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Children and Adolescents with Obsessive-Compulsive Disorder: Comorbidity and Quality of Life

Thesis for the degree of Philosophiae Doctor

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Norwegian University of Science and Technology
Faculty of Medicine
Regional Centre for Child and Youth Mental Health and Child Welfare

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Barn og ungdom med tvangslidelse (OCD): Komorbiditet og livskvalitet.

OCD er kjennetegnet av ubehagelige tvangstanker og tidskrevende tvangshandlinger og forekommer hos 0,5 -3 % av barnebefolkningen. Ubehandlet får lidelsen et kronisk forløp hos 40 -75 %. Hovedmålsettingen for avhandlingen var å belyse to viktige aspekter av OCD: Samtidig forkommende andre tilstander (komorbiditet) og livskvalitet.
Komorbiditet i form av autistiske trekk ble undersøkt hos barn og unge med OCD og sammenliknet med en kontrollgruppe fra den generelle befolkningen. Utvalget er hentet fra en svensk OCD klinikk (Göteborg), kontrollgruppen ble rekruttert i en middels stor by fra samme geografiske området. Autistiske symptomer forekom hos omtrent en femtedel av barn og unge med OCD og var dermed mye hyppigere enn i den generelle befolkningen. Allikevel hadde flertallet ikke slike symptomer som tyder på at kombinasjonen av autistiske symptomer og OCD forekommer i en undergruppe, men er ikke et generelt trekk ved OCD. I den internasjonalt pågående debatten om det er empirisk grunnlag for å betrakte tilstander som OCD, Tourettes syndrom, spiseforstyrrelser og autismespekterforstyrrelser som deler av et såkalt Obsessive-Compulsive Spectrum (OCSD) støtter våre resultater ikke klassifikasjon av autismespekterforstyrrelser som del av dette spektrum. At en undergruppe av barn med OCD har autistiske trekk må dog tas i betraktning når man skal skreddersy individuell tilpasset behandling for barn med OCD.

Å utforske livskvalitet hos barn og unge med OCD er relevant, fordi det finnes et stort antall studier av livskvalitet hos voksne med OCD, men veldig få undersøkelser hos barn. Livskvalitet ble undersøkt hos barn og unge med OCD som deltok i NordLOTS studien (Nordic Longterm OCD treatment study) og sammenliknet med livskvalitet av skoleelever i Sør-Trøndelag. NordLOTS-studien er en nordisk multisenterstudie hvor enheter som behandler OCD hos barn og ungdom har anvendt samme prosedyre for utredning, behandling og evaluering. Studien har inkludert 135 barn og ungdom i alder 7-17 år med OCD. Pasientene ble behandlet med kognitiv atferdsterapi (KAT) med eksponering i en "standartdose" på 14 timer og ble deretter evaluert. Livskvalitet og sosial kompetanse var betydelig redusert hos barn og ungdom med OCD sammenlignet med den generelle befolkningen. Hos barn med komorbide lidelser beskrev foreldrene lavere livskvalitet enn hos de med bare OCD. Etter behandlingen rapporterte de som hadde effekt av behandlingen en livskvalitet i samme nivå som i den generelle befolkningen, mens de som ikke hadde effekt beskrev ingen forbedring av livskvaliteten. Basert på våre funn anbefales å anvende livskvalitets evaluering i klinikk og forskning for å få med et mål for barns og foreldrenes subjektive opplevelse i vurderingen og dermed en mer helhetlig forståelse av OCD hos barn og unge.

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Jeg vil ikke på skolen i dag pga av framføring.
Ok, greit.
Kom igjen! Så drar du på skolen!
Nei, du skal ikke på skolen Det er alt for farlig.
Si NEI uansett!
Kom da! Du kommer forsent
Nei! Nei! Nei! Nei!
KEEP CALM
Kom igjen!
Stopp! La meg være alene!

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2 SCQ (commercial version)
3 KINDL-R Danish Translations
4 Overview of Instruments used in this thesis

1. Acknowledgements

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2. List of papers

Paper 1 (Study 1):

Bernhard Weidle, Karin Melin, Elisabeth Drotz, Thomas Jozefiak, Tord Ivarsson (2012).

Preschool and current autistic symptoms in children and adolescents with obsessive-compulsive disorder (OCD).

Journal of Obsessive-Compulsive and Related Disorders, 1, 168–174.

Paper 2 (Study 2):

Bernhard Weidle, Tord Ivarsson, Per Hove Thomsen, Thomas Jozefiak (2014).

Quality of life in children with OCD with and without comorbidity.

Health and Quality of Life Outcomes, 12:152

Paper 3 (Study 3):

Bernhard Weidle, Tord Ivarsson, Per Hove Thomsen, Stian Lydersen, Thomas Jozefiak.

Quality of life before and after treatment in children with OCD.

European Child and Adolescent Psychiatry (in press)

3. Acronyms and abbreviations

ASD	Autism spectrum disorder
ADHD	Attention deficit hyperactivity disorder
ADI-R	Autism Diagnostic Interview–Revised
CBCL	Child Behavior Checklist
CBT	Cognitive behavioural therapy
CGAS	Children’s Global Assessment Scale
CGI scale	Clinical Global Impression scale
CYBOCS	Children’s Yale–Brown Obsessive Compulsive Scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
ERP	Exposure and response prevention
FAS	Family Accommodation Scale
HFA	High-functioning autism
HRQoL	Health-related quality of life
ICD-10	International Classification of Diseases
KSADS-PL	Kiddie Schedule for Affective Disorders and Schizophrenia–Present and Lifetime Version
KINDL-R	Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents
NordLOTS	Nordic Long-term OCD Treatment Study
OCD	Obsessive–compulsive disorder
OCDS	Obsessive–compulsive disorders spectrum

OCS scale	Obsessive-Compulsive Symptom scale (of the Child Behavior Checklist)
QoL	Quality of life
SCQ	Social Communication Questionnaire
SES	Socio-economic status
SSRI	Selective serotonin reuptake inhibitor
TS	Tourette’s syndrome

4. Summary

The overall aim of the present thesis was to investigate important aspects of childhood obsessive–compulsive disorder (OCD) such as comorbidity and quality of life (QoL). Frequency and continuity of autistic symptoms from preschool age to later childhood in children with OCD were explored as a contribution to the ongoing nosological debate on whether there is an empirical base for summarizing conditions such as OCD, Tourette's syndrome, eating disorders and autism spectrum disorders as parts of a so-called obsessive–compulsive spectrum. The establishment of proper outcome measures for the evaluation of treatment interventions has been a concern in the field (Pallanti et al., 2002). The measurement of symptom reduction only, without any assessment of subjective well-being, has been criticized (Macy et al., 2013). QoL assessment is a well-established outcome measure in somatic as well as in psychiatric treatment studies. However, in contrast to adult OCD, little is known about QoL in children with OCD and next to nothing is known about the role treatment plays in their QoL. To investigate QoL in children with OCD under different conditions (with and without comorbidity, before and after treatment) is relevant because of the paucity of studies concerning children. In the first study, comorbidity in terms of autistic traits was assessed in children and adolescents seeking treatment in a Swedish OCD Clinic (Gothenburg) and compared with controls from a general population sample. In the second study, QoL was assessed at baseline, and in the third study, both at baseline and after treatment with cognitive behavioural therapy (CBT) in children and adolescents with OCD enrolled in the Nordic Long-term OCD Treatment Study (NordLOTS) and compared with the general population. The NordLOTS is a Nordic multicentre study in which OCD treatment units for children and adolescents collaborated on common procedures for assessment,

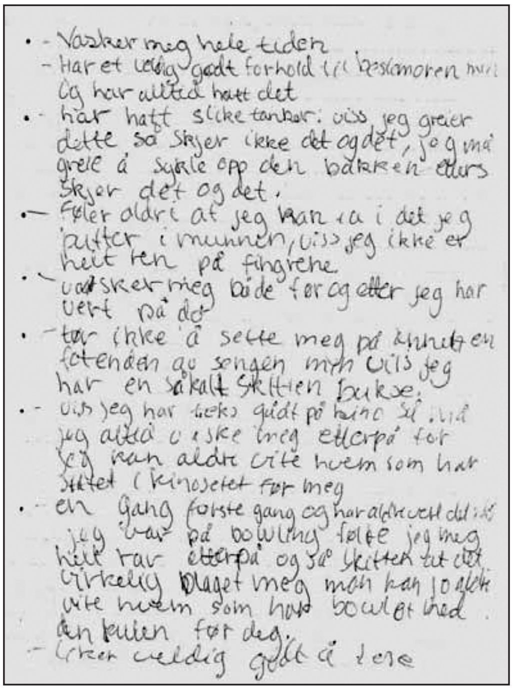
treatment and outcome evaluation (Thomsen et al., 2013). A manual for CBT with exposure and response prevention was established (Weidle et al., 2014). The QoL study included in this thesis comprised a sample of 135 children and adolescents, 7–17 years of age, with moderate to severe OCD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th edition, text rev.) (DSM-IV-TR) (2000), including nine individuals with Asperger's syndrome/high-functioning autism. QoL was assessed at baseline and after treatment with 14 sessions of CBT by self-report and caregiver proxy reports on the *Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents* (KINDL-R) and compared with an age- and gender-matched sample from the general population. Social competence and school functioning were assessed with the *Child Behaviour Checklist*, comorbidity with the *Kiddie Schedule for Affective Disorders and Schizophrenia (Present and Lifetime Version),* severity of OCD with the *Children's Yale–Brown Obsessive Compulsive Scale* and the families' involvement with the child's OCD symptoms with the *Family Accommodation Scale.* In addition, the significance of potential factors such as onset and duration of symptoms regarding QoL change were explored.

Autism spectrum disorder (ASD) symptoms occurred in about one-fifth of children with OCD and were much more common than in the general population. However, the majority of OCD patients did not have these traits, indicating that ASD and OCD co-occur in a subgroup of cases rather than in OCD as a whole. In general, ASD symptoms reported in children with OCD did not show a strong enough relationship between OCD and ASD to support a classification of ASD as a part of an obsessive–compulsive spectrum group. However, a subgroup of paediatric OCD patients had significant subclinical ASD symptom levels. This should be considered when tailoring individual treatment interventions. QoL and social competence were markedly reduced in children with OCD, both in self-reports and in parents’ reports, compared with the general population. Children with higher comorbidity had lower QoL in parents’ proxy reports. After treatment, QoL ratings in treatment responders were in the same range as in the general population, while non-responders rated no change in QoL. Comorbidity, family accommodation and psychosocial functioning were not associated with changes in QoL after treatment. To the best of our knowledge, this is the largest QoL study of paediatric patients with OCD and the first one based on the assessment of OCD and comorbid disorders by standardized semi-structured diagnostic interviews, comparing patients with matched controls from the general population. It is also the first study assessing QoL changes after treatment in paediatric OCD. QoL assessment with the KINDL-R supported outcome measures for symptom reduction used in the study to define treatment outcomes. Based on our findings, we suggest employing QoL assessment in order to have a more comprehensive understanding of childhood OCD.

5. Introduction

5.1 Obsessive–compulsive disorder

Case vignette



- Vasker meg hele tiden
  - Har et veldig godt forhold til bestamoren min
  og har alltid hatt det
- har hatt slike tanker: viss jeg greier
dette så skjer ikke det og det, jeg må
greie å sykle opp den bakken ellers
skjer det og det.
- Føler aldri at jeg kan ta i det jeg
putter i munnen, viss jeg ikke er
helt ren på fingrene
- vasker meg både før og etter jeg har
vert på do
- tør ikke å sette meg på [illegible] en
fotenden av sengen min viss jeg
har en såkalt skitten bukse.
- viss jeg har [illegible] gådt på kino så vil
jeg alltid vaske meg etterpå for
jeg kan aldri vite hvem som har
sittet i kinosetet før meg
- en gang første gang og har aldri vert det [illegible]
jeg var på bowling følte jeg meg
helt rar etterpå og så skitten at det
virkelig plaget meg man kan jo aldri
vite hvem som har bowlet med
den kulen før deg.
  - [illegible] veldig godt å lese

At the age of 13 years, K. wrote the following letter to her general practitioner:

> *I have to wash myself all the time, I have a very good relationship with my grandma, I have had such strange thoughts: if I manage this, this (disaster) will not happen, I have to cycle up the hill, if not something terrible will happen, I can't touch and eat food if my hands are not totally clean, I am washing myself before and after use of the toilet, I don’t dare to sit on my bed with so-called ‘dirty’ trousers, I have to wash my body after going to the cinema, because I can never know who used this seat before me, I had such a strange feeling after bowling, I felt so dirty, that it really disgusted me, you can never know who has used this bowling ball previously …*

This case clearly illustrates the impact of obsessive–compulsive disorder (OCD) on quality of life (QoL). K. became more and more isolated, as she always declined offers from her girlfriends to join them in their games and activities in order to avoid exposure to germs, which in turn resulted in extensive washing rituals. After some time, her friends became tired of asking her to join them, knowing she would say no. Consequently, she was not asked any more. In the end, she became seriously depressed and was referred to a child and adolescent treatment unit. This case also illustrates the complex relationship between OCD and comorbidity.

No more than 30–40 years ago, OCD was considered to be a serious psychiatric condition with a very poor prognosis. Up until the 1970s, psychoanalysis was standard treatment and no effective medication was available. In 1967, Spanish psychiatrists (Fernandez Cordoba & Lopez-Ibor Alino, 1967) found that clomipramin, a drug used against depression, had a favourable effect in treating OCD. At about the same time (in the 1960s and 1970s), intensive research led to the development of a treatment method for OCD that is now known as exposure and response prevention (ERP) (Rachman, Hodgson, & Marks, 1971). Judith Rapoport’s book *The Boy Who Couldn't Stop Washing*, published in the USA in 1989, gave rise to considerable interest in the condition from the general public and popularized this treatment method.

5.1.1 Classification

OCD is characterized by recurrent obsessions and compulsions. To fulfil the diagnostic criteria for OCD according to the ICD-10 (WHO, 1993a), either obsessions or compulsions or both should be present on most days for a period of at least two weeks and to such a degree that the symptoms will cause distress or interfere with social or individual functioning, usually by wasting time. Obsessions and compulsions should be acknowledged as originating in the mind of the patient, and not imposed by outside persons or influences. They are repetitive and unpleasant, and at least one obsession or compulsion that is acknowledged as excessive or unreasonable must be present. Carrying out the obsessive thought or compulsive act is not in itself pleasurable. According to the DSM-5 (Association, 2013), the patient only needs to acknowledge symptoms as excessive and unreasonable at least once during the course of the disorder. The DSM-5 specifies that this is not required in children. In the ICD-10, the disorder has to cause considerable distress for the sufferer. Symptoms have to interfere with daily routines, academic, occupational, social, leisure or family functioning, and occupy at least one hour per day or more. The DSM-5 has also introduced a subcategory, OCD with poor insight, for cases where the patient does not acknowledge the symptoms as unreasonable at all or only to a certain degree. This category might be useful in younger children, but in these cases it is especially important to exclude conditions such as psychosis, ASD or Tourette’s syndrome (TS). The DSM-5 has also moved OCD out of the Anxiety Disorders category, where it was placed in the DSM-IV, to a new category: Obsessive–Compulsive and Related Disorders.

5.1.2 Clinical picture

Obsessions are recurrent unwanted thoughts, preoccupations, ideas or images. They are experienced as anxiety provoking, unpleasant, disgusting, embarrassing or meaningless. Usual obsessions are preoccupation with infections from dangerous germs, and that something disgusting or dangerous will happen to one's self or family, as the case vignette in the Introduction illustrates. Other patients experience an exaggerated need for symmetry and orderliness, with an intense feeling that something is 'not right' if they don't comply with these ideas. Compulsions are repetitive stereotyped actions designed to make the thoughts go away. Normally, patients know deep down that these actions are meaningless and unnecessary. Nevertheless, it is difficult to stop them. Obsessions cause a feeling of anxiety, irritability or dislike until the action is performed or the situation is avoided. Examples are repeated handwashing, even when the hands are not dirty, counting to a certain number, checking things (that the doors are closed, that electrical devices are turned off) or avoidance of a particular situation (using the toilet, shaking hands, touching door handles) (see Figure 1).

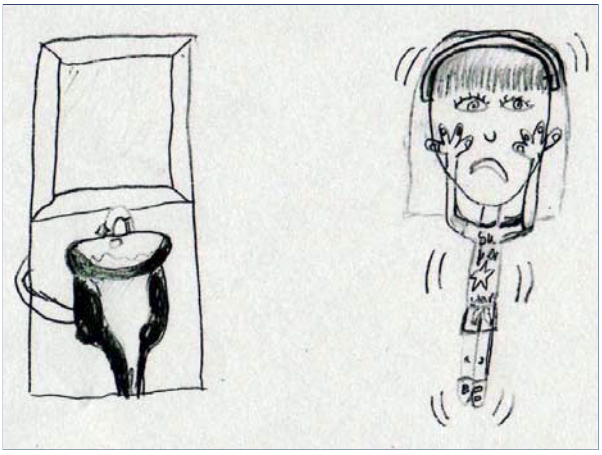


Figure 1 Obsessions: what might happen if I use the toilet?

Obsessions lead to compulsions. Thoughts about contamination or other (unrealistic) threats cause anxiety if compulsions or avoidance are resisted. It is normal behaviour to perform these actions once (for example, handwashing or checking that the door is closed), but repetition is unreasonable. Common obsessions are, for example, thoughts that something terrible will happen to the child themselves or a family member if the ritual is not performed. Obsessions and compulsions are unwanted, and perceived as disturbing and unpleasant. This should be distinguished from the temporary relief of tension or anxiety that the performance of compulsive acts conveys. Children who predominantly experience a need for symmetry may, for example, have to arrange clothes in the right order, adjust paintings on the wall or balance the right number of items on their desk. Others have a need to repeat daily routines, to move in a special pattern or to perform complex mental rituals, such as counting or repeating special words or sentences, in order to neutralize the obsessions and to avoid the threatening danger. Usually, different symptoms occur at the same time, and both obsessions and rituals change over time.

5.1.3 Prevalence

OCD is reported to have a lifetime prevalence of 2–3% in epidemiologic studies (Horwath & Weissman, 2000). Prevalence estimates for children and adolescents vary from 1% to 4% (Flament et al., 1988; Thomsen, 1998; Valleni-Basile et al., 1994; Verhulst, van der Ende, Ferdinand, & Kasius, 1997). A newer study including children aged 5–15 years reported a prevalence of 0.25% with a more frequent distribution (0.6%) in the range between 13 and 15 years of age (Heyman et al., 2001). The authors commented that the low prevalence might be due to the fact that most other studies included older children and youths up to 18 years of age. About 50% of adults with OCD report that symptoms started in childhood or adolescence (DeVeaugh-Geiss J, 1992; Ruscio, Stein, Chiu, & Kessler, 2010). Age of onset has one peak at around 10 years of age and another in early adulthood (Geller, 2006). Gender distribution is reported to be even in most adult studies. Studies with children show a preponderance of boys before puberty, while girls are in a slight majority after the onset of puberty (Geller, 2006).

5.1.4 Aetiology

Family studies have shown significant familial aggregation (Hettema, Neale, & Kendler, 2001). A review of twin studies concluded that obsessive–compulsive symptoms are heritable, with genetic influences in the range of 45–65% (van Grootheest, Cath, Beekman, & Boomsma, 2005). A number of candidate gene studies of OCD have been reported, mainly for gene variants within the serotonin, dopamine and glutamate pathways, but the only genetic association replicated by multiple groups was with a glutamate transporter gene (SLC1A1) (Bloch & Pittenger, 2010). Functional neuroimaging studies have consistently shown hyperactivity in the orbitofrontal cortex, the anterior cingulate cortex, the thalamus and the striatum of patients with OCD. Various lines of research support a causal role for the cortico-basal ganglia-thalamo-cortical loops that involve the orbitofrontal cortex and the anterior cingulate cortex in the pathogenesis of OCD in children as well as in adults (Brem et al., 2012; Maia, Cooney, & Peterson, 2008).

It is theorized that in a subgroup of children with childhood-onset OCD and/or tics, the symptoms occur as a result of group A post-streptococcal autoimmunity reactions, the so-called PANDAS (paediatric autoimmune neuropsychiatric disorders associated with streptococci) (Snider & Swedo, 2004). Murphy and colleagues (2012) found that children with PANDAS were more likely to have had dramatic onset, definite remissions, remission of neuropsychiatric symptoms during antibiotic therapy, a history of tonsillectomies/adenoidectomies, evidence of group A streptococcal infection and clumsiness than those without PANDAS. However, the aetiology in the PANDAS subgroup remains unknown and is still the subject of debate. Both a review (Shulman, 2009) and a recent study (Leckman et al., 2011) found little or no relationship between clinical exacerbations in OCD/tics and streptococcal infection in patients who met the criteria for PANDAS. Thus, it could be possible that group A streptococcal infections may be just one of many stressors that can exacerbate OCD in a subset of such patients.

5.1.5 Outcome and prognosis

The disorder has a chronic course in 40–60% of cases, with functional impairment in two-thirds of these (Micali et al., 2010; Skoog & Skoog, 1999; Stewart et al., 2004). A lifelong disposition in affected individuals is likely, especially during periods of unspecific stress, when symptoms may worsen, even to the degree of a full relapse of the disorder. CBT, where patients learn how to deal with the symptoms, might prevent relapses if the patient is able to maintain and apply the skills learned during treatment, but prospective studies with long-term follow-up are still lacking.

5.2 Treatment of OCD

Expert guidelines recommend CBT with ERP as a first line of treatment of OCD in children and adolescents, with the addition of medication, namely selective serotonin reuptake inhibitors (SSRIs), when CBT alone is not effective (NICE, 2005). A meta-analysis (Olatunji, Davis, Powers, & Smits, 2013) confirmed that CBT is efficacious and should clearly be the first line of treatment for children and adults with OCD. Furthermore, effect sizes for CBT in child studies were larger than in adult studies, suggesting that CBT may be more effective for child populations with OCD than adult populations with OCD. Another recently published meta-analysis (Skarphedinsson et al., 2014) supported the current clinical guidelines, but concluded that performance bias may have inflated previous effect estimates for CBT.

In our study, sample treatment consisted of 14 sessions of weekly individual CBT with ERP, based on the study protocol of March and Mulle, in collaboration with Foa and Kozak (1988). It was modified by adding more extensive family participation, based on the work of Piacentini and colleagues (2007), and adapted to fit Nordic cultural conditions (Weidle et al., 2014) (see Appendix 1). Parents were encouraged to actively participate during the entire course of their child’s treatment, and both the child and the parent jointly attended sessions 1–3, 7, 11 and 14. During these sessions, information was provided about treatment rationale and goals, and the parents’ role in the treatment process, and ideas about particular OCD problem areas for the child were addressed. In the remaining sessions, 45 minutes of individual CBT was offered to the child, followed by an additional 30-minute parent session (with or without the child). The purpose of the latter was to address issues such as family accommodation, family support, problem solving and other questions parents might have. The focus of the treatment was gradual exposure to threatening situations based on a detailed symptom hierarchy, including homework exposure exercises. If appropriate, parents were asked to support and closely monitor homework assignments. Towards the end of the therapy, the emphasis shifted to generalizing skills and relapse prevention. A metaphoric synopsis of the treatment process is given in Figure 2 by S., aged 8 years.

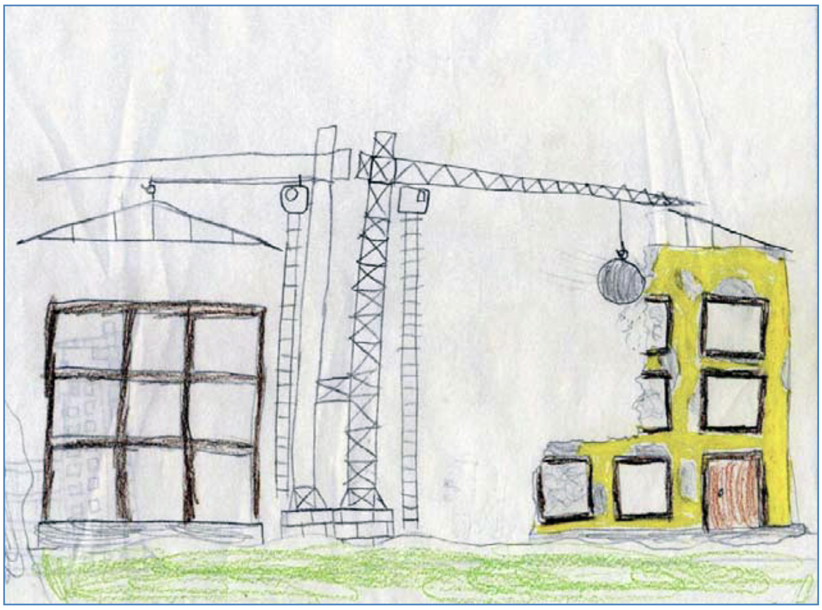


Figure 2 Therapeutic metaphor: deconstruction of OCD, reconstruction of a new life.

5.3 Comorbidity

The co-occurrence of two or more psychiatric diagnoses has frequently been reported in both adult and child populations (Andrews, Slade, & Issakidis, 2002; Ford, Goodman, & Meltzer, 2003). The term ‘comorbidity’ was introduced in the 1970s to describe cases in which a ‘distinct additional clinical entity’ occurred during the clinical course of a patient having an index disease (Feinstein, 1970). Since then, both the value and the validity of the concept have been under debate (Meghani et al., 2013). The clinical utility of the concept is apparent, potentially leading to more comprehensive treatments. In a nosological context, the complex relationships among concomitant disease entities are rather unclear and in need of more research. Are co-occurring disorders, for example, interrelated by a common underlying cause? Do they have a common genetic base? Does one lead to the other or are they just a product of the rules in our diagnostic manuals?

Current diagnostic manuals are categorical, that is, they are based on the assumption that an individual can be defined as ill or healthy based on certain criteria. However, there is little evidence that most mental disorders are separated by natural boundaries (Angold & Costello, 2009; Kendell & Jablensky, 2003). This is illustrated in a study by Fergusson and colleagues (2005) that explored the continuity of depressive symptoms from youth to adulthood. The degree of depression experienced from 17–18 years was associated with depression and suicidal behaviours later in life. Young people with subthreshold depression had a similar prognosis to those who met the criteria for major depression, suggesting that diagnostic procedures and classifying people into categorical diagnoses might obscure the fact that depressive symptoms are dimensional and range from none to severe. In their consideration of whether to view psychopathology as categorical or dimensional, Pickles and Angold (2003) concluded that because we do not observe pathology directly, but rather its properties, the same pathology can have some properties that are most easily understood using a dimensional conceptualization, while at the same time having other properties that are best understood categorically. Therefore, the central question is not whether psychopathology is scalar or categorical, but in which circumstances it is meaningful to regard psychiatric disorders as being scalar or as being categorical. They pointed to the utility of regarding psychiatric disorders as categorical even if the categories might not necessarily be valid. For example, when it comes to clinical treatment interventions, a categorical decision has to be made. For instance, before treating a child with stimulants, it is necessary to determine whether the child has symptoms of sufficient intensity to warrant treatment. Whatever assessment method is used, some cut-off point (clinical or subclinical) will have to be used to determine whether to institute treatment or not. On the other hand, it is meaningful to think in dimensional terms when the outcome is evaluated.

In the majority of cases, OCD is associated with other psychiatric conditions; as many as 77–85% of children with OCD fulfilled the criteria for one or more other psychiatric diagnoses (Hanna, 1995; Ivarsson, Melin, & Wallin, 2008). Depression, phobia and other anxiety disorders, attention deficit hyperactivity disorder (ADHD), tic disorder, oppositional defiant disorder/conduct disorder and bipolar disorder are common comorbidities in paediatric OCD (Masi et al., 2010). In addition, several researchers have reported elevated levels of ASD comorbidity with OCD. For example, 3% of an adult sample with OCD also met the DSM criteria for an ASD (LaSalle et al., 2004).

5.3.1 The relationship between OCD and ASD

Many OCD therapists will meet patients with autistic traits in their clinical practice, both with established diagnoses of ASD and with unrecognized ASD symptoms. Bejerot and colleagues (2001) described a relatively high proportion (20%) of individuals with autistic traits among adults receiving treatment for OCD. Some of them had an established diagnosis of ASD, some had ASD symptoms but were border-line in receiving a diagnosis, some were misdiagnosed with a personality disorder and some were undiagnosed. Cath and colleagues

(2008) reported a considerable symptom overlap between ASD and OCD. In the high-functioning group of individuals with ASD/Asperger's syndrome, the diagnosis might have been overlooked, and anxiety or OCD symptoms may be the first signs of the disorder in adolescence or young adulthood. With regard to paediatric OCD, Ivarsson and Melin (2008) found that 8.2% of children and adolescents treated for OCD fulfilled the diagnostic criteria for ASD.

The other way round is even more likely: ASD therapists will certainly meet patients with OCD, as OCD is a frequent comorbid condition with ASD. Epidemiologic studies describe the prevalence of OCD in ASD as 8–37% (Leyfer et al., 2006; Mattila et al., 2010; Simonoff et al., 2008). In a recent Norwegian study, OCD prevalence in ASD was found to be 10% (Gjevik, Eldevik, Fjaeran-Granum, & Sponheim, 2011). Russell and colleagues (2005) reported similar frequencies of OCD symptoms in adults with high-functioning ASD compared with a gender-matched group with OCD. In order to distinguish OCD symptoms from stereotypic behaviours and interests, symptoms were only rated if they caused some degree of discomfort and interfered with the patient's daily life. Obsessions and compulsions were found to be frequent and distressing in individuals with ASD, suggesting that OCD symptoms should be carefully distinguished from repetitive behaviours and special interests, as patients with ASD and OCD may benefit from standard treatments. Successful treatment of OCD in adolescents with ASD has been reported (Lehmkuhl, Storch, Bodfish, & Geffken, 2008; Reaven & Hepburn, 2003). The first randomized treatment study with adolescents and young adults with ASD and OCD compared CBT and 'anxiety management' (Russell et al., 2013). Both treatments resulted in a significant reduction of OCD symptoms, assessed with the YBOCS. The CBT group had more responders to the treatment (45% vs. 20%), but between-group differences were not significant. The authors concluded that psychological treatment (anxiety management and CBT) was effective for OCD in adolescents and young adults with ASD.

Without a good understanding of both conditions, OCD therapists may overlook ASD cases, misinterpreting the symptoms as OCD. In the same way, ASD therapists may regard OCD comorbidity as a part of ASD, preventing the patient from receiving adequate therapeutic interventions. Successfully treated OCD can lead to an important increase in QoL in affected individuals, even when the basic ASD symptoms remain unchanged.

5.3.2 Comorbidity or obsessive–compulsive spectrum disorders

Besides the implications for treatment interventions, another interesting aspect of studying the relationship between ASD symptoms and OCD is an ongoing debate about the nosological placement of OCD. OCD has, for decades, been classified both in the ICD and in the DSM as an anxiety disorder in view of the anxiety associated with obsessions and the function of rituals to ease it. In the DSM-5, OCD was removed from the Anxiety Disorders category and placed in a new category: Obsessive–Compulsive and Related Disorders. In this new category, OCD is now placed together with body dysmorphic disorder, trichotillomania (hair-pulling disorder), excoriation (skin-picking) disorder and hoarding disorder. The latter is now classified as a separate disorder, having previously been categorized as a subtype of OCD.

Some researchers have suggested including OCD together with ASD, tic disorders, hypochondriasis, body dysmorphic disorder and trichotillomania as one part of the so-called obsessive–compulsive spectrum disorders (OCSD) (Bartz & Hollander, 2006; Hollander, Kim, Khanna, & Pallanti, 2007). The basis for this suggestion was that these disorders share a common underlying feature (i.e., repetitive behaviour), present with similarities in phenotype, brain circuitry and neurotransmitter abnormalities and familial/genetic factors, and respond to treatment with similar drugs. The OCSD proposition has been the subject of considerable debate. Storch and colleagues, for example, argued that the OCSD construct is a misleading concept (E. A. Storch, Abramowitz, & Goodman, 2008).

5.4 Quality of life (QoL)

In 1946, the World Health Organization (WHO) published their famous definition of health as "*a state of complete physical, mental, and social well-being, not merely the absence of disease or infirmity"* (Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946 signed on 22 July 1946 by the representatives of 61 States and entered into force on 7 April 1948 (WHO, 1946). In 1995, the WHO's position paper followed, describing the development of a QoL instrument (the WHOQOL). Based on collaborative development in several culturally diverse centres and some 4500 respondents in 15 cultural settings, the WHOQOL assesses "*individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"*, producing a multidimensional profile of scores across six domains and 24 subdomains of QoL (WHO, 1995). Since then, research on QoL has increased markedly. QoL research was originally driven by the need to obtain a measure of treatment benefits in patients who had survived previously fatal conditions where the goal was not to cure the disease. The patients' perceptions of the intensity of symptoms associated with different invasive treatments and consequences for QoL emerged as an important point of assessment. First addressed in research involving adult patients with cancer (Finkelstein et al., 1988), this issue was later extended to paediatric research following the realization that there was a need for similar information specific to children, as results from adult research could not be extended to paediatric cases for a variety of developmental, perceptual and other reasons (Eiser & Jenney, 1996). Another aspect in this context was the fact that assessment of QoL in palliative care was vital, as this was the only variable of real importance to families, children and clinicians (Eiser & Jenney, 2007).

A second line of interest in QoL measurements derives from the need for patient-reported outcomes in medication trials. Traditionally, relatively few medication trials have been conducted in paediatric populations because of ethical concerns about testing experimental treatments on children and an expectation of a limited return on investment for research applied to paediatric populations compared with the larger group of adult patients. This lack of paediatric clinical trials has resulted in many 'off-label' treatments in paediatric populations, without marketing authorization or evidence of safety and efficacy. As a consequence, both the US Food and Drug Administration (FDA) and European Medicines Agency (EMEA) have issued legislation to stimulate paediatric research (Arbuckle & Abetz-Webb, 2013). Concurrently, both agencies have advocated the use of patient-reported outcomes , including health-related QoL (HRQoL), as an important part of outcome assessment in clinical trials and have published guidance on the development of reliable measures (EMEA, 2004; FDA, 2006). From this important role in the somatic field, QoL assessment has been extended to child and adolescent psychiatric research.

5.4.1 Why should we measure QoL?

Eiser and Morse (2001b) used the example of growth hormone replacement to illustrate the need for assessment of different dimensions to cover all important aspects of a medical intervention. Traditionally, increased height was the most important outcome measure indicating success after growth hormone therapy. However, for children and their families, other aspects, such as increased self-esteem or future work opportunities may be much more important for their evaluation of treatment outcome. Thus, success may be deemed to a lesser degree by centimetres gained and more by the child's ability to keep up with daily activities and to enjoy life. While height can be measured easily, the measurements of QoL and self-esteem are more difficult because of their subjective nature. However, the more elusive and subjective outcomes may, in the end, be equally or even more important. An equivalent rationale applies to children with mental health conditions. In parallel with chronic somatic disorders, psychiatric conditions quite often have a chronic nature where the goal is not a complete remission of symptoms, but an improvement of function and QoL. As Bastiaansen and colleagues (2005) demonstrated, psychopathology does not have a simple linear relationship to well-being. They assessed changes in psychopathology and their relation to QoL over a one-year follow-up in children with high levels of psychopathology. Roughly one-third showed neither psychiatric symptom reduction nor QoL improvement, another third showed symptom reduction and QoL improvement, and the last third showed either psychiatric symptom reduction or QoL improvement. Surprisingly, QoL improved in 10% of all children, even when the level of psychopathology remained high. The authors concluded that QoL may be improved by reducing psychiatric symptoms, but it is also possible to improve QoL without symptom reduction. Therefore, they argued that QoL should be included both as a treatment goal and as an outcome measure of psychiatric treatment programmes, especially in cases where psychopathology tends to persist.

The measurement of QoL in children with mental health problems offers several benefits:

1. It allows comparison of the burden of a given disorder with the burden of another, which is important in enabling policymakers and clinicians to set priorities.
2. It may help clinicians to assess and balance short-term gains against long-term outcomes, for example, to balance the advantages of a given medication against the negative consequences of side effects.
3. On an individual level, the subjective perception of QoL might be more important for the children and their families than symptom evaluation alone. Thus, appropriate measuring of QoL substantiates treatment planning including the assessment of treatment success.
4. In outcome research, adding a subjective perspective to outcome measures contributes to better ecological validity. In addition, it facilitates the comparison of outcomes in clinical trials with different interventions.

5.4.2 From concept to measurement: can QoL be assessed in a valid and reliable way?

Over a decade ago, Wallander and colleagues (2001) stated: “*There is increasing interest in measuring quality of life in children and adolescents, but this interest has developed without* *careful attention given numerous important issues. Consequently, there is much diversity and confusion in this measurement area."* Of course, measurement is a crucial issue; without reliable measurements that are sensitive to the changes in QoL that can be expected to occur after treatment, the effort of applying such measures in studies would be meaningless.

QoL can be defined as the *subjective* well-being in several life domains (Koot, 2001). The main domains usually assessed in children (and in adults) are physical, social and psychological/emotional well-being, as well as global perceptions of function and well-being. Other domains (for example, cognitive or spiritual) are less often assessed (Eiser & Morse, 2001b). However, the term 'quality of life' has been defined in many different ways and for different purposes, encompassing everything from good health status to psychosocial well-being, a sense of satisfaction with life and the perception of happiness. As Wallander and colleagues (2001) pointed out, QoL is a construct, and as such has no physical or temporal basis. It is not a directly measurable entity or 'thing'. Until now, there have been few attempts to validate the QoL concept empirically. However, a confirmatory factor analysis has provided empirical support that QoL and depressiveness are related but distinct concepts (Jozefiak, 2012). In research, different concepts, definitions, criteria and measurements are applied in the assessment of QoL. Consequently, it has been difficult to compare results across studies and populations. To narrow the issue, the term 'health-related quality of life' (HRQoL) was coined to describe the effects of health disorders and their treatment on QoL, omitting the wider aspects of QoL applied in philosophy and social science.

There is no gold standard for the definition of QoL, and definitions of HRQoL vary widely. However, the following two central aspects of this construct are encompassed in most definitions (Matza, Swensen, Flood, Secnik, & Leidy, 2004). First, HRQoL is subjective, and therefore it should be assessed from the patient's perspective whenever possible. Second, HRQoL is a multidimensional construct that integrates a broad range of outcomes. A widely applied definition of HRQoL is "an individual's subjective perception of the impact of health status, including disease and treatment, on physical, psychological, and social functioning and well-being" (Leidy, Revicki, & Geneste, 1999).

5.4.3 Can we rely on children's reports of their QoL?

Children with the same objective health status can report different subjective QoL. For example, children who survived cancer reported higher QoL than healthy children (De Clercq, De Fruyt, Koot, & Benoit, 2004), and children with ADHD rated their QoL significantly higher than their parents did (Klassen, Miller, & Fine, 2006). However, the subjectivity of the evaluation is intrinsic to the concept. The perception of QoL is in part dependent on hope and expectations in relation to an individual's personal goals. If these individual goals are not realistic, from a therapeutic point of view, it is possible to improve QoL by helping a patient to accept reality or to achieve more realistic goals. This insight might be difficult to convey if the patient is not able to differentiate between realistic and achievable goals and unrealistic dreams (Eiser & Morse, 2001b).

The general definition of QoL can be applied to children, but it is important to ensure that measurement covers the specific aspects of QoL relevant to a child's life. Thus, paediatric

QoL instruments should use items corresponding to experiences, activities and contexts that are directly relevant to the age of the sample (Matza et al., 2004). Children are found to be able to reliably and validly self-report their QoL by the age of 5 years if the instrument that is applied is age-appropriate (Varni, Limbers, & Burwinkle, 2007). Recent recommendations (Arbuckle & Abetz-Webb, 2013) underline the importance of using developmentally appropriate language and techniques to ensure that outcomes have content validity. The instrument should measure QoL as generally defined, reflect the aspects of QoL that are important to the patients themselves, and the key dimensions expected to change with therapy should be adequately represented (Leidy et al., 1999).

The Mental Health Division of the WHO (WHO, 1993b) has issued guidelines for developing HRQoL instruments for children and adolescents. According to these guidelines, measures should be child-centred, employ subjective self-reporting wherever possible, be age-related or at least developmentally appropriate, be cross-culturally comparable, have a generic core and specific modules, and include both positive and negative aspects of the relevant domains (e.g., family/social relations, physical function, social and material environment). A recent review (Ravens-Sieberer, Karow, Barthel, & Klasen, 2014) evaluated existing instruments for measuring QoL in paediatric populations according to the following criteria: (1) psychometric quality; (2) age-appropriate measurement; (3) versions for self-reporting and external rating; and (4) cross-cultural measurement. In addition, QoL instruments had to meet the quality criteria for psychometric procedures (reliability, validity and sensitivity to change). The overall conclusions were that international instruments for measuring QoL in children and adolescents are available. However, no single QoL measure covers the entire universe of HRQoL, but the QoL dimensions that are relevant to a specific subject of investigation can be measured. QoL of children and adolescents can and should be measured through self-reporting, and age-appropriate measures that take maturity and cognitive development into account must be used.

5.4.4 Can we rely on parents’ reports of their children’s QoL?

In their 2001 review titled “Can parents rate their child’s health-related quality of life?”, Eiser and Morse (2001a) could find no clear answer to the question. They found that agreement is better between parents and chronically sick children than between parents and healthy children, but that all results may be dependent on differences in measures of QoL employed in the different studies. Their overall conclusion was that there remain strong arguments for obtaining information from both parents and children whenever possible. In a later review on parent–child agreement in QoL measurement (Upton, Lawford, & Eiser, 2008), parents of children in a non-clinical sample tended to report higher child QoL scores than the children themselves, while parents of children with health conditions tended to under-estimate their children’s QoL. Jozefiak and colleagues (2010) observed the same trend, with parents by proxy reporting higher child QoL in the general population, while an inverse trend was observed in the clinical sample. However, Sattoe and colleagues (2012) found reasonable agreement (i.e., in 43–51% of cases) and most disagreement tended to be minor, suggesting that the proxy problem may be smaller than presented in the literature and its extent may differ between populations. In addition, one must bear in mind that not only children’s reports, but also the reports of parents can be biased (Davis, Davies, Waters, & Priest, 2008). In any case, both children’s reports and parents’ proxy reports should be obtained in the assessment of QoL to cover both informants' unique perspectives. Given the definition of QoL as a measure of subjective well-being, the children's report should be considered as the prime authentic report, with the parents' proxy report representing important supplemental information (Jozefiak, 2014).

5.4.5 Why we chose the KINDL-R to measure QoL

As indicated above, despite the controversies discussed, the assessment of QoL has been established as an important outcome factor independent of symptom-level assessment. The purposes of our study required a generic rather than a disorder-specific questionnaire to allow comparison of the OCD sample with a general population sample. Three main properties of a QoL instrument were crucial for our choice: availability, practicability and reliability.

Availability in all languages was essential. Swedish and Norwegian versions of the questionnaire were available, and a Danish translation was prepared and approved during the inclusion process. Study participants had to undergo a comprehensive assessment including completing a number of questionnaires at baseline and at repeated time points for treatment evaluation and follow-up. This demanded a practical, child-friendly, relatively short instrument to avoid overburdening participants with too many questions and thereby compromising compliance. The KINDL-R questionnaire (www.kindl.org) was developed with the help of focus groups involving children and adolescents as a QoL measure for healthy and ill children and adolescents (Ravens-Sieberer et al., 2014). The measurement had to be appropriate for different ages (children and adolescents) and include the perspectives of parents by proxy. The KINDL-R is available in self-report versions for children of different age groups and proxy versions for parents. The questionnaire can be filled out within approximately 10 minutes.

Concerning reliability, psychometric properties that are reliable for detecting change should have been established, which was the case for the KINDL-R (see section 7.3.2). Last but not least, a Norwegian normative study provided a large comparison sample from the general paediatric population and also confirmed satisfactory psychometric properties of a Scandinavian (i.e., Norwegian) version (Jozefiak, Larsson, & Wichstrom, 2009; Jozefiak, Larsson, Wichstrom, Mattejat, & Ravens-Sieberer, 2008).

5.4.6 What do we know about QoL in OCD?

Possibly in response to the potentially serious consequences of a chronic disorder, a considerable body of research has investigated numerous aspects of QoL in adult populations with OCD. To date, four review articles on QoL in adults with OCD have been published (Koran, 2000; Macy et al., 2013; Moritz, 2008; Subramaniam, Soh, Vaingankar, Picco, & Chong, 2013), all of which concluded that there had been an overall reduction in QoL. In fact, adult studies have found that QoL in OCD individuals was comparable with or worse than QoL levels found in schizophrenia, depression, panic disorder and substance dependence (Bobes et al., 2001; Kugler et al., 2013; Stengler-Wenzke, Kroll, Matschinger, & Angermeyer, 2006). In some studies, treatment improved QoL, but in others, symptom reduction did not lead to improved QoL (Moritz, 2008).

Macy and colleagues (2013) recently reviewed 58 studies that examined QoL in adult patients with OCD, including the influence of comorbidities and the impact of treatment. Overall, the results showed that QoL was gravely impaired in patients with OCD compared with QoL in the general population. In addition, they found evidence that comorbid conditions, particularly depression, were major contributing factors to the reduced QoL in OCD patients. The authors underlined the importance of QoL assessment in both clinical and research settings for examining the disease burden, monitoring treatment effectiveness, determining the grade of recovery from OCD and developing treatment plans. The other review, published at about the same time (Subramaniam et al., 2013), concluded that overall, studies indicated that individuals with OCD had diminished QoL across all domains relative to normative comparison subjects. Patients with OCD scored better on QoL domains than patients with major depressive disorder, whereas they scored the same as or worse than patients with schizophrenia. Research on socio-demographic correlates of QoL in OCD is largely contradictory; most studies suggest that symptom severity and comorbid depression or depressive symptoms are predictors of decreased QoL in OCD. Studies assessing QoL as an outcome of treatment have found an improvement in QoL in people with OCD after treatment with pharmacotherapy or CBT, with some studies suggesting that this improvement in QoL is correlated with an improvement in symptoms.

In contrast to adult studies, little is known about the QoL of children and adolescents with OCD, and nothing at all is known about the relation between treatment for OCD and QoL. The most recent of the mentioned reviews on QoL in adults with OCD (Subramaniam et al., 2013) stated clearly: *"…little is known about the impact of OCD on QoL in paediatric patients.*

As there is a substantial prevalence of OCD in childhood and adolescence due to its early age of onset, there is an obvious need for further exploration of QoL in these populations; however, this is currently lacking."

5.5 Contribution of this thesis to the body of knowledge

As outlined above, both comorbidity and QoL are important aspects of OCD research, and both concepts have gained increased attention during the last decade. However, in both areas, there are controversies and insufficient knowledge, especially regarding paediatric OCD. The present thesis contributes to the body of knowledge by aiming to address the lack of information about comorbidity and QoL in paediatric OCD. Study 1 contributes to the ongoing nosological debate about whether there is an empirical base for summarizing conditions such as OCD, TS, eating disorders and ASDs as parts of a so-called obsessive–compulsive spectrum.

To the best of our knowledge, study 2 is the largest QoL study of paediatric patients with OCD and the first one based on the assessment of OCD and comorbid disorders by standardized diagnostic interviews, comparing those patients with matched controls from the general population. In study 3, we report on the relation between a treatment intervention with CBT and QoL. To date, no study has assessed prospective QoL before and after treatment interventions in children and adolescents with OCD.

6. Aims of the thesis/research questions

The overall aim of this thesis was to explore important aspects, such as comorbidity and quality of life in children with OCD, as outlined in the following research questions:

Study 1: How frequent are comorbid autistic symptoms in children with OCD compared with the general childhood population and is there continuity between autistic symptoms from preschool age to later childhood?

Study 2: Do children with OCD with and without comorbidity experience reduced quality of life before treatment compared with healthy school children (general childhood population)?

Is their social competence and school functioning reduced compared with the general population?

Are comorbid disorders such as ASD, ADHD, TS, other anxiety disorders and depression associated with their perceived QoL?

Are other factors, such as duration and severity of symptoms and the family's accommodation to their rituals, associated with their perceived QoL?

Study 3: Are there changes in perceived quality of life among children and adolescents with OCD during treatment, and if so, how are they related to changes in symptom level and psychosocial functioning?

Do children with OCD report quality of life within normal population levels after treatment or will their quality of life still be below the level reported by the general population?

Do factors such as comorbidity, psychosocial functioning and family accommodation have an influence on treatment outcome?

7. Methods

7.1 Study samples study 1

7.1.1 Participants

The study group consisted of all patients with a DSM-IV diagnosis of primary OCD who were consecutively assessed and treated at the specialized OCD unit in Gothenburg, Sweden from January 2001 to December 2005. The total number of cases eligible for participation in the study was 140. Thirty-one patients declined to participate in the study and data were missing for four patients. Thus, 105 patients (girls/boys = 61/44) were included in the study, yielding a response rate of 75%. The mean age of the children was 13 years (range: 7–17). Neuropsychiatric comorbidity was common; 20 patients (19.2%) met the DSM-IV criteria for ADHD and 17 (16.2%) met the criteria for TS. Most patients had intact families (68%) and Swedish ethnicity; 7% had one non-Swedish parent and 12% had two non-Swedish parents.

7.1.2 Comparison group

As controls, children and adolescents (n = 108) from schools and participants in swimming activities in a mid-sized Swedish town in the same geographical area were recruited and matched for age and gender with the patients. Exclusion criteria for controls were a diagnosis of a neuropsychiatric disorder or the fact that a sibling was already a participant in the study. The mothers competed the Social Communication Questionnaire (SCQ) (M. Rutter, Bailey, & Lord, 2010) and the Child Behavior Checklist (CBCL) (Achenbach & Rescorla, 2001), the latter to check for possible psychiatric problems other than ASD. Two candidates who were originally eligible for the study received an ASD diagnosis during the study period and were therefore excluded. No other psychiatric problems warranting exclusion were identified in CBCL reports. Of all eligible families invited, only two declined to participate in the study.

7.2 Study sample, studies 2 and 3

7.2.1 Participants

The QoL study was a substudy of a multicentre treatment research project, the Nordic Long-term Treatment Study (NordLOTS), in which 269 children and adolescents 7–17 years of age were treated for OCD with CBT between September 2008 and June 2012 (Figure 3). Ethnicity was primarily Scandinavian; 97% of the participants had one or both parents of Scandinavian origin. The NordLOTS trial has been described in detail elsewhere (Ivarsson et al., 2010; Thomsen et al., 2013; Torp et al., 2014).

Figure 3 Main sites of the NordLOTS study.

The QoL study started later than the Nordic Long-term Treatment Study and at different time points in the three participating countries, because of the availability and approval of the national translations of the QoL questionnaire used. The Danish translation was prepared during the inclusion process and approved by the original authors only in March 2011. The first patients available for QoL assessment were included in September 2009 in Norway, in August 2010 in Sweden and in April 2011 in Denmark, leading to the following distribution: 76 participants (56.3%) from Norway, 33 (24.4%) from Sweden and 26 (19.3%) from Denmark. Altogether, 155 of the 269 patients included in the main treatment study were eligible for participation in the QoL study after the QoL questionnaire (KINDL-R) was introduced in the various countries (Figure 4).

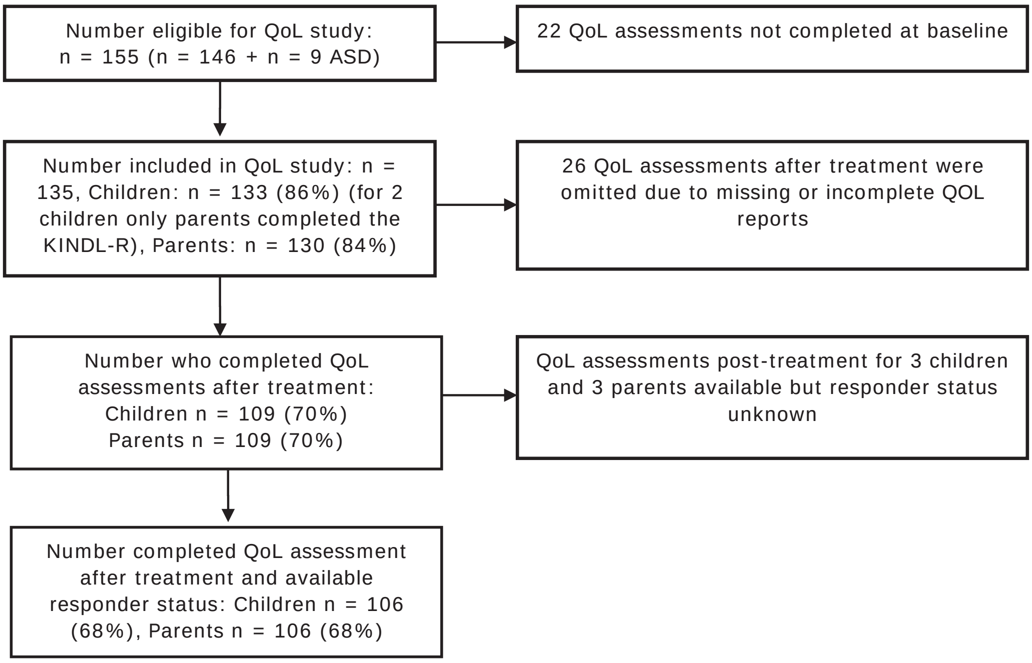


Figure 4 Flow chart for the QoL study.

Both children and one of their caregivers completed QoL questionnaires, resulting in 135 completed forms from either children and/or one of their caregivers (133 child forms and 130 parent forms, including two cases where only the parents completed the questionnaire and five cases where only the children completed the questionnaire) at baseline, yielding response rates of 86% for eligible children and 84% for the parents. Post-treatment QoL assessment was available for 109 participants (70%). In three cases with QoL assessment, post-treatment responder status was missing at the time of the data analysis. Attrition from missing QoL reports or responder status resulted in a response rate of 68% (n = 106) of all invited participants (children and parents) who completed QoL assessments before and after treatment. ASD was an exclusion criterion in the main treatment study, but nine individuals with Asperger's syndrome/HFA were included in a substudy at one site (Trondheim). Complete QoL assessment was available for eight of the ASD patients.

7.2.2 Age and gender

At baseline, the mean age of the participants was 13 years (*SD* 2.7 years, range: 7–17). Gender distribution was approximately even, with 65 girls (48.1%) and 70 boys (51.9%). Thus, the QoL substudy sample was representative of the whole sample of the treatment study, where mean age was 12.8 (*SD* 2.7) years, and only slightly more girls were represented (51.3%). If the comparison was made without the nine male participants from the ASD substudy, gender distribution was equal in both samples (51.3% versus 51.6% girls in the QoL study).

7.2.3 Socio-economic status

Socio-economic status (SES) was calculated using the highest education level of either the mother or the father (whichever was highest), assessed as suggested by Hollingshead (2011), with scores ranging from 1 to 7 (7 = university education).

The education level of the parents was generally quite high (*M* = 5.30; *SD* 1.39). The participants in the QoL study were not significantly different (*t*(270) = .92; *p* = .357) from the sample of the main NordLOTS study with regard to socio-economic status (*M* = 5.14, *SD* = 1.47).

7.2.4 Comorbidity

Comorbidity was common, especially with neuropsychiatric conditions, other anxiety disorders and, to a lesser degree, depression. In fact, only 69 patients (52.3%) had 'pure' OCD without any comorbidity (hereafter termed 'OCD only'). Eighteen patients (13.6%) met DSM-IV criteria (Association, 2000) for ADHD and 37 (28%) met the criteria for tic disorder, while 14 had a combination of both. Conduct disorders were diagnosed in six patients (4.5%). Other anxiety disorders were diagnosed in 28 patients (21.2%); two patients suffered from separation anxiety, 16 from specific phobia (12.1%), eight from social phobia (6.1%), six from generalized anxiety disorder (4.5%) and two from anxiety not specified. Four patients had two, and one patient three, additional anxiety disorders. Depression was diagnosed in seven patients (5.3%), MDD in six patients and unspecified depression in one patient. No other psychiatric comorbidity was diagnosed. The HFA group (n = 9) contributed heavily to the load of comorbidity; only one of the HFA patients had OCD only, seven patients had other neuropsychiatric conditions (three tic disorder, two ADHD and two both tic disorder and ADHD) and one patient had another anxiety disorder (specific phobia).

7.2.5 Treatment

Treatment consisted of 14 weekly sessions of individual exposure-based CBT. Clinical response was defined as a Children's Yale–Brown Obsessive Compulsive Scale (CYBOCS) total score ≤ 15, assessed by independent evaluators as a primary outcome measure, and a 30% reduction in CYBOCS score as a secondary outcome measure. Of the 106 children with complete QoL data, 71 (67%) were treatment responders and 35 (33%) were non-responders.

7.2.6 Comparison group

A large normative data sample consisting of students from schools in Sør-Trøndelag county, which represents a comparable geographical area with both urban and rural settlement, was used as a control group (Jozefiak et al., 2009). Every child or adolescent with OCD was individually matched and randomly allocated to a child of comparable gender and age from the general population sample (n = 1821, 8–16 years). With regard to parent education, there was no significant difference between patients ($M = 5.19$) and the allocated controls from the general population ($M = 5.29$) ($t(118) = 0.51$, $p = 0.61$, paired samples t-test). Because of the cluster design of the general population study (sampling data from grades 4, 6, 8 and 10) we had to stratify the samples before matching patients and controls in groups with a relatively large age range; 7–10 years, 11–14 years and 15–17 years. Therefore, we explored the differences in chronological age between patients and controls. The mean of the difference scores between patients' and controls' ages after matching was 0.39 years ($SD = 1.24$). Further, the mean age of patients (12.70 years, $SD = 2.71$) was significantly higher ($t(134) = 3.64$, $p < .001$, paired t-test) than that of controls ($M = 12.31$, $SD = 2.39$). However, the largest differences (2.5–3 years) comprised a total of only five patients (3.7%) who were randomly allocated to controls. All other patient–control pairs lay within a two-year-difference range, with 95 cases (70.3%) within a one-year-difference range. Controls who had been in contact with health or school psychological services were not excluded to avoid an 'artificially healthy' comparison group from the general population. Thus, the parents of seven (5.2%) matched controls had replied in the affirmative to the question *"Has your child received any help during the last year due to mental health problems or learning difficulties?"*

7.3 Instruments

7.3.1 Assessment of quality of life (QoL)

The Kinder Lebensqualität Fragebogen (Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents, revised version, KINDL-R) (Ravens-Sieberer & Bullinger, 2000) is a well-established QoL instrument used in several clinical and epidemiological studies. Swedish and Norwegian versions of the questionnaire were available, and the Danish translation was prepared and approved by the original authors (see Appendix 2). We used the self-report questionnaire for children and adolescents, as well as the proxy version, which was completed by one of the parents. The questionnaire consists of 24 items equally distributed into six subscales: *physical well-being*, *emotional well-being*, *self-esteem*, *family*, *friends*, and *school*. Each item addresses the child's experiences over the past week and is rated on a 5-point scale (1 = never, 5 = always). Mean item scores are calculated for all subscales and for the total QoL scale, and these are transformed to a 0–100 scale, with 100 indicating very high QoL. In addition, it provides a disorder-related subscale yielding information about the perception of the disorder burden. We modified the form by adding the sentence “Concerning your OCD…” for children and “Concerning your child's OCD…” for parents to the disorder-related questions to ensure we tracked the informants' perception of OCD and not a concurrent somatic or other disorder. Psychometric testing of the KINDL-R revealed good scale utilization and scale fit, and internal consistency of the children's self-report total score was $\alpha = .82$ (Bullinger, Brutt, Erhart, Ravens-Sieberer, & Group, 2008). In a review of QoL measures in children and adolescents, the KINDL-R was found to have acceptable sensitivity to change, which has been reported for only 10% of the identified generic QoL instruments (Solans et al., 2008). A Norwegian normative study had confirmed satisfactory internal consistency and test–retest reliability (Jozefiak et al., 2008).

7.3.2 Resources and emotional and behavioural problems

The Achenbach Child Behavior Checklist (CBCL) is widely used in Scandinavia to enable parents to assess competence and emotional and behavioural problems in general among children (Achenbach & Rescorla, 2001). Approved translations are available in all Scandinavian languages. The CBCL consists of two sections, one addressing competences and the other assessing emotional and behavioural problems in children aged 6–18 years. The CBCL yields scores for activities, social competence and school performance, which all add to a total summary competence score. The Total Competence scale includes 20 items where parents report the amount and quality of their child’s participation in sports, hobbies, activities, jobs and chores, their friendships, how well the child gets along with others and school functioning. From these items, activities, social and school subscale scores can be calculated. The problem section of the CBCL consists of 113 emotional and behavioural problem items rated on a three-point scale: 0 = “Not true”; 1 = “Somewhat or sometimes true”; and 2 = “Very true or often true”. Parents are asked to rate problems the child experienced in the last six months. Two broad dimensions, internalizing and externalizing scales, can be calculated. Some CBCL items also cover OCD symptoms, and different obsessive–compulsive symptom (OCS) subscales have been formed and studied (Geller et al., 2006; Ivarsson & Larsson, 2008; Nelson et al., 2001). In study 1, the OCS subscale proposed by Geller et al. (2006) was used to find possible OCD cases in the control group. In studies 2 and 3, the social and school subscale scores were used as an additional measurement of the psychiatric problem load and correlated with QoL data. Psychometric properties are good, with mean test–retest reliability between .95 and 1.00 and internal consistency from .78 to .97 (Achenbach, 1991). Two Norwegian normative studies confirmed satisfactory reliability and validity of the CBCL (Jozefiak, Larsson, Wichstrom, & Rimehaug, 2012; Novik, 1999).

7.3.3 Autistic traits or symptoms

The Social Communication Questionnaire (SCQ) (M. Rutter et al., 2010) (see Appendix 2) is a screening questionnaire for parents, covering both current and preschool autistic symptoms. The SCQ was originally validated under the name Autism Screening Questionnaire (ASQ) (Berument, Rutter, Lord, Pickles, & Bailey, 1999). The SCQ lifetime form can be used as a screening tool for identifying ASD symptoms as well as to get a dimensional measure of ASD symptom severity for both the preschool period and the current period. A total score of 15 is suggested as a cut-off for a probable ASD diagnosis (Berument et al., 1999). The SCQ produces subscale scores for social interaction (range: 0–15), communication (range: 0–13), and repetitive/stereotyped behaviour (range: 0–8) that parallel the basic domains of the Autism Diagnostic Interview–Revised (ADI-R) (M Rutter, Le Couteur, & Lord, 2003).

The SCQ total score can be divided into two subscales; one describing toddler autistic symptoms and the other describing current autistic symptoms. The scale showed good reliability, as indicated by its internal consistency (Cronbach's $\alpha = .90$) (Berument et al., 1999). SCQ scores can be used to compare levels of ASD symptoms across different samples, as well as to map changes in ASD symptomatology over time.

7.3.4 OCD diagnosis and comorbidity

The Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime Version (KSADS-PL) (Kaufman et al., 1997) is a widely used semi-structured interview for diagnostic assessment of DSM-IV psychiatric disorders and subsyndromal symptomatology in children and adolescents. The KSADS-PL was used to confirm the diagnosis of OCD according to the DSM-IV and to evaluate comorbidity. Diagnoses are scored as definite, probable or not present; in NordLOTS, only definite and not present were used. The KSADS-PL was administered by interviewing the parent(s) and the child. Approved translations of the revised version of the KSADS-PL (Axelson, Birmaher, Zelazny, Kaufman, & Gill, 2009) used in the study were available for all three languages. Inter-rater reliability showed 93–100% agreement, and test–retest reliability (Cohen's κ) was .80 for any anxiety disorders. The instrument had high concurrent validity when compared with questionnaires on depression, anxiety, ADHD and behavioural problems (Kaufman et al., 1997; Miller, Miller, Newcorn, & Halperin, 2008).

7.3.5 OCD symptom severity

Symptom severity was assessed using the CYBOCS (Goodman et al., 1989), which includes a scale for global severity assessment, the Clinical Global Impression (CGI) scale. The CYBOCS is a semi-structured interview containing checklists of obsessions and compulsions. Scales assessing the severity of obsessions and compulsions separately (range: 0–20) are added to provide a CYBOCS total score (range: 0–40). The checklists and severity ratings were based on interviews with each child and parent/adult informant. The CYBOCS showed reasonable reliability and validity, high internal consistency (α = .90) and test–retest reliability for the total score (ICC = .79), and good inter-rater agreement (ICC = .84 for the total score) (Scahill et al., 1997; Eric A. Storch et al., 2004).

7.3.6 Duration of symptoms

As a measure of chronicity of symptoms, the duration of OCD was calculated as age minus year of symptom onset. We used this calculation as an indicator of how long the child had struggled with OCD, suggesting that a child suffering from OCD for only a short time might have a different QoL from a child who has struggled with OCD for many years.

7.3.7 Family accommodation

The Family Accommodation Scale (FAS) (Calvocoressi et al., 1999) is a 12-item clinician-rated questionnaire that is designed to assess the families' accommodation of the child's OCD symptoms. The FAS items measure the extent to which family members provide reassurance or objects needed for compulsions, decrease behavioural expectations of the child, modify family activities or routines and help the child to avoid objects, places or experiences that cause distress. The FAS has demonstrated good psychometric properties including good internal consistency (α = .76–.80) (Calvocoressi et al., 1999; Geffken et al., 2006) good inter-rater reliability (ICC = .72–1.0) and positive correlations with measures of OCD symptom severity (E. A. Storch, Geffken, et al., 2007) and family discord (Calvocoressi et al., 1999).

7.3.8 Children’s Global Assessment Scale

The Children’s Global Assessment Scale (CGAS) is a rating scale for the assessment of children’s general level of psychosocial functioning, primarily for clinicians (Shaffer et al., 1983). It is widely used as a measure of the overall severity of disturbance in children, for example, for treatment evaluation, and as an index of impairment in epidemiological studies. Scores range from 1 (most impaired) to 100 (healthiest). The CGAS has demonstrated adequate inter-rater reliability (ICC = .84) and test–retest reliability (ICC = .63 to .93) (Bird, Canino, Rubio-Stipec, & Ribera, 1987; Rey, Starling, Wever, Dossetor, & Plapp, 1995; Schorre & Vandvik, 2004).

7.4 Statistics

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS), versions 19 (study 1) and 21 (studies 2 and 3) (IBM SPSS Inc., Chicago). In study 1, 0.9–4.2% of the SCQ values were missing. In cases with one or two missing values, the series mean was used instead. In categorical analyses for individual items, these replacements were not used. In studies 2 and 3, missing values analysis showed that missing values were generally low. At baseline, missing values were between 0% and 9.2% in the first five subscales of the KINDL-R parents’ report and between 10.8% and 13.1% in the disorder subscale. In the children’s and adolescents’ self-report, missing values were between 0% and 6.0% in the first five subscales and between 5.3% and 8.3% in the disorder subscale. At post-treatment, missing values were between 0% and 6.6% in the first five subscales of the KINDL parents’ report and between 10.7% and 13.9% in the disorder subscale. In the children’s and adolescents’ self-report, missing values were between 0.8% and 7.3% in the first five subscales, and between 10.6% and 12.2% in the disorder subscale. Missing values were substituted by the mean in accordance with the KINDL manual; if more than two questions in a section of four were not answered, no subscale score or total QoL score was produced. Accordingly, the number of participants varied across subscales and total QoL scores. Because missing values and attrition were generally low (< 10% in the first five subscales and < 14% in the disorder subscale), statistical calculations were conducted as complete case analyses. Concerning the other instruments, available case analyses using the number of cases with available data for the analyses showed very low proportions of cases with missing data, ranging from 0% (CYBOCS) to 3.7% (FAS). Only the CBCL internalizing scale (11.1%) and externalizing scale (10.4%) had a slightly higher proportion of missing data.

In study 1, we used independent t-tests to analyse descriptive data for continuous variables and chi-square for categorical variables. Effect sizes for t-tests were calculated by using Pearson's r. Pearson's correlations were used for investigating the association between preschool and current ASD symptoms and between ASD symptoms and CBCL social competence and problem scores. In the item-level analyses, we applied a stringent alpha-level of significance ($p < .01$) to account for multiple comparisons. Generalized linear model analysis was used to study whether the SCQ total score reflected a non-specific psychiatric symptom burden rather than having OCD. Internal consistency of the SCQ scales in our samples was analysed with Cronbach's alpha. The SCQ total scale showed an acceptable internal consistency of $\alpha = .718$. When analysed separately, internal consistency was $\alpha = .613$ for the cases and $\alpha = .753$ for the controls. The SCQ subscale for preschool symptoms showed internal consistency of $\alpha = .743$, while the subscale for current ASD symptoms was somewhat lower ($\alpha = .620$).

In studies 2 and 3, total QoL scores and subscale scores from both patients and caregivers by proxy were compared with the matched controls from the general population using paired sample t-tests. To explore the relation between comorbid disorders in general and QoL, we compared QoL ratings of children with any type of comorbidity with those of children with OCD only. To differentiate between disorders such as ADHD, TS, ASD, other anxiety disorders and depression, three groups were created based on the presence of comorbidity: (1) OCD only, (2) OCD with ADHD, tic disorder or a combination of both, and (3) OCD with another anxiety disorder, depression or a combination of both. General linear model analysis was conducted with the KINDL total QoL scores and all subscale scores, with both children's self-reports and parents' proxy reports as dependant variables. We used as post hoc procedure Hochberg's test because of the differences in the sizes of the analysed subgroups. With regard to parents' reports of total QoL and the subscale of physical well-being, we used the Games–Howell test because of significant differences in the variances of the groups. Age and gender proved to have no significant impact on QoL in the present study (general linear model with QoL as dependent variable), nor did we observe any interaction effects. Age and gender were therefore not included as covariates in the general linear model analysis of the comorbidity groups. Twenty-five cases had mixed or multicomorbidity with three or more diagnoses, making a detailed analysis meaningless, and were subsequently excluded from this set of analyses. With this approach, we excluded six of the seven cases with depression and all the cases with ASD. To explore a possible specific relation between the mentioned comorbidities and QoL, we created contrasts between each of them and the rest of the sample.

To explore possible associations with QoL other than comorbidity, Pearson's correlations were conducted for OCD symptom severity (CYBOCS score), age of onset, family accommodation and duration of OCD. Correlations were interpreted according to Cohen's conventions to interpret effect size (Cohen, 1992); a correlation of .10 is considered to represent a small correlation, a correlation of .30 represents a moderate association, and a correlation of .50 or larger represents a large association. To explore whether a high symptom load or a threshold of a certain symptom severity was associated with poorer QoL, we compared QoL scores in the group of children with more severe OCD (CYBOCS score ≥ 24) with the group with less severe OCD (CYBOCS 16–23). Because of multiple comparisons, the significance level was set to $p = .01$ for all analyses (F-tests and correlations), except for post hoc tests, where p was set to .05.

Changes in the participants' total QoL scores before treatment (T1) and after treatment (T2) and level of QoL after treatment compared with QoL level in the general population were analysed with paired sample t-tests. Linear regression analyses with the difference of QoL scores between T2 and T1 as the dependent variable, dichotomized into responders or non-responders to treatment, were used to estimate changes in QoL. All linear regression analyses were adjusted for gender, age, and SES as potential confounders. The Pearson chi-square test was used to analyse differences in total QoL scores between T1 and T2 in participants who were not classified as responders to treatment.

7.5 Ethics

Study 1 was approved by the Internal Review Board of the University of Gothenburg. The QoL study was approved by the Regional Committees for Medical and Health Research Ethics in Denmark, Norway and Sweden. All parents gave written informed consent and permission for their children to participate prior to their inclusion in the studies.

8. Summary of results

8.1 Study 1: Preschool and current autistic symptoms in children and adolescents with OCD

8.1.1 Aims of study 1

The aims were to assess and explore ASD symptoms in children and adolescents with OCD (1) using a dimensional approach, covering both current and preschool ASD symptoms, (2) using a normal comparison group to control for the presence of such symptoms in children generally, and (3) to control for overall psychiatric symptoms in both patients and the comparison group.

8.1.2 Main results

ASD symptoms were more common in children with OCD than in controls. However, few (one in each group) had scores in the clinical range for ASD. Symptom prevalence was low, except for symptoms that could be confused with OCD or tics. Figure 5 shows that controls tended to have a skewed distribution, with few children receiving a score of more than five, while the distribution of SCQ scores in the OCD group was closer to the normal distribution, although the mean score was quite low. The correlation between preschool and current ASD symptoms was also low. Thus, the presence of ASD symptoms in paediatric OCD seems to indicate that ASD and OCD co-occur in a subgroup of cases rather than in OCD as a whole.

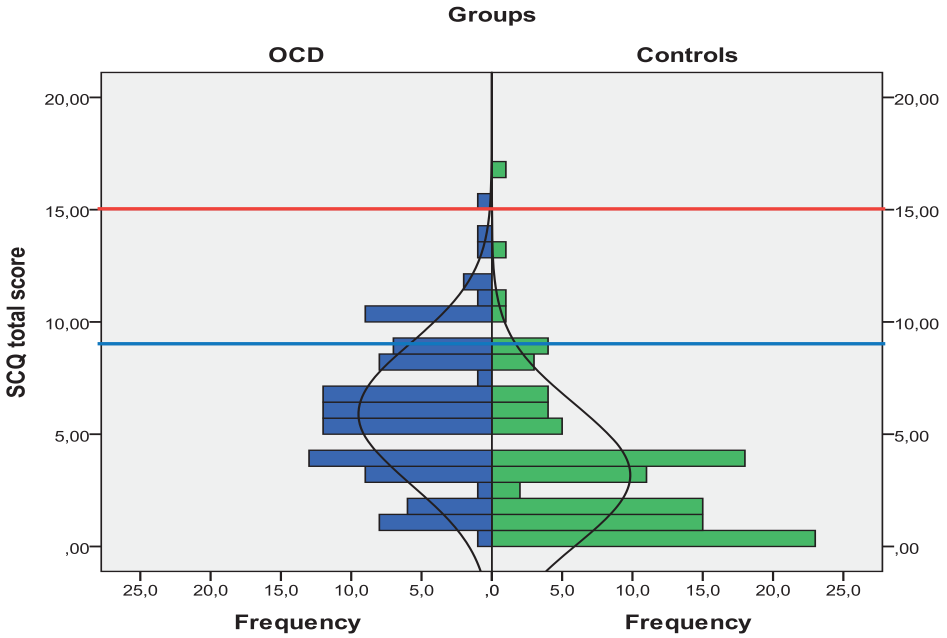


Figure 5 Distribution of SCQ total scores in the OCD (n = 105) and control group (n = 108). The red line represents the cut-off for the SCQ total score to indicate ASD (n = 15). The blue line represents an alternative cut-off score based on the 95th percentile in the control group (n = 9).

8.2 Study 2: Quality of life in children with OCD with and without comorbidity

8.2.1 Aims of study 2

The aims were (1) to assess quality of life as reported by both paediatric patients with OCD and their caregivers before treatment compared with an age- and gender-matched sample of students from the general population, (2) to compare social competence and school functioning of these patients with those of the general population, (3) to investigate the relation between comorbid disorders such as ADHD, TS, other anxiety disorders, depression and QoL, and (4) to explore the significance of other factors for perceived QoL, such as duration, severity and the family's accommodation of the OCD symptoms.

8.2.2 Main results

Overall, we found a clear reduction in QoL in children with OCD affecting total QoL measurements and most of the subdomains reported by both patients and their caregivers compared with the general population (Figure 6). Children's self-report revealed lower scores for total QoL and for all subscales, except self-esteem and school. Parents' proxy reports had a similar pattern, with reduced total QoL scores and subscale scores. In the CBCL, parents also reported highly impaired social functioning of the children with OCD compared with the general population. School functioning was also significantly lower than in the general population, but not as low as for social competence scores.

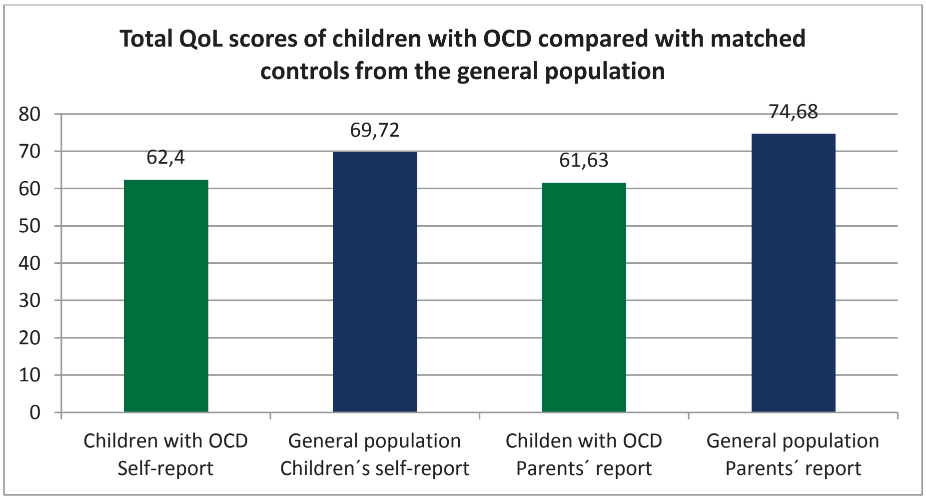


Figure 6 Quality of life: children's self-report (n = 121–133) and parents' proxy report (n = 100–110) compared with matched controls from the general population (*p* = < .001).

Parents reported a significant impact of comorbidity on QoL with respect to total scores and the subscales physical well-being, emotional well-being, friends and school. In the children's ratings, we found a tendency for lower QoL scores in children's self-reports in the comorbidity group compared with the OCD-only group; however, none of the observed differences were statistically significant. Table 1 gives an overview of the correlations between different parameters and total QoL scores assessed by children's self-report and by parents' report.

Table 1 Pearson correlations between different parameters and total QoL scores as assessed with the KINDL-R children's self-report and parents' proxy report (n = 113–135).

	Children's self-report	**Parents' proxy report**
OCD severity (CYBOCS score):	–.19, *p* = .025	–.28, *p* = **.001**
Family accommodation (FAS score):	–.10, *p* = .253	–.40, *p* < **.001**
Age of OCD onset:	–.02, *p* = .786	.08, *p* = .353
Duration of OCD:	–.18, *p* = .036	–.19, *p* = .032
CBCL internalizing score:	–.35, *p* < **.001**	–.59, *p* < **.001**
CBCL externalizing score:	–.33, *p* < **.001**	–.50, *p* < **.001**

Severity of OCD and family accommodation were negatively correlated with QoL in parents' proxy reports, but not in children's reports. Correlations were all low to moderate. The CBCL internalizing score showed overall significantly negative correlations with QoL both in children's reports and parents' proxy reports except on two subscales in the children's reports (family and school). Externalizing problems scores showed a similar pattern with low to moderate negative correlations between QoL and the CBCL externalizing score for parents' reports of total QoL and all subscales except self-esteem. For children's reports, total QoL scores and emotional well-being and family subscale scores were significantly negatively correlated with externalizing scores, with correlations being somewhat lower than for the parents' reports.

8.3 Study 3: Quality of life before and after treatment in children with OCD

8.3.1 Aims of study 3

The aims were (1) to assess changes in QoL after treatment with CBT in children and adolescents with OCD, as reported by both children and their caregivers, compared with QoL in individually matched and randomly allocated children with comparable gender and age from the general population, and (2) to assess whether treatment response, comorbidity, psychosocial functioning and family accommodation are associated with QoL changes when controlled for gender, age and SES.

8.3.2 Main results

QoL, as reported by children with OCD and their caregivers, had improved markedly after treatment. Changes in total QoL scores and all subscale scores were significant except for the friends and school subscales in the children's report. The QoL improvement was mainly loaded by CBT responders (total QoL scores mean change was 7.4 for children's reports and 9.2 for parents' reports), while non-responders had almost no change (mean change 0.23 for children's reports and 1.2 for parents' reports). After treatment, QoL ratings in treatment responders were in the same range as in the general population (Figure 7). The presence of comorbidity, defined as OCD only versus OCD with any comorbidity as assessed at baseline, was not associated with changes in QoL. Family accommodation, defined by FAS score at baseline, was not associated with changes in QoL after treatment.

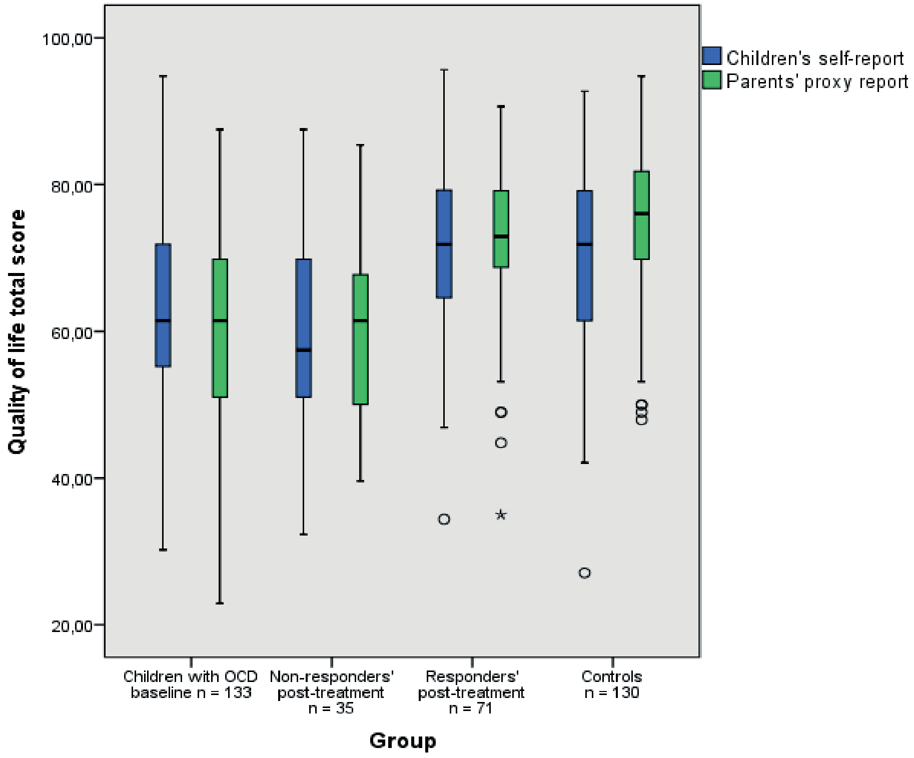


Figure 7 Total quality of life by children's and parents' report in responders and non-responders compared with matched controls from the general population. Participants consisted of 133 children who reported QoL at baseline and 106 children who reported post-treatment (71 responders, 35 non-responders).

9. Discussion

To provide a complete picture of the burden of a disorder, it is recommended to not only assess symptoms and their severity but also to add a measure of the subjective perception of the impact the disorder has on the individual. Our study acknowledged the following factors: categorical diagnoses for OCD and comorbid disorders were established with the KSADS-PL, dimensional aspects were addressed with the CYBOCS to measure severity, and the subjective perspectives of both children and caregivers were provided by QoL assessment with the KINDL-R.

9.1 Comorbidity and classification

9.1.1 Is autism an obsessive–compulsive spectrum disorder?

Beside the implications for treatment interventions outlined in the Introduction, another interesting aspect of studying the relationship between ASD symptoms and OCD is the ongoing debate about the nosological placement of OCD. Some researchers have suggested including OCD together with ASD, tic disorders, hypochondriasis, body dysmorphic disorder and trichotillomania as one part of the so-called obsessive–compulsive spectrum disorders (OCSD) (Bartz & Hollander, 2006; Hollander et al., 2007). The reasons for this unification are fourfold: the OCSDs share a core feature of repetitive thoughts and behaviour; the presence of phenotypic similarities such as age of onset, comorbidity, and family loading; the sharing of brain circuitry abnormalities, familial and genetic factors, and neurotransmitter abnormalities; and the disorders may be treated pharmacologically with similar drugs. Others have strongly questioned this approach. Storch and co-workers (2008) argued forcibly that the symptoms of these disorders have different cognitive, motivational and functional underpinnings. The functional role of compulsions was specifically pointed out as being different from that of behaviours in the other OCS disorders. Consequently, they argued, the OCSD construct is misleading.

One aspect of the OCD–ASD overlap is the elevated level of ASD comorbidity in OCD, which several researchers have reported in adults as well as in paediatric samples (Ivarsson & Melin, 2008; Ivarsson et al., 2008) (see section 5.3.1). Correspondingly, when appropriately assessed, OCD comorbidity is high in autistic samples (Leyfer et al., 2006; Russell et al., 2005). Another reason for the hypothesis of an OCSD was the phenomenological overlap between OCD, ASD and tics/TS (Hollander et al., 2007). The presence of, for example, repetitive behaviour in these disorders would be a common underlying feature. In ASD, repetitive behaviour is one of three defining symptom clusters, often meeting the need for sameness. In OCD, repetitive rituals are likewise present in most patients. However, as Storch and colleagues (2008) pointed out, repetitive behaviour in OCD has a different function, namely that of regulating anxiety. In a similar manner, Baron-Cohen (1989) suggested that the terms obsession and compulsion should be used with caution to describe autistic behaviours because they may fail to satisfy the definitions of OCD with regard to the ego-dystonic aspects (unwantedness, distress, resistance, senselessness), and recommended using the more descriptive term ‘repetitive activities’ instead. However, many patients with OCD have compulsions concerning ordering and symmetry, as well as repetition, in order to satisfy the need for a ‘just right’ feeling (Livingston-Van Noppen, Rasmussen, Eisen, & McCartney, 1990; Rapoport, 1989), which could be difficult to differentiate. Repetitive behaviour is the autistic symptom that is closest to the proposed core feature of the OCSD

(Hollander et al., 2007). Thus, if the theory of repetitiveness as a core feature of ASD holds, repetitiveness should be present during the preschool years at the onset of ASD symptoms, as well as in later childhood following the onset of OCD symptoms, which is usually at around 9–10 years of age (Masi et al., 2005). In addition, one would expect substantial continuity between ASD symptoms at preschool age and later in childhood and adolescence across all patients. To explore whether this is the case, we assessed ASD symptoms in children with OCD using a dimensional approach, covering both current and preschool ASD symptoms, compared with the general population. The comparison group was used to control for the presence of ASD symptoms in children and adolescents in general and for overall psychiatric symptoms in both groups.

Our results (study 1) showed that autistic symptoms were indeed more common in children with OCD than in the general population. Even if autistic symptoms that could be confused with OCD symptoms or tic-like symptoms were excluded, ASD symptoms occurred at a greater prevalence than in controls. However, in the sample as a whole, ASD symptom prevalence was low. The vast majority of OCD patients did not have these traits. Thus, the presence of ASD symptoms in paediatric OCD seems to indicate that ASD and OCD co-occur in a subgroup of cases rather than in OCD as a whole. In addition, those with autistic traits, who made up approximately a fifth of the OCD group, tended to have symptoms concerning communication difficulties more often than social difficulties in their preschool years. The most autism-specific symptoms (i.e., gaze avoidance, absence of social smile, and lack of shared attention, reciprocal social interaction and interest in peers) were not endorsed either. Thus, it would be difficult to construct evidence of a strong continuity between early

ASD traits in children who later develop OCD from the preschool symptoms alone. Moreover, only a few cases had high levels of preschool ASD symptoms. Contrary to the current symptom subscale of the SCQ (see Appendix 2), the preschool subscale does not include items related to repetitive/stereotyped behaviour. Therefore, repetitiveness might have been overlooked and missed in some cases. The current symptoms subscale generates a different problem, as several items overlap with both OCD (verbal rituals, compulsions and rituals) and comorbid tic disorder (hand and finger mannerisms and complex body movements). For example, is the SCQ question on compulsions and rituals worded in such a way that OCD compulsions could be included, namely ''Does she/he ever have things that she/he seems to have to do in a very peculiar way or order or rituals that she/he insists that you go through?" Similarly, tics might be confounded with the SCQ question ''odd ways of moving his/her hands or fingers''. In general, the association between preschool and current ASD symptoms was weak. Only the OCD subgroup with the highest level of preschool ASD symptoms demonstrated substantial continuity with current ASD symptoms.

The argument by Hollander (2007) and Bartz (2006) that OCD as a whole should be reclassified together with ASDs, tics/TS and various other disorders into an obsessive–compulsive spectrum group seems out of proportion, and was not supported by the level or type of current comorbid ASD symptoms, nor by the presence of preschool ASD symptoms in our study. However, the higher level of ASD symptoms in our OCD patients compared with controls, which existed independently of other psychiatric problems, might indicate that there is an underlying relationship in a subgroup of OCD patients.

9.2 QoL in children with OCD

9.2.1 QoL is reduced in children with OCD

In our study, we found a marked reduction in QoL in children with OCD compared with the general population, affecting total QoL measurements and most of the subdomains reported both by patients and their caregivers. This is consistent with studies of OCD in adults and the two studies offering data for paediatric OCD (Lack et al., 2009; Vivan Ade, Rodrigues, Wendt, Bicca, & Cordioli, 2013), despite the variety of QoL assessment instruments used. Our findings corroborate their finding of significantly impaired QoL in children with OCD with a larger sample size and a methodologically stringent design.

Social competence and school functioning in children with OCD, as reported by parents on the CBCL, were highly impaired compared with the general population. School functioning was also significantly lower than in the general population, but not as low as social competence scores. These results seem to be in accordance with the clinical experience that OCD symptoms might have a more profound impact on social life than on school performance. Taken together, it is noteworthy that patients with OCD have shown both 'subjectively' reduced QoL and correspondingly decreased levels of functioning as evaluated 'objectively' by external observers in important domains of life.

9.2.2 Comorbidity is associated with reduced QoL

Caregivers of children with OCD and at least one comorbid condition, such as ADHD, TS, other anxiety disorders or depression, reported considerably reduced QoL compared with children with 'pure' OCD. In children's reports, we observed the same tendency but without reaching significance levels. That only parents reported reduced QoL in children with comorbid conditions might be due to the general tendency of children to rate their QoL with a more optimistic view than their parents, as seen in other studies. In studies of parent–child agreement on QoL, parents of children in non-clinical samples tend to report higher QoL scores than their children (Jozefiak et al., 2010; Upton et al., 2008), while parents of children with disorders tend to under-estimate QoL compared with their children. In Lack and co-workers' (2009) study, parents generally rated QoL lower than their children did, suggesting that young people may minimize the impact of their condition on QoL.

Another possible explanation for our results could be that the numbers of children with a categorical DSM-IV comorbidity diagnosis might be too low to reach significance levels in children's QoL reports. The disadvantage of categorical DSM-IV diagnoses is that patients on a subclinical level falling short of fulfilling diagnostic criteria are not taken into account, despite having considerable problems. Accordingly, on the symptom level, internalizing and externalizing problems assessed with CBCL by parents were associated with reduced QoL. Both children's and parents' reports of QoL total scores and scores in most of the subdomains were inversely associated with the CBCL internalizing and externalizing problem scores. The dimensional assessment approach of the CBCL, summarizing symptoms into quantitative externalizing and internalizing problem scores, might have been more sensitive than the diagnostically categorical approach to detecting QoL impairment associated with comorbidity in all domains. Although the correlations between the load of comorbid internalizing and externalizing problems and reduced QoL were low to moderate, they underline the importance of keeping these factors in mind as part of the assessment procedure for children with OCD.

Because OCD affected children with a variety of other disorders in almost half of the patients in our sample, it was a challenge to disentangle the impact of different comorbidities on QoL because of statistical power problems caused by the low numbers in the comorbidity subgroups. In our analysis of two subgroups with specific comorbidity (ADHD, tic disorder or both, and anxiety disorder, depression or both) compared with the OCD-only children, we found a tendency for the children in both subgroups to report lower QoL. On the other hand, parents reported significantly worse total QoL and relationship to friends' scores for the group with OCD and neuropsychiatric disorders compared with the OCD-only group, while comorbid anxiety disorders were not associated with worse QoL.

Both ADHD and TS are associated with poor QoL in children and adolescents (Cutler, Murphy, Gilmour, & Heyman, 2009; Klassen, Miller, & Fine, 2004; E. A. Storch, Merlo, et al., 2007). Bernard and colleagues (2009) found that OCD and ADHD were significant contributors to poor QoL in a study of 56 young people with TS (age 5–17). In a study of 50 young people (aged 11–17), Eddy and colleagues (2012) showed reduced QoL in the presence of both ADHD and OCD. In this study, severity of OCD symptoms was negatively related to QoL in several domains, whereas ADHD symptoms appeared to have a negative impact on self and relationship domains only, suggesting that comorbid OCD could have a more widespread negative impact on QoL. While confirming the additional negative impact of a comorbid neuropsychiatric disorder on QoL in paediatric patients with OCD, we were not able to differentiate between the potential effects of ADHD versus TS because of the sample size and overlapping comorbidity. Parent reports showed a tendency to poor total QoL, emotional well-being, relationships with friends and school scores for children with tics, but without reaching significance levels. Because our tic disorder group contained many different types of comorbidity, it was impossible to draw firm conclusions concerning these results.

Severe depression with suicidal ideation was an exclusion criterion in the NordLOTS study. This could be one of the reasons why we had a comparable low prevalence of depression in our sample. The seven patients with depressive disorder and their caregivers tended to report lower QoL scores than other patients, with regard to total QoL, emotional well-being and school, although these differences were not significant. In addition, the children reported poorer physical well-being. One must bear in mind that six of the seven patients with depression had one or more other comorbidities; thus, the reduced QoL may well be a reflection of the general high load of comorbidity. On the other hand, the additive impact of comorbid depression on QoL is well documented in previous studies, at least in adults (Hollander, Stein, Fineberg, Marteau, & Legault, 2010; Macy et al., 2013). Emotional well-being and school were the two most affected domains in the depression group, and were reported congruently by children and parents. An interpretation of this finding could be that depression is probably more negatively associated with emotional well-being and perceived school functioning than OCD alone. That this pattern emerged in comparison with even this small group with comorbid depression, but not in comparison with the group including all comorbidities, could indicate a specific association between QoL and depression in these two domains.

Children with ASD and their caregivers rated QoL in the same range as the other patients. Previous papers have discussed whether subjectively perceived QoL can be reliably measured in children with ASD because of differences in perception (Mitchell & O'Keefe, 2008). Shipman and colleagues (2011) provided preliminary evidence that adolescents with ASD were able to report on their QoL in a valid and reliable manner. However, children with ASD and comorbid OCD are reported to have poorer insight into the exaggerated nature of their obsessions, and they may experience their compulsions in a less ego-dystonic way (Baron-Cohen, 1989; Ruta, Mugno, D'Arrigo, Vitiello, & Mazzone, 2010). OCD symptoms usually have a great impact on social life, while children with ASD may be likely to report better QoL because of their reduced interest in social activities. Both factors may contribute to perceptions of less impaired QoL. On the other hand, a possible explanation could be that OCD affects QoL to such an extent that there is no room for further QoL reduction in ASD patients. Regardless, the small number of children with ASD included in our study does not allow us to draw firm conclusions.

9.2.3 QoL before and after treatment

QoL, as reported by both children with OCD and their caregivers, improved to a great extent after treatment. Responders to treatment had a significant increase in total QoL scores and achieved the same levels of QoL reported by the general population, while non-responders reported almost no change. These findings suggest that the CBT treatment intervention was highly effective, not only in reducing symptoms in responders, but also in improving QoL to a level corresponding to that of the general population. Also, in a nine-year follow-up study by Palermo and colleagues (2011), remitters to treatment showed no QoL impairment in adulthood, while non-remitters had only mild QoL impairment. However, the studies cannot be compared directly. The therapeutic intervention consisted of medications and/or behavioural therapy throughout the study interval, but some of the participants were still receiving active psychiatric treatment, including 60% who had continued their medication, when QoL was assessed at a mean of 21 years of age. In addition, baseline assessment or a general population control was not available in the Palermo study, and long-term follow-up data are not yet available from our study.

Our findings of QoL improvement to normal levels after treatment contradict the findings in studies of adults. Huppert and colleagues (2009) found that QoL levels in individuals in remission tended to lie between healthy controls and individuals with current OCD, with no significant difference when compared with healthy controls, or with patients who had current OCD. Moritz and colleagues (2005) found significantly improved QoL in therapy responders relative to non-responders, but compromised QoL persisted in most patients across time. OCD severity was only modestly correlated with QoL, suggesting that QoL improvement after treatment reflected several influencing factors on QoL and not just improved OCD symptoms. In addition, in Hertenstein's study (2013), QoL was significantly improved after 12 months of intensive state-of-the-art treatment, but the QoL indices remained considerably lower than population norm values. In contrast, our results showed that QoL was improved after appropriate treatment to normal population levels in children and adolescents who were treatment responders. One explanation might be that treatment effects in children are larger than in adults, consequently leading to improvement in QoL, because it is likely that children had a shorter course of the disorder than adults. In addition, in paediatric patients, treatment may lead to more cases with complete remission of symptoms, while study samples of adult patients may include a higher frequency of chronic patients. However, Hertenstein assessed QoL at baseline and at follow-up 12 months after the inpatient treatment and continuing outpatient treatment, while QoL in our sample was assessed after 14 weeks of treatment intervention. Thus, it is not clear whether QoL scores will be maintained in the normal range one year after the therapeutic intervention. In our study, a follow-up over three years post-treatment is intended, to explore whether treatment gains of symptom reduction and QoL improvement will be stable over time.

9.2.4 Comorbidity, treatment and QoL

Surprisingly, the presence of comorbidity was not associated with changes in QoL after treatment in either children’s or parents’ reports. One might presume that the presence of comorbidity could lead to a lower impact of OCD treatment gains on QoL, because the comorbid conditions will still have a negative influence on QoL after treatment. However, the presence of comorbidity at baseline was not associated with QoL changes in either responders or non-responders to treatment. This could be due to an expanding effect of CBT to other symptoms and problems beyond the reduction of OCD symptoms. On the other hand, the marked treatment impact on QoL in responders might override the lack of improvement in the comparatively small group of non-responders. Interestingly, in Palermo and colleagues’ (2011) study, childhood comorbid conditions such as tic disorders, ADHD, depression and other anxiety disorders had no significant value for predicting QoL in early adulthood.

In adults with OCD, the additive impact of comorbid depression on QoL is well documented (Hollander et al., 2010; Macy et al., 2013). In Hertenstein's (2013) study, QoL improvement after treatment was predicted by improvements in depressive symptoms. Moritz and colleagues (2005) found the most pronounced correlations with QoL for depression severity and number of OCD symptoms. Hupert and colleagues (2009) found that participants with OCD and comorbid psychiatric diagnoses showed the poorest QoL, with comorbid depression accounting for much of the variance. The only available study providing information about depressive symptoms in adolescents with OCD (Vivan Ade et al., 2013) found a significant negative relationship between QoL and depressive symptoms as evaluated with the Beck Depression Inventory. The KSADS-PL was used to confirm the diagnosis of OCD in the study, but no information about the relationship between QoL and depression above the diagnostic threshold was offered. Severe depression with suicidal ideation was an exclusion criterion in the NordLOTS study. This could be one of the reasons why we had a comparatively low prevalence of depression in our sample. At baseline assessment, only seven patients were diagnosed with depressive disorder, reporting a non-significant tendency for poorer QoL compared with the other patients. In addition to low prevalence, six of the seven patients with depression had one or more additional comorbidities. Thus, an analysis of QoL change in patients with comorbid depression during treatment would not allow any conclusion to be drawn at all.

9.2.5 Severity of OCD, age of onset, duration of symptoms and QoL

As expected, we found a negative association between symptom severity and QoL, mainly as reported by parents. Although significant, the correlations were low to moderate. In children's self-reports, the negative association between symptom severity and QoL emerged in the disorder subscale only. To explore whether a high symptom load or a threshold of a certain severity was associated with poorer QoL, we compared QoL ratings of children with more severe OCD with those of the group with less severe OCD. The majority of children in our sample had more severe OCD, with CYBOCS scores of 24 or above. These children and their parents reported significantly lower scores on the disorder subscale than children with less severe OCD. The disorder section of the KINDL reflects the children's subjective perception of how well they are able to cope with OCD problems. That more severe symptoms are associated with a perception of reduced coping abilities is consistent with our expectation. Interestingly, there was high congruence between children's ratings in the other QoL domains displaying non-significant tendencies to reduced total QoL, emotional well-being and self-esteem, and parents' reports, confirming this pattern. The broad agreement between children and parents in this area seems to support the argument that a threshold of severity is associated with poorer QoL, at least in the mentioned domains, despite the fact that they did not reach significant levels.

There was no association between QoL and age of onset of OCD. Duration of OCD was significant for parents' reports only with regard to the physical well-being subscale. Surprisingly, duration of symptoms did not emerge as an important factor. A possible explanation could be that both children and parents are adjusting to the disorder burden over time, which is reflected in their perception of QoL. Taken together, all correlations that we found between QoL and the investigated factors were low to moderate. The correlation between severity of symptoms and load of comorbid internalizing and externalizing problems and reduced QoL underlines the importance of having these factors in mind as part of the assessment procedure for children with OCD. Although all of these factors were correlated with QoL, none of them showed a high correlation, indicating the value of assessing QoL. This finding seems to support our view that QoL evaluation covers different and important aspects of the disorder that are not accounted for in the framework of symptomatic and functional assessment only.

9.2.6 Family accommodation, psychosocial functioning and QoL

The term ‘family accommodation’ describes the involvement of family members of patients with OCD in their rituals, either by assisting or by direct participation. In parents’ reports, we found low to moderate inverse associations between levels of family accommodation and total QoL scores and all subscale scores except the school subscale. In children’s self-reports, we found no association between family accommodation and QoL. As the family accommodation score by definition reflects the involvement of the parents in their children’s OCD symptoms, this result was predictable. The finding that parents’ perception of QoL affects the total score and all other domains, except school, is consistent with the clinical observation that OCD symptoms are often more dominant in the home environment than at school. Alternatively, it may simply reflect the fact that parents are less involved in OCD while the children are at school.

Family accommodation and psychosocial functioning at baseline were not associated with changes in QoL after treatment, either in children's or in parents' reports. Our findings may indicate that CBT was highly effective in most cases, independent of baseline psychosocial functioning and family accommodation. In Diefenbach et al.'s (2007) study of adults, more impaired family functioning was the only demographic or clinical characteristic to differentiate the subgroup of patients whose improvements in OCD symptoms corresponded with improvements in QoL. The authors considered the possibility that this subgroup may have received more treatment specifically targeting family functioning, because patients had more family involvement in rituals. Because of a lack of measures of family accommodation in rituals, this hypothesis could not be tested. In our study, a considerable amount of effort was put into family work, encouraging caregivers to actively participate during their children's treatment. A possible interpretation of our results could be that even non-responders had an unspecific benefit from the family components of the treatment.

9.3 Outcome criteria and QoL measurement

In our study, QoL improvement was clearly associated with symptom reduction. There is an ongoing discussion in the field about the standards for treatment evaluation in terms of optimal definitions for treatment response, remission criteria and symptom reduction, and about the need to include other outcome parameters, such as functional impairment and health-related QoL measurements (Pallanti et al., 2002; Tolin, Abramowitz, & Diefenbach, 2005). The latter group questioned the external validity of clinical trial results: do gains seen on standardized clinical measures correspond to clinically meaningful changes in real-world functioning (Tolin et al., 2005)? Lack and colleagues (2009) strongly recommended QoL assessments as a parameter for treatment evaluation in paediatric OCD patients, noting their relevance for both assessment and treatment. According to the authors, “targeting symptoms only without attending to QoL may result in the confounding of assessment data as the patient may have reduced symptoms that do not translate into improved day-to-day functioning.”

In many studies, treatment response is defined as a 25–35% reduction from baseline on the YBOCS or CYBOCS score (Pallanti et al., 2002; Tolin et al., 2005). In the NordLOTS study, responders were defined by a CYBOCS score < 16. This decision was based on the Paediatric OCD Treatment Study (POTS), where the same value was used to define clinically relevant OCD symptoms (Franklin et al., 2011). Another reason for a comparably high cut-off score was the fact that non-responders were randomized to either CBT or SSRI. To avoid the ethical problems of treating children with only mild symptoms with medication, the criterion CYBOCS score < 16 was used to indicate response. As a secondary outcome measure, a 30% reduction in CYBOCS score was added to ensure that the primary outcome measure of CYBOCS < 16 did not inflate the rate of responders. In the above-mentioned study by Palermo and colleagues (2011), remission was used to define treatment response (remitters’ YBOCS score: < 8, mild OCD: 8–15, moderate OCD: 16–23 and severe OCD: > 23). Consequently, they reported a larger number of individuals without QoL impairment (57%) than remitters (42%), and found that non-remitters had only mild QoL impairment in adulthood. These results could suggest that QoL was not directly related to symptom level, in spite of the strong correlation between QoL and severity of residual symptoms. However, if a definition of responders with YBOCS score < 16 including the participants with only mild

OCD is applied, the responder rate would increase to 80%, supporting our finding that QoL impairment was closely related to symptom level in children with OCD.

In a medication study with adults, Hollander and colleagues (2010) found that improvements in QoL were closely correlated with improvements in YBOCS score. They suggested, as an important step toward achieving a consensus for any given outcome based on a YBOCS criterion, that such a criterion should demonstrate to distinguishing patients on the basis of a clinically meaningful assessment that varies as a function of YBOCS score. When they defined response using the YBOCS criterion of at least a 25% improvement in total score relative to baseline, the mean QoL scores for responders and non-responders were clearly distinguishable. We also found a clear relationship between symptomatic improvement and QoL, suggesting that QoL assessment with the KINDL-R is sensitive to treatment outcomes supporting the CYBOCS cut-off scores used in the study to define treatment outcomes. However, a small subsample of six individuals reported clinically important QoL improvement without being classified as responders to treatment. Of these participants, five showed a large reduction in their CYBOCS score (> 9), but not to the extent that they met the criteria for clinical response. Only one participant reported QoL improvement without clinical improvement. Thus, without QoL evaluation or additional outcome criteria, treatment response in these individuals could have been overlooked.

The results showing a close relationship between symptom reduction and QoL improvement are consistent with the results from Diefenbach et al.'s (2007) adult OCD sample. However, there are several other reports suggesting independence between symptom response and

QoL improvement in adults (Bystritsky et al., 2001; Tenney, Denys, van Megen, Glas, & Westenberg, 2003). Again, the reason for our findings could be that treatment in children was related to a more profound improvement in QoL, as it is likely that children had a shorter course of the disorder than adults. Another, rather methodological, explanation could be the different sensitivity levels of the various QoL assessment instruments used and their ability to detect changes.

9.4 Limitations and strengths

This study has a number of limitations. Some of the symptoms or traits we measured might be an artefact of assessment. When children and parents fill in questionnaires, we depend on their interpretations and observations. Although, most questions were descriptively oriented, some scores might be the result of faulty observations and/or interpretations. Using semi-structured interviews such as the KSADS and CYBOCS is considered to give more reliable estimates and thereby solve this problem.

In study 1, the use of screening tools such as the SCQ for the patients, and the CBCL to verify that the children in the control group had no bias in terms of high load of psychiatric symptoms or suspected psychiatric disorders, are not, of course, equivalent to a diagnostic interview. Using a semi-structured interview such as the Autism Diagnostic Interview - Revised (M Rutter et al., 2003) for children with OCD and the KSADS for controls would probably give more reliable estimates, but this study was limited by resources. Because of the homogeneous socio-demographic factors and similarities in culture and language of the populations in the Nordic countries, our sample consisted mostly of relatively well-educated families of Caucasian origin. Inability to understand one of the Nordic languages was an exclusion criterion. This represents a clear limitation to the generalization value for other populations. Although studies 2 and 3 were based on a relatively large sample of paediatric patients with OCD, some subgroups of comorbid disorders were very small, leading to problems of statistical power, which limited the analysis of each individual comorbid disorder group. A third limitation lies in the cross-sectional design of the study; this design generally does not allow conclusions to be drawn about causality or the effect of the observed associations between QoL and the examined factors. Another limitation is the lack of a treatment control group in study 3. Although our results offer strong empirical support that QoL in children and adolescents with OCD is improved after CBT, conclusions about the causal relationship between CBT and QoL improvement cannot be drawn. A final limitation is the lack of follow-up data in study 3, as QoL was assessed directly after the therapeutic intervention. There is no information available about the long-term impact of CBT on QoL in children with OCD. Thus, it is not clear whether QoL scores will be maintained in this range or deteriorate over time.

The study also has a number of strengths. The first study explored a theoretical nosological concept, namely the classification of ASD as part of an obsessive–compulsive spectrum group, empirically. Our results do not support this concept.

The QoL study is, to date, the largest study of QoL in children and adolescents with OCD. Assessments of OCD and comorbid disorders were based on standardized semi-structured diagnostic interviews. QoL ratings were available from both the children and their caregivers by proxy. QoL scores were compared with scores of individually assigned and matched controls from the general population rather than just with community norms. QoL was assessed prospectively before and after the treatment intervention. Altogether, attrition was low, and both children and parents had a high compliance rate in terms of completing the questionnaires.

9.5 Suggestions for future research

To overcome limitations, for example, in comparing comorbidity groups, much larger samples are needed for further research. This would demand not only regional multicentre studies, but also collaboration across different countries. In disorders with a low prevalence, it is necessary to join forces, collaborating in multicentre or even multinational studies. To investigate the causal relationship between treatment effect and QoL, randomized controlled trials are needed. Another crucial issue is the development of reliable instruments and agreement on their use in studies, allowing comparison across studies. Of course, this is a prerequisite for any collaboration project. Follow-up data on the stability of treatment outcomes over time are required to improve the development of individual treatment plans and to inform health policy decision making.

10. Conclusions

This thesis contributes to an understanding of the burden of OCD in childhood and adolescence, providing an empirical basis for theoretical concepts of comorbidity and QoL and how they are interrelated. ASD symptoms were more common in children with OCD than in the general population. We found significant levels of autistic symptoms in children with OCD. However, the majority of OCD patients did not have these traits, indicating that ASD and OCD co-occur in a subgroup of cases rather than in OCD as a whole. In general, the association between preschool and current ASD symptoms was weak. ASD symptoms, as reported in children with OCD, did not show a strong enough relationship between OCD and ASD to supporting the classification of ASD as part of an obsessive–compulsive spectrum group. However, a subgroup of paediatric OCD patients had significant subclinical ASD symptom levels. Possible implications of this should be considered in tailoring individual treatment interventions.

Children and adolescents with OCD had reduced QoL and social competence compared with the general population. OCD with comorbidity showed lower QoL than OCD without any comorbidity. Treatment with CBT was associated with improvement in QoL ratings. Responders to treatment rated improved QoL to such a degree that they reached the QoL levels reported in the general population. Non-responders reported no QoL changes after treatment, with the exception of one case. Severity and duration of symptoms, family accommodation and comorbid internalizing and externalizing problems were associated with reduced QoL at baseline. However, the associations were only weak to moderate, indicating that QoL evaluation covers different aspects of the disorder than symptomatic and functional assessment. Comorbidity, family accommodation and psychosocial functioning were not associated with changes in QoL after treatment. QoL assessment in the present study supported established outcome criteria of clinically meaningful symptom reduction in children and adolescents with OCD. The assessment of QoL beyond symptoms and function in children with OCD has been shown to be reliable and informative. Based on our findings, we suggest employing QoL assessment as an additional outcome measure in treatment plans in order to obtain a more comprehensive understanding of childhood OCD.

A simplified overview of the complex relationship between OCD, treatment and QoL is given by O., aged 9 years (Figure 8).

Figure 8 Correct attitude of the CBT therapist: thumbs up!

11. References

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12. Papers 1–3

Paper I

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Preschool and current autistic symptoms in children and adolescents with obsessive-compulsive disorder (OCD)

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ABSTRACT

Objective: Contemporaneous nosological debates include the presence of an Obsessive-Compulsive Spectrum Disorder (OCSD) group incorporating disorders as OCD, Tourette's syndrome, eating and autism spectrum disorders (ASD). If true, we propose, ASD symptoms should occur in the early childhood of OCD patients, show substantial continuity to later childhood and be present in a large proportion of cases. This study explores whether this is the case or not.
Methods: Paediatric patients with OCD ($n=105$) according to DSM IV were studied using parent ratings of the Social Communication Questionnaire. A general population group without ASD ($n=108$) was used to control for ASD symptoms in the normal population.
Results: ASD symptoms were more common in children with OCD than in controls ($m=5.9$ versus 3.1; $p=.0001$). However, few (one in each group) had scores in the clinical range for ASD. Symptom prevalence was low, except for symptoms that could be confused with OCD or tics. The correlation between preschool and current ASD symptoms was low.
Conclusion: ASD symptoms in OCD as reported here do not support claims about OCD as strongly related to ASD. However, a subgroup of paediatric OCD patients has significant subclinical ASD symptom levels.

1. Introduction

1.1. OCD nosology debate

Obsessive-compulsive disorder (OCD) is a common disorder among children and adolescents (Heyman et al., 2001), that often takes a chronic course (Stewart et al., 2004) and has for decades been classified in the DSM as an anxiety disorder in view of the anxiety associated with obsessions and the function of rituals to ease it. However, there has been considerable debate about the nosological placement of OCD. Arguments for a unifying relationship between OCD and autism spectrum disorders in a family of Obsessive-Compulsive Spectrum Disorders (OCSD) also containing tic disorders and disorders such as hypochondriasis, body dysmorphic disorder and trichotillomania have been raised (Bartz & Hollander, 2006; Hollander, Kim, Khanna, & Pallanti, 2007). The grounds for this unification are fourfold: that the OCSDs share a core feature, i.e. repetitive thoughts and behaviour; the presence of phenotypic similarities like age of onset, comorbidity, and family loading; the sharing of brain circuitry abnormalities, familial/genetic factors, and neurotransmitter/peptide abnormalities; and finally that the disorders may be treated pharmacologically with similar drugs.

Others have strongly questioned this attempt. Storch, Abramowitz, and Goodman (2008) argued forcibly that the symptoms of these disorders have different cognitive, motivational and functional underpinnings. The functional role of compulsions was specifically pointed out as different from that of behaviours in the other OCS-disorders. Consequently, he argued, the OCSD construct is misleading.

One reason for the hypothesis of an OCSD was the phenomenological overlap between OCD, ASD, and tics/Tourette's syndrome (Hollander, et al., 2007). The presence of, for example, repetitive behaviour in these disorders would be one unifying feature. In ASD, repetitive behaviour is one out of three defining symptom clusters, often serving the need for sameness. In OCD, repetitive rituals are likewise present in most patients, although

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as Storch (2008) pointed out, the repetitive behaviour in OCD has a different function, namely that of regulating anxiety and promoting a sense of security (''Classical OCD''). In similar manner Baron-Cohen (1989) suggested that the terms obsession and compulsion should be used with caution to describe autistic behaviours, because they may fail to satisfy the definitions of OCD with regard to the egodystone aspects (unwantedness, distress, resistance, senselessness). In his paper he used the more descriptive term ''repetitive activities''. However, many patients have ordering and/or symmetry compulsions, as well as repetition compulsions, harbouring a wish for a ''just right'' feeling (Livingston-Van Noppen, Rasmussen, Eisen, & McCartney, 1990; Rapoport, 1989). This type of compulsion is in many ways different from classical OCD, even to the extent that it can be thought of as a particular OCD-factor, i.e., ''Symmetry and Ordering'' (Baer, 1994; Leckman, Grice, Boardman, & Zhang, 1997) or as a subgroup of patients with such symptoms (Calamari, Wiegartz, & Janeck, 1999; Ivarsson & Valderhaug, 2006).

Another aspect of the OCD-ASD overlap is the elevated level of ASD comorbidity in OCD, which several researchers have reported in adult (Bejerot, 2007; Bejerot, Nylander, & Lindstrom, 2001; Cath, Ran, Smit, van Balkom, & Comijs, 2008; LaSalle et al., 2004) as well as in paediatric samples (Ivarsson & Melin, 2008; Ivarsson, Melin, & Wallin, 2008). Correspondingly, OCD comorbidity when appropriately assessed seems to be high in autistic samples. Leyfer et al. (2006) found OCD as the second most frequent DSM IV disorder (37%) in a sample of 109 children with autism, assessed with a modified version of the K-SADS. Russell, Mataix-Cols and Anson (2005) reported similar frequencies of OCD symptoms in adults with high functioning ASD compared to a gender-matched group with OCD. In order to distinguish OCD-symptoms from stereotypic behaviours and interests, symptoms were only rated if they caused some degree of discomfort and interfered with the patient's daily life. In both studies the authors reported considerable functional impairment warranting implications for treatment. Besides functional impairment, the function of behaviours is an important distinction to differentiate in cases where ASD symptoms or complex motor tic symptoms were present: Compulsions are negatively reinforced (Turner, 2006), ASD behaviour is mainly positively reinforced, tics are again negatively reinforced, but are a response to somatic phenomena (urge) (Steinberg et al., 2010), while OCD rather is a response to mental phenomena (cognitions and affects).

Could other predictions be made from the OCSD concept? One is that repetitiveness, the autistic symptom which is closest to the proposed core feature of the OCSD (Hollander, et al., 2007), should be present during the preschool years at the onset of ASD symptoms (American Psychiatric Association, 1994) as well as in later childhood following the onset of OCD symptoms, usually around 9–10 years of age (Masi et al., 2005). If the theory of repetitiveness as a core feature in ASD holds, language- and social deficits should, on the other hand, be less prominent. Moreover, there should be a substantial continuity between preschool and ''current'' ASD symptoms across all patients; especially in those that are most seriously affected.

1.2. Aims

The aim of the present study was to assess and explore ASD symptoms in paediatric OCD patients (1) using a dimensional approach, covering both current and preschool ASD symptoms, (2) using a normal comparison group to control for the presence of such symptoms in children and adolescents generally and (3) to control for overall psychiatric symptoms in both patients and comparison group.

2. Methods

2.1. Subjects

The study group consists of all patients with a diagnosis of primary OCD according to the DSM-IV who were consecutively assessed and treated at the specialized OCD unit in Gothenburg, Sweden from January 2001 to December 2005. The total number of cases eligible for participation in the study was 140. Thirty-one patients declined participation in the study and in four patients data were missing. Thus 105 patients (girls/boys$=$61/44) were included in the study, yielding a response rate of 75%. Mean age of the children was 13 years (range 7–17). Neuropsychiatric comorbidity was common; 20 patients (19.2%) filled DSM-IV criteria for ADHD and 17 (16.2%) for Tourettes syndrome. Most patients had intact families (68%) and Swedish ethnicity; 7% had one and 12% both non-Swedish parents. However, the socio-economic status of our patients did not differ due to ethnicity, both groups were relatively close (5.76 and 6.05) to the mean SES we found in a population based study (evaluating an anxiety scale) (Ivarsson & Valderhaug, 2006).

2.1.1. Comparison group

For use as controls we recruited children and adolescents ($n=108$) from schools and participants in swimming activities in a mid-sized Swedish town in the same geographical area. The controls were identified with the intention to constitute a representative sample of the normal population and were matched for age and gender with the patients. Exclusion criteria for controls were a diagnosis of a neuropsychiatric disorder or the fact that a sibling already was a participant in the study. The mothers filled in the SCQ and the CBCL, the latter to check for possible psychiatric problems other than ASD. Two candidates, who were originally eligible for the study, received an ASD diagnosis during the study period and were therefore excluded. No other psychiatric problems warranting exclusion were identified in CBCL reports. Of all eligible families invited, only two denied to participate in the study.

2.2. Procedures and methods

All patients seeking treatment for obsessive compulsive symptoms at the OCD clinic at the Queen Silvia Children's hospital in Gothenburg were assessed using a comprehensive diagnostic workup. When a diagnosis of primary OCD was established, the patients received oral and written information about the study. Parent rating scales (see below) were distributed together with instructions for filling in the scales. At the following visit, written informed consent was obtained, and the scales were collected. The diagnostic assessment of the psychiatric disorders of the patients was based on interviews using the Kiddie Schedule for Affective Disorders and Schizophrenia-Present state and Lifetime version (KSADS-PL) (Kaufman et al., 1997). An independent confirmation of the OCD diagnosis was obtained through the Children's Yale-Brown Obsessive-Compulsive Scale (CYBOCS) (Goodman, Rasmussen, Price, & Rapoport, 1986). The interviews were completed by a board certified child- and adolescent psychiatrist or by resident doctors under training during a separate visit in the initial assessment phase. In all cases where residents performed the assessment, the interviews were videotaped and quality checked by the same child- and adolescent psychiatrist. In addition, the diagnostic work up consisted of clinical interviews and the use of other rating scales including the Swedish version of the Achenbach Child Behaviour Check List (CBCL). The sample included all cases that fulfilled criteria for

OCD according to the DSM-IV, regardless of severity as expressed through the CYBOCS scores.

2.3. Instruments

2.3.1. Autistic traits or symptoms

The Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2010) is a screening questionnaire for parents, covering both current and preschool autistic symptoms. The SCQ was originally validated under the name Autism Screening Questionnaire (ASQ) (Berument, Rutter, Lord, Pickles & Bailey (1999). The SCQ lifetime form can be used as a screening tool for identifying ASD symptoms as well as to get a dimensional measure of ASD symptom severity for both the preschool period and for the current period. A total score of 15 is suggested as cut-off for a probable ASD diagnosis (Berument et al., 1999). The SCQ produces subscale scores for social interaction (range: 0–15), communication (range: 0–13), and repetitive/ stereotyped behaviour (range: 0–8), that parallel the basic domains of the Autism Diagnostic Interview - Revised (ADI-R) (Rutter, Le Couteur, & Lord (2003) Autism Diagnostic Interview - Revised Manual: Western Psychological Services). The SCQ total score may be divided into two subscales; one subscore describing toddler- and one describing current autistic symptoms. The scale showed god reliability as indicated by its internal consistency (Cronbach's Alpha=.90, Berument et al., 1999). SCQ scores can be used to compare levels of ASD symptoms across different samples, as well as to map changes in ASD symptomatology over time.

2.3.2. OCD symptoms

The Children's Yale-Brown Obsessive-Compulsive Scale (CYBOCS) (Goodman et al., 1986) is a parent-, and child interview that yields most of the information needed for a DSM diagnosis of OCD and was used to validate the diagnosis. The CYBOCS is a semi-structured interview containing checklists of obsessions and compulsions. Scales assessing the severity of obsessions and compulsions separately (range 0–20) are added to a CYBOCS total score (range 0–40). Furthermore, lack of insight, avoidance, indecisiveness, inertia, and pathological doubt can be gauged using scores ranging from 0 to 4. Finally, a global severity score is assigned based on all information gathered during the interview. This includes behaviour, such as high "avoidance" that tend to lower compulsion sub-scores and other OCD behaviour, such as "inertia" that contribute to OCD severity without necessarily elevating the obsessions or compulsions sub-scores. The checklists and the severity ratings were based on interviews with each child and each parent/adult informant.

2.3.3. Comorbidity

The Kiddie Schedule for Affective Disorders and Schizophrenia-Present state and Lifetime version (KSADS-PL) (Kaufman et al., 1997) is a widely used semi-structured interview for diagnostic assessment of DSM-IV psychiatric disorders and subsyndromal symptomatology in children and adolescents. The K-SADS was used to confirm the diagnosis of OCD according to the DSM-IV and to evaluate comorbidity. The K-SADS-PL is usually administered by interviewing the parent(s) and the child, and finally achieving summary ratings which include both sources of information. The Swedish version of the KSADS used in the study was back translated and accepted by J. Kaufman.

2.3.4. Emotional and behavioural problems

The Swedish version of the Achenbach Child Behaviour Check List (CBCL) was used for parents to assess emotional and behavioural problems more generally among the children (Achenbach, 1991; Larsson & Frisk, 1999). It consists of two parts, one addressing social competence and the other assessing emotional and behavioural problems in children aged 4 to 18 years. Social competence covers relationships with peers (e.g. number of friends and time spent with friends) and family (behaviour against parents and siblings), school performance but also free time activities (interests, hobbies and jobs). The CBCL yields scores for social activities, school performance as well as a total summary competence score. The problem part consists of 113 problem items rated on a three-point scale: 0="Not true"; 1="Somewhat or sometimes true"; 2="Very true or often true". Parents are asked to rate current problems in the child or occurring in the last six months. Two broad-band dimensions, internalising and externalising syndromes can be formed. The internalising broad-band syndrome consists of three narrow-band syndromes: Withdrawn, Somatic complaints and Anxious/ depressed and the broad-band externalising syndrome includes the Aggression and Delinquent problem scales. In addition, Social, Thought and Attention problem scales can be formed. Total scores range between 0 and 226. Some CBCL items cover OCD symptoms as well and several different Obsessive-Compulsive sub-scales have been formed and studied (Geller et al., 2006; Ivarsson & Larsson, 2008; Nelson et al., 2001). The sub-scale proposed by Geller (2006) was used to find possible OCD cases in the control group. One such case was found. The Swedish CBCL has been studied with regard to its psychometric properties and was found to be sound (Larsson & Frisk, 1999).

2.3.5. Ethics

The study was approved by the internal review board (IRB) of the University of Gothenburg.

2.4. Statistics

We used independent *t*-tests for descriptive data with regard to continuous and chi-square to categorical variables. Effect sizes for t-tests were calculated by using Pearson's r. In cases with two or less missing data, the series means was used instead. In categorical analyses for individual items, these replacements were not used. Pearson correlations were used for investigating the association between preschool and current ASD symptoms and between ASD symptoms and CBCL social competence- and problem scores. In the item level analyses, we applied a stringent alpha-level of significance ($p<.01$) to account for multiple comparisons. Generalised Linear Models was used to study whether the SCQ total score rather reflects an unspecific psychiatric symptom burden than having OCD.

Concerning reliability, in our sample the SCQ total scale showed an acceptable internal consistency as indicated by a Cronbach's Alpha=.718. If analysed separately, Cronbach's Alpha was=.613 for the cases and=.753 for the controls. The SCQ subscale for preschool symptoms showed a Cronbach's Alpha=.743, while the subscale for current ASD symptoms was somewhat lower (Cronbach's Alpha=.620).

3. Results

3.1. Autistic symptoms in OCD patients

SCQ total scores were statistically significant higher in the OCD group (m=5.9, SD=3.2) than in the control group (m=3.2, SD=3.1) (t(df 211)=6.38, p=.0001), the effect size of the difference was moderate (r=.40). However, they were much lower than the scores from a sample with autistic disorder (m=24.2, SD=7.11) published by Berument et al. (1999). Fig. 1 shows that

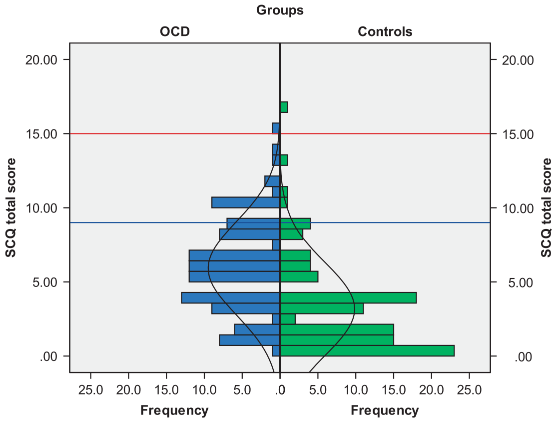

Fig. 1. Distribution of SCQ total scores in the OCD ($n=105$) and control group ($n=108$). The red line represents the cut-off for the SCQ total score to indicate ASD ($=15$). The blue line represents an alternative cut-off score based on the 95th percentile in the control group ($=9$).

controls tended to have a skewed distribution with few children receiving a score of more than 5, while the distribution of SCQ-scores in the OCD-group was closer to the normal distribution, although the mean score was quite low. Only one case in each group had scores above the cut-off score of 15 suggested by Berument et al. (1999) to indicate ASD. The case in the control group was the same one, which might have OCD according to the CBCL OCS scale.

Regarding the SCQ sub-scales, OCD-patients had higher symptom scores on both scales: Preschool subscale $m=3.14$, SD$=2.26$, compared to controls $m=2.07$, SD$=2.63$ (t(df 211)$=3.17$, $p=.002$), small effect size ($r=.21$) and current autistic symptoms subscale $m=2.78$, SD$=1.89$, compared to controls $m=1.10$, SD$=1.65$ (t(df 205.8)$=6.89$, $p=.0001$), moderate effect size ($r=.43$).

3.2. Item level analysis

As some SCQ items intended to reflect ASD-symptoms are possible to confound with OCD-symptoms, we analysed the items which were rated as positive most frequently in the OCD-group to see to what extent OCD phenomenology and SCQ items with OCD-like properties might overlap. Moreover, as tics are common in OCD (Hanna, 1995; Ivarsson, et al., 2008), one has also to consider that some SCQ-items might share features with tics, e.g. "Hand and finger mannerisms" and "Complex body mannerisms". Indeed, as Table 1 shows, mothers of children with OCD very often endorsed items "Verbal rituals", "Compulsions and rituals" as well as having "hand and finger mannerisms" and "Complex body mannerisms" as being present. Moreover, the pattern of which items discriminate between the two groups in our sample was different from Berument's et al. (1999) findings (see Table 1 for an explanation). We did find that mothers of children with OCD described more often than controls the following items as current symptoms: "unusual sensory interests" and "self-injury".

Items of autistic behaviour in toddlers that were more often endorsed by the mothers of OCD patients compared to controls mostly had to do with early problems in communication: failure to use gestures (like nods and head-shakes) or a restricted range of facial expressions, but also some social deficits (poor quality of social overtures). In the preschool section of the SCQ, no items ask for OCD- or tics-like symptoms, or repetitive behaviour (Table 1). Also in the case with current ASD-symptoms, most preschool ASD symptoms were not endorsed as present.

3.3. Continuity of ASD-symptoms

Using an alternative cut-off score, based on the 95th percentile in the control group, a score above 9 showed that 21% of children in the OCD-group were high scorers. (Fisher's exact test, $p=.001$). Excluding those SCQ-items that could be confounded with OCD-symptoms and using the 95th percentile in the control group as cut-off, 13.7 per cent of the OCD-patients had scores of 8 or above (Fisher's exact test, $p=.037$).

The correlation between preschool and current SCQ scores ($r=.16$, $p=.018$) was low, also when analysed solely in the OCD sample (Pearson $r=.15$, n.s.). Put differently, only 1 out of 3 subjects that had high preschool scores (above the 95th percentile in the control group) had high current SCQ symptom scores (above the 95th percentile in the control group). Similarly, only 2 out of 15 individuals who had current SCQ scores above the 95th percentile (a score of 5 or above) had preschool SCQ scores (also above the 95th percentile in the control group). The contingency table fell short of statistical significance. However, in the small sub-group of children with high preschool SCQ-scores in the OCD group ($n=6$), the correlation between preschool and current SCQ scores was high ($r=.63$), but not statistical significant due to lack of statistical power.

3.4. Social competence and other psychiatric problems

Patients with OCD showed lower social competence as defined by the total social competence score (OCD/$m=13.4$, SD$=4.56$ versus controls/$m=23.4$, SD$=4.25$) in the CBCL. They had fewer friends (44% had no friend, and most just one friend 48%) compared with controls (3% had no friend and 87% had two or more friends (X^2 (df3)$=123.2$, $p=.0001$). Moreover, they spent less time with friends (33% never, 28% once a week and 39% twice a week) than controls (8% never, 25% once a week and 67% twice a week) (X^2 (df3)$=24.3$, $p=.0001$). Parents rated them less well behaving with siblings and peers ($m=1.1$, SD$=.48$) compared with controls ($n=1.4$, SD$=.39$) (t (df209)$=4.90$, $p=.0001$). Furthermore, their total competence score in school was lower ($m=4.1$, SD$=2.5$) than in controls ($m=5.2$, SD$=.84$) (t (df209)$=4.90$, $p=.0001$) (t (df158.96)$=6.69$, $p=.0001$) and they were rated as less independent ($m=.97$, SD$=.71$) compared with controls ($m=1.5$, SD$=.52$) (t (df209)$=4.90$, $p=.0001$) (t (df209)$=6.48$, $p=.0001$).

The total symptom load on the problem scale was heavier in the OCD group ($m=46.45$, SD$=20.91$) than in controls ($m=11.90$, SD$=11.92$) (t (df156,5)$=14{,}54$, $p=.0001$), consisting both of internalising ($m=16.26$, SD$=8.25$ versus $m=3.97$, SD$=4.62$) (t (df156.7)$=13{,}20$, $p=.0001$) and externalising symptoms ($m=10.62$, SD$=8.19$ versus $m=3.56$, SD$=3.67$) (t (df143.20)$=8{,}08$, $p=.0001$). High levels of social problems were rated as common in OCD ($m=2.41$, SD$=2.41$) compared with controls ($m=.81$, SD$=1.31$) (t (df159.23)$=6{,}04$, $p=.0001$) as well as attention problems ($m=5.46$, SD$=3.74$ versus $m=1.44$, SD$=1.88$) (t (df152.16)$=9.85$, $p=.0001$) and thought problems ($m=5.2$, SD$=2.49$ versus $m=.72$, SD$=1.79$) (t (df188.49)$=15{,}06$, $p=.0001$).

Correlations between SCQ total scores and CBCL total-, dimensions and subsyndromal scores were moderately high: CBCL total score ($r=.43$, p.0001); Externalising ($r=.33$, p.0001); Internalising ($r=.36$, p.0001); Social Problems ($r=.33$, p.0001); Attention Problems ($r=.45$, p.0001); and Thought Problems ($r=.44$, p.0001). Moreover, SCQ current scores were moderately correlated with CBCL Social Competence scores e.g. Total Competence ($r=-.42$, p.0001), Total School ($r=-.30$, p.0001) and Total Social ($r=-.44$, p.0001), while preschool SCQ scores had lower

Table 1
SCQ-items endorsement by mothers in the OCD group ($n=105$) and in the control group ($n=108$). See symbols below denoting significance of differences.

SCQ Item	Group	Not endorsed	Endorsed
Current autistic symptoms question 2–19			
2. Conversation (n.s.)	OCD	102	3
	Controls	106	3
3. Stereotyped utterances (n.s.)	OCD	78	26
	Controls	87	21
4. Inappropriate questions (n.s.)	OCD	94	9
	Controls	103	5
5. Pronoun reversal (n.s.)	OCD	104	1
	Controls	105	3
6. Neologisms (n.s.)	OCD	98	6
	Controls	97	11
7. Verbal rituals***	OCD	77	27
	Controls	103	5
8. Compulsions and rituals***	OCD	24	81
	Controls	99	9
9. Inappropriate facial expressions (n.s.)	OCD	92	8
	Controls	95	13
10. Use of other's body to communicate (n.s.)	OCD	93	12
	Controls	105	3
11. Unusual preoccupations (n.s.)	OCD	102	3
	Controls	107	1
12. Repetitive use of objects (n.s.)	OCD	101	3
	Controls	104	4
13. Circumscribed interests (n.s.)	OCD	89	15
	Controls	99	5
14. Unusual sensory interests**	OCD	93	10
	Controls	107	1
15. Hand and finger mannerisms**	OCD	86	18
	Controls	102	6
16. Complex body mannerisms**	OCD	82	22
	Controls	101	7
17. Self injury***	OCD	86	19
	Controls	104	4
18. Unusual attachment to objects (n.s.)	OCD	98	7
	Controls	105	3
19. Friends (n.s.)	OCD	94	10
	Controls	105	3
Autistic symptoms from 4–5 years of age questions 20–40			
20. Social chat (n.s.)	OCD	95	10
	Controls	99	9
21. Imitation (n.s.)	OCD	73	32
	Controls	81	26
22. Pointing to express interest (n.s.)	OCD	91	13
	Controls	92	15
23. Gestures (n.s)	OCD	41	64
	Controls	54	52
24. Nodding to mean "yes"***	OCD	47	57
	Controls	82	24
25. Head shaking to mean "no"***	OCD	47	55
	Controls	84	22
26. Eye gaze (n.s.)	OCD	98	7
	Controls	101	6
27. Social smiling (n.s.)	OCD	102	3
	Controls	101	6
28. Showing and directing attention (n.s.)	OCD	101	3
	Controls	103	4
29. Offering to share (n.s.)	OCD	94	11
	Controls	102	5
30. Seeking to share enjoyment (n.s.)	OCD	105	0
	Controls	103	4
31. Offering comfort (n.s.)	OCD	101	4
	Controls	99	8
32. Quality of social overtures**	OCD	90	15
	Controls	103	4
33. Range of facial expressions**	OCD	105	0
	Controls	105	2
34. Imitative social play (n.s.)	OCD	93	12
	Controls	99	8
35. Imaginative play (n.s.)	OCD	90	13
	Controls	98	9
36. Interest in children (n.s.)	OCD	85	18
	Controls	99	8
37. Response to other children's approaches (n.s.)	OCD	99	4
	Controls	103	4
38. Attention to voice (n.s.)	OCD	102	2
	Controls	104	3
39. Imaginative play with peers (n.s.)	OCD	88	11
	Controls	98	9
40. Group play (n.s.)	OCD	102	3
	Controls	106	1

correlations (e.g. Total Competence ($r=-.29$, p.0001). To test whether there might be a specific association between OCD and ASD symptoms (in accordance with the OCSD hypothesis), we used Generalised Linear Models with SCQ total score as dependent variable and CBCL total score as a control for the possibility that SCQ scores reflect other problems. We controlled also for gender and parent reported total emotional and behavioural problems (Table 2). In a first run, we included a gender by CBCL total score predictor. However, it was not significant, so the model was run and reported without it. The model was significant (LRX^2 (df4)$=70.9$, $p=.0001$).

4. Discussion

The study indicates that autism spectrum disorder traits are quite common in OCD-patients, much more common than in the control group. Whether one considers ASD-symptoms across the whole SCQ scale, or whether one uses a cut-off score of 8 or 9 (excluding OCD- and tic-like symptoms), ASD symptoms occur at a greater prevalence then in controls. Significant levels of ASD symptoms occur in about a fifth of our OCD patients, and in one out of six, if SCQ-questions that might be confounded with OCD or tics are taken out from the SCQ-score. However, the majority of OCD-patients did not have these traits (Fig. 1 and Table 1). Thus, the presence of ASD-symptoms in paediatric OCD seems to indicate that ASD and OCD co-occur in a subgroup of cases rather than in OCD as a whole.

In addition, for the fifth with such symptoms, the symptoms during the preschool years tended to be those concerning communication difficulties (three out of five), while the social difficulties (two out of eleven) were less often endorsed. Likewise, none of three items concerning lack of imagination and imitation were endorsed. The most autism specific symptoms, i.e. gaze avoidance, absence of social smile, and lack of shared attention, reciprocal social interaction, and interest in peers, were not endorsed either. Thus, it would be difficult from the preschool symptoms alone, to construct a strong continuity between early ASD traits in children who later get OCD. Moreover, only few cases had high levels of preschool ASD-symptoms.

With regard to current ASD symptoms, the situation is more difficult as several items overlap with OCD (i.e. verbal rituals, compulsions and rituals) or with comorbid tic disorder (i.e. hand and finger mannerisms and complex body movements). In reassurance- or goodnight rituals, it is usual that the child wants the parent to use exactly the same words and the same tone of voice, and repeat them until the child feels better. The SCQ question on compulsions and rituals is worded in a way that OCD compulsions could be included, i.e. "have to do things in a very peculiar way or order", or rituals insisting that the parent goes through. Similarly, tics might be confounded with the SCQ question "odd ways of moving his/her hands or fingers". Moreover, the SCQ probe on

Table 2
Generalised Linear Model with SCQ total score as dependent variable, gender and group status (OCD versus Controls) and CBCL total score as covariate. The final model included an interaction between group and CBCL total score.

Parameter	B	SE	95% Wald Confidence Interval		Hypothesis Test	
			Lower	Upper	Wald (df)	*p*
Intercept	2.53	.47	1.61	3.45	29.0 (1)	.0001
Gender (girls)	−1.23	.40	−2.0	−.44	9.2 (1)	.002
Group (OCD)	3.41	.80	1.84	4.99	18.1 (1)	.0001
CBCL	.11	.02	.07	.16	23.55 (1)	.0001
CBCL*group	−.10	.03	−.15	−.05	13.17 (1)	.0001

complex body movements like "spinning or repeatedly bouncing" could be confounded with complex tics. Other current ASD symptoms, e.g. self-injurious behaviour might be endorsed in OCD-patients as well, because some in frustration, when rituals do not reduce anxiety, may hit their head against the wall or even bite themselves.

Only the OCD sub-group with highest level of preschool ASD symptoms (5.5%) demonstrated a substantial continuity with "current" ASD symptoms shown by a high (though not significant) Pearson correlation. However, using cut-off scores (95% percentiles), the continuity was less prominent.

On the other hand, using the Generalised Linear Model with SCQ total score as the dependent variable, we could control for possible confounders such as gender and CBCL total score. In this model, group status i.e. OCD versus Controls, was a strong predictor. Thus, OCD has an independent relation to elevated ASD symptoms and it seems less probable that the high levels of comorbidity present in these patients (Geller, 2006; Ivarsson, et al., 2008) is really what makes parents assess them as ASD-like. Indeed, the negative B-coefficient for the interaction between Group and CBCL total score shows that parents might be quite judicious in their ratings: OCD patients with high CBCL total scores had lower SCQ total scores.

4.1. Limitations

Some of the symptoms or traits we measured using the SCQ, might be an artefact of assessment. When parents fill in questionnaires, we depend on their interpretations and observations. Although, most questions are descriptively oriented, some scores might be the result of faulty observations and/or interpretations. Using the CBCL to control for other psychiatric problems mitigates, but does not solve the problem. Moreover, as stated earlier, not all SCQ-questions are specific to ASD, but may represent an overlap. Possibly, using a semi-structured interview like the Autism Diagnostic Interview - Revised (Rutter Le Couteur, & Lord (2003) or the Diagnostic Interview of Social- and Communication disorders (DISCO) (Wing, Leekam, Libby, Gould, & Larcombe, 2002), where problems in different social and communicative situations are elicited might give more reliable estimates. However, to conduct all interviews would demand much more resources. The same limitation applies to the use of the CBCL as screening tool to verify that the children in the control group had no bias in terms of high load of psychiatric symptoms or suspected psychiatric disorders. This screening procedure is of course not equivalent with a diagnostic interview. To use the K-SADS in all controls would solve this problem, but was again a question of resources.

Applying the SCQ once, pre-school ASD-symptoms and current ASD-symptoms were rated at the same time, which may cause a recall bias, affecting the results (probably mainly in direction of underrating pre-school symptoms). A longitudinal design would avoid this problem, but at the expense of much more resources. Another limitation is that the preschool subscale of the SCQ does not include items of the repetitive/stereotyped behaviour domain. Therefore repetitiveness was not directly assessed in the preschool questionnaire and might have been overlooked and missed in some cases. The applied version of the K-SADS (Swedish translation authorised by J. Kaufman) was based on version 1.0 of the K-SADS PL from 1996 and did not include the scale and the supplement for assessment of Autism Spectrum Disorders (including assessment of PDD NOS and Asperger's Disorder) which was added in the 2009 version. Therefore we were not able to differentiate reliably between patients with clinical autistic symptoms and a possible diagnosis of PDD NOS or Asperger's Disorder in the OCD-group, except for the fact that only one had a SCQ-score slightly above cut off of 15 (=16).

5. Conclusion

The argument by Hollander (2007) and Bartz (2006), that OCD as a whole should be re-classified together with Autism Spectrum Disorders, tics/Tourette's syndrome and various other disorders into an Obsessive- Compulsive Spectrum group seems out of proportion and is not supported by the level or type of current comorbid ASD symptoms nor the presence of preschool ASD symptoms in our study. However the contention is not finally disproved; the higher level of ASD symptoms in our OCD patients compared with controls (Fig. 1), existing independent of other psychiatric problems, and the pattern of individual responses outlined in Table 1, might indicate that there is an underlying relationship in a subgroup of OCD patients.

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Paper II

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HEALTH AND QUALITY
OF LIFE OUTCOMES

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Quality of life in children with OCD with and without comorbidity

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Abstract

Background: Quality of life (QoL) is a well-established outcome measure. However, in contrast to adult obsessive-compulsive disorder (OCD), little is known about QoL in children with OCD. This study aimed to assess QoL, social competence and school functioning of paediatric patients with OCD by comparing them with the general population and assessing the relations between comorbidity, duration and severity of symptoms, family accommodation and QoL.

Methods: Children and adolescents (n = 135), aged 7–17 (mean 13 [*SD* 2.7] years; 48.1% female) were assessed at baseline for treatment. QoL was assessed by self-report and caregiver's proxy report on the Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents (KINDL-R) and compared with an age- and sex-matched sample from the general population. Social competence and school functioning were assessed with the Child Behavior Checklist, comorbidity with the Kiddie Schedule for Affective Disorders and Schizophrenia (Present and Lifetime Version), severity of OCD with the Children's Yale-Brown Obsessive Compulsive Scale and the families' involvement with the child's OCD symptoms with the Family Accommodation Scale.

Results: QoL and social competence were reduced ($p < .001$) in patients with OCD compared with controls (KINDL-R mean score 62.40 [*SD* 13.00] versus 69.72 [12.38] in self-reports and 61.63 [*SD* 13.27] versus 74.68 [9.97] in parent reports). Patients with comorbidity had lower QoL ($p = .001$) in proxy ratings than those with OCD only (mean score 56.26 [*SD* 12.47] versus 64.30 [*SD* 12.75]). In parent proxy reports, severity of OCD ($r = -.28$) and family accommodation ($r = -.40$) correlated moderately negatively with QoL.

Conclusions: To our knowledge, this is the largest QoL study of paediatric OCD. QoL was markedly reduced in children with OCD, especially in those with comorbid psychiatric disorders. Based on our findings, we suggest employing QoL assessment in order to have a more comprehensive understanding of childhood OCD.

Clinical trials registration information: This study was registered in Current Controlled Trials; Nordic Long-term Obsessive Compulsive disorder (OCD) Treatment Study (ISRCTN66385119).

Keywords: Pediatric OCD, Quality of life, Comorbidity, Assessment

Background

Obsessive-compulsive disorder (OCD) is reported with a prevalence of 0.25% in paediatric cases, with a more frequent distribution (0.6%) in the range between 13 and 15 years of age [1]. Earlier studies suggested higher rates of between 1% and 3% [2,3]. The disorder has a chronic course in 40–75% of cases [4-6]. Between 30% and 50% of adults with OCD report that symptoms started in childhood or adolescence [7]. In the majority of cases, OCD is associated with other psychiatric conditions; as many as 77–85% of children with OCD fulfilled criteria for one or more other psychiatric diagnoses [8,9]. Depression, phobias and other anxiety disorders and neuropsychiatric conditions, such as attention deficit hyperactivity disorder (ADHD) and tic disorder are frequent comorbidities in paediatric OCD. In addition, several researchers have reported elevated levels of autism spectrum disorder

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comorbidity in OCD, in adult [10-12] as well as in paediatric samples [13].

Quality of life (QoL) assessment is established as an important outcome factor in clinical trials [14], independent from symptom-level assessment, as pathology does not have a simple linear relationship to well-being [15]. Despite a variety of assessment instruments and focuses, most studies of QoL in adult populations agree that QoL is reduced in patients with OCD and that QoL changes seem to be associated with symptom severity [16,17]. A recent review showed that QoL in adults with OCD is significantly impaired, when compared with QoL in the general population [18]. Comorbid conditions, particularly depression, were major contributing factors to the reduced QoL in OCD. The authors underlined the importance of QoL assessment in both clinical and research settings to examine disease burden, to monitor treatment effectiveness, to determine grade of recovery from OCD and to take these factors into account for the development of treatment plans.

In paediatric OCD, there is still a paucity of studies. In the above-mentioned review [18], a systematic literature search on OCD and QoL identified only seven articles concerning children or adolescents, which were subsequently excluded from the review because of the selection criterion of “studies evaluating adults”. Our own search strategy did not reveal additional research papers. A longitudinal cohort study [19] evaluated baseline characteristics of 36 children, obtained at a mean age of 12 years, with regard to their predictive value for QoL in young adulthood after an average of nine years follow-up. QoL measurement was applied at follow-up only. OCD appeared to most strongly impair the interpersonal relationships and work domains of QoL. QoL and severity of OCD and anxiety symptoms were significantly associated in early adulthood. In a long-term follow-up of 142 children and adolescents with OCD over five years [4], the persistence rate of OCD was 41%; functional impairment and QoL were mildly to moderately affected. QoL was assessed at follow-up at a point in time when the mean age of the participants was 18.6 years (*SD* =3.5, range 11–28) and 61% reported very much or much improvement of OCD symptoms. Baseline data were not available. In a survey exploring QoL among members of the Danish OCD Association, about half of the 219 individuals with OCD who completed the self-report questionnaire were beyond age 18 [20]. Because of the nature of the survey, there were several limitations, such as sample selection and lack of formal assessment. Nevertheless, it is noteworthy that 72% of the respondents reported affected social and daily life functioning and 26.5% reported dissatisfaction with their quality of life.

Lack and colleagues [21] assessed baseline QoL in 62 children and adolescents (8–17 years) presenting for an initial treatment evaluation. QoL scores were significantly lower than for healthy controls, and moderately associated with OCD symptom severity as reported by parents. In addition, the presence of comorbid externalizing and internalizing symptoms was a strong predictor for lower QoL scores. The authors described the lack of structured interviews to make the diagnoses of OCD and comorbidities as a limitation. To our knowledge, the present study is the largest QoL study of paediatric patients with OCD and the first one based on the assessment of OCD and comorbid disorders by standardized semi-structured diagnostic interviews.

Aims

The aims of the present study were: (1) to assess QoL, as reported both by paediatric patients with OCD and their caregivers, compared with an age- and sex-matched sample of student and parent reports from the general population; (2) to compare the social competence and school functioning of these patients with that of the general population; (3) to investigate the relations between comorbid disorders such as ADHD, Tourette’s syndrome, other anxiety disorders, depression and QoL; and (4) to explore the significance of other factors for the perceived quality of life, such as duration, severity, and the family’s adjustment to the OCD symptoms.

Methods

Participants

In the framework of a multicentre treatment research project (the Nordic Long-term Treatment Study [22]), QoL was assessed in children and adolescents 7–17 years of age, diagnosed with OCD and presenting for a baseline evaluation between September 2008 and June 2012. The present QoL study was initiated later than the Nordic Long-term Treatment Study and at different time points in the three participating countries, due to availability and approval of the national translations of the QoL questionnaire used. The Danish translation was prepared during the inclusion process and approved by the original authors only in March 2011. The first patients available for QoL assessment were included in September 2009 in Norway, in August 2010 in Sweden and in April 2011 in Denmark, leading to a total of 135 participants with the following distribution: 76 participants (56.3%) from Norway, 33 (24.4%) from Sweden and 26 (19.3%) from Denmark. Details of patient characteristics and results of the Nordic Long-term Treatment Study are described elsewhere [23] (Figure 1).

Comparison group

A large norm data sample consisting of students from schools in Sør-Trøndelag county [24], representing a comparable geographical area with both urban and rural

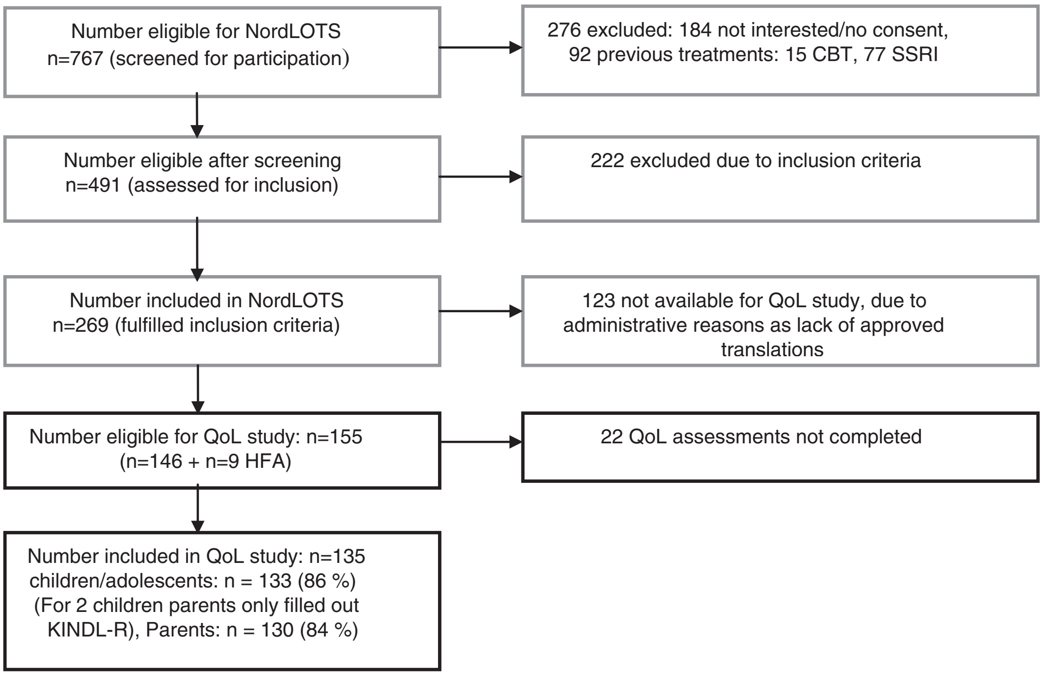

Figure 1 Flow chart. NordLOTS main study (boxes with a grey border) and QoL study (boxes with a black border). Abbreviations: NordLOTS = Nordic Long-term Obsessive-compulsive disorder Treatment Study; QoL = Quality of Life; HFA = High functioning autism; KINDL-R = Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents; CBT = Cognitive behaviour therapy; SSRI = Selective Serotonin Reuptake Inhibitor.

settlement, was used as a control group. Every child or adolescent with OCD was individually matched to a student from the general population sample (n =1821, 8–16 years). This sample was stratified according to sex and age, and students were consecutively numbered in each stratum. Using computer-generated random numbers, we then allocated each patient to a control. With regard to parent education, there was no significant difference between patients (M = 5.19) and the allocated students from the general population (M = 5.29) ($t(118) = .51$, $p = .61$, paired samples t test).

Because of the cluster design of the general population study (sampling data from grades 4, 6, 8 and 10), we had to stratify the samples before matching patients and students in groups with a relatively large age range: 7–10 years, 11–14 years and 15–17 years. Therefore, we explored the differences in chronological age between patients and students. The mean of the difference scores of age between patients and students after matching was 0.39 years (SD = 1.24). Further, the mean age of patients (12.70 years, SD =2.71) was significantly higher ($t(134)$ = 3.64, $p < .001$, paired t test) than in students (M = 12.31, SD = 2.39). Yet the largest differences (by 2.5–3 years) comprised only five patients (3.7%) who were randomly allocated to students. All other patient–student pairs lay within a range of two years difference, with the majority of 95 cases (70.3%) within a range of one year. We decided not to exclude students who had been in contact with health or school psychological services to avoid an "artificially healthy" comparison group from the general population. The parents of seven matched students (5.2%) responded affirmatively to the question *"Has your child received any help during the last year due to mental health problems or learning difficulties?"*.

Instruments

Quality of life (QoL)

The Kinder Lebensqualität Fragebogen (Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents, revised version, KINDL-R) [25] is a well-established QoL instrument used in several clinical and epidemiological studies. Swedish and Norwegian versions of the Questionnaire were available, and the Danish translation was prepared and approved by the original authors. We used the self-report questionnaire for children and adolescents as well as the proxy version completed by one of the parents. The questionnaire consists of 24 items equally distributed into six subscales: *physical well-being, emotional well-being, self-esteem, family, friends,* and *school*. Each item addresses the child's experiences over the past week and is rated on a five-point scale (1 = never, 5 = always). Mean item scores are calculated for all subscales and for the *total QoL* scale, which is transformed to a 0–100 scale, with 100 indicating very high QoL. In addition, it provides a disorder-related subscale yielding information about the perception of the disorder burden. We modified the form by adding the sentence "*Concerning your OCD…*" for children, and "*Concerning your child's OCD…*" for parents to the disorder-related questions to ensure we tracked the informants' perception of OCD and not a concurrent somatic or other disorder. Psychometric testing of the KINDL-R revealed good scale utilization and scale fit as well as moderate internal consistency [26]. A Norwegian normative study also confirmed satisfactory internal consistency and test–retest reliability [27].

Resources and emotional and behavioural problems

The Achenbach Child Behavior Checklist (CBCL) is widely used in Scandinavia for parents to assess competence and emotional and behavioural problems more generally among the children [28], and approved translations are available in all languages. It consists of two sections, one addressing competences and the other assessing emotional and behavioural problems in children aged 6–18 years. The CBCL yields scores for activities, social competence and school performance, which all add to a total summary competence score. The Total Competence scale includes 20 items where parents report the amount and quality of their children's participation in sports, hobbies, activities, jobs and chores, their friendships, how well the child gets along with others and school functioning. From these items, activities, social and school subscale scores can be calculated. In the present study, only the social and school subscale scores were used. The problem section of the CBCL consists of 113 emotional and behavioural problem items rated on a three-point scale: 0 = "Not true"; 1 = "Somewhat or sometimes true"; 2 = "Very true or often true". Parents are asked to rate problems the child experienced in the last six months. Two broad dimensions, internalizing and externalizing scales, can be calculated; in the present study, these scales were used as an additional measurement of the psychiatric problem load and correlated with QoL data. Two Norwegian normative studies confirmed satisfactory reliability and validity of the CBCL [29,30].

OCD diagnosis and comorbidity

The Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (K-SADS-PL) [31] is a widely used semi-structured interview for diagnostic assessment of DSM-IV [32] psychiatric disorders and subsyndromal symptomatology in children and adolescents. The K-SADS was used to confirm the diagnosis of OCD according to the DSM-IV, and to evaluate comorbidity. The K-SADS-PL was administered by interviewing the parent(s) and the child. Approved translations of the revised version of the K-SADS [33] used in the study were available for all three languages.

OCD symptom severity

Symptom severity was assessed with the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) [34] including Clinical Global Impression (CGI). The CY-BOCS is a semi-structured interview containing checklists of obsessions and compulsions. Scales assessing the severity of obsessions and compulsions separately (range 0–20) are added to a CY-BOCS total score (range 0–40). Finally, a global severity score (CGI) is assigned based on all information gathered during the interview. The checklists and the severity ratings were based on interviews with each child and each parent or adult informant. CGI is a widely used rating scale for clinicians to assess global severity of illness with a score ranging from 0 ("no illness") to 6 ("serious illness").

Family accommodation

The Family Accommodation Scale (FAS) [35] is a 12-item clinician-rated questionnaire, designed to assess the families' accommodation to the child's OCD symptoms. The FAS items measure the extent to which family members provide reassurance or objects needed for compulsions, decrease behavioural expectations of the child, modify family activities or routines, and help the child avoid objects, places or experiences that cause distress. The FAS has demonstrated good psychometric properties including good internal consistency ($\alpha = .76, -.80$) [35,36], and positive correlations with measures of OCD symptom severity [37] and family discord [35].

Duration of symptoms

As a measure of chronicity of symptoms, the duration of OCD was calculated as age minus year of symptom onset. We used this calculation as an indicator of how long the child had struggled with OCD, suggesting that a child suffering from OCD for only a short time might have a different QoL from a child who has struggled with OCD for many years.

Socio-economic status

Socio-economic status (SES) was calculated using the highest education level of either mother or father (whichever was highest) assessed as suggested by Hollingshead [38], with scores ranging from 1 to 7 (7 = university education).

Statistics

All statistical procedures were performed with the Statistical Package for the Social Sciences (SPSS), version 19 (IBM SPSS Inc., Chicago).

In the first five of six subscales of the KINDL-R parent report (n =130), missing values were between 0% and 3.1%; in the *school* subscale, between 7.7% and 9.2%; and in the *disorder* subscale, between 10.8% and 13.1%. In the first five subscales of the KINDL-R children and adolescent's self-report (n =133), missing values were between 0% and 3.0%; in the *school* subscale, between 5.3% and 6.0%; and in the *disorder* subscale, between 5.3% and 8.3%. Missing values were substituted by the mean according to the KINDL-R manual. In all other instruments, the number of cases with available data for the analyses showed low proportions of cases with missing data, ranging from 0% (CY-BOCS) to 3.7% (FAS). Only the CBCL internalizing scale (11.1%) and externalizing scale (10.4%) had slightly higher proportions of missing data.

QoL total scores and subscales from both patients and caregivers by proxy were compared with those of the matched controls from the general population using paired samples *t* tests. To explore the relation of comorbid disorders in general and QoL, we compared QoL ratings of children with any type of comorbidity with the children with OCD only. To differentiate between disorders such as ADHD, Tourette's syndrome, autism spectrum disorder, other anxiety disorders and depression, three groups were created based on the presence of comorbidity: (1) OCD only, (2) OCD with ADHD, with tic disorder or with a combination of both, and (3) OCD with another anxiety disorder, with depression or with a combination of both. A general linear model analysis was conducted with the KINDL-R QoL total score and all subscale scores for both children's self-reports and parent proxy reports as dependant variables. We used Hochberg post hoc tests because of differences in the size of the analysed subgroups. With regard to parent reports of total QoL and the subscale *physical well-being*, we used the Games–Howell test because of significant differences in the variances of the groups. Age and sex proved not to have a significant impact on QoL in the present study (general linear model with QoL as dependent variable), nor did we observe any interaction effects. Age and sex were therefore not included as covariates in the general linear model analysis of the comorbidity groups. Twenty-five cases had mixed or multicomorbidity with three or more diagnoses, making a detailed analysis meaningless, and were subsequently excluded from this set of analyses. With this approach, we excluded six of the seven cases with depression and all with high-functioning autism (HFA). To explore a possible specific relation between the mentioned comorbidities and QoL, we created contrasts between each of them versus the rest of the sample.

To explore possible associations with QoL, other than comorbidity, Pearson's correlations were conducted for OCD symptom severity (CY-BOCS score/GGI), age of onset, family accommodation and duration of OCD. To explore whether a high symptom load or a threshold of a certain severity was associated with poorer QoL, we compared QoL scores in the group of children with more severe OCD (CY-BOCS score ≥24) with those of the group with less severe OCD (CY-BOCS 16–23). Because of multiple comparisons, the significance level was set to $p = .01$ for all analyses (F-tests and correlations), except for post hoc tests, where p was set to .05.

Ethics

The study was approved by the Regional Committees for Medical and Health Research Ethics in Denmark, Norway and Sweden. All parents gave written informed consent and the permission for their children to participate prior to inclusion in the study.

Results

Sample description

Of 155 patients eligible for participation in the study, 22 refused to participate or did not complete the QoL instrument (KINDL-R). Each child and one of the caregivers completed QoL questionnaires resulting in 135 completed forms from either child or/and one of the caregivers (130 parent forms and 133 child forms =128 complete child and parent pairs), yielding a response rate of 86% of eligible children and 84% of the parents (Figure 1). Autism spectrum disorder (ASD) was an exclusion criterion in the main treatment study, but nine individuals with Asperger's syndrome/HFA were included in a substudy at one site (Trondheim). Complete QoL assessment was available for eight of these nine patients; in the ninth case, only the mother filled in the questionnaire.

The mean age of the participants was 13 years (*SD* 2.7 years, range 7–17). Gender distribution was even with 65 girls (48.1%). Thus, the QoL study sample was representative of the whole sample of the treatment study, where mean age was 12.8 (*SD* 2.7) years, while gender distribution diverged slightly with more girls represented (51.3%). If compared without the nine male participants from the HFA substudy, gender distribution was equal in both samples (51.3% versus 51.6% girls in the QoL study). Ethnicity was primarily Scandinavian; 97% of the participants had one or both parents of Scandinavian origin. The education level of parents was generally quite high (*M* =5.30; *SD* 1.39). The participants in the QoL study were not significantly different from the sample of the main NordLOTS study with regard to SES ($t(270) = .92$; $p = .357$; $M = 5.14$, $SD = 1.47$).

Comorbidity was common, especially with neuropsychiatric conditions, other anxiety disorders and, to a lesser degree, depression. In fact, only 69 patients (52.3%) had "pure" OCD without any other comorbidity (hereafter named "OCD only"). Eighteen patients (13.6%) met DSM-IV criteria [32] for ADHD and 37 (28%) for tic disorder; 14 had a combination of both. Conduct disorders were diagnosed in six patients (4.5%). Other anxiety disorders were diagnosed in 28 patients (21.2%): Two patients suffered from separation anxiety, 16 from specific phobia (12.1%), eight from social phobia (6.1%), six from generalized anxiety disorder (4.5%) and two from not specified anxiety. Four patients had two, and one patient three, additional anxiety disorders. Depression was found in seven patients (5.3%), with a diagnosis of major depressive disorder in six of them and unspecified depression in one case. No other psychiatric comorbidity was diagnosed. The HFA group (n =9) contributed heavily to the load of comorbidity: Only one of the HFA patients had OCD only, seven had other neuropsychiatric conditions (three tic disorder, two ADHD and two both tics and ADHD) and one patient had another anxiety disorder (specific phobia).

QoL in OCD compared with the general population

Quality of life as reported by both paediatric patients with OCD and their caregivers was significant lower than QoL reported by the controls (Table 1). Children's self-report revealed lower scores of total QoL as well as of all subscales except *self-esteem* and *school*. Parent proxy reports had a similar pattern with reduced QoL total score and all subscale scores.

Social competence and school functioning

Parents reported a great deal of impairment in the social functioning of children with OCD compared with the general population (Table 2). Also school functioning subscale scores were rated significantly lower in the children with OCD, but not as low as the social competence scores. Because of only approximate normal distribution of the social competence and school functioning scores, we confirmed the results with non-parametric tests. Both scales showed the same highly significant differences ($p < .001$ by Wilcoxon signed-rank test).

Comorbidity and QoL

In a first analysis, we compared QoL ratings of children with any type of comorbidity (n = 62) with the children with OCD only (n =68) (Table 3). We found a tendency for lower QoL scores of children's self-reports in the comorbidity group compared with the children with only OCD. None of the observed differences were statistically significant, though *physical well-being* was nearly significant. For parent reports, we observed a significant impact of comorbidity on QoL with respect to total score and the subscales *physical well-being*, *emotional well-being*, *friends* and *school.*

In a subsequent analysis of two subgroups with specific comorbidity (see above under Methods/Statistics) we again found a tendency towards lower QoL scores of children's self-reports in both comorbidity groups, but these did not reach statistical significance. Parents reported a significant impact of comorbidity on *friends* subscale scores [F (2,97) = 7.65, p = .001]. Subsequent post hoc analysis also showed significantly higher QoL on the subscale *friends* for the OCD only group (M = 66.36; SD = 17.11, n = 68) compared with the group with OCD and comorbid neuropsychiatric disorders (M = 47.79; SD = 20.37, n = 17, p = .001). Parents reported a borderline significant impact on total QoL scores (F [2,97] = 4.51, p = .013). Post hoc testing showed higher QoL total scores

Table 1 Quality of life in children with OCD compared to controls from the general population assessed by self-reports and parent proxy reports

	QoL Total score	Physical well-being	Emotional well-being	Self-esteem	Family	Friends	School
	Mean (*SD*)	Mean (*SD*)	Mean(*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)
Children with OCD self-reports	62.40 (13.00)	62.47 (18.07)	63.24 (16.73)	51.24 (20.66)	67.86 (19.49)	65.98 (18.56)	63.55 (19.76)
General population self-reports	69.72 (12.38)	70.03 (19.28)	76.53 (14.37)	54.88 (19.34)	76.56 (18.47)	75.98 (18.27)	66.72 (17.73)
p-value	**<.001**	**.003**	**<.001**	.147	**<.001**	**<.001**	.175
Children with OCD parent reports	61.63 (13.27)	63.35 (20.19)	63.07 (17.05)	49.16 (16.62)	67.44 (17.04)	62.56 (18.26)	63.98 (19.82)
General population parent reports	74.68 (9.97)	78.62 (16.97)	78.58 (12.60)	65.08 (13.56)	73.41 (12.74)	77.49 (13.15)	74.81 (12.73)
p-value	**<.001**	**<.001**	**<.001**	**<.001**	**.009**	**<.001**	**<.001**

n = 121-133 for children's self-reports.
n = 100-110 for parents' reports.
Bold letters indicate significant p-values.

Table 2 Social competence and school functioning of children with OCD as rated by parents on the CBCL compared to controls from the general population

	Mean	Standard deviation	*t*	*df*	*p*
Children with OCD: Social competence score	1.99	1.94	−27.58	103	**< .001**
General population: Social competence score	8.79	1.70			
Children with OCD: School functioning score	4.20	1.12	−3.90	85	**< .001**
General population: School functioning score	4.77	1.07			

Social competence n = 104.
School functioning n = 86.
Bold letters indicate significant p-values.

for the OCD only group (*M* = 64.03; *SD* = 12.75, n = 68) than for the group with OCD and comorbid neuropsychiatric disorders (*M* = 55.04; *SD* = 10.31, n = 17, *p* = .013). Further, we found non-significant tendencies for the OCD only group to show higher QoL than the group with neuropsychiatric disorders on three additional subscales, as reported by the parents: *physical well-being* (*F* [2,100] = 3.29, *p* = .041), *emotional well-being* (*F* [2, 100] =2.98, *p* = .055) and *school* (*F* [2,92] = 3.01, *p* = .054).

Children with tic disorder did not differ significantly in QoL from any other group, irrespective of other comorbidities. Parent ratings showed a tendency to score children with tics lower on total QoL and on different subscales (*emotional well-being, friends* and *school),* but this difference did not reach statistical significance. Patients with comorbid depressive disorder (n = 7) and their parents reported lower total QoL and scores on the subscales *physical well-being*, *emotional well-being* and *school* than all other patients, but again, without reaching significance levels. Children with HFA and OCD and their parents reported similar QoL scores to the other patients on all scales.

Symptom severity

For children's self-reports, we found a significant (*p* < .001) negative association between symptom severity expressed by CY-BOCS scores and the KINDL-R *disorder* subscale only (Table 4). For parent proxy reports, a significant association was found between CY-BOCS score and QoL total score (*r* = −.28) and four subscales (*emotional well-being, friends, school* and the *disorder* subscale score) (*p* < .01). Although significant, the correlations were low to moderate (range −.24 to −.45). Children with more severe OCD (CY-BOCS score ≥24, n = 81) and their parents reported significantly lower scores on the *disorder* subscale (children: *M* = 59.22, *SD* = 16.30 and parents: *M* = 54.16, *SD* = 16.38)

Table 3 Quality of life in children with OCD only compared to children with OCD and different comorbidities assessed by self-reports and parent proxy reports

	QoL Total score	Physical well-being	Emotional well-being	Self-esteem	Family	Friends	School	Disorder subscale
	Mean (*SD*)	**Mean (*SD*)**	**Mean (*SD*)**	**Mean (*SD*)**	**Mean (*SD*)**	**Mean (*SD*)**	**Mean (*SD*)**	**Mean (*SD*)**
Children with OCD only self-reports	64.20 (13.30)	65.38 (16.67)	65.21 (16.07)	53,89 (20.81)	68.29 (20.24)	68.29 (17.12)	63.59 (21.40)	62.14 (17.00)
Children with comorbidity self-reports	60.66 (12.14)	59.07 (18.99)	60.96 (17.22)	48.19 (19.38)	67.83 (18.95)	63.51 (19.95)	64.83 (17.71)	66.58 (16.98)
(df)	(1,128)	(1,128)	(1,126)	(1,128)	(1,127)	(1,128)	(1,122)	(1,119)
F -value	2.52	4.07	2.08	2.60	0.02	2.16	0.12	2.07
p-value	.115	.046	.152	.109	.894	.144	.727	.153
Children with OCD only parent reports	64.03 (12.75)	66.82 (20.15)	65.07 (16.56)	49.26 (17.26)	68.29 (16.06)	66.36 (17.11)	68.42 (19.96)	60.31
Children with comorbidity parent reports	56.26 (12.47)	57.73 (17.34)	57.11 (17.54)	47.33 (16.61)	64.11 (17.35)	54.76 (18.98)	56.84 (19.24)	57.32 (18.55)
(df)	(1,121)	(1,125)	(1,124)	(1,123)	(1,124)	(1,122)	(1,115)	(1,108)
F -value	11.51	11.51	6.85	0.40	1.96	12.78	10.09	0.77
p-value	**.001**	**.008**	**.010**	.527	.164	**.001**	**.002**	.383

n = 64-68 for children with OCD only and n = 53-62 for children with OCD and comorbidity.
Bold letters indicate significant p-values.

Table 4 Pearson correlations between different parameters and quality of life assessed by children's self-reports and parent proxy reports

n =113-135	QoL Total score	Physical well-being	Emotional well-being	Self-esteem	Family	Friends	School	Disorder subscale
OCD severity: CYBOCS score								
QoL Self-report	- .19	- .16	- .17	- .16	- .15	- .12	- .06	- .38
p-value	.025	.067	.048	.073	.096	.188	.54	**<.001**
Parents report	- .28	- .17	- .24	- .13	- .19	- .26	- .24	- .45
p-value	**.001**	.053	**.006**	.148	.033	**.003**	**.010**	**<.001**
Family Accommodation: FAS score								
QoL Self-report	- .10	- .16	- .15	- .07	- .15	.00	.10	- .14
p-value	.253	.075	.092	.414	.087	.974	.273	.143
Parents report	- .40	- .29	- .39	- .26	- .30	- .30	- .21	- .49
p-value	**<.001**	**.001**	**<.001**	**.004**	**.001**	**.001**	.026	**<.001**
Age of onset of OCD: Year								
QOL Self-report	- .02	.15	- .02	- .08	- .1	- .03	- .11	- .15
p-value	.786	.077	.821	.355	.909	.708	.230	.106
Parents report	.08	.16	.10	.10	.04	- .03	- .01	- .004
p-value	.353	.077	.258	.257	.635	.750	.950	.968
Duration of OCD: In years								
QoL Self-report	- .18	- .13	- .16	- .09	- .08	- .09	- .20	- .12
p-value	.036	.147	.064	.323	.369	.307	.024	.180
Parents report	- .19	- .29	- .14	- .13	- .06	- .05	- .22	- .07
p-value	.032	**.001**	.126	.140	.522	.564	.019	.460
CBCL internalizing score								
QoL Self-report	- .35	- .34	- .39	- .22	- .14	- .25	- .09	- .22
p-value	**<.001**	**<.001**	**<.001**	.015	.130	**.007**	.358	.022
Parents report	- .59	- .51	- .57	-.32	- .32	- .44	- .39	- .47
p-value	**<.001**	**<.001**	**<.001**	**.001**	**.001**	**<.001**	**<.001**	**<.001**
CBCL externalizing score								
QoL Self-report	- .33	- .21	- .31	- .22	- .31	- .21	- .05	.01
p-value	**<.001**	.020	**.001**	.014	**.001**	.023	.636	.910
Parents report	- .50	- .24	- .48	- .17	- .56	- .40	- .30	- .33
p-value	**<.001**	**.008**	**<.001**	.067	**<.001**	**<.001**	**.002**	**.001**

Bold letters: Correlation is significant at the .01 level (2-tailed).

than children with less severe OCD (n = 51) (*M* = 71.90, *SD* = 15.63; parents *M* = 67.05, *SD* = 17.43, $p < .001$, not shown in table). In addition, children's ratings showed non-significant tendencies in the same direction for total QoL ($p = .027$), *emotional well-being* ($p = .030$) and *self-esteem* ($p = .032$). Parents' reports confirmed this pattern with non-significant tendencies to lower scores for total QoL ($p = .032$) and the subscale *emotional well-being* ($p = .016$).

Family accommodation

In children's self-reports, we found no association between levels of family accommodation expressed by the FAS score and QoL (Table 4). In parent proxy reports, significant low to moderate negative correlations were found between FAS score and QoL total score ($r = -.40$) and all subscales ($p < .01$), except the *school* subscale, which showed a non-significant ($p = .026$) tendency only.

Age of onset and duration of OCD

There was no association between QoL and age of onset of OCD. Parents' reports showed the duration of OCD symptoms was significant with regard to *physical well-being* yielding a moderate negative correlation ($r = -.29$, $p = .001$). Total QoL and *school* reported by parents and children showed a non-significant tendency (Table 4) with low negative correlations.

CBCL internalizing and externalizing problems

The CBCL internalizing score showed overall significant correlations with QoL in children's and parent proxy reports ($p < .01$): Parents' reports of QoL total score and all subscales were negatively correlated with the CBCL internalizing score (low to medium correlations). In children's reports, the correlation was significant for QoL total score and three subscales only (*physical well-being, emotional well-being* and *friends*). For the externalizing problems, a pattern similar to that shown for internalizing problems emerged. We found significant low to moderate negative correlations between QoL and CBCL externalizing score for parents' reports of total QoL and all subscales except *self-esteem.* For children's reports, the total QoL, *emotional well-being* and *family* subscales were significantly ($p < .01$) negatively correlated with externalizing scores, with the correlations being somewhat lower than for the parents' report.

Discussion

We found a clear reduction of quality of life in children with OCD, which affected total QoL measurements and most of the subdomains reported by both patients and their caregivers. Lack and colleagues [21] underlined the relevance of examining QoL in children with OCD as a source of useful information for treatment planning. Our findings are in accordance with this study [21], corroborating their results of heavily impaired QoL in children with OCD with a larger sample size and a methodologically stringent design.

We compared parents' ratings of the children with OCD on the CBCL social competence and school functioning scales with the general population to add the parents' more "objective" rating of functional aspects as an external perspective to the QoL analysis, which measures by definition subjective aspects of well-being. Parents reported markedly impaired social functioning of the children with OCD compared with the general population. School performance was also reduced but to a lesser degree. This result seems to be in accordance with the clinical experience that OCD symptoms might have a more profound impact on social life than on school performance.

Concerning comorbidity, we found considerably reduced QoL in the comorbidity group compared with children with "pure" OCD, at least in the view of their caregivers. In children's reports, we observed the same tendency but without reaching significance levels. That K-SADS-diagnosed DSM-IV comorbidity showed significantly reduced QoL only in parent reports might be due to the general tendency of children to rate their QoL with a more optimistic view than their parents, as seen in other studies. In studies of parent–child agreement in QoL, parents of children in non-clinical samples tend to report higher QoL scores than their children [39], while parents of children with disorders tend to underestimate QoL compared with the children's ratings. In Lack and colleagues' study [21], parents generally rated QoL as lower than the youths did. We agree with the authors' suggestion that young people may minimize the impact on QoL of their condition. Another possible explanation could be that the numbers of children with a categorical DSM-IV comorbidity diagnosis might be too low to reach significance levels in children's QoL reports. The disadvantage of categorical DSM-IV diagnoses is that patients on a subclinical level, who fall short of fulfilling diagnostic criteria, are not taken into account despite having considerable problems. Accordingly, on the symptom level, CBCL internalizing and externalizing problems showed a clear moderate negative association with QoL. The dimensional assessment approach of the CBCL, summarizing symptoms into quantitative externalizing and internalizing problem scores, might have been more sensitive than the diagnostic categorical approach to detect QoL impairment associated with comorbidity in all domains.

Almost half of the OCD patients in our sample were also affected with a variety of other disorders, and it was difficult to disentangle the relationships between different comorbidities and QoL, especially as statistical power was reduced by the low numbers in the comorbidity subgroups. In our analysis of two subgroups with specific comorbidity (ADHD, tic disorder or both, and anxiety disorder, depression or both) compared with the children with only OCD, we again found the tendency for lower QoL to be reported by the children in both comorbidity subgroups. On the other hand, parents reported significantly worse total QoL and relation to *friends* for the group with OCD and neuropsychiatric disorders than for the OCD only group, while comorbid anxiety disorders were not associated with worse QoL.

Both ADHD and Tourette's syndrome are associated with poor QoL in children and adolescents [40-42]. The presence of both OCD and ADHD is associated with reduced QoL in young people with Tourette's syndrome [43,44]. While confirming the additional negative impact of a comorbid neuropsychiatric disorder on QoL in paediatric patients with OCD, we were not able to differentiate the potential effects of ADHD versus Tourette's syndrome because of the sample size and overlapping comorbidity. Severe depression with suicidal ideation was an exclusion criterion in the NordLOTS study. This could be one of the reasons why we had a comparatively low prevalence of depression in our sample. The seven patients with depressive disorder and their caregivers reported a non-significant tendency towards lower QoL compared with the other patients. One must bear in mind that six of the seven patients with depression had one or more other comorbidities; the reduced QoL may well be a reflection of the general high load of comorbidity. On the other hand, the additive impact of comorbid depression on QoL is well documented in previous studies, at least in adults [17,18].

Children with high-functioning autism and their caregivers rated QoL in the same range as the other patients. Previous papers have discussed whether subjectively perceived QoL can be reliably measured in children with ASD because of differences in perception [45]. Shipman and colleagues [46] provided preliminary evidence that adolescents with ASD were able to report on their QoL in a valid and reliable manner. However, children with ASD and comorbid OCD are reported to have poorer insight into the exaggerated nature of their obsessions and they may perceive their compulsions as less egodystonic [47,48]. OCD symptoms usually have a great impact on social life, but children with ASD may be prone to report better QoL because of their reduced interest in social activities. Both factors may contribute to less impaired QoL perception. On the other hand, a possible explanation could be that OCD affects QoL to such an extent that there is no room for further QoL reduction in the HFA patients. However, the number of children with ASD included in our study does not allow us to draw firm conclusions.

Finally, we explored the significance of other factors for the perceived QoL, such as severity of OCD, the family's adjustment to the symptoms, age of onset and duration. As expected, we found a negative association between symptom severity and QoL, mainly reported by parents. Although significant, the correlations were low to moderate. In children's self-reports, the negative association between symptom severity and QoL emerged in the *disorder* subscale only. To test the hypothesis that a threshold of a certain severity must be crossed to have a stronger impact on QoL, we compared QoL ratings of children with more severe OCD with the group with less severe OCD. The majority of children in our sample had more severe OCD with CY-BOCS scores of 24 or above. These children and their parents reported significantly lower scores on the *disorder* subscale than children with less severe OCD. The *disorder* section of the KINDL-R reflects the children's subjective perception of how well they are able to cope with their OCD problems. That more severe symptoms were associated with a perception of reduced coping abilities is consistent with our expectation. We also found low to moderate inverse associations between levels of family accommodation and QoL total score and all subscales, except for the *school* subscale in parents' reports. As the Family Accommodation Scale score by definition reflects the involvement of the parents in their children's OCD symptoms, this result was expected. The finding that parents' perceptions of QoL affect total score and all other domains except *school* is consistent with the clinical observation that OCD symptoms are often more dominant in the home environment than at school. Alternatively, it may simply reflect the fact that parents are less involved in OCD while their children are at school. There was no association between QoL and age of onset of OCD. Duration of OCD was significant in the parents' report only with regard to *physical well-being.* Surprisingly, the duration of symptoms did not emerge as an important factor. A possible explanation could be that both children and parents adjust to the disorder burden over time, and this is reflected in their perception of QoL.

Both children's and parents' reports of QoL total score and most of the subdomains were inversely associated with the CBCL internalizing and externalizing problems. The correlation between severity of symptoms, family accommodation and load of comorbid internalizing and externalizing problems, and reduced QoL underlines the importance of having these factors in mind as part of the assessment procedure of children with OCD. Although all of these factors were correlated with QoL, none of them showed a high correlation, indicating the separate value of assessing QoL. This finding seems to support our view that QoL evaluation covers different and important aspects of the disorder, which are not accounted for in the frame of symptomatic and functional assessment only.

Limitations

Because of the homogeneous socio-demographic factors and similarities in culture and language of the population in the Nordic countries, our sample consisted mostly of relatively well-educated families of Caucasian origin. For example, the inability to understand one of the Nordic languages was an exclusion criterion. This represents a clear limitation to the generalization value for other populations. Although our study was based on a relatively large sample of paediatric patients with OCD, some subgroups of comorbid disorders were small, leading to problems of statistical power, which limited an analysis of each single comorbid disorder group. To overcome this limitation in further research, much larger samples are needed, which would demand not only regional multicentre studies but also collaboration across different countries. Another limitation lies in the cross-sectional design of the study; this design generally does not allow conclusions to be drawn about causality and effect of the observed associations between QoL and the examined factors.

Conclusions

QoL and social competence are significantly reduced in children and adolescents with OCD compared with the general population. OCD with comorbidity showed the lowest QoL compared with OCD without any comorbidity. Severity and duration of symptoms, family accommodation and comorbid internalizing and externalizing problems were associated with reduced QoL, but with low to moderate correlations only. The assessment of QoL beyond symptoms and function in children with OCD has been shown to be reliable and informative. Thus, we recommended QoL as an additional outcome measure in the treatment plans of children with OCD.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

BW and TJ conceived of the study and its design, participated in data collection and coordination, carried out the data analyses and drafting of the manuscript. PTH and TI made significant contributions to the design of the study and critically revised the manuscript. All authors read and approved the final manuscript.

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Paper III

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Quality of life in children with OCD before and after treatment

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Abstract Quality of life (QoL) is a well-established outcome measure. In contrast to adult obsessive–compulsive Disorder (OCD), little is known about the effects of treatment on QoL in children with OCD. This study aimed to assess QoL after cognitive behavioural therapy (CBT) in children and adolescents with OCD compared with the general population and to explore factors associated with potential changes in QoL after treatment. QoL was assessed in 135 children and adolescents (ages 7–17; mean 13 [*SD* 2.7] years; 48.1% female) before and after 14 CBT sessions, using self-report and a caregivers proxy report of the *Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents (KINDL-R)*. QoL was compared with an age- and gender-matched sample from the general population. Before treatment, QoL was markedly lower in children with OCD compared with the general population. QoL improved significantly in CBT responders (mean score change 7.4), to the same range as QoL in the general population. Non-responders reported no QoL changes after treatment, except for one patient. Comorbidity, family accommodation and psychosocial functioning were not associated with changes in QoL after treatment. To our knowledge, this is the first study of the changes in QoL after treatment of paediatric OCD. The assessment of QoL beyond symptoms and function in children with OCD has been shown to be reliable and informative. The results of this study support the application of QoL assessment as an additional measure of treatment outcome in children and adolescents with OCD.

Keywords Pediatric OCD, Quality of Life, Comorbidity, Cognitive behavioural therapy, Assessment

Introduction

Obsessive–compulsive disorder (OCD) is reported with a prevalence of 0.5–3% in children and adolescents [1-3]. This disorder has a chronic course in 40–75% of cases [4-6]. In most cases, OCD is associated with other psychiatric conditions, and 77–85% of children with OCD fulfil the criteria for one or more other psychiatric diagnoses [7,8]. Depression, phobias, other anxiety disorders and neuropsychiatric conditions such as attention deficit hyperactivity disorder (ADHD) and tic disorder are frequent comorbidities in paediatric OCD. In addition, several researchers have reported elevated levels of autism spectrum disorder (ASD) comorbidity in OCD, in adult [9-11] as well as in paediatric [12] samples. Cognitive behavioural therapy (CBT) in the form of exposure and response prevention (E/RP) is well documented as an efficacious treatment for OCD. Several international guidelines recommend E/RP as the first-line treatment for paediatric OCD [13-16].

The assessment of quality of life (QoL) is established as an important outcome factor that is independent of symptom level because pathology does not have a simple linear relationship with well-being [17]. QoL is defined as *subjective* well-being on several domains of life [18]. The European Agency for the Evaluation of Medicinal Products and the U.S. Department of Health and Human Service Food and Drug Administration support the use of patient-rated outcomes, including QoL measures, as outcomes in clinical trials and have published guidance on the development of reliable measures [19,20]. In contrast to adult OCD, little is known about QoL of children and adolescents with OCD and nothing at all about the relationship between treatment of OCD and QoL in young people. To our knowledge, no study has assessed QoL before and after treatment interventions in paediatric patients with OCD.

In adults, changes in QoL seem to be associated with OCD symptom severity [21,22] and with the presence of comorbid conditions, particularly depression. To date, four review articles on QoL in adults with OCD have been published [23-26], all of which concluded that QoL was markedly lower in patients with OCD compared with the general population. Hupert and colleagues [27] for example, found significantly lower QoL in the OCD group compared with healthy controls. In their paper, they described the shortcomings of many of the previous studies as follows: (1) lack of comparison between individuals in remission with individuals who continue to have the disorder, (2) comparison only with population norms and lack of comparison with a matched normal sample and (3) lack of consideration of the impact of comorbidity in some studies. Macy and colleagues [24] underlined the importance of QoL assessment in both clinical and research settings to examine disease burden, to monitor treatment effectiveness, to determine the extent of recovery from OCD and to take these factors into account when developing treatment plans.

A variety of studies have evaluated QoL changes after different treatment options. The common feature of all studies is that they have focused on adults only. A few studies evaluated QoL after a CBT intervention. For example, Diefenbach and colleagues [28] observed significant improvement in QoL among 70 adults with OCD before and after CBT. Changes in OCD symptoms and QoL were highly related, although there was a subset of participants whose symptoms improved without corresponding improvement in QoL.

Volpato Cordioli and colleagues [29] evaluated the efficacy of group CBT on QoL after 12 weeks of treatment and a 3-month follow-up. They found significantly improved QoL in the participants compared with the waiting list controls. After the 3-month follow-up, treatment gains in terms of symptom reduction were largely maintained or improved, although the slightly lower QoL scores suggested no additional improvements in QoL. Norberg [30] evaluated treatment responses and QoL changes after non-standardized CBT programs, during which most participants received medications concurrently with CBT. They identified three distinct subgroups that exhibited changes after treatment. One group of treatment responders reported strong symptom reduction and consistent QoL improvement, a second group of partial responders had significant symptom reduction but less robust QoL improvements and a third group of treatment non-responders had decreased QoL.

Other studies have explored the relationship of more complex treatment conditions with QoL including inpatient treatment, medication and behavioural interventions, or combinations of these conditions. These studies probably included more severely impaired patients. Moritz and colleagues [31] explored the predictors of decreased QoL in 79 adults with OCD and changes in QoL after treatment, and the association between QoL changes and symptom-related outcomes. Overall, QoL improved significantly in therapy responders relative to non-responders. In another study of 73 adults with OCD, Hertenstein and colleagues [32] investigated QoL before and after treatment in an inpatient setting followed by outpatient treatment. At baseline, participants had significantly lower QoL compared with the general population. QoL improved significantly at the 12-month follow-up but remained below the values in the general population. Stewart and colleagues [33] evaluated the effects of intensive residential treatment, an inpatient program developed for severe refractory OCD that included medication and 2–4 hours of daily CBT. They reported a 30% improvement in the *Yale–Brown Obsessive Compulsive Scale* (Y-BOCS) score between admission and discharge, and a corresponding and significant improvement in QoL of 26–32% in various QoL measures.

A third group of studies examined the treatment effects on QoL after a medication trial either alone or in combination with CBT. Hollander and colleagues [22] found evidence that long-term pharmacological treatment of OCD improved QoL and that symptom relapse was associated with deterioration in QoL. Tenney and colleagues [34] reported that QoL improved following pharmacological interventions. Interestingly, treatment responders, defined by a 35% reduction in the Y-BOCS score, did not differ in their improvement in QoL, which suggests that the improvement in QoL was not associated with symptom reduction.

The findings related to QoL from adult OCD research cannot be generalized to children, who experience continuous development [35] and different perceptions of subjective well-being compared with adults [36]. In addition, the evidence from one informant does not represent a sufficiently complete picture in paediatric QoL studies because child and parent reports have shown low agreement [37,38]. Both perspectives are important because they are not the same, but both are “part of the social reality we call child well-being” [39]. Therefore, both perspectives need to be considered to obtain reliable outcome information.

Only a few studies have assessed QoL in children and adolescents with OCD. Palermo and colleagues [40] assessed adult QoL outcomes and evaluated baseline characteristics of 36 children at a mean age of 12 years to evaluate their predictive value for QoL in young adulthood after an average of 9 years of follow-up. QoL was measured at follow-up only. Remitters demonstrated significantly better QoL than non-remitters. QoL in early adulthood correlated strongly with the severity of residual OCD symptoms but not with OCD symptom severity in childhood. A general population control was not available in this study. In a study of long-term outcomes of 142 children and adolescents with OCD, Micali and colleagues [4] reported mildly to moderately affected QoL assessed at follow-up when the mean age of the participants was 18.6 years (*SD* = 3.5, range 11–28). At this time, 61% reported very much or much improvement in OCD symptoms; QoL was not assessed at baseline. Lack and colleagues [41] found significantly lower QoL scores in 62 children and adolescents (8–17 years) than in healthy controls for QoL assessed at baseline as part of the initial treatment evaluation. QoL was only moderately associated with OCD symptom severity, as reported by parents. Therefore, the authors suggested that OCD symptom severity and QoL are two related but distinct constructs. In addition, the presence of comorbid externalizing and internalizing symptoms was a strong predictor of lower QoL scores. A previous study from our group [42] reported on QoL and baseline characteristics before treatment. This study confirmed the findings of Lack and colleagues in a larger sample size showing considerably impaired QoL in children with OCD. Children with OCD and comorbidity had the lowest QoL compared with those with OCD only. A recent epidemiological study from Brazil [43] found poorer QoL in 75 adolescents with OCD (14–18 years of age) compared with adolescents without OCD, especially in those with comorbid depressive symptoms. Lack and colleagues stated in 2009 that evidence from studies of adults with OCD suggests that both CBT and pharmacotherapy are associated with improved QoL following treatment, but this has yet to be studied in youth. The most recent of the mentioned reviews on QoL in adults with OCD [26] stated clearly: "…little is known about the impact of OCD on QoL in paediatric patients. As there is a substantial prevalence of OCD in childhood and adolescence due to its early age of onset, there is an obvious need for further exploration of QoL in these populations; however, this is currently lacking."

In this paper, we report on the relationship between a treatment intervention with CBT and QoL in children and adolescents with OCD, assessing prospectively QoL before and after treatment.

Aims

The aims of the present study were: (1) to assess changes of QoL after treatment with CBT in children and adolescents with OCD reported both by children and their caregivers, compared with QoL rating in an age- and gender-matched sample of student and parent reports from the general population, and (2) to assess whether the treatment response, comorbidity, psychosocial functioning or family accommodation are associated with QOL changes after controlling for gender, age and socio-economic status (SES).

Methods

Participants

Sample description

The present QoL study is a substudy of a multicentre treatment research project, the Nordic Long-term OCD Treatment Study (NordLOTS), in which 269 children and adolescents, aged 7–17 years, were treated for OCD with CBT between September 2008 and June 2012. The NordLOTS trial has been described in detail elsewhere [44-46]. We use the term “children” to denote children and adolescents in this paper. The present QoL study was initiated later than the NordLOTS and at different time points in the three participating countries because of differences in the availability and approval of the national translations of the QoL questionnaire used. Of 155 patients eligible for participation in the study, 22 refused to participate or did not complete the QoL instrument *Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents*, revised version (KINDL-R). Each child and one of his or her caregivers completed the QoL questionnaire at baseline, giving 135 completed forms from either a child and/or one caregiver. Completed QoL assessments after treatment were available for 106 children and parents (Figure 1). ASD was an exclusion criterion in the main treatment study, but nine individuals with Asperger’s syndrome/high-functioning autism (HFA) were included in a substudy at one site (Trondheim). Complete QoL assessment was available for eight of these nine patients. Details are described elsewhere [42].

Treatment

Treatment comprised 14 sessions of weekly individual CBT with E/RP based on the study protocol of March and Mulle in collaboration with Foa and Kozak [47]. The treatment was modified to include more extensive family participation based on the work of Piacentini and colleagues [48] and adapted to fit Nordic cultural conditions. Parents were encouraged to participate actively during the entire course of their child’s treatment and both the child and the parent to jointly attend sessions 1–3, 7, 11 and 14. During these sessions, information was provided about treatment rationale and goals, and the parents’ role in the treatment process, and ideas about particular OCD problem areas for the child were addressed. In the remaining sessions, 45 minutes of individual CBT was offered to the child, followed by an additional 30 minutes for a parents’ session (with or without the child). The purpose of the latter was to address issues such as family accommodation, family support, problem solving and questions parents might have. The focus of the treatment was the gradual exposure to threatening situations based on a detailed symptom hierarchy, including homework exposure exercises. If appropriate, parents were asked to support and closely monitor homework assignments. Towards the end of the therapy, the emphasis shifted to generalizing skills and relapse prevention.

Treatment response

A clinical response was defined as a Children's Y-BOCS (CY-BOCS) total score of ≤15, assessed by independent evaluators as the primary outcome measure and a 30% reduction in the CY-BOCS score as a secondary outcome measure. Among the 106 children with complete QoL data, 71 (67%) were treatment responders and 35 (33%) non-responders.

Age, gender, ethnicity and SES

At baseline, the mean age of the participants was 13 years (*SD* 2.7 years, range 7–17). The gender distribution was even, with 65 girls (48.1%). Thus, the QoL study sample was representative of the NordLOTS, in which the mean age was 12.8 (*SD* 2.7) years, whereas the gender distribution diverged slightly with more girls represented (51.3%). If compared without the nine male participants from the ASD substudy, the gender distribution was equal in both samples (51.3% versus 51.6% girls in the QoL study). Ethnicity was primarily Scandinavian: 97% of the participants had one or both parents of Scandinavian origin. SES was calculated using the highest educational level of either the mother or father (whichever was highest) and assessed as suggested by Hollingshead [49]; the scores ranged from 1 to 7 (7 = university education). The educational level of parents was generally high ($M = 5.30$; *SD* 1.39). . The SES in the QoL study participants did not differ significantly from that of the participants in the main NordLOTS study ($t(270) = 0.92$; $p = 0.357$; $M = 5.14$, $SD = 1.47$).

Comorbidity

Comorbidity at baseline was common, especially neuropsychiatric conditions, other anxiety disorders and, to a lesser degree, depression. Only 69 patients (52.3%) had "pure" OCD without any other comorbidity (hereafter named "OCD only"). Eighteen patients (13.6%) met the *Diagnostic and Statistical Manual of Mental Disorders* 4th edition (DSM-IV) [50] criteria for ADHD and 37 (28%) for tic disorder; 14 had both. Conduct disorders were diagnosed in six patients (4.5%). Other anxiety disorders were diagnosed in 28 patients (21.2%): two patients had separation anxiety, 16 specific phobia (12.1%), eight social phobia (6.1%), six generalized anxiety disorder (4.5%) and two unspecified anxiety. Four patients had two and one patient had three additional anxiety disorders. Seven patients (5.3%) had depression; six of these seven had a diagnosis of major depressive disorder and the other had unspecified depression. No other psychiatric comorbidity was diagnosed. The ASD group (*n* = 9) contributed heavily to the load of comorbidity: only one of the ASD patients had OCD only, seven had other neuropsychiatric conditions (three with tic disorder, two with ADHD and two with both tics and ADHD) and one patient had another anxiety disorder (specific phobia).

Attrition

Baseline assessment of QoL resulted in 135 completed forms from either children and/or one of their caregivers (133 child forms and 130 parent forms, including two cases where only the parents completed the questionnaire and five cases where only the children completed the questionnaire), yielding response rates of 86% for eligible children and 84% for the parents. Post-treatment QoL assessment was available for 109 participants (70%). In three cases with QoL assessment, post-treatment responder status was missing at the time of the data analysis. Attrition from missing QoL reports or responder status resulted in a response rate of 68% (n = 106) of all invited participants (children and parents) who completed QoL assessments before and after treatment.

Insert Figure 1 about here.

Comparison group

A large normative data sample comprising students from schools in Sør-Trøndelag county [51,52], which represents a comparable geographical area as the study area with both urban and rural settlement, was used as a control group. Every child or adolescent with OCD was matched individually with a control from the general population sample (*n* = 1821, aged 8–16 years). This sample was stratified according to gender and age, and controls were numbered consecutively in each stratum. Using computer-generated random numbers, we then allocated each patient to a control. The parents' educational level did not differ significantly between patients (M = 5.19) and the allocated controls from the general population (M = 5.29) (*t*(118) = 0.51, *p* = 0.61, paired-samples *t* test). Details of the general population sample are described elsewhere [42].

Instruments

QoL

The KINDL-R [53] is a well-established QoL instrument used in several clinical and epidemiological studies. Swedish and Norwegian versions of the questionnaire were available, and the Danish translation was prepared and approved by the original authors. We used the self-report questionnaire for children and adolescents as well as the proxy version completed by one of the parents. The questionnaire comprises 24 items, whose scores are equally distributed into six subscales: *physical well-being, emotional well-being, self-esteem, family*, *friends* and *school*. Each item addresses the child's experiences over the past week and is rated on a five-point scale (1 = never, 5 = always). The mean item scores are calculated for all subscales and for the *total QoL* scale, which is transformed to a 0–100 scale, with 100 indicating very high QoL. The instrument also provides a disorder-related subscale yielding information about the perception of the disorder burden. We modified the form by adding the sentence "*Concerning your OCD …*" for children, and "*Concerning your child's OCD …*" for parents to the disorder-related questions to ensure we tracked the informants' perception of OCD and not a concurrent somatic or other disorder. Psychometric testing of the KINDL-R revealed good scale utilization and scale fit as well as moderate internal consistency [54]. A Norwegian normative study also confirmed satisfactory internal consistency and test–retest reliability [52] and ceiling effects [51]. In a review of QoL measures in children and adolescents, Solans and colleagues [55] found that the KINDL-R is one of the few identified generic instruments for which acceptable sensitivity to change has been reported.

OCD diagnosis and comorbidity

The *Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime* version (K-SADS-PL) [56] is a widely used semi-structured interview for diagnostic assessment of DSM-IV [50] psychiatric disorders and subsyndromal symptomatology in children and adolescents. The K-SADS-PL was used to confirm the diagnosis of OCD according to the DSM-IV and to evaluate comorbidity. The K-SADS-PL was administered by interviewing the parent(s) and the child. Approved translations of the revised version of the K-SADS-PL [57] used in the study were available for all three languages.

OCD symptom severity

Symptom severity was assessed with the CY-BOCS [58] including the *Clinical Global Impression* (CGI). The CY-BOCS is a semi-structured interview containing checklists of obsessions and compulsions. Scales assessing the severity of obsessions and compulsions separately (range 0–20) are added to a CY-BOCS total score (range 0–40). Finally, a global severity score (CGI) is assigned based on all information gathered during the interview. The checklists and the severity ratings were based on interviews with each child and each parent or adult informant. CGI is a widely used rating scale for clinicians to assess the global severity of illness with a score ranging from 0 (“no illness”) to 6 (“serious illness”).

Family accommodation

The *Family Accommodation Scale* (FAS) [59] is a 12-item clinician-rated questionnaire, designed to assess the family’s accommodation to the child’s OCD symptoms. The FAS items measure the extent to which family members provide reassurance or objects needed for compulsions, decrease behavioural expectations of the child, modify family activities or routines and help the child avoid objects, places or experiences that cause distress. The FAS has demonstrated good psychometric properties including good internal consistency (α = 0.76–0.80) [59,60] and positive correlations with measures of OCD symptom severity [61] and family discord [59].

Children’s Global Assessment Scale

The *Children’s Global Assessment Scale* (CGAS) is a rating scale for assessing children’s general level of psychosocial functioning and is used primarily by clinicians [62]. It is used widely as a measure of the overall severity of disturbance in children; for example, for treatment evaluation as well as an index of impairment in epidemiological studies. Scores range from 1 (most impaired) to 100 (healthiest). The CGAS has demonstrated adequate inter-rater and test–retest reliability [63,64].

Statistics

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 21 (IBM Corp., Armonk, NY).

At baseline, 0–9.2% of the parents’ reports had missing values for the first five of six KINDL-R subscales, and 10.8–13.1% had missing values in the disorder subscale. The corresponding percentages of missing values in the children’s reports were 0–6.0% for the first five subscales and 5.3–8.3% for the disorder subscale. At the post-treatment assessment 0–6.6% of the parents' reports had missing values for the first five subscales of the KINDL-R and 10.7–13.9% had missing values for the disorder subscale. The corresponding percentages of missing values in the children's reports were 0.8–7.3% for the first five subscales and 10.6–12.2% for the disorder subscale. Missing values were substituted with the mean according to the KINDL-R manual, which states that if more than two questions in a section of four were not answered, no subscale score nor a total QoL score is produced. Accordingly, the number of participants varied between subscales and QoL total scores.

In all other instruments, there were low percentages of missing values: 0% (CY-BOCS) to 3.7% (FAS). Missing values and attrition were in general low. Therefore, statistical calculations were conducted as complete case analyses.

Changes in the participants' total QoL scores before (T1) and after treatment (T2) and level of QoL after treatment compared with QoL level in the general population were analysed by paired sample *t* tests. Linear regression analyses of the difference in QoL scores between T2 and T1 as the dependent variable, dichotomized as responders and non-responders to treatment, were used to estimate the changes in QoL after treatment. All linear regression analyses were adjusted for gender, age and SES as potential confounders. The Pearson chi-squared test was used to analyse differences in QoL total score between T1 and T2 in participants who were not classified as responders to treatment.

Ethics

The study was approved by the Regional Committees for Medical and Health Research Ethics in Denmark, Norway and Sweden. All parents gave written informed consent and the permission for their children to participate before inclusion in the study.

Results

QoL in children with OCD before and after treatment

QoL as reported by children with OCD and their caregivers improved markedly after treatment (Table 1). The changes in QoL total scores and all subscale scores except the friends and school subscale in the children's report were significant.

Insert Table 1 about here.

QoL changes in responders versus non-responders to treatment

QoL total score changed significantly in the responders (mean change 7.4 for children's reports and 9.2 for parents' reports) but changed only slightly in non-responders (mean change 0.23 for children's and 1.2 for parents' reports). Being a responder was associated with QoL improvement from T1 to T2 in both the children's reports ($\beta = 0.30$; $p = 0.002$) and parents' reports ($\beta = 0.32$; $p = 0.001$) (Figure 2). There was no significant effect of potential confounders (gender, age and SES) on parents' or children's reports.

In a subsequent analysis, we identified six children (and five parents) who reported clinically important QoL improvement, defined as a difference in QoL total score between baseline (T1) and post-treatment assessment (T2) of >9 without being classified as responders to treatment (CY-BOCS total score <16). The difference was significant: $\chi^2(1) = 10.31$; $p = 0.002$ in children's reports and $\chi^2(1) = 5.35$; $p = 0.027$ in parents' reports. Further inspection of the data showed that the CY-BOCS scores decreased markedly from T1 to T2 in these participants, although not to the extent that they met the criteria for a clinical response (i.e., CY-BOCS <16). One participant reported QoL improvement without clinical improvement (no change in CY-BOCS score).

Comorbidity and changes in QoL after treatment

The presence of comorbidity, defined as OCD only versus OCD with any comorbidity as assessed at the baseline, was not associated with changes in QoL. The QoL change between T1 and T2 did not differ significantly in children with comorbidity compared with those without comorbidity as indicated in both the children's reports ($\beta = 0.001$, $p = 0.989$) and parents' reports ($\beta = 0.018$, $p = 0.854$).

This was also the case when the study population was dichotomized as responders and non-responders: children's report responders $\beta = –0.039$ ($p = 0.751$) and non-responders $\beta = 0.180$ ($p = 0.300$); and parents' report responders $\beta = –0.023$ ($p = 0.853$) and non-responders $\beta = 0.149$ ($p = 0.424$).

Family accommodation and changes in QoL after treatment

Family accommodation, defined by the FAS score at the baseline, was not associated with changes in QoL after treatment for the total group: children's reports $\beta = 0.102$ ($p = 0.301$) and parents' reports $\beta = 0.142$ ($p = 0.158$). When dichotomized into responders and non-responders to treatment and after controlling for confounders (gender, age and SES), the baseline FAS score was not associated with changes in QoL total scores in the children's reports (non-responders: β = 0.315, *p* = 0.098; responders β = 0.073, *p* = 0.594) and in the parents' reports (non-responders: β = 0.294, *p* = 0.115; responders β = 0.132, *p* = 0.274).

Psychosocial functioning and changes in QoL after treatment

Psychosocial functioning, defined by the CGAS score at baseline, was not associated with changes in QoL after treatment: children's reports β = –0.004 (*p* = 0.965) and parents' reports β = 0.017 (*p* = 0.871). When dichotomized into responders and non-responders, the CGAS score at baseline was not associated with QoL changes.

Changes in QoL after treatment compared with QoL levels in the general population

In the analysis of responders and non-responders together, the post-treatment QoL total score reported by children did not differ significantly from that in the general population: QoL total score mean difference –2.25 (*p* = 0.178). However, parents' rating of QoL total score differed between responders and non-responders: mean difference –7.30 (*p* < 0.001) (Figure 2). When dichotomized into responders and non-responders, the QoL scores for non-responders were significantly different from those of the matched cases from the general population in both the children's and parents' rating: QoL total score mean difference –10.78 (*p* < 0.001) for the children's reports and –18.36 (*p* < 0.001) for the parent reports. By contrast, after treatment, the responders achieved the same QoL as reported in the matched cases in the general population: QoL total score mean difference 1.76 (*p* = 0.347) for the children's reports and 2.17 (*p* = 0.210) for the parents' reports.

Insert Figure 2 about here.

Discussion

QoL as reported by both children with OCD and their caregivers improved largely after treatment. QoL total scores increased significantly in the responders to treatment and to such an extent that they were similar to that of the matched controls in the general population. The presence of comorbidity, degree of family accommodation and level of psychosocial functioning were not associated with changes in QoL after treatment.

QoL levels after treatment corresponding to QoL in the general population

In our sample, the baseline QoL was markedly lower in children with OCD compared with the general population. This is consistent with studies of OCD in adults and the two published studies of baseline or population data for paediatric OCD patients [41,43]. We found that, after treatment, the QoL ratings in the responders were in the same range as in the general population, whereas non-responders to treatment exhibited almost no change in QoL except for one patient. These findings suggest that the CBT treatment intervention was highly effective in reducing symptoms in responders and in improving QoL to the level observed in the general population. Similarly, in the previously mentioned follow-up study of Palermo and colleagues [40], remitters to treatment showed no impaired QoL in adulthood, and non-remitters had mild QoL impairment only. However, these studies cannot be compared directly. The therapeutic intervention in the study by Palermo and colleagues included medications and/or behavioural therapy throughout the study interval, but some of the participants continued to receive active psychiatric treatment, including medication in 60% of participants, when QoL was assessed at a mean age of 21 years. In addition, data from the baseline assessment and for a general population control were not available in the study by Palermo and colleagues, and long term follow-up data are not yet available for our study.

Our findings of QoL improvement to normal levels after treatment contradict the findings from studies in adults. For example, Huppert and colleagues [27] found that QoL scores in individuals in remission tended to be between those of healthy controls and individuals with current OCD, and to not differ significantly from either group. Moritz and colleagues [31] found significantly improved QoL in therapy responders relative to non-responders but that compromised QoL persisted in most patients over time. OCD severity correlated only modestly with QoL suggesting that QoL improvement after treatment reflected several factors that influence QoL and not just improved OCD symptoms. In Hertenstein’s study [32], QoL improved significantly after 12 months of intensive state-of-the-art treatment, but the QoL indices remained considerably lower than the population norm values. By contrast, our results showed that appropriate treatment of children and adolescents who were treatment responders improved QoL to levels in the normal population. One explanation might be that treatment in children has a more profound effect on QoL because it is likely that children have a shorter course of the disorder than do adults. In addition, in paediatric patients, treatment may increase the number of patients who experience complete remission of symptoms, whereas samples of adult patients may include a higher frequency of chronic patients. However, Hertenstein assessed QoL at baseline and at follow-up 12 months after the inpatient treatment, which included continuing outpatient treatment, whereas QoL in our sample was assessed after 14 weeks of treatment intervention. Thus, it is not clear whether the QoL scores in our study will be maintained in the normal range 1 year after the therapeutic intervention. Our study includes a follow-up over 3 years after treatment to explore whether the treatment gains in terms of symptom reduction and QoL improvements will be stable over time.

Treatment evaluation and QoL measurement

There is an ongoing discussion in the field about the standards for treatment evaluation in terms of the optimum definitions of treatment response, remission criteria, symptom reduction and the need to include other outcome parameters such as functional impairment and health-related QoL measurements [65,66]. Tolin and colleagues [66] questioned the external validity of clinical trial results; i.e., whether the gains seen on standardized clinical measures correspond to clinically meaningful changes in real-world functioning. Lack and colleagues [41] strongly recommended QoL assessment in paediatric OCD patients as a relevant parameter for both assessment and treatment evaluation. According to the authors, "targeting symptoms only without attending to QoL may result in the confounding of assessment data as the patient may have reduced symptoms that do not translate into improved day-to-day functioning".

In many studies, a treatment response is defined as a 25–35% reduction from baseline in the Y-BOCS or CY-BOCS score. [65,66]. In the NordLOTS study, responders were defined by a CY-BOCS score of <16. This definition was based on the experience in the Pediatric OCD Treatment Study, in which the same value was used to define clinically relevant OCD symptoms [67]. Another reason for the comparably high cut-off score was the fact that non-responders were later randomized to receive either CBT or a selective serotonin reuptake inhibitor (SSRI). To avoid ethical problems treating children with only mild symptoms with medication, the criterion of a CY-BOCS score of <16 was used to indicate response. As a secondary outcome measure, a 30% reduction in the CY-BOCS score was added to ensure that the primary outcome measure of a CY-BOCS score <16 did not inflate the number of responders.

In the abovementioned study by Palermo and colleagues [40], remission was used to define a treatment response as: remitters Y-BOCS score, < 8; mild OCD, 8–15; moderate OCD, 16–23; and severe OCD, >23. Consequently, they reported a larger number of individuals without

QoL impairment (57%) than the number of remitters (42%) and that non-remitters had only mild QoL impairment in adulthood. These results may suggest that QoL was not directly related to symptom level despite the strong correlation between QoL and severity of residual symptoms. However, if a definition of responders with a Y-BOCS score of <16 including the participants with only mild OCD is applied, the percentage of responders would increase to 80%, which supports our finding that QoL impairment was closely related to symptom level in children with OCD.

In a study of adults treated with medication, Hollander and co-workers [22] found that improvements of QoL correlated closely with improvements in the Y-BOCS score. They suggested that an important step towards achieving a consensus for any given outcome based on the Y-BOCS criterion is to demonstrate that such a criterion distinguishes patients on the basis of a clinically meaningful assessment that varies as a function of the Y-BOCS score. When they defined a response as a ≥25% improvement in the Y-BOCS total score relative to the baseline, the mean QoL scores for responders and non-responders were clearly distinguishable.

We also found a clear relationship between symptomatic improvement and QoL, suggesting that QoL assessed using the KINDL-R is sensitive to treatment outcomes. Thus, QoL assessment was consistent with the CY-BOCS cut-off scores used in this study to define treatment outcomes. However, a small subsample comprising six individuals reported clinically important QoL improvement without being classified as responders to treatment. Five of these participants had a large reduction in their CY-BOCS score (>9), but this change was not to an extent that they met the criteria for a clinical response. Only one participant reported QoL improvement without clinical improvement. Thus, without QoL evaluation or additional outcome criteria, a treatment response in these individuals could have been overlooked.

Our results of a close relationship between symptom reduction and QoL improvement are consistent with the results of Diefenbach and Hollander in adults with OCD. However, other reports have suggested an independence between a symptom response and QoL improvement in adults [68,34]. Again, the reason for our findings could be that treatment in children has a more profound effect on QoL because it is likely that children have a shorter course of the disorder than adults. Another explanation, related more to the methodology, is that the various QoL assessment instruments have different sensitivities in terms of their ability to detect changes.

Comorbidity and QoL

Surprisingly, the presence of comorbidity was not associated with changes in QoL after treatment in both the children's and parents' reports. At the baseline evaluation, children with comorbidity and especially neuropsychiatric conditions had lower QoL compared with those without comorbidity. Comorbid internalizing and externalizing problems are associated with reduced QoL, although the correlations are low to moderate [42]. One could presume that the presence of comorbidity may result in fewer effects on QoL after OCD treatment because the comorbid conditions will continue to have a negative influence on QoL after treatment. However, the presence of comorbidity at the baseline was not associated with QoL changes in responders or in non-responders to treatment. This may reflect an expanding effect of CBT to other symptoms and problems beyond the reduction in OCD symptoms. On the other hand, the marked treatment impact on QoL in responders might override the lack of improvement in the small group of non-responders. Interestingly, in the study of Palermo and colleagues [40], childhood comorbid conditions such as tic disorders, ADHD, depression and other anxiety disorders also had no significant value for predicting QoL in early adulthood.

In adults with OCD, the additive impact of comorbid depression on QoL is well documented [22,24]. In Hertenstein's study [32], QoL improvement after treatment was predicted by improvements in depressive symptoms. Moritz and colleagues [31] found the strongest correlations with QoL for depression severity and number of OCD symptoms. Hupert and co-workers [27] found that participants with OCD and comorbid psychiatric diagnoses showed the poorest QoL and that comorbid depression accounted for much of the variance. In the study of Kugler and colleagues [69], depressive symptoms mediated the relationships between obsessive–compulsive symptom severity and emotional health, social functioning and general health QoL. In the only available study providing information about depressive symptoms in adolescents with OCD, Vivan Ade and co-workers [43] found a significant negative relationship between QoL and depressive symptoms as evaluated with the Beck Depressive Inventory. K-SADS-PL was used to confirm the diagnosis of OCD in the study, but no information about the relationship between QoL and depression above the diagnostic threshold was offered.

Severe depression with suicidal ideation was an exclusion criterion in the NordLOTS study. This could be one of the reasons why we had a low prevalence of depression in our sample. At the baseline assessment, only seven patients were diagnosed with depressive disorder . These patients and their parents reported tendencies to lower QoL compared with all other patients, but without reaching significance levels. Six of the seven patients with depression had one or more additional comorbidities. Thus, an analysis of the change in QoL in patients with comorbid depression during treatment would not allow any conclusion at all. The impact of comorbid depression on QoL may as well reflect the total load of all comorbidities, which was not significant, as noted above.

Impact of family accommodation and psychosocial functioning on QoL

Family accommodation and psychosocial functioning at the baseline was not associated with changes in QoL after treatment in the children's and in the parents' reports. At the baseline evaluation, family accommodation was associated with low QoL, but the correlations were low to moderate [42]. Our findings may indicate that CBT was highly effective in most patients independent of the baseline psychosocial and family function. In the study of adults by Diefenbach and colleagues [28], more impaired family functioning was the only demographic or clinical characteristic to differentiate the subgroup of patients whose improvements in OCD symptoms corresponded with improvements in QoL. The authors considered that this subgroup may have received more treatment that specifically targeted family functioning because the patients had more family involvement in rituals. However, because of the lack of measures of family accommodation in rituals, this hypothesis could not be tested. In our study, considerable effort was put into family work by encouraging caregivers to actively participate during their child's treatment. One interpretation of our results is that even non-responders had a non-specific benefit of the family component of the treatment.

Limitations

Because of the homogeneous socio-demographic factors and similarities in culture and language of the population in the Nordic countries, our sample comprised mostly relatively highly educated families of Caucasian origin. For example, the inability to understand one of the Nordic languages was an exclusion criterion. This represents a clear limitation to the generalization value for other populations. Another limitation is the lack of a treatment control group in our study. Although our results offer strong empirical support that QoL in children and adolescents with OCD is improved following CBT, conclusions about the causal relationship between CBT and QoL improvement cannot be drawn. A third limitation is the lack of follow-up data because QoL was assessed directly after the therapeutic intervention. There is no information available about the long-term impact of CBT on QoL in children with

OCD. Thus, it is not clear whether the improved QoL scores will be maintained in this range or will deteriorate over time.

Conclusion

Children and adolescents with OCD had significantly lower QoL before treatment compared with the general population of children and adolescents. Responders to treatment exhibited improved QoL to the level reported in the general population. Non-responders reported no QoL changes after treatment except in one patient. Our findings suggest that QoL assessment with the KINDL-R is valid, informative and sensitive to treatment outcomes in paediatric OCD patients and supports the use of the CY-BOCS cut-off scores used in the study to define treatment outcomes. The results of this study support the application of QoL assessment as an additional measure of treatment outcome in children and adolescents with OCD.

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Conflict of interest The authors declare that they have no conflict of interest.

Table 1 Quality of life assessed by the KINDL Questionnaire, children's self-reports and parent proxy reports before and after treatment[a]

	QoL total score Mean (*SD*)	Physical well-being Mean (*SD*)	Emotional well-being Mean (*SD*)	Self-esteem Mean (*SD*)	Family Mean (*SD*)	Friends Mean (*SD*)	School Mean (*SD*)	Disorder subscale (*SD*)
Children with OCD:	62.55	62.16	63.38	51.28	68.18	66.20	63.65	64.41
Self-report at baseline	(12.67)	(17.74)	(16.88)	(19.72)	(19.18)	(18.48)	(19.87)	(17.16)
Self-report after	67.80	69.78	72.08	57.44	72.21	68.73	67.09	75.30
treatment	(13.17)	(16.53)	(16.05)	(19.46)	(18.32)	(17.74)	(17.73)	(17.34)
p-value	**<0.001**	**<0.001**	**<0.001**	**0.001**	**0.031**	0.150	0.091	**<0.001**
Parents report at	60.51	63.51	61.32	47.60	67.28	61.33	63.79	58.75
baseline	(11.96)	(18.77)	(16.12)	(16.53)	(16.17)	(17.01)	(19.41)	(16.78)
Parents report after	68.12	72.70	72.52	56.90	71.00	66.55	70.88	73.44
treatment	(12.24)	(18.13)	(17.07)	(16.59)	(15.19)	(16.89)	(15.24)	(17.43)
p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.006**	**0.004**	**<0.001**	**<0.001**

[a] The sample sizes were 92–109 for the children's self-reports before (T1) and after treatment (T2) and 90–106 for the parent proxy reports.

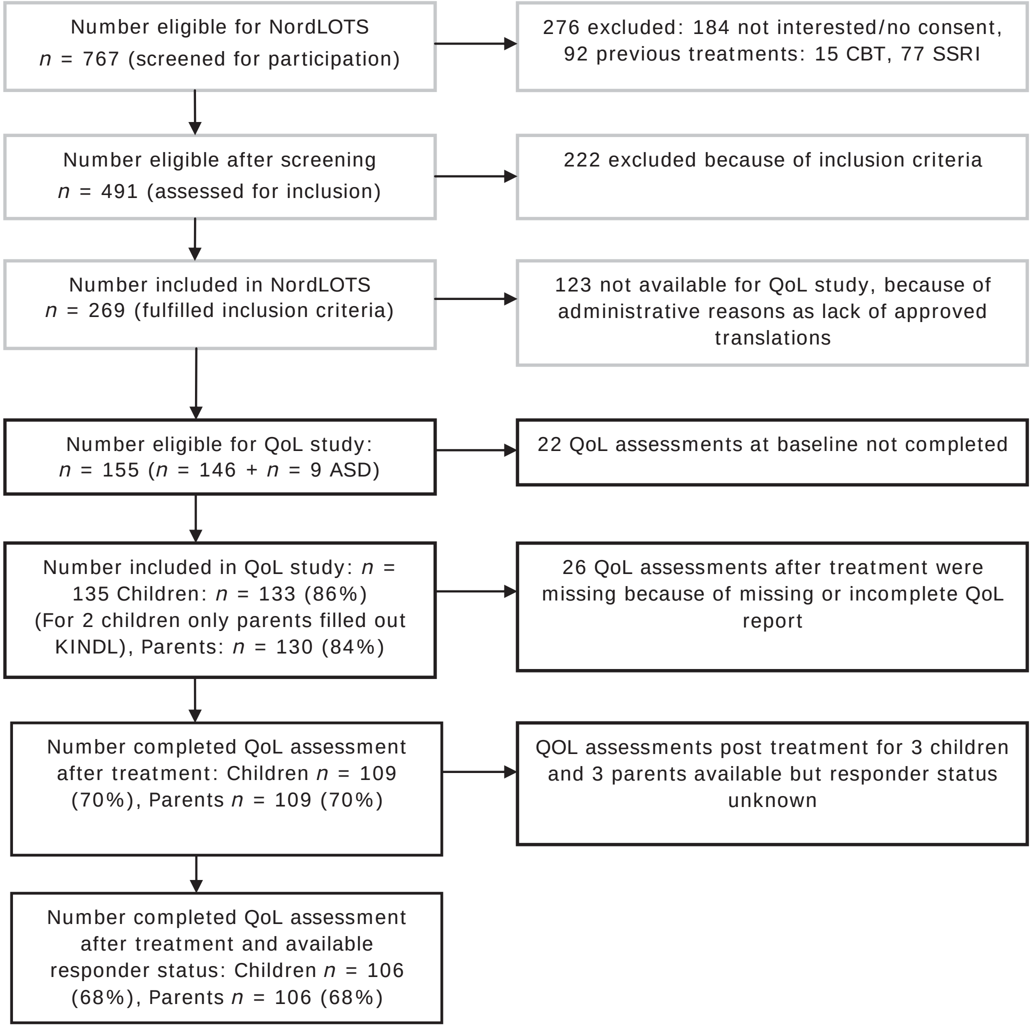

Fig. 1 Flow chart. NordLOTS main study (boxes with a grey border) and QoL study (boxes with a black border).

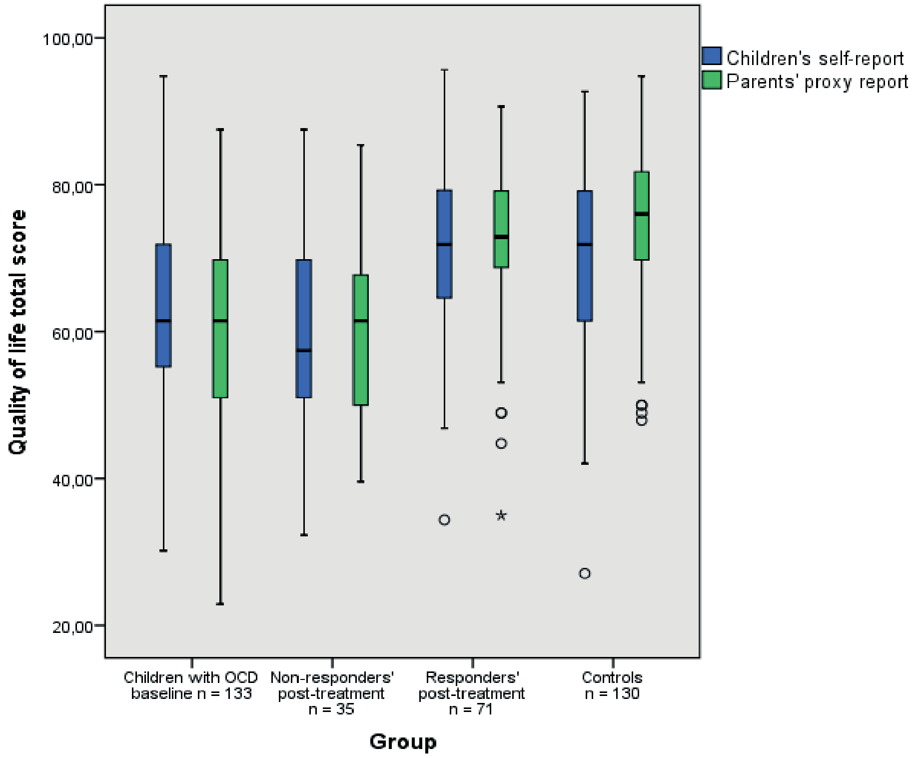

Fig. 2 Total quality of life (QoL) reported by children and parents in responders and non-responders compared with controls from the general population. Participants (*n* = 133) were children who reported QoL at baseline; the post-treatment sample size was 106 (71 responders and 35 non-responders).

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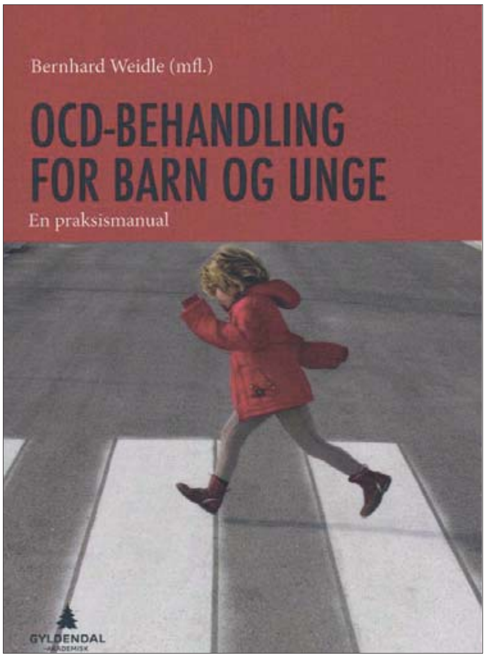
13. Appendices

Appendix 1

Bernhard Weidle mfl. **OCD-behandling for barn og unge. En praksismanual**. Oslo: Gyldendal, 2014

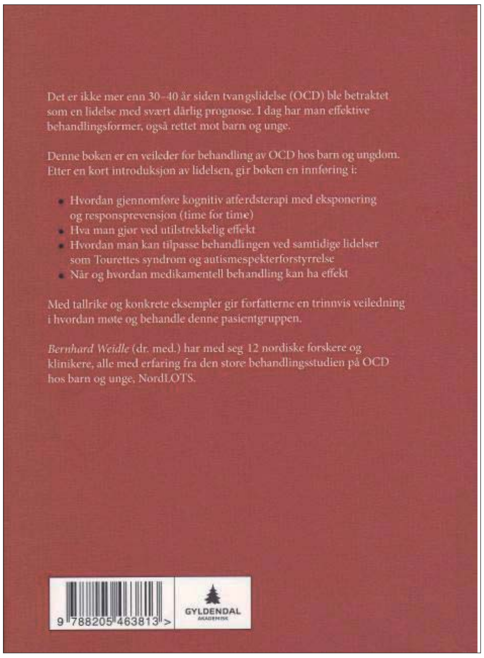


Bernhard Weidle (mfl.)

OCD-BEHANDLING FOR BARN OG UNGE

En praksismanual

GYLDENDAL AKADEMISK



Det er ikke mer enn 30–40 år siden tvangslidelse (OCD) ble betraktet som en lidelse med svært dårlig prognose. I dag har man effektive behandlingsformer, også rettet mot barn og unge.

Denne boken er en veileder for behandling av OCD hos barn og ungdom. Etter en kort introduksjon av lidelsen, gir boken en innføring i:

- Hvordan gjennomføre kognitiv atferdsterapi med eksponering og responsprevensjon (time for time)
- Hva man gjør ved utilstrekkelig effekt
- Hvordan man kan tilpasse behandlingen ved samtidige lidelser som Tourettes syndrom og autismespekterforstyrrelse
- Når og hvordan medikamentell behandling kan ha effekt

Med tallrike og konkrete eksempler gir forfatterne en trinnvis veiledning i hvordan møte og behandle denne pasientgruppen.

Bernhard Weidle (dr. med.) har med seg 12 nordiske forskere og klinikere, alle med erfaring fra den store behandlingsstudien på OCD hos barn og unge, NordLOTS.

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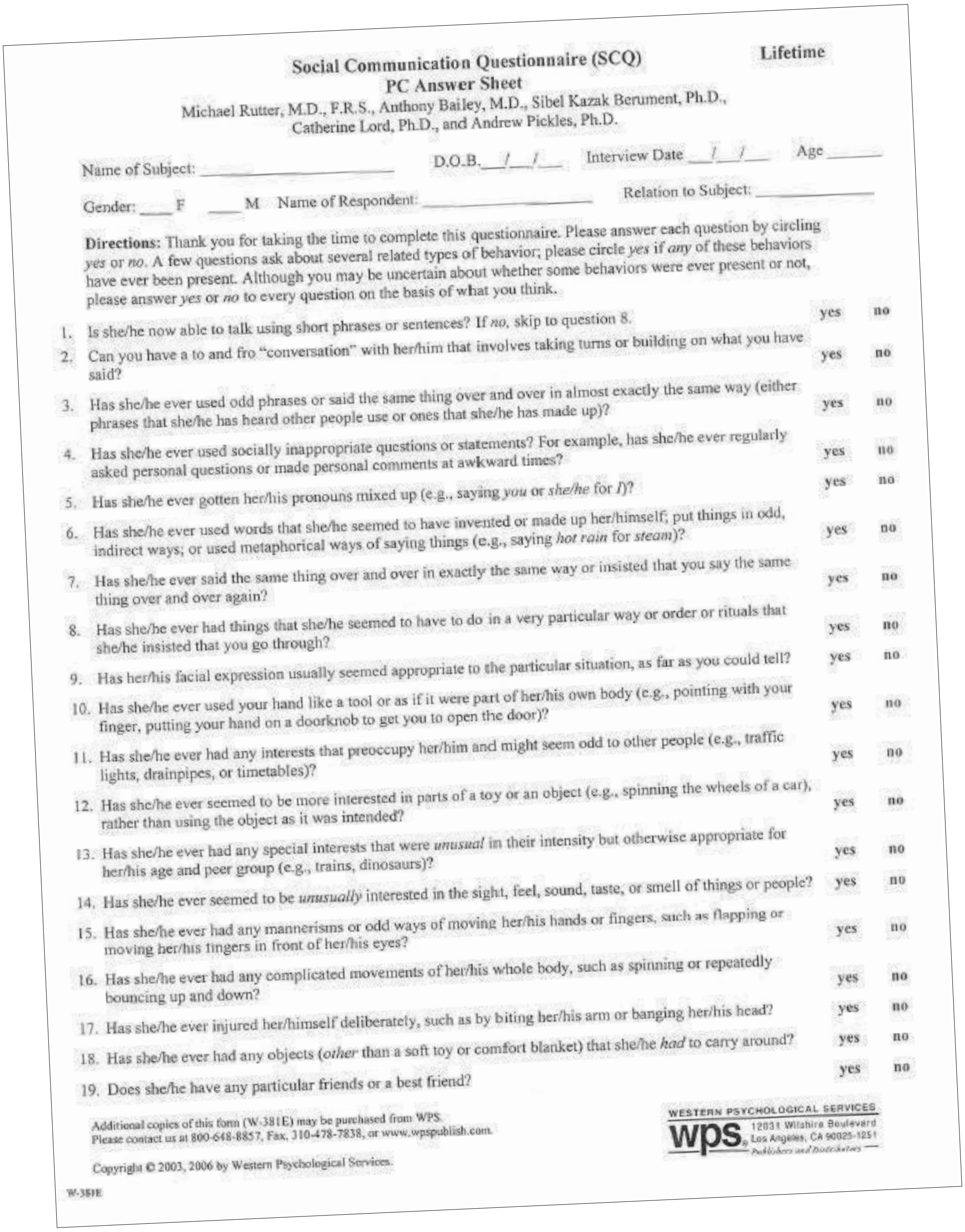
GYLDENDAL AKADEMISK

Appendix 2 Social Communication Questionnaire (SCQ)



Lifetime

Social Communication Questionnaire (SCQ)
PC Answer Sheet

Michael Rutter, M.D., F.R.S., Anthony Bailey, M.D., Sibel Kazak Berument, Ph.D.,
Catherine Lord, Ph.D., and Andrew Pickles, Ph.D.

Name of Subject: ____________________ D.O.B. __/__/__ Interview Date __/__/__ Age ______

Gender: ____ F ____ M Name of Respondent: ________________ Relation to Subject: ____________

Directions: Thank you for taking the time to complete this questionnaire. Please answer each question by circling *yes* or *no*. A few questions ask about several related types of behavior; please circle *yes* if *any* of these behaviors have ever been present. Although you may be uncertain about whether some behaviors were ever present or not, please answer *yes* or *no* to every question on the basis of what you think.

1.	Is she/he now able to talk using short phrases or sentences? If *no*, skip to question 8.	yes	no
2.	Can you have a to and fro "conversation" with her/him that involves taking turns or building on what you have said?	yes	no
3.	Has she/he ever used odd phrases or said the same thing over and over in almost exactly the same way (either phrases that she/he has heard other people use or ones that she/he has made up)?	yes	no
4.	Has she/he ever used socially inappropriate questions or statements? For example, has she/he ever regularly asked personal questions or made personal comments at awkward times?	yes	no
5.	Has she/he ever gotten her/his pronouns mixed up (e.g., saying *you* or *she/he* for *I*)?	yes	no
6.	Has she/he ever used words that she/he seemed to have invented or made up her/himself; put things in odd, indirect ways; or used metaphorical ways of saying things (e.g., saying *hot rain* for *steam*)?	yes	no
7.	Has she/he ever said the same thing over and over in exactly the same way or insisted that you say the same thing over and over again?	yes	no
8.	Has she/he ever had things that she/he seemed to have to do in a very particular way or order or rituals that she/he insisted that you go through?	yes	no
9.	Has her/his facial expression usually seemed appropriate to the particular situation, as far as you could tell?	yes	no
10.	Has she/he ever used your hand like a tool or as if it were part of her/his own body (e.g., pointing with your finger, putting your hand on a doorknob to get you to open the door)?	yes	no
11.	Has she/he ever had any interests that preoccupy her/him and might seem odd to other people (e.g., traffic lights, drainpipes, or timetables)?	yes	no
12.	Has she/he ever seemed to be more interested in parts of a toy or an object (e.g., spinning the wheels of a car), rather than using the object as it was intended?	yes	no
13.	Has she/he ever had any special interests that were *unusual* in their intensity but otherwise appropriate for her/his age and peer group (e.g., trains, dinosaurs)?	yes	no
14.	Has she/he ever seemed to be *unusually* interested in the sight, feel, sound, taste, or smell of things or people?	yes	no
15.	Has she/he ever had any mannerisms or odd ways of moving her/his hands or fingers, such as flapping or moving her/his fingers in front of her/his eyes?	yes	no
16.	Has she/he ever had any complicated movements of her/his whole body, such as spinning or repeatedly bouncing up and down?	yes	no
17.	Has she/he ever injured her/himself deliberately, such as by biting her/his arm or banging her/his head?	yes	no
18.	Has she/he ever had any objects (*other* than a soft toy or comfort blanket) that she/he *had* to carry around?	yes	no
19.	Does she/he have any particular friends or a best friend?	yes	no

Additional copies of this form (W-381E) may be purchased from WPS.
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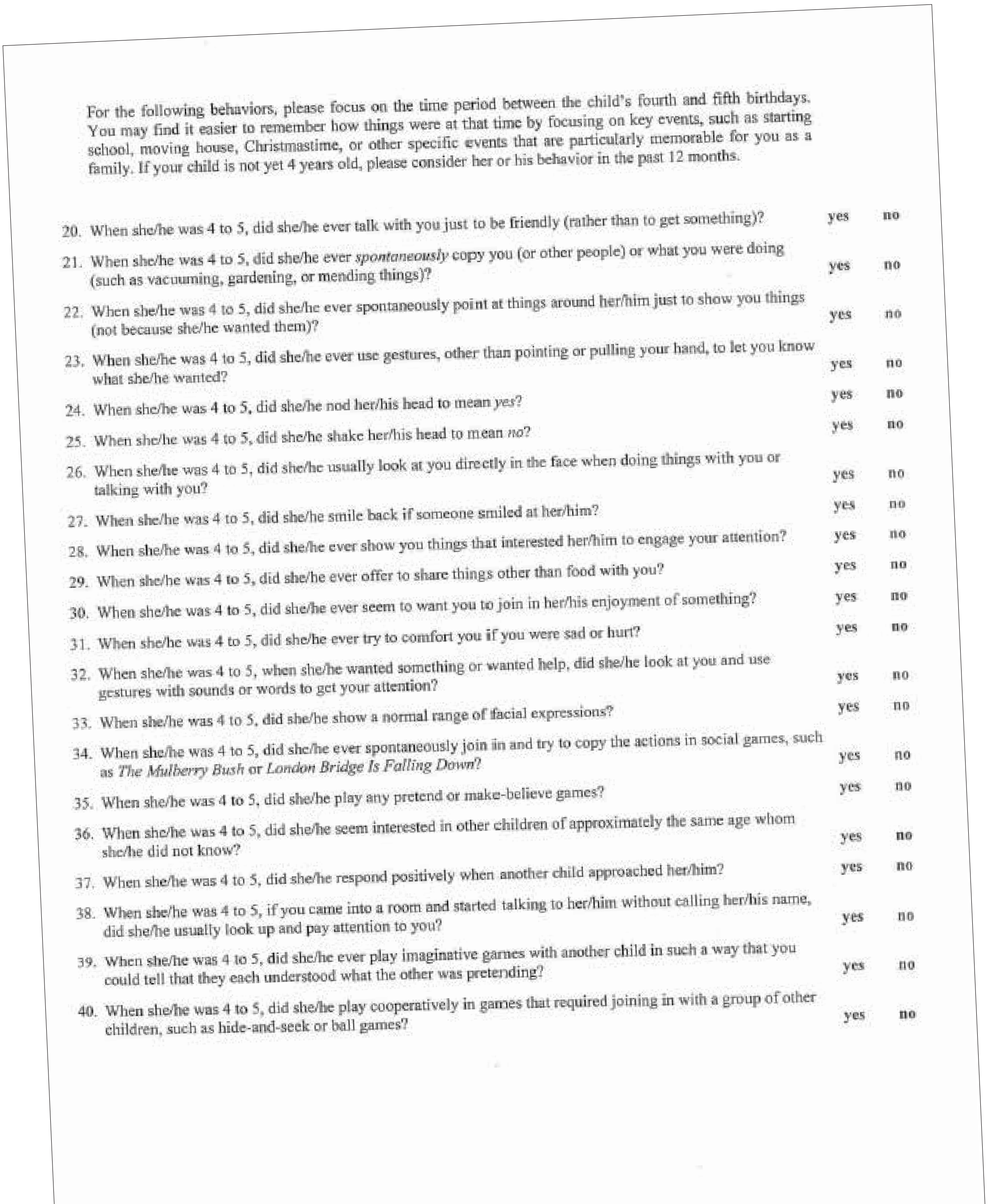
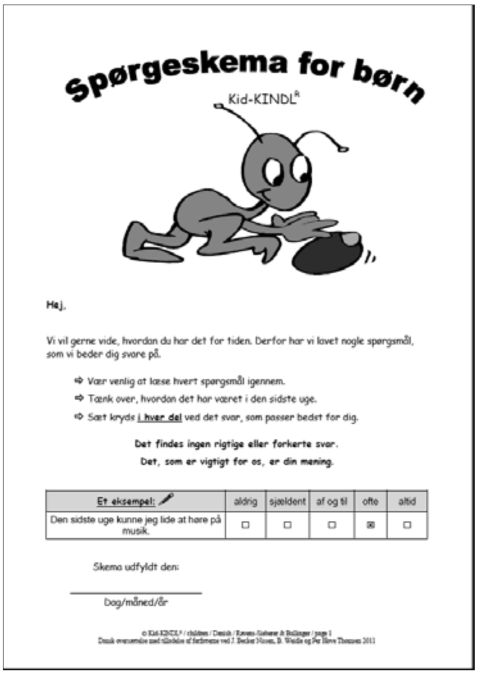


For the following behaviors, please focus on the time period between the child's fourth and fifth birthdays. You may find it easier to remember how things were at that time by focusing on key events, such as starting school, moving house, Christmastime, or other specific events that are particularly memorable for you as a family. If your child is not yet 4 years old, please consider her or his behavior in the past 12 months.

20. When she/he was 4 to 5, did she/he ever talk with you just to be friendly (rather than to get something)?	yes	no
21. When she/he was 4 to 5, did she/he ever *spontaneously* copy you (or other people) or what you were doing (such as vacuuming, gardening, or mending things)?	yes	no
22. When she/he was 4 to 5, did she/he ever spontaneously point at things around her/him just to show you things (not because she/he wanted them)?	yes	no
23. When she/he was 4 to 5, did she/he ever use gestures, other than pointing or pulling your hand, to let you know what she/he wanted?	yes	no
24. When she/he was 4 to 5, did she/he nod her/his head to mean *yes*?	yes	no
25. When she/he was 4 to 5, did she/he shake her/his head to mean *no*?	yes	no
26. When she/he was 4 to 5, did she/he usually look at you directly in the face when doing things with you or talking with you?	yes	no
27. When she/he was 4 to 5, did she/he smile back if someone smiled at her/him?	yes	no
28. When she/he was 4 to 5, did she/he ever show you things that interested her/him to engage your attention?	yes	no
29. When she/he was 4 to 5, did she/he ever offer to share things other than food with you?	yes	no
30. When she/he was 4 to 5, did she/he ever seem to want you to join in her/his enjoyment of something?	yes	no
31. When she/he was 4 to 5, did she/he ever try to comfort you if you were sad or hurt?	yes	no
32. When she/he was 4 to 5, when she/he wanted something or wanted help, did she/he look at you and use gestures with sounds or words to get your attention?	yes	no
33. When she/he was 4 to 5, did she/he show a normal range of facial expressions?	yes	no
34. When she/he was 4 to 5, did she/he ever spontaneously join in and try to copy the actions in social games, such as *The Mulberry Bush* or *London Bridge Is Falling Down*?	yes	no
35. When she/he was 4 to 5, did she/he play any pretend or make-believe games?	yes	no
36. When she/he was 4 to 5, did she/he seem interested in other children of approximately the same age whom she/he did not know?	yes	no
37. When she/he was 4 to 5, did she/he respond positively when another child approached her/him?	yes	no
38. When she/he was 4 to 5, if you came into a room and started talking to her/him without calling her/his name, did she/he usually look up and pay attention to you?	yes	no
39. When she/he was 4 to 5, did she/he ever play imaginative games with another child in such a way that you could tell that they each understood what the other was pretending?	yes	no
40. When she/he was 4 to 5, did she/he play cooperatively in games that required joining in with a group of other children, such as hide-and-seek or ball games?	yes	no

Appendix 3 a KINDL-R Danish translation (Children´s questionnaire):



Spørgeskema for børn

Kid-KINDL®

Hej,

Vi vil gerne vide, hvordan du har det for tiden. Derfor har vi lavet nogle spørgsmål, som vi beder dig svare på.

- ➪ Vær venlig at læse hvert spørgsmål igennem.
- ➪ Tænk over, hvordan det har været i den sidste uge.
- ➪ Sæt kryds **i hver del** ved det svar, som passer bedst for dig.

Det findes ingen rigtige eller forkerte svar.

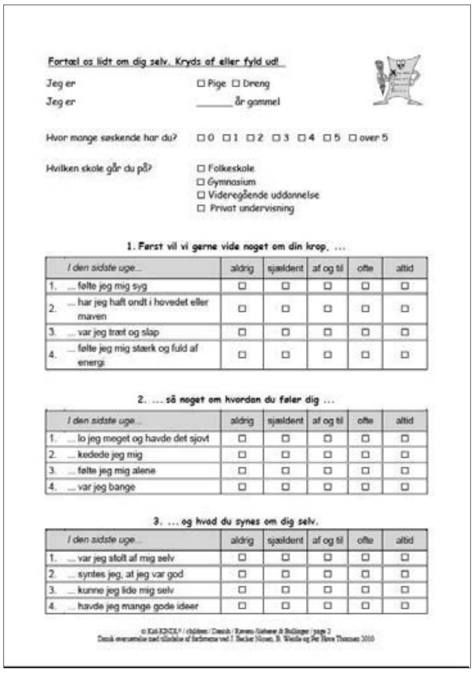
Det, som er vigtigt for os, er din mening.

Et eksempel:	aldrig	sjældent	af og til	ofte	altid
Den sidste uge kunne jeg lide at høre på musik.	☐	☐	☐	☒	☐

Skema udfyldt den:

____

Dag/måned/år



Fortæl os lidt om dig selv. Kryds af eller fyld ud!

Jeg er ☐ Pige ☐ Dreng

Jeg er ______ år gammel

Hvor mange søskende har du? ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ over 5

Hvilken skole går du på?
☐ Folkeskole
☐ Gymnasium
☐ Videregående uddannelse
☐ Privat undervisning

1. Først vil vi gerne vide noget om din krop, …

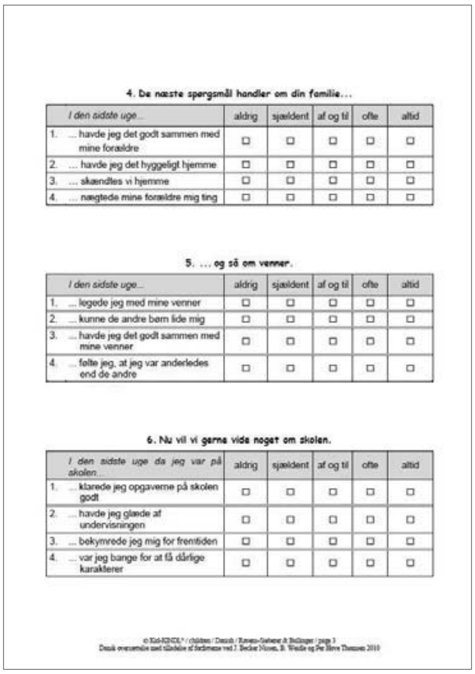
I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … følte jeg mig syg	☐	☐	☐	☐	☐
2. … har jeg haft ondt i hovedet eller maven	☐	☐	☐	☐	☐
3. … var jeg træt og slap	☐	☐	☐	☐	☐
4. … følte jeg mig stærk og fuld af energi	☐	☐	☐	☐	☐

2. … så noget om hvordan du føler dig …

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … lo jeg meget og havde det sjovt	☐	☐	☐	☐	☐
2. … kedede jeg mig	☐	☐	☐	☐	☐
3. … følte jeg mig alene	☐	☐	☐	☐	☐
4. … var jeg bange	☐	☐	☐	☐	☐

3. … og hvad du synes om dig selv.

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … var jeg stolt af mig selv	☐	☐	☐	☐	☐
2. … syntes jeg, at jeg var god	☐	☐	☐	☐	☐
3. … kunne jeg lide mig selv	☐	☐	☐	☐	☐
4. … havde jeg mange gode ideer	☐	☐	☐	☐	☐



4. De næste spørgsmål handler om din familie…

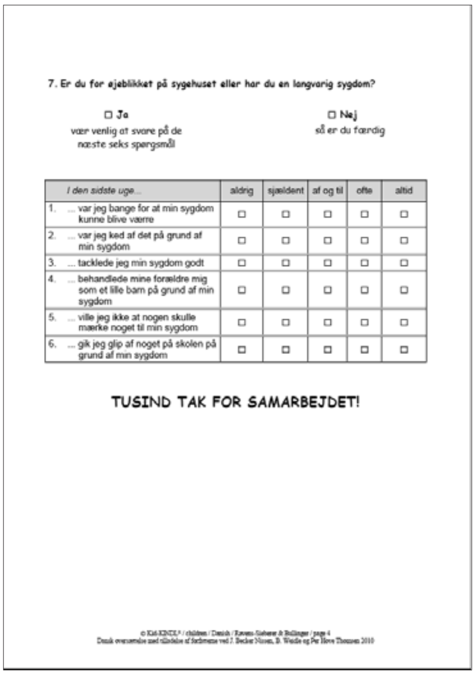
I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … havde jeg det godt sammen med mine forældre	☐	☐	☐	☐	☐
2. … havde jeg det hyggeligt hjemme	☐	☐	☐	☐	☐
3. … skændtes vi hjemme	☐	☐	☐	☐	☐
4. … nægtede mine forældre mig ting	☐	☐	☐	☐	☐

5. … og så om venner.

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … legede jeg med mine venner	☐	☐	☐	☐	☐
2. … kunne de andre børn lide mig	☐	☐	☐	☐	☐
3. … havde jeg det godt sammen med mine venner	☐	☐	☐	☐	☐
4. … følte jeg, at jeg var anderledes end de andre	☐	☐	☐	☐	☐

6. Nu vil vi gerne vide noget om skolen.

I den sidste uge da jeg var på skolen…	aldrig	sjældent	af og til	ofte	altid
1. … klarede jeg opgaverne på skolen godt	☐	☐	☐	☐	☐
2. … havde jeg glæde af undervisningen	☐	☐	☐	☐	☐
3. … bekymrede jeg mig for fremtiden	☐	☐	☐	☐	☐
4. … var jeg bange for at få dårlige karakterer	☐	☐	☐	☐	☐



7. Er du for øjeblikket på sygehuset eller har du en langvarig sygdom?

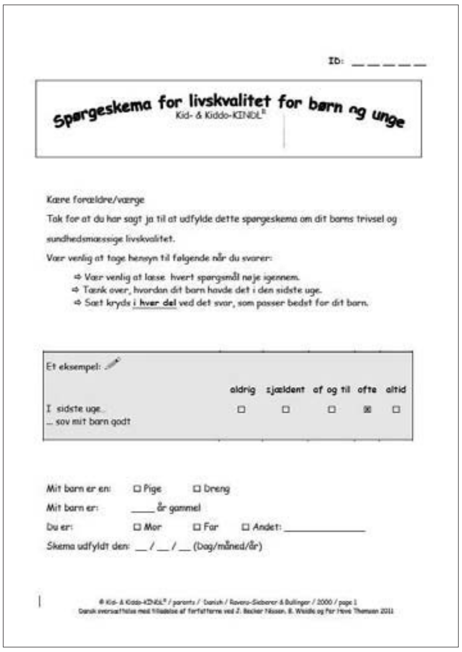
☐ **Ja**
vær venlig at svare på de
næste seks spørgsmål

☐ **Nej**
så er du færdig

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … var jeg bange for at min sygdom kunne blive værre	☐	☐	☐	☐	☐
2. … var jeg ked af det på grund af min sygdom	☐	☐	☐	☐	☐
3. … tacklede jeg min sygdom godt	☐	☐	☐	☐	☐
4. … behandlede mine forældre mig som et lille barn på grund af min sygdom	☐	☐	☐	☐	☐
5. … ville jeg ikke at nogen skulle mærke noget til min sygdom	☐	☐	☐	☐	☐
6. … gik jeg glip af noget på skolen på grund af min sygdom	☐	☐	☐	☐	☐

TUSIND TAK FOR SAMARBEJDET!

Appendix 3 b KINDL-R Danish translation (Parents' questionnaire):



ID: _ _ _ _ _

Spørgeskema for livskvalitet for børn og unge
Kid- & Kiddo-KINDL®

Kære forældre/værge

Tak for at du har sagt ja til at udfylde dette spørgeskema om dit barns trivsel og sundhedsmæssige livskvalitet.

Vær venlig at tage hensyn til følgende når du svarer:

⇨ Vær venlig at læse hvert spørgsmål nøje igennem.
⇨ Tænk over, hvordan dit barn havde det i den sidste uge.
⇨ Sæt kryds i hver del ved det svar, som passer bedst for dit barn.

Et eksempel:

	aldrig	sjældent	af og til	ofte	altid
I sidste uge… … sov mit barn godt	☐	☐	☐	☒	☐

Mit barn er en: ☐ Pige ☐ Dreng
Mit barn er: ____ år gammel
Du er: ☐ Mor ☐ Far ☐ Andet: ______________
Skema udfyldt den: __ / __ / __ (Dag/måned/år)

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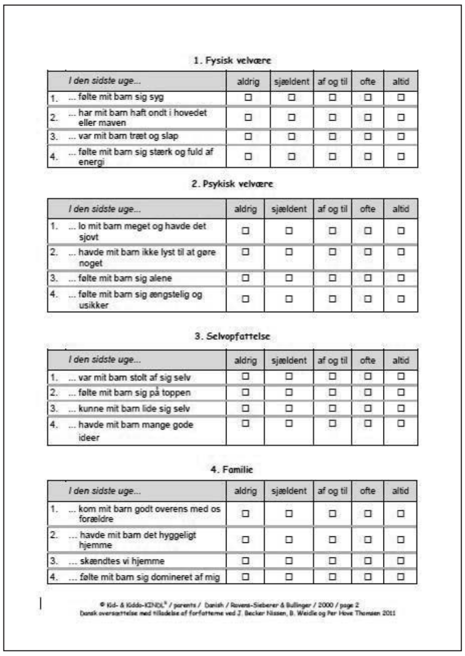

1. Fysisk velvære

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … følte mit barn sig syg	☐	☐	☐	☐	☐
2. … har mit barn haft ondt i hovedet eller maven	☐	☐	☐	☐	☐
3. … var mit barn træt og slap	☐	☐	☐	☐	☐
4. … følte mit barn sig stærk og fuld af energi	☐	☐	☐	☐	☐

2. Psykisk velvære

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … lo mit barn meget og havde det sjovt	☐	☐	☐	☐	☐
2. … havde mit barn ikke lyst til at gøre noget	☐	☐	☐	☐	☐
3. … følte mit barn sig alene	☐	☐	☐	☐	☐
4. … følte mit barn sig ængstelig og usikker	☐	☐	☐	☐	☐

3. Selvopfattelse

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … var mit barn stolt af sig selv	☐	☐	☐	☐	☐
2. … følte mit barn sig på toppen	☐	☐	☐	☐	☐
3. … kunne mit barn lide sig selv	☐	☐	☐	☐	☐
4. … havde mit barn mange gode ideer	☐	☐	☐	☐	☐

4. Familie

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … kom mit barn godt overens med os forældre	☐	☐	☐	☐	☐
2. … havde mit barn det hyggeligt hjemme	☐	☐	☐	☐	☐
3. … skændtes vi hjemme	☐	☐	☐	☐	☐
4. … følte mit barn sig domineret af mig	☐	☐	☐	☐	☐

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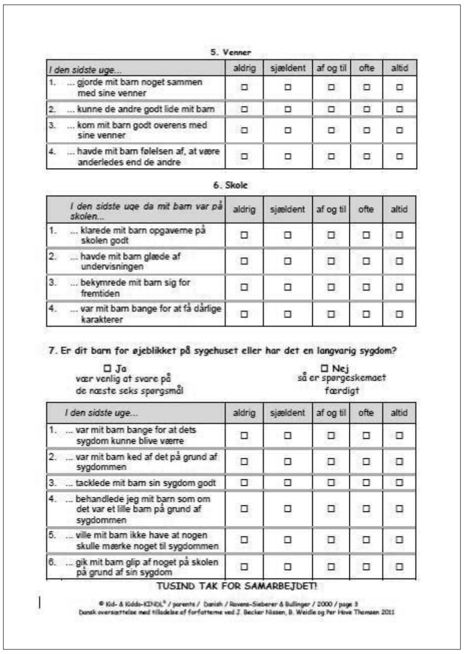

5. Venner

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … gjorde mit barn noget sammen med sine venner	☐	☐	☐	☐	☐
2. … kunne de andre godt lide mit barn	☐	☐	☐	☐	☐
3. … kom mit barn godt overens med sine venner	☐	☐	☐	☐	☐
4. … havde mit barn følelsen af, at være anderledes end de andre	☐	☐	☐	☐	☐

6. Skole

I den sidste uge da mit barn var på skolen…	aldrig	sjældent	af og til	ofte	altid
1. … klarede mit barn opgaverne på skolen godt	☐	☐	☐	☐	☐
2. … havde mit barn glæde af undervisningen	☐	☐	☐	☐	☐
3. … bekymrede mit barn sig for fremtiden	☐	☐	☐	☐	☐
4. … var mit barn bange for at få dårlige karakterer	☐	☐	☐	☐	☐

7. Er dit barn for øjeblikket på sygehuset eller har det en langvarig sygdom?

☐ Ja
vær venlig at svare på
de næste seks spørgsmål

☐ Nej
så er spørgeskemaet
færdigt

I den sidste uge…	aldrig	sjældent	af og til	ofte	altid
1. … var mit barn bange for at dets sygdom kunne blive værre	☐	☐	☐	☐	☐
2. … var mit barn ked af det på grund af sygdommen	☐	☐	☐	☐	☐
3. … tacklede mit barn sin sygdom godt	☐	☐	☐	☐	☐
4. … behandlede jeg mit barn som om det var et lille barn på grund af sygdommen	☐	☐	☐	☐	☐
5. … ville mit barn ikke have at nogen skulle mærke noget til sygdommen	☐	☐	☐	☐	☐
6. … gik mit barn glip af noget på skolen på grund af sin sygdom	☐	☐	☐	☐	☐

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Appendix 4 Overview of instruments used in this thesis

Instrument	Description	Age	Use	Scores	Psychometric properties	References
Questionnaire for Measuring Health-related Quality of Life in Children and Adolescents, revised version, (KINDL-R)	Rating of subjectively perceived QoL, Six subscales, disorder subscale and total QoL scale	6–16 years	Self-report questionnaire for children / adolescents and proxy version for caregivers	Mean item scores are calculated for all subscales and the *total QoL scale*, which are transformed to a 0 to 100 scale, 100 indicating very high QoL	Good scale utilization and scale fit, internal consistency of children's self-report total score α = .82 Satisfactory internal consistency, test-retest reliability and floor/ceiling effects in Scandinavian (Norwegian) version.	(Bullinger et al., 2008) (Jozefiak et al., 2008) (Jozefiak et al., 2009)
Achenbach Child Behavior Check List (CBCL)	Ratings of behavioural and emotional problems and adaptive functioning	6–18 years	Parent's rating scale	Activities, social competence, school performance and total competence scores. Internalizing and externalizing problems and total problems score. Higher scores indicate more problems	Syndrome profiles: mean test–retest: .90 (Pearson's correlation), internal consistency: .78–.97 (Cronbach's α), high concurrent validity. Scandinavian (Norwegian) version showed satisfactory reliability and validity	(Achenbach, 1991), (Achenbach & Rescorla, 2001) (Novik, 1999) (Jozefiak et al., 2012)
Social Communication Questionnaire (SCQ)	Screening for current and preschool autistic symptoms	4 years to adults	Screening questionnaire for parents	Subscale scores parallel domains of the ADI-R. Cut-off score for a probable ASD diagnosis: a total score of 15	Reliability: Internal consistency (Cronbach's α): .90	(Berument et al., 1999)
Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL) Revised version 2009	Psychiatric DSM-IV diagnoses (present and life-time)	6–18 years	Semi-structured interview (child/adolescent and parents). Trained interviewer	Diagnoses are scored as definite, probable or not present. In NordLOTS, only definite and not present were used	Inter-rater reliability: 93–100% agreement, test–retest reliability: (Cohen's κ): .80 for anxiety disorders. Validity: high concurrent validity when compared with questionnaires on depression, anxiety, ADHD and behavioural problems	(Kaufman et al., 1997), (Miller et al., 2008), (Axelson et al., 2009)
Children's Yale-Brown Obsessive Compulsive Scale (CYBOCS)	Scales assessing severity of obsessions and compulsions separately adding to a total score	6–17 years	Semi-structured interview (child / adolescent and parents). Trained interviewer	Severity of obsessions and compulsions 0–20, total score 0–40	Internal consistency (α = .90) and test-retest stability for the total score (ICC = .79). Validity: Good inter-rater agreement (ICC .84 for the total score)	(Goodman et al., 1989), (Scahill et al., 1997), (E. A. Storch et al., 2004)
Family Accommodation Scale (FAS)	Assessment of the families' accommodation to the child's OCD symptoms	6–17 years	12-item clinician-rated questionnaire	Severity of families' accommodation, score from 0 to 48	Internal consistency (α = .76 to .80), good inter-rater reliability (ICC = .72–1.0). Positive correlations with measures of OCD symptoms, severity and family discord	(Lisa Calvocoressi et al., 1999), (Geffken et al., 2006), (Storch, Geffken, et al., 2007)
Children's Global Assessment Scale (CGAS)	Index of psychosocial functioning	4–16 years	Lowest level for a specified time period	Scoring 1–100: Lowest 1–10 (= Needs 24-hour-care) to 91–100 (= Superior Functioning)	Inter-rater reliability: (ICC): .84, test–retest stability: (ICC): .69–.95. Discriminant validity: significantly lower scores for inpatients than outpatients	(Shaffer et al., 1983), (Bird et al., 1987), (Rey et al., 1995), (Schorre & Vandvik, 2004)