The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC)

Validity, reliability, and the measurement of autism in males and females

Caroline Mårland

Department of Psychiatry and Neurochemistry
Institute of Neuroscience and Physiology
Sahlgrenska Academy, University of Gothenburg

UNIVERSITY OF GOTHENBURG

Gothenburg 2022

Cover illustration: Pia Moberg

The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC)
Validity, reliability, and the measurement of autism in males and females

caroline.marland@gu.se

ISBN 978-91-8009-717-8 (PRINT)
ISBN 978-91-8009-718-5 (PDF)
http://hdl.handle.net/2077/70530

Printed in Borås, Sweden 2022
Printed by Stema Specialtryck AB

In memory of Professor Henrik Anckarsäter,
the founder of CELAM,
whose kind invitation turned out to be the starting point
of my adventures in the world of research

ABSTRACT

The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC) is a broad-band screening instrument for neurodevelopmental disorder (e.g., autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and learning disorder (LD)), and commonly co-occurring disorders within child and adolescent psychiatry (e.g., oppositional defiant disorder (ODD)). The overarching aim of this thesis is to further evaluate the psychometric properties of the A–TAC, with a particular focus on ASD. All papers are based on data from the Child and Adolescent Twin Study in Sweden, which includes a parental interview with the A–TAC and provides a linkage to the National Patient Register in Sweden. **Paper I** examines the previous and predictive validity of the A–TAC. The results show that the A-TAC is particularly strong as a screening instrument for ASD, ADHD, LD and ODD. In **paper II**, a *short form* of the ASD domain is developed by utilizing item response theory. Four items were selected for the *short form*, which showed excellent previous validity. **Paper III** aims to compare males and females with regard to degree of ASD symptomatology by way of a sex-specific standardized score. The results indicate that females diagnosed with ASD represent an even more extreme end of the distribution of ASD traits in the general population of females than do males diagnosed with ASD. **Paper IV** examines the items in the ASD domain in the A–TAC for differential item functioning and investigates whether a subset of items are better at capturing ASD traits in males and females. The results show that the ASD domain is largely equivalent (i.e., the same construct is measured across sexes). **In conclusion**, the A–TAC is a well-validated broad-band screening instrument that can be used in research and clinical practice. The ASD *short form* can be particularly useful in large-scale studies. Females with ASD may present with quantitatively fewer symptoms of ASD, which highlight the need to consider the quality of the manifest symptoms during clinical assessments. The limited psychometric difference between males and females diminishes the need for sex-specific scoring for the ASD domain. However, the possible differences in the manifestation of ASD across sex and age need to be further examined in order to ensure content validity and the usage of appropriate cut-off values.

Keywords: neurodevelopmental disorders, autism, ADHD, A–TAC, screening, sex, item response theory, differential item functioning

ISBN 978-91-8009-717-8 (PRINT)
ISBN 978-91-8009-718-5 (PDF)
http://hdl.handle.net/2077/70530

SAMMANFATTNING PÅ SVENSKA

Screeninginstrumetet Autism–Tics, ADHD, och andra komorbiditeter, A–TAC, är utvecklat för att fånga utvecklingsrelaterade funktionsavvikelser, så som autismspektrumtillstånd (AST), aktivitets- och uppmärksamhets-störning (ADHD) och inlärningssvårigheter samt andra vanligt förekommande diagnoser inom barn- och ungdomspsykiatrin, exempelvis trotssyndrom. Det övergripande syftet med denna avhandling är att genomföra ytterligare utvärderingar av A–TACs psykometriska egenskaper, med ett särskilt fokus på AST. Alla delstudier är baserade på data från barn- och ungdomsstudien i Sverige (CATSS) som inkluderar en föräldraintervju med A–TAC samt länkning till det svenska patientregistret. **Delstudie I** undersöker A–TACs bekräftande och prediktiva validitet. Resultatet visar på att A–TAC har en särskild styrka som ett screeninginstrument för AST, ADHD, inlärningssvårigheter och trotssyndrom. I **delstudie II** utvecklas en kortskala för AST domänen i A–TAC genom att använda modern mätteori (item response theory). Fyra frågor valdes ut till kortskalan som uppvisar en utmärkt bekräftande validitet. **Delstudie III** syftar till att jämföra graden av AST symtomatologi hos pojkar och flickor genom att studera könsspecifika standardiserade poäng. Resultatet visar på att flickor med en AST diagnos representerar en mer extrem ände av distributionen av AST drag i en generell population av flickor jämfört med pojkar diagnostiserade med AST. I **delstudie IV** används den statistiska metoden Differential Item Functioning för att undersöka om frågorna som utgör AST domänen mäter samma konstrukt hos pojkar och flickor. Resultatet visade på att AST domänen på ett likvärdigt sätt mäter AST drag hos pojkar och flickor, endast små skillnader upptäcktes mellan pojkar och flickor. **Sammanfattningsvis** är A–TAC ett väl validerat och omfattande screeninginstrument som kan användas inom både klinik och forskning. Kortskalan av AST domänen kan vara särskilt värdefull i storskaliga studier. Flickor med AST kan uppvisa kvantitativt färre symtom på AST, vilket tyder på att kvalitén av de manifesta symtomen bör beaktas vid utredning. Den psykometriska skillnaden mellan pojkar och flickor var liten vilket minskar behovet av könsspecifika versioner avseende den totala ASD-domänen. Den möjliga skillnaden mellan hur AST drag tar sig i uttryck hos pojkar och flickor och i olika åldersgrupper behöver undersökas framöver för att säkerställa innehållsvaliditet samt användandet av lämpliga gränsvärden

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. **Mårland C**, Lichtenstein P, Degl'Innocenti A, Larson T, Råstam M, Anckarsäter H, Gillberg C, Nilsson T, & Lundström S. The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC): Previous and predictive validity. *BMC Psychiatry*. 2017;17:403.

II. **Mårland C**, Lubke G, Degl'Innocenti A, Råstam M, Gillberg C, Nilsson T, & Lundström S. The development of a brief screener for autism using item response theory. *BMC Psychiatry*. 2019;19:337.

III. Lundström S, **Mårland C,** Kuja-Halkola R, Anckarsäter H, Lichtenstein P, Gillberg C, & Nilsson T. Assessing autism in females: The importance of a sex-specific comparison. *Psychiatry Research*. 2019;282:112566.

IV. **Mårland C**, Nilsson T, Larsson H, Gillberg C, Lubke G, & Lundström S. Measuring autism in males and females with a differential item functioning approach: Results from a nation-wide population-based study. *Submitted*.

CONTENT

ABBREVIATIONS

2PL	Two-Parameter Logistic Model
ADHD	Attention Deficit Hyperactivity Disorder
AIC	Akaike Information Criterion
ASD	Autism Spectrum Disorder
A–TAC	Autism–Tics, ADHD and other Comorbidities Inventory
AUC	Area Under the Receiver Operating Characteristic Curve
BCC	Boundary Characteristics Curve
BIC	Bayesian Information Criterion
CATSS	Child and Adolescent Twin Study in Sweden
CD	Conduct Disorder
CTT	Classical Test Theory
DAMP	Deficits in Attention, Motor Control, and Perceptual Abilities
DCD	Developmental Coordination Disorder
DIF	Differential Item Functioning
DOR	Diagnostic Odds Ratio
DSM	Diagnostic and Statistical Manual of Mental Disorders
ED	Eating Disorder
EFA	Exploratory Factor Analysis
ESSENCE	Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations
FP	False Positive

FN	False Negatives
GRM	Graded Response Model
ICD	International Classification of Diseases
ID	Intellectual Disability
IIF	Item Information Function
IRT	Item Response Theory
LD	Learning Disorder
LRT	Likelihood Ratio Test
NDD	Neurodevelopmental Disorders
NPR	National Patient Register
NPV	Negative Predictive Value
OCD	Obsessive Compulsive Disorder
ODD	Oppositional Defiant Disorder
ROC	Receiver Operating Characteristic Curve
PPV	Positive Predictive Value
TD	Tic Disorder
TN	True Negatives
TP	True Positives

1 INTRODUCTION

1.1 NEURODEVELOPMENTAL DISORDERS

Neurodevelopmental disorders (NDDs) are characterized by onset during the childhood years and manifested in functional deficits. Impairment can range from specific learning problems to global impairment that affects all aspects of everyday life. In the Diagnostic and Statistical Manual of Mental Disorders – fifth edition (DSM-5), NDD is an umbrella term encompassing intellectual disability (ID), communication disorders (language disorder, speech sound disorder, social communication disorder, and childhood-onset fluency disorder), autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), motor disorders (developmental coordination disorder (DCD), stereotypic movement disorder, and tic disorder (TD)) and specific learning disorders (i.e. related to reading, writing, or arithmetic skills).[1]

NDDs affect at least 7%–10% of all children[2] and are generally diagnosed more often in boys than in girls.[3] The heritability of NDDs is high[4-6] and a shared genetic liability has been reported across disorders.[7-9] The distribution of NDDs is considered to be dimensional rather than categorical.[10-13] Thus, a clinical diagnosis of NDD is, in most instances, considered to represent the extreme end of the dimensional distribution. Today, it is widely acknowledged that co-occurrence of NDDs is high (i.e., the presence of one NDD predicts the presence of another, which has been described as the rule rather than the exception).[2] In the case of ASD, studies using both clinical and population-based samples have reported that 70%–95% of the children with ASD have at least one additional diagnosis. The substantial rate of co-occurrence also includes other well-known psychiatric disorders (e.g., anxiety and depression).[14-20]

The term Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations, or ESSENCE for short, was created by Professor Christopher Gillberg to emphasize the symptomatic overlap between disorders. Gillberg emphasizes the need for a holistic perspective and multidisciplinary assessment in order to provide interventions that address the specific needs of each child and family. Therefore, children who show impairing symptoms before the age of five in one or more of the following areas – general development, communication and language, social inter-relatedness, motor coordination, attention, activity, behavior, mood, or sleep – should be referred to a multidisciplinary team.[2]

When a child presents with impairing symptoms, concerns are commonly expressed by parents or by professionals (e.g., during a mandatory developmental check-up or in a school setting). In a primary care setting, an initial visit may include a short clinical interview and observation followed by the use of screening instruments. By utilizing broad-band screening instruments, several relevant aspects of a child's development can be assessed which may assist in the referral process by highlighting different areas of deficit and impairment that are in need of further clinical investigation. There may be various aspects to a diagnostic assessment of NDDs based on the reason for the referral. There are numerous guidelines that generally recommend multidisciplinary teams and that the diagnostic process potentially include developmental and psychiatric history, physical examination, assessment through interaction and observation, diagnostic instruments and/or rating scales, assessment of the child's need and impairments in different settings, psychological testing, and consideration of any possible coexisting disorders.[21-28]

1.1.1 DEFINITION OF DISORDERS

Although this thesis focuses mainly on ASD, it also encompasses disorders that commonly overlap with ASD during childhood and adolescence: ADHD, learning disorders (LDs), DCD, TD, and the following psychiatric disorders: opposition defiant disorder (ODD), conduct disorder (CD), obsessive compulsive disorder (OCD), and eating disorders (EDs). A brief description according to the DSM-5[1] of the disorders included are presented here, with the exception of ASD, which is discussed extensively in this thesis and is therefore presented under a separate heading below.

The diagnostic features of **ADHD** include symptoms of inattention, hyperactivity, and impulsivity. Inattention is defined by difficulties with sustained attention, organization of tasks and activities, avoidance of tasks that require mental effort, and being easily distracted and absentminded. Hyperactivity is characterized by excessive motor activity which may be manifested by fidgeting, tapping and difficulties with being still or playing calmly. Impulsivity can be described as acting without thinking and includes difficulties waiting one's turn and intrusion on other people's conversations or activities. Furthermore, symptom presentation should be inconsistent with developmental level and have a negative impact on development or daily functioning in various settings.[1] The prevalence of ADHD among children and adolescents has been reported as 7.2%.[29] A diagnosis of ADHD commonly overlaps with ASD, TD, ODD, and/or CD.[30,31] Additionally, ADHD is

associated with an increased risk for anxiety, depression, substance use disorder, antisocial behavior, and criminality.[32-36]

A diagnosis of **ID** (in this thesis the abbreviation LD (i.e., learning disorder) encompasses ID) is based on deficits in intellectual and adaptive functioning. A diagnosis of ID is partly based on standardized testing of IQ, and a diagnosis of ID is indicated according to its category of severity: mild, moderate, severe, or profound via IQ scores ranging from 50-70, 35-49, 20-34 and below 20 respectively. Deficits in adaptive functioning refer to difficulties in meeting socio-cultural standards of personal independence and social responsibility. Support in everyday life is required in order to compensate for deficits in adaptive functioning. However, one's need for support can vary greatly and depends on the severity of symptoms.[1] The prevalence of ID is reported at around 1%[37] and ID commonly co-occurs with other NDDs (e.g., ASD[38] and ADHD[39,40]), and medical conditions such as cerebral palsy[41] and epilepsy.[42] A co-occurring diagnosis of ID is important to consider since it may affect the individual's outcome and prognosis.[1]

The diagnostic features of **DCD** include deficits in motor coordination inconsistent with expectations for the chronological age. The achievement of developmental milestones (e.g., crawling and walking) may be delayed. Additionally, there may be difficulties such as clumsiness and slow and/or inaccurate execution of movement (e.g., dropping things, bumping into objects, imprecise and/or slow handwriting, difficulty using zippers and cutlery, and participating in sports). A requirement for a diagnosis of DCD is that deficits in motor coordination significantly hinder and impair daily life.[1] Prevalence has been reported as 5%.[43] Even though DCD can co-occur with several NDDs, such as ASD or a specific learning disorder (e.g., difficulty writing or reading), a considerable co-occurrence of approximately 50% has been reported with ADHD.[44-46] In the long term, individuals with DCD are at increased risk of educational underachievement[47] and mental health problems (e.g., depression[48] and anxiety[49]).

The diagnostic criteria for **TD** include both motor and vocal tics. Tics are unexpected, fast and frequent motor movements or vocalizations that are involuntary, although tics can be suppressed to some extent by the individual. The variety of tics is considerable, but common symptoms include eye-blinking or throat clearing, and complex TD may include the imitation of movements or the repetition of words or phrases. Tourette's disorder is a subtype of TD defined by severe motor and vocal tics. A diagnosis of TD requires persistent symptoms of at least one year's duration and onset before 18 years of age. In most cases, TDs are temporary.[1] The prevalence of TDs

was reported as 6.6% in a Swedish study of children aged 7–15 years[50] and the reported prevalence of Tourette's disorder is 1%.[51] Co-occurrence with ADHD and OCD is considerable; about 60% of individuals with Tourette's disorder have a diagnosis of ADHD and 27% have a diagnosis of OCD.[52]

The diagnostic features of **ODD** or **CD** include problems with the self-control of behavior and emotions. ODD is characterized by irritable moods that can be manifested in the recurrent and/or persistent loss of temper, easily being annoyed or angry, and resentfulness. Defiant behavior includes frequent arguments with adults or authority figures, refusal to comply with rules or requests, knowingly annoying other people, blaming other persons for one's own mistakes, and being spiteful or vindictive. A diagnosis of ODD also requires symptoms to be present for at least six months. CD is characterized by a more severe problem constellation and is often preceded by ODD. The symptomatology of CD includes aggression towards people and animals, destruction of property, deceitful behavior, and theft or the violation of rules (e.g., running away from home).[1] The prevalence of ODD and CD varies extensively, with approximate estimates ranging from 2% to 10%.[53-56] ADHD commonly co-occurs with both ODD and CD.[32,57] Longitudinal studies have reported an increased risk of lower academic achievement, anxiety, depression, substance use, criminality, and for suicide attempts among individuals diagnosed with ODD and/or CD.[58-62]

A diagnosis of **OCD** is typically based on the presence of time-consuming obsessions or compulsions. Obsessions are persistent, frequent and intrusive thoughts, images, or urges. Compulsions are behaviors or mental acts that an individual is compelled to perform, often as a response to an obsession, in order to feel calm or reduce distress. The content of OCD varies extensively, but common themes include fear of contamination, washing of hands, forbidden thoughts (e.g., sexuality, aggression), fear of doing harm to oneself or others, and a need for symmetry.[1] Lifetime prevalence has been estimated as 1%.[63] The mean age of early onset of OCD has been reported as approximately 11–13 years, while the mean age of late onset is around 23–25 years.[64,65]

The main characteristics of an **ED** are eating disturbances or eating-related behavior which turns into a preoccupation with food or another consumption pattern that causes a significant impairment in everyday life. In DSM-5, pica (eating nonnutritive and/or nonfood substances), rumination disorder (recurring vomiting of food), avoidant/restrictive food intake disorder (limited eating that leads to weight loss and nutritional deficiency), anorexia nervosa (restricted energy intake that turns into significant low body weight), bulimia nervosa (binge eating in combination with compensatory behavior (e.g.,

vomiting)), and binge-eating disorder (excessive intake of food) have been included under the heading for feeding and eating disorders.[1] The lifetime prevalence of any ED is 8.4% among women and 2.2% among men.[66] Compared to the general population, ED symptomatology has been reported as more common among individuals with NDDs.[67] In particular, considerable overlap has been found between ASD or ADHD and EDs.[68-71]

1.2 AUTISM SPECTRUM DISORDER

1.2.1 A BRIEF HISTORICAL BACKGROUND

Over a century ago, the Swiss psychiatrist Eugen Bleuler coined the term "autism" as a description of the withdrawal from reality in schizophrenic patients.[72] For many years, ASD was considered to be a sub-type of schizophrenia and the term "childhood schizophrenia" was thus used to describe deficits in social communication.[73]

In 1926, the child psychiatrist Grunya Efimovna Sukhareva published a paper based on the case studies of six boys with psychiatric problems. Sukhareva observed several distinct features that she subsumed under the term "schizoid (eccentric) psychopathy" (e.g., odd behavior, lack of facial expression, an unusual voice (nasal, hoarse or high pitch), difficulties with peers and superficial emotions). Later, Sukhareva replaced the term "schizoid (eccentric) psychopathy" with "autistic (pathological avoidant) psychopathy". Sukhareva's pioneering work was in German and Russian and has received increased attention since being translated into English in 1996.[74]

The psychiatrist Leo Kanner is widely recognized for his work in the field of ASD. In 1943, nearly 20 years after Sukhareva, Kanner published the paper *Autistic disturbances of affective contact*, in which he wrote about his observations of eight boys and three girls and noted severe impairment in social interaction early in life, stereotyped movement, a desire for sameness and abnormal language (e.g., echolalia). Later, Kanner argued that the children's symptoms were related to a lack of warmth from their parents. The development of the concept of ASD has also been influenced by the work of the pediatrician Hans Asperger, who described a group of four boys with high intelligence, good verbal skills, narrow interests and social difficulties.[75] The work of Asperger was acknowledged and introduced to the scientific community by Lorna Wing in 1981.

During the 1970s, ASD began to be considered a separate condition that did not fit with descriptions of childhood schizophrenia. In 1978, Michael Rutter proposed a set of diagnostic criteria for childhood autism that included onset before 30 months of age and deviance in social development and language abilities, as well as insistence on sameness.[75] As of writing, five editions (including the revised versions) of DSM have been published, each with definitions of ASD that both overlap and differ.

1.2.2 AUTISM IN THE DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS

Autism was defined as a distinct disorder, separate from childhood schizophrenia, for the first time in DSM-III, published in 1980. The diagnosis "infantile autism" was subsumed under the overarching term "pervasive developmental disorders" and the diagnostic criteria were greatly influenced by Rutter's definition in 1978.[75] In 1987, the diagnostic criteria were revised, and DSM-III-R used the term "autistic disorder" and added the broader diagnosis of "pervasive developmental disorder – not otherwise specified", which included children who did not fully meet the required criteria for autistic disorder. Furthermore, the revision excluded the requirement of onset before 30 months of age. A diagnosis of autistic disorder required that at least eight of the sixteen diagnostic criteria to be fulfilled. The diagnostic criteria were organized into three categories: qualitative impairments in social reciprocity and interaction, impairments in verbal and non-verbal communication and restricted activities and interests.[76]

The fourth edition of DSM was published in 1994 and included autistic disorder, Asperger's disorder, pervasive disorder not otherwise specified, childhood disintegrative disorder, and Rett's disorder under the umbrella term of "pervasive developmental disorders". A diagnosis of autistic disorder could be made when six of the twelve diagnostic criteria were fulfilled. The diagnostic criteria were organized into three categories: social interaction, social communication, and restrictive, repetitive, or stereotyped patterns of behavior. At least one of the fulfilled symptoms should have onset before the age of three.[77]

The DSM-5 was published in May 2013 and its full diagnostic criteria are reproduced in **Box 1**. The latest edition includes several changes that should be acknowledged. First, ASD is described as a spectrum without subtypes in order to highlight the variability in symptom presentation.[1] The diagnostic subtypes have been eliminated due to insufficient evidence of reliable distinctions.[78] Instead, DSM-5 introduces specifiers (e.g., "ASD with or

without accompanying intellectual impairment") that should be used to describe symptom presentation. Second, the three overarching features of impairment were replaced with two: deficits in social communication and social interaction, and restrictive, and repetitive behaviors, interests or activities. Third, sensory reactivity was for the first time added as a symptom of restrictive and repetitive behavior. Fourth, age at onset is not strictly specified; instead DSM-5 states that the deficits should have onset during early development and points out that the deficits may become manifest later in life when demands exceed capacities in an individual. Lastly, the diagnostic criteria include the statement that a diagnosis of ASD requires a clinically significant impairment in relevant areas of everyday life.[1]

Box 1: The diagnostic criteria for Autism Spectrum Disorder in DSM-5 without severity specifiers.[1]

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive, see text):

1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):

1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns or verbal nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat food every day).
3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g, strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interest).
4. Hyper- or hypo reactivity to sensory input or unusual interests in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement)

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

Note: Individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified should be given the diagnosis of autism spectrum disorder. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.

Specify if:

- **With or without accompanying intellectual impairment**
- **With or without accompanying language impairment**
- **Associated with another neurodevelopmental, mental, or behavioral disorder**
- **With catatonia**
- **Associated with a known medical or genetic condition or environmental factor**

1.2.3 EPIDEMIOLOGY OF AUTISM

In 1966, Victor Lotter published the first epidemiological study of autistic conditions in the United Kingdom and reported a prevalence of 0.04%.[79] Since then, a substantial increase in the estimated prevalence of ASD has been reported. Over the past decade, a prevalence of approximately 1% has been widely accepted[1,80-82] although several studies have reported higher estimates of prevalence in the range of 1.5%–3.0%.[83-89] The reasons behind the rapid increase in the prevalence rate are likely multifactorial. To some extent, the rise in prevalence can be attributed to changes in and a broadening of the diagnostic criteria[90,91] diagnostic substitution[92,93] and access to support and services that require an official diagnosis of ASD.[94,95] This notion has been supported in three studies from Sweden. A large population-based study reported a considerable increase in the number of registered diagnoses of ASD despite the level of ASD symptomatology being assessed as stable over the same time period.[96] Similarly, a decrease in the number of ASD symptoms required for a clinical diagnosis has been reported.[97] Furthermore, the notion of an association between the increase in prevalence and possible genetic or environmental changes was not supported in a population-based sample of nearly 38,000 twins.[98]

A consistent finding in epidemiological studies of ASD is its preponderance in males. In DSM-5, a widely cited male-to-female ratio of 4:1 is reported.[1] However, the most recent meta-analytic study has reported a slightly lower ratio of 3:1.[99] The male-to-female ratio is associated with intellectual functioning. A decrease in the male-to-female ratio has been reported in cases where ASD is accompanied by intellectual disability,[100-102] while a substantial increase in the range of 8:1–10.8:1 has been reported for individuals without intellectual disability.[103-105] However, two Nordic studies have reported a similar male-to-female ratio in the range of 1.7:1–2.3:1 for individuals diagnosed with ASD with or without intellectual disability,[81,106] thus not supporting the suggested association between the male-to-female ratio and intellectual disability.

A diagnosis of ASD is associated with a considerable health loss across the life span. A systematic review for the global burden of disease study in 2010 reported a disability adjusted life years of 58 per 100 000 population for ASD (i.e. a measure of the number of years of life that are lost due to early death and years lived with an disability).[107]

1.2.4 AUTISM IN MALES AND FEMALES

The preponderance of males with ASD has been present since ASD was first described by Sukhareva, Kanner, and Asperger. The skewed ratio has received increased attention over the past decade, and several proposals have been made to partly explain the phenomenon. The findings range from biological differences to the diagnostic features of ASD and the possibility of a female autism phenotype.

Etiology

The skewed sex ratio can to some extent be explained by a female protective effect. According to the multifactorial model of disease transmission, the genetic liability of ASD is dimensionally distributed in the population. However, males and females are subjected to different thresholds of liability and a higher threshold is required for females in order to meet the diagnostic criteria for ASD.[108,109] This notion has been examined in twin and familial studies which hypothesize that female probands (i.e., the affected individuals in a family that are being studied) carry a higher genetic load than male probands. Therefore, the effect of familial transmission would generate a higher genetic load in the relatives of female proband.[110] The results of two large population-based twin samples showed a higher level of ASD traits among siblings of autistic females than among siblings of autistic males[111] Similarly, higher recurrence rates have been reported among siblings of female probands than among siblings of male probands.[112] A study of multiplex families (i.e., families with more than one individual diagnosed with ASD) have examined genetic liability across sex in respect of social communication and repetitive behavior. Higher levels of repetitive behavior were found among males in families with an affected female than in families without affected females. Thus, a higher genetic liability for females has been suggested with regard to repetitive behavior, whereas no differences have been found with regard to social communication.[113] Additional support for the female protective effect comes from molecular studies, in which an increased etiological burden has been reported for females. More deleterious autosomal copy-number variants have been found in females with ASD alongside slightly more deleterious single-nucleotide variants (i.e., a greater quantity of genetic "hits" are required to push females over the diagnostic threshold).[114-117] However, it should be mentioned that the notion of a female protective effect has been contested in several studies, which have reported no association between the recurrence rate and the sex of the proband.[118-121] Furthermore, a recent epidemiological study has reported similar levels of relative risk for ASD among the male and female offspring of individuals with a sibling diagnosed with ASD.[122]

In 2002, the British researcher Baron-Cohen proposed the extreme male brain theory. According to this theory, sex differences can be understood through two dimensions: empathizing and systemizing. The male brain is characterized by a significantly better ability to systemize than to empathize and the opposite cognitive pattern is representative of the female brain. Both dimensions are considered to be continuous, and ASD is hypothesized as being represented at the extreme end of the distribution of the cognitive profile of males.[123,124] It has been argued that the key biological mechanism behind the differences in cognitive profiles is elevated levels of fetal testosterone that affect the structure of the developing brain.[125-128] However, the association between testosterone and cognitive empathy in men was not confirmed in two randomized control trials.[129]

Diagnostic features of ASD

There is a growing concern that the identification of females with ASD is obscured by diagnostic criteria that have been developed and standardized based upon observations in predominantly male samples.[130] This becomes evident in the field trials for DSM-IV, which included a sample of 454 individuals with an ASD diagnosis and in which the male-to-female ratio was reported to be 4.5:1.[131] Females are, on average, diagnosed at a later age than boys.[132-135] Two large population studies compared males and females with comparable levels of ASD traits and showed that males were more likely to be diagnosed with ASD.[136,137] Thus, additional behavioral and emotional problems, or a concurrent intellectual disability, appear to be required in females in order to cross the diagnostic threshold,[133,136,138] possibly because it is a more noticeable cause for referral. The identification of females with ASD may also be obscured by symptoms of secondary conditions such as anxiety, depression, anorexia nervosa, or OCD.[139,140] Moreover, it has been argued that the socialization process puts different demands and expectations on males and females, which may generate an interpretation bias.[141,142] Therefore, a female may be considered to be "just shy" while a male with the same level of impairment in social interaction is perceived as unresponsive.[141] An alternative hypothesis is that females with a more "male" or "traditional" manifestation of ASD are recognized and diagnosed at an earlier age, while females that present with a different manifestation of ASD are identified later in life.[110] Furthermore, parents have reported higher levels of social difficulty among males during childhood while an increase in social difficulties is reported for females during adolescence. Thus, parents may not be able to identify the more subtle deficits in social interaction in females until these become evident during early and mid-adolescence, when social interactions become more complex and demanding.[143]

The 'female autism phenotype'

In recent years, evidence has emerged in support of the notion of a female autism phenotype, being a qualitatively different, or less pronounced, phenotypical manifestation of ASD. In an empirical study, females with ASD exhibited better abilities in terms of reciprocal conversation, sharing of interests, integration of verbal and nonverbal behavior, imagination, initiation of friendships, and adjustment of behavior according to the situation.[144] Furthermore, several studies have reported lower levels of restricted and repetitive behaviors in females.[145-150] However, it has been suggested that females with ASD present with interests that are more socially acceptable (e.g., people, animals,[110] pop/rock groups, soap operas,[151] books and arts/crafts[152]) or appear to be random (e.g., stickers or pen collections) than the fixated interests in males[144] (e.g., transport, technology, math/science, dinosaurs and science fiction[152]). The intensity and functional impairment of narrow interests may be overlooked if the content is gender-typical, which may explain why females generally receive lower scores on widely used clinical instruments (e.g., the Autism Diagnostic Interview–Revised, Autism Diagnostic Observation Schedule and Social Responsiveness Scale.[153]

In recent years, the concept of "camouflaging" has attracted widespread attention. Camouflaging refers to the use of different coping strategies to appear socially competent or to hide (i.e., "mask") behavior and difficulties associated with ASD.[154] Coping strategies may include imitation of social behavior, facial expressions or gestures, making eye contact, use of learned or pre-prepared phrases or jokes, and learning to follow social scripts.[155] Camouflaging is more common in autistic females without an intellectual disability[156-158] and it has been argued that camouflaging contributes to the delayed diagnosis and under identification of ASD in females.[159,160] Furthermore, camouflaging is demanding for the individual and several studies have reported adverse outcomes (i.e., exhaustion, change in self-perception (i.e., not being true to oneself), depression, stress, anxiety, and suicidal risk).[154,157,161,162] However, it has been suggested that camouflaging is more related to social anxiety and, importantly, that camouflaging is a consequence of ASD (and possibly other disorders) and should therefore not be viewed as an inherent part of the ASD phenotype.[163]

1.3 SCREENING INSTRUMENTS FOR NEURODEVELOPMENTAL DISORDERS

Screening instruments can be used as a brief and structured/systematic method of identifying individuals who acknowledge problems and symptoms that may indicate the presence of a disorder.[164] The benefits of using structured screening instruments include minimized variability in item presentation and the coverage of relevant areas of the disorder/s of interest.[165] The World Health Organization describes screening as a rough sorting process in order to identify individuals who have a higher risk for a health problem. A positive screening result does not indicate the presence of a disorder but the increased likelihood of one. In clinical practice, a positive screening result should be followed by a referral for further assessment in order to identify true cases who should be offered information and early intervention in order to achieve a better health outcome. Nonetheless, the usage of screening instruments must be balanced against the cost of over referrals and under identification, as well as the possible worry and harm for the individual.[166]

A screening instrument should be selected according to the purpose of the assessment. Broad-band screening instruments are intended to deal with several disorders or certain aspects of disorders (e.g., developmental domains such as motor skills, concentration etc.) and may be valuable during the initial assessment in order to capture a wider range of the symptomatology that is present. Narrow-band screening instruments are intended to capture a single developmental domain or a specific disorder.[164] The choice of screening instrument should be informed by the instrument's reported reliability and validity and by the sample characteristics during evaluation since estimates may differ across settings.[167] Furthermore, the screening process may include assessment by different informants (e.g., self report, parent report, or teacher report). In the case of NDDs, the usage of different informants is likely to generate a high degree of variation in ratings, which may be valuable in order to capture the behavior and deficits of a child in different settings.[168] This notion was supported in a population-based sample of children where the Autism Spectrum Screening Questionnaire was utilized, and in which there was a low level of agreement between parent and teacher reports, which most likely was associated with their different situational contexts.[169]

1.4 FUNDAMENTAL ASPECTS OF PSYCHOLOGICAL ASSESSMENT

Psychometrics can be defined as the science of psychological assessment. The different forms of assessment all share the same overarching aims: to be accurate and able to capture a given construct, and to provide a measurement capable of generating scores which can be interpreted meaningfully and which are free of bias.[170] In 1999, a revision of the *Standards for Educational and Psychological Testing*, henceforth referred to as the *Standards*, was published, which provides a contemporary perspective on the gold standard of testing practice and qualitative evaluation of tests. The *Standards* were developed by the American Educational Research Association, the American Psychological Association, and the National Council on Measurement in Education. The *Standards* emphasize three fundamental aspects of psychological testing: validity, reliability, and fairness in testing.[171]

1.4.1 VALIDITY

A crucial, or perhaps the most fundamental, aspect of the psychometric quality of an instrument is validity. The most basic definitions of validity often state that it is the degree of an instrument's ability to measure the construct that it is supposed to measure.[172] Over the years, several definitions of validity have been suggested, but the contemporary perspective of validity is based on the interpretation of test scores (i.e., the proposed use of test scores). The latest edition of the *Standards* states that the validity of an instrument is based upon the degree of evidence that supports the given interpretation of test scores. Therefore, validity is not considered to be a property of an instrument; instead validation is concerned with the evaluation of test score interpretations.[171] Test score interpretations should be based on empirical evidence and theory. It is important to keep in mind that test score interpretations can be valid to different degrees; they cannot be minimized as either valid or invalid.[172]

Validity evidence can be gathered from five sources: (a) test content (i.e., items should adequately represent the construct of interest); (b) response processes (e.g., it examines whether the response process of an observer who rates the performance of a test taker matches the proposed interpretation of test scores); (c) internal structure (i.e., it examines the relationship between the items and the proposed construct and test score (e.g., factor analysis)); (d) relations to other variables (i.e., it examines how the scores from an instrument relate to other relevant variables (e.g., convergent validity (examination of the relationship between two instruments designed to measure similar constructs) or test-criterion validity (the relationship between test score and a criterion

(e.g., a specific outcome or disorder))); and (e) consequences of testing, including both intended and unintended consequences of the interpretation of test scores (e.g., a test should not disadvantage any sub-group of test takers).[171]

1.4.2 RELIABILITY

Reliability, or precision, of a measurement is broadly defined in the *Standards* as score consistency across different parts of the testing procedure. A higher degree of reliability is warranted in situations where the test score interpretation is related to decisions or consequences for test takers. In practice, reliability can be assessed in different ways depending on the measurement theory and model used.[171]

The conceptual framework of reliability has traditionally been based on principles from classical test theory (CTT). In CTT, the theory of measurement is based on three fundamental components: observed score, true score, and measurement error. The observed score represents the score that is obtained by a measurement, and the true score represent the real amount of the measured construct. Measurement error represents other factors that contribute to inconsistency between the observed score and the true score. In CTT, reliability can be described as the degree of variance in the observed scores that is accounted for by the measured construct.[172] CTT offers several ways of estimating reliability, a common way being to include an estimation of the internal consistency in an instrument which is generally calculated by Cronbach's alpha. Inter-item correlations are used to estimate the degree of homogeneity in a test. Cronbach's alpha can be increased by adding more items or better (i.e., highly correlated) items to a scale.[173] One common way of improving reliability is by adding more items.[171]

Item and response theory (IRT), or modern test theory, provides an alternative way of gaining reliability. There are similarities between CTT and IRT. Both perspectives require that the items in a test to be unidimensional (i.e., the items should measure the same construct). CTT and IRT acknowledge that item variance arises from differences in the measured construct and from error. The error of measurement is presented as a single term in CTT. In IRT, the characteristics of each item can be examined. Therefore, CTT commonly refers to the reliability of the whole instrument, whereas IRT allows for examining the reliability of each item. Reliability can be gained for a test developed under IRT by selecting the items that best capture a specific range of the continuum of the measured construct, with a high degree of precision and a minimal amount of measurement error.[173]

1.4.3 FAIRNESS

The latest edition of the *Standards* has recognized fairness as a fundamental part of validity. The definition of fairness is broad: the same construct should be measured in the intended population and the interpretation of scores should have the same meaning for all test takers. Measurement bias is a risk to fairness that may occur when a specific subgroup (e.g., females) has a different probability of giving a correct or affirmative response to an item. This is commonly examined by way of differential item functioning (DIF) analysis.[171]

1.5 THE AUTISM–TICS, ADHD AND OTHER COMORBIDITIES INVENTORY

The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC) was developed at the Department of Child and Adolescent Psychiatry, a precursor of the Gillberg Neuropsychiatry Centre, at the University of Gothenburg, Sweden. Originally, the A–TAC was designed as part of the Child and Adolescent Twin Study in Sweden (CATSS), a large-scale longitudinal study. There was a need for an easy-to-administer interview that could be carried out by laymen over the phone. The aim was to design a dimensional and comprehensive interview that covered NDDs as well as commonly overlapping problem areas or disorders in child and adolescent psychiatry.[174]

The items in the A–TAC were formulated to encompass the symptom criteria included in the DSM-IV[77] definition of NDDs (ASD, ADHD, DCD, TD, and LD). Items for "other" psychiatric disorders were based on a selection of the symptom criteria in DSM-IV[77] (eating disorders, ODD, CD, depression, separation anxiety, and psychosis).[174] Furthermore, additional items were phrased to cover symptoms listed in the Gillberg and Gillberg algorithm for Asperger syndrome[175] and to capture relevant facets included in other questionnaires such as the Autism Spectrum Screening Questionnaire,[176] the Asperger Syndrome Diagnostic Interview,[177] and the Five-to-Fifteen questionnaire.[178]

Development of the A–TAC

A preliminary version of the A–TAC, which included 178 items, was developed and evaluated before CATSS was launched. Hansson et al. performed the first validation study, which was based on telephone interviews with parents of children who were patients at the Child Neuropsychiatric Clinic in Gothenburg (84 subjects) and a control group (27 subjects). The age range of the included subjects was 7–18 years, and two medical students unaware of the child's status conducted the interviews. In short, the diagnostic domains

generally showed excellent inter-rater agreement and test–retest reliability was good to excellent. Receiver operating characteristic curves (ROC) were calculated in order to estimate validity using the area under the curve (AUC), which indicates how well an instrument can distinguish between cases and non-cases. The results showed excellent predictive ability for ADHD (AUC 0.91), good predictive ability for ASD (0.88) and TD (0.84), and fair predictive ability for LD (0.74), and DCD (0.71). However, other child psychiatric disorders included in the A–TAC were not included in the preliminary validation study as too few children had received diagnoses of OCD or ED, for instance.[179]

Based on the results of the first validation study, additional items were included with the aim of improving specificity, and new modules were developed in order to capture overlapping symptoms. The second version of the A–TAC consisted of 327 items, and was used in a pilot study of CATSS, which included 736 subjects (aged 9 or 12). The internal consistency (i.e., Cronbach's alpha) was calculated for the different modules in order to guide the reduction of items. For the final version of A–TAC, items that yielded inconsistent answers or reduced the internal consistency within a module were removed. However, in the case of ASD and ADHD, all items that were based on the DSM-IV criteria were included in the screening algorithms without consideration of their psychometric properties.[174]

The final version of the A-TAC consists of 264 items, 96 of which are "gate" items intended to be used for screening and to provide proxies for clinical diagnoses. The 96 gate items also correspond to the version of the A–TAC included in Papers I–IV. The gate items are organized into 20 theoretically defined modules. Each module, or in some instances two or three, corresponds to a diagnostic domain (the ASD domain comprises the modules on language, social interaction, and flexibility, and the ADHD domain comprises the modules on concentration and attention, and impulsiveness and activity). The remaining items "under the gate" can be used to get a more detailed description of the problems/symptoms described in a module: these tap into more specific symptoms and should be asked only if the gate item is partly or fully endorsed and an additional 72 items (four items per module, excluding the miscellaneous module) address psychosocial dysfunction and subjective suffering in connection with the problems addressed in the specific module, as well as age at onset and a final item regarding whether the problems are present or in remission. Two of the items, "psychosocial dysfunction" and "subjective suffering", can be used to calculate a problem load score for the corresponding module.[180] An overview of the structure in A –TAC is given in **Table 1**.

Each module in the A–TAC begins with the following statement: "The essential aspect of each question is whether the problem/peculiarity has been pronounced compared to peers during any period of life." This is to remind the respondent to assess the items within a whole-life context. The modules are assessed without taking diagnostic hierarchies or exclusion criteria into account. All items are coded on a dimensional scale with three response categories: "Yes" scored as 1, "Yes, to some extent" scored as 0.5 and "No" scored as 0. A module is assessed as missing if three or more items receive a response of "Do not know" or "Do not want to respond".[180]

Previous validations of the final version of A–TAC

The A–TAC has been validated in a cross-sectional study in which three different samples have been used: a clinical sample with 91 subjects on a waiting list for neuropsychiatric assessment (71 boys, 20 girls, age range 6 to 19 years), a control group with 366 subjects from CATSS without any reported psychiatric diagnoses (181 boys, 185 girls, aged 9 or 12), and a community-recruited sample of 319 subjects in CATSS whose parents have reported one or more psychiatric diagnoses (230 boys, 89 girls, aged 9 or 12). The psychometric properties of ASD, ADHD, TD, DCD, and LD previously reported in Hansson et al. were replicated, and only small differences between boys and girls were reported. Furthermore, the 96 gate items showed a high degree of specificity and the addition of a sum score from the total scale (i.e., of 264 items) did not improve the specificity values to a significant extent. Thus, the 96 gate items are sufficient to capture a clinical diagnosis for an individual, and additional items may be used to collect valuable clinical information. Finally, cut-off values were established: a "low" cut-off value for screening purposes with high sensitivity and for certain domains a "high" cut-off value with high specificity that can be considered a clinical proxy in epidemiological settings.[180]

An independent research group in Spain has validated the ASD domain in the A–TAC. The group's sample included 140 subjects (60 boys, 80 girls, age range 6–16). The ASD domain showed a high degree of internal consistency (Cronbach's alpha = 0.93), and the AUC for the group with ASD was reported to be excellent (0.96).[181]

The construct validity of the A–TAC has been examined for convergent validity with the Child Behavior Checklist. A sample was retrieved from CATSS and included 106 subjects (94 boys, 118 girls) whose parents had participated in the A–TAC interview and responded to the Child Behavior Checklist questionnaires. The result indicated mostly moderate correlations between related subscales in the A–TAC and the Child Behavior Checklist.[182]

The test–retest reliability of the A–TAC has been examined in a sample with 400 subjects from CATSS. The interviews were conducted by laymen and, on average, there were ten weeks between interviews. The results showed good intra-rater and inter-rater reliability. Excellent test–retest intraclass correlations were reported for ASD and ADHD, although agreement (Cohen's κ) varied between slight and substantial for most of the other domains.[183]

Lastly, one longitudinal study has been conducted with a sample which included a subset of 452 subjects from CATSS (aged 9 or 12). A comprehensive clinical follow-up study was conducted at age 15 of twins who screened positive at age 9 or 12 (144 boys, 103 girls), together with their co-twin (88 boys, 69 girls), and healthy controls who were randomly selected (30 boys, 16 girls). The results showed excellent predictive properties for ASD (AUC = 0.91), although the result was only fair for ADHD (0.77), LD (0.80) and TD (0.79).[184]

Table 1. Overview of A–TAC modules and corresponding diagnostic domain, giving number of gate items and number of additional items, with number of items addressing dysfunction and suffering provided in brackets.

A–TAC module	Domain	Gate items	Additional items
A. Motor Control	DCD[c]	1	4 (4)
B. Perception	DAMP[b,c]	5	5 (4)
C. Concentration & Attention	ADHD[c]	9	2 (4)
D. Impulsiveness & Activity	ADHD[c]	10	1 (4)
E. Learning	LD	3	6 (4)
F. Planning & Organizing Tasks	Supplement	2	5 (4)
G. Memory	Supplement	3	8 (4)
H. Language	ASD	6	9 (4)
I. Social Interaction	ASD	6	15 (4)
J. Flexibility	ASD	5	0 (4)
K. Tics	TD	3	1 (4)
L. Compulsions	OCD	2	0 (4)
M. Feeding	Eating disorder	2	6 (4)
N. Separation	Anxiety	5	3 (4)
O. Opposition	ODD	6	5 (4)
P. Conduct	CD	4	13 (4)
Q. Anxiety	Anxiety	3	3 (4)
R. Mood	Depression/Bipolar	5	8 (4)
S. Concept of reality	Psychosis	1	2 (4)
T. Miscellaneous[a]	Supplement	15	0 (0)
Total		96	168

Note:

[a] *Clinically specific problem areas include sleep, food fads, severe overweight, bodily functions and substance abuse.*

[b] *DAMP is an acronym for "Deficits in Attention, Motor Control, and Perceptual Abilities." DAMP is not a diagnostic category in the DSM but a well-known sub-type of concomitant deficits that has been used in clinical practice in Scandinavia for many years.*[185]

[c] *In the A–TAC, the modules "Motor Control", "Perception", "Concentration & Attention" and "Impulsiveness & Activity" comprise the DAMP domain.*

The table is adapted from Larson 2013.[186]

1.6 STUDY RATIONALES

1.6.1 PAPER I

The substantial co-occurrence of NDDs and other psychiatric disorders highlight the need for a comprehensive perspective during both screening and diagnostic assessments. However, the number of broad-band screening instruments within the field of NDDs is limited. The A–TAC may be considered a well-validated and viable option for screening both in clinical practice and in research settings, however some issues remain to be addressed. First, only a limited number of individuals were involved in the longitudinal validation study (i.e., the clinical examination included only 20 cases of ASD and 23 cases of LD).[184] Second, the previous validation studies did not include ODD and CD due to the low prevalence in the studied sample, and there is a risk of disorders such as ODD and CD being underrepresented in clinical studies. For this reason, the cut-off values for ODD and CD were established on the basis of a sample of institutionalized adolescents in combination with a control group from CATSS.[187] Third, the longitudinal validation study was based on clinical follow-up at age 15. However, the initial age of onset for EDs varies, occurring between 10 and 20 years of age,[188] which shows the need to establish the predictive validity in a follow-up study in older groups. Lastly, the ecological validity of the A–TAC may not have been sufficiently captured in previous studies, as there may be differences in the symptomatology and impairment of participants and non-participants. Thus, the remaining issues related to the validity of the A–TAC need to be examined in a larger sample with follow-up when that sample is older.

1.6.2 PAPER II

Screening instruments are widely used in both research and clinical settings in order to gather information about the symptomatology of an individual. In the case of ASD, numerous screening instruments are available of different lengths and abilities to capture the manifestation of ASD in different age groups. The ASD domain in the A–TAC includes 17 items; the other widely used screening instruments include 23 items (Modified Checklist for Autism in Toddlers[189]), 27 items (Autism Spectrum Screening Questionnaire[176]), 40 items (Social Communication Questionnaire[190]), and 65 items (Social Responsiveness Scale[191]). These instruments may be considered brief and reliable, but the response burden may nonetheless be excessive and time-consuming. IRT allows all items in an instrument to be examined in order to identify items with maximal precision. By using the advantages of IRT, it may be possible to develop a short and reliable screening instrument for ASD with a minimal response burden. A reliable short form for ASD could be an asset in

epidemiological studies and also enhance the likelihood of early identification of individuals who present with symptoms of ASD.

1.6.3 PAPER III

The skewed male–female ratio in ASD is likely due to multiple factors. It has been argued that the diagnostic threshold is higher for females (i.e., females need to manifest more symptoms or additional problems in order to receive an ASD diagnosis[136,138]). A large-scale study reported greater impairment in females diagnosed with ASD than in males, including greater deficits in social communication, lower cognitive and language abilities, lower adaptive function and further additional problems with externalizing behavior, albeit with less restricted interest.[147] At the same time, several studies based on samples from the general population have reported lower mean scores for females using established instruments, including Social Responsiveness Scale,[12,192] Autism Spectrum Screening Questionnaire,[169,193] Social Communication Questionnaire,[194] and the Childhood Autism Spectrum Test.[195] Additionally, it has been suggested that the available screening instruments may be better at detecting a male manifestation of ASD,[130] and thus not fully capture a female representation of ASD. Taken together, it is possible that females with ASD represent a more extreme end of the distribution of ASD traits than do males with ASD and it is uncertain whether this is an artefact of norms collapsed over sex.

1.6.4 PAPER IV

There is a growing concern that existing screening and diagnostic instruments are more prone to capture a male manifestation of ASD.[130,142,196] Previous studies on sex differences in ASD have shown that males with ASD present with higher levels of repetitive and restrictive behavior.[145-150] Furthermore, a meta-analysis has reported comparable deficits in social communication for males and females with ASD,[146] while other studies have shown that females with ASD tend to have more,[147,194] or possibly subtler,[197,198] deficits in social communication. Many instruments today are based on diagnostic criteria that have been tested in predominantly male samples, which may indicate that scores and items cannot be compared uncritically across sex. Therefore, it is essential to examine ASD instruments for item-level measurement equivalence (or invariance), which would indicate that an item measures the same construct (i.e., ASD) across sex. Additionally, an investigation of item-level measurement equivalence would further inform possible differences across sex and indicate whether some items are better at capturing ASD in males or females.

2 AIM

This thesis is based on four papers and specifically aims to:

I. establish the previous and predictive validity of the A–TAC by using a nation-wide sample of twins and registered diagnoses in the National Patient Register.

II. determine the psychometric properties of each item in the ASD domain in the A–TAC by using item response theory and to construct and validate a short form of the ASD domain.

III. compare males and females with regard to the degree of symptomatology of ASD, ADHD, LD, and ODD by using a sex-specific standardized score.

IV. examine each item in the ASD domain in the A–TAC for differential item functioning and to evaluate whether a sub-set of items detects ASD better in males or females.

3 METHODS

3.1 SUBJECTS

3.1.1 THE CHILD AND ADOLESCENT TWIN STUDY IN SWEDEN

The CATSS, initiated in 2004, is an ongoing nation-wide longitudinal twin study. The overall aim is to study somatic and mental health problems in childhood and adolescence. The data collection emanates from the Swedish Twin Registry at Karolinska Institutet. The parents of all twins born in Sweden as of July 1, 1992, have been contacted and invited to participate in a telephone interview in connection with the twins' ninth birthday. In addition, the first three years of CATSS also included 12-year-old twins (born between July 1992 and June 1995). These age groups were chosen because most NDDs and child psychiatric problems are established by this age, whereas other problems associated with puberty and adolescence generally have not yet begun.[174] The twins and their parents are invited to participate in follow-up studies at the age of 15, 18 and 24 (only self-report for twins).

Since the beginning of CATSS, the A–TAC has been included as a telephone interview for parents. The overall response rate in CATSS is ≈ 70%[199] and has declined over the years; the mother has been the informant in the majority of the interviews (87.5%). In an overview study of CATSS, systematic analyses revealed small differences between responders and non-responders. In the case of NDDs, a merge with the National Patient Register (NPR) showed that 0.84% of responders and 0.95% of non-responders had a registered diagnosis of ASD. The corresponding number for ADHD was 1.6% among responders compared to 2.1% among non-responders; for LD, the result was 0.99% versus 2.0%.[174]

This thesis is based on A–TAC data from CATSS-9/12. Data was retrieved on four different occasions, thus, the sample size is different in each paper. For Paper I, data was extracted in July 2015 and the total sample included 25,828 subjects. For Paper II, data was extracted in May 2018 and the total sample included 30,898 subjects. For Paper III, data was extracted in December 2017 and the total sample included 30,392 subjects. For Paper IV, data was extracted in April 2020 and the total sample included 34,033 subjects.

3.1.2 THE NATIONAL PATIENT REGISTER

The NPR is authorized by the National Board of Health and Welfare (Socialstyrelsen), a government agency in Sweden. The NPR was established in 1964 with the aim of collecting information on inpatient care at public hospitals. Since 1987, the NPR has encompassed all inpatient care in Sweden and the participation of all county councils has been mandatory. In 2001, specialized outpatient care (e.g., psychiatric outpatient care and habilitation units) was incorporated, including both public and private caregivers. The NPR includes information regarding doctoral visits only within specialized care and does not include primary care visits. The medical data in the NPR includes the diagnostic codes of assigned diagnoses according to the International Classification of Diseases (ICD).[200] In clinical practice in Sweden, it is customary to assign a diagnosis according to the prevailing DSM manual. Therefore, a DSM diagnosis is "translated" into the corresponding ICD code.

The coverage of the NPR is monitored annually. During the registration year, 2019, the main diagnosis was missing for 1% of doctoral visits in inpatient care and for 2.8% in specialized outpatient care.[201] The level of underreporting is generally considered to be low as regards inpatient care, while the quality and coverage in respect of specialized outpatient care have improved since beginning in 2001. In the first few years, roughly 25%–30% of registered doctoral visits in specialized outpatient care did not include the code of the main diagnosis.[200]

The validity of the NPR has been examined in different diagnostic categories. In the case of ASD, Idring et al. were able to confirm 96% of the assigned ASD diagnoses in the NPR and other medical registers by examining medical records.[81] Similarly, a high level of validity, with a positive predictive value in the range of 81%–97%, has been reported for TD, OCD,[202] social anxiety disorder,[203] bipolar disorder,[204] personality disorders,[205] and schizophrenia[206,207] in the NPR.

Diagnostic data was retrieved by linking the subjects in CATSS to the NPR and searching for relevant ICD-9[208] and ICD-10[209] codes. It is possible to merge data across registers thanks to the personal identification number that is given to all individuals born in Sweden or in connection with the acquisition of Swedish citizenship. An individual's personal identification number is recorded in every case of contact with governing bodies in Sweden and is therefore included with patient data in the NPR[200]. The diagnostic codes retrieved are reported in **Table 2**.

Table 2. Overview of diagnostic codes retrieved from the National Patient Register.

Disorder	ICD-9	ICD-10
ASD	299.0,[a] 299.8, 299.9	F84.0, F84.1, F84.5, F84.8,[b] F84.9
ADHD	314	F90
LD	317–319	F70–F79
DCD	315.4	F82
TD	307.2	F95
ODD	313.8	F91.3
CD	312	F91, excluding F91.3
OCD	300.3	F42
ED	307.1 307.50, 307.51	F50

Note:
[a] *Only 299.0 was retrieved for Paper III and Paper IV.*
[b] *F84.8 was excluded in Paper I and Paper II.*

3.2 MEASURES

3.2.1 THE AUTISM–TICS, ADHD AND OTHER COMORBIDITIES INVENTORY

As described in the introduction, the A–TAC has been included in CATSS since its beginning in 2004. Interviews are conducted over the telephone by laymen from a professional company (Intervjubolaget) who have received a brief introduction to child and adolescent psychiatry and research methodology. The data is collected through a computerized version of the A–TAC inventory in which responses are entered directly into a database. The A–TAC is an open access instrument and can be downloaded in Swedish or English from the Gillberg Neuropsychiatry Centre website.[210] It is also available as an appendix in this thesis.

In **Table 3**, the established cut-off values for several diagnostic domains in the A–TAC are presented. These have been constructed with the sum score from the gate items. These are replicated in Paper I, and the ASD domain is examined in Paper II and Paper IV. For ASD, ADHD, LD, and DCD, a low (screening) and a high (clinical proxy) cut-off value have been established. The diagnostic domains of TD, ODD, CD, OCD, and ED have a single corresponding cut-off value.

Table 3. Overview of the diagnostic domains included from the A–TAC, number of gate items and cut-off values used for each paper.

Paper	Diagnostic domain	No. of gate items	Cut-off value		
			Gate	Gate – Low	Gate – High
I–IV	ASD	17		4.5 [a]	8.5 [a]
I, III	ADHD	19		6 [a]	12.5 [a]
I, III	LD	3		1 [a]	3 [a]
I	DCD	1		0.5 [a]	1 [a]
I	TD	3	1.5 [a]		
I, III	ODD	6	3 [b]		
I	CD	4	2 [b]		
I	OCD	2	1 [c]		
I	ED	2	1 [c]		

Note:
[a] *Larson, et al.*[180]
[b] *Kerekes et al.*[187]
[c] *Mårland et al.*[211]

In Paper II and Paper IV, each item in the ASD domain is examined in depth. The 17 items that correspond to the ASD domain are therefore reproduced in **Table 4**.

Table 4. The 17 items included in the ASD domain in the A–TAC.[210]

The essential aspect of each question is whether the problems/characteristics has been pronounced compared to peers during any period of life.		Yes	Yes, to some extent	No
H. Language				
H34	Was his/her language development delayed or doesn't he/she speak at all?	☐	☐	☐
H35	Does he/she have difficulties sustaining a conversation?	☐	☐	☐
H36	Does he/she like to repeat words and expressions or does he/she use words in a way that other people find strange?	☐	☐	☐
H37	Does he/she have difficulties with games of make-believe or does he/she imitate others considerably less than other children?	☐	☐	☐
H38	Does he/she talk in too high a pitch or too quietly?	☐	☐	☐
H39	Does he/she have difficulties keeping "on track" when telling other people something?	☐	☐	☐
I. Social interaction				
I40	Does he/she have difficulties expressing emotions and reactions with facial gestures, prosody, or body language?	☐	☐	☐
I41	Does he/she exhibit considerable difficulties interacting with peers?	☐	☐	☐
I42	Is he/she uninterested in sharing joy, interests, and activities with others?	☐	☐	☐
I43	Can he/she only be with other people on his/her terms?	☐	☐	☐
I44	Does he/she have difficulties behaving as expected by peers?	☐	☐	☐
I45	Do other people easily influence him/her?	☐	☐	☐

J. Flexibility				
J46	Does he/she get absorbed by his/her interests in such a way as being repetitive or too intense?	☐	☐	☐
J47	Does he/she get absorbed by routines in such a way as to produce problems for him/herself or others?	☐	☐	☐
J48	Has he/she ever engaged in strange hand movements or toe-walking when he/she was happy or upset?	☐	☐	☐
J49	Does he/she get obsessed with details?	☐	☐	☐
J50	Does he/she dislike changes in daily routines?	☐	☐	☐

Note.
Reproduced from the A–TAC with some amendments.

3.3 STATISTICAL ANALYSES

All the statistical analyses included in each of the papers are presented in **Table 5**. The statistical calculations were performed in SPSS (Paper I and Paper II: version 22.0, Paper IV: version 27.0), STATA (Paper II: version 15, Paper IV: version 16) and SAS (Paper III: version 9.3).

Table 5. Overview of the statistical methods used in each paper.

Statistical Analyses	I	II	III	IV
Diagnostic Accuracy				
Sensitivity and specificity	x	x		x
Predictive values	x	x		
Receiver operating characteristic curve	x	x		x
Diagnostic odds ratio	x	x		
Comparisons Between Groups				
Standardized scores			x	
Linear regression			x	
Item Response Theory				
Graded response model		x		
Unidimensionality				
Exploratory factor analysis		x		x
Differential Item Functioning				
Two-parameter logistic model				x
Likelihood ratio test				x
Akaike information criterion				x
Bayesian information criterion				x

3.3.1 DIAGNOSTIC ACCURACY (PAPER I, II & IV)

Sensitivity and specificity

The overall aim of screening is to sort individuals who most likely have problems or symptoms related to a specific disorder from those who most likely do not have problems or symptoms related to a specific disorder.[164] The accuracy of a screening instrument can be examined by calculating its sensitivity and specificity, which are considered to be fixed properties of a test and therefore not affected by the prevalence of a disorder in the population.[212]

Sensitivity is defined as the proportion of individuals with a disorder who have received a positive screening result (i.e., a score equal to or higher than the cut-off value). Specificity is defined as the proportion of individuals without a

disorder who have received a negative screening result (i.e., a score below the cut-off value).[164] When a binary classifier is used, the result from a screening instrument can produce four possible outcomes. The result can be classified as a true positive (a correct prediction of a disorder), a true negative (a correct prediction of the absence of a disorder), a false positive (an incorrect prediction of a disorder) or a false negative (an incorrect prediction of the absence of a disorder). The four possible outcomes can be visualized in a 2 x 2 table (see **Table 6**).[212]

Table 6. The four possible combinations of the presence or absence of a disorder and a positive or negative result from a screening instrument.

	Disorder is present	Disorder is absent
Positive screening result	True positive (TP)	False positive (FP)
Negative screening result	False negative (FN)	True negatives (TN)

Sensitivity and specificity are calculated using the 2 x 2 table according to the following formulae:
Sensitivity = TP/TP+FN
Specificity = TN/FP+TN

In Paper I, Paper II, and Paper IV, the sensitivity and specificity values were derived from the ROC curves as described below.

Predictive values
Calculations of sensitivity and specificity are based on knowledge of the presence or absence of a disorder. However, this is rarely the case in real-world settings; therefore, predictive values are calculated in order to get an estimate of the probability of the presence or absence of a disorder. The positive predictive value (PPV) is defined as the probability of the presence of a disorder given a positive screening result. The negative predictive value (NPV) is defined as the probability of the absence of a disorder given a negative screening result.[164] The PPV and NPV are dependent on the prevalence of the disorder in the population used for the calculations. If the prevalence is high, the PPV will be high. Conversely, if the prevalence is low, the NPV will be high.[212]

The PPV and NPV can be calculated from **Table 6** according to the following formulae:

PPV = TP/TP+FP
NPV = TN/FN+TN

Calculations of PPV and NPV were used only in Paper I and Paper II.

Receiver Operating Characteristics Curve

Use of the receiver operating characteristics curves dates to World War II and the development of radar. The methods used to separate signals from noise were refined during the 1950s to create signal detection theory. This methodology turned out to be highly useful in the medical field, where the signal represents the presence of a disease or disorder, while the noise represents findings that can be misinterpreted as a true signal (i.e., a disease or disorder).[213]

The performance of a screening instrument can be evaluated by calculating ROC curves, which are generated by plotting the true positive rate (i.e., sensitivity) on the Y-axis against the false positive rate (i.e., 1 – the specificity) on the X-axis for various cut-off values on a continuous scale. Thus, ROC curves can be used to derive sensitivity and specificity values for different cut-off values and signal the tradeoff between sensitivity and specificity (an increase in sensitivity will in most cases lead to a decrease in specificity and vice versa).[213]

The area under the curve (AUC, see **Figure 1**) is used as a measurement of an instrument's ability to discriminate between two groups. The AUC is defined as the probability of a randomly selected subject with a disorder receiving a higher score on a test than a randomly selected subject without a disorder.[214] A perfect instrument would have an AUC of 1.0 and the ROC curve would go straight up to the top of the Y-axis and then sharply turn right and proceed horizontally. If the instrument is not better than a random prediction, the AUC would be 0.5 and the ROC curve would be a straight diagonal line. The predictive ability of an instrument can be categorized according to the AUC, where AUC = 0.5 suggests random prediction, 0.60 < AUC 0.70 suggests poor validity, 0.70 < AUC suggests 0.80 fair validity, 0.80 < AUC 0.90 suggests good validity and AUC > 0.90 suggests excellent validity.[215]

In Paper I, Paper II, and Paper IV, ROC curves were calculated in order to obtain the AUC and sensitivity and specificity estimates at the cut-off values. The A–TAC domains were used as independent predictors and the registered

diagnoses in the NPR were used as dependent variables. In all of the papers, the age at diagnosis was taken into account and the results are reported in three different groups: previous (a registered diagnosis in the NPR before or the same year as the A–TAC interview), predictive (a registered diagnosis in the NPR after the A–TAC interview) and total (i.e., the total sample without consideration of age at diagnosis). In Paper II and Paper IV, the calculations were conducted in a specific validation sample, which was obtained by way of a random split of the total sample.

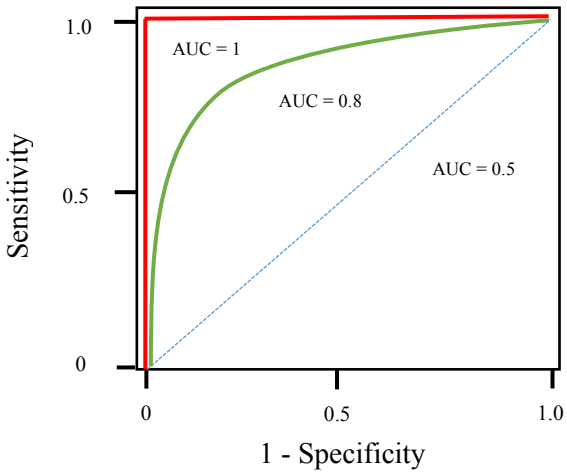

Figure 1. Graphical illustration of three ROC curves with different AUC.

Diagnostic Odds Ratio

The diagnostic odds ratio (DOR) can be used as a measure of diagnostic accuracy. The DOR is defined as the ratio of the odds of a positive test for individuals with a disorder relative to the odds of a positive test for individuals without a disorder. The DOR value ranges from zero to infinity, a value of 1 indicating that the instrument is not capable of discriminating between individuals with and without the disorder. Higher DOR values demonstrate an increased discriminatory test performance. The DOR depends not on the prevalence of the disorder but on the sensitivity and specificity of the instrument. Consequently, instruments with high sensitivity and specificity will produce a high DOR.[216]

The DOR can be calculated from **Table 6** according to the following formulae:

DOR = (TP/FN) / (FP/TN)

Calculations of DOR were used only in Paper I and Paper II.

3.3.2 COMPARISON BETWEEN GROUPS (PAPER III)

Standardized scores
Standardized scores, or z-scores, can be used to convert a distribution of observations into a distribution of z-scores with a mean of 0 and a standard deviation of 1. A z-score is obtained by subtracting the mean of the population from each individual observation and dividing the result by the standard deviation of the population. Standardized scores do not affect the relationship between variables.[217]

In Paper III, standardized scores are used to compare males and females in respect of the degree of their ASD, ADHD, LD and ODD symptomatology.

Linear regression
Linear regression is widely used to model the relationship between an independent and a dependent variable by the fitting of a linear equation. The independent variable, or explanatory variable, is used to predict the dependent variable, or outcome (e.g., to what extent does sex affect the mean score).[217]

In Paper III, four separate linear regressions were calculated using sex as the independent variable and mean scores from A–TAC domains (ASD, ADHD, LD, and ODD) as the dependent variable.

3.3.3 ITEM RESPONSE THEORY (PAPER II & IV)

IRT refers to a family of psychometric models that provide an alternative approach to CTT. IRT can be used to inform the development and refinement of instruments as well as to provide insights for the interpretation of a specific item or for the complete instrument. An IRT model requires that the response variance in an item is determined by an underlying latent trait.[218] Stated differently, the probability of an individual giving a specific response to an item is determined by the individual's level of the underlying latent trait that the item is assumed to measure.[172] In Paper II and Paper IV, the underlying latent trait is based on the ASD domain and can be described in terms of the severity of ASD traits.

Graded Response Model

The graded response model (GRM) is an IRT model for polytomous items (i.e., items with more than two response options). The performance of an item can be summarized in a boundary characteristic curve (BCC) (see **Figure 2**) that serves as a model of the relation between an individual's response to an item and the underlying latent trait.[218] The x-axis represents the level of theta (i.e., the underlying latent trait), which follows a normal distribution with a mean of 0 and a standard deviation of 1. The y-axis represents the probability of an endorsement in each response category. The shape of a BCC is dependent on the item's difficulty and discriminatory parameters.

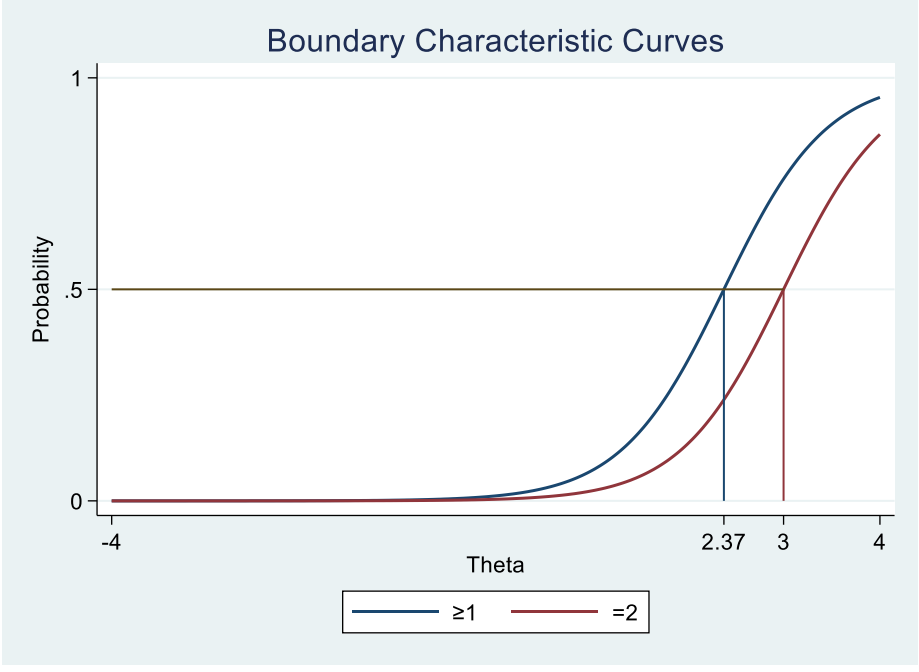

Figure 2. Hypothetical example of boundary characteristic curves based on cumulative probabilities for an instrument with three response categories (0, 1 and 2) with different difficulty parameters. An individual with a theta (underlying latent trait) level of 2.37 has a 50% probability of responding 0 rather than a figure greater than or equal to 1, and a theta level of 3 is required to have a 50% probability of responding 0 or 1 rather than 2.

The difficulty parameter for an item can be described as the level of a trait an individual must possess in order to "pass" or affirm a specific response category. In other words, item difficulty, denoted as *b*, represents the location on the latent trait continuum at which an individual has a 0.5 probability of endorsing a specific response category or a higher category.[219] Therefore, higher difficulty levels indicate that higher levels of a trait are required in order to have a 50% probability of giving an affirmative answer.[172]

The discrimination parameter for an item can be described as the item's ability to discriminate between individuals with high and low levels of a trait. The discrimination parameter, denoted as *a*, is related to the slope, or point of inflection, of the BCC at its difficulty value. A steeper slope signals a better discriminatory ability[219].

The GRM was used in order to estimate item difficulty and item discrimination for each item in the ASD domain in Paper II. A developmental sample was generated by way of a random split of the total sample in order to fit the GRM and obtain parameter estimates for each item in the ASD domain.

The results from the GRM can also be used to plot an item information function (IIF). In short, an IIF is a graphical illustration of the relationship between the amount of information an item provides and the underlying latent trait (see **Figure 3**). An IIF is based on the item's difficulty and the discrimination parameter: the difficulty parameter is mirrored at the peak of the IIF, while the steepness is dependent on the discrimination parameter.[220] Furthermore, the IIF can be used to examine the precision of an item since the error of measurement is inversely proportional to the IIF. Thus, a high and narrow IIF mirrors the range of the underlying latent trait where the error of measurement is low and the precision is high.[221] An examination of the IIF can be used to identify reliable items with high precision and minimal error of measurement. This procedure was used in Paper II and Paper IV.

3.3.4 UNIDIMENSIONALITY (PAPER II & IV)

A fundamental assumption in IRT is unidimensionality: a single underlying dimension should be able to account for the covariance among items. Exploratory factor analysis (EFA) is commonly used to examine the underlying structure of all items included in an instrument. The assumption of unidimensionality can be evaluated by examining the eigenvalues, scree plot, and item loadings on the first factor.[222]

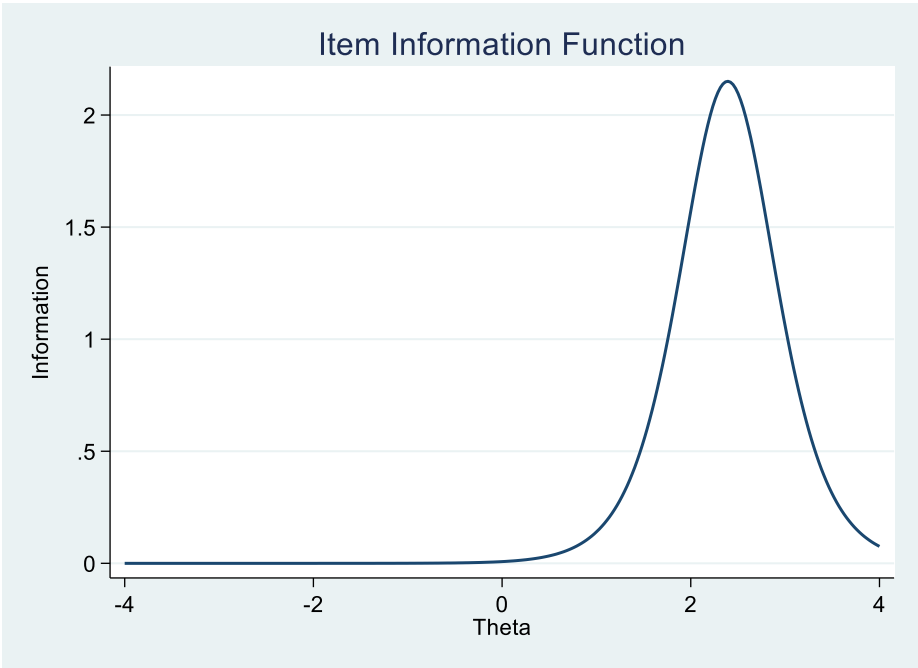

Figure 3. A graphical illustration of an IIF. Thus, if an individual with a theta (i.e., underlying latent trait) in the range of the IIF responds to this item, the answer will provide useful information for estimating the individual's theta. If an item is too easy or too difficult, or not discriminative, the answer will provide only a limited amount of information.

In Paper II and Paper IV, unidimensionality was examined by way of an EFA with principal axis factoring and a promax rotation in order to take account of the correlation between items.[217] Calculations were made in a small subset of the total sample in order to avoid capitalizing on chance. In Paper II, approximately 1% of the total sample was used. In Paper IV, the calculations were conducted for males and females separately in approximately 2% of the total sample of males or females.

Calibration of IRT models requires that the items also demonstrate local independence. Technically, this assumption is included in the concept of unidimensionality and requires that no additional systematic covariance be found among the items. Local dependence may, for example, arise if a subset of items displays similar content, which could generate remarkably high slope estimates.[222] In Paper II, items were examined for local dependence by way of an examination of the item parameters, particularly the discrimination parameter, from the GRM calibrations.

3.3.5 DIFFERENTIAL ITEM FUNCTIONING (PAPER IV)

Investigations of DIF can inform the validity of an instrument and the establishment of measurement equivalence, or invariance, which indicates that the same construct is measured across groups (e.g., sex or ethnicity). Different statistical techniques or strategies can be used to detect DIF, a common way being to utilize the methods within the IRT framework. When DIF arises in an item, the response patterns are affected by both the underlying latent trait and a grouping variable, which will generate different item parameters across groups. Stated differently, DIF occurs when different subgroups (e.g., males and females) with the same level of an underlying trait have different probabilities of giving an affirmative response.[172] An important aspect of DIF is that, to some extent, it must be systematic. Inconsistency in response patterns must affect almost all of the individuals in a sub-group in a predictable manner. Therefore, DIF should be understood at the group level.[223]

A subgroup of individuals who are believed to have an advantage are, according to convention, categorized as the reference group, while the focal group consists of the possibly disadvantaged individuals. The simplest form of DIF arises when the reference group has an advantage over the entire continuum of the underlying latent trait. This is commonly referred to as uniform DIF, which becomes evident when the difficulty parameter is different across groups while the discrimination parameter is comparable (see **Figure 4**). A more complex form is non-uniform DIF, which arises when the advantage shifts in degree or direction along the theta (i.e., the underlying latent trait) continuum. The reference group may have a small advantage at the lower end of the theta continuum while the advantage is considerably higher at the extreme end of the same continuum. Non-uniform DIF can also arise when the reference and focal groups differ in both difficulty and discrimination. The focal group may have an advantage at one part of the theta continuum while the reference group may have a larger advantage at a higher level of the underlying latent trait.[223]

An investigation of DIF within the IRT framework includes examining the potential difference in item difficulty and discrimination across groups. This can be accomplished by comparing two models: a constrained model in which the item parameters are constrained to be equal across groups and a DIF model in which item difficulty or item discrimination (or both) is allowed to differ across groups. In the next step, a likelihood ratio test (LRT) can be used to test the null hypothesis (i.e., that item difficulty or discrimination is invariant across groups). The LRT roughly follows the chi-square distribution and a significant result ($p < 0.05$) indicates a better fit for the model that assumes the

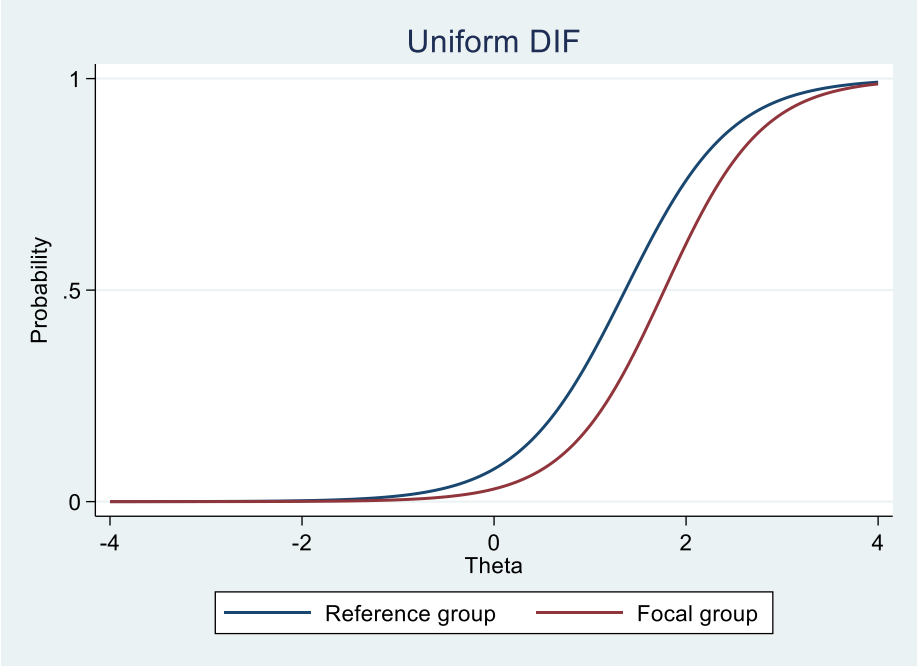

Figure 4. Graphical illustration of uniform DIF. The visible difference between the groups shows that a test taker from the reference group has a higher probability of giving an affirmative response than a test taker from the focal group with a comparable level of theta.

DIF. Caution is needed in large samples as the LRT may be significant even when the difference across models is small. Therefore, LRT calculations are often accompanied by the Akaike information criterion (AIC) and the Bayesian information criterion (BIC). The AIC and BIC are used to compare models by introducing a penalty term for the increased complexity in a model (i.e., the number of parameters included in the models). The preferred model is the one associated with the lowest AIC and BIC values.[224] According to Raftery, a difference in the BIC of 2 to 6 can be categorized as "weak" evidence for the model with a better fit, 6 to 10 as "positive" evidence and > 10 as "strong" evidence.[225]

In Paper IV, each item in the ASD domain was examined for DIF across sex. A developmental sample was generated by way of a random split of the total sample, which was used to calibrate a two-parameter logistic model (2PL). A 2PL model was used because the two higher response categories (i.e., "Yes, to some extent" and "Yes") were collapsed into a single response category, thus developing a binary scale, since low response frequencies were reported for

some items. A 2PL model is comparable with a GRM, the difference lying in the number of response categories utilized. In Paper IV, the DIF analysis includes three different 2PL models that were calibrated utilizing the slope intercept parameterization. A *constrained model* (i.e., in which the slope and intercept were constrained to be equal across sex) was compared to a *DIF difficulty model* (allowing only the intercept to vary across sex) and a *DIF discrimination model* (allowing only the slope to vary across sex). *DIF difficulty* was considered the main focus of the analysis because the difference in the probability of giving an affirmative response may have more significant consequences during a screening process.

3.4 ETHICAL CONSIDERATIONS

All of the procedures used for this thesis comply with the Helsinki Declaration of 1975, as revised in 2008, and with relevant national regulations and guidelines for research. The participants were protected by informed consent and their confidentiality was ensured by research identification codes in the raw data files that precluded any linkage to individuals.

The data collection in CATSS and the linkage to the NPR have received ethical approval from the Karolinska Institutet ethical review board (DNR 02-289) and from the Regional Ethical Review Board in Stockholm (DNR 2010/597-31/1 and 2016/2135-31).

4 RESULTS

4.1 PAPER I: PREVIOUS AND PREDICTIVE VALIDITY

The number of individuals with a registered diagnosis in the NPR are reported in **Table 7** together with the number of individuals with a screen-positive result in the corresponding diagnostic domain of the A–TAC. Of the total sample, 2.8% had a registered diagnosis of ADHD, 1.2% of ASD, and 1% of LD, while the remaining diagnoses included had a prevalence in the NPR of < 0.6%. Age at diagnosis was taken into account, which showed that a diagnosis of LD or DCD was commonly registered before the age of 9 or 12 years (i.e., before the A–TAC interview). The opposite pattern emerged for all other included diagnoses, and, for instance, a registered diagnosis of OCD or ED was more common after the age of 9 or 12 years (i.e., after the A–TAC interview).

The previous and predictive validity for each diagnosis is reported in **Table 8** together with the results from the total sample (i.e., with no consideration taken of the age at diagnosis). The previous validity was good to excellent for most disorders (AUC 0.82–0.99), the exception being eating disorders, with fair validity (0.72). The specificity values were high (> 0.90), while the sensitivity values varied between 0.37 and 0.88. The predictive validity was excellent for LD (0.92) and several disorders showed good validity (ASD, ADHD, TD, and ODD). However, poor predictive validity was reported for DCD, CD, OCD, and ED (AUC < 0.70). The specificity values were high and ranged from 0.85 to 0.99, while the sensitivity values were lower and ranged extensively, from 0.10 to 0.89. Additionally, the same pattern of sensitivity/specificity emerged for the diagnoses with two cut-off values (i.e., ASD, ADHD, LD, and DCD). The “low” cut-off value (screening) had higher sensitivity, while the “high” cut-off value (clinical proxy) had higher sensitivity in both the previous and the predictive groups.

The low prevalence of the disorders included resulted in low PPV values (0.01–0.22), while the NPV values were high (> 0.98) in both the previous and the predictive groups. The highest DOR value for each diagnosis was found in the previous group, the only exception being LD, which had the highest DOR in the predictive group. For ASD, ODD, CD, and OCD, the DOR values were > 100 in the previous group (calculations are presented in the supplementary material for Paper I).

The calculations for previous and predictive validity were also conducted in age-specific groups (i.e., nine-year-olds and twelve-year-olds). The ODD and OCD modules showed excellent previous validity for the 12-year-olds (AUC = 0.99) and the proposed cut-off values showed exceptional sensitivity (1.0) and specificity (0.97). For all other diagnoses, the age-specific calculations did not yield any considerable decrease or increase regarding the previous or predictive validity results (calculations are presented in the supplementary material for Paper I).

Table 7. Individuals with a registered diagnosis in the NPR (N (%)) and screen-positives in the corresponding diagnostic domain of the A–TAC (N (%)).

	Diagnosis in the NPR			A-TAC	
Diagnosis	Before	After	Total	Cut-off	Screen-positive
ASD	127 (0.5)	171 (0.7)	298 (1.2)	4.5	924 (3.6)
				8.5	266 (1.0)
ADHD	231 (0.9)	492 (1.9)	723 (2.8)	6	2707 (10.5)
				12.5	524 (2.0)
LD	145 (0.6)	104 (0.4)	249 (1.0)	1	3961 (15.3)
				3	428 (1.7)
DCD	70 (0.3)	18 (0.1)	88 (0.3)	0.5	2050 (7.9)
				1	469 (1.8)
TD	41 (0.2)	47 (0.2)	88 (0.3)	1.5	847 (3.3)
ODD	8 (0.0)	20 (0.1)	28 (0.1)	3	795 (3.1)
CD	27 (0.1)	50 (0.2)	77 (0.3)	2	278 (1.1)
OCD[a]	9 (0.0)	61 (0.2)	70 (0.3)	1	479 (1.9)
ED[a]	32 (0.1)	127 (0.5)	159 (0.6)	1	1371 (5.4)

Note:
N = 25,828.
The diagnoses in the NPR have been reported in three different groups: before (i.e., a registered diagnosis before or the same year as the A–TAC interview), after (i.e., a registered diagnosis after the A–TAC interview) and total (the before and after groups in collapsed fashion). The number of individuals with a gate score equal to or higher than the cut-off values is reported for each of the corresponding diagnostic domains in the A–TAC.
[a] *No previously established cut-off value.*
This table is reproduced with small amendments from Paper I.

Table 8. Previous and Predictive Validity of A–TAC.

		Previous		Predictive		Total	
Disorder	Cut-off	AUC	sens/spec	AUC	sens/spec	AUC	sens/spec
ASD	4.5 (low)	0.98	0.85/0.97	0.81	0.42/0.97	0.89	0.60/0.97
	8.5 (high)		0.48/0.99		0.17/0.99		0.30/0.99
ADHD	6 (low)	0.93	0.79/0.90	0.82	0.56/0.90	0.86	0.64/0.91
	12.5 (high)		0.46/0.98		0.19/0.98		0.28/0.99
LD	1 (low)	0.87	0.83/0.85	0.92	0.89/0.85	0.89	0.86/0.85
	3 (high)		0.37/0.99		0.40/0.99		0.39/0.99
DCD	0.5 (low)	0.82	0.70/0.92	0.57	0.22/0.92	0.77	0.60/0.92
	1 (high)		0.38/0.98		0.11/0.98		0.32/0.98
TD	1.5	0.86	0.59/0.97	0.80	0.47/0.97	0.83	0.52/0.97
ODD	3	0.99	0.88/0.97	0.80	0.45/0.97	0.85	0.57/0.97
CD	2	0.90	0.52/0.99	0.70	0.20/0.99	0.77	0.31/0.99
OCD[a]	1	0.88	0.67/0.98	0.65	0.25/0.98	0.68	0.30/0.98
ED[a]	1	0.72	0.38/0.95	0.52	0.10/0.95	0.56	0.16/0.95

Note:
Previous and predictive validity: area under the curve (AUC) and sensitivity/specificity.
[a] No previously established cut-off value.
The table is reproduced from Paper I with some amendments.

4.2 PAPER II: DEVELOPMENT OF A BRIEF SCREENER FOR AUTISM

Preliminary analysis: EFA

The initial analysis of eigenvalues before rotation showed that the single factor solution explained 35.72% of the total variance. Five factors had eigenvalues over Kaiser's criterion of 1 (eigenvalues: 6.07, 1.69, 1.3, 1.24 and 1.1) and an examination of the scree plot showed an inflection point that justified a single factor solution. In sum, the ASD domain was considered to be a reasonably unidimensional scale and we proceeded with the GRM.

Item parameter estimates

The item difficulty and discrimination and the corresponding standard error from the GRM are reported in **Table 9**. The discrimination parameter (a) ranged from 1.15 to 3.4. At the first threshold (b_1 "Yes, to some extent"), the range of the difficulty parameter was 1.11 to 2.81, and the range at the second threshold (b_2) was 2.32 to 3.57. The result indicates that a higher level of ASD traits (i.e., theta greater than 0) is required to get an affirmative response for any of the items in the ASD domain.

Item selection

The item selection for the *short form* was based on the examination of the item parameters and the IIFs (an example from the language module can be found in **Figure 5**). Both item I41 ("Does he/she exhibit considerable difficulties interacting with peers?") and item I44 ("Does he/she have difficulties behaving as expected by peers?") showed very high discrimination values which may indicate local dependence. Item I41 was therefore excluded as a candidate for the *short from* given the existence of both statistical and content similarities. The final candidates for the *short form*, with high and narrow IIFs, included item H35 from the language module, items I40 and I44 from the social interaction module and item J47 from the flexibility module.

Validation of short form

The previous and predictive validity of the *short form* are presented in **Table 10,** which reports the AUC estimates with the sensitivity and specificity values for each possible scale step. The *short form* showed excellent previous validity (AUC = 0.95), while the predictive validity was fair (0.72). Two cut-offs were established: a low cut-off (> = 0.5) for screening with a high sensitivity but lower specificity and a higher cut-off (> = 1.5) as a clinical proxy for ASD.

Table 9. Item parameter estimates and standard errors from the graded response model in the developmental sample.

Module	Item	Item content	*a*	SE	b_1	SE	b_2	SE
Language	H34	delayed language development?	1.15	.04	2.45	.07	2.97	.09
	H35	**difficulties sustaining a conversation?**	**2.54**	**.1**	**2.28**	**.04**	**2.98**	**.06**
	H36	repeat words and expressions / use words in a strange way?	2.02	.07	2.16	.04	2.78	.06
	H37	difficulties with games of make-believe / less imitation	1.96	.07	2.38	.05	3.0	.07
	H38	talk in too high a pitch or too quietly?	1.2	.04	2.22	.06	3.57	.10
	H39	difficulties keeping "on track" when telling other people something?	1.80	.05	1.74	.03	2.69	.06
Social Interaction	**I40**	**difficulties expressing emotions and reactions?**	**2.73**	**.12**	**2.44**	**.05**	**3.01**	**.07**
	I41	difficulties interacting with peers?	3.29	.11	1.75	.02	2.39	.04
	I42	uninterested in sharing joy, interests and activities?	2.36	.1	2.52	.05	3.27	.08
	I43	be with other people on his/her terms?	2.41	.07	1.83	.03	2.62	.05

	I44	**difficulties behaving as expected?**	**3.4**	**.11**	**1.64**	**.02**	**2.42**	**.04**
	I45	easily influenced by others?	1.28	.03	1.11	.03	2.61	.06
Flexibility	J46	absorbed by interests, repetitive or too intense?	1.98	.06	1.62	.03	2.48	.05
	J47	**absorbed by routines?**	**2.64**	**.09**	**2.11**	**.03**	**2.81**	**.06**
	J48	strange hand movements/toe-walking?	1.46	.06	2.81	.08	3.31	.10
	J49	obsessed with details?	2.32	.06	1.52	.02	2.41	.04
	J50	dislike changes in daily routines?	2.13	.06	1.42	.02	2.32	.04

Note:
a = item discrimination, SE = standard error, b_1 & b_2 = item difficulty.
The table is a reprint from Paper II with some amendments.

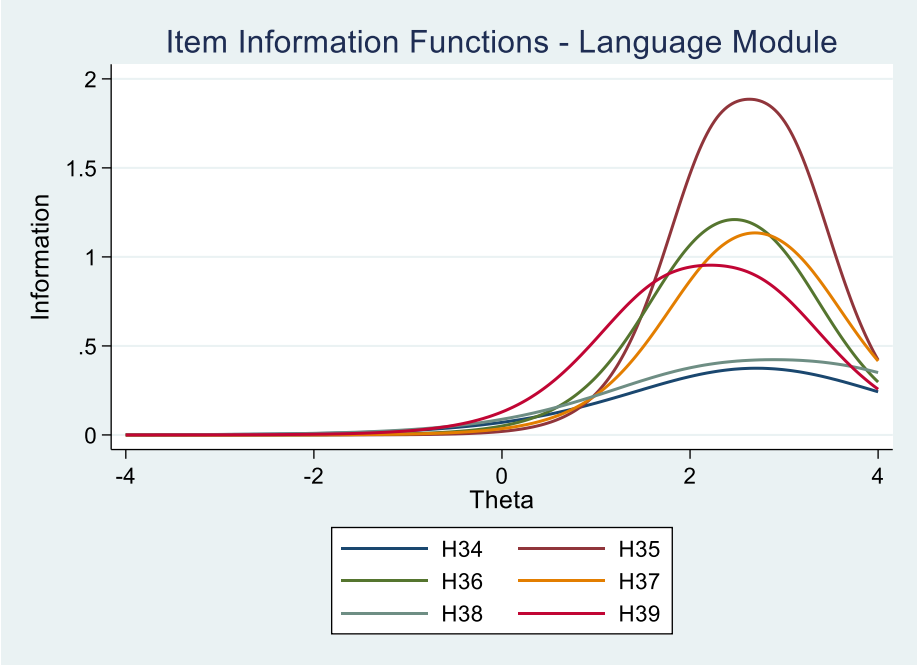

Figure 5. Item information functions from all of the items in the language module. Item H35 provided the highest IIF and was therefore selected as a candidate for the short form. In contrast, items H34 and H38 did not yield a substantial amount of information.

Table 10. Previous and predictive validity of the ASD domain short form

	Previous	Predictive	Total
AUC	.95	.72	.81
Scale step	sens/spec	sens/spec	sens/spec
0.5	**.949/.899**	**.519/.898**	**.681/.902**
1	.782/.964	.349/.963	.512/.967
1.5	**.654/.984**	**.248/.983**	**.401/.986**
2	.50/.99	.155/.989	.285/.992
2.5	.372/.995	.07/.994	.184/.995
3	.295/.997	.039/.996	.135/.997
3.5	.128/.999	.016/.998	.058/.999
4	.09/.999	.008/.999	.039/1.0

Note:
N = 15,490. Previous and predictive validity: area under the curve (AUC) and sensitivity/specificity.
The table is reproduced with minor amendments from Paper II.

4.3 PAPER III: A SEX-SPECIFIC COMPARISON

The population means for boys were consistently higher than for girls in all of the included domains (see **Table 11**).

Table 11. Population means of the 30,392 individuals.

Raw mean score (95%) confidence intervals for the entire population		
	♂	♀
ASD	.99 (.96–1.02)	.62 (.59–.64)
ADHD	2.49 (2.44–2.55)	1.58 (1.53–1.62)
LD	.31 (.30–.33)	.25 (.24–.27)
ODD	.51 (.50–.53)	.39 (.37–.40)

Note: The table is reproduced from Paper III.

The mean raw and standardized scores from each A–TAC domain are reported for males and females with an ASD diagnosis in **Table 12** together with the linear regression estimates. Males diagnosed with ASD had significantly higher raw mean scores in the ASD and ADHD domains, while no significant difference was found in the LD and ODD domains. The opposite pattern emerged when standardized scores were used; females diagnosed with ASD consistently received higher standardized scores, however only statistically significant in the ODD domain. In the ASD domain, females had a mean standardized score of 3.23, while the corresponding result for males was 2.75. Thus, when males and females with an ASD diagnosis are compared against a standardized and sex-specific mean value, the females' scores were 0.48 standardized scores above the sex-specific mean value of the boys.

Table 12. Raw mean and standardized A–TAC domain scores for the 308 boys and 122 girls with an NPR diagnosis plus ASD and linear regression estimates.

	Raw and Standardized scores (95% confidence intervals) together with linear regression estimates for individuals with an ASD diagnosis			
	Raw ♂	Raw ♀	Standardized ♂	Standardized ♀
ASD	6.05 (5.55–6.54)	4.86 (4.07–5.59)	2.75 (2.48–3.02)	3.23 (2.65–3.81)
	1.21, t=2.59, p=0.0100		-0.48, t=1.68, p=0.0945	
ADHD	8.16 (7.55–8.75)	6.45 (5.49–7.41)	1.63 (1.46–1.81)	1.85 (1.48–2.21)
	1.70, t=2.95, p=0.0033		-0.21, t=-1.18, p=0.2403	
LD	1.20 (1.07–1.32)	1.21 (1.00–1.42)	1.35 (1.16–1.54)	1.61 (1.26–1.96)
	-0.01, t=-0.12, p=0.9053		-0.26, t=-1.37, p=0.1705	
ODD	1.74 (1.56–1.88)	1.71 (1.43–1.98)	1.32 (1.15–1.49)	1.70 (1.43–2.05)
	0.01, t=.09, p=0.9273		-0.37, t=-2.09, p=0.0376	

Note:
N ♂ = 308, N ♀ = 112.
The table is reproduced from Paper III with minor amendments.

4.4 PAPER IV: MEASUREMENT OF AUTISM IN MALES AND FEMALES

Preliminary analyses: EFA

The initial analysis from the EFA in the male and female sample showed a sufficiently unidimensional scale. The examination of eigenvalues, before extraction and rotation, showed that a single factor solution in the male sample explained 33.80% of the total variance (first five eigenvalues: 5.75, 1.67, 1.22, 1.17, and 1.04). The corresponding examination in the female sample showed that a single factor solution explained 23.36% of the total variance (first six eigenvalues: 3.97, 1.72, 1.29, 1.30, 1.03, and 1.02). The scree plots were examined, which sufficiently supported the one factor solution for both males and females.

Differential item functioning

The parameter estimates from the *DIF difficulty model* are presented in **Table 13** together with the results from the DIF analysis with LRT, AIC, and BIC (i.e., the comparison with the *constrained model*). The initial analysis with LRT flagged eight items with DIF: H34, H37, and J146 favored males, while H38, H39, I43, J47, and J49 favored females. When the AIC and BIC values were examined, six items were flagged with DIF. Items H34, H37, and J46 showed significant DIF in favor of males; in other words, given comparable levels of ASD traits, males still have a higher probability of giving an affirmative response than females In contrast, significant DIF in favor of females is reported for items H38, H39, and I43. The AIC and BIC values showed a better fit of the constrained model for items J47 and J49 (i.e., no significant level of DIF). A graphical illustration of DIF in items H38 and J46 is presented in **Figure 6 and Figure 7**.

The DIF analysis with LRT, AIC and BIC for the *DIF discrimination model* yielded similar results. The initial analysis with LRT flagged the same eight items with DIF as did the DIF difficulty model. The examination of AIC and BIC indicated significant DIF in three items: item J46 had better discriminatory ability among males, while items H38 and I43 had better discriminatory ability among females (calculations are presented in a separate table in paper IV).

Table 13. Difficulty and discrimination estimates from the DIF difficulty model together with the DIF analysis utilizing the likelihood ratio test, Aikaike information criterion and Bayesian information criterion.

Item number and item content	Male *a*	Male *b*	Female *a*	Female *b*	LRT χ^2	*p*	AIC*	BIC*
H34 delayed language development?	1.10	2.19	1.10	2.72	89.29	<0.001	87.3	79.6
H35 difficulties sustaining a conversation?	2.64	2.06	2.64	2.08	0.17	0.68	-1.9	-9.5
H36 repeat words/ expressions or use words in a strange way?	2.00	2.04	2.00	2.04	0.01	0.94	-2	-9.7
H37 difficulties with games of make-believe / less imitation	1.80	2.21	1.80	2.42	15.69	<0.001	13.7	6
H38 talk in too high a pitch or too quietly?	1.21	2.17	1.21	1.85	44.44	<0.001	42.4	34.7
H39 difficulties keeping “on track” when telling other people something?	1.72	1.68	1.72	1.53	18.70	<0.001	16.7	9
I40 difficulties expressing emotions and reactions?	2.92	2.25	2.92	2.25	0.00	0.97	-2	-9.7
I41 difficulties interacting with peers?	3.56	1.57	3.56	1.54	1.78	0.18	-0.3	-7.9
I42 uninterested in sharing joy,	2.67	2.21	2.67	2.21	0.01	0.93	-2	-9.7

I43 be with other people on his/her terms?	2.66	1.68	2.66	1.47	47.66	<0.001	45.6	37.9
I44: difficulties behaving as expected?	3.54	1.47	3.54	1.44	1.09	0.30	-0.9	-8.6
I45 easily influenced by others?	1.09	1.09	1.09	1.02	3.52	0.06	1.5	-6.2
J46 absorbed by interests, repetitive or too intense?	1.89	1.32	1.89	1.79	196.73	<0.001	194.7	187
J47 Absorbed by routines?	2.62	1.98	2.62	1.90	4.30	0.04	2.3	-5.4
J48 strange hand movements/toe-walking?	1.47	2.59	1.47	2.64	0.81	0.37	-1.2	-8.9
J49 obsessed with details?	2.29	1.38	2.29	1.30	7.79	0.01	5.8	-1.9
J50 dislike changes in daily routines?	2.00	1.26	2.00	1.30	1.75	0.19	-0.3	-8

Note:
N = 8,359 males and 8,270 females.
a = item discrimination, b = item difficulty, SE = standard error, LRT χ^2 = likelihood ratio test, AIC = Aikaike information criterion, BIC = Bayesian information criterion.
** The reported AIC and BIC values represent the difference between the constrained model and the DIF difficulty model. Negative values indicate a better fit of the constrained model.*
Item number and item content in italics denote inclusion of item in the previously established short form.

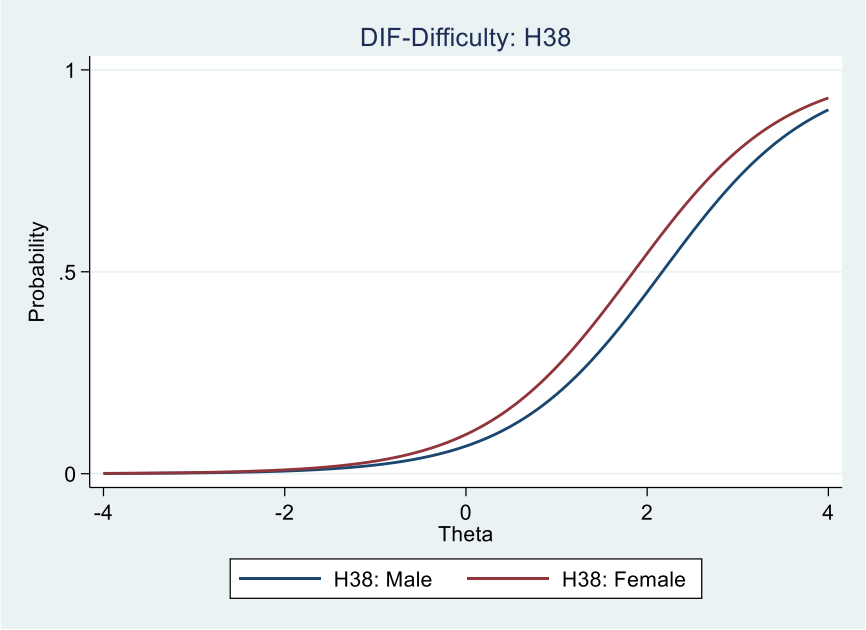

Figure 6. Item characteristic curves for males and females in item H38, which show significant DIF in favor of females.

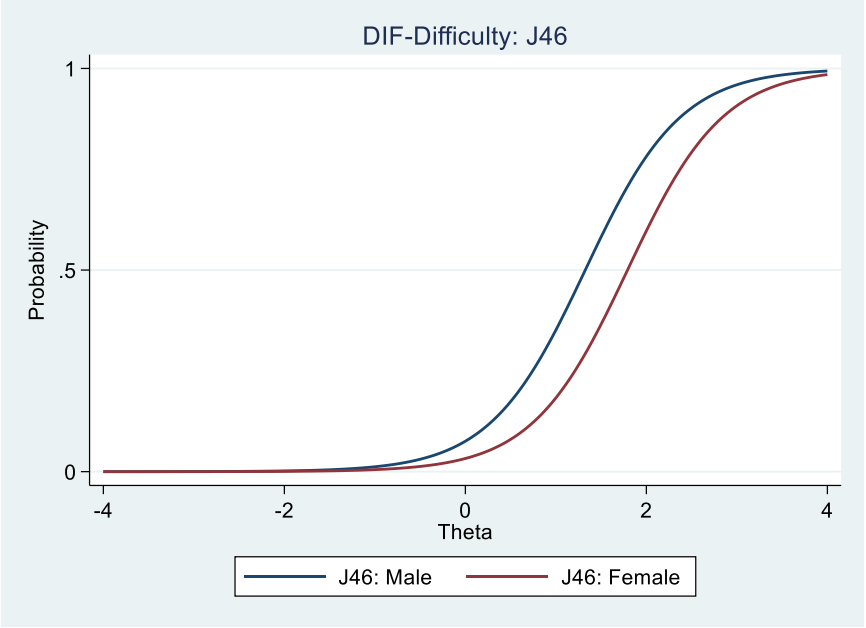

Figure 7. Item characteristic curves for males and females in item J46, which show significant DIF in favor of males.

Item selection: male and female short form

Six items showed narrow and moderately high to high IIFs at the higher end of the continuum of ASD traits: H35, I40, I41, I44, J47, and J49. Four of these items (H35, I40, I44, and J47) are included in the *short form* that was developed in Paper II.[226]

The results from the DIF analysis and the examination of IIFs were used to develop separate *male* and *female short forms* that might have the potential to better detect ASD in males and females. The four items in the previously established *short form* showed no DIF and high IIFs. Therefore, these items served as the foundation for both the *male* and *female short form*. The *male short form* also included the three items with DIF in favor of males (H34, H37, and J46), while the *female short form* included the three items with DIF in favor of females (H38, H39, and I43).

Validation

The AUC values for the ASD domain, previously established *short form*, *male short form* and *female short form* are reported in **Table 14**. Previous validity was excellent for both males and females (AUC = 0.93–0.98) in all versions of the ASD domain, whereas the corresponding predictive validity was fair (AUC = 0.71–0.79). The original ASD domain (i.e., 17 items) showed the highest AUC estimates, and an ever so slight increase was reported for both the *male* and *female short forms* as compared to the previously established *short form*.

Table 14. Area under the curve (AUC) for males and females in the previous, predictive, and total groups for the ASD domain, previously established short form and male and female short forms.

	Previous – AUC		Predictive – AUC		Total – AUC	
	♂	♀	♂	♀	♂	♀
ASD domain	0.96	0.98	0.79	0.76	0.86	0.83
Short form	0.94	0.93	0.75	0.71	0.82	0.77
Male short form	0.95	0.97	0.78	0.75	0.85	0.81
Female short form	0.94	0.97	0.77	0.74	0.84	0.81

Note:
N ♂ = 8,517 (ASD = 186), N ♀ = 8,202 (ASD = 83).

5 DISCUSSION

5.1 COMMENTS ON MAIN FINDINGS

5.1.1 PAPER I

In Paper I, the previous and predictive validity of the A–TAC was examined in a large population-based sample of twins. Our findings suggest that the A–TAC has a better ability to identify individuals who has been assigned a diagnosis before or in the same year as the A–TAC interview (i.e., previous validity). There are two possible explanations for these results. First, the A–TAC was rated by parents who are aware of their children's existing diagnoses. It is thus plausible to assume that the parents of children with a diagnosis are more prone to recognizing and affirming the corresponding symptoms included in the items. Second, it is plausible that the age at diagnosis has an impact on the manifestation of symptoms (e.g., there is a difference between a diagnosis of ASD and ADHD in childhood compared to one in adolescence). Most likely, a diagnosis in childhood indicates a quantitatively more severe symptom presentation in combination with poor adaptive functioning. This notion is supported by Arvidsson et al. who in a study of ASD symptom levels (measured by the ASD domain in the A–TAC) reported that those who received a diagnosis aged 1–6 years displayed quantitatively more symptoms than those who were diagnosed at a later age.[97] Therefore, it is plausible to assume that children who receive an ASD diagnosis after the age of nine years (i.e., after the A–TAC interview) have a less severe ASD phenotype, which is, reasonably, also coupled with a later assessment.

Furthermore, attention is warranted during the A–TAC assessment of individuals aged 12 years or older as their parental ratings may be influenced by behavior and problems associated with puberty and adolescence. For instance, social demands increase and become more complex during the adolescent years. Furthermore, internalizing disorders may develop during adolescence that may yield a more ambiguous symptomatology. For instance, the mean age of onset for separation anxiety disorder, specific phobia, and social phobia is under 15 years of age.[227] Related to this, our findings from the age-specific groups showed excellent validity for OCD for twelve-year-olds but "only" good validity was established for nine-year-olds. Thus, it is plausible to assume that results are affected by age, as the mean age of onset has been reported as 11.1 years for early onset OCD.[65] Taken together, our findings of considerably lower sensitivity values in the predictive group (except for the low cut-off for LD) offer an argument against the uncritical use

of the A–TAC in clinical settings when the results are being used to identify adolescents in need of further assessment.

5.1.2 PAPER II

In Paper II we developed a *short form* that yielded validity estimates comparable to those of the full 17-item ASD domain. The benefits of the *short form* include the quick yet reliable identification of individuals who present with symptomatology indicative of a possible ASD. A short screening instrument may be a valuable asset in primary care settings (e.g., as a part of mandatory developmental check-ups, which commonly include several developmental areas such as gross and fine motor skills, language, and communication). Today, there is ongoing discussion about the utility of general screening for ASD in primary care settings, which is recommended by some organizations.[228,229] The use of structured screening instruments as opposed to brief observation has been reported to improve the accuracy of referrals for further assessment[230] and clinical judgement.[231,232] Furthermore, structural disparities in clinical settings may be lessened by the use of a structured screening instrument, particularly in the case of children who come from a minority background or have a low socioeconomic status, who are reported to receive a diagnosis at a later age, which delays access to services.[233] A positive screening result may draw attention to the need for referral, which is the first step toward an early diagnosis. By extension, this may allow access to early interventions that can reduce the severity and/or impact of symptoms, improve language ability and adaptive behavior and provide extra resources in pre/school settings, which may improve overall functioning.[234] Taken together, our results show that the *short form* may be a viable option for screening children prior to the age of 9 or 12 years when concerns are raised during a mandatory developmental check-up or primary care visit or within a school setting. However, our findings followed the pattern of the results in Paper I, and the proposed cut-off values for the *short form* yielded low sensitivity values in the predictive group (0.519 and 0.248). Thus, the short form should not be used uncritically for assessment in older age groups.

Brief screening instruments with a minimal response burden can be valuable in large-scale epidemiological studies, particularly when the research question does not comprise the broader variance of the ASD phenotype. The *short form* may be a practical option, because it is free of charge and can be conducted by laymen over the telephone. Additionally, the *short form* may also be valuable in countries with limited societal resources. It should be noted, however, that it is not yet known how possible cultural differences may influence parental ratings in the *short form*.

5.1.3 PAPER III

Paper III aimed to compare the degree of boys' and girls' symptoms of ASD, ADHD, LD, and ODD by using a sex-specific standardized score. Our findings suggest that females diagnosed with ASD represent a more extreme end of the distribution of ASD traits in a general population of females than males diagnosed with ASD do in a distribution of ASD traits in a general population of males. This result raises questions about the degree of symptomatology that is present in males and females with a diagnosis of ASD. Garcia et al. have shown that a percentile-based distribution of NDD symptomatology is positively correlated with the degree of dysfunction and suffering.[235] Thus, it is reasonable to assume that this association is similar across sex, which would suggest that females diagnosed with ASD experience a higher degree of dysfunction than boys, even though the females are rated as having fewer symptoms. Taken as a whole, this indicates a need to consider the impairment associated with the symptomatology (i.e., make a qualitative assessment) and not just take count of symptoms during clinical assessments.

The finding that females receive lower raw mean scores in the general population has been supported in several studies utilizing different screening instruments for ASD, including Social Responsiveness Scale,[12,192] Autism Spectrum Screening Questionnaire,[169,193] the Social Communication Questionnaire,[194] and the Childhood Autism Spectrum Test.[195] Additionally, two studies have reported different distributions of ASD traits across sex where, compared to females, males tended toward the extreme end of the distribution.[236,237] The noticeable difference in the mean raw scores of males and females (i.e., 6.05 and 4.86 respectively) draws attention to the need to evaluate the possible value of sex-specific cut-off values.[238] Furthermore, our findings suggest that certain females are not adequately captured by the use of established cut-off values in the A–TAC. This emphasizes the need to examine whether different constellations of symptoms should be weighted and/or assessed differently in males and females.

5.1.4 PAPER IV

Paper IV aimed to evaluate each item in the ASD domain for DIF and to examine whether a subset of the items is better at detecting ASD traits in males or females. The finding that the full ASD domain is largely equivalent, albeit with six items being flagged with DIF, suggests that there is a limited need for sex-specific scoring for the total score (i.e., on all 17 items). This is in line with a study by Kaat et al. in which a large sample was created by bringing together females diagnosed with ASD from several sites. The results show only a minimal difference between males and females on the Autism Diagnostic

Observation Schedule, Autism Diagnostic Interview–Revised, and Social Responsiveness Scale after controlling for age, non-verbal IQ, and language level.[239]

The finding that six items were flagged with DIF indicates that caution is warranted in single-item, rather than whole-scale, interpretation. Attempts to detect DIF can have ambiguous results, particularly in large samples where small differences can easily become significant. Therefore, a reasonable explanation for the DIF is required, such as the finding that item J46 (*"Does s/he get absorbed by his/her interests in such a way as being repetitive or too intense")* favored males, which is supported by several studies that have found lower levels of restricted and repetitive behavior in females in the general population[194] and in clinical samples.[146,148,149] Similarly, females with ASD have been reported to have a higher liability threshold for ASD symptomatology in general, but particularly for restricted and repetitive interests.[113] In contrast, the DIF in item H38 ("*Does s/he talk in too high a pitch or too quietly?"*) can probably be explained by the item content and wording. In an examination of Autism Spectrum Screening Questionnaire- revised extended version, Kopp and Gillberg found that an item on robot-like language was commonly endorsed by males, while an item on different voice/speech was endorsed by females.[151] However, caution is warranted in treating this as a defining feature of ASD in males, as a recent study has found DIF in favor of males in an item in Social Responsiveness Scale on awareness of the effect of voice volumes.[240] It is likely that the contrasting results described above are influenced by the age of the participants and sample ascertainment. Taken together, the detection of DIF indicates a need for the careful writing of items and the psychometric evaluation of existing instruments in order to ensure fairness during assessment.

Our results indicate relatively small differences in ASD traits across sex. However, the possibility remains that females present with a different phenotype, which would suggest that other items are required in order to adequately capture females with ASD. For instance, the ASD symptomatology may be less pronounced in females, which may be attributable to a better ability to camouflage.[197,198] Additionally, females may be rated as less impaired at a surface level in clinical settings,[144] as well as in parent and teacher reports.[241] The ASD domain is mainly based on the diagnostic criteria for pervasive developmental disorder in DSM-IV[77], which may lack the sensitivity to capture a broader variation of ASD symptomatology. Taken as a whole, this suggests a need to examine the content validity of existing ASD instruments.

5.2 CLINICAL IMPLICATIONS

The A–TAC's primary strength is its ability to provide a broad assessment, which includes NDDs as well as commonly co-occurring psychiatric disorders. In clinical settings, it is essential to be aware of co-occurring disorders during assessment and the planning of treatment and interventions. It has been argued that the potential negative outcomes of NDDs are underpinned by the co-occurrence of "other" disorders (i.e., the risk of negative outcomes increases in the presence of co-occurring disorders, such as ASD in combination with ID and ADHD).[241-244] Additionally, a continuous measurement of NDDs may be capable of detecting the presence of subthreshold traits. Symptoms of NDDs may wax and wane over time,[245] and the manifestation of subthreshold traits may indicate the presence of a condition which at that time has not attained clinical significance and/or a prodromal pathology which may arise when the individual is older.[246,247] Furthermore, it is likely that an individual trajectory may be influenced by subthreshold traits from another diagnostic category. For instance, one study has found that individuals with bipolar disorder and ASD traits show a specific clinical phenotype which includes a higher degree of suicidal ideation.[248] Taken together, broad-band screening instruments, such as the A–TAC, should be recommended in clinical practice in order to obtain an initial assessment that taps into a broad range of symptomatology that is frequently present in child and adolescent psychiatry.

In Paper I, Paper II, and Paper IV, the calculations from the AUC indicate a decrease in validity for the predictive group. As noted in the discussion of Paper I and Paper II, clinicians should not use the established cut-off values uncritically in older age groups. Symptoms of NDDs may become visible at different points in time in an individual's life. This became evident in a study by Mandy et al. that examined the developmental trajectories of males and females with ASD traits in a large population-based sample. While males had higher levels of ASD traits at age 7, a decline was found between the ages of 7 and 10, followed by a slight increase in ASD traits between the ages of 10 and 16. On the other hand, females had lower scores than males at age 7, but a substantial increase in ASD traits was reported for females during adolescence.[143] This indicates that, on the one hand, parents may not adequately capture subtle deficits in their children until they become manifest, possibly due to an increase in social demands. On the other hand, one may also argue that ASD deficits or traits that are not detectable by parents are of limited clinical relevance. Our findings nevertheless support the need to take into account the age of the child during screening for NDDs.

Our findings in Paper IV indicate that the ASD domain is largely equivalent across sex. Therefore, differences in the total score reflect a meaningful variation in ASD traits and are not the consequence of measurement error. Additionally, our results in Paper III show that females diagnosed with ASD had lower raw mean scores than did males diagnosed with ASD. Thus, our findings in Paper III indicate that females diagnosed with ASD are rated with a quantitatively lower level of ASD traits even though a higher rate of impairment may be present. Our findings suggest that clinicians need to consider the number of symptoms in combination with the degree of dysfunction and suffering.

5.3 METHODOLOGICAL CONSIDERATIONS

5.3.1 GENERALIZABILITY

All of the papers in this thesis are based on a twin sample, which raises questions about generalizability. For instance, an excess of twin pairs has been found among families with two or more siblings with ASD, which may suggest that the process of twinning is a risk factor for developing ASD.[249,250] However, this notion is not supported by three large population-based studies from California,[251] Australia,[252] and Sweden.[253] Additionally, similar levels of ASD traits,[254,255] ADHD traits,[256] and general psychiatric outcomes[257,258] (e.g. depression, affective disorders and psychotic disorders) have been reported for twins and singletons. Therefore, it is reasonable to assume that the results from Papers I–IV can be generalized to a non-twin population.

A declining participation rate has been reported for CATSS and it is possible that parents of children with NDDs or other psychiatric disorders are overrepresented among non-responders. This notion is supported by two studies from Norway in which an increased likelihood of a higher degree of impairment or mental health problems has been found among non-responders.[259,260] It is also plausible, however, that parents of children with NDDs are more likely to participate as they may be more inclined to contribute to research within this field. Systematic analyses of the responders and non-responders in CATSS have shown relatively small differences in socio-economic circumstances, registered diagnoses in the NPR, and pharmacological treatment.[174] However, these analyses were published in 2011 and it is not yet known how the declining participation rate has affected the direction of the difference between responders and non-responders.

The previous and predictive validity was examined by way of ROC curves utilizing registered diagnoses in the NPR as dependent variables. In Paper I,

low prevalence rates (i.e., < 0.6%) were reported for DCD, TD, ODD, CD, OCD, and ED in the NPR. It is plausible that clinicians may be more prone to assign a primary diagnosis without specifying any co-occurring disorders. For instance, the ADHD symptomatology may be expanded to include symptoms of ODD or CD. However, the prevalence estimates for ASD and ADHD were also low (1.2% and 2.8% respectively in Paper I), while the prevalence of 1% seems reasonable for LD. In the most recent data sample from CATSS and the NPR, extracted during 2020, the prevalence of ASD was 2.4%. Thus, the trend of an increase in registered ASD diagnoses was also evident within CATSS. The issue of prevalence taps into the changing panorama of child and adolescent psychiatric disorders.

The A–TAC was developed early in the 21st century, when the reported prevalence of ASD was around 1% in children and somewhat lower in adults.[80] In 2018, the reported prevalence of ASD was approximately 4% among children and young adults (i.e., aged 0–24 years) in Stockholm County.[261] Thus, a remarkable increase in the number of diagnoses has occurred. This is also the case outside of Sweden. Similar prevalence estimates have been reported in South Korea,[83] USA,[86] and Japan.[88] the However, despite the increase in the number of registered diagnoses of ASD, the symptomatology constituting the ASD phenotype has remained stable at all levels of the population.[96] Furthermore, a decrease in the number of symptoms required for an ASD diagnosis has been reported; in children diagnosed between the ages of 7 and 12, a 50% reduction in reported symptoms was observed in the years 2004–2014.[97] Furthermore, a meta-analytic study has reported a gradual decrease in neurological and psychological constructs between individuals with and without ASD, which suggests that the construct of ASD has (1) become substantially less demarcated and (2) developed into a heterogeneous population.[262] It is also important to note that there is no evidence of a changing etiology, which is evident from a large twin study showing a very similar genetic and environmental ratio despite rapidly increasing prevalence.[98] The changes described above are indeed relevant to the A–TAC. The current cut-off scores for the ASD domain in the A–TAC were established in 2010, and it is plausible that the high cut-off of 8.5, developed to mirror a clinical proxy of ASD, does not adequately capture the predominantly older individuals who are diagnosed with ASD today. Instead, it may be assumed instead that the high cut-off of 8.5 reflects a narrower definition of ASD and that the low cut-of value of 4.5 is representative of the ASD phenotype diagnosed today. The question of whether this represents a dilution of the diagnosis is beyond the scope of this thesis; however, it must be acknowledged that the resources of child and adolescent psychiatry are limited and a continuous surge in ASD

diagnoses create the risk of individuals having less access to habilitation services and special education in schools.

5.3.2 MEASUREMENT ERROR AND MISCLASSIFICATION

Mothers were the informants in the vast majority of the interviews in CATSS.[174] In a study of the Child Behavior Checklist, van der Valk et al. showed that separate ratings from mothers and fathers contributed unique information about a child.[263] Therefore, reliance on a single informant may not fully capture the possible symptomatology in a child. Furthermore, it has been argued that the environmental context influences the manifest behavior of a child and thus that the use of multiple informants may reduce the risk of misclassification.[236] Furthermore, informant type may affect a study's results (e.g., higher heritability estimates for ASD have been reported when the data has been based on parent report as opposed to teacher and/or self-report).[264] However, it is rarely feasible, for practical and financial reasons, to collect data from multiple informants in large-scale studies. In the A–TAC, the items should be assessed within a whole-life context and the behavior of the child should be compared with that of their peers, which makes parents, rather than the twins themselves, more suitable as raters, even though there is a risk of misclassification. Related to this, it can be argued that nine-year-old children may not yet possess the meta-cognitive skills required to compare their own behavior to that of their peers.

In Paper II and Paper IV, we make the assumption that the total score from the ASD domain is representative of the underlying latent trait (i.e., theta). We have defined theta so that the extreme end represents a clinical diagnosis of ASD. This is justified, as the results from the EFA were sufficiently unidimensional, indicating that it measures a single construct. Furthermore, the items in the ASD domain are mostly based on the diagnostic criteria for pervasive developmental disorders in the DSM-IV[77] and are dimensionally distributed in the population; the same genetic liabilities are associated with autistic-like traits and a diagnosis of ASD.[13] The notions of a shared etiology and of dimensional distribution of ASD traits are supported in several large-scale studies.[10,12,264,265] Furthermore, there is considerable overlap between ASD and syndromic ASD (i.e., disorders with a well-known etiology and different developmental trajectory as compared to non-syndromic ASD).[266] These syndromes have a phenotypical presentation that may include symptoms of ASD (e.g., Down's syndrome,[267] Rett syndrome,[268] fragile X syndrome,[269] 22q11-deletions syndrome,[270] tuberous sclerosis,[271] and neurofibromatosis type 1.[272] Unlike ASD, these syndromes have a clear demarcation from the general population. Nonetheless, it seems likely that an A–TAC assessment would also capture children with syndromic ASD. These syndromes are rare,

and we believe that the total score from the ASD domain is sufficiently representative as the theta in the IRT calibrations in Paper II and Paper IV.

In Paper III and Paper IV, the validation estimates are based on data from ASD diagnoses retrieved from the NPR. However, ascertainment bias may have affected the results, as females with an ASD diagnosis may be at greater risk of under identification and/or misclassification. Thus, it is important to note that our findings in Paper II and Paper IV can be generalized only to children and adolescents who have already been diagnosed with ASD in service based registers. This has recently been indicated in a meta-analysis reporting a male-to-female ratio of 4:56 in studies based on participants with a pre-existing ASD diagnosis. By way of contrast, a lower ratio of 3.25:1 has been reported in studies that actively included participants without taking consideration of registered ASD diagnoses.[99] However, in Paper IV, the male-to-female ratio was 2.26:1, which suggests only minor, if any, underrepresentation in CATSS.

6 CONCLUSION

In conclusion, the papers included in this thesis have shown that:

I. the A–TAC is particularly strong as a parent-rated screening instrument for ASD, ADHD, LD, and ODD in children aged 9 or 12 and makes it possible to obtain phenotypical information for several child psychiatric disorders.

II. the *short form* of four items from the ASD domain can satisfactorily discriminate among individuals at the higher end of the autism trait continuum – the previous validity was excellent for children under the ages of nine or twelve.

III. females diagnosed with ASD represent an even more extreme end of the distribution of ASD traits in the general population of females than do males diagnosed with ASD.

IV. the ASD domain in the A–TAC is largely equivalent across sex and the differences observed in mean scores reflect a meaningful variation in ASD traits – the need for a sex-specific scoring procedure is diminished when the total score for the ASD domain is utilized.

7 FUTURE PERSPECTIVES

The A–TAC was developed nearly two decades ago. The items in it are based on diagnostic criteria from the DSM-IV[77] and on well-known clinical features. Thus, a possible future direction may be to evaluate the A–TAC against diagnoses assigned by the DSM-5[1] and the forthcoming ICD-11. Similarly, the potential need for age-specific cut-off values suggested by our findings can also be examined in future studies.

Assessment by way of the A–TAC provides a "problem load score" (i.e., two items on the perceived dysfunction and suffering on the part of the child and two items on the age at onset and on remission or persistence of the perceived problems). A cut-off score of 1 has previously been suggested by Garcia et al. as mirroring significant problems.[235] However, previous validation studies have excluded the "problem load score" as the addition of these items has not substantially improved diagnostic accuracy. Future studies may benefit from an examination of the clinical utility of the "problem load score", particularly since the presence of dysfunction and suffering is explicitly required for a diagnosis of ASD in the DSM-5.[1] Given the rising prevalence of ASD, and that this increase is predominantly driven by individuals without intellectual disability, the arenas in which dysfunction and suffering arise should be thoroughly examined.

This thesis includes a thorough validation of the ASD domain in the A–TAC; similar analyses of possible sex differences can be conducted for the other domains and may be particularly important for the ADHD domain. As with ASD, ADHD is commonly diagnosed in males, with the DSM-5 reporting a male-to-female ratio of 2:1.[1] Similarly, the manifestation of symptomatology has been reported as differing across sex (i.e., females have more symptoms of inattention and internalizing problems and fewer symptoms of hyperactivity and impulsivity).[273]

It is important to establish measurement equivalence, or invariance, both at an item level and for the total scale, because the mean difference is commonly utilized in order to examine differences across groups. If an instrument exhibits measurement variance across groups, then the mean scores are not comparable across the groups being examined. In Paper IV, we examine DIF for males and females, but this methodology can also be used to investigate other subgroups of interest. The diagnostic criteria of ASD may have gained a general acceptance in western countries, but it remains to be discovered how different cultural backgrounds may affect A–TAC assessment. This is an important

consideration with regard to ensuring fairness in screening and diagnostic evaluation. In a recent study from Sweden, the prevalence of ASD among immigrant and multiethnic populations was reported as being at least 3.66% in children aged 2–5 years[274] which shows the need to evaluate existing instruments for possible cultural differences in responses, perception of disability and access to healthcare. For instance, it has been reported that the Childhood Autism Rating Scale has shown measurement invariance in diverse samples from six different countries. Items on social interaction and communication have been reported to show lower levels of variance across the six countries than do items on stereotyped behavior and sensory sensitivity.[275] Cultural adaption of a screening instrument may also include the modification of established cut-off values, which has been proposed for the Finnish version of Autism Spectrum Screening Questionnaire.[276]

As stated above, the detection of similarities and possible differences between male and female manifestation may be obscured by the usage of clinically ascertained samples. It is possible that existing instruments lack the female-specific content needed to capture females who likely have a less pronounced ASD symptomatology. This notion could be further examined in samples that are representative of the general population. Another possibility is to take clinical knowledge and experience into account and develop new items based on observed behavioral differences between males and females. This type of knowledge and experience was previously utilized by Kopp and Gillberg in the development of the Autism Spectrum Screening Questionnaire- revised extended version.[151]

ACKNOWLEDGEMENTS

This thesis would not have seen the light of the day without the contribution and support of many people. I would like to express my sincerest gratitude to each and every one of them who have made this project possible.

First of all, thank you to all of the 34,033 consenting parents of the twins in the Child and Adolescent Twin Study in Sweden. This research could not have been conducted without you.

I am grateful beyond words to my main supervisor, **Sebastian Lundström**, who has generously shared his time and knowledge with me for a decade. Thank you for your endless support and guidance during this journey. I admire your passion for research and your humor, together with your intellectual brilliance.

I would also like to thank the following people:

My co-supervisor **Thomas Nilsson** for providing stability and firm advice to me, as to so many others. The CELAM corridor would not be the same without you.

My co-supervisor **Alessio Degl'Innocenti** for all of your help and support, particularly in practical matters. As head of the forensic psychiatric clinic in Gothenburg, Rågården, you allowed me to work part-time on my doctoral studies. This project would not have been possible without this support.

Christopher Gillberg, as a leading scientist in the field of child and adolescent psychiatry, he was key in the development of A-TAC and his vast scientific contributions has included the development of several concepts included in this thesis.

Henrik Anckarsäter, now in loving memory, my second cousin whom I met up with for the first time in the spring of 2012 when my path through life led me to explore the field of forensic psychiatry – Henrik kindly invited me to write my master's thesis at CELAM, and the rest is history. I have learned a great deal about both research and life from you and I am very grateful that I had the chance to meet you.

My co-authors (besides those mentioned above) **Paul Lichtenstein, Tomas Larson, Maria Råstam, Gitta Lubke, Ralf Kuja-Halkola** and **Henrik Larsson**, for sharing their vast knowledge and expertise with me by providing valuable input that has improved our papers as well as my understanding of research.

My employer and the current head of the department of forensic psychiatry at Sahlgrenska University Hospital, **Eirini Alexiou** – I am very grateful for the opportunity to conduct research as part of my employment! Special thanks are due to my current boss, **Veronica Stenberg**, for all the help and guidance you provided that allowed me to find a balance between my clinical work and doctoral studies.

All my past and present colleagues at CELAM, above all **Peter Andiné, Malin Hildebrand Karlén, Susanna Radovic, Stefan Axelsson, Anna-Kari Sjödin, Sabrina Doering, Anja Fernqvist and Carl Delfin -** thank you for all of the discussions about different aspects of life (and research) and the (ever so important) coffee breaks, laughter, and support at times when everything just seemed rather grey. I have also received a lot of support from my past and present colleagues at Rågården – I would not be the clinical psychologist that I am today without you! A special thanks to **Erik Myhrman** and **Louise Parkdahl,** who endured several visits from me when I was unable to concentrate enough to write this thesis. I would also like to express my sincerest gratitude to **Sven Pedersen** and **Henrik Bergman**, who have been my fellow clinicians and doctoral students since the start. Thank you for always taking time to talk to me when I dropped by to chat about my various concerns, big or small, and for keeping me sane when the circumstances have been tough. Thank you to **Karin Trägårdh** for all the energy that you always bring with you and for letting me partake of your clinical wisdom: I have learned a lot from you. Thank you also to **Pauline Mileikowsky**, for keeping me on my toes with all of your intriguing questions and thoughts about forensic psychiatry and research, and to **Åse Holl**, for your assistance in practical matters and for all of our conversations in the corridor that made the workday more pleasant.

Each and every one of my fantastic friends – you know who you are. Some of you have been right beside me since preschool or elementary school, and some of you have come along later in life. Life is an adventure, and I am grateful for all the experiences we have shared, and will share in the years to come.

My parents, **Marianne** and **Lennart**, for teaching me the value of persistence and for your endless support on my various ventures in life, and my sister, **Charlotte**, who embodies the role of the caring older sister – thank you for keeping me warm with your fantastic knitting projects and endless cups of tea or coffee.

Henrik, oh captain, my captain, thank you for always believing in me, particularly at times when I fail to do it myself. My beloved children, **Alma** and **Wilhelm**, who always reminds me of the important parts of life.

This research was supported by grants from ALF agreement, grant number ALFGBG-776031, Drottning Silvias Jubileumsfond, and Systrarna Greta Johansson och Brita Anderssons Minnesfond.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, Fifth Edition. Arlington, Va: American Psychiatric Association; 2013.

2. Gillberg C. The ESSENCE in child psychiatry: Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations. Res Dev Disabil. 2010;31(6):1543-51.

3. Rutter M, Caspi A, Moffitt TE. Using sex differences in psychopathology to study causal mechanisms: unifying issues and research strategies. J Child Psychol Psychiatry. 2003;44(8):1092-115.

4. Ronald A, Hoekstra RA. Autism spectrum disorders and autistic traits: A decade of new twin studies. Am J Med Genet Part B. 2011;156(3):255-74.

5. Deary IJ, Johnson W, Houlihan LM. Genetic foundations of human intelligence. Hum Genet. 2009;126(1):215-32.

6. Willcutt EG, Pennington BF, Duncan L, Smith SD, Keenan JM, Wadsworth S, et al. Understanding the complex etiologies of developmental disorders: behavioral and molecular genetic approaches. J Dev Behav Pediatr. 2010;31(7):533-44.

7. Lichtenstein P, Carlström E, Råstam M, Gillberg C, Anckarsäter H. The genetics of autism spectrum disorders and related neuropsychiatric disorders in childhood. Am J Psychiatry. 2010;167(11):1357-63.

8. Pettersson E, Anckarsäter H, Gillberg C, Lichtenstein P. Different neurodevelopmental symptoms have a common genetic etiology. J Child Psychol Psychiatry. 2013;54(12):1356-65.

9. Ronald A, Simonoff E, Kuntsi J, Asherson P, Plomin R. Evidence for overlapping genetic influences on autistic and ADHD behaviours in a community twin sample. J Child Psychol Psychiatry. 2008;49(5):535-42.

10. Anckarsäter H, Larson T, Hansson S, Carlström E, Ståhlberg O, Gillberg C, et al. Child Neurodevelopmental and Behavioural Problems are Intercorrelated and Dimensionally Distributed in the General Population. The Open Psychiatry Journal. 2008;2.

11. Rutter M. Research Review: Child psychiatric diagnosis and classification: concepts, findings, challenges and potential: Research Review: Child psychiatric diagnosis and classification. J Child Psychol Psychiatry. 2011;52(6):647-60.

12. Constantino JN, Todd RD. Autistic traits in the general population: a twin study. Arch Gen Psychiatry. 2003;60(5):524-30.

13. Lundström S, Chang Z, Råstam M, Gillberg C, Larsson H, Anckarsäter H, et al. Autism Spectrum Disorders and Autisticlike Traits: Similar Etiology in the Extreme End and the Normal Variation. Arch Gen Psychiatry. 2012;69(1):46-52.

14. Levy SE, Giarelli E, Lee LC, Schieve LA, Kirby RS, Cunniff C, et al. Autism spectrum disorder and co-occurring developmental, psychiatric, and medical conditions among children in multiple populations of the United States. J Dev Behav Pediatr. 2010;31(4):267-75.

15. Höglund Carlsson L, Norrelgen F, Kjellmer L, Westerlund J, Gillberg C, Fernell E. Coexisting Disorders and Problems in Preschool Children with Autism Spectrum Disorders. Sci World J. 2013;2013:213979-6.

16. Joshi G, Petty C, Wozniak J, Henin A, Fried R, Galdo M, et al. The Heavy Burden of Psychiatric Comorbidity in Youth with Autism Spectrum Disorders: A Large Comparative Study of a Psychiatrically Referred Population. J Autism Dev Disord. 2010;40(11):1361-70.

17. Simonoff E, Pickles, Charman T, Chandler S, Loucas T, Baird G. Psychiatric Disorders in Children With Autism Spectrum Disorders: Prevalence, Comorbidity, and Associated Factors in a Population-Derived Sample. J Am Acad Child Adolesc Psychiatry. 2008;47(8):921-9.

18. Brookman-Frazee L, Stadnick N, Chlebowski C, Baker-Ericzén M, Ganger W. Characterizing psychiatric comorbidity in children with autism spectrum disorder receiving publicly funded mental health services. Autism. 2018;22(8):938-52.

19. Mattila M-L, Hurtig T, Haapsamo H, Jussila K, Kuusikko-Gauffin S, Kielinen M, et al. Comorbid psychiatric disorders associated with Asperger syndrome/high-functioning autism: a community-and clinic-based study. J Autism Dev Disord. 2010;40(9):1080.

20. van Steensel F, Bögels S, de Bruin E. Psychiatric comorbidity in children with autism spectrum disorders: A comparison with children with ADHD. Journal of child and family studies. 2013;22(3):368-76.

21. Wolraich M, Hagan J, Allan C, Chan E, Davison D, Earls M, et al. Clinical Practice Guideline: Diagnosis and Evaluation of the Child With Attention-Deficit/Hyperactivity Disorder. Pediatrics. 2019;144(4): e20192528.

22. Hyman S, Levy S, Myers S, Council on children with disabilities, section on developmental and behavioral pediatrics. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. Pediatrics. 2020;145(1): e20193447.

23. Penner M, Anagnostou E, Andoni LY, Ungar WJ. Systematic review of clinical guidance documents for autism spectrum disorder diagnostic assessment in select regions. Autism. 2018;22(5):517-27.

24. Blank R, Barnett AL, Cairney J, Green D, Kirby A, Polatajko H, et al. International clinical practice recommendations on the definition, diagnosis, assessment, intervention, and psychosocial aspects of developmental coordination disorder. Dev Med Child Neurol. 2019;61(3):242-85.

25. National Institute for Health and Care Excellence. Attention deficit hyperactivity disorder: diagnosis and management [Internet]. London: NICE 2018 [updated 2019 Sep 13; cited 2022 Jan 30]. Available from: https://www.nice.org.uk/guidance/ng87.

26. National Institute for Health and Care Excellence. Autism spectrum disorder in under 19s: recognition, referral and diagnosis [Internet]. London: NICE 2011 [updated 2017 Dec 20; cited 2022 Jan 30]. Available from: https://www.nice.org.uk/guidance/cg128.

27. Szejko N, Robinson S, Hartmann A, Ganos C, Debes NM, Skov L, et al. European clinical guidelines for Tourette syndrome and other tic disorders—version 2.0. Part I: assessment. Eur Child Adolesc Psychiatry. 2021;18:1-20.

28. Siegel M, McGuire K, Veenstra-VanderWeele J, Stratigos K, King B, Bellonci C, et al. Practice Parameter for the Assessment and Treatment of Psychiatric Disorders in Children and Adolescents With Intellectual Disability (Intellectual Developmental Disorder). J Am Acad Child Adolesc Psychiatry. 2020;59(4):468-96.

29. Thomas R, Sanders S, Doust J, Beller E, Glasziou P. Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics. 2015;135(4):e994-e1001.

30. Yoshimasu K, Barbaresi WJ, Colligan RC, Voigt RG, Killian JM, Weaver AL, et al. Childhood ADHD is strongly associated with a broad range of psychiatric disorders during adolescence: a population-based birth cohort study: Childhood ADHD adolescent psychiatric comorbidity and gender. J Child Psychol Psychiatry. 2012;53(10):1036-43.

31. Stevens T, Peng L, Barnard-Brak L. The comorbidity of ADHD in children diagnosed with autism spectrum disorder. Res Autism Spectr Disord. 2016;31:11-8.

32. Biederman J, Monuteaux MC, Mick E, Spencer T, Wilens TE, Silva JM, et al. Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. Psychol Med. 2006;36(2):167-79.

33. Biederman J, Petty CR, Woodworth KY, Lomedico A, Hyder LL, Faraone SV. Adult outcome of attention-deficit/hyperactivity disorder: a controlled 16-year follow-up study. J Clin Psychiatry. 2012;73(7):941-50.

34. Dalsgaard S, Mortensen PB, Frydenberg M, Thomsen PH. Long-term criminal outcome of children with attention deficit hyperactivity disorder: Criminality outcome of children with ADHD. Crim Behav Ment Health. 2013;23(2):86-98.

35. Lundström S, Forsman M, Larsson H, Kerekes N, Serlachius E, Långström N, et al. Childhood Neurodevelopmental Disorders and Violent Criminality: A Sibling Control Study. J Autism Dev Disord. 2013;44(11):2707-16.

36. Mannuzza S, Klein RG, Moulton JL. Lifetime criminality among boys with attention deficit hyperactivity disorder: A prospective follow-up study into adulthood using official arrest records. Psychiatry Res. 2007;160(3):237-46.

37. Maulik PK, Mascarenhas MN, Mathers CD, Dua T, Saxena S. Prevalence of intellectual disability: A meta-analysis of population-based studies. Res Dev Disabil. 2011;32(2):419-36.

38. Tonnsen BL, Boan AD, Bradley CC, Charles J, Cohen A, Carpenter LA. Prevalence of Autism spectrum disorders among children with intellectual disability. Am J Intellect Dev Disabil. 2016;121(6):487-500.

39. Dekker MC, Koot HM. DSM-IV Disorders in Children With Borderline to Moderate Intellectual Disability. I: Prevalence and Impact. J Am Acad Child Adolesc Psychiatry. 2003;42(8):915-22.

40. Emerson E, Einfeld S. Emotional and behavioural difficulties in young children with and without developmental delay: a bi-national perspective. J Child Psychol Psychiatry. 2010;51(5):583-93.

41. Reid SM, Meehan EM, Arnup SJ, Reddihough DS. Intellectual disability in cerebral palsy: a population-based retrospective study. Dev Med Child Neurol. 2018;60(7):687-94.

42. Robertson J, Hatton C, Emerson E, Baines S. Prevalence of epilepsy among people with intellectual disabilities: A systematic review. Seizure. 2015;29:46-62.

43. Gillberg C. Essence : om autism, adhd och andra utvecklingsavvikelser. Första utgåvan. Stockholm: Natur & Kultur; 2018.

44. Watemberg N, Waiserberg N, Zuk L, Lerman-Sagie T. Developmental coordination disorder in children with attention-deficit–hyperactivity disorder and physical therapy intervention. Dev Med Child Neurol. 2007;49(12):920-5.

45. Kadesjö B, Gillberg C. Developmental Coordination Disorder in Swedish 7-Year-Old Children. J Am Acad Child Adolesc Psychiatry. 1999;38(7):820-8.

46. Kadesjö B, Gillberg C. Attention deficits and clumsiness in Swedish 7-year-old children. Dev Med Child Neurol. 1998;40(12):796-804.

47. Harrowell I, Hollén L, Lingam R, Emond A. The impact of developmental coordination disorder on educational achievement in secondary school. Res Dev Disabil. 2018;72:13-22.

48. Harrowell I, Hollén L, Lingam R, Emond A. Mental health outcomes of developmental coordination disorder in late adolescence. Dev Med Child Neurol. 2017;59(9):973-9.

49. Sigurdsson E, Van Os J, Fombonne E. Are impaired childhood motor skills a risk factor for adolescent anxiety? Results from the 1958 U.K. birth cohort and the National Child Development Study. Am J Psychiatry. 2002;159(6):1044-6.

50. Khalifa N, von Knorring A-L. Prevalence of tic disorders and Tourette syndrome in a Swedish school population. Dev Med Child Neurol. 2003;45(5):315-9.

51. Rothenberger A, Banaschewski T. Tic disorders. In: Gillberg C, Steinhausen H-C, Harrington R, editors. A Clinician's Handbook of Child and Adolescent Psychiatry. Cambridge: Cambridge University Press; 2006. p. 598-624.

52. Freeman RD, Fast DK, Burd L, Kerbeshian J, Robertson MM, Sandor P. An international perspective on Tourette syndrome: selected findings from 3500 individuals in 22 countries. Dev Med Child Neurol. 2000;42(7):436-47.

53. Nock MK, Kazdin AE, Hiripi E, Kessler RC. Lifetime prevalence, correlates, and persistence of oppositional defiant disorder: results from the National Comorbidity Survey Replication. J Child Psychol Psychiatry. 2007;48(7):703-13.

54. Nock MK, Kazdin AE, Hiripi EVA, Kessler RC. Prevalence, subtypes, and correlates of DSM-IV conduct disorder in the National Comorbidity Survey Replication. Psychol Med. 2006;36(5):699-710.

55. Sacco R, Camilleri N, Umla-Runge K. The prevalence of oppositional defiant disorders among young people in europe: A systematic review and meta-analysis. Eur Psychiatry. 2021;64(1):S639-S40.

56. Sacco R, Camilleri N, Umla-Runge K. The prevalence of conduct disorders among young people in europe: A systematic review and meta-analysis. Eur Psychiatry. 2021;64(1):S637-S8.

57. Kadesjö C, Bruno H, Kadesjö B, Gillberg C. Attention-deficit-hyperactivity disorder with and without oppositional defiant disorder in 3- to 7-year-old children. Dev Med Child Neurol. 2003;45(10):693-9.

58. Biederman J, Petty CR, Dolan C, Hughes S, Mick E, Monuteaux MC, et al. The long-term longitudinal course of oppositional defiant disorder and conduct disorder in ADHD boys: findings from a controlled 10-year prospective longitudinal follow-up study. Psychol Med. 2008;38(7):1027-36.

59. Burke JD, Rowe R, Boylan K. Functional outcomes of child and adolescent oppositional defiant disorder symptoms in young adult men. J Child Psychol Psychiatry. 2014;55(3):264-72.

60. Boylan K, Vaillancourt T, Boyle M, Szatmari P. Comorbidity of internalizing disorders in children with oppositional defiant disorder. Eur Child Adolesc Psychiatry. 2007;16(8):484-94.

61. Goldston DB, Daniel SS, Erkanli A, Reboussin BA, Mayfield A, Frazier PH, et al. Psychiatric Diagnoses as Contemporaneous Risk Factors for Suicide Attempts Among Adolescents and Young Adults: Developmental Changes. J Consult Clin Psychol. 2009;77(2):281-90.

62. Linker J, Gillespie NA, Maes H, Eaves L, Silberg JL. Suicidal Ideation, Depression, and Conduct Disorder in a Sample of Adolescent and Young Adult Twins. Suicide Life Threat Behav. 2012;42(4):426-36.

63. Fawcett EJ, Power H, Fawcett JM. Women Are at Greater Risk of OCD Than Men: A Meta-Analytic Review of OCD Prevalence Worldwide. J Clin Psychiatry. 2020;81(4): 19r13085.

64. Anholt GE, Aderka IM, van Balkom AJ, Smit JH, Schruers K, van der Wee NJ, et al. Age of onset in obsessive–compulsive disorder: admixture analysis with a large sample. Psychol Med. 2014;44(1):185-94.

65. Delorme R, Golmard J-L, Chabane N, Millet B, Krebs M-O, Mouren-Simeoni MC, et al. Admixture analysis of age at onset in obsessive–compulsive disorder. Psychol Med. 2005;35(2):237-43.

66. Galmiche M, Déchelotte P, Lambert G, Tavolacci MP. Prevalence of eating disorders over the 2000-2018 period: a systematic literature review. Am J Clin Nutr. 2019;109(5):1402-13.

67. Karjalainen L, Gillberg C, Råstam M, Wentz E. Eating disorders and eating pathology in young adult and adult patients with ESSENCE. Compr Psychiatry. 2016;66:79-86.

68. Nickel K, Maier S, Endres D, Joos A, Maier V, Tebartz van Elst L, et al. Systematic Review: Overlap Between Eating, Autism Spectrum, and Attention-Deficit/Hyperactivity Disorder. Front Psychiatry. 2019;10:708.

69. Wentz E, Lacey JH, Waller G, Råstam M, Turk J, Gillberg C. Childhood onset neuropsychiatric disorders in adult eating disorder patients. Eur Child Adolesc Psychiatry. 2005;14(8):431-7.

70. Råstam M, Täljemark J, Tajnia A, Lundström S, Gustafsson P, Lichtenstein P, et al. Eating Problems and Overlap with ADHD and Autism Spectrum Disorders in a Nationwide Twin Study of 9- and 12-Year-Old Children. Scientific World Journal, 2013. 2013.

71. Yao S, Kuja-Halkola R, Lu Y, Birgegård A, Yilmaz Z, Coleman J, et al. Associations Between Attention-Deficit/Hyperactivity Disorder and Various Eating Disorders: A Swedish Nationwide Population Study Using Multiple Genetically Informative Approaches. Biol Psychiatry (1969). 2019;86(8):577-86.

72. Crespi BJ. Revisiting Bleuler: relationship between autism and schizophrenia. Br J Psychiatry. 2010;196(6):495.

73. Wolff S. The history of autism. Eur Child Adolesc Psychiatry. 2004;13(4):201-8.

74. Ssucharewa GE, Wolff S. The first account of the syndrome Asperger described? Translation of a paper entitled "Die schizoiden Psychopathien im Kindesalter" by Dr. G.E. Ssucharewa scientific assistant, which appeared in 1926 in the Monatsschrift für Psychiatrie und Neurologie 60:235-261. Eur Child Adolesc Psychiatry. 1996;5(3):119-32.

75. Rosen NE, Lord C, Volkmar FR. The Diagnosis of Autism: From Kanner to DSM-III to DSM-5 and Beyond. J Autism Dev Disord. 2021;51(12):4253-70.

76. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, Third edition - Revised. Washington: Cambridge: American Psychiatric Association; 1987.

77. American Psychiatric Assocation. Diagnostic and statistical manual of mental disorders, Forth edition. Washington, D.C.: American Psychiatric Association; 1994.

78. Lord C, Petkova E, Hus V, Gan W, Lu F, Martin DM, et al. A Multisite Study of the Clinical Diagnosis of Different Autism Spectrum Disorders. Arch Gen Psychiatry. 2012;69(3):306-13.

79. Lotter V. Epidemiology of autistic conditions in young children: 1. Prevalence. Soc Psychiatry. 1966;1(3):124-35.

80. Baird G, Simonoff E, Pickles A, Chandler S, Loucas T, Meldrum D, et al. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). Lancet. 2006;368(9531):210-5.

81. Idring S, Rai D, Dal H, Dalman C, Sturm H, Zander E, et al. Autism spectrum disorders in the Stockholm Youth Cohort: design, prevalence and validity. PLoS One. 2012;7(7):e41280.

82. Fombonne E. Epidemiology of autistic disorder and other pervasive developmental disorders. J Clin Psychiatry. 2005;66 Suppl 10:3-8.

83. Kim YS, Leventhal BL, Koh Y-J, Fombonne E, Laska E, Lim E-C, et al. Prevalence of Autism Spectrum Disorders in a Total Population Sample. Am J Psychiatry. 2011;168(9):904-12.

84. Baron-Cohen S, Scott FJ, Allison C, Williams J, Bolton P, Matthews FE, et al. Prevalence of autism-spectrum conditions: UK school-based population study. Br J Psychiatry. 2009;194(6):500-9.

85. Russell G, Rodgers LR, Ukoumunne OC, Ford T. Prevalence of parent-reported ASD and ADHD in the UK: findings from the Millennium Cohort Study. J Autism Dev Disord. 2014;44(1):31-40.

86. Blumberg SJ, Bramlett MD, Kogan MD, Schieve LA, Jones JR, Lu MC. Changes in prevalence of parent-reported autism spectrum disorder in school-aged U.S. children: 2007 to 2011-2012. Natl Health Stat Report. 2013;20;(65):1-11.

87. Maenner MJ, Shaw KA, Baio J, Washington A, Patrick M, DiRienzo M, et al. Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2016. MMWR Surveill Summ. 2020;69(4):1-12.

88. Saito M, Hirota T, Sakamoto Y, Adachi M, Takahashi M, Osato-Kaneda A, et al. Prevalence and cumulative incidence of autism spectrum disorders and the patterns of co-occurring neurodevelopmental disorders in a total population sample of 5-year-old children. Mol Autism. 2020;11(1):35.

89. Christensen DL, Baio J, Van Naarden Braun K, Bilder D, Charles J, Constantino JN, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. MMWR Surveill Summ. 2016;65(3):1-23.

90. Hansen SN, Schendel DE, Parner ET. Explaining the Increase in the Prevalence of Autism Spectrum Disorders: The Proportion Attributable to Changes in Reporting Practices. JAMA Pediatr. 2014;169(1):56-62.

91. King M, Bearman P. Diagnostic change and the increased prevalence of autism. Int J Epidemiol. 2009;38(5):1224-34.

92. Coo H, Ouellette-Kuntz H, Lloyd JE, Kasmara L, Holden JJ, Lewis ME. Trends in Autism Prevalence: Diagnostic Substitution Revisited. J Autism Dev Disord. 2007;38(6):1036-46.

93. Shattuck PT. The Contribution of Diagnostic Substitution to the Growing Administrative Prevalence of Autism in US Special Education. Pediatrics. 2006;117(4):1028-37.

94. Taylor LJ, Eapen V, Maybery MT, Midford S, Paynter J, Quarmby L, et al. Diagnostic evaluation for autism spectrum disorder: a survey of health professionals in Australia. BMJ open. 2016;6(9):e012517.

95. Skellern C, Schluter P, McDowell M. From complexity to category: Responding to diagnostic uncertainties of autistic spectrum disorders. J Paediatr Child Health. 2005;41(8):407-12.

96. Lundström S, Reichenberg A, Anckarsäter H, Lichtenstein P, Gillberg C. Autism phenotype versus registered diagnosis in Swedish children: prevalence trends over 10 years in general population samples. BMJ. 2015;350:h1961.

97. Arvidsson O, Gillberg C, Lichtenstein P, Lundström S. Secular changes in the symptom level of clinically diagnosed autism. J Child psychol Psychiatry. 2018;59(7):744-51.

98. Taylor MJ, Rosenqvist MA, Larsson H, Gillberg C, D'Onofrio BM, Lichtenstein P, et al. Etiology of Autism Spectrum Disorders and Autistic Traits over Time. JAMA Psychiatry. 2020;77(9):936-43.

99. Loomes R, Hull L, Mandy WPL. What Is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis. J Am Acad Child Adolesc Psychiatry. 2017;56(6):466-74.

100. Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of Autism in a US Metropolitan Area. JAMA. 2003;289(1):49-55.

101. Gillberg C, Steffenburg S, Schaumann H. Is Autism More Common Now than Ten Years Ago? Br J Psychiatry. 1991;158(3):403-9.

102. Wing L. Sex ratios in early childhood autism and related conditions. Psychiatry Res. 1981;5(2):129-37.

103. Scott FJ, Baron-Cohen S, Bolton P, Brayne C. Brief Report Prevalence of Autism Spectrum Conditions in Children Aged 5-11 Years in Cambridgeshire, UK. Autism. 2002;6(3):231-7.

104. Banach R, Thompson A, Szatmari P, Goldberg J, Tuff L, Zwaigenbaum L, et al. Brief Report: Relationship Between Non-verbal IQ and Gender in Autism. J Autism Dev Disord. 2008;39(1):188-93.

105. Gillberg C, Cederlund M, Lamberg K, Zeijlon L. Brief Report: "The Autism Epidemic". The Registered Prevalence of Autism in a Swedish Urban Area. J Autism Dev Disord. 2006;36(3):429-35.

106. Mattila ML, Kielinen M, Linna SL, Jussila K, Ebeling H, Bloigu R, et al. Autism Spectrum Disorders According to DSM-IV-TR and Comparison With DSM-5 Draft Criteria: An Epidemiological Study. J Am Acad Child Adolesc Psychiatry. 2011;50(6):583-92.e11.

107. Baxter AJ, Brugha TS, Erskine HE, Scheurer RW, Vos T, Scott JG. The epidemiology and global burden of autism spectrum disorders. Psychol Med. 2015;45(3):601-13.

108. Reich T, Cloninger CR, Guze SB. The Multifactorial Model of Disease Transmission: I. Description of the Model and its use in Psychiatry. Br J Psychiatry. 1975;127(1):1-10.

109. Tsai LY, Beisler JM. The Development of Sex Differences in Infantile Autism. Br J Psychiatry. 1983;142(4):373-8.

110. Lai MC, Lombardo MV, Auyeung B, Chakrabarti B, Baron-Cohen S. Sex/gender differences and autism: setting the scene for future research. J Am Acad Child Adolesc Psychiatry. 2015;54(1):11-24.

111. Robinson EB, Lichtenstein P, Anckarsäter H, Happe F, Ronald A. Examining and interpreting the female protective effect against autistic behavior. Proceedings of the National Academy of Sciences - PNAS. 2013;110(13):5258-62.

112. Werling DM, Geschwind DH. Recurrence rates provide evidence for sex-differential, familial genetic liability for autism spectrum disorders in multiplex families and twins. Mol Autism. 2015;6:27.

113. Szatmari P, Liu X-Q, Goldberg J, Zwaigenbaum L, Paterson AD, Woodbury-Smith M, et al. Sex differences in repetitive stereotyped behaviors in autism: Implications for genetic liability. Am J Med Genet B Neuropsychiatr Genet. 2012;159B(1):5-12.

114. Jacquemont S, Coe BP, Hersch M, Duyzend MH, Krumm N, Bergmann S, et al. A higher mutational burden in females supports a "female protective model" in neurodevelopmental disorders. Am J Hum Genet. 2014;94(3):415-25.

115. Levy D, Ronemus M, Yamrom B, Lee Y-h, Leotta A, Kendall J, et al. Rare De Novo and Transmitted Copy-Number Variation in Autistic Spectrum Disorders. Neuron. 2011;70(5):886-97.

116. Sanders Stephan J, Ercan-Sencicek AG, Hus V, Luo R, Murtha Michael T, Moreno-De-Luca D, et al. Multiple Recurrent De Novo CNVs, Including Duplications of the 7q11.23 Williams Syndrome Region, Are Strongly Associated with Autism. Neuron. 2011;70(5):863-85.

117. Iossifov I, O'Roak BJ, Sanders SJ, Ronemus M, Krumm N, Levy D, et al. The contribution of de novo coding mutations to autism spectrum disorder. Nature. 2014;515(7526):216-21.

118. Sandin S, Lichtenstein P, Kuja-Halkola R, Larsson H, Hultman CM, Reichenberg A. The Familial Risk of Autism. JAMA. 2014;311(17):1770-7.

119. Messinger DS, Young GS, Webb SJ, Ozonoff S, Bryson SE, Carter A, et al. Early sex differences are not autism-specific: A Baby Siblings Research Consortium (BSRC) study. Mol Autism. 2015;6:32.

120. Ozonoff S, Young GS, Carter A, Messinger D, Yirmiya N, Zwaigenbaum L, et al. Recurrence risk for autism spectrum disorders: a Baby Siblings Research Consortium study. Pediatrics. 2011;128(3):e488-e95.

121. Goin-Kochel RP, Abbacchi A, Constantino JN, Autism Genetic Resource Exchange Consortium. Lack of evidence for increased genetic loading for autism among families of affected females: A replication from family history data in two large samples. Autism. 2007;11(3):279-86.

122. Bai D, Marrus N, Yip BHK, Reichenberg A, Constantino JN, Sandin S. Inherited Risk for Autism Through Maternal and Paternal Lineage. Biol Psychiatry. 2020;88(6):480-7.

123. Baron-Cohen S. The extreme male brain theory of autism. Trends Cogn Sci. 2002;6(6):248-54.

124. Greenberg DM, Warrier V, Allison C, Baron-Cohen S. Testing the Empathizing–Systemizing theory of sex differences and the Extreme Male Brain theory of autism in half a million people. Proc Natl Acad Sci USA. 2018;115(48):12152-57.

125. Auyeung B, Baron-Cohen S, Ashwin E, Knickmeyer R, Taylor K, Hackett G. Fetal testosterone and autistic traits. Br J Psychol. 2009;100(Pt 1):1-22.

126. Auyeung B, Taylor K, Hackett G, Baron-Cohen S. Foetal testosterone and autistic traits in 18 to 24-month-old children. Mol Autism. 2010;1(1):11.

127. Baron-Cohen S, Knickmeyer RC, Belmonte MK. Sex Differences in the Brain: Implications for Explaining Autism. Science. 2005;310(5749):819-23.

128. Chapman E, Baron-Cohen S, Auyeung B, Knickmeyer R, Taylor K, Hackett G. Fetal testosterone and empathy: Evidence from the Empathy Quotient (EQ) and the "Reading the Mind in the Eyes" Test. Soc Neurosci. 2006;1(2):135-48.

129. Nadler A, Camerer CF, Zava DT, Ortiz TL, Watson NV, Carré JM, et al. Does testosterone impair men's cognitive empathy? Evidence from two large-scale randomized controlled trials. Proc Biol Sci. 2019;286(1910):20191062.

130. Halladay AK, Bishop S, Constantino JN, Daniels AM, Koenig K, Palmer K, et al. Sex and gender differences in autism spectrum disorder: summarizing evidence gaps and identifying emerging areas of priority. Mol Autism. 2015;6(1):36.

131. Volkmar FR, Klin A, Siegel B, Szatmari P, Lord C, Campbell M, et al. Field trial for autistic disorder in DSM-IV. Am J Psychiatry. 1994;151(9):1361-7.

132. Begeer S, Mandell S, Wijnker-Holmes B, Venderbosch S, Rem D, Stekelenburg F, et al. Sex differences in the timing of identification among children and adults with autism spectrum disorders. J Autism Dev Disord. 2013;43(5):1151-60.

133. Giarelli E, Wiggins LD, Rice CE, Levy SE, Kirby RS, Pinto-Martin J, et al. Sex differences in the evaluation and diagnosis of autism spectrum disorders among children. Disabil Health J. 2010;3(2):107-16.

134. Petrou AM, Parr JR, McConachie H. Gender differences in parent-reported age at diagnosis of children with autism spectrum disorder. Res Autism Spectr Disord. 2018;50:32-42.

135. Shattuck PT, Durkin M, Maenner M, Newschaffer C, Mandell DS, Wiggins L, et al. Timing of Identification Among Children With an Autism Spectrum Disorder: Findings From a Population-Based Surveillance Study. J Am Acad Child Adolesc Psychiatry. 2009;48(5):474-83.

136. Dworzynski K, Ronald A, Bolton P, Happé F. How Different Are Girls and Boys Above and Below the Diagnostic Threshold for Autism Spectrum Disorders? J Am Acad Child Adolesc Psychiatry. 2012;51(8):788-97.

137. Russell G, Steer C, Golding J. Social and demographic factors that influence the diagnosis of autistic spectrum disorders. Soc Psychiatry Psychiatr Epidemiol. 2010;46(12):1283-93.

138. Duvekot J, van der Ende J, Verhulst FC, Slappendel G, van Daalen E, Maras A, et al. Factors influencing the probability of a diagnosis of autism spectrum disorder in girls versus boys. Autism. 2017;21(6):646-58.

139. Trubanova A, Donlon K, Kreiser NL, Ollendick TH, White SW. Underidentification of Autism Spectrum Disorder in Females: A Case Series Illustrating the Unique Presentation of this Disorder in Young Women. Scand J Child Adolesc Psychiatr Psychol. 2014;2(2):66-76.

140. Kopp S, Gillberg C. Girls with social deficits and learning problems: Autism, atypical Asperger syndrome or a variant of these conditions. Eur Child Adolesc Psychiatry. 1992;1(2):89-99.

141. Goldman S. Opinion: Sex, gender and the diagnosis of autism—A biosocial view of the male preponderance. Res Autism Spectr Disord. 2013;7(6):675-9.

142. Kreiser NL, White SW. ASD in females: are we overstating the gender difference in diagnosis? Clin Child Fam Psychol Rev. 2014;17(1):67-84.

143. Mandy W, Pellicano L, St Pourcain B, Skuse D, Heron J. The development of autistic social traits across childhood and adolescence in males and females. J Child Psychol Psychiatry. 2018;59(11):1143-51.

144. Hiller RM, Young RL, Weber N. Sex Differences in Autism Spectrum Disorder based on DSM-5 Criteria: Evidence from Clinician and Teacher Reporting. J Abnorm Child Psychol. 2014;42(8):1381-93.

145. Tillmann J, Ashwood K, Absoud M, Bölte S, Bonnet-Brilhault F, Buitelaar JK, et al. Evaluating Sex and Age Differences in ADI-R and ADOS Scores in a Large European Multi-site Sample of Individuals with Autism Spectrum Disorder. J Autism Dev Disord. 2018;48(7):2490-505.

146. Wijngaarden-Cremers PJ, van Eeten E, Groen WB, Van Deurzen PA, Oosterling IJ, Van der Gaag RJ. Gender and age differences in the core triad of impairments in autism spectrum disorders: a systematic review and meta-analysis. J Autism Dev Disord. 2014;44(3):627-35.

147. Frazier TW, Georgiades S, Bishop SL, Hardan AY. Behavioral and Cognitive Characteristics of Females and Males With Autism in the Simons Simplex Collection. J Am Acad Child Adolesc Psychiatry. 2014;53(3):329-40.e3.

148. Mandy W, Chilvers R, Chowdhury U, Salter G, Seigal A, Skuse D. Sex Differences in Autism Spectrum Disorder: Evidence from a Large Sample of Children and Adolescents. J Autism Dev Disord. 2012;42(7):1304-13.

149. Charman T, Loth E, Tillmann J, Crawley D, Woolidge C, Goyard D, et al. The EU-AIMS Longitudinal European Autism Project (LEAP): clinical characterisation. Mol Autism. 2017;23(8):27.

150. Wilson CE, Murphy CM, McAlonan G, Robertson DM, Spain D, Hayward H, et al. Does sex influence the diagnostic evaluation of autism spectrum disorder in adults? Autism. 2016;20(7):808-19.

151. Kopp S, Gillberg C. The Autism Spectrum Screening Questionnaire (ASSQ)-Revised Extended Version (ASSQ-REV): an instrument for better capturing the autism phenotype in girls? A preliminary study involving 191 clinical cases and community controls. Res Dev Disabil. 2011;32(6):2875-88.

152. Sutherland R, Hodge A, Bruck S, Costley D, Klieve H. Parent-reported differences between school-aged girls and boys on the autism spectrum. Autism. 2017;21(6):785-94.

153. Lai M-C, Szatmari P. Sex and gender impacts on the behavioural presentation and recognition of autism. Curr Opin Psychiatry. 2020;33(2):117-23.

154. Hull L, Petrides KV, Allison C, Smith P, Baron-Cohen S, Lai M-C, et al. "Putting on My Best Normal": Social Camouflaging in Adults with Autism Spectrum Conditions. J Autism Dev Disord. 2017;47(8):2519-34.

155. Lai MC, Baron-Cohen S. Identifying the lost generation of adults with autism spectrum conditions. Lancet Psychiatry. 2015;2(11):1013-27.

156. Hull L, Lai M-C, Baron-Cohen S, Allison C, Smith P, Petrides KV, et al. Gender differences in self-reported camouflaging in autistic and non-autistic adults. Autism. 2020;24(2):352-63.

157. Lai M-C, Lombardo MV, Ruigrok ANV, Chakrabarti B, Auyeung B, Szatmari P, et al. Quantifying and exploring camouflaging in men and women with autism. Autism. 2017;21(6):690-702.

158. Schuck RK, Flores RE, Fung LK. Brief Report: Sex/Gender Differences in Symptomology and Camouflaging in Adults with Autism Spectrum Disorder. J Autism Dev Disord. 2019;49(6):2597-604.

159. Bargiela S, Steward R, Mandy W. The Experiences of Late-diagnosed Women with Autism Spectrum Conditions: An Investigation of the Female Autism Phenotype. J Autism Dev Disord. 2016;46(10):3281-94.

160. Livingston LA, Shah P, Happé F. Compensatory strategies below the behavioural surface in autism: a qualitative study. Lancet Psychiatry. 2019;6(9):766-77.

161. Cage E, Troxell-Whitman Z. Understanding the Reasons, Contexts and Costs of Camouflaging for Autistic Adults. J Autism Dev Disord. 2019;49(5):1899-911.

162. Cassidy S, Bradley L, Shaw R, Baron-Cohen S. Risk markers for suicidality in autistic adults. Mol Autism. 2018;9(1):42.

163. Fombonne E. Camouflage and autism. J Child Psychol Psychiatry. 2020;61(7):735-8.

164. Glascoe FP. Screening for developmental and behavioral problems. Ment Retard Dev Disabil Res Rev. 2005;11(3):173-9.

165. Aboraya A, France C, Young J, Curci K, Lepage J. The Validity of Psychiatric Diagnosis Revisited: The Clinician's Guide to Improve the Validity of Psychiatric Diagnosis. Psychiatry (Edgmont). 2005;2(9):48-55.

166. World Health Organization. Regional Office for Europe. Screening programmes: a short guide. Increase effectiveness, maximize benefits and minimize harm. Copenhagen: World Health Organization. Regional Office for Europe. 2020.

167. Fisher P, Chin, E., Vidair, H. Use of structured interviews, rating scales, and observational methods in clinical settings. In: Thapar AP, Daniel; Leckam, James; Scott, Stephen; Snowling, Margaret; Taylor, Eric, editor. Rutter's Child and Adolescent Psychiatry. 6 ed. Hoboken: Wiley; 2015.

168. Achenbach TM, McConaughy SH, Howell CT. Child/Adolescent Behavioral and Emotional Problems: Implications of Cross-Informant Correlations for Situational Specificity. Psychol Bull. 1987;101(2):213-32.

169. Posserud MB, Lundervold AJ, Gillberg C. Autistic features in a total population of 7-9-year-old children assessed by the ASSQ (Autism Spectrum Screening Questionnaire). J Child Psychol Psychiatry. 2006;47(2):167-75.

170. Rust J. Modern psychometrics : the science of psychological assessment. Fourth edition. Kosinski M, Stillwell D, editors. Milton Park, Abingdon, Oxon; New York: Routledge; 2021.

171. American Educational Research Association, American Psychological Association, & National Council on Measurement in Education (Eds.). Standards for educational and psychological testing. American Educational Research Association; Washington, DC; 2014.

172. Furr RM. Psychometrics : an introduction. Second edition. Bacharach VR, editor. Los Angeles: Sage Publications; 2014.

173. DeVellis RF. Scale development : theory and applications. Third edition. London: SAGE; 2011.

174. Anckarsäter H, Lundström S, Kollberg L, Kerekes N, Palm C, Carlström E, et al. The Child and Adolescent Twin Study in Sweden (CATSS). Twin Res Hum Genet. 2011;14(6):495-508.

175. Gillberg IC, Gillberg C. Asperger syndrome--some epidemiological considerations: a research note. J Child Psychol Psychiatry. 1989;30(4):631-8.

176. Ehlers S, Gillberg C, Wing L. A screening questionnaire for Asperger syndrome and other high-functioning autism spectrum disorders in school age children. J Autism Dev Disord. 1999;29(2):129-41.

177. Gillberg C, Gillberg C, Råstam M, Wentz E. The Asperger Syndrome (and high-functioning autism) Diagnostic Interview (ASDI): a preliminary study of a new structured clinical interview. Autism. 2001;5(1):57-66.

178. Kadesjö B, Janols LO, Korkman M, Mickelsson K, Strand G, Trillingsgaard A, et al. The FTF (Five to Fifteen): the development of a parent questionnaire for the assessment of ADHD and comorbid conditions. Eur Child Adolesc Psychiatry. 2004;13 Suppl 3:3-13.

179. Hansson SL, Svanstrom Röjvall A, Råstam M, Gillberg C, Gillberg C, Anckarsäter H. Psychiatric telephone interview with parents for screening of childhood autism - tics, attention-deficit hyperactivity disorder and other comorbidities (A-TAC): preliminary reliability and validity. Br J Psychiatry. 2005;187:262-7.

180. Larson T, Anckarsäter H, Gillberg C, Ståhlberg O, Carlström E, Kadesjö B, et al. The autism-tics, AD/HD and other comorbidities inventory (A-TAC): further validation of a telephone interview for epidemiological research. BMC Psychiatry. 2010;10:1.

181. Cubo E, Saez Velasco S, Delgado Benito V, Ausin Villaverde V, Garcia Soto XR, Trejo Gabriel YGJM, et al. [Psychometric attributes of the Spanish version of A-TAC screening scale for autism spectrum disorders]. An Pediatr (Barc). 2011;75(1):40-50.

182. Halleröd SL, Larson T, Ståhlberg O, Carlström E, Gillberg C, Anckarsäter H, et al. The Autism-Tics, AD/HD and other Comorbidities (A-TAC) telephone interview: convergence with the Child Behavior Checklist (CBCL). Nord J Psychiatry. 2010;64(3):218-24.

183. Larson T, Kerekes N, Selinus EN, Lichtenstein P, Gumpert CH, Anckarsäter H, et al. Reliability of Autism-Tics, AD/HD, and other Comorbidities (A-TAC) inventory in a test-retest design. Psychol Rep. 2014;114(1):93-103.

184. Larson T, Lundström S, Nilsson T, Selinus EN, Råstam M, Lichtenstein P, et al. Predictive properties of the A-TAC inventory when screening for childhood-onset neurodevelopmental problems in a population-based sample. BMC Psychiatry. 2013;13:233.

185. Gillberg C. ADHD and DAMP: A General Health Perspective. Child and adolescent mental health. 2003;8(3):106-13.

186. Larson T. A-TAC The Autism-Tics, ADHD and other Comorbidities inventory: studies in reliability and validity [Doctoral thesis]: Lund University; 2013.

187. Kerekes N, Lundström S, Chang Z, Tajnia A, Jern P, Lichtenstein P, et al. Oppositional defiant- and conduct disorder-like problems: neurodevelopmental predictors and genetic background in boys and girls, in a nationwide twin study. PeerJ (San Francisco, CA). 2014;2:e359-e.

188. Preti A, Girolamo Gd, Vilagut G, Alonso J, Graaf Rd, Bruffaerts R, et al. The epidemiology of eating disorders in six European countries: Results of the ESEMeD-WMH project. J Psychiatr Res. 2009;43(14):1125-32.

189. Robins DL, Fein D, Barton ML, Green JA. The Modified Checklist for Autism in Toddlers: an initial study investigating the early detection of autism and pervasive developmental disorders. J Autism Dev Disord. 2001;31(2):131-44.

190. Rutter M, Bailey A, Lord C. The Social Communication Questionnaire. Los Angeles: Western Psychological Services; 2003.

191. Constantino J, Gruber J. Social Responsiveness Scale (SRS) Manual, . Los Angeles: Western Psychological Services; 2005.

192. Kamio Y, Inada N, Moriwaki A, Kuroda M, Koyama T, Tsujii H, et al. Quantitative autistic traits ascertained in a national survey of 22 529 Japanese schoolchildren. Acta Psychiatr Scand. 2013;128(1):45-53.

193. Ryland H, Hysing M, Posserud M-B, Gillberg C, Lundervold A. Autistic features in school age children: IQ and gender effects in a population-based cohort. Res Autism Spectr Disord. 2014;8:266–74.

194. Evans SC, Boan AD, Bradley C, Carpenter LA. Sex/Gender Differences in Screening for Autism Spectrum Disorder: Implications for Evidence-Based Assessment. J Clin Child Adolesc Psychol. 2019;48(6):840-54.

195. Williams JG, Allison C, Scott FJ, Bolton PF, Baron-Cohen S, Matthews FE, et al. The Childhood Autism Spectrum Test (CAST): sex differences. J Autism Dev Disord. 2008;38(9):1731-9.

196. Ratto AB, Kenworthy L, Yerys BE, Bascom J, Wieckowski AT, White SW, et al. What About the Girls? Sex-Based Differences in Autistic Traits and Adaptive Skills. J Autism Dev Disord. 2018;48(5):1698-711.

197. Lai M-C, Lombardo MV, Pasco G, Ruigrok ANV, Wheelwright SJ, Sadek SA, et al. A behavioral comparison of male and female adults with high functioning autism spectrum conditions. PLoS One. 2011;6(6):e20835-e.

198. Rynkiewicz A, Schuller B, Marchi E, Piana S, Camurri A, Lassalle A, et al. An investigation of the 'female camouflage effect' in autism using a computerized ADOS-2 and a test of sex/gender differences. Mol Autism. 2016;7(1):10.

199. Karolinska Institutet. The Child and Adolescent Twin Study in Sweden (CATSS) [Internet]. Stockholm: Karolinska institutet 2021 [updated 2021; cited 2021 Okt 23]. Available from: https://ki.se/en/meb/the-child-and-adolescent-twin-study-in-sweden-catss.

200. Socialstyrelsen. Patientregistret [Internet]. Stockholm: Socialstyrelsen 2018 [updated 2021; cited 2021 Okt 23]. Available from: https://www.socialstyrelsen.se/statistik-och-data/register/alla-register/patientregistret/.

201. Sköldin K. Information om Patientregistret, regsiterår 2019, version 3 [Internet]. Stockholm: Socialstyrelsen 2020. [updated 2020; cited 2021 Okt 23]. Available from: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/dokument-webb/statistik/information-for-patientregistret-registerar-2019.pdf.

202. Rück C, Larsson KJ, Lind K, Perez-Vigil A, Isomura K, Sariaslan A, et al. Validity and reliability of chronic tic disorder and obsessive-compulsive disorder diagnoses in the Swedish National Patient Register. BMJ Open. 2015;5(6):e007520.

203. Vilaplana-Perez A, Isung J, Krig S, Vigerland S, Jolstedt M, Bjureberg J, et al. Validity and reliability of social anxiety disorder diagnoses in the Swedish National Patient Register. BMC Psychiatry. 2020;20(1):242.

204. Sellgren C, Landén M, Lichtenstein P, Hultman CM, Långström N. Validity of bipolar disorder hospital discharge diagnoses: file review and multiple register linkage in Sweden: Validity of register-based bipolar disorder. Acta Psychiatr Scand. 2011;124(6):447-53.

205. Kouppis E, Ekselius L. Validity of the personality disorder diagnosis in the Swedish National Patient Register. Acta Psychiatr Scand. 2020;141(5):432-8.

206. Ekholm B, Ekholm A, Adolfsson R, Vares M, Ösby U, Sedvall GC, et al. Evaluation of diagnostic procedures in Swedish patients with schizophrenia and related psychoses. Nordic journal of psychiatry. 2005;59(6):457-64.

207. Lichtenstein P, Björk C, Hultman CM, Scolnick E, Sklar P, Sullivan PF. Recurrence risks for schizophrenia in a Swedish National Cohort. Psychol Med. 2006;36(10):1417-25.

208. World Health Organization. ICD-9: The International classification of diseases: ninth revision. Washington, D.C: World Health Organization 1980.

209. World Health Organization. ICD-10: International statistical classification of diseases and related health problems: tenth revision. Geneva: World Health Organization; 1992.

210. Gillberg Neuropsychiatry Centre. A-TAC screening questionnaire [Internet]. Göteborg: Gillberg Neuropsychiatry Centre 2020. [updated 2020; cited 2021 Okt 4]. Available from: https://www.gu.se/en/gnc/gncs-resources/screening-questionnaires/a-tac-screening-questionnaire.

211. Mårland C, Lichtenstein P, Degl'Innocenti A, Larson T, Råstam M, Anckarsäter H, et al. The Autism–Tics, ADHD and other Comorbidities inventory (A–TAC): previous and predictive validity. BMC Psychiatry. 2017;17(1):403.

212. Streiner DL. Diagnosing Tests: Using and Misusing Diagnostic and Screening Tests. J Pers Assess. 2003;81(3):209-19.

213. Streiner DL, Cairney J. What's under the ROC? An Introduction to Receiver Operating Characteristics Curves. Can J Psychiatry. 2007;52(2):121-8.

214. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982;143(1):29-36.

215. Tape T. Interprenting diagnostic tests [Internet]. [cited 2021 Okt 10]. Available from: http://darwin.unmc.edu/dxtests.

216. Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PMM. The diagnostic odds ratio: a single indicator of test performance. J Clin Epidemiol. 2003;56(11):1129-35.

217. Field A. Discovering statistics using IBM SPSS statistics: forth edition. London: Sage: 2013.

218. Reise SP, Waller NG. Item response theory and clinical measurement. Annu Rev Clin Psychol. 2009;5(1):27-48.

219. Thomas ML. The Value of Item Response Theory in Clinical Assessment: A Review. Assessment. 2011;18(3):291-307.

220. DeMars C. Item Information Function. Frey BB, editor. The SAGE Encyclopedia of Educational Research, Measurement, and Evaluation: SAGE Publications; 2018.

221. Carlson JE. Introduction to item response theory models and applications. London: Routledge; 2020.

222. Edelen MO, Reeve BB. Applying Item Response Theory (IRT) Modeling to Questionnaire Development, Evaluation, and Refinement. Qual Life Res. 2007;16(S1):5-18.

223. Osterlind SJ, Everson HT. Differential Item Functioning. Los Angeles: SAGE Publications; 2009.

224. Raykov T, Marcoulides GA. A course in item response theory and modeling with Stata. Texas: Stata Press; 2018.

225. Raftery AE. Bayesian Model Selection in Social Research. Sociol Methodol. 1995;25:111-63.

226. Mårland C, Lubke G, Degl'Innocenti A, Råstam M, Gillberg C, Nilsson T, et al. The development of a brief screener for autism using item response theory. BMC Psychiatry. 2019;19(1):337.

227. Lijster J, Dierckx B, Utens E, Verhulst F, Zieldorff C, Dieleman G, et al. The age of onset of anxiety disorders: A meta-analysis. Can J Psychiatry. 2017;62(4):237-46.

228. American Academy of Pediatrics. Identifying Infants and Young Children With Developmental Disorders in the Medical Home: An Algorithm for Developmental Surveillance and Screening. Pediatrics. 2006;118(1):405-20.

229. Volkmar F, Siegel M, Woodbury-Smith M, King B, McCracken J, State M. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Autism Spectrum Disorder. J Am Acad Child Adolesc Psychiatry. 2014;53(2):237-57.

230. Gabrielsen TP, Farley M, Speer L, Villalobos M, Baker CN, Miller J. Identifying autism in a brief observation. Pediatrics. 2015;135(2):e330-e8.

231. Miller JS, Gabrielsen T, Villalobos M, Alleman R, Wahmhoff N, Carbone PS, et al. The Each Child Study: Systematic Screening for Autism Spectrum Disorders in a Pediatric Setting. Pediatrics. 2011;127(5):866-71.

232. Robins DL. Screening for autism spectrum disorders in primary care settings. Autism. 2008;12(5):537-56.

233. Fountain C, King MD, Bearman PS. Age of diagnosis for autism: individual and community factors across 10 birth cohorts. J Epidemiology Community Health. 2011;65(6):503-10.

234. Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. Pediatrics. 2010;125(1):e17-23.

235. Garcia D, Anckarsäter H, Lundström S. Self-Directedness and Cooperativeness, Psychosocial Dysfunction and Suffering in ESSENCE. TheScientificWorld. 2013;2013:416981-10.

236. Constantino JN. The quantitative nature of autistic social impairment. Pediatr Res. 2011;69(5 Pt 2):55R-62R.

237. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The Autism-Spectrum Quotient (AQ): Evidence from asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. J Autism Dev Disord. 2001;31(1):5-17.

238. Constantino JN, Charman T. Gender Bias, Female Resilience, and the Sex Ratio in Autism. J Am Acad Child Adolesc Psychiatry. 2012;51(8):756-8.

239. Kaat AJ, Shui AM, Ghods SS, Farmer CA, Esler AN, Thurm A, et al. Sex differences in scores on standardized measures of autism symptoms: a multisite integrative data analysis. J Child Psychol Psychiatry. 2021;62(1):97-106.

240. Frazier TW, Hardan AY. Equivalence of symptom dimensions in females and males with autism. Autism. 2017;21(6):749-59.

241. Posserud M, Hysing M, Helland W, Gillberg C, Lundervold AJ. Autism traits: The importance of "co-morbid" problems for impairment and contact with services. Data from the Bergen Child Study. Res Dev Disabil. 2018;72:275-83.

242. Gillberg C, Fernell E. Autism Plus Versus Autism Pure. J Autism Dev Disord. 2014;44(12):3274-6.

243. Chiang H-L, Gau SS. Comorbid psychiatric conditions as mediators to predict later social adjustment in youths with autism spectrum disorder. J Child Psychol Psychiatry. 2016;57(1):103-11.

244. Sprenger L, Bühler E, Poustka L, Bach C, Heinzel-Gutenbrunner M, Kamp-Becker I, et al. Impact of ADHD symptoms on autism spectrum disorder symptom severity. Res Dev Disabil. 2013;34(10):3545-52.

245. Lahey BB, Loeber R, Burke J, Rathouz PJ, McBurnett K. Waxing and Waning in Concert: Dynamic Comorbidity of Conduct Disorder With Other Disruptive and Emotional Problems Over 7 Years Among Clinic-Referred Boys. J Abnorm Psychol. 2002;111(4):556-67.

246. Stice E, Ng J, Shaw H. Risk factors and prodromal eating pathology. J Child Psychol Psychiatry. 2010;51(4):518-25.

247. Klein DN, Shankman SA, Lewinsohn PM, Seeley JR. Subthreshold Depressive Disorder in Adolescents: Predictors of Escalation to Full-Syndrome Depressive Disorders. J Am Acad Child Adolesc Psychiatry. 2009;48(7):703-10.

248. Dell'Osso L, Carpita B, Bertelloni CA, Diadema E, Barberi FM, Gesi C, et al. Subthreshold autism spectrum in bipolar disorder: Prevalence and clinical correlates. Psychiatry Res. 2019;281:112605.

249. Greenberg DA, Hodge SE, Sowinski J, Nicoll D. Excess of twins among affected sibling pairs with autism: implications for the etiology of autism. Am J Hum Genet. 2001;69(5):1062-7.

250. Betancur C, Leboyer M, Gillberg C. Increased rate of twins among affected sibling pairs with autism. Am J Hum Genet. 2002;70(5):1381-3.

251. Croen LA, Grether JK, Selvin S. Descriptive epidemiology of autism in a California population: who is at risk? J Autism Dev Disord. 2002;32(3):217-24.

252. Hallmayer J, Glasson EJ, Bower C, Petterson B, Croen L, Grether J, et al. On the twin risk in autism. Am J Hum Genet. 2002;71(4):941-6.

253. Hultman CM, Sparen P, Cnattingius S. Perinatal risk factors for infantile autism. Epidemiology. 2002;13(4):417-23.

254. Hoekstra RA, Bartels M, Verweij CJH, Boomsma DI. Heritability of Autistic Traits in the General Population. Arch Pediatr Adolesc Med. 2007;161(4):372-7.

255. Curran S, Dworzynski K, Happé F, Ronald A, Allison C, Baron-Cohen S, et al. No major effect of twinning on autistic traits. Autism Res. 2011;4(5):377-82.

256. Moilanen I, Linna SL, Ebeling H, Kumpulainen K, Tamminen T, Piha J, et al. Are twins' behavioural/emotional problems different from singletons'? Eur Child Adolesc Psychiatry. 1999;8(S4):S062-S7.

257. Kendler KS, Martin NG, Heath AC, Eaves LJ. Self-report psychiatric symptoms in twins and their nontwin relatives: are twins different? Am J Med Genet. 1995;60(6):588-91.

258. Kendler KS, Pedersen NL, Farahmand BY, Persson PG. The treated incidence of psychotic and affective illness in twins compared with population expectation: a study in the Swedish Twin and Psychiatric Registries. Psychol Med. 1996;26(6):1135-44.

259. Posserud M, Lundervold AJ, Lie SA, Gillberg C. The prevalence of autism spectrum disorders: impact of diagnostic instrument and non-response bias. Soc Psychiatry Psychiatr Epidemiol. 2009;45(3):319-27.

260. Stormark KM, Heiervang E, Heimann M, Lundervold A, Gillberg C. Predicting Nonresponse Bias from Teacher Ratings of Mental Health Problems in Primary School Children. J Abnorm Child Psychol. 2007;36(3):411-9.

261. Kosidou K, Edvin, V., Magnusson, C., Dahlman, C. Autismspektrumtillstånd och ADHD bland barn och unga i Stockholms län: Förekomst i bedolkningen samt vårdsökande under åren 2011 till 2016. Faktablad. Centrum för epidemiologi och samhällsmedicin; 2017.

262. Rødgaard EM, Jensen K, Vergnes JN, Soulières I, Mottron L. Temporal Changes in Effect Sizes of Studies Comparing Individuals With and Without Autism: A Meta-analysis. JAMA Psychiatry. 2019;76(11):1124-1132.

263. van Der Valk JC, van Den Oord EJ, Verhulst FC, Boomsma D. Using Parental Ratings to Study the Etiology of 3-year-old Twins' Problem Behaviors: Different Views or Rater Bias? J Child Psychol Psychiatry. 2001;42(7):921-31.

264. Ronald A, Happé F, Plomin R. A twin study investigating the genetic and environmental aetiologies of parent, teacher and child ratings of autistic-like traits and their overlap. Eur Child Adolesc Psychiatry. 2008;17(8):473-83.

265. Robinson EB, Munir K, Munafò MR, Hughes M, McCormick MC, Koenen KC. Stability of Autistic Traits in the General Population: Further Evidence for a Continuum of Impairment. J Am Acad Child Adolesc Psychiatry. 2011;50(4):376-84.

266. Sztainberg Y, Zoghbi HY. Lessons learned from studying syndromic autism spectrum disorders. Nat Neurosci. 2016;19(11):1408-17.

267. Wester Oxelgren U, Åberg M, Myrelid Å, Annerén G, Westerlund J, Gustafsson J, et al. Autism needs to be considered in children with Down Syndrome. Acta Paediatr. 2019;108(11):2019-26.

268. Percy AK. Rett Syndrome: Exploring the Autism Link. Arch Neurol. 2011;68(8):985-9.

269. Abbeduto L, McDuffie A, Thurman AJ. The fragile X syndrome-autism comorbidity: what do we really know? Front Genet. 2014;5:355.

270. Niklasson L, Rasmussen P, Óskarsdóttir S, Gillberg C. Autism, ADHD, mental retardation and behavior problems in 100 individuals with 22q11 deletion syndrome. Res Dev Disabil. 2009;30(4):763-73.

271. Gipson TT, Poretti A, Thomas EA, Jenkins KT, Desai S, Johnston MV. Autism Phenotypes in Tuberous Sclerosis Complex: Diagnostic and Treatment Considerations. J Child Neurol. 2015;30(14):1871-6.

272. Morris SM, Acosta MT, Garg S, Green J, Huson S, Legius E, et al. Disease Burden and Symptom Structure of Autism in Neurofibromatosis Type 1: A Study of the International NF1-ASD Consortium Team (INFACT). JAMA Psychiatry. 2016;73(12):1276-84.

273. Gershon J. A Meta-Analytic Review of Gender Differences in ADHD. J Atten Disord. 2002;5(3):143-54.

274. Linnsand P, Gillberg C, Nilses Å, Hagberg B, Nygren G. A High Prevalence of Autism Spectrum Disorder in Preschool Children in an Immigrant, Multiethnic Population in Sweden: Challenges for Health Care. J Autism Dev Disord. 2020;51(2):538-49.

275. Stevanovic D, Costanzo F, Fucà E, Valeri G, Vicari S, Robins DL, et al. Measurement invariance of the Childhood Autism Rating Scale (CARS) across six countries. Autism Res. 2021;14(12):2544-54.

276. Mattila M-L, Jussila K, Linna S-L, Kielinen M, Bloigu R, Kuusikko-Gauffin S, et al. Validation of the Finnish Autism Spectrum Screening Questionnaire (ASSQ) for Clinical Settings and Total Population Screening. J Autism Dev Disord. 2012;42(10):2162-80.

APPENDIX: A–TAC FV

A-TAC: FV
Collateral version

This questionnaire is in particular detail focused on a number of abilities and behaviours in children. Every child is different from everybody else. This means that their abilities in various areas as well as their conduct and behaviour vary a great deal.

To gain as complete a picture as possible of your child, we ask you to answer a considerable number of questions.

Children naturally function in different ways at different ages. State your perception of your child's functioning as compared to his or her peers. If your child has had a certain problem or specific characteristic during *any period of life*, answer the question with "yes" even if the problem or characteristic is no longer present.

Name of child/youth: _____

Date of birth/personal identity number: _____

Age: _____ Sex: _____

Date of interview: _____

Informant (the person answering the questions): _____

Informant's relationship to the child/youth (i.e. mother, father, etc): _____

Henrik Anckarsäter Björn Kadesjö
Carina Gillberg Maria Råstam
Christopher Gillberg Ola Ståhlberg

Developed at the Department of Child and Adolescent Psychiatry, University of Gothenburg

English translation: Sheila Allein, Henrik Anckarsäter, Christopher Gillberg, Ola Ståhlberg

A. Motor control		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
1	Does he/she have problems coordinating movements smoothly?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to this question:				
A1	Is he/she clumsy?		☐	☐	☐
A2	Is he/she fumbling?		☐	☐	☐
A3	Does he/she have balance problems?		☐	☐	☐
A4	Does he/she easily stumble and fall?		☐	☐	☐
A5	Have motor problem/characteristic caused significant impairment in school, among age peers or at home?		☐	☐	☐
A6	Does the motor problem/characteristic cause him/her significant suffering?		☐	☐	☐
A7	At what age did the motor problem/characteristic commence?		Age:		
A8	Are they still present?		Yes ☐	No ☐	

B. Perception		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
2	Does he/she seem disturbed by height differences such as in connection with climbing stairs etc.?		☐	☐	☐
3	Does he/she have difficulty judging distance or size?		☐	☐	☐
4	Is he/she oversensitive to touch or by tight clothing?		☐	☐	☐
5	Is he/she particularly sensitive to certain sounds/noise?		☐	☐	☐
6	Is he/she particularly sensitive to certain flavours, smells, or consistencies?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
B1	Does he/she have difficulty comprehending orientation and spatial directions, e.g. turns clothes back to front?		☐	☐	☐
B2	Does he/she often bump into other people?		☐	☐	☐
B3	Does he/she have poor concepts of time?		☐	☐	☐
B4	Does he/she have difficulty imitating other people's movements?		☐	☐	☐
B5	Does he/she have difficulty recognizing people?		☐	☐	☐
B6	Have perception problems/characteristics caused significant impairment in school, among age peers or at home?		☐	☐	☐
B7	Do the perception problems/characteristics cause him/her significant suffering?		☐	☐	☐
B8	At what age did the perception problems/characteristics commence?		Age:		
B9	Are they still present?		Yes ☐	No ☐	

C. Concentration and attention	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
7	Does he/she often fail to pay close attention to details or make careless mistakes in schoolwork, or other activities?	☐	☐	☐
8	Does he/she often have difficulty sustaining attention in tasks or play activities?	☐	☐	☐
9	Does he/she often seem not to listen when spoken to directly?	☐	☐	☐
10	Does he/she often fail to follow instructions and to finish tasks?	☐	☐	☐
11	Does he/she often have difficulty organizing tasks and activities?	☐	☐	☐
12	Does he/she often avoid tasks that require sustained mental effort (such as homework)?	☐	☐	☐
13	Does he/she often lose things?	☐	☐	☐
14	Is he/she often easily distracted or disturbed?	☐	☐	☐
15	Is he/she often forgetful in daily activities?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
C1	Does he/she have difficulty getting started on tasks/activities?	☐	☐	☐
C2	Does he/she have difficulty completing a task/activity?	☐	☐	☐
C3	Have concentration and/or attention problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
C4	Do the concentration and/or attention problems/characteristics cause him/her significant suffering?	☐	☐	☐
C5	At what age did the concentration and/or attention problems/characteristics commence?	Age:		
C6	Are they still present?	Yes ☐ No ☐		

D. Impulsiveness and activity	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
16	Does he/she have difficulties holding his/her hands and feet still or can he/she not stay seated?	☐	☐	☐
17	Does he/she get up and move about in school or in other situations when he/she is supposed to remain seated?	☐	☐	☐
18	Does he/she often run about or climb excessively compared to peers?	☐	☐	☐
19	Does he/she have difficulty playing calmly and quietly?	☐	☐	☐
20	Is he/she often"on the go" or does he/she often act as if "driven by a motor"?	☐	☐	☐
21	Does he/she often talk excessively?	☐	☐	☐
22	Does he/she often blurt out answers before the question has been completed?	☐	☐	☐
23	Does he/she have difficulty awaiting turns?	☐	☐	☐
24	Does he/she often interrupt or intrude on others?	☐	☐	☐
25	Does he/she easily get bored?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
D1	Is he/she unusually intrepid in physically dangerous situations?	☐	☐	☐
D2	Have impulsiveness and/or activity problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
D3	Do the impulsiveness and/or activity problems/characteristics cause him/her significant suffering?	☐	☐	☐
D4	At what age did the impulsiveness and/or activity problems/characteristics commence?	Age:		
D5	Are they still present?	Yes ☐	No ☐	

E. Learning	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
26	Has he/she had more difficulties than expected acquiring reading skills?	☐	☐	☐
27	Is learning slow and laborious?	☐	☐	☐
28	2. Does he/she have difficulties with basic maths?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
E1	Is he/she a slow reader?	☐	☐	☐
E2	Does he/she dislike reading (e.g., avoids reading books)?	☐	☐	☐
E3	Does he/she have difficulties with maths problems given in written form?	☐	☐	☐
E4	Does he/she have difficulties understanding or using abstract terms?	☐	☐	☐
E5	Does he/she have difficulties spelling?	☐	☐	☐
E6	3. Does he/she get special education in school?	☐	☐	☐
E7	Have learning problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
E8	Do the learning problems/characteristics cause him/her significant suffering?	☐	☐	☐
E9	At what age did the learning problems/characteristics commence?	Age:		
E10	Are they still present?	Yes ☐ No ☐		

F. Planning and organizing tasks	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
29	Does he/she have difficulties shifting plan or strategy when this is required?	☐	☐	☐
30	Does he/she find it difficult to keep basic order around him/her?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
F1	Does he/she have difficulties understanding consequences of his/her own actions?	☐	☐	☐
F2	Is he/she dependent and in very much in need of support?	☐	☐	☐
F3	Does he/she find it difficult to take care of his/her personal hygiene and his/her clothes?	☐	☐	☐
F4	Does he/she have difficulties postpone rewards until later and to find the meaning in things that are not immediately rewarding?	☐	☐	☐
F5	Does he/she experience simple, everyday-activities as tiring or energy consuming?	☐	☐	☐
F6	Have planning and organizing problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
F7	Do the planning and organizing problems/characteristics cause him/her significant suffering?	☐	☐	☐
F8	At what age did the planning and organizing problems/characteristics commence?	Age:		
F9	Are they still present?	Yes ☐ No ☐		

G. Memory	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
31	Does he/she have difficulties remembering where he/she put things?	☐	☐	☐
32	Does he/she have difficulties remembering long or multiple-step instructions?	☐	☐	☐
33	Does he/she have difficulties learning rhymes, songs, multiplication tables etc by heart?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
G1	Does he/she have difficulties remembering information about personal data, such as date of birth, home address etc.?	☐	☐	☐
G2	Does he/she have difficulties remembering the names of other people?	☐	☐	☐
G3	Does he/she have difficulties remembering the names of weekdays, months and seasons?	☐	☐	☐
G4	Does he/she have difficulties remembering non-personal facts learned at school (e.g. historic events, chemical formulas etc.)?	☐	☐	☐
G5	Does he/she have difficulties remembering specific situations that have occurred recently, as what has happened during the day or what he/she ate in school?	☐	☐	☐
G6	Does he/she have difficulties remembering events that occurred some time ago, such as what happened on a trip, what Christmas presents he/she got etc.?	☐	☐	☐
G7	Does he/she have difficulties remembering appointments with peers or what home-work he/she has got?	☐	☐	☐
G8	Does he/she have difficulties acquiring new skills, such as rules of new play or games?	☐	☐	☐
G9	Have memory problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
G10	Do the memory problems/characteristics cause him/her significant suffering?	☐	☐	☐
G11	At what age did the memory problems commence?	Age:		
G12	Are they still present?	Yes ☐ No ☐		

H. Language		The essential aspect of each question is whether the problems/characteristics has been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
34	Was his/her language development delayed or doesn't he/she speak at all?		☐	☐	☐
35	Does he/she have difficulties participating in discussions with others?		☐	☐	☐
36	Does he/she like to repeat words and expressions or does he/she use words in a way other people find strange?		☐	☐	☐
37	Has he/she difficulties with pretend play or does he/she imitate considerably less than other children?		☐	☐	☐
38	Does he/she talk in too high a pitch or too quietly?		☐	☐	☐
39	Does he/she have difficulties keeping "on track" when telling other people something?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
H1	Does he/she have difficulties expressing him/herself in whole sentences?		☐	☐	☐
H2	Does he/she speak with a monotonous or strange voice?		☐	☐	☐
H3	Does he/she have difficulties telling about experiences or situations so that the listener understands?		☐	☐	☐
H4	Does he/she have difficulties explaining what he/she wants?		☐	☐	☐
H5	Does he/she have difficulties speaking fluently without any breaks?		☐	☐	☐
H6	Does he/she have difficulties pronouncing complex words?		☐	☐	☐
H7	Does he/she have difficulties verbally explaining emotions?		☐	☐	☐
H8	Does he/she use strange neologisms, old-fashioned words, or too elegant words?		☐	☐	☐
H9	Does he/she speak so rapidly that it is difficult to comprehend what he/she is saying?		☐	☐	☐

H10	Have language problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
H11	Do the language problems/characteristics cause him/her significant suffering?	☐	☐	☐
H12	At what age did the language problems/characteristics commence?	Age:		
H13	Are they still present?	Yes ☐ No ☐		

I. Social interaction	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
40	Does he/she have difficulties expressing emotions and reactions with facial gestures, prosody, or body language?	☐	☐	☐
41	Does he/she exhibit considerable difficulties interacting with peers?	☐	☐	☐
42	Is he/she uninterested in sharing joy, interests, and activities with others?	☐	☐	☐
43	Can he/she only be with other people on his/her terms?	☐	☐	☐
44	Does he/she have difficulties behaving as expected by peers?	☐	☐	☐
45	Do other people easily influence him/her?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
I1	Is he/she self-centred/self-absorbed?	☐	☐	☐
I2	Is he/she perceived by peers as different, odd, or eccentric?	☐	☐	☐
I3	Does he/she have difficulties understanding other people's social cues, e.g., facial expressions, gestures, tone of voice, or body language?	☐	☐	☐
I4	Does he/she have difficulties understanding the feelings of other people?	☐	☐	☐
I5	Does he/she have difficulties showing other people respect?	☐	☐	☐

I6	Does he/she get exaggerated when there are a lot of people around?	☐	☐	☐
I7	Does he/she usually leave in the middle of a conversation, or abruptly change the topic of a conversation?	☐	☐	☐
I8	Does he/she have difficulties realising how to behave in different social situations?	☐	☐	☐
I9	Does he/she inadvertently make a fool of him/herself or does he/she make naïve and embarrassing remarks?	☐	☐	☐
I10	Does he/she often seem to lack common sense?	☐	☐	☐
I11	Does he/she find eye contact difficult?	☐	☐	☐
I12	Does he/she think that relationships are not very important and does he/she prefer to be on his/her own?	☐	☐	☐
I13	Is his/her body language awkward, gauche, clumsy, strange or unusual?	☐	☐	☐
I14	Does he/she have difficulties interpreting other people's gaze intentions?	☐	☐	☐
I15	Is his/her gaze stiff, strange, peculiar, abnormal or odd?	☐	☐	☐
I16	Have social interaction problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
I17	Do the social interaction problems/characteristics cause him/her significant suffering?	☐	☐	☐
I18	At what age did the interaction problems/characteristics commence?	Age:		
I19	Are they still present?	Yes ☐ No ☐		

J. Flexibility	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
46	Does he/she get absorbed by his/her interests in such a way as being repetitive or too intense?	☐	☐	☐
47	Does he/she get absorbed by routines in such a way as to produce problems for himself or for other?	☐	☐	☐
48	Has he/she ever engaged in strange hand movements or walking high on tiptoe when he/she was happy or upset?	☐	☐	☐
49	Does he/she get absorbed by details?	☐	☐	☐
50	Does he/she dislike changes in daily routines?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
J1	Have flexibility problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
J2	Do the flexibility problems/characteristics cause him/her significant suffering?	☐	☐	☐
J3	At what age did the flexibility problems/characteristics commence?	Age:		
J4	Are they still present?	Yes ☐ No ☐		

K. Tics	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
51	Was there ever a time when he/she would make unmotivated sounds such as throat clearing, sneezing, swallowing, barking, or shouting?	☐	☐	☐
52	Was there ever a time when he/she had involuntary movements, tics, twitches or facial grimaces?	☐	☐	☐
53	Does he/she have difficulties keeping quiet, e.g., whistles, hums, mumbles?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
K1	Does he/she use dirty words or language in an exaggerated way?	☐	☐	☐
K2	Have tics problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
K3	Do the tics problems/characteristics cause him/her significant suffering?	☐	☐	☐
K4	At what age did the tics problems/characteristics commence?	Age:		
K5	Are they still present?	Yes ☐ No ☐		

L. Compulsions	The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
54	Does he/she have obsessive/fixed ideas?	☐	☐	☐
55	Does he/she have compulsive behaviours such as washing hands, touch things, control things, repeat things or procedures, arrange or ordering thing, or counting?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
L1	Have compulsion problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
L2	Do the compulsion problems/characteristics cause him/her significant suffering?	☐	☐	☐
L3	At what age did the compulsion problems/characteristics commence?	Age:		
L4	Are they still present?	Yes ☐ No ☐		

M. Feeding		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
56	Has he/she ever failed to gain enough weight for more than a year?		☐	☐	☐
57	Has he/she seemed fearful of gaining weight or growing fat?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
M1	Has he/she dieted hard enough to cause underweight or no weight gain for any length of time?		☐	☐	☐
M2	Has he/she exaggerated physical training or has he/she been excessively interested in his/her appearance?		☐	☐	☐
M3	Girls only: Has she failed to menstruate for at least 3 months due to weight loss?		☐	☐	☐
M4	Has he/she had periods of overeating followed by vomiting?		☐	☐	☐
M5	Has he/she tried to lose weight in spite of already being thin?		☐	☐	☐
M6	Has he/she ever had anorexia nervosa?		☐	☐	☐
M7	Have feeding problems/characteristics caused significant impairment in school, among age peers or at home?		☐	☐	☐
M8	Do the feeding problems/characteristics cause him/her significant suffering?		☐	☐	☐
M9	At what age did the feeding problems/characteristics commence?		Age:		
M10	Are they still present?		Yes ☐ No ☐		

N. Separations		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
58	Has he/she difficulties functioning outside family house?		☐	☐	☐
59	Does he/she often voice fears that family members may die or get hurt?		☐	☐	☐
60	Does he/she have unreasonable fear of being alone?		☐	☐	☐
61	Does he/she have difficulties sleeping if family members are not around?		☐	☐	☐
62	Does he/she complain of recurring headaches, bellyaches, nauseas or vomits after separation from loved ones?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
N1	Does he/she have difficulties going off to school for fear of separation from family?		☐	☐	☐
N2	Does he/she have recurring nightmares about being separated from family?		☐	☐	☐
N3	Does he/she react unusually strong when friendship comes to an end?		☐	☐	☐
N4	Have separation problems/characteristics caused significant impairment in school, among age peers or at home?		☐	☐	☐
N5	Do the separation problems/characteristics cause him/her significant suffering?		☐	☐	☐
N6	At what age did the separation problems/characteristics commence?		Age:		
N7	Are they still present?		Yes ☐ No ☐		

O+P. Opposition/Conduct		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
63	Has there ever been a time when he/she would be angry to the extent that he/she cannot be reached?		☐	☐	☐
64	Does he/she often argue with adults?		☐	☐	☐
65	Does he/she often tease others by deliberately doing things that are perceived as provocative?		☐	☐	☐
66	Is he/she easily offended, or disturbed by others?		☐	☐	☐
67	Is he/she easily teased?		☐	☐	☐
68	Does he/she often lie or cheat?		☐	☐	☐
69	Has he/she ever engaged in shoplifting?		☐	☐	☐
70	Has he/she ever deliberately been physically cruel to anybody?		☐	☐	☐
71	Does he/she often get into fights?		☐	☐	☐
72	Does he/she steal things at home or outside home?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
O1	Does he/she often lose temper?		☐	☐	☐
O2	Does he/she often refuse to follow the instructions of adults?		☐	☐	☐
O3	Is he/she often vindictive or cruel?		☐	☐	☐
O4	Does he/she often treat significant others badly or without respect?		☐	☐	☐
O5	Does he/she often blame others for own mistakes or bad actions?		☐	☐	☐
P1	Does he/she often threaten, harass or humiliate others?		☐	☐	☐
P2	Is he/she cruel to insects?		☐	☐	☐
P3	Is he/she cruel to other animals?		☐	☐	☐
P4	Has he/she ever started a fire?		☐	☐	☐
P5	Has he/she ever sexually abused others?		☐	☐	☐
P6	Has he/she ever been detained by the police?		☐	☐	☐

P7	Has he/she ever used a deadly weapon?	☐	☐	☐
P8	Has he/she ever robbed anyone or unlawfully acquired other people's property?	☐	☐	☐
P9	Has he/she ever purposely destroyed other people's property?	☐	☐	☐
P10	Has he/she ever broken into someone else's home, premises or car?	☐	☐	☐
P11	Is he/she often out late at night without consent (beginning before 13 years of age)?	☐	☐	☐
P12	Has he/she ever ran away from home and stayed away over night at least two times (or one time if it was for an extended period of time)?	☐	☐	☐
P13	Is he/she often absconding (beginning before 13 years of age)?	☐	☐	☐
OP14	Have opposition or conduct problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
OP15	Do the opposition or conduct problems/characteristics cause him/her significant suffering?	☐	☐	☐
OP16	At what age did the opposition or conduct problems/characteristics commence?	Age:		
OP17	Are they still present?	Yes ☐	No ☐	

Q. Anxiety		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
73	Does he/she have panic attacks with sudden fear or anxiety?		☐	☐	☐
74	Does he/she fear leaving home alone, crowds, waiting in line or going on a bus or train?		☐	☐	☐
75	Is he/she particularly nervous or anxious?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:				
Q1	Is he/she extremely shy and reticent?		☐	☐	☐
Q2	Is he/she silent in situations you are not expected to be silent?		☐	☐	☐
Q3	Is there anything he/she fears doing in front of other people, i.e. talking, eating or writing (excludes presentations of reports)?		☐	☐	☐
Q4	Have anxiety problems/characteristics caused significant impairment in school, among age peers or at home?		☐	☐	☐
Q5	Do the anxiety problems/characteristics cause him/her significant suffering?		☐	☐	☐
Q6	At what age did the anxiety problems/characteristics commence?		Age:		
Q7	Are they still present?		Yes ☐ No ☐		

R. Mood		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
76	Does he/she have poor self-confidence?		☐	☐	☐
77	Does he/she often complain about bellyaches, headaches, breathing difficulties or other bodily symptoms?		☐	☐	☐
78	Has he/she had recurrent episodes with extremely high activity level and flight of ideas?		☐	☐	☐

79	Does he/she have recurrent periods of obvious irritability?	☐	☐	☐
80	Does his/her self-confidence very from situation to situation?	☐	☐	☐
	If "Yes" or "Yes, to some extent" to any of these questions:			
R1	Does he/she seem to be unhappy, sad, or depressed?	☐	☐	☐
R2	Does he/she often complain about feelings of loneliness?	☐	☐	☐
R3	Does he/she often express a feeling of being worthless or inferior to other children?	☐	☐	☐
R4	Has there ever been a period when nothing, or almost nothing, could make him/her feel happy?	☐	☐	☐
R5	Has he/she been thinking of or talked about committing suicide?	☐	☐	☐
R6	Has he/she tried to commit suicide	☐	☐	☐
R7	Has he/she often had a feeling of emptiness?	☐	☐	☐
R8	Does he/she feel that his/her qualities and talents are ignored by others?	☐	☐	☐
R9	Have mood problems/characteristics caused significant impairment in school, among age peers or at home?	☐	☐	☐
R10	Do the mood problems/characteristics cause him/her significant suffering?	☐	☐	☐
R11	At what age did the mood problems/characteristics commence?	Age:		
R12	Are they still present?	Yes ☐ No ☐		

S. Concept of reality		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
81	Has he/she ever seen things no one else could see?		☐	☐	☐
	If "Yes" or "Yes, to some extent" to this question:				
S1	Has he/she ever perceived him/herself as traced or haunted by others not this being reality?		☐	☐	☐
S2	Has he/she ever heard voices or sounds, which no one else could hear?		☐	☐	☐
S3	Have problems/characteristics with concept of reality caused significant impairment in school, among age peers or at home?		☐	☐	☐
S4	Do the problems/characteristics with concept of reality cause him/her significant suffering?		☐	☐	☐
S5	At what age did the problems/characteristics with concept of reality commence?		Age:		
S6	Are they still present?		Yes ☐ No ☐		

T. Miscellaneous		The essential aspect of each question is whether the problems/characteristics have been **pronounced compared to peers during any period of life**	Yes	Yes, to some extent	No
82	Does he/she stutter?		☐	☐	☐
83	Is or has she/she been bullied by other children in school?		☐	☐	☐
84	Has he/she been severely overweight?		☐	☐	☐
85	Does he/she often have sleeping problems?		☐	☐	☐
86	Does he/she often have nightmares?		☐	☐	☐
87	Does he/she walk in sleep or have nocturnal attacks when he/she cannot be ”reached” or comforted?		☐	☐	☐
88	Has he/she tried to inflict bodily damage to him-/herself?		☐	☐	☐
89	Has he/she repeatedly tried to inflict bodily damage to him-/herself?		☐	☐	☐
90	Is there anything else he/she fears, i.e. flying, heights, cramped rooms, or certain kind of animals or insects?		☐	☐	☐
91	Has he/she wet him/herself during daytime after the age of 5?		☐	☐	☐
92	Has he/she soiled him/herself on several occasions after the age of 4 except in connection with gastro-intestinal infection?		☐	☐	☐
93	Does he/she smoke?		☐	☐	☐
94	Does he/she use tobacco in other form?		☐	☐	☐
95	Has he/she ever used alcohol?		☐	☐	☐
96.	Has he/she ever had a period after age 5 when he/she only wanted to eat particular types of food?		☐	☐	☐