD (Marques 2013)	63.33	20.3929	45	70.66	16.787	43	8.9%	−7.33 [−15.12, 0.46]
ID (Golubovic 2013)	71.87	20.45	67	76.97	14.38	122	12.7%	−5.10 [−10.62, 0.42]
ADHD (Göker 2011)	71	22.9	50	72.8	16	30	7.9%	−1.80 [−10.35, 6.75]
Total (95% CI)			**987**			**5351**	**100.0%**	**−10.23 [−13.23, −7.24]**

Heterogeneity: Tau^2 = 10.41; Chi^2 = 19.00, df = 8 (P = 0.01); I^2 = 58%

Test for overall effect: Z = 6.70 (P < 0.00001)

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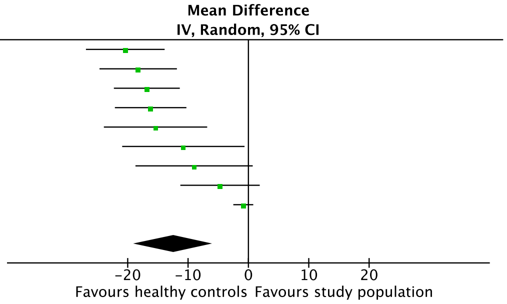
Study or Subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
ADHD (Varni and Burwinkle 2006)	65.55	28.12	72	85.95	16.49	3256	11.3%	−20.40 [−26.92, −13.88]
ADHD (Jafari 2011)	66.11	24.88	72	84.37	17.19	140	11.4%	−18.26 [−24.67, −11.85]
ID (Golubovic 2013)	76.94	21.9	67	93.77	8.61	122	11.7%	−16.83 [−22.29, −11.37]
ADHD (Coghill and Hodgkins 2015)	75	22.4245	174	91.2	25.7391	106	11.5%	−16.20 [−22.13, −10.27]
ADHD (Marques 2013)	65.77	26.6316	45	81.16	11.9345	43	10.5%	−15.39 [−23.95, −6.83]
SLEEP−DISORDERED BREATHING (Crabtree 2004)	73.25	23.2	40	84.03	20.3	31	9.8%	−10.78 [−20.92, −0.64]
ENURESIS (Al−Zaben and Sehlo 2015)	73.7	26.6888	43	82.7	17.8985	40	10.0%	−9.00 [−18.72, 0.72]
ADHD (Göker 2011)	83.3	18.2	50	88	11.8	30	11.3%	−4.70 [−11.28, 1.88]
TOURETTE (Hao 2010)	89.19	16.03	424	90.04	12.85	1583	12.6%	−0.85 [−2.50, 0.80]
Total (95% CI)			**987**			**5351**	**100.0%**	**−12.42 [−19.00, −5.83]**

Heterogeneity: $Tau^2 = 88.63$; $Chi^2 = 101.32$, df = 8 ($P < 0.00001$); $I^2 = 92\%$

Test for overall effect: Z = 3.70 (P = 0.0002)



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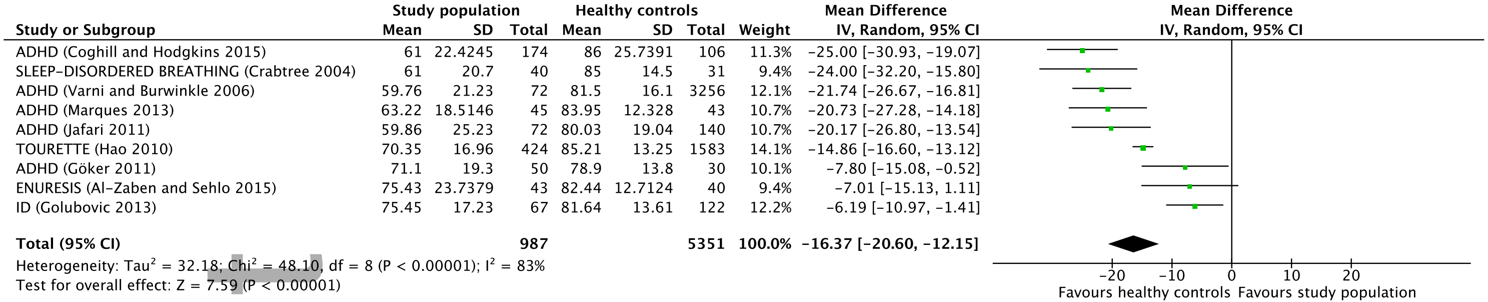

Study or Subgroup	Study population Mean	SD	Total	Healthy controls Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
ADHD (Coghill and Hodgkins 2015)	61	22.4245	174	86	25.7391	106	11.3%	−25.00 [−30.93, −19.07]
SLEEP−DISORDERED BREATHING (Crabtree 2004)	61	20.7	40	85	14.5	31	9.4%	−24.00 [−32.20, −15.80]
ADHD (Varni and Burwinkle 2006)	59.76	21.23	72	81.5	16.1	3256	12.1%	−21.74 [−26.67, −16.81]
ADHD (Marques 2013)	63.22	18.5146	45	83.95	12.328	43	10.7%	−20.73 [−27.28, −14.18]
ADHD (Jafari 2011)	59.86	25.23	72	80.03	19.04	140	10.7%	−20.17 [−26.80, −13.54]
TOURETTE (Hao 2010)	70.35	16.96	424	85.21	13.25	1583	14.1%	−14.86 [−16.60, −13.12]
ADHD (Göker 2011)	71.1	19.3	50	78.9	13.8	30	10.1%	−7.80 [−15.08, −0.52]
ENURESIS (Al−Zaben and Sehlo 2015)	75.43	23.7379	43	82.44	12.7124	40	9.4%	−7.01 [−15.13, 1.11]
ID (Golubovic 2013)	75.45	17.23	67	81.64	13.61	122	12.2%	−6.19 [−10.97, −1.41]
Total (95% CI)			**987**			**5351**	**100.0%**	**−16.37 [−20.60, −12.15]**

Heterogeneity: Tau^2 = 32.18; Chi^2 = 48.10, df = 8 (P < 0.00001); I^2 = 83%

Test for overall effect: Z = 7.59 (P < 0.00001)