The Quality of Life of Children with Attention Deficit/Hyperactivity Disorder and Related Disorders: A Systematic Review

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Abstract

Background: Quality of life (QoL) is increasingly considered an important outcome in child mental health research, and measures of QoL are increasingly included in studies of the impact of childhood disorders on everyday functioning and as an outcome in treatment ADHD trials. In the current paper we provide a systematic review of empirical studies of ADHD and QoL. Method: In part one, we summarise key conceptual and methodological issues. Part two provides a review of studies of the impact of ADHD on QoL. Three questions are asked. Is QoL reduced in ADHD cases compared to non-clinical controls? Is QoL reduced in ADHD cases compared to children with other mental or physical health disorders? Can factors other than ADHD itself (such as social class or comorbid disorders) explain the impact of ADHD on QoL. Part three reviews treatment studies which have included QoL as an outcome variable. Results: ADHD has a negative impact on a broad range of QoL outcomes to a degree which is equivalent to other chronic mental and physical disorders, effects which are not accounted for by comorbidities or confounding factors alone. Treatment-related improvements in ADHD symptoms are frequently associated with improvements in QoL. Conclusion: ADHD seriously compromises QoL especially when see from the perspective of the parents. QoL outcomes should be included as a matter of course in all treatment studies.

As medicine has moved on from a "life preserving" to a "health promoting" science (World Health Organisation, 1947), Quality of Life (QoL) has become an increasingly important concept in the study of medical conditions, their impact and their outcome (Coghill et al., submitted). The QoL concept is subject to a multiplicity of definitions, but all, to a greater or lesser extent, emphasise the ideal state as one of general well-being in which an individual's day-to-day functioning, across a wide range of domains, is unencumbered by the potentially adverse impact of disease or disorder. Although QoL is influenced by many proximal (i.e., family, friendship) and distal (socio-economic and cultural) forces, illness is one of the most potent influences (Eiser & Morse, 2001). In addition to the effects of physical illness on QoL, there is now substantial support for mental illness also having major impact (Bastiaansen et al., 2004; Moss et al., 2007; Rudnick, 2001). Where children or adults suffer mental disorders these impact on their capacity to engage effectively in daily activities with knock on consequences for their general sense of well-being. In childhood, these effects are perhaps most obvious for the most severe of extreme forms of mental health problem (e.g. autism) or those that impact directly on an individual's sense of self worth (e.g. anxiety and depression). However, there is growing evidence that the, so called, externalising disorders such as oppositional defiant disorder and attention deficit/hyperactivity disorder (ADHD) also substantially reduce the QoL of children and young people in terms of their subjective sense of wellbeing and their capacity for everyday functioning. The goal of the current paper is to address the issue of QoL in externalising disorders through a systematic review of the published literature on QoL in ADHD and related childhood disorders.

ADHD is a high prevalence disorder of childhood and adolescence marked by early onset, persistent and pervasive patterns of inattention, overactivity and impulsivity. It is associated with impairment across a range of domains. More specifically it is associated with educational under-achievement (Wilson & Marcotte, 1996), family-related and peer

relationship problems (August, Braswell, & Thuras 1998; Bagwell et al. 2001; Erhardt & Hinshaw 1994) and increased anti-social and delinquent activity (Satterfield et al, 1994). Long term adverse outcomes include increased risk of substance abuse (Biederman et al., 1998), reduced vocational opportunities (Barkley et al., 2006) and increased criminal activity (Satterfield & Schell, 1997). ADHD is often comorbid with other disorders such as oppositional defiant disorder (ODD), conduct disorder (CD), depression and anxiety (Biederman et al., 2006; Biederman, Faraone, & Lapey, 1992). ADHD can be successfully managed by a combination of stimulant medication and psychosocial approaches which reduce both symptoms and global levels of impairment. While generally well tolerated stimulant medication has a range of side-effects in a substantial minority of children (Banaschewski et al., 2006; Barkley et al., 1990; Graham & Coghill, 2008). Key questions for the current paper therefore are (i) what are the relationships between ADHD symptoms, functional impairment and QoL for the child with ADHD?(ii) Does symptom reduction, and improved daily functioning following treatment, translate into an improved QoL? (iii) How do the side effects of treatment affect QoL? (iv) Do different treatment combinations have different effects on QoL? (v) Is it ADHD itself or its comorbidities that impact on QoL?

These questions are important for a number of reasons. First, QoL is arguably the most important treatment outcome, for the patient and those around them, often outweighing short-term symptom reduction. If a treatment reduces symptoms but does not increase QoL can it be considered effective? Second, assessing QoL, allows one to directly compare the impact of ADHD against the impact of other physical and mental health conditions – this has the potential to provide an evidence base for a rational reconsideration of the ways that resources are allocated within health services. Third, within each individual child and adolescent mental health service, the use of QoL data could assist with service planning and audit – by focusing attention on the outcomes that the patients themselves feel are important.

Fourth, QoL measurement is central to the calculation of cost-effectiveness of different treatments and hence to the choices between treatments, both at an economic level (e.g. reimbursement of drug treatment costs) and at an individual patient level.

1) A brief overview of conceptual and measurement issues

Despite the obvious importance of the issue at hand, the QoL concept has been difficult to define precisely and its measurement has been problematic. A comprehensive and broad-based review of these issues can be found in a recent paper by the authors (Coghill et al., submitted). By definition some impairment from the symptoms of ADHD should be present in two or more settings (e.g., at school and at home) in order to fulfil either of the DSM-IV-TR (American Psychiatric Association, 2000) or ICD-10 (World Health Organization, 1996) diagnostic criteria However the concepts of symptoms, associated functional impairments, and QoL, have not been delineated clearly and consistently. For instance, items relating to each of these elements are often being included in QoL instruments and there is great potential for overlap between instruments and items used to measure ADHD symptoms and those used to measure QoL. It is therefore vital that, as far as possible, we draw clear distinctions between the symptoms (e.g., poor concentration) and their potential effects (i.e., functional impairment and reduced QoL). If this is not achieved there is a risk that apparent QoL effects are so closely related to symptoms and impairment that their association with the disorder will become a tautology.

Of the many instruments available to measure QoL, not all have been developed according to accepted guidelines nor do they have good psychometric properties. The concept of "validity" with regards QoL instruments is particularly difficult given the lack of an agreed and objective gold standard of QoL to measure them against; current approaches to testing the validity of the QoL concept employ quantitative (e.g. factor analysis) and qualitative (e.g. patient debriefing questionnaires and patient panels) techniques.

There is also value in considering the usefulness of both generic and condition-specific measures, both in general and in relation to ADHD specifically. Generic measures are designed to be more comprehensive, but may be less sensitive to treatment-related change. ADHD-specific measures or modules focus in on areas of particular concern in relation to that specific disorder; (e.g., the issue of stimulant drug treatments and/or their side effects). Two disorder-specific instruments for measurement of disease and treatment impact in children with ADHD are known to the authors: the AIM, (*ADHD Impact module*), developed by Landgraf and colleagues (Landgraf, Rich, & Rappaport, 2002) and the WFIRS (*Weiss Functional Impairment Rating Scale*) which is currently being used in several pharmacological studies (Weiss, personal communication). Published psychometric data are still largely lacking on these instruments. The AIM has shown statistically significant differences between ADHD-combined and ADHD-inattentive subtypes, with better functioning at home for the latter (Landgraf, Rich, & Rappaport, 2002).The WFIRS is a 50-item parent-rated Likert-based measure of functioning across 6 domains: *family, learning and school, life skills, child's self concept, social activities and risky activities*. Overlap with ADHD-symptoms is deliberately avoided.

While generic QoL measures allow comparison between ADHD and other conditions, they may not capture certain aspects of its impact or its treatment response. However, there may be a particular risk of overlap between items measuring ADHD symptoms and those measuring QoL. For instance, items relating to concentration have been included in generic QoL scales.

Measures that have been used in studies of QoL and ADHD, while covering the accepted core QoL domains (physical, psychological, cognitive and social) each measure defines these domains in different ways and includes different sub-domains. This means that there is a considerable amount of inter-instrument non-overlap between studies which can make direct

comparisons problematic. As a consequence we cannot simply assume equal coverage by different measures or that all generic QoL measures cover the necessary ground – there is therefore a need to interrogate instruments at the sub-scale and even the item-level to ensure appropriate coverage.

The majority of studies in relation to ADHD have used parent/carers as informants which will allow only a partial sense of the overall impact of the condition on QoL. This may be an especially important constraint on the validity of studies because QoL is seen primarily as a patient-reported outcome (Matza et al., 2004; Spitzer et al., 1995) with a key distinction being between independent assessment (e.g., he/she cannot concentrate and this stops him or her functioning at school and I think he/she should feel bad about this) and the "subjective" appraisal (I can't concentrate, this stops me working at school and I feel badly about this and it impacts generally on how I feel about myself). For this reason parent and/or carer ratings are often described as proxy ratings of a child's perspective. A child report seems essential to capture their QoL, in the sense implied by current definitions. However, young children (e.g., before the age of seven or eight years of age) may lack the understanding, insight or communication skills to provide valid self ratings (Bibace & Walsh, 1980). This may be a particular problem for children with learning disabilities, where mental health conditions impact on the ability to reflect and report upon ones state accurately (e.g., depression), or, as is often the case with ADHD, children are unable to concentrate and apply themselves to answering a questionnaire. In these cases one may have to rely on a rating by parents or carers. However, one should be aware that the levels of child-other informant agreement are low, especially in regard to non-observable aspects of QoL. Parent/carer ratings may however be useful as they provide an important alternative perspective to that of the child. Whilst parents or guardians are usually considered the most valuable alternative informant, teachers and clinicians can also be used and can sometimes provide important insights. In situations

where it is felt important to have both self- and other informant-rated QoL then it is essential to select an instrument with both child and adult versions that can provide an integrated index of overall QoL.

It is likely that in addition to having different abilities to report on their QoL at different ages, there will also be major age-related differences in the way individuals value different aspects of QoL, the ways in which they can express these and the ways that they interact with each other. It is inevitable that in selecting an instrument for a particular age group one will have to trade-off the age specificity of item content with the benefits of potential comparability across ages (Matza et al., 2004). If one focuses too much on adapting instruments for use by a specific age group then it is likely that it will become more difficult to compare or to pool data collected from subjects of different ages. On the other hand, if an instrument does not cover the necessary constructs within an age then the validity of the instrument will inevitably be compromised. Careful piloting of proposed instruments within the age range to be studied is therefore essential. Ways in which instruments can be tailored to the age of their child participants include; ensuring that questionnaires are short and written in simple (age appropriate) language; changing questionnaires into interviews (Rebok et al., 2001; Juniper et al., 1997); attempting to reduce the influence of the adult over the child's responses during face-to-face administration; using pictorial response formats such as *smiley*, *neutral* and *sad* faces (Christie et al. 1993; Rebok et al., 2001; Eiser & Morse, 2001; Harter & Pike, 1984); using props and puppets (Mize & Ladd, 1988); possibly, computer-administered measures (Eiser et al,. 1999; Gringras et al., 2006); and ensuring that an appropriate recall period is selected as younger children can have difficulties with the time concepts such as 1 week or 1 month (Rebok et al., 2001).

2) Studies of quality of life in children with ADHD

We conducted a systematic literature search through PubMed using ADHD and "quality of life" as key words and searched from 1990-2007. Included were English-language articles that contained at least some empirical data on QoL measurement in children or adolescents with ADHD and used a QoL instrument. Excluded were studies in adults. It would be inaccurate to say that the QoL of children with ADHD has not been studied in the past. However early studies which investigate the impact of ADHD on day-to-day functioning across a broad set of domains (Barkley et al., 1990, 1991; Biederman et al., 1994) lacked; (i) an assessment of general overall well-being and; (ii) the patient-reported and subjective element so central to contemporary definitions of QoL.

Functional impairment is a necessary component of an ADHD diagnosis, and clinical guidelines (Taylor et al., 2004) have encouraged its measurement using instruments such as the Children's Global Assessment Scale (CGAS) by Shaffer et al. (1983) which makes a rating based on the clinician's judgement. Rimmer et al. (2007) found low correlations between the CGAS and child ratings of QoL. As it involves general ratings the CGAS, do not capture the diversity of QoL domains or the distinctiveness of the parent or the child perspectives. Despite the aforementioned requirement for functional impairment in the diagnosis of ADHD, assessment of the therapeutic effects of treatment has historically been almost exclusively restricted to measurement of symptom change. Over the past few years, however, a broader focus has started to emerge which encompasses measurement of QoL in both the assessment of ADHD and the measurement of the effects of treatment. Below we review the published studies.

(i) Case-controls differences in QoL

Several studies have compared QoL in samples of children and adolescents with ADHD with normal controls or against existing normative data on QoL from standardised instruments.

With two exceptions (Sawyer et al., 2002; Varni & Burwinkle, 2006) all studies included only clinical samples.

Parent/carer report: During the development of the parent version of the *Child Health Questionnaire* (CHQ-PF50), Landgraf et al. (1999) were the first to report that an ADHD sample showed significantly lower scores on CHQ-*psychosocial* and *family* subscales (*behaviour, mental health, self-esteem, role limitations – emotional/behavioural, parental impact – emotional and time, family activities and family cohesion*) and the psychosocial summary score, compared to their norm group. Later, these findings were replicated in different clinical ADHD samples when compared to either US norms (Brown et al., 2006; Klassen, Miller, & Fine, 2004; Matza et al., 2004; Matza et al., 2005; Perwien et al., 2004; Perwien et al., 2006; Rentz et al., 2005) or controls (Hakkaart-van Roijen et al., 2007; Sawyer et al., 2002). These differences were found, both for male and female subjects. The largest differences were observed on subscales of *family impact* (*family activities, parental time emotional*), *behaviour* and *role-emotional/behavioural*. The *psychosocial* summary score for children with ADHD in the different studies ranged between 27.6 and 34.4, which is between 1.5 and 2 SD below the US norms. Comparing different ADHD-subtypes on this measure, all three subtypes had worse scores than controls on the psychosocial summary scale and most subscales. The combined and inattentive subtypes had significantly lower scores on some of the subscales than the hyperactive-impulsive type and the combined subtype in turn showed worse scores on some subscales than the inattentive subtype (Graetz et al., 2001).

On the *physical* domain parents did not rate children with ADHD to have lower QoL (Klassen, Miller, & Fine, 2004; Matza et al., 2004; Perwien et al., 2004; Rentz et al., 2005). Children with ADHD were also reported by their parents to have similar physical health compared to controls in a Thai sample, using the *PedsQL-4.0* (Varni, Seid, & Rode, 1999), which contrasted with the lower total and *psychosocial* scores on the *emotional, social* and

school subscales (Pongwilairat et al., 2005). In two studies, few parents of children with ADHD-related problems reported difficulties on the *physical* items (e.g.,*mobility* and *pain/discomfort*) of the EQ-5D (EuroQol Group, 1990) parent version. In contrast the majority endorsed problems with emotions and the ability to exert usual activities (Matza et al., 2005). In a community study, however, (Sawyer et al., 2002; Varni & Burwinkle, 2006) small but significant differences were found on the parent-reported *physical* subscales of the CHQ-PF50. This may be due to the broader scope of this study. Escobar et al. (2005) was the only study to report a significantly lower *physical* summary score in children with newly diagnosed ADHD, compared to a control sample.

Klassen (2005) computed the effect sizes for several of the above studies, using the CHQ-PF 50 and the criterion of Norman et al. (2003) which proposes that, in QoL research, a difference of at least half a standard deviation is required for a "clinically meaningful difference". There were clinically important deficit in QoL on all *psychosocial* and *family* subscales (*mental health* -.55, *self-esteem* -.75, *parental impact-time* -.85, *role emotional/behavioural* -1.22, *behaviour* -1.44, *parental impact-emotions*, -1.45 and *family activities* -1.67).

In a pan-European ADHD observational study (ADORE; Preuss et al., 2006), the QoL of some 1500 children with ADHD was dramatically lower at baseline, than that of community youth, with mean scores on the parent report form of the CHIP-CE (*Child Health and Illness Profile-Child Edition;* Riley et al., 2004) between 1.5 and 2 standard deviations below community norms in all areas, except the comfort domain. Scores were below 35 (mean of 50 with SD of 10) for the sub-domains, *satisfaction with self, social problem solving*, *threats to achievement* and *academic achievement* and between 40 and 35 for satisfaction with *health*, *emotional comfort, family involvement, individual risk avoidance* and *peer relations*. Only three sub-domains were near normal: *physical comfort*, *restricted*

activities and *physical activities*. These findings were consistent across all ten participating countries (Riley et al., 2006). Equally compromised QoL, as measured by the CHIP-CE, was found in 200 children with ADHD entering an open label treatment study in the UK (Prasad et al., 2007).

Self-report; Despite the importance of the individual's self-perception of QoL, few studies of children with ADHD have included child ratings of QoL. Klassen et al. (2006) reported that children and adolescents with ADHD (10-17 years old) rated their own QoL as significantly better than did their parents for their *behaviour*, *self-esteem*, *mental health* and *family cohesion* and significantly poorer for *physical function* on the self-report version of the CHQ-CF87 (Landgraf & Abetz, 1997). In general the physical subscales showed higher correlations (between $r = .75$ and $r = .60$) than the psychosocial subscales (between $r = .40$ to $r = .48$) between child and parent ratings. More importantly, in most domains children perceived themselves as no different from the general child population. They only considered themselves slightly worse for *physical function* and *behaviour* and significantly worse for *family activities*. Landgraf & Abetz (1997) reported very similar mean scores across these domains in children with ADHD (9-16 years). In contrast , using the *Youth Quality of Life Instrument – Research Version* (Edwards et al., 2002), Topolski et al. (2004) found that adolescents with ADHD (11-18 years) reported poorer QoL, compared with a control group without a chronic condition, especially in the domains of *self* (belief in self, mental and physical health) and *relationships* (peers, friends, family, adults). However, these differences were no longer significant when a Bonferroni correction was applied.

The total, *physical* and *psychosocial* PedsQL scores (Varni, Seid, & Rode, 1999) reported by children with ADHD, regardless of their medication status, were significantly lower than those reported by control children in a Thai sample (Pongwilairat et al., 2005). Children with ADHD (5-16 years) also reported significantly lower PedsQL scores on

dimensions of *psychosocial health* and small, but not statistically significant differences on *physical functioning* in a large population-based study, compared to healthy children (Varni & Burwinkle, 2006). In the latter study, the inter-correlations of the PedsQL subscales between parent and child report were in the medium to large range (between r = .50 and r = .75), with no higher correlation in the physical domain than in the psychosocial domains. Rimmer et al. (2007) reported similar correlations (r = 0.67) between child and parent ratings on the PedsQL measured in an independent clinic based sample.

In summary, according to parents ADHD affects QoL across a broad range of psycho-social, achievement and self evaluation domains but no effects in physical functioning domains. Effects were less robust and broadly-based when self report was the main outcome – very often children with ADHD did not see themselves as functioning less well than controls and rated their own QoL as good. The possibility that this discrepancy between child and parent QoL ratings is due to a lack of self awareness on the part of the ADHD child cannot be ruled out.

(ii) QoL in children with ADHD, compared to children with other conditions

In order to assess the significance of the effects of ADHD on QoL it is useful to compare effects with other physical and mental health conditions. Compared to children with asthma and sickle cell disease, children with ADHD were more affected on the psychosocial subscales of the CHQ-PR50 and showed higher scores on the physical subscales (Rentz et al., 2005). Escobar et al. (2005) confirmed these findings in a comparison between children with newly diagnosed ADHD and asthma. Compared to children with newly-diagnosed cancer and children with cerebral palsy, children with ADHD reported significantly better physical functioning, but comparable psychosocial health decrements (Varni & Burwinkle, 2006). In the only study employing child reported QoL on the CHQ-CF87, children with ADHD rated

their QoL far better than children with end stage renal failure, not only on the physical subscales but also on role/social behaviour and mental health (Landgraf & Abetz, 1997).

Whilst there have been few studies addressing QoL in mental health disorders other than ADHD there have been some direct comparisons between ADHD and other mental health conditions. In a large community sample, the QoL of children and adolescents with different mental disorders was compared after the exclusion of comorbid cases (Sawyer et al., 2002). Children with ADHD had more behavioural and fewer emotional problems than those with major depressive disorder, and also had more interference with family activities and impact on parental time (effect sizes all $\geq$ 0.3 SD). Interference with peer and school activities or emotional impact on parents varied little for children as a function of different mental disorders. No significant differences were found between children with ADHD and CD. Scores of children with mental disorders (including a majority with ADHD) were significantly lower on four of the five CHQ scales than for children with physical disorders (including asthma, diabetes and epilepsy).

In a clinical sample, Bastiaansen et al. (2004) did not find any overall differences in QoL of children with ADHD/disruptive disorders compared to those with other disorders such as anxiety disorders, pervasive developmental disorders, mood disorders, "other" diagnosis or even to those without a formal diagnosis but who were seeking help. However, children with disruptive disorders including ADHD showed significantly lower scores on the psychosocial sub-domain of the PedsQL than children in the other or no diagnosis category.

In summary, ADHD has shown more adverse effects on psychosocial domains than common chronic physical illnesses and comparable impact to other mental health conditions and severe physical disorders.

(iii)Factors related to QoL in ADHD; Symptom severity, comorbidity and family background

If we are to understand the nature of QoL in ADHD it is important to examine the characteristics of the ADHD child that drive the reduction in QoL.

Severity: The scores on the *psychosocial* scales of the CHQ-PF50 have been shown to significantly negatively correlate with parent and clinician symptom ratings (Klassen, Miller, & Fine, 2004; Matza et al., 2004; Rentz et al., 2005). Correlations are usually in the small to moderate range (between r = -.21 to r = -.60), which suggests that these measures are tapping into related but distinct constructs. The highest correlations with symptom severity are found on *behaviour* and *family activities* subscales. The *psychosocial* subscales correlated equally highly with both the hyperactivity/impulsivity and the inattention symptom subscales (Klassen, Miller, & Fine 2004; Matza et al., 2004). Correlations between the parent-reported QoL psychosocial scores and teacher-reported *Child and Adolescent Symptom Inventory* were not statistically significant (Klassen et al. 2004). Using the PedsQL Rimmer et al. (2007) also found relatively low correlations between parent and child ratings of QoL and clinician ratings of severity using the CGAS (parent/clinician r = 0.42; child/clinician r = 0.29). Coghill et al. (2004) using the EQ-5D found that utility scores deteriorated as severity increased and that patients with improved symptom severity since the last consultation had a utility value of .88, those who did not improve, had a utility value of .78 suggesting that patients who had improved symptoms valued their health state more than those whose symptoms did not improve.

Comorbidity; Within a sample of children with ADHD, those with multiple comorbid disorders had poorer *psychosocial* QoL on the CHQ-PF50 than children with no or only one comorbid disorder (Klassen, Miller, & Fine, 2004). The combination of comorbid ODD/CD and another comorbid disorder (e.g. tic disorder, depression, anxiety disorder but not learning

disability) was also associated with significantly lower scores (Klassen, Miller, & Fine, 2004).

Discrepancies between parent and child report of the CHQ behaviour and mental health scales were larger in the presence of ODD/CD (Klassen et al., 2006). Comparing youth with ADHD with and without ODD, those with ODD generally had lower scores on the psychosocial summary score of the CHQ-PF-50, as well as on most subscales (Newcorn et al., 2005). The presence of a psychosocial stressor (e.g. parental separation/divorce; move; conflict with siblings or peers) was also related to a larger difference in the behaviour scale in this study, and higher parent reported ADHD symptom severity was associated with more discrepant findings for self-esteem. In the ADORE study twenty-six independent factors were investigated for their relationship to aspects of ADHD children's QoL on the CHIP-CE (Riley et al., 2006). High emotional symptoms, conduct problems, peer relationship problems, coordination problems, asthma or two or more somatic symptoms, and having a parent with mental health or health problems, were all negatively related to several aspects of the child's QoL, over and above the association with ADHD.

Demographic factors; Also in the ADORE study neither demographic variables, nor having a parental history of ADHD had influence on the quality of life, whereas living with both parents was associated with a stronger sense of well-being (Riley et al., 2006).

In summary ADHD symptom severity and the presence of comorbid conditions or psychosocial stressors predict QoL in samples of ADHD children.

3) Is QoL in children with ADHD responsive to treatment?

The final question of significance that we will address relates to the broader effectiveness of ADHD treatments. We are unaware of any psycho-social treatment studies that have utilized QoL measures of outcome. In an observational study of QoL, both medicated and un-medicated children with ADHD were found to have significantly lower scores than controls

on the total score and psychosocial subscales of the PedsQL (Pongwilairat et al., 2005), but did not differ from each other. Controlled studies, however, do suggest improvements in QoL mirror symptom reductions for those pharmacological treatments that have been studied. Unfortunately there is insufficient data published for the full range of currently licensed medications for a comparison of the efficacy of different treatments. Indeed almost all of the currently published studies focus on one molecule, atomoxetine, measured either against placebo, treatment as usual or an active comparator (methylphenidate). All these studies were funded by Eli Lilly. Combining data from 3 randomized double-blind controlled trials, Perwien et al. (2004) documented that improvements in the *psychosocial* domains of the parent version of the CHQ-PF-50 over and above those for placebo could be demonstrated after 7-8 weeks treatment. Lower baseline QoL scores, no prior stimulant use and absence of ODD were factors associated with improvement. No difference was found between once or twice daily dosing schedules and there was no apparent dose response curve for the doses tested. Response rates in terms of having scores at the endpoint of the trial within 1.5 standard deviations of the normative mean were lower for QoL than for ADHD symptoms. A subsequent meta-analysis of 9 randomized placebo-controlled trials with atomoxetine confirmed the improvement of QoL in atomoxetine treated children and adolescents (Cheng et al., 2007). Both children with ADHD with and without ODD showed significant changes in the psychosocial summary score and on most subscales of the CHQ-PF-50 after 8 weeks of treatment with atomoxetine (Newcorn et al., 2005). The findings of this study were endorsed by a meta-analysis of the results of this and two other studies (Biederman et al., 2007). However, although the CHQ and symptom-based findings were generally similar, they varied to some extent as a function of group and dose, with some subscales separating from placebo in the 1.8-mg/kg/day dose group and not the 1.2-mg/kg/day group. This underscores the importance of looking beyond symptomatic control when evaluating treatments for ADHD

(Newcorn et al., 2005). A recent meta-analysis of four studies (Buitelaar et al., in press) comparing symptomatic and QoL outcomes following atomoxetine treatment found a high correlation between the two outcomes as measured on the life participation scale (r=.67). The association was higher for ratings on the self control than for happy/social scale.

Brown et al. (2006) found only a trend toward a better response to active treatment with atomoxetine than to placebo after a seven week double-blind trial in children with ADHD, while significant improvements were found on both parent and teacher symptom ratings. The effect size relative to placebo was small (ES= .32). With response defined as a total T-score below 60 on the CHQ, significantly more children responded to active medication (43.8%) than to placebo (22.2%). In a UK study, children were randomized to open label atomoxetine or standard current treatment (Prasad et al., 2007). Over a ten-week period, overall QoL in children with ADHD improved significantly, as measured with the CHIP-CE total score. A differential effect was found between the study treatments, in favour of atomoxetine over standard treatment (mainly methylphenidate). In the atomoxetine group children's mean total score increased from 23.2 (+/- 12.2) to 38.4 (+/- 1.3), still more than one standard deviation below the norm of 50. After 10 weeks all five parent-reported sub-domains of the CHiP-CE (*satisfaction, comfort, risk avoidance, resilience and achievement*) were improved. Much less improvement was seen on the patient-reported Harter Self Perception Profile, with only one scale (social acceptance domain) showing significant change. Possible reasons for the larger improvement for atomoxetine than methylphenidate suggested by the authors are, a more persistent effect of atomoxetine, with less fluctuations and a possible additional effect on anxiety or tic symptoms (Prasad et al., 2007).

Hardly any studies have looked at the long term treatment effects on QoL. Perwien et al. (2006) report on the changes in the CHQ-PF-50 over a 10-week period and over 24 months open label treatment with atomoxetine. Although significant effects were found for

the psychosocial scales in the acute treatment phase and these were preserved over the long term, no additional improvement in QoL was observed between 10 weeks and 24 months. Using an unlicensed novel inhibitor of noradrenaline and dopamine reuptake, a statistically significant improvement was observed in the *psychosocial* summary score of the shorter CHQ-PF-28 by DeVeaugh-Geiss et al. (2002).

All published treatment studies used generic QoL scales rather than ADHD-specific scales.

In summary, there is evidence for broader efficacy of ADHD treatment – but this evidnce is almost entirely limited to atomoxetine because of a lack of studies on effects of other drugs and issues about the overlap between QoL improvements and symptom reduction have not been addressed.

Discussion

QoL is widely acknowledged as an important element in a comprehensive assessment of childhood disorders, in general, and ADHD, in particular. However, the QoL concept remains problematic in a number of ways, with multiple competing definitions and measurement approaches. These complicate the interpretation of the existing data relating to QoL in ADHD. Despite these limitations, in the current review we bring together the existing published data on QoL in ADHD, draw out its implications, reflect on issues of interpretation and identify areas for future study.

QoL, defined broadly, appears to be impaired in children with ADHD according to parental report. ADHD children are between 1.5 to 2 SD below the appropriate population norms. Furthermore as the severity of disorder increases, and/or is complicated by the presence of comorbidity or psychosocial stressors, QoL impairment increases. The most robust effects are found with *psycho-social* and *achievement*-related scales and impact on

family life. Both types of ADHD symptoms (inattention and hyperactivity/impulsivity) appear equally related to this broader concept of the child's well-being. Furthermore, there is evidence to support treatment effects on QoL that to some extent mirror their effects on ADHD symptoms, although with smaller effect sizes.

Interpreting these general findings is complicated by a large number of factors. First, there are differences between child and parent reports of QoL. This can be seen in the, at best, modest correlations between parent and child reports, as is also seen in relation to parent-child discrepancy for ADHD symptoms themselves, and in the differences in effects of ADHD on QoL as seen from these two perspectives. Inconsistencies between child and parent ratings of QoL may reflect age, instrument or sample differences as well as error or true differences. In contrast to children with other (mental) conditions (e.g., depression), children with ADHD specifically may have an over-optimistic view of their situation, described as a positive illusory bias (Hoza et al., 2002; Owens & Hoza 2003). Klassen et al. (2006) describe several other possible reasons for these findings. First, children may want to conceal their problems. Second, they may ignore them in an attempt to cope with them. Third, they may undergo a process of adaptation to disorder leading to a shift in their internal standards leading to changes in evaluation. Fourth, they may be making systematic mistakes in rushing through the questionnaires because of their impulsive cognitive style. The finding of larger discrepancies between self- and parent-ratings in children with comorbid ODD/CD and those with additional psychosocial stressors, may support the first two hypotheses. This pattern of inter-informant discrepancy raises a fundamental conceptual issue given that, at its core, QoL has a strong element of self evaluation. If this view was taken to its logical conclusion the child's view would trump that of the parents. However, at this stage a pragmatic approach would involve developing ways to combine proxy and child measures in order to provide a more integrated assessment (Varni & Burwinkle, 2006). Future research,

should address the differing ways by which children and parents construct the experience and impact of ADHD. There will also need to be more work exploring the psychometric properties of child-report instruments.

Second, there needs to be more work aimed at better delineating the different levels of analysis that comprise a child's overall functioning (e.g. ADHD symptoms, associated functional impairment and QoL) as these are currently not well delimited within the different scales. Different questionnaires contain different mixes of items which tap into all three levels. This means that there is inevitably item-overlap between symptoms rating scales and QoL measures and it becomes difficult to tease out any independent effects that the disorder or its treatment may be having on symptoms on the one hand and QoL on the other. This begs the question of whether an apparent treatment related change in QoL, as measured by current instruments is really nothing more than reduction in ADHD symptoms. Future research needs to address the contribution of these different elements in characterising ADHD and its relationship to QoL. The major question would be; does the concept of QoL add any value to our understanding of ADHD over and above the concepts of symptoms and more specific functional impairment. One study: (Sawyer et al., 2000) has explicitly studied aspects of this overlap and found that the removal of potentially overlapping items made little difference to the relationships they had previously established between mental illness and QoL. Answering this question would hopefully lead to the refining of instruments towards a clearer delineation of the key characteristics at the core of QoL that are independent of both symptoms and general functional impairment.

Third, even within the limited domain of QoL in children with ADHD there is little consistency in terms of the instruments that have been used to measure QoL. The different instruments have substantially different sub-scale structures and content (Coghill et al., submitted). This makes it very hard to compare across studies and disorders. This is likely to

reflect different opinions regarding the best conceptualisation of QoL and the lack of a core QoL paradigm. Sufficient data has not yet been collected to perform a meta-analysis of studies and instruments that could lead to the development of a core set of items that could lead to a common instrument.

Fourth, most studies have relied on clinic-referred samples, and thus have the potential for referral and Berkson's bias (Berkson, 1946) as well as the issues of reduced range in outcomes and associated limitations on the power of statistical tests. Further studies are required, to anchor these effects within the wider population.

Fifth, most studies have used parental reports both for symptom severity and QoL. This introduces the problem of shared-rater variance due to common raters and may induce a possible source bias. First, this will potentially lead to a spurious association between ADHD symptoms and QoL. Second, it leaves both measures open to undue influence by parent characteristics: There have been no studies of the effect of parental mental health on measures of their ADHD children's QoL. Studies should, as a matter of course, take independent ratings of QoL and symptoms. The choice of who should act as the other informant raises a number of issues itself. In the broader field of ADHD, teachers' ratings are often used to address this problem. However, the low correlations found between different raters' ratings of QoL and teacher-reported symptoms may be accounted for by the fact that teachers observe different maladaptive and adaptive behaviours in the classroom, or that they often only see the children when they are medicated. It is also possible that parents may have exaggerated both symptoms and impact on well-being.

Finally, treatment studies have, to date, been extremely limited in their scope. First, studies have focused almost exclusively on one treatment modality (pharmacological) and one molecule (atomoxetine). Stimulants (dexamfetamine, methylphenidate) are also

recommended for the treatment of ADHD. At present there is no systematic published data on the impact of stimulants on QoL in ADHD. Furthermore, systematic studies of psychological therapies either on their own or in multimodal combinations with medication have not been carried out. A number of trials of stimulants are currently underway. Second, studies have, on the whole, had relatively short follow-up periods. It has been presumed that some aspects of QoL may take more time for change and would therefore not be seen in these short term clinical trials. However, Perwien et al's (2006) longer term study failed to show any additional improvement in QoL after the acute treatment period. Third, there has been no analysis of the extent to which changes in QoL are mediated by symptom changes, changes in functional impairment or other factors. This task is complicated enormously by the fact that the concept of QoL appears to be somewhat confounded in current scales with ADHD symptoms and functional impairment. Fourth, the role of adverse events, in determining QoL following treatment, has not been reported in any studies. QoL, in relation to medication response, will probably be influenced by a mixture of positive treatment responses and side effects. Fifth, studies have failed to control for comorbid disorders such as ODD, anxiety and depression, either at baseline or when assessing responsiveness of QoL to treatment, while several subscales of the QoL measures contain items on behaviour problems, depressive symptoms and anxiety. At the same time, it seems clear that some of the QoL effects demonstrated in ADHD are clearly distinct from symptoms, e.g. peer and family relation impact. In the future, head-to-head studies of different treatment packages should be conducted with a broad range of outcomes over extended periods of time, with multiple testing points. These studies should be designed in such a way to allow the exploration of the natural history of changes in QoL following treatment as well as the mediating effects of symptom reductions and other factors on longer term changes in well-being. These studies should include both proxy and child completed measures.

In summary, published studies to a degree support an impact of ADHD on QoL, which is at least as great as seen for many physical disorders. These effects are greatest, and most consistent, with parent ratings than child-self ratings. Future research needs to distinguish QoL effects from those related only to symptoms and functional impairment; study the differences between child and parent perceptions of ADHD and its impact; identify common elements across the multiple measures currently in use; use population as well clinical samples; include independent ratings of QoL and ADHD symptoms; study the effects of a broader range of treatments in a way that allows the assessment of mediating and moderating factors.

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