Subgroups in Pediatric Obsessive-Compulsive Disorder

Exploring Age Groups, Latent Profile Classes, and Latent Class Trajectories of Functional Impairment

Orri Smárason

Thesis for the degree of Philosophiae Doctor

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Undirhópar barna og unglinga með áráttu- og þráhyggjuröskun

Könnun á aldurshópum, undirliggjandi þversniðsklösum og ferilklösum hæfnisskerðingar

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Ágrip

Bakgrunnur: Áráttu- og þráhyggjuröskun hjá börnum (ÁÞR) er hamlandi, langvinn geðröskun sem veldur oft alvarlegri lífsgæðaskerðingu ásamt truflun á félagslífi og námi. ÁÞR getur komið fram með mjög fjölbreyttum hætti og með ólíkum einkennamynstrum. Þó megineinkenni röskunarinnar sé samspil þráhyggju og árátttu er innihald þráhyggjuhugsana og framkvæmd árátttuhegðunar mjög ólík á milli einstaklinga. Einkenni geta auk þess breyst með tímanum. Að bera kennsl á undirhópa barna og unglinga með ÁÞR út frá einkennamynd og tengdum eiginleikum, eins og fylgiröskunum, getur hugsanlega varpað enn frekara ljósi á algengar klínískar birtingarmyndir, veitt innsýn varðandi undirliggjandi geðræna þætti og leitt til bættrar einstaklingsmiðaðrar meðferðar.

Markmið: Þessi ritgerð miðar að því að bera kennsl á, kanna og bera saman undirhópa barna og unglinga með ÁÞR. Undirhóparnir eru byggðir á aldri við greiningu, aldurs þegar einkenni koma fyrst fram, tímalengd einkenna, birtingarmynd einkenna, lýðfræði, fylgiröskunum og meðferðarsvörun út frá hæfnisskerðingu.

Aðferð: Í rannsókn I voru undirhópar skilgreindir út frá aldri. Borin voru saman börn (7-11 ára) og unglingar (12-17 ára) sem tóku þátt í meðferðarrannsókn fyrir ÁÞR (n=269). Að auki voru bornir saman hópar byggðir á því hvort ÁÞR kom fyrst fram fyrir kynþroska eða á unglingsárum. Að lokum voru bornir saman undirhópar sem byggðir voru á tímalengd ÁÞR veikinda. Undirhóparnir voru, í öllum tilfellum, bornir saman hvað varðar (1) alvarleika ÁÞR, (2) birtingarmynd ÁÞR, (3) fylgiraskanir og (4) hæfnisskerðingu. Í rannsókn II var notað samsett alþjóðlegt úrtak 830 barna og unglinga með ÁÞR. Í upphafi var gerð þáttagreining til að ákvarða þáttabyggingu birtingarmyndar ÁÞR einkenna. Í öðru lagi var líkan fyrr blandaðar dreifingar (e. *dependent mixture model*) notað til að bera kennsl á undirliggjandi klasa (e. *Latent classes*) sem tákna undirhópa barna og unglinga með ÁÞR. Líkanið byggði á þáttaskorum einkennaþátta, alvarleika einkenna og tegundum fylgiraskana. Í þriðja lagi voru tengsl undirhópaaðildar við aðrar klínískt mikilvægar breytur könnuð, þar á meðal aldur við upphaf einkenna, forðun, hæfnisskerðingu og fjölskylduhliðrun. Í rannsókn III var langtímaferill OCD-tengdrar hæfnisskerðingar skoðaður, bæði á meðan meðferð stóð og eftir að henni lauk. Sama úrtak var notað og í rannsókn I. Undirliggjandi þroskalíkan (e. *latent class growth analysis*) var notað til að bera kennsl á ólíka ferla hæfnisskerðingar barna og ungmenna með ÁÞR yfir þriggja ára tímabil (eða 170 vikur). Eiginleikar ólíkra ferilklasa (e. *trajectory classes*) voru svo bornir saman. Til að bera kennsl á breytur sem mögulega spá fyrir um aðild að hverjum og einum ferilklasa var

notast við aðhvarfslíkan. Ólíkir ferlar hæfnisskerðingar voru svo bornir saman við sambærilega ferilklasa byggða á alvarleika ÁÞR einkenna úr fyrri rannsókn.

Niðurstöður: Í rannsókn I reyndust yngri börn hafa lakara innsæi í ÁÞR einkenni ásamt hærri tíðni ADHD og hegðunarvandamála. Eldri hópurinn var með hærri tíðni hugrænnar áráttu, meira af óskilgreindum þráhyggjum og áráttum, og að eigin mati, með meiri hæfnisskerðingu. Enginn munur fannst á algengi kvíða, kipparöskunar, eða þunglyndis milli aldurshópa, né heldur á alvarleika ÁÞR einkenna. Þegar undirhópar voru skilgreindir eftir upphafsaldri einkenna og lengd veikinda, í stað aldurs þegar mat fór fram, breytti það ekki niðurstöðum. Í rannsókn II var sex-þátta líkan af ÁÞR einkennum auðkennt og notað sem grunnur fyrir frekari greiningar. Matsgildi studdu fjögurra klasa líkan. Einkennamynd og fylgiraskanir voru þeir þættir sem helst aðgreindu klasa. Matsgildi fyrir þriggja til sjö klasa lausnir voru aðeins lítillega frábrugðin hvort öðru. Eiginleikar flestra klasa héldust að mestu leyti stöðugir á milli lausna, þó minni og sértækari klasar hafi bæst við í flóknari lausnum. Í rannsókn III kom fram að breytingar á hæfnisskerðingu voru á þrenna vegu. Stærsti hópurinn (70,7%) hóf meðferð með nokkuð væga hæfnisskerðingu sem minnkaði nokkuð yfir meðferðartíman og hélst væg í eftirfylgd. Annar flokkurinn (24,4%) hóf meðferð með mikla skerðingu á starfshæfni sem minnkaði svo hratt á meðferðartímanum. Þriðji og minnsti flokkurinn (4,9%) hóf meðferð með miðlungs mikla skerðingu á hæfni sem hélst stöðug og minnkaði ekki yfir meðferðartímann. Það sem helst aðgreindi hópana var alvarleiki ÁÞR einkenna við upphaf meðferðar og ólíkar fylgiraskanir.

Ályktanir: Í rannsókn I reyndist minni munur á milli aldurshópa en í flestum fyrri rannsóknum. Hins vegar voru niðurstöður sem bentu til lakara innsæis, hærra algengi ADHD og meiri hegðunarvandi hjá yngri börnum, ásamt vísbendingum um meiri hæfnisskerðingu hjá unglingum, í góðu samræmi við fyrri rannsóknir. Niðurstöður úr rannsókn II styðja notagildi þess að samþætta upplýsingar um einkenni, þroskastöðu og fylgiraskanir við kortlagningu vanda barna og unglinga með ÁÞR. Klasarnir sem tilgreindir eru í rannsókn II benda til þess að einkenni sem snúast um smit og þrif spili lykilhlutverk í ÁÞR og að tengsl séu á milli víðtækari einkennamyndar og hærri tíðni fylgiraskana. Einnig koma fram sjaldgæfar birtingarmyndir þar sem fara saman ÁÞR einkenni og frávik í taugaþroska. Rannsókn III leiddi í ljós að flestir sjúklingar tóku framförum og héldu lágu stigi hæfnisskerðingar í meira en þrjú ár, óháð alvarleika skerðingar við upphaf meðferðar. Hins vegar hélst lítill undirhópur þátttakennda á sama stigi starfshæfnisskerðingar allan meðferðar- og eftirfylgdartímann. Sá hópur skar sig eingöngu úr að því leyti að hann hafði meira af ADHD einkennum en hinir hóparnir.

Lykilorð: Árátta- og þráhyggja, hæfnisskerðing, fylgiraskanir, undirliggjandi klasar, aldursmunur.

Abstract

Background: Pediatric obsessive-compulsive disorder (OCD) is debilitating and often chronic, associated with significant social and educational impairment as well as reduced quality of life. OCD can present with highly heterogenous symptom profiles. Although it is characterized by the functional relationship between obsessions and compulsions, the specific content of the obsessions and the topology of the compulsions varies greatly between individuals and can fluctuate over time within individuals. Identifying subgroups of children and adolescents with OCD based on symptom expression and associated features, such as comorbid psychopathology, can potentially shed additional light on common clinical presentations, offer insights regarding potential underlying transdiagnostic processes, and lead to improved specificity of care.

Aims: The current thesis aims to identify, explore, and compare subgroups of children and adolescents based on their age at assessment, age of OCD symptom onset, duration of OCD symptoms, symptom expression, demographics, comorbid psychopathology, and long-term functional impairment treatment response.

Method: Study I examined subgroups based on age, comparing adolescents (age 12-17) and children (age 7-11), participating in an OCD treatment trial (n=269). In addition, subgroups based on age of OCD onset, prepubertal or adolescent, were compared within the older age group. Lastly, subgroups based on the duration of OCD illness were compared. The subgroups were, in all instances, compared in terms of: (1) OCD severity, (2) OCD symptom profile, (3) comorbid symptoms, and (4) OCD-related functional impairment. Study II used an aggregated international sample of 830 OCD-affected children and adolescents, presenting to OCD specialty centers. First, a factor analysis was conducted to establish a factor structure of OCD symptoms. Second, a dependent mixture model was employed to identify latent clusters representing subgroups of OCD-affected children and adolescents based on symptom factor scores, symptom severity, and the presence or absence of comorbid disorders. Third, relationships of subgroup membership with other clinically relevant variables, including the age of symptom onset, avoidance, impairment, and family accommodation were explored. Study III examined the long-term trajectory of OCD-related functional impairment during and after stepped-care treatment, in a longitudinal analysis of the same sample as used in study I. A latent class growth analysis was conducted to identify trajectories of child and adolescent self-reported OCD-related functional impairment over three years (170 weeks). Trajectory classes were compared on pretreatment characteristics. To identify predictors of trajectory class membership a multinomial

logistic regression model was used. The overlap of the identified functional impairment trajectory classes with previously established OCD symptom severity trajectory classes was also explored.

Results: In study I, younger children were found to have poorer level of insight, higher rates of ADHD, and disruptive disorders. The older group had higher levels of mental compulsions, miscellaneous obsessions and compulsions, and self-rated functional impairment. No differences were found in the prevalence of anxiety, tic, or depressive disorders between the age groups, nor in overall OCD severity. Defining groups by age of OCD onset and duration of illness rather than age at evaluation did not change results, with no further clear differences emerging. In study II, a six-factor model of OCD symptoms was identified and used as a basis for the dependent mixture model. Fit statistics favored a four-cluster latent class model with groups distinguished primarily by symptom expression and comorbidity type. Fit indices for three to seven cluster models were only marginally different and characteristics of the clusters remained largely stable between solutions with small clusters of distinct presentations added in more complex models. In study III, three distinct long-term functional impairment trajectory classes were identified. The largest class (70.7%) initiated treatment with lower functional impairment. This group experienced a moderate reduction in impairment, which was maintained over the long term. The second class (24.4%) initiated with higher functional impairment which rapidly diminished over time. The third and smallest class (4.9%), initiated with moderate functional impairment which remained unchanged over the study period. The classes differed on measures of OCD severity and comorbid symptoms.

Conclusions: Study I found fewer overall differences between the age groups than most previous studies. However, in line with extant literature, less insight, higher levels of ADHD, and more disruptive problems in younger children, and higher self-rated functional impairment in older children, was found. Rather than identifying a single classification system, the findings from study II support the utility of integrating dimensional, developmental, and transdiagnostic information in the conceptualization of OCD-affected children and adolescents. The clusters identified in study II point to the centrality of contamination concerns in OCD, relationships between broader symptom expression and higher levels of comorbidity, and the potential for complex/neurodevelopmental presentations. Study III found that most patients receiving stepped-care treatment improved and maintained low levels of impairment for over three years, regardless of initial level of impairment. However, a small subgroup, distinguished by higher levels of ADHD symptoms, remained at pretreatment levels of impairment throughout.

Keywords: obsessive-compulsive disorder, functional impairment, comorbidity, latent classes, age differences

Acknowledgements

Since starting my PhD project, I have been asked several times if I can provide any advice for someone considering a PhD. My answer is always the same. I only have one piece of advice to give: choose your main advisor very carefully! In this regard I believe I made the best choice possible. I will forever be extremely grateful for my main advisor, Dr. Gudmundur Skarphedinsson, who not only provided me with this wonderful opportunity in the first place, but who through his support, encouragement, academic acumen, and wisdom expertly guided me through the whole process. I not only consider him a mentor, a role model, and a first-rate colleague, but also a dear friend.

Gudmundur did, however, not act alone. His co-advisor, Dr. Davíð R.M.A Højgaard, was someone I first met when this project started but immediately found very easy to get along- and collaborate with. I am very grateful for the academic guidance and assistance Davíð provided through the whole journey. He made invaluable contributions to the papers this thesis consists of. Davíð also has a way of making you believe that any problem or issue you are currently facing, however difficult or impossible it seems at the time, is entirely solvable. That attitude has often been helpful, and he is usually right.

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My thesis would not have been possible if not for the tremendous efforts of the NordLOTS research team. It has been a privilege to be able to work with data from

such a landmark study. Many of the NordLOTS team co-authored the papers presented in this thesis and along the way provided great training in academic writing and research skills.

I thank Dr. Sigurgrímur Skúlason for his help with translating statistical terms into Icelandic.

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This thesis focuses on pediatric OCD and that has also been the focus of my clinical work these past few years. I must thank every child, teenager, and parent affected by this disorder that I have worked with. Every client has taught me something new and helped to further my understanding, not only of the disorder itself but the importance of studying it further.

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Contents

List of Abbreviations

ADHD	Attention deficit hyperactivity disorder
AIC	Akaike Information Criterion
ANOVA	Analysis of variance
ASD	Autism spectrum disorder
ATRC	Anxiety
BIC	Bayesian Information Criterion
CBT	Cognitive behavioral therapy
CY-BOCS	Children's Yale-Brown Obsessive-Compulsive Scale
CD	Conduct disorder
CBCL	Child Behavior Checklist
CFA	Confirmatory factor analysis
CFI	Comperative fit index
COIS-R	Child Obsessive-Compulsive Impact Scale – Revised
DCS	D-Cycloserine CBT trial
DSM	Diagnostic and Statistical Manual of Mental Disorders
EFA	Exploratory factor analysis
FAS	Family accommodation scale
GAD	Generalized anxiety disorder
ICC	Intra-class correlation
K-SADS-PL	Schedule for Affective Disorders and Schizophrenia for School Age Children - Present and Lifetime version
LCA	Latent class analysis

LCGA	Latent class growth analysis
MFQ	The Moods and Feelings Questionnaire
MICE	Multiple imputation by chained equations
NordLOTS	The Nordic Long-Term OCD Treatment Study
OCD	Obsessive compulsive disorder
ODD	Oppositional defiant disorder
PANS	Pediatric acute neuropsychiatric syndrome
PANDAS	Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection
RI-CLPM	Random intercept cross-lagged panel model
RMSEA	Root mean square error of approximation
RMSR	Root mean square residual
SCARED	Screen for Child Anxiety Related Emotional Disorders
SD	Standard deviation
SPSS	Statistical Package for Social Sciences
SRI	Serotonin reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
TLI	Tucker-Lewis Index
UBC POP	University of British Columbia Provincial Obsessive Compulsive Disorder Program
χ^2	Chi-squared

List of Figures

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List of Original Papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I, II, III):

I. Orri Smárason, Bernhard Weidle, David R.M.A. Højgaard, Nor Christian Torp, Tord Ivarsson, Judith Becker Nissen, Per Hove Thomsen, Gudmundur Skarphedinsson (2021). "Younger versus older children with obsessive-compulsive disorder: Symptoms, severity, and impairment. Journal of Obsessive Compulsive and Related Disorders." Volume 29, April 2021, DOI: https://doi.org/10.1016/j.jocrd.2021.100646

II. Orri Smárason, Robert R. Selles, Davíð R.M.A. Højgaard, John R. Best, Karin Melin, Tord Ivarsson, Per Hove Thomsen, Nicole Michelle McBride, Eric A. Storch, Daniel Geller, Sabine Wilhelm, Lara J. Farrell, PhD, Allison M. Waters, PhD, Sharna Mathieu, PhD, Noam Soreni, S. Evelyn Stewart & Gudmundur Skarphedinsson. "Exploring Latent Clusters in Pediatric OCD based on Symptoms, Severity, Age, Gender, and Comorbidity." (Submitted for publication, under review)

III. Orri Smárason, Davíð R.M.A. Højgaard, Sanne Jensen, Eric A. Storch, Gudmundur B. Arnkelsson, Lidewij H. Wolters, Nor Christian Torp, Karin Melin, Bernhard Weidle, Judith Becker Nissen, Katja Anna Hybel, Per Hove Thomsen, Tord Ivarsson, Gudmundur Skarphedinsson. "Long-term functional impairment in pediatric OCD after and during treatment: An analysis of distinct trajectories." *Psychiatry Research*, Volume 324, June 2023. https://doi.org/10.1016/j.psychres.2023.

Declaration of Contribution

I, Orri Smárason (OS), conceived and designed the study under the supervision of Gudmundur Skarphedinsson (GS) and Davíð R.M.A. Höjgaard (DRMAH). The NordLots study team collected the data. OS analyzed the data, interpreted the results, and wrote the manuscript under the supervision of GS and DRMAH. All co-authors read and approved the final version of the manuscript.

II: OS, Robert Selles (RS), Evelyn Stewart (ES), John Best (JB), GS, and DRMAH conceived and designed the study. Data was collected by specialized OCD treatment and study centers. OS analyzed the data, interpreted the results, and wrote the manuscript under the supervision of GS, DRMAH, RS, and JB. All co-authors read and approved the final version of the manuscript.

III: Orri Smárason (OS) conceived and designed the study under the supervision of Gudmundur Skarphedinsson (GS) and Davíð R.M.A. Höjgaard (DRMAH). The NordLots study team collected the data. OS analyzed the data and wrote the manuscript under the supervision of GS and DRMAH. All co-authors read and approved the final version of the manuscript.

1 Introduction

Obsessive-compulsive disorder (OCD) is characterized by obsessions or compulsions that are time-consuming (lasting more than an hour each day) or significantly distressing, anxiety-inducing, or debilitating. Obsessions are defined as distressing or anxious, invasive, and persistent thoughts, visions, or impulses. Compulsions are characterized as unpleasurable repetitive behavioral or mental acts made in response to obsessions to lessen worry, anxiety, or distress (American Psychiatric Association, 2013). As compulsive behaviors provide temporary relief of the distress from obsessions, they are reinforced and thus become more likely to be re-enacted in the future, even though they are not realistically related to the distressing obsessive thought, or are clearly excessive (Abramowitz, Taylor, & McKay, 2009).

The functional impact of OCD can be severely debilitating. It is associated with significant social, educational, and occupational impairment, reduced quality of life (Huppert, Simpson, Nissenson, Liebowitz, & Foa, 2009; Kugler et al., 2013; Perez-Vigil et al., 2018) and is a significant source of disability in the developed world (Lopez & Murray, 1998). If left untreated, OCD can become chronic and severely disrupt the developmental pathway of a young person, as well as increase the risk of developing multiple concurrent psychiatric disorders and of suicide (Fernández de la Cruz et al., 2017; Flament et al., 1988; Taylor, 2011). At least half of all adults diagnosed with OCD report a pediatric onset of their symptoms (Rasmussen & Eisen, 1990). Early diagnosis and treatment of OCD is therefore crucial to prevent possible lifelong impairment (Fineberg et al., 2019; Heyman et al., 2001).

1.1 Pediatric obsessive-compulsive disorder

The occurrence of OCD in children and adolescents was considered rare about 40 years ago (Quay & Werry, 1979), likely leading to severe underdiagnoses and inadequate treatment at the time. Reliable diagnostic criteria were introduced in 1980 with the third edition of the *Diagnostic and Statistical Manual of Mental Disorders*. DSM-III, (American Psychiatric Association, 1980) which led to an increase in clinical reports describing the serious and impairing nature of OCD (Rasmussen & Tsuang, 1986). This sparked greater research interest and resulted in a systematic inquiry of pediatric OCD, which has led to major breakthroughs, such as evidence that OCD is a neurobiological disorder (Azari et al., 1993; Benkelfat et al., 1990) that can be treated with both psychotherapy (Marks, 1997) and medication (McDonough & Kennedy, 2002). Diagnostic criteria

1.2 Diagnostic criteria

The current criteria for a diagnosis of OCD are presented in both the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition (DSM-5) (American Psychiatric Association, 2013) and the *International Classification of Diseases* 11th Revision (ICD-11) (World Health Organization, 2018). The current DSM criteria are presented in Table 1.

The data presented in this thesis was collected using the diagnostic criteria from the fourth edition of the DSM (American Psychiatric Association, 2000). These criteria have remained largely the same since the DSM-III. However, in the DSM-5 (and ICD-11) OCD is no longer categorized as an anxiety disorder. Instead, a new category of obsessive-compulsive and related disorders is included, comprised of OCD as well as body dysmorphic disorder, hair-pulling disorder (trichotillomania), and two new disorders: hoarding disorder, and excoriation (skin-picking) disorder. The rationale for this was that OCD, and related disorders, have been shown to be closely related in terms of diagnostic validity and clinical utility and should therefore be made distinct from anxiety disorders (American Psychiatric Association, 2013). This has been criticized on the grounds that such a change in classification lacks expert consensus and empirical support (Storch, Abramowitz, & Goodman, 2008). Two further notable differences in the DSM-5 compared to earlier editions are that the fifth edition classifies hoarding as a distinct disorder within the OCD spectrum (although OCD- related hoarding is still also acknowledged) and allows for more variation in the level of patient's symptoms insight, ranging from absent to good, while earlier editions only allowed for categorical classification of good or poor insight (American Psychiatric Association, 2013).

Table 1: DSM-5 diagnostic criteria for OCD.

A. Presence of obsessions, compulsions, or both:

Obsessions are defined by (1) and (2):

1. Recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress.

2. The individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).

Compulsions are defined by (1) and (2):

1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly.

2. The behaviors or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviors or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive.

Note: Young children may not be able to articulate the aims of these behaviors or mental acts.

B. The obsessions or compulsions are time-consuming (e.g., take more than one hour per day) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The obsessive-compulsive symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

D. The disturbance is not better explained by the symptoms of another mental disorder (e.g., excessive worries, as in generalized anxiety disorder; preoccupation with appearance, as in body dysmorphic disorder; difficulty discarding or parting with possessions, as in hoarding disorder; hair pulling, as in trichotillomania [hair-pulling disorder]; skin picking, as in excoriation [skin-picking] disorder; stereotypies, as in stereotypic movement disorder; ritualized eating behavior, as in eating disorders; preoccupation with substances or gambling, as in substance-related and addictive disorders; preoccupation with having an illness, as in illness anxiety disorder; sexual urges or fantasies, as in paraphilic disorders; impulses, as in disruptive, impulse-control, and conduct disorders; guilty ruminations, as in major depressive disorder; thought insertion or delusional preoccupations, as in schizophrenia spectrum and other psychotic disorders; or repetitive patterns of behavior, as in autism spectrum disorder).

1.3 Prevalence and Onset

The prevalence rates of child and adolescent OCD have been estimated between 0.25% and 4% (Canals, Hernandez-Martinez, Cosi, & Voltas, 2012; Heyman et al., 2003; Valleni-Basile et al., 1996; Zohar, 1999). Prevalence seems to increase somewhat with children's age, and for adolescents, the prevalence is the same as in the adult populations (2-3%) (Canals et al., 2012; Ruscio, Stein, Chiu, & Kessler, 2010). However, once adulthood is reached, prevalence appears to decrease with advancing age (Torres et al., 2006). Clinical studies seem to indicate that OCD is more common in boys, but this may be the result of a selection bias as recent population-based and clinical studies indicate no gender differences for children and adolescents, and higher lifetime OCD prevalence rates in women (Fawcett, Power, & Fawcett, 2020; Moore, Mariaskin, March, & Franklin, 2007; Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015).

The mean age of onset of pediatric OCD is estimated to be between the ages of 10-13 years (Geller et al., 1998; Pinto, Mancebo, Eisen, Pagano, & Rasmussen, 2006; Swedo, Rapoport, Leonard, Lenane, & Cheslow, 1989). Boys tend to have an earlier age of onset than girls (Bellodi, Sciuto, Diaferia, Ronchi, & Smeraldi, 1992; H. L. Leonard et al., 1989). It is also common for parents to recall minor OCD-like symptoms occurring in their children for a few years before they became severe enough to warrant intervention (Geller et al., 1998; Mancebo et al., 2014).

1.4 Clinical presentation and symptom profiles

OCD is a highly heterogeneous disorder. Although it is characterized by the functional relationship between obsessions and compulsions, the specific content of the obsessions and the topology of the compulsions varies greatly between individuals and can fluctuate over time within individuals (American Psychiatric Association, 2013; Højgaard, Mortensen, et al., 2017). The core features of OCD are obsessions; thoughts, images, or impulses that are experienced as intrusive. Even when these obsessions are unrealistic or excessive, they cause feelings of anxiety, disgust, or distress and compel the sufferer to act to minimize that distress or the likelihood of a feared event. Compulsions, the other core symptom of the disorder, are behaviors or mental acts performed to prevent or reduce distress caused by obsessions. Compulsions are usually only effective for a short time and therefore quickly become highly repetitive and excessive. The most common obsessions in pediatric OCD are fears of contamination (often perceived as caused by dirt or germs), the fear of causing harm to oneself or a significant other, and a strong urge for exactness or symmetry (Rettew, Swedo, Leonard, Lenane, & Rapoport, 1992). The most common compulsions, carried out to neutralize the feelings of distress caused by the obsessions, include washing, checking, ordering, and mental compulsions such as repeating words silently,

praying, or counting (American Psychiatric Association, 2013; Geller & March, 2012; Rettew et al., 1992).

Certain obsessions are often paired with related compulsions, leading to identifiable symptom profiles (Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008; Leckman et al., 1997). Factor analyses of OCD symptom structure in children and adolescents have indicated that at least three or four distinct factors exist (Bernstein, Victor, Nelson, & Lee, 2013; Delorme et al., 2006; Højgaard, Mortensen, et al., 2017; Mataix-Cols, Nakatani, Micali, & Heyman, 2008; McKay et al., 2006; Stewart et al., 2007). The most stable of these factors consists of contamination obsessions and cleaning compulsions. The three other common OCD symptom factors are: 1) symmetry and order: comprised of symmetry obsessions and repeating and counting compulsions; 2) forbidden thoughts: comprised of aggressive, sexual, religious, or somatic obsessions and checking compulsions, and 3) hoarding: comprised of hoarding obsessions and compulsions (although the fifth edition of the DSM classifies hoarding as a distinct disorder within the OCD spectrum, hoarding symptoms are considered OCD-related when the hoarding behavior is a direct consequence of obsessions or compulsions, such as difficulty discarding things to avoid harm or when discarding results in a feeling of incompleteness (American Psychiatric Association., 2013)). In pediatric samples, these symptom factors have been shown to be temporally stable (Fernandez de la Cruz et al., 2013) and to have partly different etiologies (López-Solà et al., 2016). However, frequent within-individual endorsement of symptoms across multiple dimensions limits the utility of these factors for informing individual-level classification of OCD-affected children and adolescents (Bernstein et al., 2013; Stewart et al., 2008).

Developmental factors appear to influence symptom expression in pediatric OCD (Nakatani et al., 2011; Selles, Storch, & Lewin, 2014; Smarason et al., 2022), and so do interactions with common comorbid conditions (Højgaard, Hybel, et al., 2018; Højgaard, Mortensen, et al., 2018; Nestadt et al., 2009), such as anxiety, tic disorders, and attention deficit hyperactivity disorders (ADHD, Selles et al., 2018). Identifying clusters of OCD-affected children and adolescents based on symptom expression, comorbid psychopathology, and demographic factors is consistent with recommendations towards dimensional and psychometrically-informed conceptualizations of psychopathology (Krueger & Markon, 2006) and may shed additional light on common clinical presentations. If identified, such clusters may offer insights regarding potential underlying transdiagnostic processes, and lead to improved specificity in care (Gillan, Fineberg, & Robbins, 2017).

Among pediatric samples, cluster analyses examining symptom expression have found similar groupings to factor-analytic studies (Hybel, Lykke Mortensen, Højgaard, Lambek, & Hove Thomsen, 2017; Ivarsson & Valderhaug, 2006). Højgaard et al. (2018) examined comorbidity profiles among OCD-affected children and adolescents and

identified a three-class solution, characterized by those with no comorbidity, those with neurological/behavioral conditions (e.g., ADHD, tics, ODD), and those with comorbid anxiety disorders. Although OCD symptom types were not included in the model, secondary analyses suggested symmetry/hoarding symptoms were associated with both comorbid classes, harm/sexual symptoms were associated with the comorbid anxiety class, and comorbidity was less common among those with contamination/cleaning symptoms. There is strong evidence suggesting that symptoms of psychopathology, including the symptoms of OCD, are best described as overlapping, dimensional phenomena without clear distinctions between normal and abnormal (Abramowitz et al., 2014; Kotov et al., 2017). As most studies examining the interplay of OCD symptoms and comorbidity profiles use a diagnostic interview, which marks diagnoses as simply present or absent, it is possible that more nuanced symptom associations are missed (Cervin, Lázaro, et al., 2020). To address this limitation, network analyses have been conducted where symptoms of OCD and anxiety and depression are included in network models. This network approach to psychopathology conceptualizes mental disorders as networks of symptom-to-symptom relationship and is well suited to outline symptom relationships within and between mental disorders (Borsboom, 2017). Network analysis results have indicated that depression is linked to OCD mainly through obsession-related distress, in both adult and pediatric samples. Specifically, the frequency of obsessions and not being able to control them is linked to a self-reported sense of failure, leading to increased depression levels (Cervin, Lázaro, et al., 2020; Jones, Mair, Riemann, Mugno, & McNally, 2018; McNally, Mair, Mugno, & Riemann, 2017). Network analysis has also found links between the OCD symptom dimensions of obsessing, doubting, and checking to symptoms of panic and generalized anxiety disorders, which in turn are linked to depression (Cervin, Lázaro, et al., 2020). This has led to the suggestion that children and adolescents that do not respond well to standard OCD treatment may benefit from interventions targeting panic and generalized anxiety. However, this remains an untested hypothesis (Cervin, Lázaro, et al., 2020).

Cluster-based analytic methods (e.g., dependent mixture modeling and latent class analysis [LCA]) have also demonstrated utility in producing meaningful subgroups among youth with mental health concerns (Petersen, Qualter, & Humphrey, 2019). While such methods have been utilized to explore either OCD symptom expression or comorbid disorder presentations among OCD-affected individuals, these methods have not yet been utilized to examine both domains simultaneously, which may produce novel and clinically relevant insights by identifying meaningful subgroups which may have unique characteristics regarding etiology and treatment response.

1.5 Comorbidity

Pediatric OCD is highly comorbid with other psychiatric disorders. Recent estimates are that around 64% of patients with OCD present with a secondary co-occurring diagnosis

(Sharma et al., 2021), and some studies have found that as many as 86% of youth have a secondary comorbid diagnosis, and up to 74% present with a third psychiatric condition (Farrell, Waters, Milliner, & Ollendick, 2012). This high degree of comorbidity contributes strongly to the impairing nature of OCD and the high complexity involved in treating pediatric OCD (Farrell et al., 2012; Krebs & Heyman, 2010; Storch, Larson, et al., 2008). The most common comorbid diagnoses in pediatric OCD are anxiety disorders (e.g., social anxiety disorder, generalized anxiety disorder (26-70%), depression (10-73%), tic disorders (17-59%), attention deficit/hyperactivity disorders (10-50%), and behavioral disorders (e.g., oppositional defiant disorder (10-57%), Farrell et al., 2012, Sharma, 2021). Other less common, yet fairly frequently co-occurring disorders include developmental disorders (e.g., autism spectrum disorder), eating disorders, and other OCD-related disorders, in particular, body dysmorphia, and trichotillomania (Farrell et. al., 2012). The proposed reasons for the high co-occurrence of other disorders in OCD samples include diagnostic practices (e.g., the tendency to ascribe additional diagnoses to psychiatric patients) (Cervin, Lázaro, et al., 2020), shared genetic risk factors (Bolhuis et al., 2013; López-Solà et al., 2016), and direct causal mechanisms through which OCD symptoms and their resulting impairment give rise to other psychiatric symptoms, such as those of anxiety and depression (Rickelt et al., 2016; Voltas, Hernández-Martínez, Arija, Aparicio, & Canals, 2014; Zandberg et al., 2015). When assessing and treating pediatric OCD, comorbidity should be assumed, and the successful treatment of individuals with OCD must take the potential impact of comorbid conditions into account. In general, comorbidity in pediatric OCD is associated with a higher degree of functional impairment and attenuated response to treatment; however, an exception to this general rule is comorbid anxiety, which does not seem to greatly impact treatment response to first-line OCD interventions (Storch, Bjorgvinsson, et al., 2010). This may be, in part, because of similarity in key treatment components for both anxiety disorders and OCD, as cognitive behavioral therapy (CBT) with an emphasis on exposures and serotonin reuptake inhibitors (SRI) are regarded as the first-line treatment options for children and adolescents in both conditions (National Institute for Heath and Clinical Excellence, 2005, 2014).

1.6 Age and development

There are several developmental and familial characteristics unique to the pediatric presentation of OCD (Selles et al., 2014; Skriner et al., 2016). OCD is equally prevalent in child and adolescent males and females but seems more prevalent for females among adults (Fawcett et al., 2020; Geller et al., 1998; Masi et al., 2005; Moore et al., 2007; Tukel et al., 2005). Children and adolescents with OCD have higher rates of comorbid disruptive behavior disorders, anxiety disorders, and tic disorders compared to adults with OCD (Chabane et al., 2005; do Rosario-Campos et al., 2005; Geller, 2006; Masi et al., 2006), and level of insight is also typically poorer

in children and adolescents with OCD (Geller, 2006; Geller et al., 1998). Studies in adult samples have consistently shown that OCD is often chronic and lifelong; however, studies in pediatric populations indicate a more episodic course (Mancebo et al., 2014).

Studies comparing older and younger subsamples of children and adolescents with OCD have shown mixed results on variables regarding symptom structure and clinical correlates (Farrell, Barrett, & Piacentini, 2006; Geller et al., 2001; Mancebo et al., 2008; Nakatani et al., 2011; Skriner et al., 2016). Despite methodological differences between studies, different age groupings, and varying sample sizes, some common patterns emerge in the literature. For symptom profile, a higher occurrence of ordering, repeating, and checking compulsions (Farrell et al., 2006; Nakatani et al., 2011) and sexual obsessions (Geller et al., 2001; Selles et al., 2014) are commonly found in adolescents while a higher occurrence of hoarding compulsions has been found in younger children (Selles et al., 2014). Comorbid depression has also been found to be more prevalent among adolescents in some studies (Geller et al., 2001; Peris et al., 2017; Selles et al., 2014; Skriner et al., 2016). Preadolescent children tend to have poorer insight, a higher prevalence of tic disorders, and higher incidence of ADHD, ODD, and anxiety symptoms (Geller et al., 2001; Nakatani et al., 2011; Peris et al., 2017; Selles et al., 2014; Skriner et al., 2016). Adolescents also tend to show greater levels of functional impairment compared to younger children (Piacentini, Peris, Bergman, Chang, & Jaffer, 2007; Valderhaug & Ivarsson, 2005). It is, however, important to note that none of these developmental or age-related differences are consistently found in all studies, and more work is needed to confirm any reliable developmental patterns. A summary of previous studies of age differences in pediatric OCD samples is presented in Table 2.

A possible limitation of most previous studies is that data on the age of onset was not collected (Selles et al., 2014). It is possible that differences found between the younger and older groups might be better explained by the early or late onset of OCD symptoms. Duration of OCD illness might also, relatedly, be associated with greater severity and comorbidity, as some research has suggested (de Mathis et al., 2013; Nakatani et al., 2011). Furthermore, it is worth noting that most previous studies on developmental differences in pediatric OCD (5 of 7) have been conducted in the USA, and all the previous studies are situated within an English-speaking cultural context. It is important to examine OCD symptoms and developmental differences in more diverse samples, as there is a possible cultural effect on the presentation and development of OCD symptoms in addition to the potential effect of different systems of social support and healthcare. Extending previous research by using large representative samples outside of an English language societal and cultural context, and by including the age of onset and duration of illness in the analyses, is an important step in determining the nature and extent of possible developmental differences in pediatric OCD presentations.

Table 2: Studies comparing characteristics of younger versus older youth with OCD. Adapted and expanded from Selles, Storch, and Lewin, 2014.

Study	Younger group	Older group	Age used	Data source	Main difference: Younger group	Main difference: Older group
Geller et al. (2001)	Under 12 yrs. (*n*=46, 67.4% male)	12 and older (*n*=55, 63.6% male)	Age at time of evaluation.	Consecutive referrals at OCD clinic.	Poorer insight. Higher occurrence of comorbid separation anxiety disorder and tics.	Higher occurrence of religious and sexual obsessions. Higher occurrence of comorbid major depressive disorder.
Farrell et al. (2006)	6-11yrs (*n*=40, 57.5% male)	12-17yrs (*n*=44. 43.2% male)	Age at time of evaluation.	Baseline evaluations from a CBT trial.	Higher occurrence of comorbid specific phobia and oppositional defiant disorder.	Higher occurrence of contamination obsessions, washing and checking rituals. Shift to female preponderance.
Mancebo et al. (2008)	6-12yrs (*n*=20, 65% male)	13-18yrs (*n*=44, 68.2% male)	Age at time of evaluation.	Evaluations as part of naturalistic follow-up.		Higher occurrence of aggressive obsessions.
Nakatani et al. (2011)	3-9yrs (*n*=151, 58.9% male)	10-17yrs (*n*=214, 58,4% male)	Retrospective age of onset.	Archival analysis on routine clinical practice data.	Higher occurrence of comorbid tics.	Higher occurrence of ordering and repeating compulsions.
Selles et al. (2014)	3-9yrs (*n*=99, 54.5% male)	10-18yrs (*n*=193, 48.2%)	Age at time of evaluation.	Baseline evaluations from a CBT trial combined with data from a single time-point evaluation study on pediatric OCD characteristics.	Poorer insight. Higher occurrence of comorbid ADHD. Higher parent-rated anxiety symptoms. Higher occurrence of hoarding compulsions.	Higher occurrence of comorbid depression. Higher occurrence of sexual, magical thinking, and somatic obsessions. Higher occurrence of checking, counting, and magical thinking compulsions.
Skriner et al. (2016).	5-8yrs (*n*=127, 47.2% male)		Age at time of evaluation.	Baseline evaluations from a CBT trial.	Severity levels similar to studies with older children. High rates of comorbid ADHD, ODD, tics, and anxiety disorders. Low rates of depression.	
Peris et al. (2017)	7-9yrs (*n*=58)	10-13 (*n*=148) and 14-17 (*n*=116)	Age at time of evaluation.	Baseline assessments at a university-based clinic.		Higher rates of externalizing and internalizing comorbid disorders. Adolescents had a sixfold increase in comorbid depression compared to children.

1.7 Etiology

The pathogenesis of OCD appears to involve a combination of genetic, neurological, behavioral, cognitive, and environmental factors. Twin and genetic studies on OCD have shown an estimated heritability of 40-65%, and point to the involvement of many different genes associated with serotonin, dopamine, and glutamate neurotransmitter systems (Arnold et al., 2009; Arnold, Sicard, Burroughs, Richter, & Kennedy, 2006; Pauls, 2008, 2010; Pauls, Abramovitch, Rauch, & Geller, 2014; van Grootheest et al., 2008; van Grootheest, Cath, Beekman, & Boomsma, 2005). Compared to anxiety and mood disorders, OCD has significantly higher heritability rates (Eley et al., 2003); in particular, heritability is high for childhood-onset OCD (van Grootheest et al., 2005). However, there are few replicated genetic risk variants for OCD. Gene discovery has been hampered by relatively small and homogeneous samples, which international consortia are currently working to overcome (Burton et al., 2018; Crowley et al., 2023; International Obsessive Compulsive Disorder Foundation Genetics & Studies, 2017).

1.7.1 Behavioral models

Behavioral models postulate that both classical and operant conditioning play a part in OCD. Mowrer´s two-stage theory is a learning model of OCD and suggests that fear develops when a neutral stimulus is paired with an aversive stimulus, through classical conditioning. This is referred to as stage one. Stage two involves operant conditioning through negative reinforcement, when avoidance behavior develops to reduce the anxiety associated with the (initially neutral) stimulus (Dollard & Miller, 1950; Mowrer, 1960). In other words, obsessions become associated with anxiety, and that association is perpetuated and reinforced via operant conditioning of subsequent responses. This model led to the treatment rationale of exposing OCD patients to situations or items that cause them distress while preventing them from carrying out any of their compulsions, which proved successful for cases with severe and protracted OCD (Meyer, 1966; Meyer, Levy, & Schnurer, 1974). Subsequently, further experiments showed that when the urge to carry out a compulsion was provoked in OCD patients, those urges, along with the associated anxiety and discomfort, decreased with time, even though the patients were prevented from carrying out the compulsive behavior (Rachman, De Silva, & Roper, 1976). It was further discovered that with repetition, this "spontaneous decay" of the urge to carry out a compulsion happened faster over time (Likierman & Rachman, 1980). These insights underpin the first randomized controlled trial of exposure and response prevention (ERP) (Rachman et al., 1979), which is a core ingredient of the current gold-standard treatment (McKay et al., 2015; Olatunji, Davis, Powers, & Smits, 2013).

1.7.2 Cognitive models

Cognitive models of OCD assume that either a dysfunction in general cognitive

information processing, or certain kinds of dysfunctional beliefs and thought processes, underpin OCD. Researchers have proposed that OCD might be caused by abnormalities in information processing, potentially due to dysregulated neural circuitry, and point to evidence indicating that individuals with OCD tend to perform worse on neuropsychological measures of executive function and memory, in comparison to those without OCD (Taylor & Jang, 2011). Deficits in neuropsychological domains are, however, only found in a subset of individuals with OCD, and often only at a relatively mild level. Further, similar neuropsychological deficits are found across several other psychological disorders, and it is unclear as to whether poorer performance on neuropsychological tests is a cause or effect of OCD. Dysfunctional cognitive information processing should therefore likely be viewed as a nonspecific vulnerability factor rather than a direct causal factor for OCD (Taylor et al., 2010).

The manner in which dysfunctional beliefs and thought processes lead to obsessions and compulsions is explained by the cognitive behavioral theory of OCD (Salkovskis, 1985, 1989, 1996). This model is based on the observation that intrusive thoughts are quite common and essentially non-pathological, as they are experienced by around 90% of the general population, the vast majority of whom are not significantly troubled or impaired by them (Rachman & de Silva, 1978). This view proposes that the difference between intrusive thoughts that are dismissed as meaningless, and those that develop into obsessions, is the individual's appraisal of the thought. In OCD, intrusive thoughts are appraised as a threat linked to harm to oneself or others, in a way that is personally meaningful to the individual (Rachman, 1997; Salkovskis, 1985). If the intrusive thought is interpreted to mean that the individual may be, or may become, responsible for harm or its prevention, then OCD symptoms will likely occur (Rachman, 1997; Salkovskis, 1985, 1989). It is this interpretation that mediates the distress that is caused by the intrusive thought and therefore leads to reactions, such as compulsive or neutralizing behaviors, which can consequently strengthen the belief in the appraisal of threat and responsibility (Barrera & Norton, 2011; Purdon & Clark, 2001). Research has shown that obsessions are likely to be most distressing when their content is in opposition to the individual's personal values or sense of self (Rowa, Purdon, Summerfeldt, & Antony, 2005).

The traditional view of cognitive behavioral theory suggests that an inflated sense of responsibility is at the core of the disorder. This has been challenged by the view that OCD symptoms are mainly driven by diminished confidence, conviction, or certainty in the ability to assimilate the information necessary to come to a decision, in other words; that doubt is at the core of the disorder, rather than over-inflated responsibility (Nestadt et al., 2016; Samuels et al., 2017). However, it has been found that the severity of doubt is highly variable in OCD and a sizeable proportion of patients are rated as having no, or little, doubt. This suggests that doubt may not be a core feature of all cases of OCD, but rather a frequently occurring symptom of, or trait related to, the disorder (Samuels et al., 2017). It has also been argued that factors other than just the

appraisal of an intrusive thought might be important in distinguishing thoughts from obsessions. Evidence suggests that compared to non-OCD- related intrusive thoughts, obsessions occur more often without an identifiable trigger (Rachman & de Silva, 1978). Obsessions appear to be distinct from intrusive worry thoughts, such as occur in generalized anxiety disorder, as obsessions more often occur without any basis in reality (Audet, Wong, Radomsky, & Aardema, 2020; Langlois, Freeston, & Ladouceur, 2000).

1.7.3 Neurobiological models

Proposed neurobiological models of OCD all focus on several substructures within the frontal-striatal-thalamic-cortical network of the brain (Alexander, DeLong, & Strick, 1986; Huey et al., 2008). Specifically, findings show abnormal metabolic activity in the orbitofrontal cortex, anterior cingulate/caudal medial prefrontal cortex, and the caudate nucleus (Saxena, Brody, Schwartz, & Baxter, 1998). This network tends to show increased activity both "at rest" and during symptom provocation among OCD patients, as well as a reduced activity following successful treatment (Graybiel & Rauch, 2000). This neural circuit has been implicated in the formation of habits, suggesting its excessive activation could facilitate highly repetitive thoughts (obsessions) and actions (compulsions). Importantly, OCD seems to be a network pathology rather than a specific anatomical one. It has also been suggested that OCD may be a heterogenous condition with various neural pathologies resulting in common psychiatric symptoms (Menzies et al., 2008; Piras et al., 2015).

The discovery of clomipramine as an effective pharmacological intervention led to an interest in the role of the neurotransmitter serotonin in the pathogenesis of OCD (Barr, Goodman, & Price, 1993; Charney et al., 1988; Fernandez & Lopez-Ibor, 1967). Clomipramine is a tricyclic antidepressant that, unlike other tricyclics, impacts serotonin (Rapoport, Elkins, & Mikkelsen, 1980) and, in general, OCD responds to medication that inhibits the synaptic reuptake of serotonin. This has led to a serotonin deficiency hypothesis, which proposes that OCD is caused by a significant deficit in serotonin (Barr et al., 1993; Westenberg, Fineberg, & Denys, 2007, Fineberg, 2007 #3939). However, no unified theory regarding the role of serotonin in the etiology of OCD has been accepted and, to date, the mechanisms by which medications impacting serotonin provide their effects remain poorly understood (Fineberg, Pampaloni, Pallanti, Ipser, & Stein, 2007; Westenberg et al., 2007). There is growing evidence, from both preclinical and clinical studies, that the dopamine system may also be involved in the pathogenesis of OCD, and that dopaminergic and serotonergic pathways play a role in the genesis and maintenance of obsessive-compulsive symptoms (Westenberg et al., 2007). Another neurotransmitter implicated in OCD pathology is glutamate, the main excitatory neurotransmitter within frontal-striatal-thalamic-cortical network (Marinova, Chuang, & Fineberg, 2017). Glutamatergic pharmacological agents have recently become a focus of interest, particularly for treatment-resistant OCD. Although some

promising findings have been made (e.g., for glutamate modulators like memantine, riluzole and n-acetyl cysteine), this research is still mostly preliminary, and in the case of riluzole some concerning side effects have been found (Grant et al., 2014; Jalal, Chamberlain, & Sahakian, 2023; Oliver et al., 2015; Pittenger, 2015).

There is increasing evidence for secondary immune-mediated forms of OCD, as subgroups of OCD patients have been found to have elevated levels of proinflammatory cytokines and autoantibodies against targets that include the basal ganglia (Endres et al., 2022). The most well-known of auto-immune OCD symptom onset forms is associated with pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection, or PANDAS (Orlovska et al., 2017; Swedo et al., 1998; Westwell-Roper et al., 2019). The term pediatric acute neuropsychiatric syndrome (PANS) has also been introduced when other pathogens are identified as possible causes of immune-related OCD symptom onset (Chang et al., 2015). Whether immune-mediated secondary OCD could also develop as a consequence of COVID-19 poses a highly relevant research question to be elucidated in the near future (Pallanti, Grassi, Makris, Gasic, & Hollander, 2020; Steardo Jr, Steardo, & Verkhratsky, 2020). Recognition and further understanding of the potential autoimmune causes of OCD could inform additional therapeutic options for the affected patients to enhance treatment response and reduce chronicity (Endres et al., 2022).

1.8 Treatment of pediatric OCD

1.8.1 Cognitive behavioral therapy

Cognitive behavioral therapy (CBT) with exposure and response prevention (ERP) is the most efficacious and well-studied psychotherapy for pediatric OCD. Numerous studies have demonstrated the efficacy of CBT with ERP compared with medication alone and other active control conditions (Abramowitz, Whiteside, & Deacon, 2005; McGuire et al., 2015; Sánchez-Meca, Rosa-Alcázar, Iniesta-Sepúlveda, & Rosa-Alcázar, 2014; Watson & Rees, 2008). In child and adolescent samples, 45-65% of OCD patients show symptom reduction after CBT with ERP, and 40-88% achieve remission (Barrett, Healy-Farrell, & March, 2004; Bolton et al., 2011; Franklin et al., 2011). These substantial treatment gains have been shown to last for several years and even into adulthood (Mancebo et al., 2014; Micali et al., 2010).

CBT with ERP in standard format is delivered in an outpatient setting, typically over 12 to 20 weeks. CBT for OCD is an active, goal-oriented therapy in which the patient and therapist work collaboratively to develop a shared understanding of the patient´s OCD symptoms and to identify their maintaining factors. Exposure and response prevention (ERP) is known to be the primary active ingredient in CBT for OCD (Foa, Yadin, & Lichner, 2012; Krebs & Heyman, 2015). ERP involves the patient confronting a feared situation or stimulus while resisting the urge to perform the compulsion typically used to

neutralize the anxiety or discomfort (Olatunji et al., 2013). Families are often highly involved and impacted by the OCD symptoms in their children and adolescents. Family members can inadvertently accommodate their child's anxiety to smooth interactions and ease distress, and greater levels of such family accommodation have been related to more severe OCD symptoms (Albert et al., 2010; Marien, Storch, Geffken, & Murphy, 2009; Storch, Geffken, Merlo, Jacob, et al., 2007). It is therefore crucial to involve parents and other family members in OCD treatment and, during the ERP phase, family members should be present during treatment sessions and they should monitor at-home exposures to ensure they are completed with fidelity and to provide encouragement or coaching (Marien et al., 2009). There is evidence to suggest that treatment effects are enhanced when families are intensively engaged in CBT with ERP for children and adolescents (Thompson-Hollands, Edson, Tompson, & Comer, 2014).

1.8.2 Intensive treatment

Short intensive psychotherapy formats have been suggested as equally, or potentially more, effective for severe OCD than weekly, single-treatment sessions (Foa & Steketee, 1987). Intensive formats are usually based on ERP and have similar components as traditional outpatient CBT treatment but manipulate the dose of psychotherapy by providing long exposure sessions over the course of a few days. Intensive formats can be a practical and more accessible treatment option in some instances. For children and adolescents, intensive formats have shown considerable promise and may be a viable and effective treatment option for those that do not respond sufficiently to standard CBT formats or first-line pharmacotherapy (Bjorgvinsson et al., 2008; R. C. Leonard et al., 2015; Riise et al., 2016; Storch, Geffken, Merlo, Mann, et al., 2007; Storch, Lehmkuhl, et al., 2010)

1.8.3 Pharmacotherapy

Selective serotonin reuptake inhibitors (SSRIs) are the only evidence-based pharmacological treatment for pediatric OCD (National Institute for Heath and Clinical Excellence, 2005). For children and adolescents with OCD in the severe or extremely severe range (i.e., scores between 24-40 on the CYBOCS) it is recommended that SSRI medication treatment is started alongside behavioral treatment (Garcia et al, 2004; NICE, 2005). Evidence suggests that SSRI monotherapy is superior to pill placebo and, in some studies, similarly effective as CBT with ERP for children and adolescents (Garcia et al., 2010; Ivarsson et al., 2015; Varigonda, Jakubovski, & Bloch, 2016). Combined treatment, where SSRI and CBT with ERP are delivered simultaneously, has been found to be superior to either treatment alone or pill placebo (Ivarsson et al., 2015; POTS Study Team, 2004).

There are additional pharmacological treatments that have shown some effectiveness and may be recommended for children and adolescents who do not respond to a course of CBT with ERP and trials of at least two SSRIs. The tricyclic drug clomipramine,

which initially led to serotonin being targeted in OCD treatment, is often regarded as more effective than the SSRIs but has a less favorable side-effect profile (Geller et al., 2003; Geller & March, 2012; Watson & Rees, 2008). Clomipramine has been shown to be an effective medication for treatment resistant cases and may be particularly beneficial when combined with the SSRI fluvoxamine (Fung, Elbe, & Stewart, 2021; Hardy & Walkup, 2021). Augmenting SSRI therapy with a low dose of risperidone has demonstrated symptom improvement in 50% of previous non-responders in a naturalistic study but randomized trials have not yet been conducted. However, risperidone and other antipsychotic medications (e.g., aripiprazole) are generally less well-tolerated than SSRIs and are associated with serious side effects (Masi, Pfanner, & Brovedani, 2013; Gudmundur Skarphedinsson & Ivarsson, 2015).

1.9 OCD-related functional impairment

OCD tends to be a debilitating condition, negatively impacting the quality of life of affected children and adolescents (Storch et al., 2018). In one study, OCD patients reported spending an average of 5.9 hours per day engaged with obsessions and 4.6 hours a day carrying out compulsions, indicating the time burden resulting from the disorder (Ruscio et al., 2010). The core symptoms of OCD, obsessions and compulsions, can directly impair daily functioning and potentially interfere with many domains of life. This is referred to as OCD-related functional impairment (Piacentini, Bergman, Keller, & McCracken, 2003; Valderhaug & Ivarsson, 2005). Children and adolescents with OCD have been found to show higher levels of impairment in school, social, and family settings than unaffected peers (Storch, Larson, et al., 2010). Therefore, it is unsurprising that OCD in children and adolescents has been associated with a profound decrease in educational attainment (for both compulsory- and postgraduate education) and employment prospects, especially for those with early onset of the disorder (Hollander et al., 1998; Koran, 2000; Perez-Vigil et al., 2018)

Functional impairment level is correlated with symptom severity but only moderately so, (Calvo et al., 2022; Langley et al., 2014; Piacentini et al., 2003; Piacentini et al., 2007; Storch, Larson, et al., 2010; Valderhaug & Ivarsson, 2005), which indicates that functional impairment is a clinically relevant construct distinct from the severity of OCD symptoms. Factors associated with greater levels of impairment include other comorbid psychiatric disorders, which potentially interact with and add to OCD symptoms, resulting in greater overall impairment (Ivarsson, Melin, & Wallin, 2008). Lack of insight (Storch, Milsom, et al., 2008), and high family accommodation (Storch, Geffken, Merlo, Jacob, et al., 2007), has also been found to further add to OCD-related impairment. Different OCD symptom dimensions (e.g, cleaning and contamination symptoms) may also influence the specific type and level of impairment, as well as which domains of life are primarily impaired (Bloch et al., 2008; Højgaard, Mortensen, et al., 2017). Following first-line evidence-based treatment (CBT or SSRI medication) (Lewin, Park, et al., 2014; Piacentini et al., 2011; Selles et al., 2017; G.

Skarphedinsson, Weidle, et al., 2015), OCD-related functional impairment tends to decrease parallel to a decrease in symptom severity and an increase in quality of life (B. Weidle, Ivarsson, Thomsen, Lydersen, & Jozefiak, 2015; Wellen et al., 2017). However, high functional impairment has been associated with an attenuated treatment response (Garcia et al., 2010; Selles et al., 2020; Turner, O'Gorman, Nair, & O'Kearney, 2018). Not all children and adolescents with OCD respond adequately to treatment and fewer still achieve remission, with over 30% of children and adolescents classified as non-responders in some studies (McGuire et al., 2015; Ost, Riise, Wergeland, Hansen, & Kvale, 2016; Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). Factors associated with poorer treatment response in addition to higher functional impairment are older age, higher OCD symptom severity, extreme avoidance, low insight, and family accommodation (Garcia et al., 2010; Selles et al., 2020; Turner et al., 2018). There are some inconsistencies between study results; for example, Selles et al. (2020) found that insight did not significantly impact treatment response and, in contrast to earlier studies (Garcia et al., 2010; Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Hybel, et al., 2015), that lower OCD symptom severity at baseline predicted a lower likelihood of treatment response. These inconsistencies indicate that non-responders are a heterogenous subgroup requiring further study. To date, no studies have examined the impact of factors such as age, OCD symptom severity, insight, and family accommodation on the trajectory of long-term OCD-related functional impairment or the interaction of OCD symptom severity treatment response with OCD-related functional impairment. To further examine the heterogeneity of treatment response, it is likely beneficial to identify subgroups of children and adolescents with different long-term trajectories and attempt to identify factors that predict subgroup membership. Such trajectory classes are formed based on the similarities of symptom courses among patients, representing a person-centered (as opposed to variable-centered) approach (Jung & Wickrama, 2008). This approach could provide more personalized information about the prospective long-term course of OCD-related functional impairment (Mulder, Joyce, & Frampton, 2003).

Jensen et al. (2020) previously examined latent class trajectories of OCD symptom severity during and after treatment and predictors of class membership. Three distinct class trajectories were found: (a) acute, sustained responders (54.6%), where class membership was predicted by lower levels of contamination and cleaning symptoms as well as less parent-rated anxiety; (b) slow, continued responders (23.4%), where class membership was predicted by higher overall severity of psychopathology; and (c) limited long-term responders (21.9%), where class membership was predicted by adolescence, lower overall psychopathology, higher levels of contamination and cleaning symptoms, as well as higher parental ratings of anxiety. No previous studies have analyzed latent class trajectories of OCD-related functional impairment during and after treatment.

Even when symptom remission is achieved post-treatment, with corresponding improvements in quality of life and functional impairment, adults with a history of OCD continue to be more impaired than healthy controls with no such history (Huppert et al., 2009). Whether this is also the case for children and adolescents is currently unknown as the long-term development of OCD-related functional impairment following intervention has not yet been studied. Further, whether factors such as age, comorbidity, or symptom profiles impact how functional impairment changes during and after treatment remains unexplored. Improved knowledge in this area may ultimately help clinicians assess and treat OCD-related functional impairment with greater effectiveness, potentially leading to less impact on patients´ future educational and employment prospects, and increased quality of life.

2 Aims

The current thesis consists of three papers related to exploring subgroups within samples of children and adolescents with OCD. As pediatric OCD is a highly heterogenous disorder, identifying subgroups of children and adolescents with OCD based on symptom expression, comorbid psychopathology, demographic factors, and long-term functional treatment response may shed additional light on common clinical presentations, offer insights regarding potential underlying transdiagnostic processes, and lead to improved specificity of care (Gillan et al., 2017). It is further consistent with recommendations towards dimensional and psychometrically-informed conceptualizations of psychopathology (Krueger & Markon, 2006).

2.1 Study I

Study I examined subgroups based on age, comparing older adolescents (age 12-17) and younger children (age 7-11), participating in an OCD treatment trial (n=269). In addition, subgroups based on age of OCD onset, prepubertal or adolescent, were compared within the older age group. Lastly, subgroups based on the duration of OCD illness were compared. The subgroups were, in all instances, compared in terms of: (1) OCD severity, (2) OCD symptom profile, (3) comorbid symptoms, and (4) OCD-related functional impairment.

2.2 Study II

Study II used an aggregated international sample of 830 OCD-affected children and adolescents, presenting to OCD specialty centers. There were three aims for this study: 1) to establish a factor structure of OCD symptoms; 2) to identify latent clusters representing subgroups of OCD-affected children and adolescents based on symptom factor scores, symptom severity, and the presence or absence of comorbid disorders; and 3) to explore relationships of subgroup membership with other clinically relevant variables, including age of symptom onset, avoidance, impairment, and family accommodation.

2.3 Study III

Study III examined the long-term trajectory of OCD-related functional impairment during and after stepped-care treatment, in a longitudinal analysis of the same sample as used in study I. This study aimed to identify possible latent class trajectories of child and adolescent self-reported OCD-related functional impairment over three years (170 weeks) and to describe these classes according to pretreatment characteristics. Further,

the study aimed to identify predictors of trajectory class membership and to examine the overlap of functional impairment trajectory classes with OCD symptom severity trajectory classes, previously identified in the same sample (Jensen et al., 2020).

3 Materials and Methods

3.1 Study I: Subgroups based on age at assessment and age of OCD onset

3.1.1 Participants

A total of 269 children and adolescents aged 7 to 17 years, recruited from Denmark, Sweden, and Norway between September 2008 and June 2012, were included in the Nordic Long-Term Obsessive-Compulsive Disorder Treatment Study (NordLOTS) (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). Included patients were referred from primary care community health centers, general practitioners, or by parents who contacted the clinics directly, leading to a representative sample of pediatric patients seeking treatment for OCD. Inclusion criteria were an OCD diagnosis based on DSM-IV criteria confirmed with the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL), a Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) total severity score ≥16, and no treatment with CBT or effective doses of SSRIs (>50 mg) six months prior to the start of the study. Exclusion criteria included the presence of another psychiatric disorder with higher treatment priority. Study rationale (Ivarsson et al., 2010) and inclusion procedures (Thomsen et al., 2013; Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015) for the NordLOTS are described in detail elsewhere. Informed consent was obtained from all participants and their parents, and the trial was approved by the Norwegian, Swedish, and Danish Committees for Medical and Health Research Ethics and the Medical Products Agencies.

3.1.2 Measures

Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS). The CY-BOCS is a semi-structured interview evaluating OCD severity and symptom presentation. The CY-BOCS was administered by an independent evaluator. It is comprised of two parts. The first is a 74-item symptom checklist assessing a broad range of current and past obsessions and compulsions. The second part, a severity scale, consists of 10 questions (five concerning obsessions and five concerning compulsions) that measure severity on a 5-point scale, with a total score ranging from 0 to 40 (Scahill et al., 1997). The CY-BOCS has demonstrated reliability and validity in samples of children with OCD (Scahill et al., 2014; Storch et al., 2004). In the NordLOTS sample the intra-class correlation coefficients (*ICC*) of inter-rater agreement were as follows: obsessions *ICC* = 0.94 (95 % *CI* 0.85–0.97), compulsions *ICC* = 0.87 (95 % *CI* 0.67–0.93), and total score

ICC = 0.92 (95 % *CI* 0.78–0.97) (Thomsen et al., 2013).

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime (K-SADS-PL). K-SADS-PL is a diagnostic semi-structured interview designed to assess a broad range of child and adolescent mental disorders according to DSM-IV criteria. The interview comprises an introductory interview, a screening interview, and a diagnostic part. Symptoms are scored as "not present", "possible", "in remission", or "certain" (Kaufman et al., 1997). K-SADS-PL has been shown to possess good inter-rater reliability (98 %) and has a test–retest kappa of 0.80 for all included anxiety diagnoses (Kaufman et al., 1997). The interview has been shown to have good convergent and divergent validity (Kragh et al., 2018; Lauth et al., 2010; Villabo, Oerbeck, Skirbekk, Hansen, & Kristensen, 2016). This study used present diagnoses classified as "certain".

Child Obsessive-Compulsive Impact Scale – Revised (COIS-R). COIS-R is a 33-item, self-reported questionnaire designed to assess the psychosocial functioning of children and adolescents in home, school, and social settings and to assess how OCD affects such functioning. Parent and child rating versions are available. Scale items are scored on a 4-point Likert scale (0 = not at all, 1 = just a little, 2 = pretty much, and 3 = very much). The scale has moderate to high internal consistency of α = 0.92–0.94 and α = 0.78–0.92, respectively, for the parent and child versions (Piacentini et al., 2007; G. Skarphedinsson, Melin, et al., 2015).

Child Behavior Checklist (CBCL). The CBCL is used to evaluate child and adolescent behavioral and emotional problems, as well as social competence. The scale, rated by parents, has 113 items on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, and 2 = very or often true). It has been shown to have good psychometric properties across different populations, mean test–retest reliability between 0.95–1.00, and internal consistency from α = 0.78 to α = 0.97 (Achenbach, 1994; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

Family accommodation scale. The Family Accommodation Scale (FAS) (Calvocoressi et al., 1999) is a 12-item clinician-administered interview that assesses the family's accommodation of their child's OCD symptoms. The FAS has been shown to have good internal consistency (α = 0.76– 0.80) (Calvocoressi et al., 1999{Geffken, 2006 #139; Geffken et al., 2006) and to correlate positively with measures of OCD symptom severity (Storch, Geffken, Merlo, Jacob, et al., 2007) and family discord (Calvocoressi et al., 1999). In the NordLOTS study sample, the internal consistency was α = 0.87 (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015)

The Mood and Feelings Questionnaire (MFQ). The MFQ is a parent- and child-rated questionnaire that is used to assess symptoms of depression based on the DSM-III-R. The scale comprises 13 items, scored in total from 0 to 26. The assessment has sound psychometric properties, and the scale's total score has demonstrated internal consistency of α = 0.75 (Messer et al., 1995) and of α = 0.90 in the current sample

(Messer et al., 1995; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

Screen for Child-Anxiety-Related Emotional Disorders (SCARED). SCARED is a parent- and child-rated questionnaire used to measure symptoms of anxiety based on the DSM-IV, scored from 0 to 82. Its total score has demonstrated internal consistency of α = 0.92 for both child- and parent-rated versions (Ivarsson, Skarphedinsson, Andersson, & Jarbin, 2018; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

Age of onset, age at assessment, and duration of illness. Age at assessment was used primarily to divide the sample into older and younger groups. During initial evaluation, all participants were also asked when they had first been diagnosed with OCD; that age of first diagnosis was used as age of onset. The difference between age of onset and age at assessment was used to ascertain duration of illness.

3.1.3 Analysis

In this study, the sample was divided into two subgroups based on age at assessment. Children aged 7-11 years comprised the younger group (n=85) and adolescents aged 12-17 years comprised the older group (n=184). Independent sample *t*-tests were used to examine between-group differences on continuous dependent variables from symptom rating scales and Pearson's *chi square* to examine between-group differences on categorical variables, i.e., namely K-SADS-PL diagnoses and CY-BOCS symptom categories. Since previous research has suggested that age of onset and duration of illness could explain differences in symptom profiles and comorbidity between older and younger pediatric groups with OCD (Selles et al., 2014), we used the age of OCD onset to divide the sample into three subgroups: younger (and early onset group) (age 7-11 years, n=80), older and early onset group (age 12 years or older, onset before 12 years of age, n=38) and the older and later onset group (age 12 years or older, onset age 12 or later, n=114). ANOVA (for continuous variables) and logistic regression (for categorical variables) were used to examine between-group differences for these three subgroups. Tukey post-hoc tests were used where further analysis was required. Linear regression was used to examine the effect of OCD duration as a continuous variable. All statistical analyses were done using SPSS 26, and p<0.05 was considered to indicate statistical significance.

3.2 Study II: Subgroups based on symptom factor scores, OCD severity and comorbid disorders

3.2.1 Participants

This study included data from 830 OCD-affected children and adolescents, obtained by aggregating participants with completed CY-BOCS checklist data from seven international pediatric OCD programs: NordLOTS (n = 263) (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015); Sahlgrenska

University Hospital OCD Outpatient Clinic, Gothenburg, Sweden (GBG, *n*=91) (Melin, Skarsater, Haugland, & Ivarsson, 2015); D-Cycloserine Cognitive Behavioral Therapy, Tampa, Florida and Boston, Massachusetts, USA (DCS, *n* = 153) (Storch et al., 2016); University of British Columbia Provincial Obsessive Compulsive Disorder Program, Vancouver, Canada (UBC POP, *n* = 148) (Stewart et al., 2017); Griffith University, Gold Coast, and Mount Gravatt, Australia (*n* = 114) (Farrell et al., 2022); Anxiety Treatment Research Center, Hamilton, Ontario, Canada (ATRC, *n* = 56); and University of Iceland, Reykjavik (n = 4) . All participants had a confirmed OCD diagnosis. Average OCD-severity was in the moderate-severe range (mean = 24.5; SD = 5.9). The sample was 54% female and 5-19 years of age (mean = 12.9; SD = 2.9).

3.2.2 Measures

For the majority of participants, baseline diagnoses were assessed using either the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime, K-SADS-PL as described in study I, (n = 567; 68.3%) (Kaufman et al., 1997) or the Anxiety Disorder Interview Schedule for Children - Parent Version (n = 263; 31.2%) (Silverman & Albano, 1996). OCD symptoms were assessed across all sites using the CY-BOCS, a measure with well-established psychometric properties (Scahill et al., 1997; Storch et al., 2004). The CY-BOCS symptom checklist was utilized to assess OCD symptom types. Symptom severity was assessed via the CY-BOCS total score, which is comprised of 10 items rated 0 to 4, with higher scores indicating more severe symptoms. The six CY-BOCS extension items, which evaluate, on a 0 to 4 scale, additional domains related to OCD (e.g., insight, avoidance, doubt) were also completed with many participants (n = 402-728; 49%-88%). While exact measure usage varied across sites, child- and parent-ratings of OCD-related impairment were assessed using variations of the Child Obsessive-Compulsive Impact Scale (COIS) (Piacentini et al., 2003; Piacentini et al., 2007) and family accommodation was assessed using variations of the Family Accommodation Scale (FAS) (Calvocoressi et al., 1999; Flessner et al., 2011; Pinto, Van Noppen, & Calvocoressi, 2013).

3.2.3 Analysis

Data processing and statistical analyses were conducted using Mplus 8.6 (Muthén & Muthén, 1998-2017) and R version 4.0.3 (r-project.org). Two primary sets of analyses were conducted. First, an acceptable factor structure of the CY-BOCS symptom checklist variables was established. Checklist items were modeled as ordinal variables with diagonally-weighted least squares to estimate model parameters and robust standard errors. Model fit statistics, including the Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (RMSR) were calculated and compared across models, seeking the most parsimonious acceptable fit. Acceptable fit was defined as CFI and TLI values of at least 0.9. Factor structures derived from previously identified

solutions by Højgaard et.al (Højgaard, Mortensen, et al., 2017), and from an exploratory factor analysis of the current data were tested in confirmatory factor analysis (CFA). Latent factor scores for each participant were generated based on the best fitting CFA model, using the R *lavaan* package (version 0.6-7) (Rosseel, 2012).

The second primary analysis entailed dependent mixture modelling with the R-package *depmixS4* (version 1.4-2) (Visser & Speekenbrink, 2010) to identify distinct latent groups underlying the observed data. Each participant's factor scores extracted from the best-fitting CFA, total CY-BOCS score, and nine comorbidities were included as the observed variables in this analysis. Child age and gender were treated as covariates using a stepwise approach, where factors were enumerated first using age- and gender-adjusted indicators and differences in factors were then tested based on relevant covariates (i.e., age of symptom onset, avoidance, impairment, and family accommodation). Participants with CFA-derived factor scores as well as other indicators (e.g., comorbidities) were included in the mixture model.

Mixture solutions ranging from one to nine distinct groups were evaluated; Akaike information criterion [AIC] and Bayesian information criterion [BIC] were computed for each solution, with BIC providing a stronger penalty of model complexity (Masyn, 2013; Nylund, Asparoutiov, & Muthen, 2007). Additionally, entropy and average posterior probability for each observation's most likely group measures were computed to evaluate the quality of group separation, with values closer to one reflecting superior delineation of the groups (Masyn, 2013; Nylund-Gibson, 2018). The likelihood ratio tests directly compared models using the difference in χ^2 and degrees of freedom; a larger χ^2 value indicates a larger difference in the models. A final set of analyses examined between-cluster differences in secondary outcomes of interest.

3.3 Study III: Subgroups based on long-term functional impairment trajectories

3.3.1 Participants

The sample consisted of 266 children and adolescents with OCD from Denmark, Norway, and Sweden participating in the Nordic long-term OCD treatment study, NordLOTS (Thomsen et al., 2013). This is the same sample as used in study I where 269 participants were included (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). However, three participants did not provide COIS-R data for at least one assessment point and were therefore excluded from this analysis.

3.3.2 Treatment and follow-up procedures

The NordLOTS was a stepped-care, longitudinal treatment study (Thomsen et al., 2013). In step 1, patients received 14 weekly sessions of manualized, exposure-based cognitive behavioral therapy (CBT) (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle,

Melin, et al., 2015). Children and adolescents that did not respond to treatment at step 1 (CY-BOCS score > 15, *n* = 50) were randomized to either an additional 10 sessions of CBT (*n* = 28) or sertraline for 16 weeks (n = 22); non-responders to CBT in step 2 (*n* = 11) were subsequently offered sertraline (Skarphedinsson, Weidle, et al., 2015). Step 1 responders were offered up to four booster sessions during the first-year post-treatment. In cases of relapse
(CY-BOCS > 15), patients were offered up to 10 CBT sessions (including booster sessions). If the patient did not respond satisfactorily, treatment with sertraline was offered. Independent evaluators assessed all patients before treatment, in weeks 7 and 14 during step 1, and at 40, 66, 118, and 170 weeks after the end of step 1 (Jensen et al., 2020).

3.3.3 Measures

The COIS-R and the CY-BOCS were administered at all assessment points. Baseline assessment measures included in this study were the K-SADS-PL, FAS, MFQ, CBCL and SCARED, all previously described in study I.

3.3.4 Analysis

3.3.4.1 Latent trajectory classes

Latent class growth analysis (LCGA) (Nagin, 2005; Nylund et al., 2007) with linear, quadratic, and cubic terms for two to five classes was conducted on the sample (*N* = 266) using COIS-R self-report data from children and adolescents at the seven points of assessment: Pretreatment (*n* = 246), week 7 (*n* = 215), week 14 (*n* = 213), 40-week follow-up (*n* = 165), 66-week follow-up (*n* = 162), 118-week follow-up (*n* = 151), and 170-week follow-up (*n* = 147). Optimal model fit was evaluated using, primarily, the Bayesian information criterion (BIC) and the sample-size adjusted BIC (SABIC) with lower scores indicating better fit (Nylund et al., 2007). Clinical interpretability and the entropy value (with a score closer to 1 representing higher classification quality) were also considered. Missing data were handled using maximum likelihood estimation. The number of participants from each class entering step 2 treatment (either CBT or SSRI) was examined.

3.3.4.2 Pretreatment characteristics of classes

The latent classes were evaluated by differences in pretreatment demographics, OCD features, and comorbid variables using univariate analyses, ANOVA, or the Kruskal–Wallis tests and chi-squared or Fisher's exact tests, on the raw data.

3.3.4.3 Predictor analyses

Multinomial logistic regression was performed on the combined imputed datasets of the pretreatment variables. The multivariate analysis was explorative because of the novelty

of the trajectory classes. The following variables were included: age, gender, CY-BOCS total severity score, duration of OCD, insight, symptom dimension factor scores (i.e., harm/sexual factor, hoarding/symmetry factor, cleaning/contamination factor), tic disorder (K-SADS), CBCL ADHD symptom subscale, CBCL ODD symptom subscale, anxiety symptoms (SCARED-P), and depression symptoms (MFQ-P).

3.3.4.4 Comparison with OCD symptom severity (CY-BOCS) classes

The results of the LCGA for COIS-R scores were compared to those of the LCGA for symptom severity, using CY-BOCS total scores, conducted by Jensen et al. (2020), using data from the current sample. The extent to which classes shared participants was specifically examined using a Bonferroni-adjusted z-test for independent proportions.

3.3.4.5 Analysis of missing cases

Missing versus non-missing COIS-R child self-report cases were evaluated according to the pretreatment characteristics listed in Table 1, at each point of assessment, using the same univariate analysis on the raw data as was used to compare trajectory classes.

The LCGA was performed using Mplus version 8.6 (Muthén & Muthén, 1998-2017). MICE and all other analyses were performed using SPSS 28 (IBM, 2021).

4 Results

4.1 Study I: Subgroups based on age at assessment and age of OCD onset

4.1.1 Younger versus older participants

The severity of obsessions (t (266) = -1.82, p = 0.07) and compulsions (t (266) = -0.08, p = 0.94), as well as overall OCD severity as determined by the CY-BOCS total score, did not differ between the two age groups (t (266) = -1.03, p = 0.30). Both disruptive disorders, such as ODD or CD, as well as ADHD, were shown to be considerably more common in the younger group (χ^2 (1) = 4.43, p = 0.05), as was CD (χ^2 (1) = 6.97, p < 0.01). Regarding the comorbidity of tic disorders (χ^2 (1) = 0.23, p = 0.64), anxiety disorders (χ^2 (1) = 1.31, p = 0.25), and depression (χ^2 (1) = 0.02, p = 0.89), no significant differences were discovered. However, both the CBCL total problem score (t (211) = -2.52, p < 0.01) and the CBCL externalizing problem scores (t (243) = 2.24, p = 0.03) were greater for the younger group.

On continuous assessments of self- or parent-rated depressive symptoms (MFQ C/P) and family accommodation (FAS) there were no appreciable differences between the two groups. The younger group had higher parental SCARED scores overall (t (252) = 2.13, p = 0.03). The younger group also had greater separation anxiety levels on both child and adult ratings, (t (254) = 3.86, p < 0.01) and (t (252) = 4.06, p < 0.01), respectively. The older group had higher self-rated generalized anxiety (t (253) = -3.75, p < 0.01).

On the CY-BOCS, the older group displayed substantially greater levels of "miscellaneous obsessions" and "miscellaneous compulsions" (χ^2 (1) = 4.28, p = 0.04) and (χ^2 (1) = 7.33, p = 0.01), respectively. A higher prevalence of mental compulsions (χ^2 (1) = 11.8, p < 0.001) and magical/superstitious compulsions (χ^2 (1) = 5.03, p = 0.003) were also observed in the older group. More participants in the younger group (χ^2 (1) = 5.11, p = 0.02) displayed low insight.

The COIS-R self-report ratings for the older group were higher (t (244) = 2.09, p = 0.038), partially supporting the hypothesis that they would demonstrate more functional impairment. However, there was no discernible difference between the groups when it came to the parent-rated COIS-R.

4.1.2 Age of onset

Three subgroups were defined by age of onset. The average length of illness for the younger/early-onset group was 0.79 years (SD = 1.48), for the older/late-onset group it was 0.72 years (SD = 1.11), and for the older/early-onset group it was 3.6 years (SD = 2.5). We compared these three groups using every continuous metric available. On the SCARED, there were significant between-group differences for parent-rated separation anxiety, child-rated separation anxiety, and child-rated generalized anxiety, ($F(2.219) = 9.563$, $p = 0.001$, $p = 0.003$, and $F(2.216) = 6.153$, $p = 0.003$), respectively. The total score on the CBCL ($F(2.181) = 4.274$, $p = 0.01$) and the externalizing symptom score ($F(2.211) = 4.637$, $p = 0.01$) were also significantly different.

The CY-BOCS obsession subscale scores are the only significant finding in this analysis that was not found in the older vs. younger analysis ($F(2.229) = 22.374$, $p = 0.047$), demonstrating that the older/early onset group scored significantly higher than the older/late onset group (using the Tukey post-hoc test). We did not discover any appreciable variations in comorbidity across groups. The results for the older versus younger analyses are mostly reflected in the results for the symptom profile. In regard to symptom profiles, the logistic regression model found no appreciable differences between magical/superstitious compulsions. The older/later onset group had recurring compulsions more frequently than the older/earlier onset group ($\chi^2(1) = 5.74$, $p = 0.02$), which was the only novel discovery in this analysis.

4.1.3 Duration of illness

An analysis of OCD duration using a linear regression model was carried out. Higher levels of CBCL internalizing symptoms and more severe compulsive symptoms on the CY-BOCS were shown to be substantially predicted by longer OCD duration ($F(1,209) = 6.898$, $p = 0.009$ and $F(1,230) = 4.736$, $p = 0.03$). Regarding symptom profiles, longer duration was associated with a higher likelihood of contamination ($F(1,230) = 7.562$, $p = 0.006$) and religious obsessions ($F(1,230) = 7.51$, $p = 0.007$), and cleaning ($F(1,230) = 5.093$, $p = 0.025$), and miscellaneous compulsions ($F(1,230) = 6.967$, $p = 0.009$).

4.2 Study II: Subgroups based on symptom factor scores, OCD severity, and comorbid disorders

4.2.1 Factor analysis of OCD symptoms

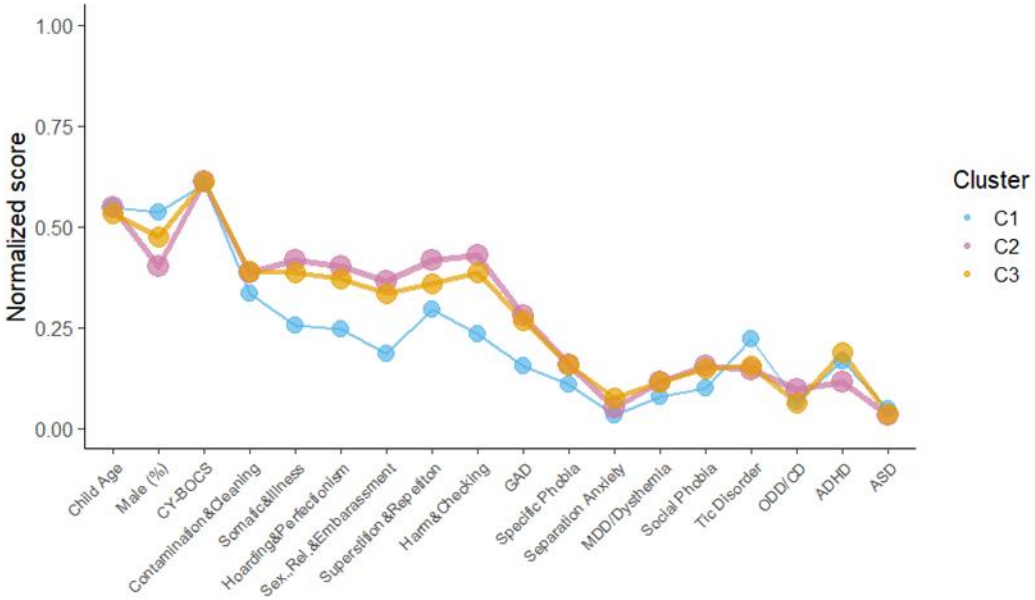
A previously identified three-factor model (Højgaard, Mortensen, et al., 2017) was initially tested in a confirmatory factor analysis (CFA) and did not meet the requirements of acceptable fit in this sample. Therefore, an exploratory factor analysis (EFA) was conducted to suggest the composition of usable factor solutions. A parallel analysis

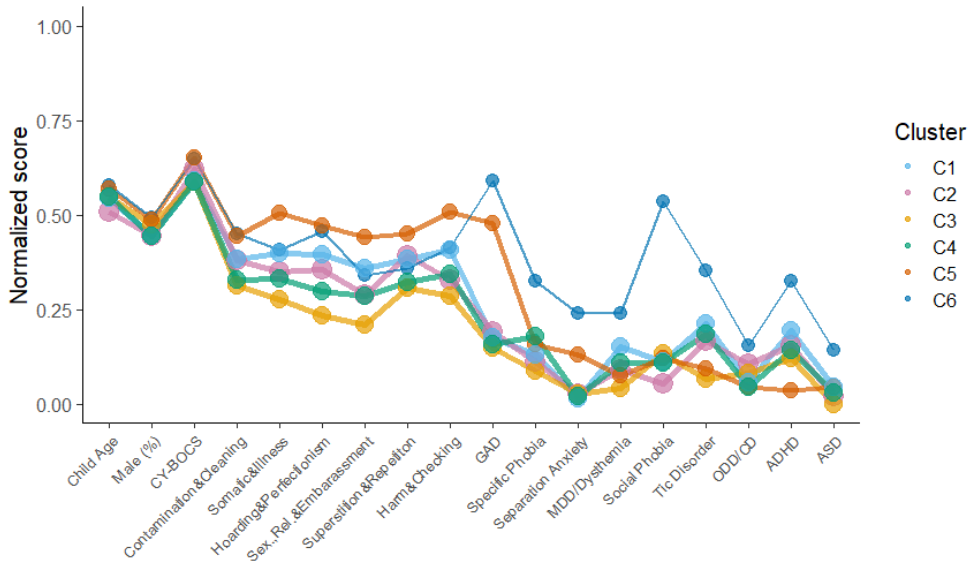
suggested a 10-factor model. A visual scree plot inspection indicated four to six factors, and the 0.7 Kaiser criterion indicated six factors. Fit measures for EFA models of three to 11 factors were examined further and all models with four factors or more had an adequate fit, with fit values improving with each added factor.

To obtain factor loadings for each participant, the exploratory factor solutions were all re-run in a confirmatory factor analysis (CFA). Again, fit values improved with each added factor. A six-factor solution provided an acceptable fit in a CFA, and better fit indexes than fewer factor models. Although EFA results potentially suggest factor solutions with more factors, models with more than six factors failed to converge on an optimal solution in a CFA. The current six-factor model suggests CY-BOCS symptom checklist items can be attributed to contamination/cleaning, sexual/ religious/embarrassment, somatic/illness, harm/checking, superstition/repetition, and hoarding/perfectionism latent factors. Factor loadings for the checklist items and correlations among the six factors were calculated.

4.2.2 Cluster analysis of OCD symptom factors, severity, comorbidity, and demographics

Nine possible solutions were generated by the dependent mixture model. Based on model fit criteria and visual interpretability, solutions involving three to sevenclusters were explored in further detail. Fit indices favored the four-cluster solution; however, all examined models demonstrated acceptable participant classification/entropy (0.8 or higher, Figure 1).




Normalized score
1.00
0.75
0.50
0.25
0.00
Child Age
Male (%)
CY-BOCS
Contamination&Cleaning
Somatic&Illness
Hoarding&Perfectionism
Sex.,Rel.&Embarassment
Superstition&Repetition
Harm&Checking
GAD
Specific Phobia
Separation Anxiety
MDD/Dysthemia
Social Phobia
Tic Disorder
ODD/CD
ADHD
ASD
Cluster
C1
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C3
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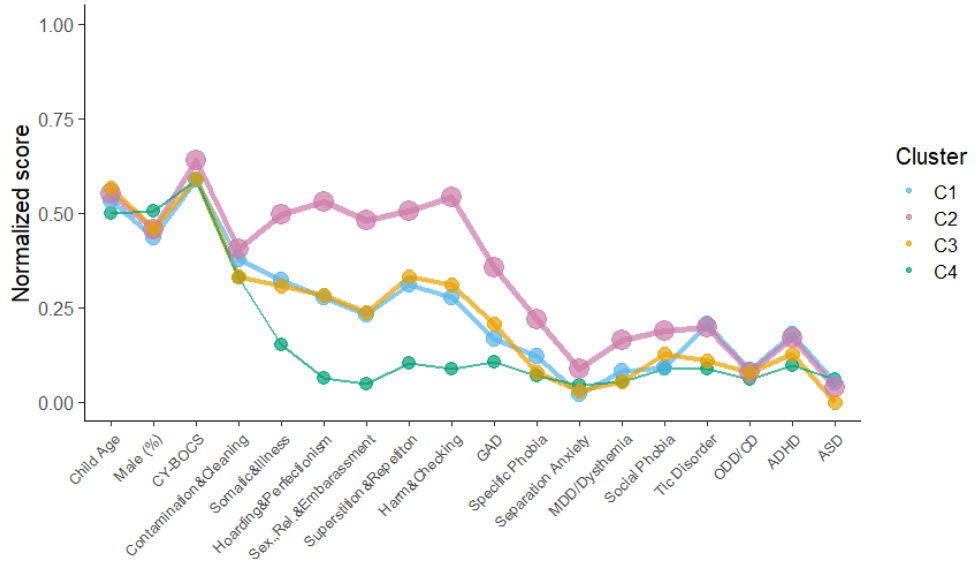
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Child Age
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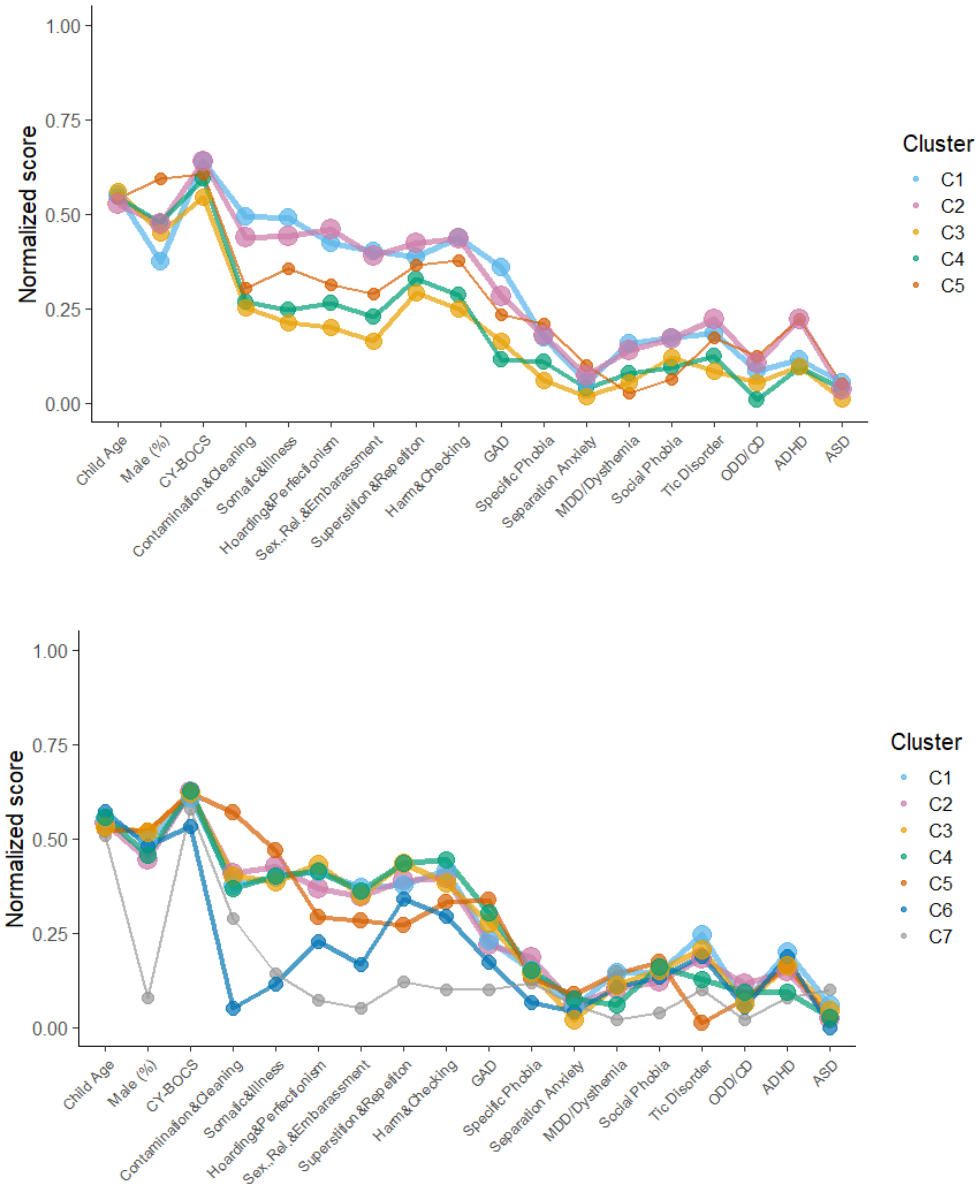

Figure 1: Plots of variable scores across three to seven-cluster, latent class models in study II.

Variation across clusters regarding contamination/cleaning symptoms, symptom severity, and gender distribution was mostly minimal except in more complex models. Clusters were most notably distinguishable by loadings on the other symptom factors and comorbidity patterns. The overall characteristics of the first three identified clusters remained observable and somewhat consistent across subsequent models. In the four-cluster model, two distinct groups emerged: C2 with a mixed symptom presentation, relatively lower contamination/cleaning scores compared to other symptom types, and high levels of comorbid disorders compared to other clusters; and C4 a smaller group, high on contamination/cleaning scores but low on other symptom types and levels of comorbidity. However, these characteristics became less distinct in later models. In the six-factor model, C6 emerged with a small but distinct subset of children and adolescents, with high rates of ASD, ADHD, tics, GAD, and social phobia. In the seven-factor model, C7 emerged with an additional small but distinct subset of mostly female youth who demonstrated high rates of ASD, low levels of other comorbidities, and almost exclusively contamination/cleaning type symptoms.

4.2.3 Cluster differences in secondary outcomes

A final set of analyses compared latent clusters on secondary measures using the four-group solution as it showed the best BIC and had an acceptable entropy value. No significant differences were observed across clusters for CY-BOCS auxiliary items (Tukey-corrected $p > 0.05$) except for slowness where C3 demonstrated higher ratings compared to C4. No differences were observed between clusters on age of onset, measures of impairment, or family accommodation (Tukey-corrected $p > 0.05$).

4.3 Study III: Subgroups based on long-term functional impairment trajectories

4.3.1 OCD-related functional impairment (COIS-R) trajectory classes

All cubic solutions with three or more classes, as well as the two-, four-, and five-class quadratic models, gave cautions about model identification issues. The three-class quadratic solution was picked for analysis, as it has superior fit indices compared to those of the linear and two-class cubic models (Figure 2).

Class 1 (green line), *low impairment-continuous improvement*, had 188 patients (70.7%) and had a relatively low level of impairment at baseline that gradually decreased throughout treatment and up until week 118 of follow-up, retaining a comparable level at the final assessment point. Twenty-eight patients from this class (14.9%) began step 2 therapy, with 12 receiving SSRIs and 18 receiving CBT.

Sixty-five (24.4%) patients were included in Class 2 (blue line), *high impairment-rapid improvement*. This class had high levels of impairment at baseline and showed rapid improvement throughout therapy and follow-up. Seventeen individuals (26.2%) from

this class went on to undergo step 2 treatment; nine received sertraline, and eight received ongoing CBT.

There were 13 individuals (4.9%) in Class 3 (red line), *moderate impairment-no improvement*. This class displayed a moderate to high level of impairment at baseline and no change throughout the treatment phase, with functional impairment scores remaining at a similar level throughout. Step 2 treatment included three individuals from this class (23.1%), two of whom received CBT and one sertraline.

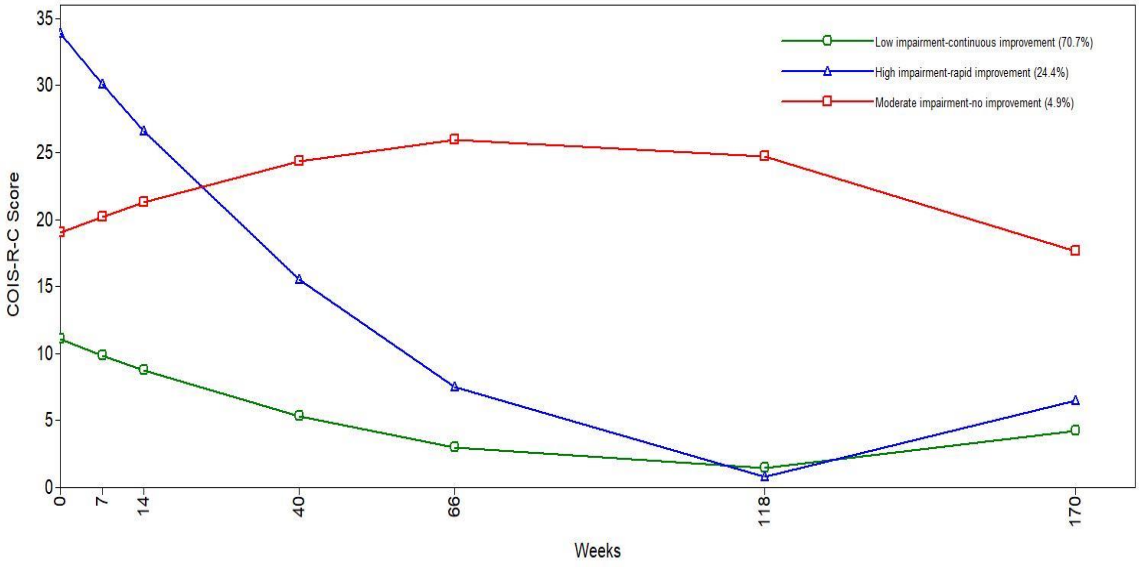

Figure 2: Three distinct latent class growth trajectories of self-reported OCD-related functional impairment for 266 pediatric OCD patients during and after stepped-care treatment, from study III.

4.3.2 Characteristics of functional impairment trajectory classes

The total OCD symptom severity, hoarding/symmetry symptoms, total psychopathology, internalizing symptoms, anxiety- and depressive symptoms, and age were all significantly lower in the *low impairment-continuous improvement* class compared to the *high impairment-rapid improvement* class.

The *moderate impairment-no improvement* class and the *high impairment-rapid improvement* class were distinguished by the latter's lower prevalence of comorbid ADHD and higher levels of OCD and depressive symptoms.

Comorbid ADHD was significantly less prevalent in the *low impairment-continuous improvement* class compared to the *moderate impairment-no improvement* class.

4.3.3 Multivariate predictor analysis of class membership

Membership in the high impairment-rapid improvement class was predicted by higher OCD symptom severity (CY-BOCS total) scores and older age, using the low impairment-continuous improvement class as a reference category.

Higher levels of ADHD symptoms and lower levels of oppositional defiant disorder (ODD) symptoms, as measured by their respective CBCL subscales, were the only significant predictors of membership in the moderate impairment-no improvement class.

4.3.4 Overlap of OCD-related functional impairment trajectory classes and OCD symptom severity trajectory classes

Of participants in the *low impairment-continuous improvement* class, 64% belong to the *acute, sustained responder* symptom severity class. The *acute, sustained responder* class mean CY-BOCS score decreased by 70% from pre- to post-treatment, which indicates a strong initial slope in the trajectory of symptom recovery. The *low impairment-continuous improvement* class, in contrast, only sees a 25% decrease in COIS-R mean scores from pre- to post-treatment.

Of participants in the *high impairment-rapid improvement* group, 43.1% fall into the *slow, continuous responders'* symptom severity class. Again, the CY-BOCS score change from pre- to post-treatment for the symptom severity class is initially steep, with a 40% improvement, compared to the *high impairment-rapid improvement* class's improvement of about 24% on mean COIS-R scores in the same timeframe.

More than half (53.8%) of the *moderate impairment-no improvement* class members belong to the *limited long-term responder* symptom severity category. While the functional impairment class does not show any signs of improvement during the therapy phase, the symptom severity class did show signs of limited improvements.

4.3.5 Analysis of missing cases

At baseline, 7.5% of COIS-R child self-report scores were missing. In comparison to the non-missing group, the missing group had lower age, higher family accommodation, and fewer symmetry/hoarding symptoms. These traits were no longer statistically different between the groups during the treatment phase (weeks 7 and 14).

At the end of the follow-up period (week 170), there had been significant attrition, with 44.7% of participants dropping out. The missing group was younger, had an earlier age of onset, and had higher levels of baseline self- and parent-reported functional impairment, which was the most consistently significant difference throughout the follow-up phase. Maximum likelihood estimate (used for the LCGA) and multiple imputation (used on the baseline data for multinomial logistic regression) both make the

assumption that data are missing at random (MAR) or missing completely at random (MCAR) (Muthén & Muthén, 1998-2017; Rubin, 1996). Non-random attrition in longitudinal data can weaken statistical precision and lead to bias (Andruff, 2009). The current data are clearly not MCAR, yet there are no indications that missingness is affected by unknown reasons and therefore MAR is assumed.

5 Discussion

The current thesis aimed to explore subgroups within samples of children and adolescents with OCD, based on developmental level, age of onset, symptom expression, comorbid psychopathology, and demographic factors. The results, discussed in detail below, may shed additional light on common clinical presentations, offer insights regarding potential underlying transdiagnostic processes, and lead to improved specificity of care.

5.1 Older adolescents and younger children with OCD

Study I examined subgroups based on age, comparing older adolescents (age 12 - 17) and younger children (age 7 - 11), participating in an OCD treatment trial. The severity of OCD symptoms, symptom profiles, comorbid disorders, and the level of functional impairment brought on by the OCD were all compared between the age groups. The severity of OCD symptoms was comparable across the age groups, which is consistent with recent literature. In contrast to what we predicted, the older group did not exhibit higher levels of checking and sexual obsessions. We did discover, however, that the older group had much greater levels of mental compulsions as well as miscellaneous obsessions. This appears to be a novel result and may suggest that adolescents experience more varied and difficult-to-categorize symptoms than younger children, although this is not reflected in higher overall severity. The CBCL total problem and externalizing problem scores were higher for the younger group, indicating a higher general level of psychopathology.

According to previous studies (Piacentini et al., 2007; Valderhaug & Ivarsson, 2005), older children often have more OCD-related functional impairment. Parent reports of functional impairment did not support this finding in our data. However, it is possible that this effect is best explained by younger children underreporting levels of impairment. This underreporting of OCD-related symptoms by children is well known, and when combined with younger children´s lower levels of insight, might explain the gap between what kids and parents describe as functional impairment in the younger group. Another possible explanation is that mental compulsions are more frequent in the older group and perhaps such compulsions are particularly impairing in the complex and demanding social context of adolescence.

We found less difference in comorbidity between the older and younger subgroups than most previous studies. This is perhaps most notable with regard to depression as, in contrast to previous studies (Geller et al., 2001; Peris et al., 2017; Selles et al., 2014), comorbid depression was not different between age groups. However, as

reported by Torp et al. (2015), the rate of comorbid depression, in this sample, was much lower than in other similar OCD samples (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). This discrepancy might be influenced by the availability of mental health services, which in Scandinavia are free and inclusive, which may reduce any subsequent secondary problems through making early intervention more accessible.

Studies comparing older and younger children with OCD have found that poor insight is more common in the younger group (Selles et al., 2018; Selles et al., 2014), and this was confirmed in the current data. Younger children's lower cognitive developmental level may account for this outcome. Lower insight might also explain why younger children self-report lower levels of functional impairment, while parents rate them equally impaired as the older group.

Although there is some evidence in the current data of increased separation anxiety symptoms in the younger group and more parental-rated anxiety symptoms overall, there was no statistically significant difference in the rates of comorbid anxiety disorders between the two age groups. In certain previous studies, younger subgroups have been found to have a greater incidence of anxiety disorders (Geller et al., 2001; Skriner et al., 2016). The finding that older children self-report more severe general anxiety disorder (GAD) scores has, to our knowledge, not been previously reported. It is likely that the older group has better insight than the younger group, making them more conscious of their general anxiety level, resulting in higher self-reported GAD scores and, perhaps, self-rated functional impairment scores. This finding is also in line with longitudinal population studies indicating that GAD prevalence rises sharply during late adolescence (Copeland, Angold, Shanahan, & Costello, 2014).

According to some earlier research (Geller et al., 2001; Nakatani et al., 2011; Skriner et al., 2016), younger children with OCD have a higher frequency of tic disorders than adolescents with OCD. We did not find this pattern in the current data. Dividing the older group into early-onset and later-onset sub-categories did not change this outcome. Lewin et al. (2014) similarly took age of onset into account in this context (although they used different age group definitions) and also found no connection between age of onset and concomitant tic disorder in OCD. However, a study of participants with comorbid tics in the NordLOTS sample found that on average they had a slightly earlier age of OCD onset (10.92 years) than those without comorbid tics (11.94 years) (Højgaard, Skarphedinsson, et al., 2017). We found greater incidence of comorbid disruptive disorders and ADHD in the younger group. When studies compare the comorbidity profiles of younger vs older children with OCD, this seems to be one of the most consistent findings.

5.2 Age of onset

Defining subgroups based on age of OCD onset, that is early (i.e., prepubertal) or late (i.e., adolescent) onset, did not impact the conclusions to a great extent. The only new significant finding from this analysis is that the later age of onset group had higher levels of repeating compulsions. In Nakatani et al. (Nakatani et al., 2011) the opposite was found, as very early onset of OCD was associated with higher levels of repeating compulsions. They argue that their finding is in line with earlier research indicating that tic disorders are associated with both earlier onset and higher levels of repeating compulsions (Scahill et al., 2003). The results of study I did not support this, and along with Lewin et al. (2014), indicate that the association between early OCD onset and comorbid tic disorders is not as robust as previously thought. Further, these results might indicate that repeating compulsions are independent of tic disorder symptoms, or at least not as strongly associated as some have previously suggested (Scahill et al., 2003).

5.3 Duration of OCD illness

Lastly, in study III, subgroups based on the duration of OCD illness were compared. Earlier studies, albeit with smaller sample sizes, have associated a long chronic course of OCD illness with higher OCD severity, more impairment, and more comorbid anxiety symptoms (Mancebo et al., 2014). Duration of OCD as a continuous variable did not predict overall OCD severity, functional impairment, or any comorbidities in study I. However, we did find that duration of illness was associated with more severe compulsions as well as a higher likelihood of having contamination obsessions and cleaning compulsions, partially supporting previous results (Mancebo et al., 2014).

5.4 OCD symptom factors

Study II used an aggregated international sample of 830 OCD-affected children and adolescents, presenting to OCD specialty centers. The first aim of this study was to establish a factor structure of OCD symptoms. Initially, the plan was to use a three-factor structure previously identified in a large aggregated international sample, including the NordLOTS sample also used in this study (Højgaard, Mortensen, et al., 2017). However, this factor solution produced inadequate fit indexes in the current sample. Previous factor analyses of the symptom checklist of the CY-BOCS (Scahill et al., 1997) have suggested that pediatric OCD symptoms coalesce around: 1) contamination obsessions and cleaning/washing compulsions; 2) harm/sexual obsessions and checking compulsions; and 3) symmetry obsessions and compulsions, with hoarding symptoms sometimes included or identified as their own factor (Bernstein et al., 2013; Bloch et al., 2008; Højgaard, Mortensen, et al., 2017; Stewart et al., 2008). It was therefore surprising that a similar factor structure did not fit these data, and perhaps that speaks to the heterogeneity of OCD symptom presentations in

children and adolescents. However, as factor scores were needed as an essential base for the LCA and it was not feasible to move forward with an ill-fitting factor structure, a new analysis was conducted. The findings revealed that a six-factor model showed the best fit and was therefore used in the LCA.

The six-factor model used corresponds in part with earlier work where contamination and cleaning symptoms form a cluster, and harm and checking symptoms also cluster together. A hoarding and perfectionism factor was also present, and such a cluster has been found in previous factor analytic studies (Bernstein et al., 2013; Bloch et al., 2008; Højgaard, Mortensen, et al., 2017; Stewart et al., 2008). However, the somatic and illness symptom factor; the sexual, religious, and embarrassment symptom factor; and the superstition and repetitions symptom factor all appear to be novel symptom clusters, not commonly identified in earlier studies. To what extent these symptom clusters are clinically relevant depends largely on whether they are found to be associated with comorbid psychiatric problems or demographic variables. Examining the variable specific entropy, a measure of how well a variable in a LCA model defines a latent cluster (Asparouhov & Muthén, 2014), reveals that the sexual, religious, and embarrassment symptom factor strongly defines latent classes (Table S7) in all models. In the best fitting LCA model, high levels of sexual, religious, and embarrassment symptoms are associated with diverse symptoms, higher rates of generalized anxiety disorder, social phobia, tic disorders, and ADHD while low levels of sexual, religious, and embarrassment symptoms are associated with predominant contamination symptoms and low comorbidity. Even though harm and checking symptoms, and hoarding and perfectionism symptoms, also distinguish between similar latent groups, variable-specific entropy coefficients suggest that sexual, religious, and embarrassment symptoms might most strongly distinguish highly diverse and comorbid subgroups in pediatric OCD. As most studies have identified fewer than six factors, it is uncertain whether the six-factor model is replicable and stable. As six factors make for a more complicated model than most previous work is based upon, further factor analyses of the CY-BOCS symptom checklist in large samples are required to confirm such a factor structure and the potential clinical usefulness of the factors. This applies particularly to the sexual, religious, and embarrassment symptoms factor which seems to be associated with diverse and highly comorbid OCD presentations.

5.5 Latent clusters based on symptom factors, severity, and comorbidity

The second aim of study II was to identify latent clusters representing subgroups of OCD-affected children and adolescents based on the obtained symptom factor scores, symptom severity, and the presence or absence of comorbid disorders. Results suggested that youth could be acceptably classified into three to seven clusters, with a four-cluster solution offering optimal fit statistics, but more complex models identifying unique and clinically relevant subgroups. Given this, and the limitation that cluster

identification is dependent on the variables included (or not included) in the model, we opted to present, describe, and note differences between clusters in the varying models, rather than highlighting a single model as "the" way that OCD-affected youth are most accurately classified. This open examination is possible in part due to the general stability of cluster characteristics across models.

5.5.1 Cluster characteristics

The largest and most stable cluster throughout all the latent class models was named C2 (and identified by the color pink in the graphs, Figure 1). It does shrink in proportion from 42% to 22% from the simplest to the most complex models, indicating that members from it are further differentiated into subgroups of less common presentations. The youths in this group had more severe OCD symptoms, endorsed a varied symptom profile, and had high comorbid tics, ADHD, and internalizing disorders. These patterns might suggest that increased diversity in symptom expression may be indicative of additional underlying fear/anxiety processes and/or cognitive-dysfunction (e.g., maladaptive beliefs, repetitive negative thinking) (Cervin, Perrin, Olsson, Claesdotter-Knutsson, & Lindvall, 2020, 2021).

Another consistent cluster, comprised of approximately 20%-35% of the sample, was named cluster C3 (and identified by the color yellow in the graphs) and seems to represent a "median" presentation of OCD in most of the models, featuring average to low severity and mixed symptom- and comorbidity profiles throughout.

The C1 cluster (light blue in the graphs) appears to feature low to moderate endorsement of symptoms across all six OCD symptom factors, average severity and demographics, and generally low frequency of internalizing comorbid disorders. Tic disorders and ADHD are, however, quite common. This cluster initially comprised the second-largest proportion of the sample (23%), but steadily lost youth as additional clusters were added, decreasing to 18% of the sample by the seven-cluster model but remaining stable regarding its characteristics.

The C4 cluster (green) emerges in the four-factor model as a small (14%) group of youth almost exclusively endorsing contamination/cleaning symptoms and showing low levels of comorbidity. Along with the consistent presence of contamination symptoms across the larger clusters, these findings suggest contamination symptoms are the most specific or central to pediatric OCD (Højgaard, Mortensen, et al., 2017; Torres et al., 2013). In subsequent models, however, C4 trends towards more mixed symptom expression and comorbidity profiles while remaining stable in size.

The C5 cluster (orange) initially identified 9% of the sample, favored males slightly, and featured high severity, relatively high levels of superstition/repetition and harm/checking symptoms in the five- and six-cluster models, but more predominant

contamination/cleaning symptoms in the seven-cluster model. C5 increases slightly in size and trends toward high levels of anxiety comorbidities in the last two models.

Two small but distinct clusters emerged in the final two models. Distinguished by significantly higher frequencies of comorbid disorders and making up 9% of the sample, C6 (dark blue) showed average severity, high levels of perfectionism/ hoarding, and the highest levels of all clusters on ASD, ADHD, and tics, indicative of a neuropsychological profile and/or difficulties in inhibitory control. In the seven-factor model, C6 is distinguished by very low levels of contamination/cleaning symptoms, low severity, and low internalizing comorbidity indicating that this is not a stable cluster between models. Making up 6% of the sample, C7 (grey) consisted mostly of females exclusively endorsing contamination/cleaning symptoms, showing overall low levels of comorbidity but higher levels of ASD.

The four-latent class model, which had the best fit indexes of the models compared, was used to examine class differences in secondary variables, which might be clinically relevant but were not included in the LCA. Only minimal differences were found on CY-BOCS auxiliary items, and no significant differences were found between clusters on the age of onset, measures of impairment, or family accommodation.

These latent class analyses results are not directly comparable to previous findings as we used a new six-factor structure for OCD-symptom dimensions. However, there are similarities with the best fitting four-cluster model and previous findings, with the almost exclusive endorsement of contamination/cleaning symptoms being associated with a low level of comorbidities (Højgaard, Hybel, et al., 2018), and a trend of more diverse OCD-symptom expressions being associated with higher comorbidity levels (Højgaard, Hybel, et al., 2018; Nestadt et al., 2009).

5.6 Long-term functional impairment trajectories

Study III examined the long-term trajectory of OCD-related functional impairment during and after stepped-care treatment, in a longitudinal analysis of the same sample as used in study I. The purpose of this study was to discover potential latent class trajectories of functional impairment caused by OCD in children and adolescents over three years (170 weeks) and to describe these latent classes in terms of pretreatment characteristics. Three distinct trajectory classes were found. The two larger classes had different initial levels of impairment, but both showed clear signs of improvement during and after treatment. The smaller third class did not improve at any point of assessment during the three-year follow-up. The trajectories of classes defined by impairment seem to be in important respects distinct from trajectories of classes defined by severity, and in some cases, improvements in severity appear to be concomitant with stagnated impairment and vice versa. However, for the two larger classes, functional improvement seems to occur after improvements in symptom severity.

5.7 Descriptions of functional impairment trajectory classes

The largest class, *low impairment-continuous improvement*, was distinguished by less severe symptoms, lower comorbidity, and less symmetry/hoarding symptoms. It also had the lowest starting level of functional impairment. The average age of this class is also lower than that of the *high impairment-rapid improvement* class. Throughout the treatment and follow-up phases, the degree of impairment gradually decreased in this group. Additionally, this class had the lowest percentage of participants beginning step 2 treatment. The *acute, sustained responder* symptom severity trajectory class from Jensen et al. (2020) greatly overlapped with the *low impairment-continuous improvement* functional impairment class. This demonstrates that a strong majority of children and adolescents with OCD improve both symptomatically and functionally with treatment and maintain their treatment gains for at least three years. This is also consistent with past research showing that functional impairment is positively predicted by symptom severity treatment response (Garcia et al., 2010; Turner et al., 2018). It has previously been shown, in the NordLOTS data, that younger age predicts a positive treatment response, and this finding appears to apply to functional impairment as well. (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Hybel, et al., 2015). Further, Jensen et al (2020) found that older age predicted membership in the *limited responder* class, which also indicates better outcomes for younger patients overall in the current sample.

High impairment-rapid improvement, the second-largest subgroup, began treatment with the highest level of functional impairment at baseline but quickly improved over the course of the first 66 weeks. This class attained and sustained a level of impairment comparable to the *low impairment-continuous improvement* class. Only 26.2% of this class entered step 2 treatment, despite having the greatest level of functional impairment 14 weeks after treatment. The *slow, continued response* symptom severity class, which also had the highest severity levels of the three classes established by Jensen et. al. (2020), shared members most frequently with the *high impairment-rapid improvement* functional impairment class. High overall psychopathology severity was a predictor of belonging to the *slow, continued response* symptom severity class (Jensen et al., 2020) and membership in the *low impairment-continuous improvemen*t class was, relatedly, predicted by OCD symptom severity. This suggests that a sizeable subset of adolescents with OCD are severely afflicted and have high levels of comorbid psychopathology. After treatment, this group is still markedly impaired and symptomatic, but they then continue to get better during follow-up and eventually reach a minimal degree of impairment. Therefore, it is crucial for clinicians to remember that symptom severity and functional impairment may still be significant in the most seriously affected OCD cases even after treatment. It seems that with ongoing care, the long-term prognoses for this subgroup could be just as good as those with less severe conditions. This also implies that post-treatment functional impairment ratings are not on their own strong predictors of a patient's future course. This is in line with recent studies showing

that post-treatment OCD symptom severity scores do not predict remission status two or three years after treatment (Jensen et al., 2022).

Moderate impairment-no improvement was the third and smallest class and has a functional impairment level that initially falls between the other two classes. This impairment class exhibits no signs of improvement, suggesting that a small subset of young OCD patients respond, at best, only partially to evidence-based therapy and maintain the same level of impairment as before treatment. These results might be highly clinically significant as this class has a very distinct trajectory, even though it is by far the smallest of the three. This class and *the limited long-term responder* symptom severity class share a significant portion of participants (Jensen et al., 2020). However, although less so than the other symptom severity classes, the *limited, long-term responder* class did exhibit early evidence of therapy response while the *moderate impairment-no improvement* impairment class showed no evidence of treatment response. The presence of more concurrent ADHD diagnoses is the only distinguishing feature of the *moderate impairment-no improvement* class. Despite having higher levels of ADHD, this group does not exhibit more externalizing symptoms, indicating that they are not more likely to exhibit behavioral problems. Surprisingly, lower levels of ODD symptoms predict membership in this group. This would suggest that these children and adolescents are primarily more disorganized and inattentive, which might make it harder for them to engage in psychological therapy or follow pharmacotherapy regimens. This is partially supported by previous research indicating that comorbid ADHD is associated with attenuated treatment response in children with OCD (Masi et al., 2006; Sukhodolsky, do Rosario-Campos, Scahill, Findley, & Leckman, 2005), while the evidence is much more mixed for other externalizing disorders (Garcia et al., 2010; Halldorsdottir & Ollendick, 2014; Storch, Larson, et al., 2010). Further, those with both OCD and ADHD are more likely to experience relapse after successful inpatient treatment compared to patients without ADHD (Walitza et al., 2008). Although the small size of this class makes this highly speculative, we believe clinicians should be aware that this comorbidity pattern may provide particular treatment challenges. However, replication would be required for any firm conclusions regarding the potential impact of comorbid ADHD on functional treatment response in pediatric OCD. It is also important to mention that most participants in the *moderate impairment-no improvement* class did not have concomitant ADHD, and it is possible that this non-ADHD element of this subclass explains why there is a link between lower ODD levels and this subclass. Further, it is possible that the COIS-R self-report is not only measuring OCD-related functional impairment, or that these children and adolescents read the questionnaires instructions less thoroughly or forget them while answering. In such cases the impairment caused by ADHD symptoms might be inflating the COIS-R scores (Guzick et al., 2017).

Non- and limited responders to stepped-care OCD treatment appear to be a heterogenous subgroup. For example, in contrast to the functional impairment non-

response group, Jensen et al. (2020) found that limited symptom treatment response was predicted by lower levels of overall psychopathology severity and greater contamination/cleaning symptoms. It is, therefore, still challenging to identify reliable predictors of worse long-term therapeutic response.

It is clear from earlier studies describing the current sample's symptom severity treatment response that the steepest decline in symptom severity occurs during the first 14 weeks of treatment, both for the entire sample and for all identified subgroups (Melin et al., 2020; Jensen et al., 2020). However, we observe a more modest pattern of improvement over time with functional impairment. This suggests a delayed effect of treatment on impairment, and that it takes time for the child or adolescent to return to their pre-OCD onset levels of functioning once symptoms have been decreased.

5.8 Comparison of functional impairment trajectories and symptom severity trajectories

The proportion of trajectory class members entering step 2 treatment is substantially less variable between functional impairment trajectory classes than for the symptom severity classes found by Jensen et al. (2020). The *low impairment-continuous improvement* functional impairment class had the most similar trajectory and highest member overlap with the *acute, sustained responders* class, yet it had 14.9% of its members enter step 2 treatment, compared with two patients (1.36%) entering step 2 from the *acute, sustained responders* severity class.

Nearly half (49.21%) of the members of the *slow, continued responders* symptom severity class entered step 2 treatment, whereas only 26.3% of *high impairment-rapid improvement* functional impairment trajectory class entered step 2. Three patients (23.1%) from the *moderate impairment-no improvement* impairment class entered step 2. More than half of this class's members also belong to the class of *limited long-term responders* symptom severity class, which also has the most limited response to treatment. As most participants in this non-response impairment group do not enter step 2 treatment, even though their trajectory would indicate a need for further treatment, the importance of taking the progress of functional impairment during and after treatment into account is highlighted. According to current recommendations for OCD treatment, symptom severity is emphasized when defining response and remission (Mataix-Cols et al., 2016). Others have claimed that this strategy may be insufficient because symptomatic improvement may not always translate into functional improvement, and that functional impairment and quality of life indicators ought to be added (Jaisoorya & Janardhan Reddy, 2023). The findings of study III support this opinion.

5.9 Strengths and limitations

The studies reported in the current thesis have certain limitations which should be acknowledged. Studies I and III both use the NordLOTS sample, which is ethnically homogenous as 97% of participants are of Scandinavian origin, which may limit the generalizability of the results, particularly to more culturally and ethnically diverse settings. Further, in study I we chose to categorize children as prepubertal and pubertal in line with Geller (2001) and Farrell (2006), which limits the accuracy of direct comparisons to studies with differently defined age groups. It is important to note that the subgroup of older children characterized by early onset and longer duration of illness was relatively small (38 children). A larger sample might lead to different results.

Study II was highly explorative in nature, and while it provides indications of cluster characteristics at the time of assessment, the study design does not inform the extent to which cluster distribution changes over time (e.g., if participants migrate from one group to another as they age), nor does it allow for direct testing of underlying mechanisms. Second, the clusters provide average scores of those included within that class, rather than clear and definable rules regarding class membership. As a result, applying these categorizations to any individual would be premature at this time. Third, secondary variables were compared between classes after making concrete class assignments (as opposed to allowing for partial class membership). This process overestimates confidence in class assignment. Entropy was strong but not perfect, meaning that there was good but not perfect confidence in identifying which participant was assigned to each cluster. Fourth, site-based variance might have been enhanced by a lack of standardization of procedures, such as in how the CY-BOCS interview was conducted. Fifth, ASD diagnoses were based on the K-SADS and ADIS which are primarily symptom screeners of ASD caseness, and not considered gold-standard measures of ASD (McCarty & Frye, 2020). ASD diagnosis (except for the DSM-IV diagnosis of pervasive developmental disorder not otherwise specified (PDD-NOS)) was an exclusion criterion in the NordLOTS study, resulting in the underrepresentation of comorbid ASD in the study sample. Sixth, the five to seven-factor models have fairly unequal class prevalence, and simulation studies have indicated that in such models, smaller classes may be difficult to recover at small sample sizes (Nylund-Gibson, 2018; Nylund-Gibson & Masyn, 2016). Seventh, the enumeration of factors through the mixture modeling process is sensitive to how covariates are treated and the assumption of different population models to ours, regarding the effects of age and gender, might yield different results (Nylund-Gibson & Masyn, 2016). Eighth, although the sample was large and combined from global centers, these centers were specialized, age-specific, located within countries with high development indexes and primarily Caucasian populations, and they utilized dichotomized, rather than continuous, assessments of comorbidity. Given that results are dependent on sample characteristics and included variables, a different formation of clusters could occur if other variables

(e.g., avoidance, other comorbidities) were included and thus the generalizability of results to other OCD-affected populations may be limited.

Study III is limited by the uneven size of the clusters; in particular, the class of *moderate impairment-no improvement* contains few participants and might not be stable or repeatable in future populations. Additionally, the multivariate regression model's statistical power is limited due to the size of that class's membership. The study is additionally restricted by the absence of any neuropsychological measurements because functional impairment may be connected to neuropsychological performance, which may improve with time if it is state-related. The study uses a dimensional factor score based on the CY-BOCS checklist. Results might have been different if dimensionality had been measured using a more refined measure like the DY-BOCS (Rosario-Campos et al., 2006). Additionally, the results are primarily generalizable to clinical scenarios where CBT is the first line of treatment. Study III also relied on a self-report measure of child and adolescent functional impairment. Although the COIS-R has been validated by its authors (Piacentini et al., 2007), the factor structure of the self-report version appears to be unstable (G. Skarphedinsson, Melin, et al., 2015). It is further possible that, especially for younger children, the COIS-R self-report is less a specific measure of OCD-related functional impairment than an overall non-specific impairment measure. There is a limitation of attrition, as there is in most all follow-up studies. Maximum likelihood equations and multiple imputation were used to handle missing data in order to minimize the impact of attrition. The LCGA did not include characteristics that were likely predictive of missingness, such as age, family accommodation, or baseline functional impairment, so some bias is unavoidable.

Notable strengths are that study I uses a large sample and employs a thorough and systematic assessment process. It also comprises the largest sample using age at evaluation to identify groups and a standardized diagnostic interview to diagnose comorbidity and OCD severity. It also represents the first sample where the age-specific presentation of OCD is explored in a non-English-speaking cultural environment.

Strengths of study II include a large aggregated international sample, a thorough assessment process at specialized OCD centers, and it is, to the best of our knowledge, the first study to simultaneously consider symptom expression, severity, comorbidity, gender, and age in the classification of OCD-affected children and adolescents.

Main strengths of study III are that it makes use of data from the largest pediatric OCD follow-up study to date. This first LCGA investigation of long-term OCD-related functional impairment was made possible by the large sample size and the study methodology, which involved several thorough successive evaluations. The same sample has also been utilized in the past for an LCGA of symptom severity scores, enabling direct comparisons with its findings and adding clinically pertinent supplemental data on the long-term evolution of OCD in children and adolescents.

6 Conclusions

In the current thesis, subgroups within pediatric OCD samples were defined and compared. These subgroups were variously defined by age at evaluation, age of onset, with a dependent mixture model in a cross-sectional sample where classes were based on demographic, symptom profile, and comorbidity information, and with a latent class growth analysis in a longitudinal sample where classes were based on OCD-related functional impairment.

Fairly few major differences between subgroups based on age at assessment were found. This particularly applied to comorbid disorders but also, to a lesser extent, to symptom expression. However, results confirm that a poorer level of insight is an established characteristic of younger children with OCD, as is a higher prevalence of ADHD and ODD. Splitting the sample by late or early age of OCD onset revealed that earlier onset was associated with higher obsession severity and less repeating compulsions, but no differences in comorbidity were found.

In a dependent mixture model conducted on a large sample, which included demographic information, symptom types, and comorbidity profile, a four-cluster model was found to have the best fit. However, all model solutions with three to seven classes had adequate fit indexes, and most classes remained relatively stable between models. The three to seven-class models were therefore all presented and compared, although the best fitting four-class solution was at the center of all further analysis. Similarities with earlier studies were found, in that lower comorbidity risk was associated with isolated contamination concerns and more extensive symptom expression was associated with comorbid internalizing disorders. Small clusters of youth with neurodevelopmental presentations and high comorbidity rates were also found. However, a direct comparison with earlier work is not entirely feasible as a new six-factor structure for OCD-symptom dimensions had to be used to obtain factor scores, due to the previously established three-factor structure not fitting the data adequately.

OCD-related functional impairment was found to improve gradually during and after stepped-care treatment, with continuous long-term improvement for most patients over three years. This contrasts with previous results from the same sample where symptom severity improved rapidly during the treatment phase but much more slowly or very little in the post-treatment phase. A small, yet clinically relevant, subgroup was found that did not improve during the treatment or follow-up phases of the study. The only distinguishing feature of this group was a high prevalence of comorbid ADHD diagnosis.

6.1 Clinical implications

The results of study I confirm the previous findings that a poorer level of insight is an established characteristic of younger children with OCD, and so is a higher prevalence of ADHD and ODD. Clinicians should be aware of these age-related differences. There is some data indicating that a lower level of insight predicts poorer CBT treatment response in pediatric OCD (Garcia et al., 2010; Turner et al., 2018), although a recent study using a large sample did not find this to be the case (Selles et al., 2018). Interestingly, in the NordLOTS sample (reported on in the current thesis) the younger group was found to have lower levels of insight, while at the same time younger age was also associated with positive treatment response, both in terms of symptom (Jensen et al., 2020; Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Hybel, et al., 2015), and functional improvements (Smárason et al., 2023). Therefore, it appears that lower levels of insight are not necessarily predictive of poorer treatment response. It is worth noting that the CBT treatment manual used in the NordLOTS trial emphasized the behavioral approach of ERP and included parental involvement (Thomsen et al., 2013), which may be well suited to younger children and less sensitive to lack of insight than more cognitive treatment approaches.

The elevated prevalence of ADHD and disruptive disorders highlights the need to assess and monitor these comorbid conditions in younger children with OCD. Previous studies have found that ADHD is comorbid in around 15-20% of pediatric OCD cases (Sharma et al., 2021), and is associated with earlier age of OCD onset (Brem, Grünblatt, Drechsler, Riederer, & Walitza, 2014). Comorbid ADHD has previously been associated with attenuated treatment response in children with OCD (Garcia et al., 2010; Storch, Merlo, et al., 2008), although results are somewhat mixed (Selles et al., 2018). Results of study III indicate that ADHD symptoms may be particularly associated with poor long-term functional outcomes in pediatric OCD. The optimal treatment strategy for comorbid OCD and ADHD in children and adolescents is yet to be determined, although current evidence suggests that treating OCD with traditional first-line treatments (SSRI and/or CBT with ERP) can improve attentional deficits in cases with comorbid ADHD (Guzick et al., 2017). In general, concurrent treatment is advised (Geller et al., 2002). The first line treatment for ADHD is stimulant medication, which may improve attention, and facilitate learning and retention of CBT skills for children with comorbid OCD, although this has only been demonstrated in case studies (King, Dowling, & Leow, 2017). However, limited evidence from case studies suggests that stimulant medication could exacerbate and provoke OCD symptoms (Jhanda, Singla, & Grover, 2016; Kouris, 1998; Woolley & Heyman, 2003). It is essential that clinicians closely monitor the severity of OCD symptoms when initiating stimulant treatment for comorbid ADHD.

There is some prior evidence that sexual obsessions might be more common in adolescence (Geller et al., 2001), which seems plausible due to the nature of sexual

development, but this effect was not found in study I. Interestingly, sexual obsessions were relatively common in both age groups with a prevalence around 10%, indicating that clinicians need to screen for such obsessive content regardless of age, and be aware that children may need help to disclose and to identify these thoughts as obsessions to address them in treatment (Bernhard Weidle et al., 2022). A novel and important finding in study I is that adolescents experience mental compulsions to a greater degree than prepubescent children and that such compulsions are present in almost half of adolescent OCD cases. As mental compulsions can be hidden and are perhaps not always voluntarily disclosed during assessment and treatment, it is crucial for clinicians to be aware of their high prevalence and to probe for them specifically. Again, a replication of this finding would be important before firmer clinical conclusions are drawn.

In study II, certain symptom and comorbidity profiles which are in accordance with previous work seem to emerge. First, a cluster of participants almost exclusively endorsed contamination/cleaning symptoms, and a relatively low level of comorbidities was found. Second, a trend of more diverse OCD-symptom expressions being associated with higher comorbidity levels emerges. In particular, higher levels of sexual, religious, and embarrassment symptoms may be indicative of more complex and comorbid OCD presentations. This pattern might suggest that increased diversity in symptom expression may be indicative of additional underlying neurodevelopmental deficits and transdiagnostic cognitive dysfunction (e.g., maladaptive beliefs and repetitive negative thinking, Cervin, Perrin, et al., 2020; Cervin et al., 2021). Clinicians should be aware of this pattern and emphasize thorough case conceptualization in such complex cases, in an attempt to target treatment towards such underlying processes.

Study III indicates that functional impairment tends to improve in a more gradual manner than OCD symptoms, during and after treatment. Clinicians should be aware that even if children and adolescents are still impaired post-treatment, it is likely that they will continue to improve functionally. The exception to this, however, is a small group, represented in Class 3, which appears to not benefit functionally from treatment. Interestingly, only three participants (23.1%) from this cluster entered step 2 treatment in the NordLOTS trial. This indicates that most cluster members were considered symptomatic responders at the end of step 1, even though they continued to be, on average, as functionally impaired as they were pretreatment. These results demonstrate the importance of assessing functional impairment throughout treatment, even in those symptomatically remitted, and taking such assessment into account when making treatment decisions. It also implies the need to develop and assess strategies to address functional impairment directly. Current guidelines emphasize symptom severity for definitions of response and remission in OCD treatment (Mataix-Cols et al., 2016). The results of study III, however, lend support to the view that such an approach might be inadequate, as measures of functional impairment and quality of life should also be included (Jaisoorya & Janardhan Reddy, 2023).

6.2 Future research directions

Further research is needed to elucidate the role of poor insight in pediatric OCD and its potential impact on treatment outcomes. It appears that insight might be best thought of as a malleable, symptom-related state among youth, rather than a stable trait (Landmann, Cludius, Tuschen-Caffier, Moritz, & Külz, 2019; Marková, Jaafari, & Berrios, 2009). This is supported by the finding that insight tends to improve over the course of CBT which might explain why it does not represent a significant barrier to CBT response (Borda, Neziroglu, Taboas, McKay, & Frenkiel, 2017; Selles et al., 2020). However, poorer insight among youth at post-treatment appears to be associated with an attenuated response to CBT (Selles et al., 2020). It is of interest for future dismantling studies to examine which treatment facets may limit or enhance the impact of poor insight on treatment response, as well as to examine interventions that might be particularly effective at improving children's level of insight. As sexual obsessions surprisingly appear to be equally common in younger and older children with OCD in our sample, a more thorough analysis of the specific content of such obsessions at different age and developmental levels might help clinicians when assessing and treating them.

The six-factor structure of the CY-BOCS symptom checklist found in study II needs to be replicated and evaluated in other samples of OCD affected youth. The finding that sexual, religious, and embarrassment type symptoms might be particularly indicative of more complex and comorbid OCD presentations would also require further validation. It would be of great interest to examine the latent classes identified in study II in a longitudinal manner, as it seems plausible that they might have different treatment response profiles. If that is the case, such classes could greatly aid efforts to improve specificity of care. In addition to the core symptoms of obsessions and compulsions, associated factors such as shame or guilt, or lack of insight and avoidance behaviors are common in children and adolescents with OCD (Lewin et al., 2010). Affected children often actively avoid things, places, people, or situations where obsessions might be evoked, thereby lessening the need for compulsive response behaviors. This pattern can be very debilitating and serves in effect to maintain the symptoms of OCD and as an obstacle for working with the symptoms clinically (Briggs & Price, 2009; Kashdan, Barrios, Forsyth, & Steger, 2006; Nissen & Parner, 2018). In addition, children can often be reluctant to talk about their symptoms because of associated feelings of shame or guilt, or lack of insight into the nature of their distress (Lewin et al., 2010). If, and how, these associated factors impact the latent class structure within pediatric OCD samples remains to be examined. A latent class analysis including these factors, in addition to symptom profile factor scores and comorbidity, would therefore be of interest.

The potential impact of comorbid ADHD on functional treatment outcomes should be examined in more detail based on the finding that it is a characteristic of the subgroup

with the poorest long-term functional outcomes. However, as this is based on a very small, and potentially unstable, latent cluster, it is difficult to draw firm conclusions. It would be of great interest to examine the long-term development of post-treatment functional impairment in other samples to see if this result replicates. If so, clearly, the OCD and ADHD comorbidity subgroup requires special attention and likely treatment adjustment. Controlled trials in clinical populations are needed to determine the best course of treatment for this relatively common comorbidity profile (Cabarkapa, King, Dowling, & Ng, 2019). It is important to note that the combined impact of poorer insight and higher prevalence of ADHD might lead to less co-operation during treatment and indicate a need for greater parental involvement. Previous studies have also found a relationship between insight and ADHD in pediatric OCD, potentially suggesting the contribution of neurodevelopmental domains to insight, such as deficits in meta-cognition, theory of mind, and other executive functions, often diminished in children with ADHD (Selles et al., 2018; Steinberg, Morris, & Jaffee, 2023). The potential impact of this interplay between insight and neurodevelopmental deficits on treatment outcomes remains to be fully examined.

Further exploration of the temporal and causal nature of the relationship between symptom severity and functional impairment, during and after OCD treatment, seems warranted. Methodological approaches such as random-intercept cross-lagged panel modeling (RI-CLPM), can be employed to establish whether changes in symptom severity reliably precede changes in functional impairment (or vice versa). If changes in symptom severity reliably precede changes in functional impairment, then specifically targeting impairment during interventions would be redundant but, if that is not the case, further research on how to improve functioning concurrently with symptoms seems warranted.

Further research is needed to confirm the long-term development of OCD-related functional impairment, and its interplay with symptom profiles and severity, during and after treatment. The results in study III are based on child self-reports of functional impairment and the logical next step would be to compare and contrast those results to parental ratings of functional impairment. Although large long-term treatment studies would be the optimal way to further examine the long-term interplay of symptom profiles, severity, and functional impairment, such research is costly and complicated. Aggregating samples from many studies using similar measurement instruments (as in study II) might provide a way to achieve similar quality of results while utilizing existing data. Distinguishing characteristics of subgroups that do not benefit from treatment would be of particular interest in such studies.

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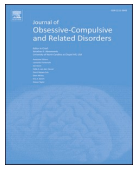

Younger versus older children with obsessive-compulsive disorder: Symptoms, severity and impairment

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ABSTRACT

Studies on child and adolescent obsessive-compulsive disorder (OCD) indicate that symptom severity is similar across age, but significant age differences of symptom profile and comorbid disorders have been observed. The current study examines these differences in one of the largest samples to date, and the first sample outside of an English-speaking cultural context. We compared children aged 11 years and younger to adolescents aged 12 years and older from the Nordic Long-Term Obsessive-Compulsive Disorder Treatment Study that included 269 children and adolescents with a primary diagnosis of OCD. The two groups were compared on measures of OCD severity, symptom profile, comorbid symptoms, and functional impairment. Results showed that the younger group had a poorer level of insight, higher rates of ADHD, and disruptive disorders. The older group had higher levels of mental compulsions, miscellaneous obsessions and compulsions, and self-rated functional impairment. No differences were found on the prevalence of anxiety, tic or depressive disorders between the age groups, nor on overall OCD severity. Overall, differences between the age groups were found to be less than in previous research. Defining groups by age of onset and duration of illness rather than age at evaluation did not change results.

1. Introduction

Obsessive Compulsive Disorder (OCD) is a debilitating psychiatric disorder with an estimated lifetime prevalence between 1 and 3% (Ruscio, Stein, Chiu, & Kessler, 2010). It is mainly characterized by anxiety or distress inducing intrusive thoughts (i.e. obsessions) and anxiety or distress reducing ritualistic behaviors (i.e. compulsions) often complicated by comorbid psychiatric conditions (Lewin et al., 2014; Piacentini, Peris, Bergman, Chang, & Jaffer, 2007). If left untreated, OCD is often a chronic disorder, and frequently associated with severe functional impairment (Piacentini, Bergman, Keller, & McCracken, 2003; Rasmussen & Eisen, 1992; Stewart et al., 2004; Sukhodolsky et al., 2005, pii; Valderhaug & Ivarsson, 2005). About one-third to half of adults diagnosed with OCD report that the onset of their symptoms began in childhood with most studies reporting a mean age of onset at about 10 years (range 6–14 years) (Rasmussen & Eisen, 1990; Skriner et al., 2016).

There are a number of developmental and familial characteristics unique to the pediatric presentation of OCD (R. Selles, Storch, & Lewin, 2014; Skriner et al., 2016). Some studies have shown that pediatric OCD seems to be more prevalent in males than in females while the opposite pattern occurs among adults (D. Geller et al., 1998; Masi et al., 2005; Tukel et al., 2005). Children and adolescents with OCD have higher rates of comorbid disruptive behavior disorders, anxiety disorders, and tic disorders than adults with OCD (Chabane et al., 2005; do Rosario-Campos et al., 2005; D.; Geller, 2006; Masi et al., 2006, pii) and level of insight is also typically poorer in children and adolescents with OCD (D. Geller, 2006).

Symptomatic differences have been observed concerning age and developmental level in some psychiatric disorders (R. Selles et al.,

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2014). For instance, in ADHD, hyperactivity has been shown to be a more prevalent symptom among younger children (Biederman, Mick, & Faraone, 2000) and in depression, somatic complaints are more common in younger children while anhedonia, hopelessness and suicidality are more common in older youths (Rohde, Lewinsohn, Klein, Seeley, & Gau, 2013). Studies evaluating age differences in anxiety disorders have shown mixed results (D. A. Geller et al., 2001; Peris et al., 2017; Skriner et al., 2016). Even though a number of studies have shown phenomenological differences between adult and pediatric OCD, further studies are needed to examine age and developmental differences in pediatric OCD. Given that age related differences have been observed in both externalizing and internalizing pediatric mental disorders it is important to examine such differences further for OCD. Earlier studies comparing older and younger subsamples of children and adolescents with OCD have shown mixed results on variables regarding symptom structure and clinical correlates (Farrell, Barrett, & Piacentini, 2006; D. A. Geller et al., 2001; Mancebo et al., 2008, pii; Nakatani et al., 2011; Skriner et al., 2016). Differences in symptom profile have emerged in some of the studies, for example a higher occurrence of ordering and repeating compulsions (Nakatani et al., 2011) and sexual obsessions (D. A. Geller et al., 2001; R. Selles et al., 2014) in older children and a higher occurrence of hoarding compulsions in younger children (R. Selles et al., 2014), but these difference mostly remain unconfirmed.

Selles et al. (2014) examined the phenomenology of OCD symptoms in a sample of 292 treatment seeking children. They divided the sample into two age groups, younger (3–9 years old) and older (10–18 years old) and found a number of differences in symptom profile and rates of comorbid disorders, such as more sexual obsessions and higher rates of comorbid depression in the older group and a lower level of insight and higher rates of ADHD and disruptive behavior in the younger group. In addition, Selles et al. (2014) summarized the state of the evidence in this area andwe have added research published since 2014 to the summary (Table 1).

These studies vary in sample sizes, define age groups differently, and one study uses retrospective age of onset while the others use age at time of evaluation to split the sample into older and younger groups. Despite methodological differences between studies, some common patterns seem to emerge. Comorbid depression is more prevalent among adolescents than children, in four of the studies (Geller, 2001, Selles, 2014, Skriner, 2016 and Peris, 2017) (Table 1), in two of the studies there is a pattern of higher levels of sexual obsessions (Geller, 2001 and Selles, 2014) and in three studies a higher occurrence of checking rituals (Farrell, 2006 and Selles, 2014) in older children and/or adolescents. Younger children have poorer insight in two studies (Geller, 2001 and Selles, 2014), a higher prevalence of tic disorders in two studies (Geller, 2001 and Nakatani, 2011), and higher incidence of ADHD (Selles, 2014; Skriner, 2016), ODD (Farrell, 2006; Skriner, 2016) and anxiety symptoms (Geller, 2001; Selles, 2014; Skriner, 2016) are also found in at least two of the studies for the younger group.

OCD related functional impairment has been shown to be considerable in social-, school, family-, and home settings for both children and adolescents (Piacentini et al., 2007; Skarphedinsson et al., 2015) and older youth tend to show greater levels of functional impairment compared to younger children (Piacentini et al., 2007; Valderhaug & Ivarsson, 2005). Furthermore, OCD related functional impairment has been shown to correlate positively with OCD symptom severity, anxiety-

Table 1
Studies comparing characteristics of younger versus older youth with OCD. Adapted and expanded from Selles et al., 2014.

	Younger group	Older group	Age used	Data source	Main difference: Younger group	Main difference: Older group
Geller et al. (2001)	Under 12 yrs (n = 46, 67,4% male)	12 and older (n = 55, 63,6% male)	Age at time of evaluation.	Consecutive referrals at OCD clinic.	Poorer insight. Higher occurrence of comorbid separation anxiety disorder and tics.	Higher occurrence of religious and sexual obsessions. Higher occurrence of comorbid major depressive disorder.
Farrell et al. (2006)	6–11yrs (n = 40, 57,5% male)	12–17yrs (n = 44.43,2% male)	Age at time of evaluation.	Baseline evaluations from a CBT trial.	Higher occurrence of comorbid specific phobia and oppositional defiant disorder.	Higher occurrence of contamination obsessions, washing and checking rituals. Shift to female preponderance.
Mancebo et al. (2008)	6–12yrs (n = 20, 65% male)	13–18yrs (n = 44, 68,2% male)	Age at time of evaluation.	Evaluations as part of naturalistic follow-up.		Higher occurrence of aggressive obsessions.
Nakatani et al. (2011)	3–9yrs (n = 151, 58,9% male)	10–17yrs (n = 214, 58,4% male)	Retrospective age of onset.	Archival analysis on routine clinical practice data.	Higher occurrence of comorbid tics.	Higher occurrence of ordering and repeating compulsions.
Selles et al. (2014)	3–9yrs (n = 99, 54,5% male)	10–18yrs (n = 193, 48,2%)	Age at time of evaluation.	Baseline evaluations from a CBT trial combined with data from a single time point evaluation study on pediatric OCD characteristics.	Poorer insight. Higher occurrence of comorbid ADHD. Higher parent rated anxiety symptoms. Higher occurrence of hoarding compulsions.	Higher occurrence of comorbid depression. Higher occurrence of sexual, magical thinking and somatic obsessions. Higher occurrence of checking, counting and magical thinking compulsions.
Skriner et al. (2016).	5–8yrs (n = 127, 47,2% male)		Age at time of evaluation.	Baseline evaluations from a CBT trial.	Severity levels similar to studies with older children. High rates of comorbid ADHD, ODD, tics and anxiety disorders. Low rates of depression.	
Peris et al. (2017)	7–9yrs (n = 58)	10-13 (n = 148) and 14–17 (n = 116)	Age at time of evaluation.	Baseline assessments at a university-based clinic.		Higher rates of externalizing and internalizing comorbid disorders. Adolescents had a sixfold increase in comorbid depression compared to children.

and depressive symptoms as well as global functional impairment (Nadeau et al., 2013; Piacentini et al., 2003, 2007; Storch et al., 2010).

Selles et al. (2014) note that it is a possible limitation of their study that data on age of onset was not collected. They speculate that the differences they find between the younger and older groups might be better explained by early or late onset of OCD symptoms. They also mention that duration of illness might be associated with greater severity and comorbidity as some research has suggested (de Mathis et al., 2013; Nakatani et al., 2011). Furthermore, it is worth noting that most previous studies on developmental differences in pediatric OCD (5 of 7) have been conducted in the US and all of the previous studies are situated within an English-speaking cultural context. It is important to examine OCD symptoms and developmental differences in more diverse samples than are reported in Table 1. There is a possible cultural effect on the presentation and development of OCD symptoms as well as a possibility of an effect of different systems of social supports and healthcare. We will extend previous research by using a large representative sample outside of an English language societal and cultural context and by including age of onset and duration of illness in our analyzes.

The aim of the current study is to compare the adolescent (12–17 years) and child (7–11 years) subgroups in a large sample of children with OCD that underwent systematic and careful diagnostic workup. In a previous study by our research group younger children (age 7–11 years) were found to respond significantly better to CBT compared to older children (age 12–17 years) (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Hybel, et al., 2015).(Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). We will use the same age cut-off in this study which was also previously used by Farrell et al. (2006) and Geller et al. (2001). We will compare the age groups in terms of (1) OCD severity, (2) OCD symptom profile (3) comorbid symptoms and (4) OCD related functional impairment. We will also examine these measures with regards to prepubertal and adolescent onset of OCD for the older group and with regards to duration of illness.

We predict, based on previous findings, that overall severity will be similar between the groups, that the younger group will have higher rates of comorbid tic disorder, ADHD, ODD and anxiety symptoms as well as poorer insight. We also predict that the older group will have higher rates of comorbid depression, higher levels of sexual obsessions and checking rituals as well as greater functional impairment.

2. Method

2.1. Participants

A total of 269 children and adolescents aged 7–17 years, recruited from Denmark, Sweden, and Norway between September 2008 and June 2012, were included in the Nordic Long-Term Obsessive-Compulsive Disorder Treatment Study (NordLOTS) (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). Included patients were referred from primary care community health centers, general practitioners or parents contacted the clinics directly, leading to a representative sample of pediatric patients seeking treatment for OCD. Inclusion criteria were an OCD diagnosis based on DSM-IV criteria confirmed with the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL), a Children's Yale-Brown Obsessive--Compulsive Scale (CY-BOCS) total severity score $\geq$16, and no treatment with CBT or effective doses of SSRIs (>50 mg) six months prior to the start of the study. Exclusion criteria included the presence of another psychiatric disorder with higher treatment priority. Study rationale (Ivarsson et al., 2010) and inclusion procedures (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015) for the NordLOTS are described in detail elsewhere. Informed consent was obtained from all participants and their parents, and the trial was approved by the Norwegian, Swedish, and Danish Committees for Medical and Health Research Ethics and the Medical Products Agencies. In the current study the sample was divided into two subgroups on the basis of age at assessment.

2.2. Measures

2.2.1. CY-BOCS

The CY-BOCS is a semi-structured interview used to evaluate OCD severity and symptom presentation. In the current study the CY-BOCS was administered by an independent evaluator. The CY-BOCS comprises two parts. The first part is a 74-item symptom checklist assessing a broad range of current and past obsessions and compulsions. The second part, a severity scale, consists of 10 questions (five concerning obsessions and five concerning compulsions) that measures severity on a five-point scale, with a total score ranging from 0 to 40 (Scahill et al., 1997). The CY-BOCS symptom checklist includes one item regarding hoarding obsessions and one item regarding hoarding compulsions as well as two additional items where the clinician can report symptoms of hoarding obsessions and compulsions other than the those defined in the checklist. If patients currently had any of these symptoms, they were classified as having hoarding symptoms in this study.

Indecision was measured with one item on the CY-BOCS (item 13), based on a Likert scale from 0 = no indecision to 4 = very indecisive. Insight was likewise measured with an item on CY-BOCS (item 11) based on a Likert scale ranging from 0 = "good insight" to 4 = "bad insight".

The CY-BOCS has demonstrated reliability and validity in samples of children with OCD (Scahill et al., 2014; Storch et al., 2004). In the NordLOTS, the intra-class correlation coefficients (*ICC*) of inter-rater agreement were as follows: obsessions *ICC* = 0.94 (95% *CI* 0.85–0.97), compulsions *ICC* = 0.87 (95% *CI* 0.67–0.93), and total score *ICC* = 0.92 (95% *CI* 0.78–0.97) (Thomsen et al., 2013).

2.2.2. K-SADS-PL

K-SADS-PL is a diagnostic, semi-structured interview designed to assess a broad range of child and adolescent mental disorders according to DSM-IV criteria. The interview comprises an introductory interview, a screening interview, and a diagnostic part. Symptoms are scored as one of "not present," "possible," "in remission," or "certain" (Kaufman et al., 1997). K-SADS-PL has been shown to possess good inter-rater reliability (98%) and has a 1–5 week test–retest kappa of 0.80 for all included anxiety diagnoses (Kaufman et al., 1997). The interview has been shown to have good convergent and divergent validity (Kragh et al., 2018; Lauth et al., 2010; Villabo, Oerbeck, Skirbekk, Hansen, & Kristensen, 2016). This study used present diagnoses classified as "certain."

2.2.3. The child obsessive-compulsive impact scale – revised (COIS-R)

COIS-R is a 33-item, self-reported questionnaire designed to assess the psychosocial functioning of children and adolescents in home, school, and social settings and to assess how OCD affects such functioning. Parent and child rating versions are available. Scale items are scored on a four-point Likert scale (0 = not at all, 1 = just a little, 2 = pretty much, and 3 = very much). The scale has moderate to high internal consistency of $\alpha = 0.92–0.94$ and $\alpha = 0.78–0.92$, respectively, for the parent and child versions (Piacentini et al., 2007; Skarphedinsson et al., 2015).

2.2.4. Child behavior checklist (CBCL)

The CBCL is used to evaluate child behavioral and emotional problems, as well as social competence. The scale, rated by parents, has 113 items on a three-point scale (0 = not true, 1 = somewhat or sometimes true, and 2 = very or often true). It has been shown to have good psychometric properties across different populations, mean test–retest reliability between 0.95 and 1.00, and internal consistency from $\alpha = 0.78$ to $\alpha = 0.97$ (Achenbach, 1994; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

2.2.5. Family accommodation scale

The Family Accommodation Scale (FAS) (Calvocoressi et al., 1999) is a 12-item clinician-administered interview that assesses the family's accommodation of their child's OCD symptoms. The FAS has been shown to have good internal consistency ($\alpha = 0.76$–0.80) (Calvocoressi et al., 1999; Geffken et al., 2006) and to correlate positively with measures of OCD symptom severity (Storch et al., 2007) and family discord (Calvocoressi et al., 1999). In the NordLOTS study sample, the internal consistency was $\alpha = 0.87$ (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015).).

2.2.6. The mood and feelings questionnaire (MFQ)

The MFQ is a parent and child rated questionnaire that is used to assess symptoms of depression based on the DSM–III–R. The scale comprises 13 items, scored in total from 0 to 26. The assessment has sound psychometric properties, and the scale's total score has demonstrated internal consistency of $\alpha = 0.75$ (Messer et al., 1995) and of $\alpha = 0.90$ in the current sample. (Messer et al., 1995; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

2.2.7. Screen for child-anxiety-related emotional disorders (SCARED)

The SCARED is a parent and child rated questionnaire used to measure symptoms of anxiety based on the DSM-IV, scored from 0 to 82. Its total score has demonstrated internal consistency of $\alpha = 0.92$ for both child- and parent-rated versions (Ivarsson, Skarphedinsson, Andersson, & ; Torp, Dahl, Skarphedinsson, Compton, et al., 2015).

2.2.8. Age of onset, age at assessment and duration of illness

Age at assessment was used primarily to divide the sample into older and younger groups. During initial evaluation, all participants were also asked when they had first been diagnosed with OCD and that age of first diagnoses is used as age of onset. The difference between age of onset and age at assessment was used to ascertain duration of illness.

2.3. Analyses

In the current study the sample was divided into two subgroups on the basis of age at assessment. Children 7–11 years comprised the younger group ($n = 85$) and children 12–17 years comprised the older group ($n = 184$). Independent sample *t*-tests were used to examine between group differences on continuous dependent variables from symptom rating scales and Pearson *Chi-Square* to examine between group differences on categorical variables, i.e., namely K-SADS-PL diagnoses and CY-BOCS symptom categories.

Since it has been suggested that age of onset and duration of illness could explain differences in symptom profiles and comorbidity between older and younger groups with OCD (R. Selles et al., 2014) we used the age of OCD onset to divide the sample into three subgroups; younger (and early onset group) (age 7–11 years, $n = 80$), older and early onset group (age 12 years or older, onset before 12 years of age, $n = 38$) and the older and later onset group (age 12 years or older, onset age 12 or later, $n = 114$). This is primarily an explorative study and therefore we do not correct for multiple comparisons.

We used ANOVA (for continuous variables) and logistic regression (for categorical variables) to examine between group differences for these three subgroups. Tukey post hoc tests were used where further analysis is called for. Linear regression was used to examine the effect OCD duration as a continuous variable.

All statistical analyses were done using SPSS 26 and $p < 0.05$ was considered to indicate statistical significance.

3. Results

Overall OCD severity as measured by the CY-BOCS total score did not differ between the two age groups ($t(266) = -1{,}03$, $p = 0{,}30$) nor did the severity of obsessions ($t(266) = -1{,}82$, $p = 0{,}07$) or compulsions ($t(266) = -0{,}08$, $p = 0{,}94$) (Table 2).

ADHD was significantly more prevalent in the younger group ($\chi^2 1) = 4.43$, $p = 0{,}05$) as well as disruptive disorders, ODD or CD (χ^2 (1) = 6.97, $p < 0{,}01$). No significant differences were found in regard to the comorbidity with tic disorders (χ^2 (1) = 0.23, $p = 0{,}64$) and anxiety disorders (χ^2 (1) = 1.31, $p = 0{,}25$). In the current sample the older group did not have higher levels of comorbid depression (χ^2 (1) = 0.02, $p = 0{,}89$) (see Table 2).

CBCL total problem score was higher for the younger group ($t(211) = -2{,}52$, $p < 0{,}01$) as well as the CBCL Externalizing problem scores (*t*

Table 2
Group differences on symptom rating scales and K-SADS-PL diagnoses.

	Age groups		
	Older (≥ 12. n = 182)	Younger (<12. n = 85)	Group difference
Percent female	53%	49%	$\chi^2 = 0.09$. p = 0.77
CBCL Internalizing, M (SD)	14.96 (9.04)	16.09 (8.61)	$t = -0.93$. p ≤ 0.37
CBCL Externalizing	8.21 (7.28)	10.85 (8.92)	**$t = -2.24$. p = 0.03**
CBCL Total	40.73 (22.45)	49.77 (25.11)	**$t = -2.52$. p < 0.01**
SCARED Panic - Parent rated	3.21 (4.11)	3.94 (4.45)	$t = -1.28$. p = 0.20
SCARED GAD - Parent rated	6.68 (4.36)	7.42 (4.22)	$t = -1.3$. p ≤ 0.20
SCARED SAD - Parent rated	5.36 (4.73)	7.72 (4.82)	**$t = 3.86$. p < 0.01**
SCARED SOP - Parent rated	4.14 (4.00)	4.19 (3.64)	$t = 0.89$. p = 0.93
SCARED OCD - Parent rated	9.16 (4.16)	8.46 (3.57)	$t = 1.23$. p = 0.20
SCARED Total - Parent rated	19.41 (13.44)	23.28 (12.85)	**t=-2.13. p=0.03**
SCARED Panic - Child rated	0.37 (0.35)	0.32 (0.32)	$t = 0.98$. p ≤ 0.33
SCARED GAD - Child rated	0.85 (0.51)	0.60 (0.41)	**$t = 3.75$. p < 0.01**
SCARED SAD - Child rated	0.41 (0.31)	0.59 (0.36)	**t=-4.06. p < 0.01**
SCARED SOP - Child rated	0.66 (0.53)	0.70 (0.51)	$t = -0.61$. p = 0.54
SCARED OCD - Child rated	1.00 (0.41)	0.92 (0.42)	$t = 1.43$. p = 0.15
SCARED Total - Child rated	21.93 (12.95)	21.67 (12.24)	$t = 0.15$. p = 0.88
MFQ - Parent rated	6.43 (5.50)	6.90 (5.69)	$t = -0.62$. p = 0.53
MFQ - Child rated	6.80 (5.07)	5.64 (4.51)	$t = 1.77$. p = 0.08
CYBOCS Obsessions	12.49 (2.66)	11.82 (3.02)	$t = 1.82$. p = 0.07
CYBOCS Compulsions	12.33 (2.65)	12.31 (2.76)	$t = 0.08$. p = 0.94
CYBOCS Total Score	24.82 (4.93)	24.13 (5.43)	$t = 1.03$. p = 0.30
FAS	15.84 (12.15)	19.14 (11.51)	$t = -1.83$. p = 0.07
COIS – Parent rated	25.55 (19.68)	25.61 (17.12)	$t = -0.25$. p = 0.98
COIS – Child rated	21.12 (14.62)	16.91 (13.41)	**$t = 2.09$. p = 0.38**
Comorbid disorders (K-SADS-PL)			
Depressive disorders, *n (%)*	7 (3.8%)	3 (3.5%)	$\chi^2 = 0.02$. p = 0.89
Anxiety disorders	32 (17.6%)	20 (23.5%)	$\chi^2 = 1.31$. p = 0.25
ADHD	10 (5.5%)	11 (12.9%)	**$\chi^2 = 4.43$. p = 0.05**
ODD or CD	3 (1.6%)	7 (8.2%)	**$\chi^2 = 6.97$. p < 0.01**
Tic disorders	32 (17.6%)	17 (20%)	$\chi^2 = 0.23$. p = 0.64

(243) = 2,24, p = 0,03).

No significant differences were found between the two groups on continuous measures of self or parent rated depressive symptoms (MFQ C/P) or family accommodation (FAS). However, several differences were observed on self or parent rated anxiety symptoms as assessed by the SCARED. Overall parental SCARED scores were higher for the younger group (t(252) = 2,13, p = 0,03). Separation anxiety scores (child- and parent rated) were higher for the younger group t(254) = 3,86, p < 0,01 and t(252) = 4,06, p < 0,01). However, self-rated generalized anxiety was higher for the older group (t(253) = -3,75, p < 0,01).

The older group showed significantly higher levels "miscellaneous obsessions" (χ^2 (1) = 4.28, p = 0,04), and "miscellaneous compulsions" (χ^2 (1) = 7.33, p = 0,01) on the CY-BOCS. With regards to miscellaneous obsessions more older children reported; "the need to know or remember" (p = 0.02) and "fear of not saying just the right thing" (p = 0.001). With regards to miscellaneous compulsions more older children reported; "the need to do things until they feel just right" (p < 0.001), and "compulsions involving blinking or staring" (p = 0.034). The older group also had higher levels of mental compulsions (χ^2 (1) = 11.8, p < 0,001) and magical/superstitious compulsions (χ^2 (1) = 5.03, p = 0,003).

In the younger group more individuals had poor insight (χ^2(1) = 5.11, p = 0,02) (see Table 3).

Our prediction that higher levels of functional impairment would be observed in the older group was partially supported as COIS-R self-report scores were higher for the older group (t(244) = 2,09, p = 0,038). There was no difference between the groups on the parent rated COIS-R, however.

We also defined three groups by age of onset. The younger/early onset group had a mean duration of illness of 0.79 (SD = 1.48) years, the older/late onset group had a mean duration of illness of 0.72 (SD = 1.11) years while the older/early onset group had a mean duration of illness of 3.6 (SD = 2.5) years. We compared these three groups using all the continuous measures reported in Table 2. The results mirror those presented in Table 2 closely with significant between group differences found for parent rated separation anxiety (F(2,219) = 9.563, p = 0.001), child rated separation anxiety on (F(2,216) = 6.153, p = 0.003), and child rated generalized anxiety (F(2,217) = 7.763, p = 0.001) on the SCARED. We also found the same significant results on the CBCL, for total score (F(2,181) = 4.274, p = 0.01) and for Externalizing symptoms (F(2,211) = 4.637, p = 0.01). The only significant finding in this analysis that was not present in the older vs younger analysis is for obsession subscale scores on the CY-BOCS (F(2,229) = 22.374, p = 0.047) showing that the older/early onset group scored significantly higher than the older/late onset group (using the Tukey post-hoc test). We didn't find any significant differences on comorbidity. With regards to symptom profile the results again mostly mirror the results for the older vs younger analysis reported in Table 3. However magical/superstitious compulsions were not significantly different in the logistic regression model. The only new finding in this analysis was that repeating compulsions were more common in the older/late onset group than in the older/early onset group (χ^2(1) = 5.74, p = 0.02).

We also examined OCD duration as a continuous variable with linear regression. Longer OCD duration turned out to significantly predict higher levels of CBCL internalizing symptoms (F(1,209) = 6.898, p = 0.009) and more severe compulsive symptoms on the CY-BOCS (F (1,230) = 4.736, p = 0.03). With regards to symptom profiles longer duration predicted a higher likelihood of having contamination (F (1,230) = 7.562, p = 0.006) and religious obsessions (F(1,230) = 7.51, p = 0.007) as well as cleaning (F(1,230) = 5.093, p = 0.025) and miscellaneous compulsions (F(1,230) = 6.967, p = 0.009).

Table 3
Age Group differences on OCD symptom categories.

CYBOCS symptoms category	Age groups		
	Older (≥ 12. n = 183)	Younger (<12. n = 85)	Group difference
Contamination obsessions, *n* (%)	117 (63.9%)	54 (63.5%)	χ^2 = 0.04. p = 0.95
Aggressive obsessions	108 (59.0%)	44 (51.8%)	χ^2 = 1.24. p = 0.27
Sexual obsessions	23 (12.6%)	8 (9.4%)	χ^2 = 0.57. p = 0.45
Hoarding obsessions	42(23.0%)	15 (17.6%)	χ^2 = 0.96. p = 0.32
Magical obsessions	69 (37.7%)	24 (28.2%)	χ^2 = 2.29. p = 0.13
Somatic obsessions	62 (33.9%)	25 (29.4%)	χ^2 = 0.53. p = 0.47
Religious obsessions	45 (24.6%)	18 (21.2%)	χ^2 = 0.38. p = 0.54
Symmetry obsessions	71 (38.8%)	26 (30.6%)	χ^2 = 1.69. p = 0.19
Miscellaneous obsessions	119 (65.0%)	44 (51.8%)	**χ^2 = 4.28. p = 0.04**
Cleaning compulsions	132 (72.1%)	56 (65.9%)	χ^2 = 1.08. p = 0.29
Checking compulsions	119 (71.7%)	47 (55.3%)	χ^2 = 2.33. p = 0.13
Repeating compulsions	100 (54.6%)	36 (42.4%)	χ^2 = 3.51. p = 0.06
Counting compulsions	62 (33.9%)	21 (25.3%)	χ^2 = 2.29. p = 0.13
Symmetry/ordering compulsions	73 (39.9%)	33 (38.8%)	χ^2 = 0.03. p = 0.87
Hoarding compulsions	42 (23.0%)	17 (20.0%)	χ^2 = 0.41. p = 0.52
Magical/superstitious compulsions	66 (36.1%)	19 (22.4%)	**χ^2 = 5.03. p = 0.03**
Involve others compulsions	113 (61.7%)	57 (67.1%)	χ^2 = 0.71. p = 0.40
Mental compulsions	88(48.1%)	22 (25.9%)	**χ^2 = 11.8. p < 0.01**
Miscellaneous compulsions	128 (69.9%)	45 (52.9%)	**χ^2 = 7.33. p < 0.01**
Poor insight	52 (28.4%)	36 (42.4%)	**χ^2 = 5.11. p = 0.024**

4. Discussion

The current study examines differences and similarities between younger children and adolescents with OCD in a large sample outside of an English language cultural context.

In line with the current literature, severity of OCD symptoms was similar between age groups. In contrary to our hypothesis, we did not find higher levels of sexual obsessions or checking compulsions in the older group. However, in the older group, we found significantly higher levels of mental compulsions as well as higher levels of miscellaneous compulsions and obsessions. To our knowledge this is a novel finding and might indicate, since these CY-BOCS items are not unitary, that older youths have more diverse and not easily categorized symptoms than younger children although this does not seem to increase overall severity. We predicted that overall severity of psychopathology would not differ between the older and younger groups. However, the CBCL total problem and externalizing problem scores were higher for the younger group, indicating a higher general level of psychopathology.

Previous research has generally indicated that older children show more OCD related functional impairment (Piacentini et al., 2007; Valderhaug & Ivarsson, 2005). This proved to be the case in this sample for self-report but not for parent report of functional impairment. It is however possible that this effect is best explained by the underreporting of impairment by younger children. The underreporting of OCD related symptoms by children is well known and taken together with poorer level of insight in younger children, the high discrepancy between child- and parent reported functional impairment in the younger group seems quite plausible. Another possible explanation is that mental compulsions are more frequent in the older group and perhaps such compulsions are

particularly impairing in the complex and demanding social context of adolescence.

We found less difference in comorbidity between the older and younger subgroups than in most previous studies, perhaps most notably with regards to depression, which might go some way towards explaining why functional impairment is similar overall. In contrast to previous studies (D. A. Geller et al., 2001; Peris et al., 2017; R. Selles et al., 2014) comorbid depression was not different between groups in the current study. However, the rate of comorbid depression, in this sample, was much lower than in other similar OCD samples (Torp, Dahl, Skarphedinsson, Thomsen, Valderhaug, Weidle, Melin, et al., 2015). In addition, the mental health services in Scandinavia are free and inclusive, thus, making early intervention more accessible, which may reduce any subsequent secondary problems. It is also possible that this difference is explained by most other studies using samples from secondary or tertiary clinical sources while the current study uses a primary care sample.

Poor insight was more prevalent in the younger group which is a consistent finding in studies comparing older and younger youths with OCD (R. Selles et al., 2014; R. R. Selles et al., 2018). This is not surprising, as development and lower degree of maturity in younger children is expected and might explain this finding.

Rates of comorbid anxiety disorders were not significantly different between the two groups although there is some evidence of more separation anxiety symptoms in the younger group and more parental rated anxiety symptoms overall. Some previous studies have indicated higher rates of anxiety disorders in the younger subgroup (D. A. Geller et al., 2001; Skriner et al., 2016). However, older children self-reported more severe general anxiety disorder scores than the younger group which is another finding not reported in any previous study to our knowledge. It is possible that a higher level of insight in the older group contributes to more awareness of their general anxiety level than the younger group, elevating the self-reported GAD score.

In previous studies, younger children with OCD have been consistently found to have a higher frequency of tic disorders compared to adolescents with OCD (D. A. Geller et al., 2001; Nakatani et al., 2011; Skriner et al., 2016). However, we did not observe that. This result remained the same when we split older children in to early and later onset subgroups. Lewin et al. (2014) have also considered age of onset in this context (although with different age group definitions) and found no significant association between age of onset and comorbid tic disorder in OCD. As in previous studies, we found higher rates of comorbid ADHD and disruptive disorders in the younger group. This seems to be among the most consistent finding in studies looking at differences in comorbidity in younger versus older children with OCD.

Our secondary analyses dividing the older groups into two subgroups by early onset and longer duration of illness or late age of onset and shorter duration of illness did not impact the conclusions to a great extent. The only new significant finding from this analysis is that the later age of onset group had higher levels of repeating compulsions. We also examined OCD duration specifically as a continuous variable and found that it did not predict overall OCD severity, functional impairment nor any comorbidities. It however did predict more severe compulsions as well as a higher likelihood of contamination obsession and cleaning compulsions.

All previous studies looking at developmental differences in the presentation and comorbidity of OCD are from English speaking countries; five studies are from the United States, one from Australia (Farrell et al., 2006) and one from the UK (Nakatani et al., 2011) (Table 1). However, the study of Farrell (2006) was limited by a small sample size and the study of Nakatani (2011) by the lack of structured diagnostic interviews. Nakatani (2011) furthermore defines younger and older groups by retrospective age of onset rather than age at evaluation rendering it methodologically different from the majority of studies in this area. The current study represents the first sample where the age specific presentation of OCD is examined in a non-English speaking cultural context and the largest sample using age at evaluation to define groups and a structured diagnostic interview to diagnose comorbidity and OCD severity. The current study was conducted within the Scandinavian health care system, i.e. patients had low or no costs for services, likely leading to a highly representative sample of children with OCD in general (Ivarsson et al., 2014). It is furthermore possible that the Scandinavian model of social- and healthcare services which is quite different from the US model could have a subtle but measurable effect on such variables as symptom severity, comorbidity and functional impairment and might partially explain the lower levels of comorbidity in this sample compared to others in similar studies.

The main strengths of the current study are a large and highly representative sample and a thorough and systematic assessment process. Unfortunately, comparisons with other studies are difficult, because no consensus exists on how to define age groups and how to divide age of onset into older and younger sub-groups. We chose to categorize children as prepubertal and pubertal in line with Geller (2001) and Farrell (2006). It is important to note that the early onset and longer duration of illness subgroup of older children was quite small (38 children) so even though we did not find it to differ greatly from other subgroups it is entirely possible that a larger sample would yield different results. In addition, the ethnic homogeneity of the sample, with 97% Scandinavian participants, may limit the generalizability of the results.

5. Conclusion

The current study used a large Scandinavian sample to examine differences in comorbidity and symptom profiles between younger and older children with OCD. We found a poorer level of insight and a higher prevalence of ADHD and ODD for the younger group which corresponds well with earlier research. Clinicians should be aware of these differences as this highlights the need to assess and monitor these comorbid disorders and to adjust treatment both to comorbidity and to level of insight, especially in younger children with OCD.

Overall, we found less differences between the age groups than previous research and defining groups by age of onset rather than age at evaluation does not seem to impact results to any great extent. Mental health services in Scandinavia are free of cost, making early intervention more accessible, which may reduce subsequent secondary problems and explain these findings.

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Contributors

All authors participated in conceptualizing and designing the paper.

OS was in charge of statistical analysis and drafting the paper under the supervision of GS.

All authors critically read, commented on and revised the paper. All authors approved the final manuscript.

Author statement

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Paper II

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Exploring Latent Clusters in Pediatric OCD based on Symptoms, Severity, Age, Gender, and Comorbidity

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Abstract

Background: Given diverse symptom expression and high rates of comorbid conditions, the present study explored underlying commonalities among OCD-affected children and adolescents to better conceptualize disorder presentation and associated features.

Methods: Data from 830 OCD-affected participants presenting to OCD specialty centers was aggregated. Dependent mixture modeling was used to examine latent clusters based on their age- and gender adjusted symptom severity (as measured by the Children's Yale-Brown Obsessive-Compulsive Scale; CY-BOCS), symptom type (as measured by factor scores calculated from the CY-BOCS symptom checklist), and comorbid diagnoses (as assessed via diagnostic interviews).

Results: Fit statistics favored a four-cluster model with groups distinguished primarily by symptom expression and comorbidity type. Fit indices for 3-7 cluster models were only marginally different and characteristics of the clusters remained largely stable between solutions with small clusters of distinct presentations added in more complex models.

Conclusions: Rather than identifying a single classification system, the findings support the utility of integrating dimensional, developmental, and transdiagnostic information in the conceptualization of OCD-affected children and adolescents. Identified clusters point to the centrality of contamination concerns to OCD, relationships between broader symptom expression and higher levels of comorbidity, and the potential for complex/neurodevelopmental presentations.

Keywords: Obsessive-compulsive disorder; assessment; symptomatology; comorbidity

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Study concept and design: Selles, Best, Stewart, Højgaard, Smárason & Skarphedinsson.

Acquisition, analysis, or interpretation of data: All authors.

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Study supervision: Selles, Stewart, Smárason, Højgaard and Skarphedinsson.

Background

Obsessive compulsive disorder (OCD) is an impairing psychiatric condition affecting approximately 1% of individuals across the lifespan [1], with onset commonly occurring between childhood and late adolescence [2]. Rather than topically-specific, OCD is defined by a psychopathological relationship (i.e., unwanted/distressing internal experiences that are avoided, reduced, or escaped via repetitive action [3] resulting in diverse symptom expression that appears influenced by developmental factors [4-6] and interactions with common comorbid concerns [7-9], such as anxiety, tic, and attention deficit hyperactivity disorders (ADHD) [10].

Various methods have been utilized to explore shared characteristics among OC-presentations. Factor analysis of the symptom checklist of the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) [11] has suggested symptoms coalesce around: 1) contamination obsessions and cleaning/washing compulsions; 2) harm/sexual obsessions and checking compulsions; and 3) symmetry obsessions and compulsions, with hoarding symptoms sometimes included or identified as their own factor [12-15] Unfortunately, frequent within-individual endorsement of symptoms across multiple dimensions limits the utility of these factors for informing individual-level classification of OCD-affected children and adolescents [12, 15].

Benefiting from a person- as compared to item-oriented approach, cluster-based analytic methods (e.g., dependent mixture modelling and latent class analysis [LCA]) have demonstrated utility in producing meaningful subgroups among youth with mental health

concerns [16]. While utilized to explore either OC-symptom expression or comorbid disorder presentations among OCD-affected individuals, these methods have not yet been utilized to examine both domains simultaneously. In OCD-affected adults, analyses based on symptom expression have identified frequency-[17] and etiologically-based clusters [18], while analyses of comorbidity among OCD-affected adults has suggested three- or four-class solutions based on number and type of comorbid disorders [8, 19]. Among pediatric samples, cluster analyses examining symptom expression have found similar groupings to factor-analytic studies [20, 21]. Højgaard et al. [9] examined comorbid profiles among OCD-affected children and adolescents and identified a three-class solution, characterized by those with no comorbidity, those with neurological/behavioral conditions (e.g., ADHD, tics, ODD), and those with comorbid anxiety disorders. Although OCD symptom types were not included in the model, secondary analyses suggested symmetry/hoarding symptoms were associated with both comorbid classes, harm/sexual symptoms were associated with the comorbid anxiety class, and comorbidity was less common among those with contamination/cleaning symptoms.

Identifying clusters of OCD-affected children and adolescents based on symptom expression, comorbid psychopathology, and demographic factors is consistent with recommendations towards dimensional and psychometrically-informed conceptualizations of psychopathology [22] and may shed additional light on common clinical presentations, offer insights regarding potential underlying transdiagnostic processes, and lead to improved specificity of care [23]. As a result, the present study seeks to replicate and expand on the work of Højgaard et al. [9, 14] by exploring latent clusters among a large, aggregated, international sample of OCD-affected children and adolescents.

Aim 1. Confirm a factor structure to develop factor loadings for use in the analysis. We hypothesized that a three-factor solution as in Højgaard et al. [14] (i.e., contamination/cleaning; harm/sexual; symmetry/hoarding) would provide an acceptable model fit. If a three-factor solution does not provide an acceptable fit in this sample, an exploratory factor analysis will be carried out to extract a usable factor structure.

Aim 2. Identify latent clusters representing sub-groups of OCD-affected children and adolescents based upon symptom factor scores, symptom severity, and the presence/absence of comorbid disorders. We hypothesized a four-class solution would emerge characterized by: A) contamination/cleaning symptoms and low comorbidity; B) harm/sexual symptoms and anxious comorbidity; C) symmetry/hoarding symptoms and neurobehavioral comorbidity; and D) multi-dimensional symptoms and multiple comorbid conditions.

Aim 3. Explore relationships of cluster membership with other available clinically relevant variables, including age of symptom onset, avoidance, impairment, and family accommodation.

Methods

Ethical Considerations:

All sites had ethics approval and obtained participant assent and family consent for participation in research and data sharing.

Participants and Procedures:

The present study includes data from 830 OCD-affected children and adolescents. Data was obtained by aggregating participants with completed CY-BOCS checklist data from seven

international pediatric OCD programs (see TableS1) (NordLOTS [24]; GBG [25]; DCS [26]; UBC POP [27]; Griffith [28]). All participants had a confirmed OCD diagnosis. Average OCD-Severity was in the moderate-severe range (mean = 24.5; SD = 5.9). The sample was 54% female and 5-19 years of age (mean = 12.9; SD = 2.9). Participant characteristics for individual programs and the combined sample are presented in Table 1.

Measures:

Diagnostic Assessments. For the majority of participants, baseline diagnoses were assessed and diagnosed using either the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime (n = 567; 68.3%) [29] or the Anxiety Disorder Interview Schedule for Children - Parent Version (n = 263; 31.2%) [30]. *OCD Symptoms and Severity.* OCD symptoms were assessed across all sites using the CY-BOCS, a measure with well-established psychometric properties [11, 31] . The CY-BOCS symptom checklist was utilized to assess presence of OCD symptom types. Symptom severity was assessed via the CY-BOCS total score, which is comprised of ten-items rated 0 to 4, with higher scores indicating more severe symptoms.

Additional Variables. The six CY-BOCS extension items, which evaluate, on a 0 to 4 scale, additional domains related to OCD (e.g., insight, avoidance, doubt) were also completed with many participants (n = 402-728; 49%-88%). While exact measure usage varied across sites (see TableS1), child- and parent-ratings of OCD-related impairment was assessed using variations of the Child Obsessive-Compulsive Impact Scale [32, 33] and family accommodation was assessed using variations of the Family Accommodation Scale [34-36]. While of interest to profile composition, less consistent measure completion across sites limited the feasibility of their

inclusion. Therefore, relationships between these variables and profiles were examined in a secondary analysis.

Analytic Plan:

Data processing and statistical analyses were conducted using Mplus 8.6[37]) and R version 4.0.3 (r-project.org). Two primary sets of analyses were conducted. First, an acceptable factor structure of the CY-BOCS symptom checklist variables was established. Checklist items were modelled as ordinal variables with diagonally weighted least squares to estimate model parameters and robust standard errors. Model fit statistics, including the comparative fit index (CFI), the Tucker-Lewis index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (RMSR) were calculated and compared across models, seeking the most parsimonious acceptable fit. Acceptable fit was defined as CFI and TLI values of at least 0.9. Factor structures derived from previously identified solutions by Højgaard et.al [14], and from an exploratory factor analysis of the current data were tested in a confirmatory factor analysis (CFA). Models were directly compared using the scaled chi-squared difference test [38] . Latent factor scores for each participant were generated based on the best fitting CFA model, using the R *lavaan* package (version 0.6-7) [39].

The second primary analysis entailed dependent mixture modelling with the R-package *depmixS4* (version 1.4-2) [40] to identify distinct latent groups underlying the observed data. Each participants factor scores extracted from the best-fitting CFA, total CY-BOCS score, and 9 comorbidities were included as the observed variables in this analysis. Child age and gender were treated as covariates using a stepwise approach, where factors were enumerated first using age and gender adjusted indicators and differences in factors then tested based on

relevant covariates (i.e., age of symptom onset, avoidance, impairment, and family accommodation). The continuous measures— the CFA-derived factors, CY-BOCS total, and child age—were normalized such that the minimum score was transformed to zero and the maximum score to one. Some checklist items were missing from specific sites ("*No concern with consequences of contamination other than how it might feel",* and "*Mental Compulsions"* were missing in Griffith; "*Checking that did not/will not harm others",* and "*Need to do things until it feels just right"* were missing in ATRC) and were excluded from the CFA analysis to maximize numbers of participants. Participants with CFA derived factor scores as well as other indicators (e.g., comorbidities) were included in the mixture model.

Mixture solutions ranging from 1 to 9 distinct groups were evaluated; Akaike Information Criterion [AIC] and Bayesian Information Criterion [BIC] were computed for each solution, with BIC providing a stronger penalty of model complexity [41, 42]. Additionally, entropy and average posterior probability for each observation's most likely group measures were computed to evaluate the quality of group separation, with values closer to 1 reflecting superior delineation of the groups [41, 43]. The likelihood ratio tests directly compared models using the difference in $\Rightarrow^2$ and degrees of freedom; a larger $\Rightarrow^2$ value indicates a larger difference in the models.

A final set of analyses examined between-cluster differences in secondary outcomes of interest. Prior to conducting between-cluster tests, children were assigned to the cluster to which they had the maximum posterior probability value of belonging. Omnibus cluster differences were identified with a p value threshold < .05 and were adjusted for study site. Follow-up pairwise comparisons used the Tukey correction for multiple comparisons.

Results

Descriptive statistics for the overall sample and each study site are provided in Table 1.

Factor Analysis of OCD Symptoms:

The previously identified three-factor model [14] was initially tested and did not meet requirements of acceptable fit in the current sample (see TableS3). Therefore, an exploratory factor analysis was conducted to suggest the composition of usable factor solutions. A parallel analysis suggested a ten-factor model. A visual scree plot inspection indicated four to six factors (Figure S1), and the 0.7 Kaiser criterion indicated six factors. Fit measures for three- to eleven-factor EFA models were examined further and all models with four factors or more had adequate fit, with fit values improving with each added factor (see TableS2).

A six-factor solution provided an acceptable fit (see TableS3) in a CFA. Although EFA results potentially suggest factor solutions with more factors, models with more than six factors failed to converge on an optimal solution in a CFA. The current six-factor model suggests CY-BOCS symptom checklist items can be attributed to contamination/cleaning, sexual/religious/embarrassment, somatic/illness, harm/checking, superstition/repetition, and hoarding/perfectionism latent factors. Factor loadings for the checklist items and correlations among the six factors are provided in TableS4 and TableS5, respectively.

Cluster Analysis of OCD Symptom Factors, Severity, Comorbidities and Demographics:

Nine possible solutions were generated by the dependent mixture model. Based on model fit criteria and visual interpretability, solutions involving 3-7 clusters were explored in further detail (See Figure 1). Table 2 provides model fit and descriptive outcomes of the

solutions and identified clusters, while Table 3 describes features associated with the identified clusters. Fit indices favored the four-cluster solution; however, all examined models demonstrated acceptable participant classification/entropy (0.8 or higher, see Table 2).

As observed in Figure 1 and described in Table 3, variation across clusters regarding contamination/cleaning symptoms, symptom severity, and gender distribution was mostly minimal except in more complex models. Clusters were most notably distinguishable by loadings on the other symptom factors and comorbidity patterns (variable specific entropy values for 3-7 cluster models are presented in TableS6). The overall characteristics of the first three identified clusters remained observable and somewhat consistent across subsequent models. In the four-cluster model, two distinct groups emerge; C2 (pink, see Figure 1) with a mixed symptom presentation, relatively lower contamination/cleaning scores compared to other symptom types, and high levels of comorbid disorders compared to other clusters; and C4 (green) a smaller group, high on contamination/cleaning scores but low on other symptom types and levels of comorbidity. However, these characteristics became less distinct in later models. C1 (light blue) and C3 (yellow) both present mixed profiles at moderate levels, mainly distinguishable by higher levels of comorbid Tics for C1. In the six-factor model, C6 (dark blue) emerged with a small but distinct subset of children and adolescents, with high rates of ASD, ADHD, tics, GAD, and Social Phobia. In the seven-factor model, C7 (grey) emerged with an additional small but distinct subset of mostly female youth who demonstrate high rates of ASD, low levels of other comorbidities and almost exclusively contamination/cleaning type symptoms.

Cluster Differences on Secondary Outcomes:

A final set of analyses compared latent clusters on secondary measures using the four-group solution as it showed the best BIC and had an acceptable entropy value (see TableS7). No significant differences were observed across clusters for CY-BOCS auxiliary items (Tukey-corrected $p > .05$) except for slowness where C3 (Yellow) demonstrated higher ratings compared to C4 (green). No differences were observed between clusters on age of onset, measures of impairment, or family accommodation (Tukey-corrected $p > .05$). TableS8 provides descriptive statistics from the 4-cluster solution for variables not included in other analyses (e.g., race, study site).

Discussion

Using dependent mixture modeling, the present study explored shared characteristics among a global sample of OCD-affected youth based on severity, symptom type, and comorbidity. After confirming a six-factor model for the CY-BOCS symptom checklist, our results suggested that youth could be acceptably classified into three to seven clusters, with a four-cluster solution offering optimal fit statistics, but more complex models identifying unique and clinically relevant sub-groups. Given this, and the limitation that cluster identification is dependent on the variables included (or not included) in the model, we have opted to present, describe, and note differences between clusters in the varying models, rather than highlighting a single model as "the" way that OCD-affected youth are most accurately classified. This open examination is possible in part due to the general stability of cluster characteristics across models.

Discussion of Cluster Characteristics:

The C1 (light blue, see Figure 1) cluster appears to feature low-moderate endorsement of symptoms across all six OCD symptom factors, average severity and demographics, and generally low frequency of internalizing comorbid disorders. Tics disorders and ADHD are however quite common. The C1 cluster initially comprised the second-largest proportion of the sample (23%), but steadily lost youth as additional clusters were added, decreasing to 18% of the sample by the 7-cluster model but remaining stable regarding its characteristics.

The C2 (pink) cluster is the largest cluster throughout all models, although it does shrink in proportion from 42% to 22%. These youth had more severe OCD symptoms, endorsed a varied symptom profile and had high comorbid Tics, ADHD as well as internalizing disorders in most models. These patterns suggest that increased diversity in symptom expression may be indicative of additional underlying fear/anxiety processes and/or cognitive-dysfunction (e.g., maladaptive beliefs, repetitive negative thinking) [44, 45] .

Comprised of approximately 20%-35% of the sample, cluster C3 (yellow) seems to represent a “median” presentation of OCD in most of the models, featuring average to low (in the five- and six factor models) severity and mixed symptom- and comorbidity profiles throughout.

C4 (green) emerges in the four-factor model as a small (14%) group of youth almost exclusively endorsing contamination/cleaning symptoms and showing low levels of comorbidity. Along with the consistent presence of contamination symptoms across the larger clusters, these findings suggest contamination symptoms are the most specific or central to OCD [14, 46]. In subsequent models however, C4 trends towards more mixed symptom expression and comorbidity profiles while remaining stable in size.

C5 (orange) initially identified 9% of the sample, favored males slightly and featured high severity, relatively high levels of superstition/repetition and harm/checking symptoms in the five and six-cluster models, but more predominant contamination/cleaning symptoms in the seven-cluster model. C5 increases slightly in size and trends toward high levels of anxiety comorbidities in the last two models.

Two small but distinct clusters emerged in the final two models. Distinguished by significantly higher frequencies of comorbid disorders and making up 9% of the sample, C6 (dark blue), showed average severity, high levels of perfectionism/hoarding and the highest levels of all clusters on ASD, ADHD and tics, indicative of a neuropsychological profile and/or difficulties in inhibitory control. In the seven-factor model C6 is distinguished by very low levels of contamination/cleaning symptoms, low severity and low internalizing comorbidity indicating that this is not a stable cluster between models. Making up 6% of the sample, C7 (grey) consisted mostly of females exclusively endorsing contamination/cleaning symptoms, showing overall low levels of comorbidity but higher levels of ASD.

The present results are not directly comparable to previous findings as we used a new six-factor structure for OCD-symptom dimensions. We, however, note similarities with the current best fitting four-cluster model and previous findings; with the almost exclusive endorsement of contamination/cleaning symptoms being associated with a low level of comorbidities [9], and a trend of more diverse OCD-symptom expressions being associated with higher comorbidity levels [8, 9] .

Limitations:

There are several limitations to note. First, while the study provides indications of cluster characteristics at the time of assessment, the study design does not inform the extent to which cluster distribution changes over time (e.g., if participants migrate from one group to another as they age), nor does it allow for direct testing of underlying mechanisms. Second, the clusters provide average scores of those included within that class, rather than clear and definable rules regarding class membership. As a result, applying these categorizations to any individual would be premature at this time. Third, secondary variables were compared between classes after making concrete class assignments (as opposed to allowing for partial class membership). This process overestimates confidence in class assignment. Entropy was strong but not perfect, meaning that there was good but not perfect confidence in identifying which participant was assigned to each cluster. Fourth, site-based variance might have been enhanced by lack of standardization of procedures, such as in how the CY-BOCS interview is conducted. Fifth, ASD diagnoses were based on the K-SADS and ADIS which are primarily symptom screeners of ASD caseness, and not adequate for establishing ASD diagnosis on their own. ASD diagnosis was an exclusion criterion in the NordLOTS study, resulting in the underrepresentation of comorbid ASD in the current sample. Sixth, the 5-7 factor models have fairly unequal class prevalence and simulation studies have indicated that in such models smaller classes may be difficult to recover at small sample sizes [43, 47]. Seventh, the enumeration of factors through the mixture modelling process is sensitive to how covariates are treated and the assumption of different population models to ours, regarding the effects of age and gender, might yield different results [47]. Eighth, although the sample was large and combined from global centers, these centers were specialized, age-specific, located within

countries with high development indexes and primarily Caucasian populations, and utilized dichotomized, rather than continuous, assessments of comorbidity. Given that results are dependent on sample characteristics and included variables, a different formation of clusters could occur if other variables (e.g., avoidance, other comorbidities) were included and the generalizability of results to other OCD-affected populations may be limited.

Conclusions:

The present study provides an explorative overview of potential latent sub-groups among OCD-affected children and adolescents. The identified clusters support efforts towards dimensional or transdiagnostic conceptualizations of psychopathology and, by identifying more homogenous subsets of OCD, based on relevant shared characteristics, may serve as translational markers for further investigations of relevant neurocircuitry and mechanisms of dysfunction, such as neurocognition, cognitive flexibility, inhibitory control, and fear extinction processes [48-51]. In informing clinical care, clusters provide an indication of potentially relevant adaptations to treatment, such as supplemental emphasis on cognitive processes and maladaptive beliefs, executive skills and impulse control, distress tolerance and emotion regulation, and/or parental roles and involvement. Replication of clusters in more diverse populations (e.g., additional countries, socio-economic groups, ages, and comorbidities) and among individuals with other primary disorders is warranted.

Key Points

- Characterization of OCD-affected youth is complicated by diverse symptom expression and comorbidity.
- This is the first study to simultaneously consider symptom expression, severity, comorbidity, gender, and age in the classification of OCD-affected youth.
- Dependent mixture modeling identified 3-7 possible clusters with symptom expression and comorbidity types as the factors most relevant to cluster composition.
- Notable patterns suggest lower comorbidity risk associated with isolated contamination concerns, more extensive symptom expression with comorbid internalizing disorders, and small clusters of youth with neurodevelopmental presentations/high comorbidity rates.
- The findings provide potential subgroupings to inform further exploration of dimensional, developmental, and transdiagnostic mechanisms of psychopathology as well as efforts to improve specificity of care.

Table 1. Participant characteristics for individual programs and the combined sample.

		Study Site							
Variable	Overall, N = 830[1]	GBG, N = 91[1]	ATRC, N = 56[1]	DCS-CBT, N = 153[1]	Griffith, N = 114[1]	Iceland, N = 4[1]	Nord-LOTS, N = 263[1]	UBC-POP, N = 148[1]	Site difference p-value[2]
Child Age	12.9 (2.9)	12.9 (2.6)	13.5 (2.8)	12.4 (3.0)	12.2 (2.6)	12.5 (2.4)	12.8 (2.8)	13.7 (3.1)	<0.001
Age of Onset	8.7 (3.4)	9.8 (2.9)	-	8.2 (3.4)	8.6 (3.2)	-	8.8 (3.5)	8.5 (3.5)	0.018
<Missing>	<103>	<26>	<56>	<8>	<9>	<4>	<0>	<0>	
Age of Diagnosis	10.8 (4.2)	-	-	-	11.1 (2.9)	-	11.6 (3.0)	10.0 (5.2)	0.056
<Missing>	<360>	<91>	<56>	<153>	<21>	<4>	<35>	<0>	
OCD Severity	24.5 (5.9)	23.0 (5.9)	22.7 (5.7)	25.1 (6.1)	26.8 (4.0)	24.2 (3.0)	24.6 (5.1)	23.2 (7.4)	<0.001
Insight	1.3 (1.0)	-	1.3 (0.6)	1.1 (1.1)	1.6 (1.0)	-	1.1 (1.0)	1.6 (0.9)	<0.001
<Missing>	<102>	<91>	<0>	<0>	<1>	<4>	<0>	<6>	
Avoidance	1.8 (1.2)		-	1.5 (1.2)	2.2 (0.9)	-	1.8 (1.1)	2.0 (1.3)	<0.001
<Missing>	<158>	<91>	<56>	<0>	<1>	<4>	<0>	<6>	
Indecision	1.1 (1.1)		-	1.0 (1.2)	1.5 (1.1)	-	1.0 (1.1)	1.1 (1.1)	<0.001
<Missing>	<154>	<91>	<56>	<0>	<1>	<4>	<0>	<2>	
Responsibility	0.8 (1.0)		-	0.6 (0.9)	1.5 (1.1)	-	0.8 (1.0)	0.6 (0.8)	<0.001
<Missing>	<157>	<91>	<56>	<0>	<1>	<4>	<0>	<5>	
Slowness	1.2 (1.1)		-	1.2 (1.1)	1.5 (1.0)	-	1.1 (1.1)	1.3 (1.0)	0.010
<Missing>	<159>	<91>	<56>	<0>	<2>	<4>	<0>	<6>	
Doubt	1.0 (1.0)		-	0.9 (1.0)	1.7 (1.0)	-	-	0.9 (1.0)	<0.001
<Missing>	<418>	<91>	<56>	<0>	<1>	<4>	<263>	<3>	

Impairment (Parent)	31.1 (24.9)	56.3 (33.8)	-	15.6 (10.9)	41.0 (24.6)	-	25.7 (18.7)	35.7 (20.3)	<0.001
<Missing>	<181>	<7>	<56>	<8>	<7>	<4>	<92>	<6>	
Impairment (Child)	25.5 (2284)	41.7 (31.3)	-	14.0 (10.4)	40.4 (30.0)	-	19.9 (14.4)	25.5 (19.1)	<0.001
<Missing>	<185>	<17>	<56>	<16>	<9>	<4>	<60>	<23>	
Family	13.3 (12.0)	-	18.0 (10.6)	15.1 (8.4)	26.1 (10.1)	-	16.7 (12.0)	0,4(0.3)	<0.001
Accommodation									
<Missing>	<221>	<91>	<1>	<0>	<66>	<4>	<53>	<6>	
Gender, male	382 (46%)	38 (42%)	19 (34%)	78 (51%)	50 (44%)	1 (25%)	129 (49%)	67 (45%)	<0.001
Child Race									<0.001
American Indian	5 (0.6%)	-	-	0 (0%)	0 (0%)	0 (0%)	-	5 (3.3%)	
Asian	27 (3.3%)	-	-	2 (1.3%)	2 (2.1%)	0 (0%)	-	23 (15.5%)	
Black	8 (1.0%)	-	-	6 (3.9%)	0 (0%)	0 (0%)	-	2 (1.4%)	
Native Hawaiian/ Pacific Islander	0 (0%)	-	-	0 (0%)	0 (0%)	0 (0%)	-	0 (0%)	
White	347 (41.8%)	-	-	142 (93%)	92 (98%)	4 (100%)	-	109 (73.6%)	
Mixed Race	2 (0.4%)	-	-	2 (1.3%)	0 (0%)	0 (0%)	-	0 (0%)	
Other	10 (1.2%)	-	-	1 (0.7%)	0 (0%)	0 (0%)	-	9 (6.1%)	
<Missing>	<339>	<91>	<56>	<0>	<20>	<0>	<263>	<0>	
Ethnicity, Hispanic	28 (3.4%)	-	0 (0%)	24 (16%)	0 (0%)	0 (0%)	-	4 (2.7%)	<0.001
<Missing>	<283>	<91>	<0>	<0>	<20>	<0>	<263>	<0>	
Any Prior Treatment	351 (74%)	-	21 (38%)	99 (65%)	55 (79%)	-	-	102 (70%)	<0.001
<Missing>	<439>	<91>	<0>	<0>	<44>	<4>	<263>	<37>	
Current SSRIs	219 (26.5%)	53 (58.2%)	14 (25%)	44 (29%)	36 (32%)	-	0 (0%)	72 (48.6%)	0.041

<Missing>	<4>	<1>	<0>	<0>	<0>	<4>	<0>	<0>	
GAD	204 (24.6%)	11 (12%)	35 (62%)	34 (22%)	63 (55%)	1 (25%)	19 (7.2%)	40 (27%)	<0.001
Social Phobia	115 (13.9%)	8 (8.8%)	26 (46%)	19 (12%)	27 (24%)	4 (100%)	12 (4.6%)	19 (12.8%)	<0.001
Sep Anxiety	45 (5.4%)	3 (3.3%)	6 (11%)	9 (5.9%)	17 (15%)	0 (0%)	6 (2.3%)	4 (2.7%)	<0.001
Specific Phobia	123 (14.8%)	25 (27.5%)	17 (30%)	16 (10%)	39 (34%)	1 (25%)	20 (7.6%)	5 (3.4%)	<0.001
ADHD	127 (15.3%)	15 (16.5%)	8 (14%)	30 (20%)	14 (12%)	0 (0%)	23 (8.7%)	37 (25%)	<0.001
ODD/CD	64 (7.7%)	8 (8.8%)	7 (12%)	18 (12%)	12 (11%)	0 (0%)	10 (3.8%)	9 (6.1%)	<0.001
MDD/Dysthymia	88 (10.6%)	27 (29.7%)	11 (20%)	18 (12%)	11 (9.6%)	1 (25%)	8 (3.0%)	12 (8.1%)	<0.001
Tic Disorder	137 (16.5%)	26 (28.6%)	9 (16%)	7 (4.6%)	15 (13%)	0 (0%)	49 (19%)	31 (20.9%)	<0.001
ASD	29 (3.5%)	5 (5.5%)	0 (0%)	0 (0%)	18 (16%)	0 (0%)	1 (0.4%)	6 (4.1%)	<0.001

[1]Mean (SD) ; n (%)

[2]Kruskal-Wallis rank sum test; Pearson's Chi-squared test

Table 2. Outcomes of the dependent mixture modeling.

	3 Cluster			**4 Cluster**			**5 Cluster**			**6 Cluster**			**7 Cluster**		
AIC	16375.24			15736.28			15938.22			15908.63			15424.94*		
BIC	17163.72			16789.16*			17255.50			17490.31			17271.01		
Entropy[a]	0.86			0.90*			0.86			0.86			0.89		
LRT $\Rightarrow^2$(df)[b]				316.8 (21)			150.9 (21)			107.8 (21)			116.9 (21)		
Factors	*Fit*[c]	*n*	*%*	*Fit*[c]	*n*	*%*	*Fit*[c]	*n*	*%*	*Fit*[c]	*n*	*%*	*Fit*[c]	*n*	*%*
C1 (Light Blue)	0.91	194	23	0.93	200	24	0.90	190	23	0.90	160	19	0.93	151	18
C2 (Pink)	0.95	345	42	0.96	350	42	0.93	265	32	0.90	200	24	0.94	183	22
C3 (Yellow)	0.94	291	35	0.92	165	20	0.89	164	20	0.92	150	18	0.90	160	19
C4 (Green)	-	-	-	0.98	115	14	0.91	130	16	0.94	140	17	0.91	118	14
C5 (Orange)	-	-	-	-	-	-	0.91	81	9	0.87	109	13	0.88	92	11
C6 (D. Blue)	-	-	-	-	-	-	-	-	-	0.87	71	9	0.95	75	9
C7 (Grey)	-	-	-	-	-	-	-	-	-	-	-	-	0.99	51	6

Notes.

AIC = Akaike information criterion. BIC = Bayesian information criterion. LRT = log-likelihood ratio test.

[a] Entropy values range from 0 to 1 (better separation between factors).

[b] The log-likelihood ratio test compares two adjacent models (e.g., 3-factor versus 4-factor). Larger values represent a bigger improvement in model fit from the simpler to more complex model. Across all comparisons, $p < .001$.

[c] Fit is defined as the average posterior probability of belonging to this particular group after assigning individuals to groups based on their maximum posterior probability. Optimally= 1.0

*indicates best fit

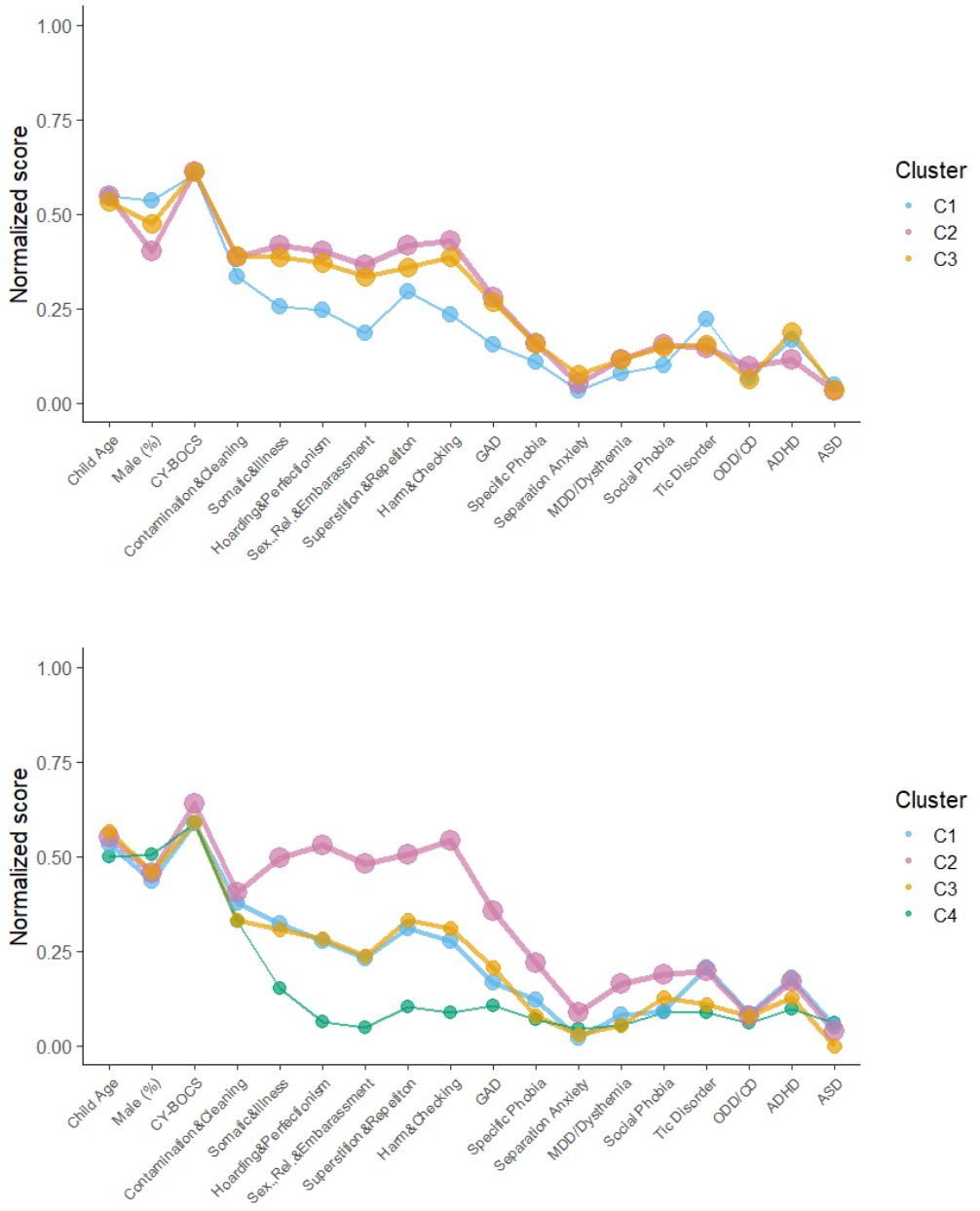
Table 3. Descriptive interpretation of identified clusters.

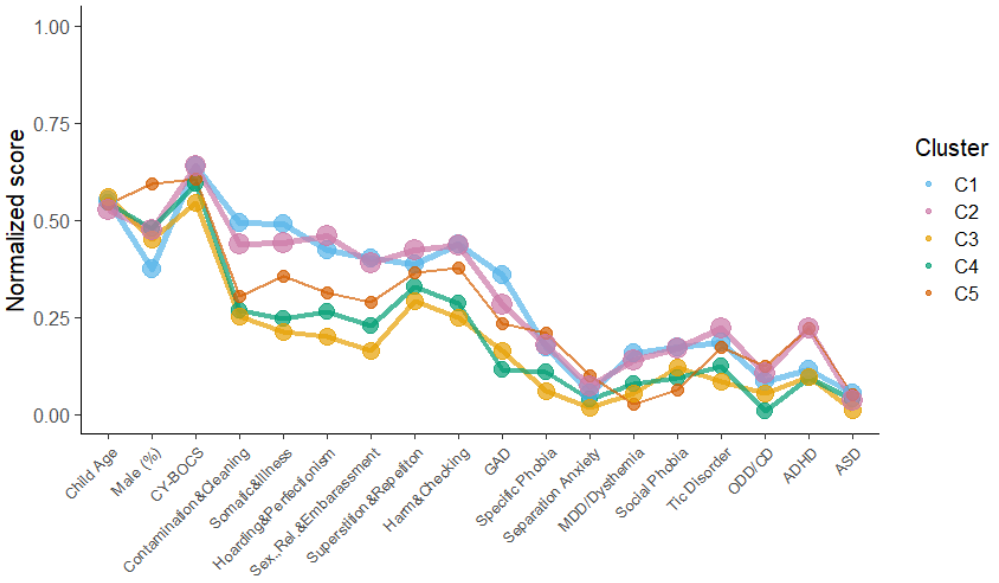
ID (Color)	Proportion of Sample	Age Distribution[a]	Gender Distribution	Severity	Symptoms	Comorbidities	Stability
C1 (L Blue)	Medium (18-24%)	Mean	Females = males	Mean	Mix at low to moderate frequency	Low internalizing comorbidity, high on Tics and ADHD	Gradually shrinks
C2 (Pink)	Medium to large (22-42%)	Mean	Females slightly> males	Slightly above Mean	Mixed at moderate frequency	Higher rates of GAD, Social Phobia, Tics and ADHD	Shrinks after 4-factor model
C3 (Yellow)	Medium (19-35%)	Mean	Females = males	Mean	Mixed at moderate frequency	Low comorbidity	Becomes smaller in 4-factor model; stable in subsequent models
C4 (Green)	Small (14-17%)	Mean	Males slightly > females	Mean	Predominant contamination with others at low frequency initially, becomes mixed in later models	Low comorbidity initially, moderate comorbidity in six and seven cluster models	Remains stable in size but gradually moves towards more mixed symptom profiles and higher comorbidity
C5 (Orange)	Small (9-13%)	Slightly older	Females= males	Above Mean	Moderate frequency, favors superstition/repetition and harm/checking in five and six-cluster models, predominant contamination in seven cluster model	Higher rates of GAD and Social Phobia in six and seven-cluster models	Moves towards more contamination symptoms and higher GAD and Social Phobia comorbidities
C6 (D Blue)	Small (9%)	Mean	Males = females	Mean	Mix at high frequency, high on contamination/cleaning and hoarding/perfectionism in 6-factor solution;	Highest comorbidity overall in 6-factor model, especially high in GAD, Social Phobia, Tics, ADHD and ASD;	Highly unstable

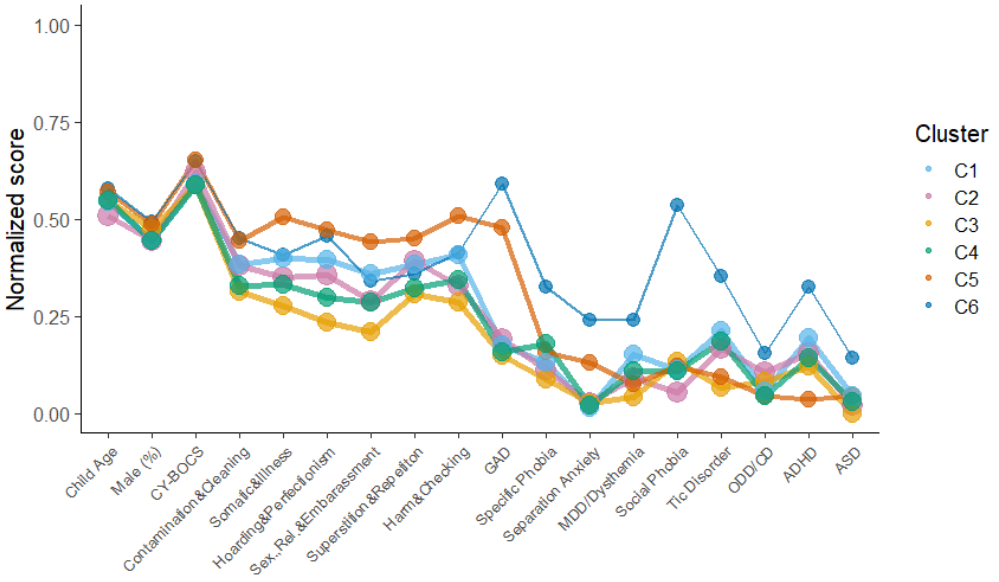
					Low frequency in the 7-factor solution with very low contamination/cleaning	Much lower in 7-factor model although ADHD is still prevalent.	
C7 (Grey)	Very Small (6%)	Mean	Females greatly > males	Below Mean	Mix at low frequency, favors contamination/cleaning	Low overall; Highest cluster on ASD in model.	n/a

[a] By normalized age: slightly older (0.51-0.63), much older (0.63-0.75), very much older (>0.75); slightly younger (0.38-0.49), much younger (0.25-0.38), very much younger (<0.25).

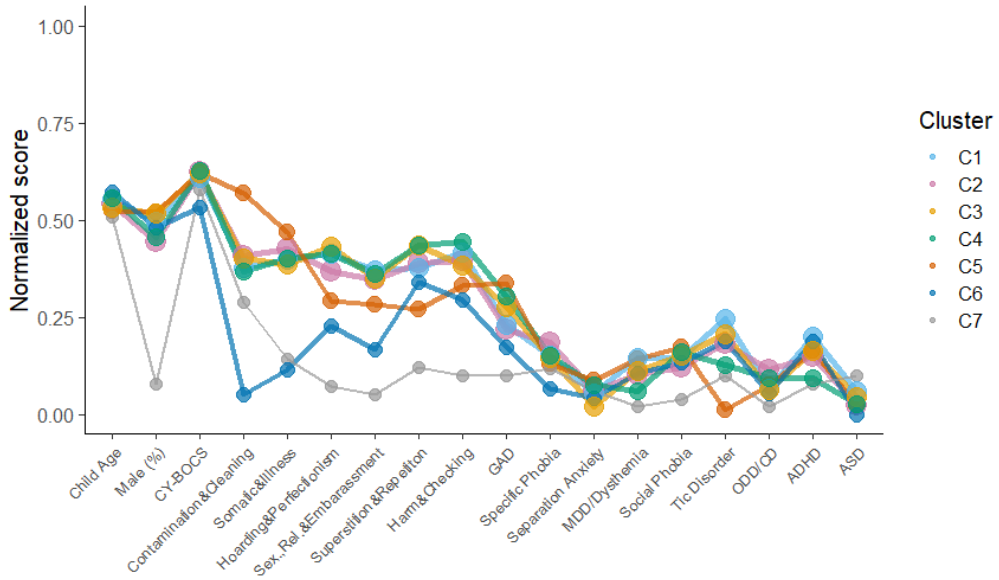
Figure 1. Plots of variable scores across 3-7 cluster models.




Normalized score
1.00
0.75
0.50
0.25
0.00
Child Age
Male (%)
CY-BOCS
Contamination&Cleaning
Somatic&Illness
Hoarding&Perfectionism
Sex.,Rel.&Embarassment
Superstition&Religion
Harm&Checking
GAD
Specific Phobia
Separation Anxiety
MDD/Dysthemia
Social Phobia
Tic Disorder
ODD/CD
ADHD
ASD
Cluster
C1
C2
C3
C4
C5


Normalized score
1.00
0.75
0.50
0.25
0.00
Child Age
Male (%)
CY-BOCS
Contamination&Cleaning
Somatic&Illness
Hoarding&Perfectionism
Sex.,Rel.&Embarassment
Superstition&Religion
Harm&Checking
GAD
Specific Phobia
Separation Anxiety
MDD/Dysthemia
Social Phobia
Tic Disorder
ODD/CD
ADHD
ASD
Cluster
C1
C2
C3
C4
C5
C6

LATENT CLUSTERS IN PEDIATRIC OCD



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Supplementary tables and figures

Table S1. Details for Programs Included in the Mega-Analysis

Program	Locations	Program/Study Description	Years	Funding	Inclusion	Exclusion	Measures
GBG (*n*=91)	Gothenburg, Sweden	Clinical diagnostic assessment conducted at a specialized outpatient pediatric OCD clinic for a naturalistic study	2001-2005	Agreement concerning research and education of doctors – Region Vestra Götaland; Claes Groschinky Memorial Fund; Iris Jonzén-Sandblom and Greta Jonzén´s Foundation	Diagnosis of OCD; 5-17 years old.	None.	Screening: K-SADS Impair: COIS Fam Accom : N/A
ATRC (*n* = 56)	Hamilton, ON, Canada	Clinical diagnostic assessments conducted in a hospital-based anxiety and OCD specialty program	2013-2017	Ontario Brain Institute	Diagnosis of OCD; and < 18 years old.	Autism, bipolar, psychosis, and known intellectual disability.	Screening: K-SADS Impair: N/A Fam Accom: FAS-PR
DCS-CBT Study (*n* = 153)	Tampa, FL, & Boston, MA, USA	Screening/baseline assessments conducted at OCD specialty centers for a randomized controlled trial examining DCS versus placebo augmentation of CBT for OCD	2011-2015	National Institute of Mental Health	Primary OCD; CY-BOCS $\geq$ 16; 7 – 17 years old; IQ > 85; and stable medications (see for details).	Interfering physical health problems (see [2] for details); active suicidality/attempt in past year; pregnancy/unprotected sex (female participants); and comorbid psychosis, bipolar, autism, anorexia nervosa, or primary hoarding.	Screening: K-SADS Impair: COIS-20 Fam Accom: FAS-IR
Griffith (*n* = 114)	Gold Coast, & Mount Gravatt, Australia	Screening/baseline assessments conducted at OCD specialty centers for an open trial of DCS for treatment refractory OCD, an open trial of group CBT for OCD, and a randomized controlled trial of intensive CBT for OCD	2008-2016	National Health and Medical Research Council; Foundation for Children; Rotary Foundation	Primary OCD; 7-17 years old; one willing parent to attend treatment; and stable dose of medication.	Psychosis or an organic mental disorder, significant learning difficulties, active suicidal ideation, and/or level two or three autism spectrum disorder.	Screening: ADIS Impair: COIS Fam Accom: FAS-PR
Iceland (n = 4)	Reykjavik, Iceland	Evaluating CY-BOCS psychometric properties	2017-2018	No funding	Diagnosis of OCD; and < 18 years old.	Inadequate language proficiency by the patient or the parent and known intellectual disability.	Screening: K-SADS Impair: N/A Fam Accom: N/A
Nord-LOTS Study (*n* = 263)	Aarhus, Denmark; Gothenburg & Stockholm, Sweden; Central & East Norway	Screening/baseline assessments conducted at OCD specialty and community centers for an international open trial of CBT for OCD.	2008-2012	TrygFonden; Danish Council for Strategic Research; Pulje til styrkelse af psykiatrisk Forskning i Region Midtjylland; The Center for Child and Adolescent Mental Health, Eastern and Southern Norway; Stiftelsen Clas Groschinskys Minnesfond; Norwegian	Primary OCD; CY-BOCS $\geq$ 16; 7 – 17 years old; IQ > 70; and $\geq$ 3 months of stable meds if comorbid ADHD was present.	Disorders with higher treatment priority (see for details), and patients already under CBT, selective-serotonin reuptake inhibitor (SSRI), or atypical neuroleptic, treatment for OCD within six months of study start.	Screening: K-SADS Impair: COIS-R Fam Accom: FAS-IR

				Research Council, Helse & Rehabilitering, Norge			
UBC POP (*n* = 148)	Vancouver, BC, Canada	Clinical diagnostic assessments conducted in a hospital-based OCD specialty program	2011-2019	Michael Smith Foundation for Health Research; British Columbia Provincial Health Services Administration	Diagnosis of OCD; and ≤ 19 years old.	None.	Screening: ADIS Impair: COIS-R Fam Accom: FAS-IR* FAS-SR

Note: GBG = Sahlgrenska University Hospital OCD Outpatient Clinic,Gothenburg, Sweden; ATRC = Anxiety Treatment Research Center; DCS-CBT = D-Cycloserine Cognitive Behavioral Therapy; NordLOTS = Nordic Long-Term OCD Treatment Study; UBC POP = University of British Columbia Provincial Obsessive Compulsive Disorder Program; K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children; ADIS = Anxiety Disorder Interview Schedule for Children – Parent Version; COIS = Children's Obsessive Compulsive Scale; COIS-20 = COIS – 20 Item Version; COIS-R = COIS – Revised Version; FAS-IR = Family Accommodation Scale – Interviewer Rated; FAS-PR = Family Accommodation Scale – Parent Rated; CBCL = Child Behavior Checklist; IQ = Intelligence Quotient.
*FAS-IR was completed by parents.

Table S2. Fit Measures for Exploratory Factor Analysis.

Number of factors	Chi-squared	Degrees of freedom	CFI	TLI	RMSEA	SRMR
3	5851.164	1650	0.887	0.875	0.027	0.087
4	3397.552	1592	0.920	0.908	0.023	0.078
5	2702.727	1535	0.939	0.928	0.020	0.073
6	1883.241	1479	0.957	0.946	0.017	0.065
7	1713.017	1424	0.969	0.960	0.015	0.060
8	1587.111	1370	0.977	0.969	0.013	0.056
9	1492.018	1317	0.981	0.974	0.012	0.053
10	1407.300	1265	0.985	0.978	0.011	0.050
11	1327.526	1214	0.988	0.982	0.010	0.048

Abbreviations: CFI = comparative fit index; RMSEA = root mean square error of approximation; SRMR = standardized root mean square residual; TLI = Tucker Lewis index.

Table S3. Outcomes of Confirmatory Factor Analysis.

	Model fit statistics						Scaled chi-squared difference test		
Model description	Scaled chi-squared	Degrees of freedom	Scaled CFI	Scaled TLI	Scaled RMSEA	SRMR	Chi-squared difference	Difference in degrees of freedom	*P* value
Eight-factor[2]	-	-	-	-	-	-	-	-	-
Seven-factor[2]	-	-	-	-	-	-	-	-	-
Six-factor	2105.5*	1300	0.910*	0.904*	0.026*	0.088*	--	--	--
Five-factor	2196.6	1273	0.888	0.878	0.030	0.089	91.1	-27	1.0
Four-factor[1]	-	-	-	-	-	-	-	-	-
Three-factor (Harm/sexual vs Symmetry/hoarding vs Contamination/cleaning)	2865.2	1476	0.824	0.816	0.033	0.108	789.7	176	<.001
Two-factor (Obsessions vs compulsions)	5091.2	1429	0.54	0.52	0.06	0.14	2985.7	129	<.001
Single factor	5134.8	1430	0.54	0.52	0.06	0.14	3029.5	130	<.001

*Indicates best fit

Abbreviations: CFI = comparative fit index; RMSEA = root mean square error of approximation; SRMR = standardized root mean square residual; TLI = Tucker Lewis index.

[1]A four-factor model based on supplemental Table 3 in Højgaard et al. 2017 was fit to the data but did not converge on an optimal solution. A separate four factor model based on an exploratory factor analysis of the current data was tested but also did not converge on an optimal solution. Therefore, no fit statistics are reported for these models.

[2]Both the seven and eight-factor models from the exploratory factor analysis had one factor comprised of only two items that also cross-loaded on another factor. When fit to the data and tested in a CFA neither model converged on an optimal solution. Therefore, no fit statistics are reported for these models.

Table S4. Factor loadings for best-fitting confirmatory factor analysis

Latent Factor	Checklist Item	Estimate	Standard Error	95% CI Lower	95% CI Upper
Contamination/ Cleaning	Excessive concern with dirt, germs	1.000	0.000	1.000	1.000
	Excessive concern with bodily waste	0.759	0.056	0.650	0.868
	Excessive concern with environmental contaminants	0.284	0.087	0.114	0.454
	Excessive concern about contamination from touching animals/insects	0.789	0.058	0.676	0.902
	Excessively bothered by sticky substances or residues	0.53	0.054	0.431	0.641
	Concerned will get ill because of contaminant	0.288	0.070	0.152	0.425
	Concerned will get others ill by spreading contaminant	0.677	0.060	0.559	0.794
	Excessive or ritualized hand washing	1.027	0.062	0.905	1.148
	Excessive or ritualized showering, grooming	0.765	0.057	0.654	0.876
	Excessive cleaning of items	0.793	0.056	0.684	0.902
	Other measures to prevent or remove contact with contaminants	0.827	0.056	0.718	0.936
	Checking associated with washing	0.421	0.059	0.305	0.538
Sexual/ Religious/ Embarrassment	Fear of blurting out obscenities or insults	1.000	0.000	1.000	1.000
	Fear will act on unwanted impulses	-0.083	0.148	-0.372	0.207
	Forbidden or upsetting sexual thoughts	0.947	0.095	0.760	1.134
	Content involves homosexuality	0.935	0.113	0.714	1.155
	Sexual behavior toward others	0.934	0.132	0.676	1.192

	Overly concerned with offending religious objects	0.976	0.093	0.794	1.158
	Excessive concern with right/wrong, morality	0.816	0.122	0.577	1.054
	Fear of saying certain things	0.800	0.092	0.620	0.981
	Fear of not saying just the right thing	0.685	0.106	0.477	0.894
	Intrusive (non-violent) images	0.746	0.097	0.556	0.935
	Intrusive sounds, words	0.766	0.092	0.586	0.947
	Excessive telling, asking, or confessing	0.939	0.084	0.774	1.103
	Fear of doing something embarrassing	0.941	0.087	0.772	1.111
	Excessive concern with body part or aspect of appearance	0.832	0.097	0.642	1.022
Somatic/ Illness	Excessive concern with environmental contaminants	1.000	0.000	1.000	1.000
	Concerned will get ill because of contaminant	0.907	0.129	0.654	1.159
	Excessive concern with illness or disease	1.028	0.121	0.791	1.264
	Checking tied to somatic obsession	1.004	0.114	0.779	1.228
	Excessive concern with dirt, germs	0.100	0.093	-0.081	0.282
	Excessive concern with contamination from household items	0.545	0.132	0.286	0.804
	Fear harm will come to others	-0.013	0.093	-0.196	0.169
	Rituals involving others	0.778	0.109	0.565	0.991
	Ritualized eating	0.474	0.100	0.277	0.670
Harm/ Checking	Fear might harm self	1.320	0.129	1.067	1.572
	Fear harm will come to self	1.144	0.120	0.908	1.380
	Fear harm will come to others	1.449	0.141	1.174	1.725
	Violent or horrific images	1.157	0.116	0.930	1.385
	Fear will act on unwanted impulses	1.314	0.202	0.918	1.710
	Fear will be responsible for something terrible to happen	1.191	0.118	0.960	1.421
	Checking associated with washing	0.503	0.106	0.296	0.711
	Checking that did not/will not harm others	1.117	0.133	0.857	1.377
	Checking that nothing terrible did/will happen	1.157	0.140	0.882	1.431
	Measures to prevent harm to self	0.814	0.123	0.573	1.055
Superstition/ Repetition	Lucky/unlucky numbers, colors, words	1.000	0.000	1.000	1.000
	Rereading, erasing, or rewriting	0.457	0.090	0.280	0.634
	Need to repeat routine activities	0.981	0.087	0.811	1.152
	Counting objects, words	0.934	0.082	0.774	1.095
	Arranging/ordering—evening up	0.891	0.090	0.714	1.067
	Magical games/superstitions	0.999	0.094	0.815	1.184
	Excessive touching, tapping, rubbing	1.047	0.088	0.874	1.219

	Hoarding obsessions	1.000	0.000	1.000	1.000
	Need to know or remember	0.823	0.083	0.660	0.985
	Checking that did not make mistake	1.028	0.083	0.866	1.190
	Difficulty throwing things away	0.903	0.072	0.761	1.044
	Excessive list making	0.739	0.096	0.550	0.928
Hoarding/ Perfectionism	Checking locks, toys, schoolbooks/items	0.844	0.084	0.680	1.009
	Excessive concern with right/wrong, morality	0.230	0.107	0.019	0.440
	Fear of saying certain things	0.444	0.102	0.243	0.645
	Rereading, erasing, or rewriting	0.659	0.088	0.486	0.832
	Excessively bothered by sticky substances or residues	0.445	0.085	0.280	0.611

Table S5. Correlations between Latent Factors

	Contamination/ Cleaning	Sexual/Religious/ Embarrassment	Somatic/ Illness	Harm/ Checking	Superstition/ Repetition	Hoarding/ Perfectionism
Contamination/Cleaning	1					
Sexual/Religious/Embarrassment	0.17	1				
Somatic/ Illness	0.504	0.535	1			
Harm/Checking	0.004	0.672	0.458	1		
Superstition/Repetition	-0.021	0.369	0.232	0.453	1	
Hoarding/Perfectionism	0.17	0.604	0.33	0.522	0.463	1

Table S6. Univariate variable specific entropy for 3-7 cluster models

	Model descriptions				
Model variables	Three Cluster	Four Cluster*	Five Cluster	Six Cluster	Seven Cluster
CY-BOCS	0.046	0.091	0.078	0.055	0.081
Contamination/Cleaning	0.049	0.279	0.208	0.222	0.295
Sexual/Religious/Embarrassment	0.614	0.54	0.497	0.403	0.425
Somatic/Illness	0.265	0.327	0.343	0.297	0.349
Harm/Checking	0.505	0.502	0.423	0.367	0.386
Superstition/Repetition	0.237	0.256	0.218	0.191	0.218
Hoarding/Perfectionism	0.502	0.408	0.373	0.301	0.316
Separation Anxiety	0.036	0.073	0.062	0.056	0.054
Specific Phobia	0.041	0.075	0.064	0.057	0.055
Social Phobia	0.035	0.07	0.061	0.063	0.074
GAD	0.053	0.079	0.07	0.07	0.067
MDD or Dysthemia	0.033	0.069	0.061	0.041	0.064
ODD or CD	0.029	0.064	0.058	0.03	0.055
ADHD	0.032	0.068	0.058	0.057	0.057
Tic Disorder	0.031	0.069	0.061	0.039	0.067
ASD	0.032	0.067	0.064	0.036	0.052

*Indicates best fitting model

Table S7. Comparison of secondary outcomes across clusters for the 4-cluster solution.

		Latent Cluster				
Variable	Overall, N = 830	C1, N = 200	C2, N = 350	C3, N = 165	C4, N = 115	Omnibus Cluster *P* value
Age of onset, Mean (SD)	8.7 (3.4)	8.9 (3.4)	8.61 (3.2)	9.1 (3.3)	8.8 (3.9)	0.28
<Missing>	<103>	<18>	<56>	<22>	<11>	
Insight, Median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	1.0 (0.0, 2.0)	1.0 (1.0, 2.0)	1.0 (0.0, 2.0)	0.29[1]
<Missing>	<102>	<25>	<48>	<17>	<12>	
Avoidance, Median (IQR)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.20[1]
<Missing>	<158>	<36>	<76>	<31>	<15>	
Indecision, Median (IQR)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	0.07[1]
<Missing>	<154>	<38>	<76>	<31>	<14>	
Responsibility, Median (IQR)	0.0 (0.0, 2.0)	0.0 (0.0, 1.0)	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.5(0.0, 2.0)	0.12[1]
<Missing>	<157>	<35>	<76>	<31>	<15>	
Slowness, Median (IQR)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)[a,b]	2.0 (1.0, 1.0)[a,b]	1.0 (1.0, 3.0)[b]	1.0 (0.0, 2.0)[a]	.015[1]
<Missing>	<159>	<35>	<77>	<31>	<16>	
Doubt, Median (IQR)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	0.361[1]
<Missing>	<418>	<102>	<160>	<87>	<69>	
Family Accommodation, Mean (SD)[2]	0.00 (1.00)	0.09 (0.95)	0.05 (0.92)	-0.07 (1.11)	-0.18 (1.07)	0.147[3]

		Latent Cluster				
Variable	Overall, N = 830	C1, N = 200	C2, N = 350	C3, N = 165	C4, N = 115	Omnibus Cluster *P* value
<Missing>	<221>	<51>	<112>	<31>	<27>	
Impairment (Parent), Mean (SD)[2]	0.00 (1.00)	-.04 (0.92)	0.06 (0.96)	-0.03 (1.15)	-0.08 (1.02)	0.44[3]
<Missing>	<181>	<34>	<76>	<28>	<28>	
Impairment (Child), Mean (SD)[2]	0.00 (1.00)	-0.01 (1.01)	0.05 (1.01)	-0.02 (1.00)	-0.11 (0.88)	0.47[3]
<Missing>	<185>	<38>	<84>	<33>	<30>	

[1]Calculated from ordinal regression model adjusting for study site.

[2]Standardized (M = 0, SD = 1) within site prior to computing cluster means and standard deviations.

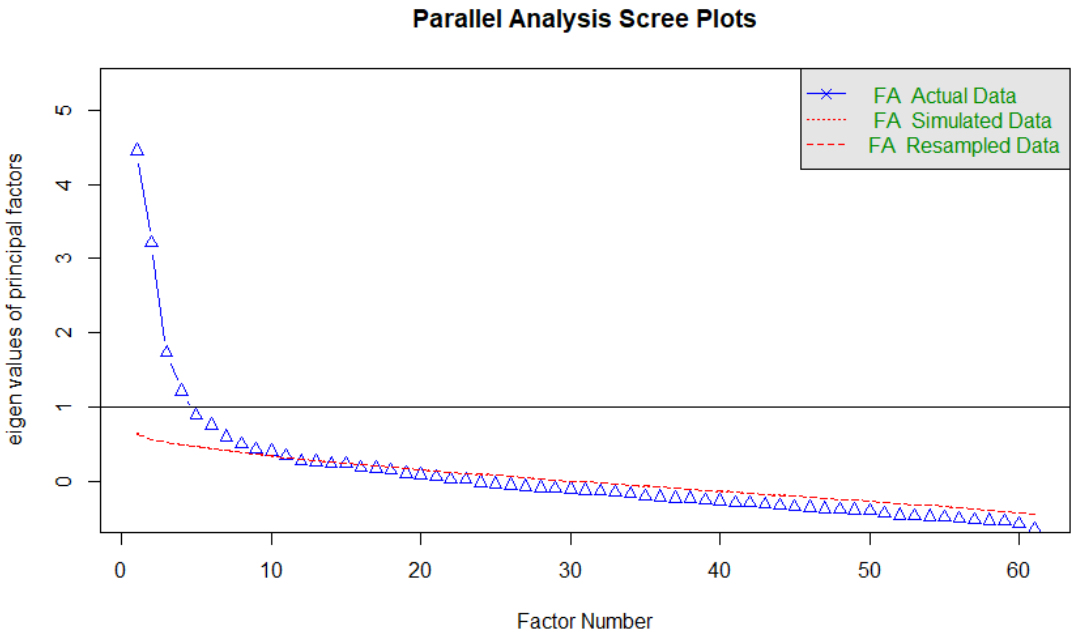
[3]Calculated from linear regression model.

For statistically-significant omnibus cluster effects ($p < .05$), pairwise comparisons were calculated with the Tukey correction for multiple comparisons. Values with shared superscripts are not statistically different from one another (Tukey-corrected $p < .05$)

Table S8. Descriptive statistics from the 4-cluster solution for variables not included in other analyses.

	Latent Cluster				
Variable	Overall, N = 830[1]	C1, N = 200	C2, N = 350	C3, N = 165	C4, N = 115
Age of Diagnosis	11.0 (3.8)	10.6 (3.8)	11.0 (3.6)	11.7 (3.8)	10.8 (4.3)
<Missing>	<361>	<71>	<172>	<78>	<40>
Child Race					
American Indian	10 (0.6%)	0 (0%)	3 (0.9%)	2 (1.2%)	0 (0%)
Asian	27 (3.3%)	13 (6.5%)	6 (1.7%)	6 (3.6%)	2 (1.7%)
Black	8 (1%)	2 (1%)	6 (1.7%)	0 (0%)	0(0%)
Native Hawaiian/Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
White	347 (41.8%)	79 (39.5%)	158 (45.1%)	69 (41.8%)	41 (35.7%)
Mixed Race	2 (0.4%)	0 (0%)	1 (0.3%)	1 (0.6%)	1 (0.4%)
Other	10 (1.2%)	2 (1%)	4 (1.1%)	2 (1.2%)	2 (1.7%)
<Missing>	<339>	<126>	<42>	<70>	<59>
Ethnicity, Hispanic	28 (3.4%)	5 (2.5%)	14 (4%)	4 (2.4%)	5 (4.3%)
<Missing>	<283>	<74>	<98>	<56>	<55>
Any Prior Treatment	277 (33.4%)	68 (34%)	126 (36%)	56 (33.9%)	27 (23.5%)
<Missing>	<348>	<87>	<126>	<69>	<66>
Current SSRIs	219 (26.5%)	53 (26.5%)	102(29.4%)	40(24.5%)	24(20.9%)
<Missing>	<5>	<0>	<3>	<2>	<0>
Study					
GBG	91 (11%)	20 (22%)	46 (50.5%)	31 (18.8%)	10 (11%)
ATRC	56 (6.7%)	10 (17.9%)	28 (50%)	14 (25%)	4 (7.1%)
DCS-CBT Study	153 (18.6%)	32 (16%)	76 (21.7%)	31 (18.8%)	15 (13%)
Griffith	114 (13.7%)	22 (19.3%)	72 (63.2%)	14 (12.3%)	6 (5.3%)
Iceland	4 (0.5%)	0 (0%)	2 (50%)	2 (50%)	0 (0%)
Nord-LOTS	263 (31.7%)	69 (26.2%)	84 (31.9%)	56 (21.3%)	54 (20.5%)
UBC POP	148 (17.8%)	47 (31.8%)	42 (28.4%)	33 (22.3%)	26 (17.6%)

Figure S1. Exploratory factor analysis scree plot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FA Actual Data
FA Simulated Data
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Factor Number
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Paper III

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Long-term functional impairment in pediatric OCD after and during treatment: An analysis of distinct trajectories

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ABSTRACT

The present study aimed to: (a) identify latent class trajectories of OCD-related functional impairment, before, during and over three years after stepped-care treatment in children and adolescents with OCD; (b) describe these classes according to pretreatment characteristics; (c) identify predictors of trajectory class membership and (d) examine the relationship of functional impairment trajectory classes with OCD symptom severity trajectory classes. The sample consisted of 266 children and adolescents (aged 7–17 years) with OCD, participating in the Nordic long-term OCD treatment study. Latent class growth analysis was conducted using *Child Obsessive-Compulsive Impact Scale-Revised (COIS-R)* data from children and parents on seven assessment points over a three-year period. A 3-class solution was identified. The largest class (70.7%) initiated treatment with lower functional impairment and obtained moderate reduction which was maintained over time. The second class (24.4%) initiated with higher functional impairment which rapidly diminished over time. The third and smallest class (4.9%), initiated with moderate functional impairment which remained stable over time. The classes differed on measures of OCD severity and comorbid symptoms. Most participants improved with treatment and maintained low levels of impairment. However, a subgroup distinguished by higher levels of ADHD symptoms, remained at pretreatment levels of impairment throughout.

1. Introduction

Obsessive-compulsive disorder (OCD) affects 0.5–3% of children and adolescents (Heyman et al., 2001; American Psychiatric Association, 2013; Fawcett et al., 2020) and often leads to chronic and severe functional impairment (Piacentini et al., 2007; Skarphedinsson et al., 2015a; Valderhaug and Ivarsson, 2005). OCD in children and adolescents has been associated with a profound decrease in educational attainment (for both compulsory- and postgraduate education) and employment prospects, especially for those with early onset of the disorder (Perez-Vigil et al., 2018; Hollander et al., 1998; Koran, 2000). Early longitudinal studies showed that children and adolescents with OCD had an inferior prognosis (Stewart et al., 2004) and indicated that the natural course of OCD tended to be chronic (Visser et al., 2014). However, recent long-term follow-up studies of evidence-based treatments show a more positive outcome, with up to 73% of children and adolescents achieving

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symptom remission (O'Leary et al., 2009; Melin et al., 2018; Melin et al., 2020; Lewin et al., 2014). OCD-related functional impairment tends to also be reduced after evidence-based treatment of OCD (Selles et al., 2017; Skarphedinsson et al., 2015b; Piacentini et al., 2011). However, even when symptom remission is achieved, with corresponding improvements in quality of life and functional impairment, adults with a history of OCD continue to be more impaired than healthy controls with no such history (Huppert et al., 2009). Whether this is also the case for children and adolescents is currently unknown as the long-term development of OCD-related functional impairment following intervention has not yet been studied.

Functional impairment refers to a limitation resulting from a psychiatric disorder that manifests as reduced capability to meet the demands of life. Across pediatric mental disorders, studies have suggested low to moderate associations between symptom severity and functional impairment. This has also been found in pediatric OCD samples (Piacentini et al., 2007; Valderhaug and Ivarsson, 2005; Piacentini et al., 2003; Storch et al., 2010; Langley et al., 2014; Calvo et al., 2022), indicating that functional impairment is a clinically relevant construct distinct from the severity of OCD symptoms. The core symptoms of OCD, obsessions and compulsions, can directly impair daily functioning and interfere with many domains of life (Valderhaug and Ivarsson, 2005; Piacentini et al., 2003). Different OCD symptom dimensions (e.g., cleaning and contamination symptoms) may also influence the specific type and level of impairment, as well as which domains of life are primarily impaired (Hojgaard et al., 2017; Bloch et al., 2008). Psychiatric comorbidity, especially depression, anxiety disorders, tic disorders and ADHD is common in OCD (occurring in around 70% of patients) (Sharma et al., 2021) (Sharma et al., 2021; Ivarsson et al., 2008), likely interacting with and adding to OCD-related functional impairment. Other factors, such as the lack of insight (Storch et al., 2008), and high family accommodation (Storch et al., 2007), may also further add to OCD-related impairment. Whether and how OCD symptom dimensions, comorbidities and associated factors impact the level and trajectories of OCD-related functional impairment during and after treatment is currently unknown. Further knowledge in this area may ultimately help clinicians assess and treat OCD-related functional impairment with greater effectiveness.

Following cognitive-behavioral treatment (Lewin et al., 2014; Selles et al., 2017; Skarphedinsson et al., 2015b; Piacentini et al., 2011) and/or treatment with selective serotonin reuptake inhibitors (SSRIs) (Skarphedinsson et al., 2015b; Storch et al., 2013), OCD-related functional impairment tends to decrease parallel to a decrease in symptom severity (Skarphedinsson et al., 2015c) and an increase in quality of life (Wellen et al., 2017; Weidle et al., 2015). However, not all children and adolescents with OCD respond adequately to treatment and fewer still achieve remission, with over 30% of children and adolescents classified as non-responders in some studies (McGuire et al., 2015; Torp et al., 2015a; Ost et al., 2016). Factors associated with poorer treatment response are higher functional impairment, older age, higher OCD symptom severity, extreme avoidance, low insight, and family accommodation (Selles et al., 2020; Garcia et al., 2010; Turner et al., 2018). There are some inconsistencies between study results, for example, Selles et al. (Selles et al., 2020) found that insight did not significantly impact treatment response and, in contrast to earlier studies (Garcia et al., 2010; Torp et al., 2015b), that lower OCD symptom severity at baseline predicted a lower likelihood of treatment response. These inconsistencies indicate that non-responders are a heterogenous subgroup requiring further study.

No studies have examined the impact of factors such as age, OCD symptom severity, insight, and family accommodation on the trajectory of long-term OCD-related functional impairment or the interaction of OCD symptom severity treatment response with OCD-related functional impairment. To examine the heterogeneity of treatment response, it is beneficial to identify subgroups of children and adolescents with different long-term trajectories and attempt to identify factors that predict subgroup membership. Such trajectory classes are formed based on the similarities of symptom courses among patients, representing a person-centered (as opposed to variable-centered) approach (Jung and Wickrama, 2008). This approach could provide more personalized information about the prospective long-term course of OCD-related functional impairment (Mulder et al., 2003).

Jensen et al. (Jensen et al., 2020) previously examined latent class trajectories of OCD symptom severity during and after treatment and predictors of class membership. Three distinct class trajectories were found:(a) acute, sustained responders (54.6%), where class membership was predicted by lower levels of contamination and cleaning symptoms as well as less parent-rated anxiety; (b) slow, continued responders (23.4%), where class membership was predicted by higher overall severity of psychopathology (CGI-S); and (c) limited long-term responders (21.9%), where class membership was predicted by adolescence, lower CGI-S severity and higher levels of contamination and cleaning symptoms as well as higher parental ratings of anxiety.

No previous studies have analyzed latent class trajectories of OCD-related functional impairment during and after treatment. Since OCD-related functional impairment is only moderately correlated with OCD symptom severity and is assessed with a different instrument utilizing a different assessment approach (clinical interview vs self-report), it provides distinct clinically relevant information to explore its long-term development in different subgroups. As distinct trajectories of OCD symptom severity response have been identified in the current sample (Jensen et al., 2020) it is of interest to examine if OCD-related functional impairment response has similar distinct subgroups and to what extent the subgroups of the two clinically relevant measures overlap. The present study aimed to: (a) identify possible latent class trajectories of child and adolescent self-reported OCD related functional impairment over three years (170 weeks) during and after stepped-care treatment; (b) describe these classes according to pretreatment characteristics; (c) identify predictors of trajectory class membership; and (d) to examine the overlap of functional impairment trajectory classes with OCD symptom severity trajectory classes identified in a previous study (Jensen et al., 2020).

2. Methods

2.1. Participants

The sample consisted of 266 children and adolescents with OCD from Denmark, Norway, and Sweden participating in the Nordic long term OCD treatment study, NordLOTS (Thomsen et al., 2013). A total of 767 children and adolescents were screened for participation, 491 met inclusion criteria and consented for assessment. Of those, 222 were excluded. Criteria for exclusion were not meeting diagnostic criteria for OCD, having a CY-BOCS score lower then 16, any comorbid psychiatric disorders with higher treatment priority than OCD (i.e., psychosis and severe depression) as assessed by an evaluator administering the K-SADS-PL at baseline, a diagnosis of autism spectrum disorder, and IQ score below 70. Therefore, 269 were included in the original treatment study (Torp et al., 2015a). Three participants did not provide COIS-R data for at least one assessment point and were therefore excluded in the current analysis. Age at inclusion ranged from 7 to 17 years (M = 12.8; SD = 2.7) and gender distribution was equal (51.3% females) with 97% being of Scandinavian ethnicity (Torp et al., 2015a). Criteria for study inclusion were a Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM-IV) OCD diagnosis and Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) (Scahill et al., 1997) severity score greater than 15.

2.2. Treatment and follow-up procedures

The NordLOTS was a stepped-care, longitudinal treatment study (Thomsen et al., 2013). In step 1, patients received 14 weekly sessions of

manualized exposure-based Cognitive Behavioral Therapy (CBT) (Torp et al., 2015a). Children and adolescents that did not respond to treatment at Step 1 (CY-BOCS score > 15, $n = 50$) were randomized to either an additional ten sessions of CBT ($n = 28$) or sertraline for 16 weeks ($n = 22$); non-responders to CBT in Step 2 ($n = 11$) were subsequently offered sertraline (Skarphedinsson et al., 2015b). Step 1 responders were offered up to four booster sessions during the first-year post-treatment. In cases of relapse (CY-BOCS > 15), patients were offered up to 10 CBT sessions (including booster sessions). If the patient did not respond satisfactorily, treatment with sertraline was offered. Independent evaluators assessed all patients before treatment, in weeks 7 and 14 during Step 1, and at 40, 66, 118, and 170 weeks after the end of Step 1 (Jensen et al., 2020). All measures included were administered at baseline, and the CY-BOCS and COIS-R were administered at all assessment points.

2.3. Instruments

The *Child Obsessive-Compulsive Impact Scale-Revised (COIS-R)* is a questionnaire consisting of 33 items (Piacentini et al., 2007). It assesses the impact of obsessive–compulsive symptoms on the child's overall functioning in home, school and social settings. The questionnaire has a child and adolescent self-report and a parent version. Each item is rated on a four-point Likert scale (0 = not at all, 1 = just a little, 2 = pretty much, and 3 = very much), with a total score range from 0 to 99 (Piacentini et al., 2007). The scale has moderate to high internal consistency of $\alpha = 0.80–0.95$ and $\alpha = 0.78–0.95$, respectively, for the parent and child versions (Skarphedinsson et al., 2015a; Calvo et al., 2022). The COIS-R has excellent test-retest reliability, with intraclass correlation scores above 0.9 for the total score and all subscales, as well as good convergent and divergent validity (Piacentini et al., 2007; Calvo et al., 2022). For this study the child and adolescent self-report version of the COIS-R was used as it has equivalent psychometric properties to the parent report version and it is accepted that patients themselves have the best perspective on the impact of illness, as they directly experience the benefits and burdens of therapeutic interventions and are also aware of hidden, indirect benefits and costs which may go unnoticed by the objective observer (Upton, 2014).

Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) is a clinician-administered semi-structured interview assessing OCD symptoms and severity on a scale from 0 to 40, as well as symptom insight (five levels from excellent to absent), and avoidance (five levels from none to extreme) in children and adolescents aged 6–17 years (Scahill et al., 1997). It has demonstrated reliability and validity in samples of children and adolescents with OCD (Thomsen et al., 2013; Storch et al., 2004). In the current study a factor analyses of the symptom checklist conducted by Højgaard et al. (Hojgaard et al., 2017) is used to examine potential differences in symptom profiles between latent trajectory classes. The three factors identified were 1) Harm/sexual symptoms, 2) Symmetry/hoarding symptoms, and 3) Cleaning/contamination symptoms. Other studies have found similar factor structures (Delorme et al., 2006; Bernstein et al., 2013). Item 11 on the CY-BOCS was used to assess level of insight on a 5-point scale (0 = excellent insight, 1 = good insight, 2 = fair insight, 3 = poor insight, 4 = completely lacks insight).

Kiddie Schedule for Affective Disorders and Schizophrenia –Present and Lifetime Version (K-SADS-PL) is a semi-structured diagnostic interview assessing a wide range of DSM-IV mental disorders in children and adolescents (Kaufman et al., 1997). The K-SADS-PL has good psychometric properties with an interrater reliability of 98% and a 1–5 week test-retest kappa of 0.80 for any anxiety disorder diagnosis (Kaufman et al., 1997). Convergent and divergent validity have been documented in a Nordic sample of adolescents (Lauth et al., 2010; Kragh et al., 2018).

Child Behavior Checklist (CBCL) is a 113-item parent-rated questionnaire assessing a wide range of behavioral and emotional problems in children aged 6–18 with well-established psychometric properties across a variety of clinical and nonclinical populations (Achenbach, 1994). The mean test–retest reliability has been reported to be between 0.95 and 1.00 and internal consistency between 0.78 and 0.97 (Achenbach, 1991). In the current study we utilize the CBCL total score as a measure of psychopathology, the internalizing (0–64) and externalizing (0–70) symptoms total score subscales, as well as the DSM-5 diagnoses oriented subscales for Attention deficit/hyperactivity (ADHD) and Oppositional defiant disorder (ODD) symptoms (Achenbach, 1994).

Screen for Child Anxiety-Related Emotional Disorders (SCARED) assesses DSM-IV child- and parent-rated anxiety symptoms with a total score from 0 to 82 (Birmaher et al., 1997). The SCARED total score has been shown to possess high internal consistency ($\alpha = 0.94$) (Muris et al., 2001). The internal consistencies of the SCARED child- and parent-report in the current study were $\alpha = 0.92$ and $\alpha = 0.92$, respectively.

Mood and Feelings Questionnaire (MFQ) assesses child- and parent rated depressive symptoms in children aged 8–18 years with a total score from 0 to 26 (Angold et al., 1987; Messer et al., 1995). The MFQ has sound psychometric properties (Messer et al., 1995), with an internal consistency of $\alpha = 0.75–0.78$ (Wood et al., 1995). The internal consistencies of the parent and child versions in the current study were $\alpha = 0.90$ and $\alpha = 0.85$, respectively.

Family Accommodation Scale (FAS) is a 12-item clinical interview conducted with parent(s) to assess the family's accommodation to the child's OCD symptoms (total score 0–48) (Calvocoressi et al., 1999). The FAS has been shown to have good internal consistency ($\alpha = 0.76–0.80$) and to correlate positively with measures of OCD symptom severity (Storch et al., 2007; Calvocoressi et al., 1999; Calvocoressi et al., 1995) and family discord (Calvocoressi et al., 1999). In the NordLOTS study sample, the internal consistency was $\alpha = 0.87$.

2.4. Ethical considerations

The National Ethical Committees and data authorities in Denmark, Norway, and Sweden approved the study, and written consent was obtained from parents and patients. Trial registry: Nordic Long-term Obsessive-Compulsive Disorder (OCD) Treatment Study; www.controlled-trials.com; ISRCTN66385119.

2.5. Statistical analyses

2.5.1. Latent trajectories

Latent class growth analysis (LCGA) (Nagin, 2005; Nylund et al., 2007) with linear, quadratic, and cubic terms for two to five classes was conducted on the sample ($N = 266$) using COIS-R self-report data from children and adolescents at the seven points of assessment: Pretreatment ($n = 246$), week 7 ($n = 215$), week 14 ($n = 213$), 40-week follow-up ($n = 165$), 66-week follow-up ($n = 162$), 118-week follow-up ($n = 151$), and 170-week follow-up ($n = 147$). Optimal model fit was evaluated using, primarily, the Bayesian information criterion (BIC) and the sample-size adjusted BIC (SABIC) with lower scores indicating better fit (Nylund et al., 2007). Clinical interpretability and the entropy value (with a score closer to 1 representing higher classification quality) were also considered. Missing data were handled using maximum likelihood estimation. The number of participants from each class entering step 2 treatment (either CBT or SSRI) was examined.

2.5.2. Pretreatment characteristics of classes

The latent classes were evaluated by differences in pretreatment demographics, OCD features, and comorbid variables using univariate analyses, ANOVA or the Kruskal–Wallis tests and chi-squared or Fisher's exact tests, on the raw data.

2.5.3. Predictor analyses

Missing data for all potentially relevant pretreatment variables were handled with multiple imputations by chained equations (MICE). One hundred imputed datasets were generated, which were combined for

predictor analyses following Rubin's rules for combining multiple imputed datasets (Rubin, 2004). Multivariate analysis (multinomial logistic regression) was performed on the combined imputed datasets of the pretreatment variables. The multivariate analysis was explorative because of the novelty of the trajectory classes. Variables were selected to cover a range of factors associated with long-term treatment outcomes from the literature. For comorbidity variables, continuous measures were preferred over dichotomous diagnostic categories where possible. To avoid multicollinearity the variable inflation factor (VIF) and tolerance index were examined for all potential variables. All included variables had a VIF under the recommended limit of 2.5 and a tolerance above the recommended limit of 0.2 (Shrestha, 2020; Senaviratna and Cooray, 2019) (Supplemental Table S1). The following variables were included age, gender, CY-BOCS total severity score, duration of OCD, insight, symptom dimension factor scores (i.e., harm/sexual factor, hoarding/symmetry factor, cleaning/contamination factor), Tic disorder(K-SADS), CBCL ADHD symptom subscale, CBCL ODD symptom subscale, anxiety symptoms (SCARED-P), and depression symptoms (MFQ-P).

2.5.4. Comparison with OCD symptom severity (CY-BOCS) classes

The results of the LCGA for COIS-R scores were compared to those of the LCGA for symptom severity, using CY-BOCS total scores, conducted by Jensen et al. (Jensen et al., 2020), using data from the current sample. The extent to which classes share participants will be specifically examined using a Bonferroni-adjusted z-test for independent proportions.

2.5.5. Analysis of missing cases

Missing versus non-missing COIS-R child self-report cases were evaluated according to the pretreatment characteristics listed in Table 1, at each point of assessment, using the same univariate analysis on the raw data as was used to compare trajectory classes.

The LCGA was performed using Mplus version 8.6 (Muthén and Muthén, 1998-2017). MICE and all other analyses were performed using SPSS 28 (IBM, IBM SPSS 2021).

Table 1
Model fit statistics of the functional impairment trajectories.

		2 Classes	3 Classes	4 Classes	5 Classes
Linear					
	BIC	9980.342	9912.299	9854.911	9830.231
	AIC	9937.340	9858.547	9790.408	9754.978
	SABIC	9942.295	9864.741	9797.841	9763.649
	Entropy	0.805	0.786	0.808	0.799
	LTR	0.1621	0.3547	0.2941	0.1449
	ALTR	0.1805	0.3672	0.3025	0.1555
	BootLTR	0.0000	0.0000	0.0000	0.0000
Quadratic					
	BIC	9857.425*	9782.548	9717.402*	9679.287*
	AIC	9803.672	9714.461	9634.982	9582.532
	SABIC	9809.866	9722.307	9644.479	9593.682
	Entropy	0.809	0.821	0.815	0.788
	LTR	0.6289	0.2134	0.1313	0.3574
	ALTR	0.6402	0.2165	0.1362	0.3654
	BootLTR	0.0000	0.0000	0.0000	0.0000
Cubic					
	BIC	9818.986	9726.592*	9665.581*	9624.839*
	AIC	9750.900	9640.588	9561.660	9503.000
	SABIC	9758.745	9650.498	9573.635	9517.040
	Entropy	0.802	0.834	0.804	0.819
	LTR	0.2717	0.2077	0.5886	0.5171
	ALTR	0.2809	0.2142	0.5975	0.5214
	BootLTR	0.0000	0.0000	0.0000	0.0000

Abbreviations: BIC=Bayesian Information Criterion, AIC=Akaike Information Criterion, SABIC= Sample-size Adjusted Information Criterion, LTR= Vuong-Lo-Mendell-Rubin Likelihood Ratio Test, ALTR=Adjusted Lo-Mendell-Rubin Likelihood Ratio Test, BootLTR=Parametric Bootstrapped Likelihood Ratio Test.
* =Indicates model misspecification warning.

3. Results

3.1. OCD-related functional impairment (COIS-R) trajectory classes - Latent class growth analysis

The three-class quadratic solution was chosen for analysis as it showed better fit indices than the linear and two-class cubic models. Table 1 presents fit values for all examined models. The two-, four- and five-class quadratic models provided warnings indicating model identification problems, as did all cubic solutions of three or more classes. Figures for individual trajectories within each class are provided in the supplemental materials (Figs. S1, S2 and S3) (Fig. 1).

Class 1 (green line), *low impairment-continuous improvement*, included 188 patients (70.7%) and showed a relatively low level of impairment at baseline that steadily declined during treatment and up until week 118 of follow-up, maintaining a similar level at the last assessment point. 28 patients from this class (14.9%) entered step 2 treatment, 12 on SSRI and 18 on CBT.

Class 2 (blue line), *high impairment-rapid improvement,* comprised of 65 (24.4%) patients, had high levels of impairment at baseline, improved rapidly during treatment and follow-up. From this class 17 patients (26.2%) entered step 2 treatment, nine on SSRI and eight on CBT.

Class 3 (red line), *moderate impairment-no improvement*, consisted of 13 patients (4.9%). This class showed a moderate to high level of impairment at baseline and no response during the treatment phase, with functional impairment scores ending up at the same level at the last assessment point as at pretreatment. Three patients (23.1%) from this class were included in step 2 treatment, one on SSRI and two on CBT.

3.2. Characteristics of functional impairment trajectory classes

Table 2 lists the differences in pretreatment characteristics of the three trajectory classes.

The *low impairment-continuous improvement* class differed significantly from the *high impairment-rapid improvement* class with lower CY-BOCS total OCD symptom severity, hoarding/symmetry symptoms, total psychopathology, internalizing symptoms, anxiety- and depressive symptoms, and younger age.

The *high impairment-rapid improvement* class differed from the *moderate impairment-no improvement* class regarding higher levels of OCD symptoms and depressive symptoms and lower rates of comorbid ADHD.

The *low impairment-continuous improvement* class differed significantly from the *moderate impairment-no improvement* class regarding lower rates of comorbid ADHD.

3.3. Multivariate predictor analysis of class membership

Using the *low impairment-continuous improvement* class as a reference category, membership in the *high impairment-rapid improvement* class was predicted by higher OCD symptom severity (CY-BOCS total) scores and older age (Table 3).

For the *moderate impairment-no improvement* class, higher levels of ADHD symptoms and lower levels of Oppositional defiant disorder (ODD) symptoms as assessed with their respective CBCL subscales, were the only significant predictors of membership.

3.4. Overlap of OCD-related functional impairment trajectory classes and OCD symptom severity trajectory classes

Table 4 displays the overlap of class membership between functional impairment and symptom severity trajectory groups.

64% of participants in the *low impairment-continuous improvement* class belong to the *acute, sustained responder* symptom severity class. The

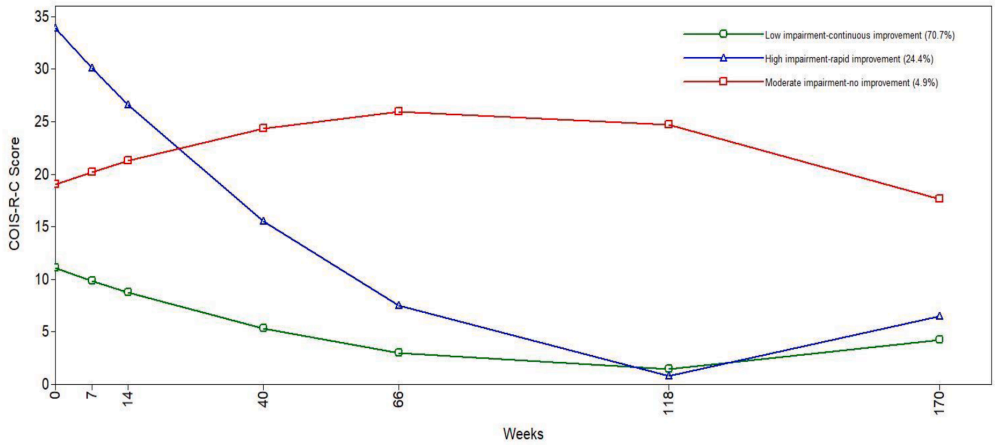

Fig. 1. Three distinct latent class growth trajectories of self-reported OCD-related functional impairment for 266 pediatric OCD patients during and after stepped-care treatment.

Table 2
Pretreatment characteristics of the three trajectory classes.

Demographics	*Low impairment-continuous improvement* (LICI)	*High impairment-rapid improvement* (HIRI)	*Moderate impairment-no improvement* (MINI)	Total	*p*	LICI vs HIRI (*p*)	LICI vs MINI (*p*)	HIRI vs MINI (*p*)	Missing N (%)
N (%)	188 (70.7%)	65 (24.4%)	13 (4.9%)	266					0
Females, N (%)	94	35	5	266	.598	.891	.679	.572	0
Age in years, mean (SD)	12.49 (2.83)	13.74 (2.27)	12.92 (2.5)	12.82 (2.74)	**.006**	**.004**	.841	.580	0
OCD constructs									
Symptom severity, CY-BOCS mean (SD)	23.91 (4.85)	26.95 (5.46)	22.77 (2.98)	24.61 (5.10)	**.001**	**.001**	.712	**.016**	0
Age of OCD onset, mean (SD)	11.38 (3.06)	12.36 (2.45)	11.58 (4.01)	11.63 (2.99)	.110	.090	.972	.693	38 (14.3%)
OCD duration, mean	1.13 (1.91)	1.32 (1.66)	1.58 (2.31)	1.19 (1.87)	.608	.777	.692	.899	38 (14.3%)
Good to excellent insight N (%)	125 (67.2%)	44 (67.7%)	9 (69.2%)	178 (67.4%)	.978	.997	.988	.994	0
Harm/sexual (factor score), mean (SD)	-0.0008 (0.9740)	-0.0253 (0.9437)	-0.0246 (0.9649)	-0.0246 (0.9649)	.422	.983	.388	.480	0
Symmetry/hoarding (factor score), mean (SD)	-0.1726 (0.8554)	.1472 (0.9905)	.1365 (1.192)	-0.0794 (0.9158)	**.035**	**0.40**	.462	.999	0
Cleaning/contamination (factor score), mean (SD)	.0217 (0.9351)	.1269 (1.077)	.3090 (0.9120)	.0613 (0.9694)	.482	.732	.557	.811	0
Family accommodation, FAS mean (SD)	16.58 (12.33)	18.01 (11.58)	12 (7.68)	16.71 (11.98)	.305	.721	.439	.280	54 (20.3%)
Comorbidity									
Tic disorders, N (%)	31 (16.7%)	13 (20.3%)	4 (30.8%)	48 (18.3%)	.394	.793	.413	.698	0
Anxiety disorders, N (%)	35 (18.8%)	13 (20.3%)	3 (23.1%)	51 (19.4%)	.911	.964	.926	.972	0
Depressive Disorders, N (%)	5 (2.7%)	4 (6.3%)	1 (7.7%)	10 (3.6%)	.33	.406	.634	.967	0
ADHD, N (%)	14 (7.5%)	3 (4.7%)	4 (30.8%)	21 (8%)	**.006**	.744	**.008**	**.004**	0
ODD, N (%)	8 (4.3%)	1 (1.6%)	1 (7.7%)	10 (3.6%)	.465	.594	.805	.543	0
CBCL total, mean (SD)	39.19 (20.78)	52.89 (28.2)	45.05 (19.56)	42.96 (23.47)	**.001**	**.001**	.690	.554	56 (21.1%)
CBCL internalizing, mean (SD)	13.76 (8.06)	19.73 (10.15)	15.09 (7.44)	15.25 (8.92)	**.001**	**.001**	.229	.871	25 (9.4%)
CBCL externalizing, mean (SD)	8.71 (7.94)	9.81 (8.11)	7.89 (5.83)	8.93 (7.89)	.587	.629	.727	.932	24 (9.0%)
Parent rated anxiety symptoms (SCARED), mean (SD)	18.83 (12.27)	25.76 (15.76)	20.82 (7.63)	20.67 (13.34)	**.002**	**.001**	.855	.431	15 (5.6%)
Parent rated depression symptoms (MFQ), mean (SD)	5.78 (5.27)	9.05 (5.83)	4.33 (2.57)	6.5 (5.5)	**.001**	**.001**	.633	**.015**	16 (6%)

Bold values are *p* values of ≤ 0.5.

Table 3
Parameters for the multinomial logistic regression model using the *low impairment-continuous improvement* class as a reference category (Pooled multiple imputation results).

Trajectory class		B	Std. Error	Wald	df	Sig.	Exp (B)	95% Confidence Interval for Exp(B)		Fraction Missing Info.	Relative Increase Variance	Relative Efficiency
								Lower Bound	Upper Bound			
High impairment-rapid improvement	Intercept	−8.111	1.464	30.704	1.660421.960	0.000				0.012	0.012	1.000
	Age	0.226	0.072	9.811	1.529910.825	**0.002**	1.254	1.088	1.445	0.013	0.013	1.000
	Gender	0.013	0.363	.001	1.210602.823	0.972	1.013	0.497	2.064	0.021	0.021	1.000
	CY-BOCS total score	0.123	0.036	11.497	1.530712.436	**0.001**	1.130	1.053	1.213	0.013	0.013	1.000
	OCD duration	−0.065	0.095	.465	1.25651.255	0.495	0.937	0.779	1.129	0.060	0.063	0.999
	Insight	0.053	0.170	.097	1.3100978.47	0.755	1.054	0.756	1.471	0.005	0.005	1.000
	Family accommodation scale	−0.011	0.018	.403	1.3353.488	0.526	0.989	0.954	1.024	0.166	0.198	0.998
	Tic disorder (K-SADS)	−0.019	0.457	.002	1.595206.837	0.967	0.982	0.400	2.406	0.012	0.013	1.000
	SCARED-P Total	0.030	0.016	3.408	1.29588.239	0.065	1.030	0.998	1.063	0.056	0.059	0.999
	MFQ- P Total	0.059	0.041	2.028	1.12845.964	0.154	1.061	0.978	1.150	0.085	0.092	0.999
	CBCL ADHD subscale	0.115	0.083	1.901	1.7914.541	0.168	1.122	0.953	1.321	0.108	0.121	0.999
	CBCL ODD subscale	−0.115	0.099	1.366	1.15119.512	0.242	0.891	0.734	1.081	0.078	0.084	0.999
	Harm/sexual (factor score)	−0.195	0.186	1.095	1.942148.798	0.295	0.823	0.572	1.185	0.010	0.010	1.000
	Symmetry/ hoarding (factor score)	0.210	0.195	1.162	1.1151029.95	0.281	1.233	0.842	1.806	0.009	0.009	1.000
	Cleaning/ contamination (factor score)	−0.048	0.189	.064	1.281874.415	0.800	0.953	0.659	1.380	0.018	0.018	1.000
Moderate impairment – no improvement	Intercept	−4.188	2.619	2.557	1.173545.866	0.110				0.023	0.023	1.000
	Age	0.057	0.138	.170	1.70952.765	0.681	1.058	0.808	1.386	0.036	0.037	1.000
	Gender	0.106	0.712	.022	1.127677.133	0.881	1.112	0.276	4.489	0.027	0.027	1.000
	CY-BOCS total score	0.008	0.075	.011	1.144179.150	0.917	1.008	0.869	1.168	0.025	0.026	1.000
	OCD duration	0.084	0.181	.212	1.28842.520	0.645	1.087	0.762	1.551	0.056	0.060	0.999
	Insight	−0.233	0.369	.399	1.220789.585	0.528	0.792	0.384	1.633	0.020	0.021	1.000
	Family accommodation scale	−0.039	0.043	.818	1.2454.203	0.366	0.962	0.884	1.047	0.194	0.240	0.998
	Tic disorder (K-SADS)	0.342	0.829	.170	1.53277.284	0.680	1.408	0.277	7.152	0.041	0.043	1.000
	SCARED-P Total	0.050	0.036	1.967	1.45804.671	0.161	1.051	0.980	1.128	0.045	0.047	1.000
	MFQ- P Total	−0.201	0.126	2.567	1.13730.616	0.109	0.818	0.639	1.046	0.082	0.089	0.999
	CBCL ADHD subscale	0.476	0.179	7.028	1.6192.795	**0.008**	1.609	1.132	2.288	0.122	0.139	0.999
	CBCL ODD subscale	−0.416	0.212	3.841	1.6936.971	**0.050**	0.660	0.435	1.000	0.115	0.130	0.999
	Harm/sexual (factor score)	−0.780	0.435	3.216	1.141722.005	0.073	0.459	0.196	1.075	0.025	0.026	1.000
	Symmetry/ hoarding (factor score)	−0.046	0.379	.015	1.314750.609	0.902	0.955	0.455	2.005	0.017	0.017	1.000
	Cleaning/ contamination (factor score)	0.541	0.399	1.832	1.115398.791	0.176	1.717	0.785	3.756	0.028	0.029	1.000

Bold values are p values of ≤ 0.5.

Table 4
Overlap with symptom severity trajectory classes from Jensen et al.

CY-BOCS trajectory class membership	COIS-R trajectory class membership		
	Low impairment responders	High impairment responders	No-improvemnet
Acute responders	119 (64%) $_{a}$	20 (30.8%) $_{a, e}$	4 (30.8%) $_{e}$
Slow responders	32 (17.2%) $_{a}$	28 (43.1%) $_{e}$	2 (15.4%) $_{a, e}$
Limited responders	35 (18.8%) $_{a}$	17 (26.2%) $_{e}$	7 (53.8%) $_{a, e}$

Each subscript letter ($_{a}$, $_{e}$) denotes a subset of COIS-R trajectory classes whose column proportions do not differ significantly from each other at the 0.05 level.

trajectory of symptom improvement for the *acute, sustained responder* symptom severity class is initially steep, with the CY-BOCS mean score improving by 70% from pre- to post treatment for the group. In contrast, COIS-R mean scores only improve by 25% from pre-to post treatment for the *low impairment-continuous improvement* class.

43.1% of participants in the *high impairment-rapid improvement* class, belong to the *slow, continuous responders* symptom severity class. Again, the trajectory of the symptom severity class is initially steep, with CY-BOCS scores improving 40% from pre- to post treatment, while the *high impairment-rapid improvement* class improves around 24% on mean COIS-R scores from pre- to post treatment.

For the *moderate impairment-no improvement* class, over half (53.8%) belong to the *limited long-term responders* symptom severity class. The symptom severity class shows limited signs of improvement during the treatment phase while the functional impairment class does not.

3.5. Analysis of missing cases

Table S2 in the supplemental material provides an overview of the missing COIS-R scores and differences between missing and non-missing groups at each point of assessment.

At baseline 7.5% of COIS-R child self-report scores were missing. The missing group was characterized by lower age, higher family accommodation and less symmetry/hoarding symptoms than the non-missing group. During treatment (weeks 7 and 14) these characteristics were no longer significantly different between the groups.

During follow-up there was considerable attrition eventually resulting in 44.7% missing at the last assessment point (Week 170). The most consistent significant difference during the follow-up phase was that the missing group was younger, had an earlier age of onset and had higher levels of self and parent reported functional impairment at baseline. Both multiple imputation (used on the baseline data for multinomial logistic regression) and maximum likelihood estimation (used for the LCGA) assume that data are missing at random (MAR) or missing completely at random (MCAR) (Muthén and Muthén, 1998-2017; Rubin, 1996). Non-random attrition in longitudinal data can weaken statistical precision and lead to bias (Andruff et al., 2009). The current data are clearly not MCAR, yet there are no indications that missingness is affected by unknown reasons and therefore MAR is assumed.

4. Discussion

This study examines latent class trajectories of long-term OCD-related functional impairment in children and adolescents before, during and after treatment. Three distinct trajectory classes were identified. Two large classes of different initial levels of impairment showed clear signs of improvement during and after treatment. A smaller third class did not improve at any point of assessment during the 3-year-follow-up. The trajectories of impairment, while in some ways similar, are in important respects distinct from trajectories of severity and, in some cases, improvements in severity may be concomitant with stagnated impairment and vice versa. However, for the larger classes, functional improvement seems to occur after improvements in symptom severity.

The largest class, *low impairment-continuous improvement,* had the lowest level of functional impairment initially. For this group, the level of impairment steadily declined throughout the treatment and follow-up phases. This class also had the lowest proportion of members entering step 2 treatment . The *low impairment-continuous improvement* class largely overlapped with the *acute, sustained responders* symptom severity trajectory class from Jensen et al. (Jensen et al., 2020), representing a strong majority of children and adolescents with OCD that improve both symptomatically and functionally with treatment, and maintain their treatment gains for at least three years. This group is characterized by less symptom severity and comorbid psychopathology and fewer symmetry/hoarding symptoms. This is in line with earlier studies indicating that lower symptom severity positively predicts symptom severity treatment response, and the same holds true for functional impairment (Garcia et al., 2010; Turner et al., 2018). This class is also younger on average than the *high impairment-rapid improvement* class. It has previously been shown that in the current sample younger age predicted positive treatment response and this seems to apply to functional impairment as well (Torp et al., 2015b). Similarly, Jensen et al. (Jensen et al., 2020) found that older age predicted membership in the *limited responders* class indicating better outcomes for younger patients overall in the current sample.

The second largest class, *high impairment-rapid improvement*, had the highest level of functional impairment initially but rapidly improved over the course of the first 66-weeks. This class eventually reached a similar level of impairment to the *low impairment-continuous improvement* class and maintained that level as well. Despite having the highest level of functional impairment post-treatment (at week 14), only 26.2% of this class entered step 2 treatment. The *high impairment-rapid improvement* class shared members most frequently with the *slow, continued responders* symptom severity class, which also had the highest severity levels of the three classes identified in Jensen et al. (Jensen et al., 2020). Membership in the *slow, continued responders* symptom severity class was predicted by high overall psychopathology severity (Jensen et al., 2020) and membership in the *low impairment-continuous improvement* class was, relatedly, predicted by OCD symptom severity. This indicates that there is a substantial subgroup of pediatric OCD patients which is severely affected, characterized by higher levels of comorbid psychopathology scores and a tendency to be older. This group is still significantly impaired and symptomatic post-treatment but continues to improve during follow-up, eventually reaching a low level of impairment.. It is therefore important for clinicians to keep in mind that for the most severely affected OCD cases, symptom severity and functional impairment may still be high after treatment. However, with continued support, it appears that their long-term outcomes can be as good as for less severely affected patients. This further means that post-treatment functional impairment scores do not determine long-term development and are on their own not indicative of the patient's subsequent trajectory. This is consistent with recent research indicating that post-treatment OCD symptom severity scores do not predict remission status at two- or three-year follow-up (Jensen et al., 2022).

The third and smallest class, *moderate impairment-no improvement*, has a level of functional impairment that initially falls between the other two classes. Even though by far the smallest class, these results are clinically important as this class has a very distinct trajectory. This class has considerable overlap with the *limited long-term responders* symptom severity class (Jensen et al., 2020). However, the *limited long-term responders* class did show signs of treatment response, although less so than the other symptom severity classes. However, this impairment class shows no signs of improvement, which indicates that a small group of pediatric OCD patients has a limited response to evidence-based treatment and remains at the same level of impairment as pretreatment.. The only significant characteristic of this group is a higher level of comorbid ADHD diagnoses. This group does not have a higher level of externalizing symptoms indicating that despite higher ADHD levels they are not more prone to behavioral difficulties. Remarkably, membership in this group is predicted by lower levels of ODD symptoms. This might indicate that these children and adolescents are primarily more inattentive and disorganized and therefore possibly impaired in their ability to engage with psychological treatment or adhere to medication regimens. Although the small number of participants in this class makes this highly speculative, we believe clinicians should be aware that this comorbidity might yield specific treatment challenges, but replication would be needed for any firm conclusions. It is, however, also important to note that the majority of the *moderate impairment-no improvement* class did not have comorbid ADHD, and it is possible that the non-ADHD portion of this subclass explains the association with lower ODD levels. It would appear that non- and limited responders are a heterogenous subgroup... Jensen et al. (Jensen et al., 2020) found that limited symptom treatment response was predicted by lower levels of overall psychopathology severity and more contamination/cleaning symptoms, which was not found for the impairment non-response group. Identification of robust predictors of poorer long-term treatment response remains difficult.

From earlier studies describing the symptom severity treatment response for the current sample (for the whole sample (Melin et al., 2020) and for distinct subgroups (Jensen et al., 2020)) it is apparent that the steepest decline in symptom severity occurs during the initial 14-week treatment phase for the total sample and all subgroups identified. For OCD-related functional impairment, however, we find a more gradual pattern of improvement over time for most patients. This demonstrates a delayed effect of treatment on impairment, such that after symptoms are reduced a period of readjustment is needed for the child or adolescent to achieve their pre-OCD onset levels of functioning.

The proportion of trajectory class members entering Step 2 treatment

is much less varied between classes for the current functional impairment trajectory classes than it was for the symptom severity classes (Jensen et al., 2020). The *acute, sustained responders* symptom severity trajectory class only had two patients (1.36%) that entered Step 2 while the functional impairment class showing the most similar trajectory and member overlap with that class, the *low impairment-continuous improvement* class, has 14.9% of its member entering Step 2. The *slow, continued responders* symptom severity trajectory class had almost half (49.21%) of its members entering Step 2 treatment while the most similar functional impairment trajectory class, the *high impairment-rapid improvement* class had 26.3% entering Step 2. The third functional impairment class, *moderate impairment-no improvement*, had 3 patients (23.1%) that entered Step 2. This class shares over half of its members with the *limited long-term responders* symptom severity class. The *moderate impairment-no improvement* class show no signs of improving with regards to functional impairment during and after treatment and shares members mostly with the symptom severity class that also has the most limited response to treatment. This suggests the importance of taking the development of functional impairment during treatment into account when deciding whether further treatment is required. Current guidelines emphasize symptom severity for definitions of response and remission in OCD treatment (Mataix-Cols et al., 2016). Others have argued that this approach might be inadequate as measures of functional impairment and quality of life should be included (Jaisoorya and Janardhan Reddy, 2023). The current results lend support to this view.

4.1. Strengths and limitations

The data for the present study comes from the largest follow-up study of pediatric OCD to date. The large sample size and the study design of conducting several successive assessments made it feasible to conduct the first LCGA study of long-term OCD-related functional impairment. The same sample has previously been used for a LCGA of symptom severity score allowing for direct comparisons with its results and adding clinically relevant supplementary information on the long-term development of OCD in children and adolescents.

The study is limited by the unequal size of the clusters, particularly the *moderate impairment-no improvement* class has few participants and may not be stable or replicable in other samples. Furthermore, the small number of members in that class results in low statistical power for the multivariate regression model. The study is also limited by not employing any neuropsychological measures as functional impairment could be related to neuropsychological performance, which may improve over time if it is state-related. The current study employs a dimensional factor score based on the CY-BOCS checklist. A more refined measure of dimensionality, such as the DYBOCS (Rosario-Campos et al., 2006), could have yielded different results. The current findings are also mostly generalizable to clinical situations where CBT is the first line of treatment for OCD. Like all follow-up studies there is a limitation of attrition. Missing data were handled by maximum likelihood equations and multiple imputation to mitigate this. However, some bias is inevitable since variables predictive of missingness (i.e., age, family accommodation, baseline functional impairment) were not included in the LCGA.

5. Conclusion

The current study demonstrated that after stepped-care treatment long-term OCD-related functional impairment can be classified based on three distinct trajectories: a *low impairment-continuous improvement* class, a *high impairment-rapid improvement* class and a *moderate impairment-no improvement* class. The two larger classes, *low impairment-continuous improvement* and *high impairment-rapid improvement,* together indicate that a large majority of children and adolescents improved with treatment and maintained low levels of impairment throughout the follow-up period regardless of differing levels of baseline severity and comorbidity. Functional impairment improves gradually with continuous long-term improvement post-treatment for most patients, which contrasts sharply with previous results from the same sample where severity improved rapidly during the treatment phase but much slower or very little in the post treatment phase. A small subgroup, *moderate impairment-no improvement*, did not demonstrate any improvement in functional impairment during or after treatment and remained at pre-treatment levels of impairment after three years. The distinguishing feature of this group is a significantly higher level of comorbid ADHD diagnoses. The current results demonstrate the importance of assessing functional impairment, even in those symptomatically remitted, and developing strategies to address functional impairment directly.

Further research is needed to confirm the long-term development of OCD-related functional impairment after treatment and distinct latent class trajectory patterns thereof. Distinguishing characteristics of subgroups that do not benefit from treatment would be of particular interest. Furthermore, the functional interplay of OCD and ADHD as comorbid disorders requires further examination.

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Author contributions

Mr. Smárason, Drs. Skarphedinsson and Højgaard had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

CRediT authorship contribution statement

Orri Smárason: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Davíð R.M.A. Højgaard:** Conceptualization, Methodology, Writing – review & editing. **Sanne Jensen:** Writing – review & editing. **Eric A. Storch:** Writing – review & editing. **Gudmundur B. Arnkelsson:** Writing – review & editing. **Lidewij H. Wolters:** Writing – review & editing. **Nor Christian Torp:** Writing – review & editing. **Karin Melin:** Writing – review & editing. **Bernhard Weidle:** Writing – review & editing. **Judith Becker Nissen:** Writing – review & editing. **Katja Anna Hybel:** Writing – review & editing. **Per Hove Thomsen:** Writing – review & editing. **Tord Ivarsson:** Writing – review & editing. **Gudmundur Skarphedinsson:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

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Supplementary materials

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