# Autism in adult psychiatry outpatients

## Prevalence, comorbidity, suicidality and cognition

Johan Nyrenius

Gillberg Neuropsychiatry Centre
Institute of Neuroscience and Physiology
Sahlgrenska Academy, University of Gothenburg

UNIVERSITY OF GOTHENBURG

Gothenburg 2023

Cover illustration: Per Ögren

Autism in adult psychiatry outpatients

johan.nyrenius@gu.se

ISBN 978-91-8069-169-7 (PRINT)
ISBN 978-91-8069-170-3 (PDF)
http://hdl.handle.net/2077/75179

Printed in Borås, Sweden 2023
Printed by Stema Specialtryck AB

*At man, naar det i Sandhed skal lykkes En at føre et Menneske hen til et bestemt Sted, først og fremmest maa passe paa at finde ham der, hvor han er, og begynde der.*

*If one is truly to succeed in leading a person to a specific place, one must first and foremost take care to find him where he is and begin there.*

Søren Kierkegaard

# ABSTRACT

**Background:** Autism Spectrum Disorder (ASD), one of the Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE), is a neurodevelopmental disorder (NDD) characterised by a pattern of deficits in reciprocal social communication and social interaction, and restricted and/or repetitive behaviours (including sensory abnormalities). Under its current DSM-5 definition, ASD occurs worldwide in 1-1.5% of the general population but is more prevalent in clinical populations. The prevalence of ASD in adult psychiatric outpatient services is not known, and adult psychiatric outpatients with ASD are often not examined "holistically".

**Aims:** Examine prevalence of ASD in adult outpatient psychiatry, psychiatric, cognitive and sociodemographic profiles, functional level, suicidality and non-suicidal self-injury (NSSI).

**Methods:** *Studies I, II and III* examined newly referred psychiatric outpatients (N = 90) at a psychiatric outpatient clinic in Helsingborg, Sweden during 2019 and 2020. Patients were screened with the Ritvo Autism Asperger Diagnostic Scale – Revised (RAADS-R) or the abbreviated RAADS-14 Screen, and patients with screening results indicating possible ASD were offered to participate in in-depth clinical assessments by experienced clinicians using well-validated psychometric instruments. In *Study IV* neuropsychological test results were analysed in outpatients (N = 30) who had received clinical diagnoses of ASD at an NDD assessment unit.

**Results:** ASD was diagnosed in 18.9% of newly referred outpatients, with an additional 5.7% showing "subthreshold" symptoms of ASD. Participants with ASD had more psychiatric comorbidity, more NDDs, more anxiety disorders and lower functional level compared to participants without ASD. No differences were found between participants with and without ASD in sociodemographic characteristics. Suicidal thoughts and behaviour, and NSSI, were common among participants with ASD; similar to what has previously been reported among psychiatric outpatients. Substantial deficits in functional level were found, regardless of Intelligence Quotient (IQ) level. Working memory and processing speed explained more than one fifth of the variance in functional level.

**Conclusions:** In summary, the results of this thesis suggest that adult psychiatric services need a substantial increase in knowledge about ASD, and to adjust and adapt protocols and routines to become more "autism-friendly".

**Keywords**: Autism, Adults, Psychiatry, Suicidality, Non-suicidal self-injury, Cognition, Outcomes

ISBN 978-91-8069-169-7 (PRINT)
ISBN 978-91-8069-170-3 (PDF)

# SAMMANFATTNING PÅ SVENSKA

Autismspektrumtillstånd (AST) är livslånga, utvecklingsrelaterade funktionsnedsättningar som karaktäriseras av stora svårigheter i social kommunikation och social ömsesidighet och av repetitiva, begränsade beteenden (och annorlunda reaktioner på sensoriska stimuli). AST förekommer, såsom tillstånden är definierade idag, hos cirka 1-1.5% av befolkningen, men förekommer oftare i olika kliniska grupper. Förekomsten av AST bland vuxna patienter i psykiatrisk öppenvård är inte känd. Gruppen vuxna patienter med AST inom allmänpsykiatrisk öppenvård är inte heller systematiskt undersökt avseende psykiatrisk, sociodemografisk och kognitiv profil, funktionsnivå, suicidalitet och icke-suicidala självskador. Syftet med denna avhandling var att estimera förekomst av AST och att systematiskt undersöka patienter med AST vid den vuxenpsykiatriska öppenvården i Helsingborg.

*Studierna I, II och III* undersökte patienter (N = 90) på nybesök vid vuxenpsykiatrisk öppenvård i Helsingborg under 2019 och 2020 genom en tvåstegsmodell. Patienterna genomgick screening med Ritvo Autism Asperger Diagnostic Scale – Revised (RAADS-R) eller den förkortade RAADS-14 Screen. Patienter som fick screeningresultat indikerande möjligt AST erbjöds att delta i en fördjupad bedömning hos erfarna kliniker som använde väl validerade instrument. Av de patienter som var på nybesök bedömdes 18.9% fylla diagnostiska kriterier för AST och ytterligare 5.7% bedömdes ha påtagliga AST-symptom, men utan att helt uppfylla kriterierna för en AST-diagnos. Två tredjedelar av alla patienter som deltog i screening fick resultat som indikerade möjligt AST. Patienter med AST hade fler samtidigt förekommande psykiatriska diagnoser, lägre funktionsnivå, oftare ångesttillstånd och oftare andra utvecklingsrelaterade funktionsnedsättningar. Sociodemografiska faktorer skilde sig inte mellan patienter med respektive utan AST. Suicidtankar, suicidala beteenden och icke-suicidala självskador var vanligt i AST-gruppen och var jämförbart med vad tidigare studier har rapporterat hos andra patienter i vuxenpsykiatrisk öppenvård. *Studie IV* analyserade neuropsykologiska utredningar av patienter (N = 30) som fått kliniska AST-diagnoser hos ett neuropsykiatriskt utredningsteam. Samtliga deltagare hade kraftigt nedsatt adaptiv funktionsnivå, oavsett begåvningsnivå. Nedsatt arbetsminne och processhastighet förklarade mer än en femtedel av variansen i adaptiv funktionsnivå. Resultaten presenterade i denna avhandling antyder ett stort behov av ökad kompetens om AST inom vuxenpsykiatrisk öppenvård. Att ändra och anpassa interventioner och bemötande till att bli mer ”autismvänligt” inom vuxenpsykiatrin borde få hög prioritet.

# LIST OF PAPERS

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

I. **Nyrenius, J.**, Eberhard, J., Ghaziuddin, M., Gillberg, C., & Billstedt, E. Prevalence of autism spectrum disorders in adult outpatient psychiatry. Journal of Autism and Developmental Disorders, 2022; 52(9): 3769-3779.

II. **Nyrenius, J.**, Eberhard, J., Ghaziuddin, M., Gillberg, C., & Billstedt, E. The "lost generation" in adult psychiatry: psychiatric, neurodevelopmental and sociodemographic characteristics of psychiatric patients with autism diagnosed in adulthood. The British Journal of Psychiatry Open, 2023; in press.

III. **Nyrenius, J.**, Waern, M., Eberhard, J., Ghaziuddin, M., Gillberg, C., & Billstedt, E. Autism spectrum disorders in adult psychiatric outpatients: non-suicidal self-injury, suicidal ideation, and suicide attempts. Submitted, 2023.

IV. **Nyrenius, J.,** & Billstedt, E. The functional impact of cognition in adults with autism spectrum disorders. Nordic Journal of Psychiatry, 2020; 74(3): 220-225.

# CONTENT

# ABBREVIATIONS

| | |
|---|---|
| ABAS-2 | Adaptive Behavior Assessment System, Second Edition |
| ADHD | Attention - Deficit/ Hyperactivity Disorder |
| ADI-R | Autism Diagnostic Interview – Revised |
| ADOS | Autism Diagnostic Observation Schedule |
| ADOS-2 | Autism Diagnostic Observation Schedule – Second Edition |
| ALT | Autistic-Like Trait |
| ANOVA | Analysis of Variance |
| AQ | Autism Spectrum Quotient |
| ASD | Autism Spectrum Disorder |
| ASDI | Asperger Syndrome (and high-functioning autism) Diagnostic Interview |
| AST | Autismspektrumtillstånd |
| AUC | Area Under Curve |
| AUDIT | Alcohol Use Disorder Identification Test |
| BRIEF-A | Behavior Rating Inventory of Executive Function – Adult version |
| CBT | Cognitive Behavioural Therapy |
| COVID-19 | Coronavirus Disease 2019 |
| CP | Cerebral Palsy |
| CWIT | Color-Word Interference Test |
| DISCO | Diagnostic Interview for Social and Communication Disorders |
| D-KEFS | Delis-Kaplan Executive Function System |
| DSM | Diagnostic and Statistical Manual of Mental Disorders |
| DSM-III | Diagnostic and Statistical Manual of Mental Disorders, Third Edition |
| DSM-III-R | Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised |
| DSM-IV | Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition |
| DSM-5 | Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition |
| DUDIT | Drug Use Disorders Identification Test |
| ESSENCE | Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations |
| FASM | Functional Assessment of Self-Mutilation |
| FSIQ | Full-Scale Intelligence Quotient |
| FTF | Five To Fifteen (questionnaire) |
| GABA | Gamma-AminoButyric Acid |
| GAC | General Adaptive Composite |
| GAF | Global Assessment of Functioning |
| ICD-10 | International statistical Classification of Diseases and Related Health Problems, 10$^{th}$ revision |
| ID | Intellectual Disability |
| IQ | Intelligence Quotient |
| LEAD | Longitudinal Expert, All Data |
| M.I.N.I | Mini International Neuropsychiatric Interview |
| NDD | Neurodevelopmental Disorder |
| NSSI | Non-Suicidal Self-Injury |
| OCD | Obsessive-Compulsive Disorder |
| PAU | Psychiatric Assessment Unit |
| PRI | Perceptual Reasoning Index |

| | |
|---|---|
| PDD-NOS | Pervasive Developmental Disorder – Not Otherwise Specified |
| PSI | Processing Speed Index |
| PTSD | Post-Traumatic Stress Disorder |
| RAADS | Ritvo Autism Asperger Diagnostic Scale |
| RAADS-R | Ritvo Autism Asperger Diagnostic Scale – Revised |
| SRS-2 | Social Responsiveness Scale – Second Edition |
| SUD | Substance Use Disorder |
| TMT | Trail Making Test |
| VABS | Vineland Adaptive Behavior Scale |
| VCI | Verbal Comprehension Index |
| VF | Verbal Fluency test |
| WAIS | Wechsler Adult Intelligence Scale |
| WAIS-III | Wechsler Adult Intelligence Scale – Third Edition |
| WAIS-IV | Wechsler Adult Intelligence Scale – Fourth Edition |
| WHODAS 2.0 | World Health Organization Disability Assessment Schedule 2.0 |
| WMI | Working Memory Index |

# 1 INTRODUCTION

Autism, or Autism Spectrum Disorder (ASD), one of the Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Exaaminations (ESSENCE; Gillberg, 2010), is a neurodevelopmental disorder characterised by social deficits and restricted, repetitive behaviours (American Psychiatric Association, 2013). ASD has become a more frequent diagnosis in child and adolescent psychiatric populations during the last few decades. ASD persists into adult age and is associated with increased risk of psychiatric disorders; over 90% of adults with ASD will suffer from at least one psychiatric disorder at some time in their life (Gillberg et al., 2016). Knowledge about ASD in children and adolescents has increased exponentially during the last 40-50 years. However, there are substantial knowledge gaps regarding the profiles and needs of adults with ASD, and even more so regarding adult psychiatric patients with ASD. There is also a lack of consensus regarding the prevalence of ASD in adult psychiatric populations.

The overall focus of this thesis is the knowledge gap regarding adults with ASD attending adult outpatient psychiatric services. Characteristics of this subgroup of adult psychiatric outpatients – not least in terms of prevalence, comorbidity, functional level, cognitive profile and suicidality – are largely unknown or "extrapolated" from the general population of adults with ASD. Most studies reporting about psychiatrically relevant characteristics of adults with ASD have been based on samples drawn from adult populations diagnosed with ASD in childhood. This thesis will instead focus on an ASD group drawn from an adult psychiatric outpatient population, describing ASD in psychiatry rather than psychiatry in ASD.

## 1.1 AUTISM SPECTRUM DISORDER

ASD is a complex neurodevelopmental disability (Joon et al., 2021). As can be seen in the current diagnostic criteria (table 1), the condition is defined by clear and persistent deficits in reciprocal social communication and social interaction, restricted and/or repetitive behaviours (sometimes stereotypic), and sensory hypo- or hyperreactivity (The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5); American Psychiatric Association, 2013). The core diagnostic features need to be evident in the early developmental period, with symptoms typically recognised during the second year of life but may be noted later than 24 months of age in cases with regression or if the symptoms are more subtle (American Psychiatric Association, 2013). The diagnostic criteria of ASD that are currently used in most clinical settings internationally are those of the DSM-5. Criteria from the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) (World Health Organization, 2004) are also widely used. The ICD-10 does not consider autism as a spectrum, but rather different diagnostic entities (autistic disorder, Asperger's syndrome and pervasive developmental disorder – not otherwise specified (PDD-NOS)). Most clinics in Sweden use the DSM-5 criteria for ASD. Autistic-like traits (ALTs) – symptoms of ASD but not to an extent where a diagnosis is warranted – are common in the general population, although at lower levels than in ASD populations (Lundström et al., 2011; Posserud et al., 2006; Ruzich, 2015), illustrated below in figure 1. ASD is widely considered to be a lifelong condition, with reported diagnostic stability rates between 76-97%, at least up to early adult age (Billstedt et al., 2005; Helles et al., 2015; Kočovská et al., 2013). ASD is equally prevalent in adults as in children and adolescents (Brugha, 2011).

*Table 1. Diagnostic criteria from DSM-5 (2013), Autism Spectrum Disorder*

| | |
|---|---|
| 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 stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases). |
| (2) | Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same 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 interests). |
| (4) | Hyper- or hyporeactivity to sensory input or unusual interest 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. |

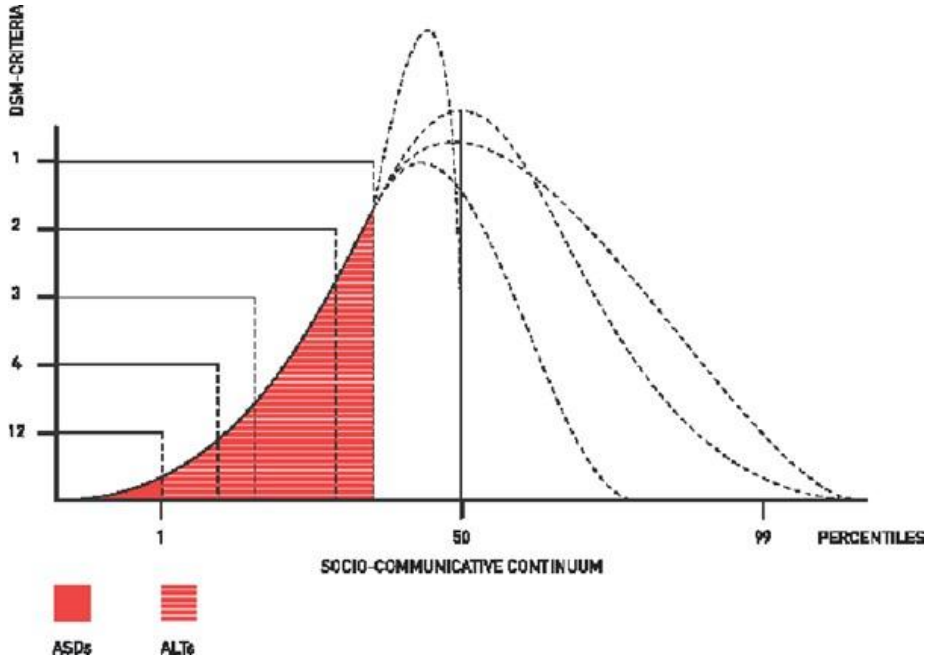


*Figure 1. Distribution of autistic-like traits (ALTs; expressed as diagnostic criteria (A1-A3) according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) in the general population (Lundström, 2011). Reprinted with permission from the author.*

### 1.1.1 ETIOLOGY OF ASD

The causes or underlying variables of ASD are not clearly known. Many erroneous assumptions were made in the past without any scientific evidence; the most harmful of which was perhaps that dysfunctional parenting or vaccines would cause ASD. Current consensus is that ASD has a multifactorial etiology with many different genetic and environmental factors involved. The genetic components or heredity were earlier (at the end of the 20th century) believed to account for almost all cases of ASD (Bailey et al., 1995). The genetic component is still considered to have the strongest impact (Taylor et al., 2020), though the percentage estimates have been adjusted down to explaining around 60-80% of the variance in ASD diagnoses (Gillberg, 2021; Modabbernia et al., 2017). The remaining variance is believed to be explained by many different environmental factors, the foremost being different pre- or perinatal complications including toxins in pregnancy, prematurity, head trauma, ischemia or hypoxia (Modabbernia et al., 2017).

### 1.1.2 STRESS AND VULNERABILITY

The biopsychosocial model (Engel, 1981) is the most widespread, currently used framework for conceptualising psychiatric or mental health problems. The model recognises biological, psychological and social factors as independent causal factors for psychiatric disorders. Recent additions to the model have clarified that conceptualizing illness- and disability-related issues also involve the interaction between the factors; top-down, bottom-up, or within-levels processes (Bolton & Gillett, 2019; Gajwani & Minnis, 2023). Taken together with the vulnerability-stress model (Zubin & Spring, 1977), biopsychosocial conditions form the vulnerability and stress would be the trigger for developing psychiatric symptoms. ASD constitutes a risk factor for a number of different biological, psychological and social risk factors for developing psychiatric disorders. Many somatic conditions are associated with ASD (Muskens et al., 2017), psychological difficulties are commonly reported in ASD (Weiss et al., 2014), and adverse social experiences (such as maltreatment or bullying) are more common in persons with ASD (Maiano et al., 2016; McDonnell et al., 2019). Taken together, persons with ASD face multiple and multi-level risk factors for psychiatric disorders.

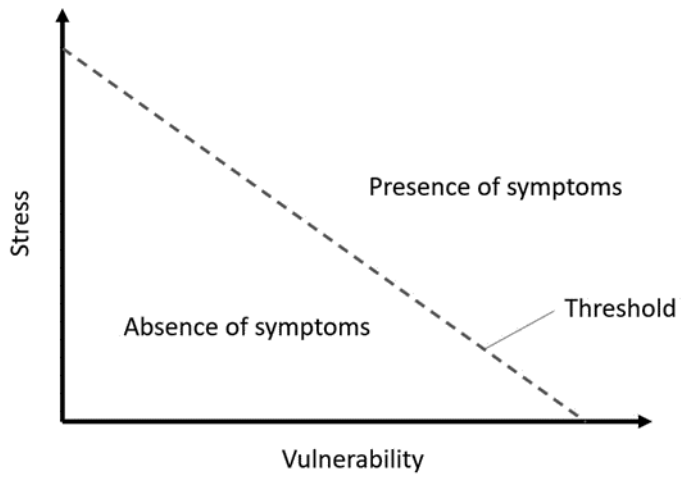


*Figure 2. Depiction of the vulnerability-stress model. A lower degree of vulnerability requires a higher degree of stress to develop symptoms, and vice versa.*

## 1.2 THE DEVELOPMENT OF THE AUTISM CONCEPT

ASD and psychiatric disorders have always been intertwined. Before Kraepelin published his famous textbook (Kraepelin, 1899), classification of the "delusional syndromes" (that later would develop into concepts of for example "dementia praecox", "paranoia", "schizophrenia" and "autism") lacked consensus as psychiatrists at the time tried to include all "delusional" patients, after organic and mood disorders were excluded (Kendler, 2019). Because of the wide inclusion, classification was difficult as it involved a broad and overlapping range of diverse "delusional" syndromes. Many symptoms that later became viewed as important in psychoses were not mentioned during this time, for example emotional blunting, verbigeration or autism.

### 1.2.1 AUTISM BETWEEN THE 1900S AND 1940S

In the early 20th century, after Kraepelin had created his classification system, consensus in the definitions of dementia praecox (and later schizophrenia) was gradually established (Bleuler, 1924; Kendler, 2016). A high grade of similarity in the defining symptoms of schizophrenia can be found between psychiatric experts in the early 20th century and our modern diagnostic system (Kendler, 2016). During this time, Bleuler described the concept of "autism" in schizophrenia as a social withdrawal, lack of interest in what is going on, even "being an inhabitant of another psychological world"; the symptoms or characteristics were in many cases described as not having a dramatic onset and were often quite noticeable already during childhood (Bleuler, 1924). Somewhat later, the shift from diagnostic descriptions to diagnostic criteria (the latter intended as a way of distinguishing between "normal" and "abnormal", rather than being a comprehensive description of a condition) came with Schneider's definition of "first-rank symptoms" of schizophrenia (Kendler & Mishara, 2019). The first-rank symptoms had an emphasis on positive psychotic symptoms (Schneider, 1939) and sparked the transition into a new consensus (established in the 1960s-1970s) of using distinguishing criteria, thereby turning away from descriptions of common (and considered clinically important) diagnostic signs (Kendler, 2019). Common signs of schizophrenia, including "autism", stereotypic movements ("movements/posture"), compulsive behaviours ("automatisms"), echolalia/echopraxia ("verbigeration") and difficulties sharing emotional states ("un-understandability") have since their removal from psychiatric textbooks and diagnostic manuals increasingly been viewed (again) as

clinically important (Kendler, 2016). Many of the symptoms we currently associate with autism were separated from the formal concept of schizophrenia, starting with Schneider in the late 1930s and becoming consensus with operationalised diagnostic criteria somewhere in the 1960s or 70s. In 1925, more than a decade before Leo Kanner and Hans Asperger published their now-famous articles, the symptoms of autism were described in Russian by Grunya Sukhareva (Wolff, 1996) (sometimes transliterated Ssucharewa), a Ukrainian child psychiatrist. Sukhareva's article was published in German in 1926 but remained largely unnoticed until the 1990s.

### 1.2.2 AUTISM BETWEEN THE 1940S AND THE 1970S

Kanner's famous article (Kanner, 1943) describing children with autism was published a few years after Schneider's diagnostic manual, as was Aspergers' definition (Asperger, 1938, 1944) of what would later be known as Asperger's syndrome. Symptoms of autism ("autistic thinking" and "avoidance of close relations with others") were included in the description of schizoid personality disorder, and children presenting with autistic symptoms were still labelled "schizophrenic reaction, childhood type" in the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 1952). Mildred Creak suggested autism to be a clinically distinguishable, congenital syndrome in the early 1950s, and she established a working group that came up with suggested diagnostic criteria in the early 1960s (Creak 1961; 1964). From the 1960s, there was increasing support for autism being a neurobiological disorder and in the early 1970s, Rutter and Kolvin established that autism was something distinct and separated from childhood schizophrenia (Volkmar & McPartland, 2014). Attempts were made to create consensus in diagnostic guidelines for autism in the late 1970s, but autism was not officially recognised as a (developmental rather than a psychiatric) disorder with clear criteria until the third edition of the DSM (DSM-III) (American Psychiatric Association, 1980).

*Table 2. Diagnostic criteria from DSM-III (1980), Infantile Autism (all criteria needed for diagnosis)*

| | |
|---|---|
| A. | Onset before 30 months of age |
| B. | Pervasive lack of responsiveness to other people (autism) |
| C. | Gross deficits in language development |
| D. | If speech is present, peculiar speech patterns such as immediate and delayed echolalia, metaphorical language, pronominal reversal |
| E. | Bizarre responses to various aspects of the environment, e.g., resistance to change, peculiar interest in or attachments to animate or inanimate objects |
| F. | Absence of delusions, hallucinations, loosening of associations, and incoherence as in Schizophrenia |



### 1.2.3 AUTISM BETWEEN THE 1980S AND THE 2010S

The diagnostic criteria in the DSM-III were narrow and inflexible; the definition of autism in the revised version (DSM-III-R) (American Psychiatric Association, 1987) that came a few years later was more flexible and widened the concept of autism (Volkmar & McPartland, 2014; Wolff, 2004). Descriptions of autism and its epidemiology were published around this time (for example Wing and Gould's landmark studies) and contributed to widening of the concept. The next edition of the DSM, the DSM-IV (American Psychiatric Association, 1994), further widened the concept or definition of autism and introduced Asperger's syndrome as a separate diagnosis. Research interest in autism had exploded by this time and major findings had been published and continued to be published by researchers such as Rutter, Gillberg and later Frith and Happé (Wolff, 2004). The idea of autism as a spectrum of disorders was introduced in the early 1990s (Gillberg, 1992) and the current edition of the DSM – the DSM-5 (American Psychiatric Association, 2013) – renamed the condition "Autism Spectrum Disorder".

Increases in the prevalence rate of autism is not only attributable to widening of the concept of autism or changes in diagnostic criteria. Knowledge about autism increased from the early 1980s onwards among professionals in children's services, not least through lectures by autism researchers and -clinicians; the increased knowledge about autism lead to better detection of cases of autism (Gillberg et al., 1991). Development of autism diagnostic

services since the 1980s have increased the availability of professional knowledge about autism, and links between autism and migration over long distances or potential environmental risk factors have been proposed (Coleman & Gillberg, 2012).

*Table 3. Diagnostic criteria from DSM-III-R (1987), Autistic Disorder (at least eight of the sixteen items needed, these to include at least two items from A, one from B and one from C)*

| | |
|---|---|
| A. | Qualitative impairment in reciprocal social interaction |
| 1. | Marked lack of awareness of the existence or feelings of others |
| 2. | No or abnormal seeking of comfort at times of distress |
| 3. | No or impaired imitation |
| 4. | No or abnormal social play |
| 5. | Gross impairment in ability to make peer friendships |
| B. | Qualitative impairment in verbal and nonverbal communication and in imaginative activity |
| 1. | No mode of communication, such as communicative babbling, facial expression, gesture, mime, or spoken language |
| 2. | Markedly abnormal nonverbal communication, as in the use of eye-to-eye gaze, facial expression, body posture, or gestures to initiate or modulate social interaction |
| 3. | Absence of imaginative activity, such as play-acting of adult roles, fantasy character or animals; lack of interest in stories about imaginary events |
| 4. | Marked abnormalities in the production of speech, including volume, pitch, stress, rate, rhythm, and intonation |
| 5. | Marked abnormalities in the form or content of speech, including stereotyped and repetitive use of speech; use of "you" when "I" is meant; idiosynchratic use of words or phrases; or frequent irrelevant remarks |
| 6. | Marked impairment in the ability to initiate or sustain a conversation with others, despite adequate speech |
| C. | Markedly restricted repertoire of activities and interests |
| 1. | Stereotyped body movements |
| 2. | Persistent preoccupation with parts of objects or attachment to unusual objects |
| 3. | Marked distress over changes in trivial aspects of environment |
| 4. | Unreasonable insistence on following routines in precise detail |
| 5. | Markedly restricted range of interests and a preoccupation with one narrow interest, E.G., interested only in lining up objects, in amassing facts about meteorology, or in pretending to be a fantasy character |
| D. | Onset during infancy or early childhood<br>Specify if childhood onset (after 36 months of age) |

*Table 4. Diagnostic criteria from DSM-IV (1994), Autistic Disorder*

| | |
|---|---|
| A. | A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3): |
| 1. | Qualitative impairment in social interaction, as manifested by at least two of the following: |
| (a) | Marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction |
| (b) | Failure to develop peer relationships appropriate to developmental level |
| (c) | A lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest) |
| (d) | Lack of social or emotional reciprocity |
| 2. | Qualitative impairments in communication as manifested by at least one of the following: |
| (a) | Delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime) |
| (b) | In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others |
| (c) | Stereotyped and repetitive use of language or idiosyncratic language |
| (d) | Lack of varied spontaneous make-believe play or social imitative play appropriate to developmental level |
| 3. | Restricted, repetitive, and stereotyped patterns of behavior, interests, and activities, as manifested by at least of one of the following: |
| (a) | Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus |
| (b) | Apparently inflexible adherence to specific, nonfunctional routines or rituals |
| (c) | Stereotyped and repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole body movements) |
| (d) | Persistent preoccupation with parts of objects |
| B. | Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years: (1) social interaction, (2) language as used in social communication, or (3) symbolic or imaginative play. |
| C. | The disturbance is not better accounted for by Rett's disorder or childhood disintegrative disorder. |

### 1.2.4 AUTISM SINCE 2010: INCREASING PREVALENCE

As the concept of autism has been gradually broadened since the emergence of common definitions, the reported prevalence has increased (Gillberg & Wing, 1999). In DSM-5 (introduced 2013), ASD replaced the DSM-IV diagnoses of Autistic Disorder, Asperger's Disorder and Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS). Before the release of DSM-5, it was expected to exclude patients from diagnosis (especially with milder forms of autism), that had met DSM-IV criteria (Volkmar & McPartland, 2014). Some that met DSM-IV definitions (of for example Asperger's syndrome) were excluded from ASD diagnosis according to DSM-5 (Helles et al., 2015), but the new definition of autism proved to contribute to further broadening of the concept of autism, and the prevalence of autism in the general population increased again.

It also seems that the level of symptom severity needed to receive a clinical ASD diagnosis has decreased. For example,the ASD symptom score of a Swedish sample of children between 7-12 years with an ASD diagnosis decreased around 50% between 2004 and 2014 (Arvidsson et al., 2018). In 2016, the percentages of persons between 0-24 years diagnosed with ASD in Stockholm county, Sweden, were higher than population estimates in all sex and age categories except in girls between 0 and 12 years; boys between 13 and 17 years showing a prevalence of 4.1% (Kosidou et al., 2017). Increased awareness of ASD might also have contributed to the increasing prevalence rates. A Faroese total-population study (Kočovská et al., 2013) that collected data at two points in time, separated by seven years, showed a distinct increase in prevalence at T2, principally in females. The new cases at T2 may be a result of increased awareness of ASD in the Faroese community, induced by conducting the study at T1.

Consensus prevalence of autism in the general population today (using the DSM-5 definition) is around 1.0 to 1.5% (Atladottir et al., 2015; Chiarotti & Venerosi, 2020; Zeidan et al., 2022). Compared to prevalence estimates of 4.5/10 000 or 0.045% in the 1960s (Lotter, 1966), the increase is enormous. In summary, the increase is widely seen as deriving from widening of the concept of autism, expansion of the diagnostic criteria, development of services and increased awareness (Fombonne, 2009; King & Bearman, 2009). The prevalence of ASD among adults with normal intelligence or mild Intellectual Disability (ID) has recently been estimated at 1%, with considerably more men than women affected (Brugha et al., 2016).

### 1.2.5 ASD IN ADULT PSYCHIATRIC POPULATIONS

Most studies on ASD in adult psychiatric populations have been published during the past 15 years. The prevalence of ASD in general adult psychiatric populations has not been thoroughly studied. Some prevalence estimates have been published for adult psychiatric subgroups. A review of prevalence estimates for ASD in adult inpatient psychiatry was recently published, finding estimations ranging from 2.4-9.9% and noting substantial differences in methodology between the few (4) studies that were eligible for inclusion (Tromans et al., 2018). In psychiatric outpatient subgroups, ASD prevalence has been estimated at 16% in a population of depressed patients (Takara & Kondo, 2014) and the average prevalence of ASD in eating disorder populations has been reported at 22.9% (Huke et al., 2013). The first study that systematically assessed the prevalence of ASD in broad outpatient psychiatric groups was published in 2001 and estimated the prevalence to be at least 1.4% (Nylander & Gillberg, 2001). The extreme variance in prevalence estimates between different studies might be (at least partly) explained by problems with screening methods for adults (further explained below under "diagnostic procedures and tools for ASD"). In summary, most (of the few) published studies estimate the prevalence of ASD in adult psychiatric populations to be substantially higher than in the general population; even the Nylander & Gillberg study from 2001, whose estimate was almost 50% higher than the consensus ASD prevalence in the general population at the time. This should not surprise anyone as co-occurring psychiatric disorders are very common in the adult ASD population as a whole and it would likely be safe to assume that adults with ASD – as well as adults without ASD – will seek psychiatric care if needed.

## 1.3 CO-OCCURRING CONDITIONS

ASD is associated with many other neurodevelopmental disorders (NDDs) and other medical conditions. Most common are tic disorders, epilepsy, ID, language disorder, motor coordination disorders and psychiatric disorders (Coleman & Gillberg, 2012). Prevalence rates of epilepsy vary with type of ASD, 10-20% has been suggested as prevalence across all types of ASD (Coleman & Gillberg, 2012). Tics occur in around 25% of children and adolescents with ASD (Coleman & Gillberg, 2012); lifetime prevalence of tics (any type) has varied between 11-50% in studies on adults with ASD and normal intelligence (Gillberg et al., 2016; Joshi et al., 2013). The prevalence of ID in ASD populations has gradually decreased over the years (details under "Cognition" below) and is now estimated at around 20%. ASD is common among patients with many different syndromes and disorders, for example Cerebral Palsy (CP), Down syndrome, Fragile X syndrome and tuberous sclerosis; as many as 30-50% of the ASD+ID – group has identifiable genetic disorders (Coleman & Gillberg, 2012; Påhlman et al., 2021). A detailed review of co-occurring psychiatric conditions is presented under a separate heading below. Partially depending on co-occurring conditions, ASD is highly heterogenous and the co-occurring conditions influence the outcomes in ASD more than the ASD in itself (Gillberg & Fernell, 2014).

### 1.3.1 PSYCHIATRIC AND NEURODEVELOPMENTAL CONDITIONS CO-OCCURRING WITH ASD

Psychiatric conditions are reported to be prevalent in adults with ASD; the lifetime prevalence of any psychiatric condition has been estimated to be over 90%, and the point prevalence above 50% (Gillberg et al., 2016). The most common psychiatric disorders / NDDs in this group are Attention-Deficit / Hyperactivity Disorder (ADHD), anxiety disorders and mood disorders. The studies published to date vary greatly in respect of which definition of autism that was used (autistic disorder, Asperger's syndrome and PDD-NOS from the DSM-IV, or ASD from the DSM-5). It should also be stressed that autism could not be diagnosed together with ADHD according to earlier diagnostic manuals. Three recent systematic reviews of psychiatric conditions co-occurring with ASD estimated current anxiety disorders at 20-27% and current depressive or mood disorders at 11-23% (Hollocks et al., 2019; Lai et al., 2019; Lugo-Marín et al., 2019). This is higher than for example in the general population in Sweden, where the prevalence of current depression has been reported at 10.8% and the prevalence of current clinically significant anxiety

has been reported at 14.7% (Johansson et al., 2013). Many studies are follow-up assessments of participants who had been diagnosed in childhood or adolescence (Buck et al., 2014; Gillberg et al., 2016; Lugnegård et al., 2011) and/or show high rates of co-occurring ID (Buck et al., 2014; Fombonne et al., 2020). Reports of co-occurring psychiatric conditions in the wider adult ASD population show considerable heterogeneity, not least due to differences with regard to age, gender, intellectual functioning, and country of study (Lai et al., 2019).

In the adult ASD group with no ID, rates of co-occurring ADHD vary between 28 and 43% (Gillberg et al., 2016; Hofvander et al., 2009; Joshi et al., 2013; Lugnegård et al., 2011), tic disorders have been estimated at 20% in samples of mixed DSM-IV categories of autism (Hofvander et al., 2009). Current depressive disorders have been estimated at up to around 30% while the rates of bipolar and related disorders have varied greatly – between 4-25% (Gillberg et al., 2016; Joshi et al., 2013). Estimations of obsessive-compulsive disorder (OCD) are also inconclusive (varying between 7-24%), showing a clearly lower prevalence in Asperger's syndrome samples (Gillberg et al., 2016; Hofvander et al., 2009; Lugnegård et al., 2011). Eating disorder prevalence has been more coherently estimated at around 5% (Hofvander et al., 2009; Lugnegard et al., 2011). Prevalence for schizophrenia and other psychotic disorders in ASD samples have not been possible to estimate in any reliable way because of difficulties separating psychotic syndromes from ASD (Ghaziuddin & Ghaziuddin, 2020). However, if turning it around – ASD has been reported to be highly prevalent in psychosis populations with estimates of up to 52% (Kincaid et al., 2017). Personality syndromes have seldomly been assessed but seems very common with prevalence estimations between 48 and 62% (Hofvander et al., 2009; Lugnegård et al., 2012). Substance Use Disorder (SUD) prevalence rate varies (0-16%) in cross-sectional studies (Gillberg et al., 2016; Hofvander et al., 2009; Joshi et al., 2013; Lugnegård et al., 2011). Recent register studies have shown up to more than twice the risk of developing an SUD in persons with ASD and co-occurring psychiatric conditions compared to persons without ASD (Huang et al., 2021), and a prevalence of 3.8% for SUD (or diagnoses associated with SUD such as for example alcohol intoxication) (Roux et al., 2022). Post-Traumatic Stress Disorder (PTSD) is one of the least investigated co-occurring psychiatric conditions to ASD and the few studies published to date report 0% (Gillberg et al., 2016) and 5% (Joshi et al., 2013).

Only a handful of studies have been published on psychiatric conditions co-occurring with ASD in adult psychiatric populations (Eberhard et al., 2022; Joshi et al., 2013; Lever & Geurts, 2016; Ryden & Bejerot, 2008). The studies

report mostly differing results; lifetime prevalence of depression varies between 49-77%, ADHD between 30.4-68%, SUDs between 15.9-33%, eating disorders between 5.9-13.2% - but similar results on lifetime prevalence of anxiety disorders (50-60%). The different results could be explained both by different methodology and differences in the samples; the samples varied in gender distribution (54-70% males), mean age (29.2-46.5 years) and distribution of autism diagnoses (DSM-IV autistic disorder 6-65%, Asperger's syndrome 25-61% and PDD-NOS 10-35%). Despite the differences in results, it seems obvious that persons with ASD in adult psychiatric services have a higher lifetime rate of cooccurring psychiatric conditions compared to the entire adult ASD population.

### 1.3.2 SUICIDALITY AND NON-SUICIDAL SELF-INJURY IN ADULTS WITH ASD

Suicide attempts and completed suicides have been proposed to be more common in individuals with ASD compared to the general population. Individuals (of all ages) with ASD without co-occurring ID have been proposed to be at between four- and fourteen-times higher risk (females and those with co-occurring ADHD presenting the higher estimates) of suicide attempts and completed suicides than the general population (Hirvikoski et al., 2020; Hirvikoski et al., 2016). A recent study estimated that possibly 41% of those who died of suicide in two regions of England between 2014 and 2017 had diagnosed autism or possible undiagnosed autism (Cassidy et al., 2022). However, results from prospective, longitudinal long-term follow-up studies of individuals diagnosed with ASD in childhood have not indicated a high rate of suicide, rather the opposite (Billstedt et al., 2005; Gillberg et al., 2015).

Non-suicidal self-injury (NSSI) is defined as injuring oneself without an intent to die. Switching between engaging in self-injury with and without suicidal intent has been shown to be common and associated with future suicidal behaviour in adult psychiatric patients (Waern et al., 2022). A lifetime history of NSSI has been reported in 50% - 73% of adults with ASD (Maddox et al., 2017; Moseley et al., 2022). Both studies were conducted online and relied on self-reported ASD diagnoses. These rates are many times higher than what has been shown in the general adult population, for example in the United States where the lifetime prevalence of NSSI has been estimated at 6% (Klonsky, 2011).

## 1.4 ASD AND COGNITION

ASD is, and has always been, associated with ID (Coleman & Gillberg, 2012; Gillberg, 1984; Rydzewska et al., 2019; Wing & Gould, 1979). With widening of diagnostic criteria over the years, epidemiologic studies have shown a decreased prevalence of ID in ASD populations; from 84.4% in 1966 (Lotter, 1966), to 40-70% around the turn of the millennium (Fombonne, 2003), to 40% in 2015 (Van Naarden Braun et al., 2015), to recent estimations that vary between 13.6 and 23.6% (Rydzewska et al., 2019; Xie et al., 2017).

Cognitive profiles or characteristics in ASD differ greatly across presentation types, comorbidities and age groups. Even within the adult ASD group, a common cognitive profile has proven difficult to define. Most studies have relied on small sample sizes and a wide range of measurement methods have been used across studies, complicating comparisons. Findings are largely inconsistent, but some reviews have been published recently. Adults with ASD show impairments across almost all domains of non-social cognitive functioning, most notably in processing speed, verbal learning, verbal memory, reasoning and problem solving; this seems stable across age groups, genders and countries (Velikonja et al., 2019). When specifically analysing results from Wechsler's Adult Intelligence Tests (WAIS variants), the results look somewhat different. Adults with ASD show better results than the general population on the subtests Similarities, Information and Block Design; impaired results on the subtests Picture Completion and Coding (Kuo & Eack, 2020). Both mentioned studies included a broad definition of ASD, and none considered co-occurring conditions, aside from neurological co-occurring conditions (which were excluded in Velikonja et al., 2019).

There are no easily measurable cognitive factors or deficits that generalise to the entire ASD group. The earlier view of the ASD population as largely homogenous, and not considering comorbid disorders, is (or was) unfortunate. It has recently been proposed that cognitive ability and the behavioural phenotype of autism might be distinct phenomena (Sarovic, 2021). If true, this would imply a need for defining cognitive profiles in clinically relevant subgroups of ASD rather than trying to find a "general" cognitive profile for "the" adult presentation of ASD. In adult psychiatric settings, executive functions are generally seen as the most clinically relevant cognitive factors and are often measured during diagnostic evaluations. Therefore, executive functions were particularly studied in this thesis, aiming to describe a cognitive profile for the study group.

### 1.4.1 EXECUTIVE FUNCTION

Executive functions are prerequisites to successfully handle independent, purposive, self-directed and self-serving behaviour . Impairments in executive functions show up globally, affecting all kinds of behaviour by compromising strategies to identifying goals and approaching, planning and carrying out tasks or monitoring own performance (Lezak et al., 2012). Poorly developed executive functions in individuals with ASD have been suggested by clinical experience, but it is not clear if there are ASD-specific executive function deficits (Coleman & Gillberg, 2012). Children and adolescents with ASD show impairments in working memory, inhibition, planning, organisation, and flexibility (Dawson, 1996; Kenworthy et al., 2008). Slow processing speed has also been shown in children and adolescents with ASD (Linnenbank et al., 2021). In adults with ASD, results from studies this far (though scarce) differ significantly and there are no "universal" executive deficits (Wallace et al., 2016). Executive deficits are associated with poorer outcomes in ASD, and it is possible that the association is stronger in individuals without ID (Coleman & Gillberg, 2012). All studies published regarding executive functions in adults with ASD have been using self- or informant-ratings such as the Behavior Rating Inventory of Executive Functioning – Adult version (BRIEF-A; Roth et al., 2005). No studies on adults with ASD using direct psychometric testing of participants' executive functions were published prior to this thesis.

### 1.4.2 OTHER COGNITIVE THEORIES

#### 1.4.2.1 Joint attention

Deficits in the ability to share focus on the same object as another individual are common in persons with ASD. Most persons with ASD have problems with self-initiated sharing of attention. Early theories of shared attention deficits as a common root of autism have not been supported by the evidence (Coleman & Gillberg, 2012). Deficits in self-initiated shared attention seems to be one of the best predictors of a later ASD diagnosis in children around 10 months of age, though not all children with autism show deficits in shared attention (Coleman & Gillberg, 2012).

#### 1.4.2.2 Theory of mind

Uta Frith, among others, hypothesised that an underlying "core" of autism is deficits or complete inability to understand other peoples' mental states (for example beliefs, intentions, emotions or desires) (Frith, 1989). The theory claims that mental states are not directly observable – but rather something we attribute to ourselves and others. This "theory of mind" – the ability to make such attributions intuitively and most of the time correctly – develops gradually and is probably built on (among other things) joint attention skills (Coleman & Gillberg, 2012). The concept of a "theory of mind" could explain how difficulties in reciprocal social interaction, communication and imagination can co-exist with unaffected memory or visuospatial skills. There is general agreement that young children with ASD have severe problems with "theory of mind" (Coleman & Gillberg, 2012).

#### 1.4.2.3 Central coherence

Individuals with ASD generally seem to have a bias towards a detail-focused information processing, as opposed to processing styles that focus on more global or universal concepts. This processing bias is considered to be robust and not a side effect of executive dysfunction (Coleman & Gillberg, 2012). Older assumptions that this "weak central coherence" (Happe & Frith, 2006) was an underlying "core deficit" in global processing – has been questioned. Though, the phenomenon of detail-focus and difficulties switching from details to universal concepts seem to be robust (Coleman & Gillberg, 2012).

#### 1.4.2.4 Motor skills and perception

ASD is associated with both motor problems and abnormal responses to sensory stimuli (Coleman & Gillberg, 2012). Sensory abnormalities have been introduced as a criterion on its own in the current diagnostic definition of ASD (American Psychiatric Association, 2013). Any role of sensory abnormalities in the cognitive development of individuals with ASD is not clear.

## 1.5 INTERVENTIONS AND TREATMENTS

Per today, there is no available cure or treatment for the core symptoms of ASD. Trials with bumetanide, a diuretic that alters Gamma-AminoButyric Acid (GABA) neurotransmissions and GABA glutamate "balance", are promising and have shown significant reduction in severity of ASD in children and adolescents age 3-18 (Wang et al., 2021). Improvements shown in the few bumetanide trials published so far are substantial, but the trials are short-term (typically 3 months). Bumetanide has also shown positive results on young adults (age up to 28 years), though so far only in small trials (Hadjikhani et al., 2015). Acute administration of oxytocin has been shown to alleviate social difficulties in ASD, but there is very limited evidence of beneficial effects from extended oxytocin treatment (Guastella & Hickie, 2016). The few medications that are currently widely approved for use in ASD (including Risperidone) are not affecting core ASD symptoms.

Most interventions for ASD are psychoeducational (Marcus et al., 1978; Mesibov & Schopler, 1983; Peeters, 1997) and/or aimed at environmental factors, behavioural training and co-occurring conditions. Knowledge about treatment of co-occurring psychiatric conditions in adults with ASD is emerging and there is a severe lack of published studies. In general, interventions aimed at co-occurring psychiatric conditions in ASD should follow the same recommendations as to any other patient, though psychosocial interventions should be adapted for ASD and/or be delivered by staff that are familiar with ASD (National Institute for Health and Care Excellence, 2021; Swedish National Board of Health and Welfare, 2022). Regarding psychotherapy, different Cognitive Behavioural Therapy (CBT) methods are commonly recommended, adapted for ASD. Descriptions of how to adapt CBT for adult persons with ASD are rare and generally limited to the works of a few experts (e.g. Gaus, 2018). Clinical trials of CBT or CBT-related psychotherapies for adults with ASD are generally few and with small samples.

## 1.6 OUTCOME

Functional level (here synonymous with adaptive function, adaptive behaviour and/or activities in daily life) is suboptimal in ASD and has consistently been shown to decline with age, at least up to the early adult years (Chatham et al., 2018; Tillmann et al., 2019). Deficits in functional level are, unlike the cognitive deficits, quite uniform in adults with ASD (Chatham et al., 2018). Functional level is usually examined using a brief clinical assessment such as the General Assessment of Functioning (GAF). Somewhat more thorough assessments with self-rating or interview scales such as the World Health Organization Disability Assessment Scale 2.0 (WHODAS 2.0; Ustun et al., 2010), or comprehensive, highly detailed assessments e.g. the Adaptive Behavior Assessment System – Second Edition (ABAS-2; Harrison & Oakland, 2008) or the Vineland Adaptive Behavior Scales (VABS; Sparrow et al., 2005) are sometimes used. Results regarding causes of the functional level deficits in adults with ASD are inconsistent. Different studies have highlighted or downplayed co-occurring psychiatric conditions, cognitive factors, and the core symptomatology of ASD (Tillmann et al., 2019; Wallace et al., 2016). However, the studies investigating the effects of executive functions on functional level (in adults) are all based on ratings of executive function rather than direct measurements. Children with NDDs in general have recently been suggested to show a different relationship between Intelligence Quotient (IQ) and functional level, where a higher IQ is not (unlike children without NDDs) associated with higher functional level, a pattern that remains at least up to age 15 (Åsberg Johnels et al., 2021). This gap between IQ and functional level has been shown to persist into adult age in individuals with ASD (Kraper et al., 2017).

Common quality of life – associated parameters such as (self-rated) quality of social relationships, subjective well-being, emotional harmony and perceived health, have recently been shown to be lower in adults with ASD when compared to the general population (Graham Holmes et al., 2020). Earlier studies (in which a majority of study participants had co-occurring ID) have shown less favourable outcomes in terms of educational or vocational status, but at the same time a favourable (self-rated) subjective well-being (Billstedt et al., 2011).

Studies on outcomes in terms of levels of social integration and quality of life have produced inconclusive results (due to heterogeneity in the study cohorts and variability in measures), and we are currently far from identifying stable predictors of positive adult outcomes of ASD (Howlin & Magiati, 2017). The very few studies published about outcomes in normal-intelligence adults with

ASD so far show that 40-46% are in work or education, and that 62-72% are living independently (Helles et al., 2017; Roy et al., 2015).

# 1.7 DIAGNOSTICS

Clinical guidelines stress the importance of highly skilled and experienced multi-professional teams performing diagnostic assessment including a medical doctor and a psychologist as a minimum (National Institute for Health and Care Excellence, 2021; Swedish National Board of Health and Welfare, 2022). Other professions (for example speech and language therapists or occupational therapists) are sometimes included in the teams. In Sweden, most diagnostic assessments of ASD and other NDDs are performed in psychiatric settings (child and adolescent psychiatry or adult psychiatry).

## 1.7.1 DIAGNOSTIC PROCEDURES AND TOOLS FOR ASD

Diagnostic assessments of ASD comprise clinical assessment (including assessment of diagnostic criteria for ASD, conditions known to often coexist with ASD and considering differential diagnoses), assessment of developmental and medical (including psychiatric) history and assessment of functional level. Clinical assessments of diagnostic criteria (social reciprocity, social communication and motivation, repetitive / restricted behaviours and sensory hyper/hyporeactivity) for ASD in children are often assisted by autism-specific observational tools, such as the Autism Diagnostic Observation Schedule – Second Edition (ADOS/ADOS-2) (Lord et al., 2012). The ADOS/ADOS-2 is considered an "objective" instrument, assessing only the presence and intensity of symptoms/behaviours without trying to explain them. Assessments of developmental history in children are commonly made via interviews with parents or other close relatives, assisted by psychometric tools such as the Autism Diagnostic Interview – Revised (ADI-R) (Rutter et al., 2003) or the Diagnostic Interview for Social and Communication Disorders (DISCO) (Wing, 2006). These diagnostic tools, used in children, are not as commonly used in adult services.

The validity of the diagnostic tools decreases when used in adults. The ADI-R has overall been reported to show a low sensitivity (43%) but a high specificity (95%) (Fusar-Poli et al., 2017). The ADOS seems more sensitive (usually 80-90%) but less specific (60-90%) than the ADI-R (Wigham et al., 2019); the combination of the ADI-R and the ADOS (commonly considered "gold standard" for assessing ASD in children) in assessing ASD in adults does not seem to be very accurate. Specificity seems to drop further when the diagnostic tools are used in psychiatric populations (Wigham et al., 2019). The DISCO with ASD algorithm has shown good sensitivity (up to 93%) when used in

adults (Kent et al., 2013), but no studies reporting specificity in adults have been published.

Other tools, without established diagnostic cutoff scores, are sometimes used. The Five To Fifteen (FTF) (Kadesjö et al., 2004) is a 180-item parent-rating questionnaire about different aspects of development. The FTF has been proposed to be useful for gathering retrospective information about the developmental history of adults (Hirvikoski et al., 2021). The Asperger syndrome (and high-functioning autism) diagnostic interview (ASDI) (Gillberg et al., 2001) was originally developed for use with the Gillberg & Gillberg criteria for Asperger's syndrome (Gillberg & Gillberg, 1989) but is sometimes used as a structured means of assessing ASD diagnostic criteria in adults.

### 1.7.2 SCREENING TOOLS FOR ASD IN ADULTS

Several psychometric tools for ASD screening to assist in singling out which patients who may need to be referred for a diagnostic assessment have been developed over the years. Most of the screening tools have been developed for children and adolescents and usually rely on parents rating their child's symptoms. Screening tools for adolescents and adults instead rely on self-reporting of thoughts, feelings, behaviours or experiences. Difficulties with theory of mind make self-rating of symptoms problematic and could potentially worsen the validity of self-rating scales for individuals with ASD. Nevertheless, a few psychometric instruments have been developed for ASD screening in adults and show fair psychometric properties. Most notable are the Autism Spectrum Quotient (AQ) (Baron-Cohen et al., 2001), the Ritvo Autism Asperger Diagnostic Scale (RAADS; available as a long (RAADS-Revised) (Ritvo et al., 2011) or short (RAADS-14) (Eriksson et al., 2013) version), and the Social Responsiveness Scale – Second Edition (SRS-2) (Constantino & Gruber, 2012), which is available as both self-rating and informant-rating. Specificity is decreased in all screening tools when used in psychiatric populations; reported sensitivity and specificity of the screening tools in adult general populations and adult psychiatric populations are presented in table 4. It is worth noting that almost all published studies about the accuracy of self-rating questionnaires for ASD in adults in psychiatric populations are case-control studies. Controls have typically been defined as not having a clinical ASD diagnosis assigned in their medical record. Underdiagnosis of ASD in the control groups might explain part of the worsened specificity in psychiatric populations; the so far only published study on the subject using a cohort design (Brugha et al., 2020) reported better

specificity figures in psychiatric populations (for AQ and RAADS-R, see table 5). The instruments available for screening and diagnostics of ASD keep improving and, although still facing obvious problems, makes it increasingly possible and feasible to conduct epidemiological studies on adults with ASD (Brugha et al., 2012).

*Table 5. Reported sensitivity and specificity of the most widely used screening tools for ASD in adults*

| | General populations<br>Sensitivity / Specificity | Psychiatric populations<br>Sensitivity / Specificity |
|---|---|---|
| AQ | 79% / 98%[1]<br>70% / 91%[3] | 79% / 77%[2]<br>71% / 35%[4]<br>AUC > 65%[5] |
| RAADS-R | 97% / 100%[6] | 75% / 71%[7] |
| RAADS-14 | 97% / 95%[8] | 97% / 46-64%[8] |
| SRS-2 | AUC > 87%[9] | SRS: 84% / 81%[10] (males)<br>SRS: 95% / 61%[10] (females) |

AUC = Area Under Curve; AQ = Autism Spectrum Quotient; RAADS-R = Ritvo Autism Asperger Diagnostic Scale [1] (Baron-Cohen et al., 2001) (cutoff score =32) [2] (Brugha et al., 2020) (cutoff score =31) [3] (Booth et al., 2013) (cutoff score = 32) [4] (Ashwood et al., 2016) (cutoff score =32) [5] (Lugnegård et al., 2015) (in a population with schizophrenia) [6] (Ritvo et al., 2011) (cutoff score =65) [7] (Brugha et al., 2020) [8] (Eriksson et al., 2013) (cutoff score =14) [9] (Nishiyama et al., 2014) [10] (Takei et al., 2014)

### 1.7.3 CHALLENGES IN DIAGNOSTIC ASSESSMENTS OF ASD IN ADULTS

The manifest symptoms of ASD in adults (for example repetitive and/or rigid behaviours, difficulties in social interactions, lack of social motivation et cetera) are associated with many (often overlapping) psychiatric disorders and are commonly seen in psychiatric patients in general (Bejerot & Nylander, 2022). In clinical practice, a thorough assessment of developmental and psychiatric history (by experienced clinicians) is widely considered the "gold standard" in differentiating between ASD and other diagnoses. Acquiring an accurate developmental and psychiatric history is complicated by several factors. Parents or other primary caregivers are not always available to supply the information (parents are sometimes deceased, patients sometimes refuse to involve their parents in an assessment because of severe conflicts); most parents or other primary caregivers have considerable difficulties remembering

details – especially from the pre-school period; there is often a discrepancy between patients' and parents' reports; and parents often show ALTs, having own difficulties accounting for their children's developmental and psychiatric history. Though not empirically investigated, these clinical observations might at least partly explain the lower validity of diagnostic tools for ASD in psychiatric adults.

# 2 AIMS

The overall purpose of this thesis was to describe patients with ASD in adult psychiatric outpatient services. The specific aims of the four studies in the thesis were to:

(1) estimate the prevalence of ASD in an adult psychiatric outpatient population (Study I);

(2) investigate psychiatric comorbidity in adult psychiatric outpatients with ASD, and contrast findings with those obtained in adult psychiatric outpatients without ASD (Study II);

(3) estimate degree of and describe suicidal ideation, suicidal behaviour and NSSI in adult psychiatric outpatients with ASD (Study III);

(4) study cognitive factors (IQ and executive function) and their impact on adaptive functioning in adult psychiatric patients with ASD (Study IV).

# 3 MATERIALS AND METHODS

The studies included in this thesis made use of primarily quantitative measures in a naturalistic design. The study population differed between studies I, II and III compared to study IV. The data were a "snapshot" of participants' profiles at a specific moment. In studies I, II and III, that moment was at the time of the participants' first appointments at an adult outpatient psychiatric service. In study IV, it was at the time of clinical neurodevelopmental examinations of the participants.

## 3.1 CONTEXT

The adult psychiatric clinic of Helsingborg, Sweden, is part of the Swedish public healthcare system. The clinic is responsible for providing specialised adult psychiatric services in a catchment area of 10 municipalities in northwestern Skåne county. The catchment area has a total population of approximately 350 000 people, of which 70 000 are age 67 and up, 80 000 are under age 18 and 200 000 are between ages 18 and 66. One private contractor of specialised psychiatric outpatient services is responsible for a geographically defined uptake area consisting of approximately 50 000 out of the 18-66 group.

## 3.2 STUDY I, II AND III

### 3.2.1 PROCEDURE INCLUDING SCREENING

All incoming outpatient referrals to the clinic are assessed at one unit – the Psychiatric Assessment Unit (PAU). Accepted referrals of patients that have had a psychiatric contact within the last six months are sent directly to appropriate psychiatric outpatient units (the different units at the clinic have their own catchment areas and diagnostic areas of responsibility). Patients that have not had any contact with psychiatry for at least six months undergo a first psychiatric assessment at the PAU, meant as triage to determine the urgency of their need for treatment and the nature of treatment required. The exceptions to this are patients referred with well-founded suspicion of a psychotic disorder (about 1% of all new patients, taken care of at psychosis units), patients aged 67 or more (about 7%, taken care of at a special geriatric psychiatry unit), and patients referred for an SUD (about 4%, taken care of at a special SUD unit).

Patients undergoing a first psychiatric assessment at the PAU or the SUD unit during 2019 and 2020 (N = 1030) were screened for ASD. New patients at the geriatric psychiatry unit or at the three psychosis units were not included in the study for practical reasons. Initial difficulties with the screening process resulted in an unsystematic screening between January 1 and October 31 in 2019. Screening was systematic (all patients were offered screening) between November 1, 2019 and December 31, 2020. Screen-positive cases and cases eligible for inclusion as controls were contacted by telephone and offered to participate in an in-depth assessment lasting approximately two hours. The in-depth assessments were made by clinicians with extensive experience in psychiatry and diagnosing ASD in clinical settings. Participating in an in-depth assessment in the study did not affect the study participants' clinical assessments as assignment of research diagnoses were not communicated to the clinic. A follow-up of assigned clinical diagnoses in the participants' psychiatric records was performed in late August and early September, 2021. Visualisation of the study design in figure 3.

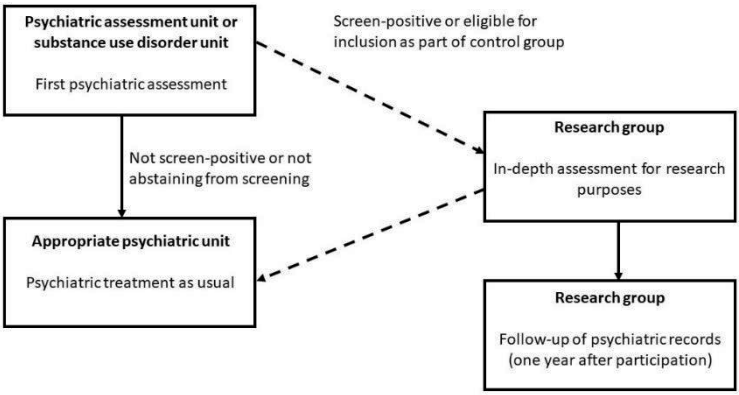


*Figure 3. Flowchart of the study design*

### 3.2.2 PARTICIPANTS

Included screen-positive participants were drawn from the unsystematic screening (January 1 – October 31, 2019, n = 33) and from the systematic screening (November 1, 2019 – December 31, 2020, n = 48). Included participants in the control group were drawn from the systematic screening (November 1, 2019 to December 31, 2020, n = 9). The control group was planned to be an age and gender – matched sample of n = 30, but very few patients met the eligibility criteria (low screening scores) even after an adjustment. To be able to recruit a large enough control group, eligibility criteria would have had to be adjusted to a level where assignment as case or control would have been arbitrary. Of the total 90 participants (cases + controls; 36 males and 54 females), mean age was 31.0 years (SD = 10.5) and age range was 18-65 years. Reasons for being referred to the clinic (with comparisons to all incoming referrals) are presented in table 6.

*Table 6. Primary reason of referral for all incoming referrals 2019 and 2020 (to the PAU and the SUD unit) and for the study participants*

| Primary reason for referral | All incoming referrals (%) | Study participants (%) |
|---|---|---|
| Neurodevelopmental disorder | 35 | 40 |
| Depression / affective disorder | 22 | 23 |
| Anxiety disorder | 9 | 12 |
| Substance or alcohol abuse/addiction | 8 | 2 |
| Not confirmed | 7 | 11 |
| Severe or post-traumatic stress | 5 | 3 |
| Personality disorder | 3 | 1 |
| Eating disorder | 3 | 3 |
| Other[1] | 8 | 5 |

[1]Severe suicidality or suicidal attempt; suspected psychotic disorder; aggression problems; adjustment disorder; crisis; organic disorder; psychosomatic symptoms; relationship problems; self-injury behaviours; sleep disorders.

### 3.2.3 INSTRUMENTS

#### 3.2.3.1 Screening

The self-rating scale RAADS-R (Ritvo et al., 2011) was initially used as screening instrument. The cutoff was set at 50 (the scoring ranges from 0 to 240), which is lower than recommended in clinical applications in Swedish contexts (72) (Andersen et al., 2011). The reason for using a lower cutoff was to increase the possibilities of including subthreshold autism cases. The size of the RAADS-R (80 items) proved to discourage many patients from participating in the screening (and was one reason for initial failures to implement systematic screening). Therefore, screening instrument was changed to the shorter RAADS-14 (Eriksson et al., 2013). The reported poor specificity of the RAADS-14 in psychiatric populations meant no need for lowering cutoff from the clinically recommended 14 (the scoring ranges from 0 to 42). Eligibility for participating as part of the control group was first set at a maximum of 5, later raised to a maximum of 6.

#### 3.2.3.2 Psychiatric conditions and NDDs

Psychiatric conditions (including ADHD) were assessed with the Mini International Neuropsychiatric Interview (M.I.N.I) (Sheehan, 1998), Swedish translation version 7.0.1 with ADHD supplement. Sections B (suicidality), I (alcohol use disorder) and J (substance use disorder) were omitted in order to save time since other instruments were included in the study to evaluate these conditions. The M.I.N.I is considered as a valid diagnostic instrument, widely used in both clinical and research settings, and identifies occurrence of the most common psychiatric disorders according to DSM-5. Core symptoms of ASD were assessed with the ASDI (Gillberg et al., 2001). Research diagnoses of ASD were not assigned based on the ASDI score; the interview was rather used as a structured means of assessing the core symptoms of ASD. Tics were assessed via observations and interviewing the participants according to DSM-5 criteria.

#### 3.2.3.3 Suicidality and self-harming behaviours

Assessment of suicidal thoughts and behaviors were made by the five questions suggested by Paykel (Paykel et al., 1974); (1) “Have you ever felt that life was not worth living?”, (2) “Have you ever wished that you were dead? For instance, that you would go to sleep and not wake up?”, (3) “Have you ever thought of taking your own life, even if you would not really do it?”, (4) “Have you ever reached the point where you seriously considered taking your own life, or perhaps made plans how you would go about doing it?”, (5) “Have you ever made an attempt to take your life?”. The questions were self-rated by the participants with the answering options (0) never, (1) more than one year ago, (2) during the past year, (3) during the past month, (4) during the past week, (5) I don’t want to answer and (6) I don’t know. Participants were asked a screening question about NSSI (“Have you ever done something to hurt yourself, or done something dangerous where you could have died, but without ANY intention to take your life?”) with answer options yes or no; those acknowledging a history of NSSI completed the Functional Assessment of Self-Mutilation (FASM) (Lloyd-Richardson et al., 2007), which is a detailed assessment of NSSI behaviours.

#### 3.2.3.4 Functional level

Functional level was rated as GAF (American Psychiatric Association, 1994). GAF is rated between 0 and 100, where 100 is indicative of a very good level of functioning. Results of 70 and above are generally considered normal.

#### 3.2.3.5 Alcohol and drug consumption

The Alcohol Use Disorder Identification Test (AUDIT) (Saunders et al., 1993) and the Drug Use Disorder Identification Test (DUDIT) (Berman et al., 2005) were used for assessing alcohol and drug consumption, hazardous or harmful alcohol use, and drug-related problems.

#### 3.2.3.6 Cognitive functions

The participants completed three subtests (Symbol Search, Coding and Matrix Reasoning) from the Wechsler Adult Intelligence Scale – fourth edition (WAIS-IV) (Wechsler, 2008). Symbol Search and Coding were used to calculate Processing Speed Index (PSI). Matrix Reasoning and Coding were used to estimate IQ, as they have previously been shown to accurately predict IQ level (Girard et al., 2015).

#### 3.2.3.7 Developmental history

The FTF (Kadesjo et al., 2004) was forwarded by the participants to their parents for completion. The parent received written instructions to answer the FTF as the participants presented at 17 years. This age was chosen to maximize the parents' ability to remember details as the FTF is comprehensive with its 180 items.

#### 3.2.3.8 Sociodemographic variables

The participants completed a questionnaire involving a wide variety of sociodemographic variables, including living arrangements, relations,

educational background, occupational status, economic background and situation, spare time activities and healthcare contacts.

### 3.2.4 DIAGNOSTIC ASSESSMENT AND CLASSIFICATION OF ASD

The diagnostic assessment of ASD was made based on all available data from the in-depth assessment, including the clinical impression of the participant. Research diagnoses were assigned based on DSM-5 criteria. All in-depth assessments and decisions regarding ASD status were carried out by 2 clinical psychologists with extensive clinical team experience diagnosing ASD. A random selection of 5 assessments were validated conjointly with the author and three collaborators from Sweden and the United States (Eva Billstedt, Mohammad Ghaziuddin and Christopher Gillberg), all three extremely senior clinicians and researchers in the field. The conjoint validations were made as Longitudinal Expert discussions using All Data (LEAD) (Kranzler et al., 1994). Total consensus was reached, initial differences arose concerning the severity of the ASD but there were no disagreements about if the subjects met criteria for ASD or not.

## 3.3 STUDY IV

### 3.3.1 PROCEDURE

Study IV used data from clinical neurodevelopmental diagnostic assessments, derived from the participants' medical records. The assessments were performed between 2010 and 2017 at the clinic's specialised NDD assessment team. The team is the expert resource team in matters of NDDs at the same psychiatric clinic as in study I, II and III, and consisted of (at the time of the study) one psychiatrist, two neuropsychologists, one occupational therapist and one social worker, all with long experience of diagnosing NDDs. Between 2010 and 2017, patients from all units at the clinic with suspected NDD were referred to this specialised team for NDD assessment. The assessments consisted of a neuropsychological assessment, a psychiatric evaluation, a functional assessment and a detailed social, developmental and psychiatric history. Diagnoses were assigned by the team, based on LEAD (Kranzler et al., 1994) discussions.

### 3.3.2 PARTICIPANTS

In total, 30 participants (21 males and 9 females; age 18-30 years) were included in the study. All participants were referred to NDD assessment for clinical purposes. The age cap was chosen because of limitations in the instrument chosen for assessing adaptive function (see under Instruments below). There were no differences in age between male and female participants. All participants had received clinical ASD diagnoses according to the ICD-10 (World Health Organization, 2004); autistic disorder (n = 10), atypical autism (n = 10), and Asperger's syndrome (n = 10). Eight of the participants were assigned additional diagnoses of attention disorders; three combined-type ADHD, one inattentive-type ADHD and four attention deficit disorder – not otherwise specified. All participants had co-occurring psychiatric disorders at the time of the assessment. Regarding educational background, 26 had completed 9 years of compulsory school and 10 had also completed upper secondary school/high school. None of the participants worked full-time; 2 worked part-time, 6 were studying and 22 were unemployed with welfare benefits.

### 3.3.3 INSTRUMENTS

#### 3.3.3.1 WAIS

The WAIS scales are the most widely used intelligence scales for adults worldwide. Index scores (M = 100; Sd = 15) are calculated for Full-Scale Intelligence Quotient (FSIQ) and four subscales – Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI) and PSI. WMI and PSI measures aspects of executive function. Two of the participants were assessed with the Wechsler Adult Intelligence Scale – third edition (WAIS-III) (Wechsler, 1997), which has a similar construction as the WAIS-IV. Results from WAIS-III and WAIS-IV are interchangeable as correlations between sub-indexes ranges between r = 0.84 – 0.91 and correlation of FSIQ is r = 0.94 (Wechsler et al., 2008).

#### 3.3.3.2 ABAS-II, parent version

The ABAS-II (Harrison & Oakland, 2008) is an instrument for assessing adaptive behaviour (adaptive function) in persons aged 5-21 years. The instrument is available as a teacher version and a parent version. The ABAS-II has previously been used up to age 56 (Makary et al., 2015). The ABAS-II presents its results as index scores (M = 100, Sd = 15), across the indexes "conceptual domain", "social domain" and "practical domain", together forming a General Adaptive Composite (GAC).

#### 3.3.3.3 Delis-Kaplan Executive Function System (D-KEFS)

The D-KEFS (Delis et al., 2001) is a widely used neuropsychological test battery that measures different executive functions in children and adults. The D-KEFS consists of nine different tests of which four were used in this study. The Trail Making Test (TMT) is a measure of mental flexibility; the participant uses a pen to follow a sequence on paper, quickly switching between numbers and letters. The primary measure is the time needed to complete the sequence, and the time used is then derived into a scaled score with M = 10 and Sd = 3. The Verbal Fluency test (VF) measures three different variants of word-generation; non-overlearned word-generation, abstract word-generation, word-generation while switching categories. The Colour-Word Interference Test (CWIT) is a variant of the classic "Stroop" test (Stroop, 1935), requiring that the participant reads a sheet of colour names printed in the "wrong" colour,

and needs to say the name of the printed colour (thereby inhibiting the overlearned and automatic impulse to read the written text). Primary measures are cognitive flexibility and verbal inhibition, but also naming speed and reading speed. The fourth test used in this study was the Proverb test, where the participant needs to interpret and explain eight different sayings. The participant needs at first to explain the saying freely, and afterwards in a multiple-choice condition. The test measures verbal abstract thinking, semantic integration, and generalization.

## 3.4 ANALYSIS AND STATISTICAL METHODS USED, BY STUDY

All statistical analyses were performed using IBM SPSS. The statistical significance level was set at $p < 0.05$ in all studies.

### 3.4.1 STUDY I

Comparisons of age and sex between screening responders and non-responders were performed; comparisons of other variables involving the non-responders were restricted by ethical permits. Among the screening responders, comparisons were made between the screen-positive and screen-negative groups regarding age, sex and RAADS-14 results. Comparisons were also made between the ASD group, the subthreshold ASD group, the non-ASD group and the screen-positive non-participant group regarding age, sex, RAADS-14 results, ASDI results, IQ estimate and GAF scores. Between-group comparisons of continuous and normally distributed variables were performed using student's t-test and analyses of variance (ANOVA). Comparisons between groups in nominal variables were performed using Chi-square tests, or Fisher's exact test (in 2x2 tables).

### 3.4.2 STUDY II

Because of similarities in degree of autism symptomatology, the ASD group and the subthreshold ASD group were collapsed into a "Merged ASD" group, intended to cover the broad autism phenotype. Between-group comparisons were then made between the Merged ASD group and the non-ASD group. Sociodemographic variables chosen for analysis were those commonly seen as clinically relevant; educational background, living situation, vocational status, social relationships, history of contacts with psychiatry and current/past support from social services. ASD-specific variables chosen were clinically assessed ASD diagnostic criteria (according to DSM-5 and Gillberg & Gillberg's criteria for Asperger's syndrome) and ASDI results.

Current psychiatric diagnoses were collapsed into DSM-5 categories, because of the diagnostic overlap between the different diagnoses. To measure the degree of psychiatric comorbidity, the number of current psychiatric non-mood disorders was used. Mood disorders were excluded because they are extremely common in psychiatry in general. Outcome, measured with GAF as degree of

disability, was explored for associations to common factors associated with functional level such as age, processing speed and IQ, presence of ADHD, degree of co-occurring psychiatric diagnoses and degree of ASD. Categorical data was analyzed using Chi-squared test or Fisher's exact test (for 2x2 tables). Correlation analyses between GAF and potentially associated factors were performed using Spearman's rho, as all independent variables were not normally distributed. Linear regression analyses were performed for exploring the association between the outcome variable (GAF) and potential predictors.

### 3.4.3 STUDY III

As in study II, the ASD and Subthreshold ASD groups were collapsed into a "Merged ASD" group. Degree of ASD symptoms was compared between depressed and non-depressed participants, to assess if ASD diagnoses (unintentionally) were assigned to symptoms of depression or vice versa. Known risk factors for suicide attempts were analysed as potentially associated to suicide attempts in the study sample. The factors were dependence on economic welfare, age, sex, degree of psychiatric comorbidity, number of depressive symptoms met during most severe depressive episode, experience of psychological trauma, ASD symptomatology, IQ and PSI.

Known risk factors for NSSI were analysed as potentially associated to NSSI in the study sample. Those factors were cluster B personality disorders, ASD symptomatology, sex, age, history of suicidal ideation and/or suicidal behaviour and occurrence of ADHD.

Between-group comparisons were performed with Mann-Whitney U test or Student's t-test (for continuous variables, depending on if the variables were normally distributed). Chi-squared or Fisher's exact test (for 2x2 tables) were used for comparisons of categorical data. Relationships between the outcome variables (suicide attempts and NSSI) and the different potential predictors were explored using logistic regression analyses.

### 3.4.4 STUDY IV

Pearson correlation analyses were performed between the different ABAS-II domains, GAC and the results from all cognitive and executive function tests. To explore any relationships between the results from cognitive / executive function tests and GAC, linear regressions were performed with GAC as

dependent variable and correlating cognitive / executive function measures as independent variables.

## 3.5 ETHICS

All procedures performed in the context of these studies comply with the ethical standards stated in the Helsinki Declaration of 1975, as revised in 2008. Written or oral informed consent was obtained from all participants. The work in this thesis was approved by the Regional Ethical Review Board in Lund, Sweden (Study I, II and III: Reference number 2018/740 and Study IV: Reference number 2015/696).

# 4 RESULTS

## 4.1 STUDY I

Between November 1, 2019, and October 31, 2020, 562 new outpatients (321 females and 241 males; age M = 33.7, Sd = 12.5) were assessed at the psychiatric assessment unit (PAU) in Helsingborg, Sweden. Out of the total 562, 304 (58%; 183 females and 121 males; age M = 33.1, Sd = 12.6) participated in screening for ASD. Out of the screening responders, 197 were screen-positive (65%; 117 females and 80 males; age M = 32.0, Sd = 11.7). Out of the screen-positive patients, 48 participated (24%; 29 females and 19 males; age M = 32.0, Sd = 11.8) in the study and were subject to in-depth assessment. Out of the participants, 26 met criteria for ASD (54%; 17 females and 9 males; age M = 31.0, Sd = 12.2), 8 (17%; 4 females and 4 males; age M = 40.6, Sd = 11.8) met criteria for subthreshold ASD and 14 did not meet criteria for ASD or subthreshold ASD (29%; 8 females and 6 males; age M = 28.9, Sd = 9.0).

Assuming (on the basis of similarities in age, sex distribution, reasons for being referred to the clinic and screening results) that the study participants were representative of all screen-positive screening responders and assuming that none of the screening non-responders and none of the screen-negative screening responders had ASD, the prevalence of ASD in this population would be 18.9% - with an additional 5.7% having subthreshold ASD. A maximum estimate, assuming that none of the screen-negative screening responders would have ASD but that the screening non-responders would have a similar distribution of screening results as the screening responders, the prevalence of ASD would be 35% with an additional 10.7% having subthreshold ASD. As an absolute minimum, assuming that we by chance managed to recruit all patients with ASD and subthreshold ASD in the entire population, the prevalence of ASD would be 4.6% with an additional 1.4% having subthreshold ASD.

## 4.2 STUDY II

Eighty-one screen-positive patients participated in the study. Patients eligible for inclusion in the control group (RAADS-14 result ≤ 6) proved difficult to recruit into the study, with only nine participating in total. Of the total 90 participants (54 females and 36 males; age M = 31.0, Sd = 10.5), 63 met criteria for ASD (n = 52; 32 females and 20 males; age M = 30.6, Sd = 9.8) or subthreshold ASD (n = 11; 4 females and 7 males; age M = 38.6, Sd = 11.7), together constituting a "Merged ASD" group. Twenty-seven (18 females and 9 males; age M = 29.0, Sd = 10.4) of the participants did not meet criteria for ASD or subthreshold ASD. Based on the distribution of RAADS-14 results (presented in detail in study I), the participants who did not meet criteria for ASD or subthreshold ASD from the original control group (n = 8), together with the participants that did not meet criteria for ASD or subthreshold ASD from the screen-positive group (n = 19; together constituting a "Non-ASD group"), were considered representative of non-ASD patients from the study population.

Psychiatric co-occurring conditions in the Merged ASD group by DSM-5 category, in order of commonness, were: NDDs other than ASD (90%; of which 67% had ADHD of any subtype); Anxiety disorders (87%); OCD and related disorders (53%), depressive disorders (40%); potential SUD (hazardous or harmful alcohol use and/or drug-related problems) (30%); bipolar disorders (29%); trauma and stressor-related disorders (21%); disruptive, impulse-control and conduct disorders (11%); eating disorders (10%); and schizophrenia spectrum and other psychotic disorders (5%). Mean number of comorbid psychiatric diagnoses were 4.1, with a standard deviation of 1.7. No differences were found between the Merged ASD group and the Non-ASD group in self-reported social relationships, living conditions, educational level, vocational status, psychiatric history or history of support in school or from social services. Psychiatric profiles for the two groups were similar, but anxiety disorders and NDDs (other than ASD) were more common in the Merged ASD group. There were non-significant trends in the data towards depressive disorders, obsessive-compulsive and related disorders and trauma- and stressor-related disorders being more common in the Merged ASD group as well. The data suggested that parent-rated developmental history show clear signs of NDD symptomatology regardless of classification (Merged ASD or Non-ASD), though the sample size was too small to be able to compare the groups statistically. The Merged ASD group had more comorbid psychiatric diagnoses and lower GAF scores than the Non-ASD group. Within the Merged ASD group, the number of comorbid psychiatric non-mood disorders and current mood disorder explained 26.7% of the variability in GAF.

## 4.3 STUDY III

This study explored suicidal thoughts, plans and attempts, as well as NSSI, in the Merged ASD group (n = 63). Active suicidal ideation (actively thinking about ending one's own life) was experienced by 58% of the participants during the past year. Suicidal plans had been prevalent in 29% of the participants during the past year and 7% of the participants had attempted suicide during the past year. One fourth of the participants had a history of at least one suicide attempt during their life. Some 32% of the participants had engaged in NSSI during the past year, 44% at any time during their life. There was a significant overlap between NSSI and suicidality. The four most common types of NSSI behaviours were hitting oneself on purpose, picking at wounds, cutting or carving oneself and biting oneself. The five most common reasons for engaging in NSSI were relief of feeling numb or empty, to feel something – even if it was pain, to get control of a situation, to punish oneself and to stop bad feelings.

Hazardous or harmful alcohol use and/or drug-related problems and severity of the worst experienced depressive episode explained between one fifth and one third or the variance in suicide attempts. Factors associated with NSSI were being female, ever having experienced suicidal plans and antisocial personality disorder; together explaining up to half of the variance in the occurrence of NSSI. No completed suicides were recorded at the follow-up of medical records. Out of the nineteen participants having a hazardous or harmful alcohol use and/or drug-related problems, only six (four out of six males and two out of thirteen females) had a clinical diagnose of harmful use or addiction at the follow-up of medical records.

## 4.4 STUDY IV

Results from the cognitive tests showed that the sample assessed (N = 30; 21 males and 9 females; age M = 21.6, Sd = 2.9; eight having additional attention-deficit diagnoses) was of normal but slightly below average IQ. Three of the four measures of executive functions were in the average range, only the Proverb test was below average. Trends in the data showed that PRI from the WAIS was higher than VCI, WMI and PSI. The trends in the data further showed that all tests of executive function except verbal fluency, condition 2 (word-generation in concrete categories), were below average. None of these trends were significantly below the normative means. However, below-average results regarding cognitive flexibility, abstract verbal fluency, inhibition and verbal abstract thinking are often seen clinically in adult psychiatric patients with ASD.

Adaptive function (expressed as GAC) was predicted by IQ, WMI and PSI, respectively. A regression model incorporating WMI and PSI explained 23.8% of the variance in GAC. IQ alone explained 11.5% of the variance. Mean GAC in the sample was 62.1 (Sd = 15.7), indicating adaptive function in the range of mild ID.

# 5 DISCUSSION

The studies included in this thesis concerned different aspects of adult psychiatric outpatients with ASD. In study I, we found a relatively high prevalence of ASD and ALTs in newly referred patients to a Swedish psychiatric clinic. In studies II and III, we found that when comparing patients with and without ASD, comorbidity patterns (including suicidal behaviours) were not very dissimilar. In study IV, we found associations between cognitive factors and functional level in patients with ASD.

## 5.1 PREVALENCE OF ASD IN ADULT OUTPATIENT PSYCHIATRY

Given that this is the first published estimation of ASD prevalence in a general psychiatric outpatient population since 2001, the figure 18.9% seems very high at first glance. The estimation is, however, roughly in line with a prevalence estimate of ASD in an adult population with depression (Takara & Kondo, 2014) and with prevalence estimates of ASD in adult eating disorder populations (Huke et al., 2013). Even if some would call almost one in five a surprisingly high prevalence, it does not seem so from a clinical, general adult psychiatric perspective. Even if one would be extremely cautious and assume that every patient with ASD during the screening period participated in the study, the prevalence of ASD would still be 4.6%, i.e. at least three to four times more common among psychiatric outpatients than in the general population.

According to the screening results, two thirds of the screening responders were screen-positive for ASD. This implies that ALTs are much more common in the screened population than in the general population, even though ALTs are quite common in the general population as well (Posserud et al., 2006). The specificity of the RAADS-14 in the study sample was 54%, i. e. in between the previously reported specificity in an ADHD population (46%) and a psychiatric population (64%) (Eriksson et al., 2013). Our distribution of screening results was similar to the ADHD population in Eriksson et al's study. This might imply a higher degree of ADHD in our population, compared to the psychiatric population in Eriksson et al (2013).

Symptoms of ASD, both expressed as DSM-5 criteria and Gillberg & Gillberg criteria, were common in both ASD and non-ASD groups. The clearest

similarities between the groups were non-verbal communication deficits and sensory hyper- or hypo-reactivity, though the non-ASD group reported that the non-verbal communication deficits were not lifelong in approximately half of the cases, as opposed to the ASD and subthreshold ASD groups. Symptoms of ASD were commonly seen in non-ASD participants – but not more than one, two or three symptoms simultaneously. In the ASD participants, the symptoms instead presented as the pattern of symptoms (two to three A-criteria and at least two B-criteria simultaneously, according to DSM-5) that is commonly associated with ASD. Both ASD and non-ASD groups were, on the group level, far above the screening cutoff scores; this might indicate that self-experienced symptoms of ASD are difficult to evaluate.

Only one participant in the whole group studied met criterion B1 (stereotyped or repetitive motor movements, use of objects or speech). Stereotyped behaviours in children with ASD are associated with lower IQ levels (Bishop et al., 2006) and the lack of stereotyped motor movement in this study group might be explained by the "non-ID nature" of the group included here. It is possible that this is a group of persons with ASD who did not present with stereotyped behaviours, or who had presented with less frequently occurring such behaviours during childhood, than other ASD groups. This would likely have made it more difficult for family or professionals to recognise the ASD during childhood, thereby contributing to the late detection of the condition. It is also possible that this group did show stereotypies during childhood and/or adolescence, but that the behaviours had faded over the years, or that the participants had learned how to mask their stereotyped behaviours as they are usually seen as stigmatising.

## 5.2 SIMILARITIES AND DIFFERENCES COMPARED TO NON-ID ADULTS WITH ASD

The findings in studies II (psychiatric and sociodemographic profiles), III (suicidality and NSSI) and IV (cognition) are generally in line with previously published studies on other adult ASD populations. The ASD *symptomatology* of our sample was slightly different from the few (two) other samples available for comparison (Helles et al., 2015; Hofvander et al., 2009). Our sample had seemingly less motor clumsiness (Gillberg & Gillberg criterion 6; 52% compared to 78%) and seemingly more rigid routines (Gillberg & Gillberg criterion 3; 94% compared to 75%) than what was reported in Hofvander et al (2009). The possibly less common motor clumsiness in our sample could imply that our sample had less overall cognitive impairment, as motor and cognitive deficits have previously been shown to be associated (Leonard et al., 2015). The more commonly occurring repetitive routines might be an effect of the pronounced higher degree of psychiatric comorbidity in our sample, as more stress in persons with ASD tends to increase repetitive routines or compulsive behaviours (Geurts et al., 2009). Our sample might have had a somewhat higher degree of ASD symptomatology (ASDI M = 23.5, Sd = 6.0) compared to a longitudinal follow-up of (now adult) boys diagnosed with Asperger's syndrome (M = 18.5, Sd = 7.3) (Helles et al., 2015). This could possibly be an effect of the symptoms of ASD being entangled with psychiatric symptoms, causing the ASD symptoms to seem more distinct at the time of the assessment. It is possible that some of the participants would not be found to meet criteria for ASD if they had a diagnostic assessment while less affected by "other" psychiatric disorders. On the other hand, it is also possible that ASD presenting with severe psychiatric comorbidity in adult age is a sub-category in itself and that disentangling ASD and psychiatric disorders in this group is not possible or even meaningful.

In line with what has been previously reported, no clear patterns or profiles in cognitive deficits could be seen in the studies, except for possible trends towards deficits in cognitive flexibility and towards higher results on perceptual reasoning compared to other subscales on the WAIS. In both study groups (study I-III and study IV), other conditions affecting cognition were common – in particular ADHD (67% of the merged ASD group in study II and 27% in study IV). The high degree of co-occurring conditions makes it more or less impossible – and clinically pointless – to draw any conclusions on what cognitive impairments are "ASD-specific". Cognition did, however, have an impact on the activities of daily life in study IV (WAIS-IV working memory

and processing speed explaining more than one fifth of the variance), and the degree of comorbid psychiatric disorders had an impact on GAF in study II (explaining slightly more than one fourth of the variance together with current depression). Previously published studies on which factors predict adaptive function in adults with ASD argue for an emphasis on cognitive functions (Wallace et al., 2016) or on co-occurring psychiatric disorders (Kraper et al., 2017). As Wallace et al. (2016) points out, cognitive deficits are intertwined with co-occurring psychiatric disorders. It seems safe to assume that both cognitive functions and co-occurring psychiatric disorders are important for understanding the functional level in this group. The gap between IQ and adaptive function among adults with ASD, reported in study IV, has been seen previously (Kraper et al., 2017) and might constitute a means of screening for ASD among psychiatric adults. The current GAF score of our participants was similar to those reported previously in non-ID adults with Asperger syndrome or ASD (Helles et al., 2015; Joshi et al., 2013).

Sociodemographic characteristics were, with certain exceptions, largely similar to what has been reported from other studies of normal-intelligence adults with ASD (Helles et al., 2017; Joshi et al., 2013; Lugnegård et al., 2011; Ryden & Bejerot, 2008). Educational levels were roughly similar to those reported in two Swedish clinical ASD cohorts (Lugnegård et al., 2011; Ryden & Bejerot, 2008), but slightly lower than in Swedish adults diagnosed with Asperger's syndrome during childhood (Helles et al., 2017) and an American clinical sample diagnosed with ASD at differing ages (Joshi et al., 2013). History of earlier contacts with psychiatric care (out- and inpatient) was comparable to the American clinical sample (Joshi et al., 2013) and dependence on social services was comparable to the Swedish clinical sample where comparisons were possible (Lugnegård et al., 2011). The most distinct differences to other ASD samples were relationships, where twice as many in our sample reported having a partner compared to both American and Swedish clinical samples (Joshi et al., 2013; Ryden & Bejerot, 2008), and 79% of our sample compared to 52% in the Swedish Asperger's syndrome follow-up (Helles et al., 2017) reported having had a partner at some point during their life. Our sample reported having had much less support in school (41%) than what was reported from the clinical American sample (Joshi et al., 2013) (71%). Our sample having had less difficulties in school might be one of the factors contributing to not being recognised as having ASD until adulthood.

Almost all psychiatric disorders that were assessed in our ASD study group were more prevalent than reported in previous studies of co-occurring psychiatric conditions in adults with ASD, this was expected as all participants were referred to a psychiatric clinic. Ranking the commonness of different

psychiatric disorders, our results showed a higher proportion of anxiety disorders and OCD (and related disorders) than what has been shown in meta-analyses (Lai et al., 2019; Lugo-Marín et al., 2019). Mood disorders, ADHD, and anxiety disorders were by far the three most common psychiatric diagnoses, echoing current consensus. Furthermore, the larger proportions as regards OCD and anxiety disorders in our study have been reported in other Swedish samples as well (Gillberg et al., 2016; Hofvander et al., 2009; Lugnegård et al., 2011; Ryden & Bejerot, 2008). By and large, the profile of co-occurring psychiatric conditions in our sample was not very dissimilar compared to those reported in previous studies of normal-intelligence adults with ASD.

Suicidal ideation (thoughts and plans of suicide) and suicide attempts, both in the past year and at a lifetime perspective, were comparable to results from other adult ASD populations that were diagnosed in adult age (Cassidy et al., 2018). Completed suicides have recently been suggested to be considerably more common in adults with ASD compared to adults without ASD (Cassidy et al., 2022; Hirvikoski et al., 2020), though most of the participants in the mentioned studies were diagnosed with ASD as adults or were not formally diagnosed with ASD at all. Longitudinal studies of those diagnosed with ASD during childhood, involving suicidality measures, so far shows clearly lower prevalence rates of suicidal ideation and suicide attempts (Culpin et al., 2018; Gillberg et al., 2016). Thus, it might be possible that receiving an ASD diagnosis during childhood has a preventive effect on suicide, with regard to development of major psychiatric diorders.

The knowledge base on NSSI in normal-intelligence adults with ASD is only emerging. The few studies published have reported substantially higher prevalence rates than those found in the present group (Maddox et al., 2017; Moseley et al., 2022). Reasons for engaging in NSSI behaviours, methods used, and experience of pain were similar to what we found. However, previous studies have relied on online surveys using self-reported diagnoses of ASD which has obvious risks of bias.

The method used in this thesis for establishing diagnoses of ASD was unorthodox, in the sense that a single psychologist assessed the diagnostic criteria. In many diagnostic guidelines, a combined psychologist – psychiatrist assessment, or an assessment drawing on a range of professions, is required (National Institute for Health and Care Excellence, 2021; Swedish National Board of Health and Welfare, 2022). The unorthodox diagnostic method might possibly have led to over- or underdiagnosis of ASD. However, the conjoint

validation showed good reliability across the rater and three different internationally well-established psychiatrists/psychologists.

## 5.3 SIMILARITIES AND DIFFERENCES COMPARED TO PSYCHIATRIC OUTPATIENTS WITHOUT ASD

This project is the first to describe a psychiatric outpatient population and comparing patients with and without ASD. No between-group differences were found in any sociodemographic variables. This might be due to the rather blunt psychometric instruments used. Slight differences in psychiatric profiles were found; NDDs and anxiety disorders were more common, and the psychiatric comorbidity was greater in patients with ASD. Previous studies have shown a high rate of comorbidity in psychiatric populations regarding depression and anxiety disorders, where the risk of meeting criteria for additional psychiatric diagnoses increases with the symptom load (Andrews et al., 2008). More than half of patients with major depressive disorder tend to meet criteria for at least one comorbid anxiety disorder (Zimmerman et al., 2000). Our findings imply that ASD is associated with higher levels of psychiatric comorbidity compared to other psychiatric outpatients, mirroring clinical experience (e.g. ASD patients showing a "messier" psychiatric presentation). It is not impossible that the "messier" psychiatric presentation might, at least partly, explain the lower GAF in the ASD group.

Regarding prevalence of suicidality and NSSI as well as type/function of NSSI behaviours, our ASD group was similar to other (non-ASD) psychiatric samples. This implies that psychiatric patients with ASD or suspected ASD need similar conceptulisation of NSSI and suicidality as do psychiatric patients without ASD; that NSSI in the ASD group is not necessarily stereotyped or repetitive. As in most populations, the most distinct predictive factor of suicide attempts was alcohol and/or substance use. In summary – when comparing ASD and non-ASD psychiatric patients, the similarities seem to clearly outweigh the differences. One important difference, though, lies in the symptoms of ASD.

## 5.4 STRENGTHS AND LIMITATIONS

The main strength of this study lies in it being based on clinical assessments, performed by experienced clinicians using well-validated psychometric instruments. Another strength is that it is a naturalistic description of a clinical population. Major limitations are the relatively low participation rate and the small sample size. A larger sample and extending the screening/inclusion period would have improved the quality of the study substantially but was not possible because of the Coronavirus Disease 2019 (COVID-19) pandemic. Another limitation is the low degree of informant-supplied developmental history of the participants, which could have led to both over- and underdiagnosis of ASD.

# 6 CONCLUSIONS AND CLINICAL IMPLICATIONS

The studies included in this thesis found that DSM-5 ASD was present in almost one in five adults attending a Swedish psychiatric outpatient clinic. Comparisons across adult psychiatric outpatients with and without ASD showed that similarities outweighed differences in terms of sociodemographic profile, suicidal ideation and suicide attempts, NSSI and, to a large extent, also as regards psychiatric comorbidities. However, there were three important differences between the groups. First and foremost of these was the pattern of symptoms commonly associated with ASD – lifelong deficits in reciprocal social communication and social interaction in combination with restricted and/or repetitive behaviours and sensory hypo- or hyperreactivity, present only in the ASD group. Second, significant deficits in functional level that had always been present in the ASD group (as opposed to cases where the onset of functional deficits coincide with the onset of psychiatric disorders). Third, the rate of psychiatric comorbidities was higher in the ASD group. The findings imply that all professionals in psychiatry need to recognise the pattern of symptoms specific to ASD, to both help identify patients with ASD and to treat patients with ASD according to their needs – whether they have a prior formal diagnosis of ASD or not.

In adult psychiatric settings in many places, not least in Sweden, professionals are struggling with attempts at determining "what is ASD?" and "what is non-ASD?". This is commonly done by trying to assess the origin and the functional aspect of the symptoms. The results of these "determinations" are most often a few lines in the assessment report, leading up to a diagnostic decision. In psychiatric assessments, professionals should rather regard ASD and other NDDs as predisposing factors in the overall clinical psychiatric symptom presentation. Given that ASD and psychiatric disorders "overlap", assessments need to be holistic even if the presenting problem is depression or anxiety or something else. How can we conceptualise the psychiatric "situation"; what are the predisposing, perpetuating and precipitating factors? If one of the predisposing factors is having "an autistic way of functioning" – meeting enough criteria for a formal diagnosis or not – then this needs to be taken into account in order to optimise intervention.

Functional level in the ASD group was affected by both co-occurring psychiatric disorders and deficits in executive functions. This implies that interventions aimed at alleviating deficits in executive functions, such as occupational therapy interventions or pharmacological treatments, might help

improve the functional level in this patient group and therefore should be considered for adult psychiatric patients with ASD. Prioritising and allocating of resources could easily be assisted by specific psychiatric and neuropsychological assessments. In many places, neuropsychological assessments have been or are in the process of being removed from the clinical "neuropsychiatric" diagnostic examination guidelines with a view to "saving resources"; in light of the results in this thesis, removing such assessments would appear to be counter-intuitive.

Finally, more and more studies on the prevalence of NDDs in adult psychiatric settings are being published. So far, it would appear that the majority of adult psychiatric outpatients have an underlying NDD – with a significant minority of about 20% having ASD (Eberhard et al., 2022). Time will tell if the results from this thesis are indeed generalisable. This thesis adds to the growing knowledge that NDDs are, in fact, not only the ESSENCE in child psychiatry (Gillberg, 2010), but in adult psychiatry as well.

# 7 FUTURE RESEARCH

It is encouraging to see that interest in the study of adults with ASD is increasing and that more and more studies are published. However, there are still no studies that have comprehensively assessed risk factors for severe "comorbid" psychiatric disorders in adulthood for individuals with ASD, and no longtitudinal studies on outcomes of psychiatric disorders in ASD. Also, there is an obvious need for further development of psychometric instruments for screening and diagnostics of ASD in adults. Several more studies using active case ascertainment, e. g. Brugha et al. (2020) are needed, not least in general psychiatric populations. It is not impossible that the instruments already developed will show better psychometric properties in psychiatric populations if validated using different methodology, as proposed in a recent article (Tromans & Brugha, 2022).

Interventions aimed at alleviating deficits in executive functions for this group need to be developed and systematically evaluated. The interventions available for increasing the functional level in this group, at least in most parts of Sweden, are of the same kind as the interventions for persons with ID, in effect limited to concrete support at home by social workers. According to clinical experience, most non-ID adults with ASD in the adult psychiatry are unwilling to accept such support due to its intrusive nature. It is not uncommon for adult psychiatric outpatients with ASD to express feeling offended because such interventions feel too extensive.

Most research on adults with ASD has been focused on those diagnosed in childhood, or in those who seek psychiatric help or help with a diagnostic assessment of ASD as adults. Is there a group of adults with ASD and mental health problems, who do not seek help? In future research it would also be important to compare outcomes in the groups that receive a formal ASD diagnosis during different stages of childhood or adolescence, as adults or never at all. These are potentially very important knowledge gaps, though study designs with a view to examining them would be challenging.

# ACKNOWLEDGEMENTS

Research in general, and clinical research in particular, is a team sport. A great number of people have helped me through the often frustrating and tedious work by unselfishly offering support, giving me a couple of kind words passing by, validating and listening patiently to my frustrated rants or giving me a pat on the shoulder when I needed it. Here are those who need to be mentioned in particular.

**Christine** – Thank you for always supporting me and putting up with all projects and shenanigans. Thank you equally much for your judgment, common sense and skills in knowing when *not* to support my weird ideas and instead keeping both my feet on the ground. You sweep me off those feet every day.

**Harry and Tyra** – Thank you for putting up with a busy and stressed dad during the years I worked with this project. You show me what's really important in life every day, just by being you. You're the most amazing humans I've ever met.

**Eva Billstedt** – My main supervisor. I've always been extremely lucky with tutors and supervisors; you are the finest example of that luck. Your magical understanding of what I needed and when I needed it was crucial in pushing me though this project. Great leaders lead by example – and what an exemplar you are. I sure hope we can keep doing projects together for many years to come. Thank you for giving me this opportunity and believing in me.

**Christopher Gillberg** – My co-supervisor. I am ever grateful that you wanted to become part of this project and for sharing your vast knowledge about all aspects of the ESSENCE umbrella. Thank you for our talks, your thoroughness, and especially for teaching me the importance of attention to detail – something I'm not the easiest person to teach (ask Eva).

**Jonas Eberhard** – My second co-supervisor. Above everything else, you've taught me the basics in the art of networking, how to balance research and clinical work, and how to make things happen. You truly are an amazing enabler. I hope we will keep working together for many years.

**Mohammad Ghaziuddin** – My unofficial third co-supervisor. Thank you for taking on that supportive role. Your contact during the years and your generosity with your time and knowledge meant more to me than you know, and much of your support came exactly when I needed it. I hope we will realise some of our project ideas.

Clinic manager **Maria Holst** – The support you have provided for this thesis – and for starting up the research group at the psychiatric clinic in Helsingborg – has been invaluable. You are a huge resource for the Scanian psychiatry in general, we are lucky to have you. Without you believing in this project and approving it, this thesis would obviously not exist. Thank you for believing in me and for appreciating research at our clinic.

**Jannice Jäderhed Linderståhl** – Thank you for supporting me in all phases of this project, for pushing me and making it happen. Thank you also for the years as my manager, you have always been there for me, not least with your ability of pointing out what I need to consider, especially when it comes to personal well-being, which I tend to forget about. I hope you will enjoy your retirement.

Secretaries **Gunnel Larsson, Frida Bjällö and Jessica Cruz** – In this whole project, you were the most important key personnel. Without the three of you and your always positive contact with our patients, this project would never have happened; no matter the funding, support from the organisation and different universities, supervision from professors, etc. You were the true key to making this work at all.

**Margda Waern** – Thank you for being part of this project and your contributions to the project design, for teaching me the basics of suicidology research and for taking such an active part in study III.

**Ingrid Vinsa** – Thank you for always knowing what to do, always fixing everything (with a smile!) and for always making me feel welcome at the GNC.

**Anna Spyrou** – Thank you for all support in all matters regarding communication, thank you especially for your thorough work with this thesis.

**Maria Marinopoulou** – Thank you for your invaluable contributions to the creation and writing of this thesis and for nice discussions along the way.

And, of course, **my friends, my family and extended family** for putting up with me.

**You others** who – knowingly or not – provided key support at times that were rough for me; sometimes just with a single comment that meant loads for me at that particular time and sometimes with nice discussions, bad jokes and/or practical support. In no particular order:

**Elisabeth Fernell, Ewa Hellberg Rosengren, Erik Jedenius, Valdemar Landgren, Kirsten Mehlig, Gudrun Olow-Schnaars, Maria Råstam, Darko Sarovic, Charlotte Stübner, Max Thorsson, Maria Unenge-Hallerbäck, Njördur Viborg, Angeline Wemmert and Eric Zander.**

Finally, **the study participants** – Thank you for willingly being a part of this project at a tough time in your lives. All things considered, I did this for you and I sincerely hope that the knowledge from this project will help improve psychiatric services for all of you with NDDs in general and ASD in particular.

This thesis was supported by grants from Region Skåne (grants from the adult psychiatric clinic in Helsingborg and grants from the regional psychiatric research and development unit), the Stig and Ragna Gorthon Foundation, the Swedish Research Concil, the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBG-965080), the AnnMari and Per Ahlqvist Foundation, the Wilhelm and Martina Lundgren Foundation, the Thorsten Birger Segerfalk Foundation and the Adlerbertska Scholarship Foundation.

# REFERENCES


American Psychiatric Association. (1952). *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association Mental Hospital Service.

American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed.). American Psychiatric Association.

American Psychiatric Association. (1987). *Diagnostic and Statistical Manual of Mental Disorders* (3rd, rev. ed.). American Psychiatric Publishing.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). American Psychiatric Publishing.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.). American Psychiatric Publishing.

Andersen, L. M., Naswall, K., Manouilenko, I., Nylander, L., Edgar, J., Ritvo, R. A., Ritvo, E., & Bejerot, S. (2011). The Swedish version of the Ritvo autism and asperger diagnostic scale: revised (RAADS-R). A validation study of a rating scale for adults. *Journal of Autism and Developmental Disorders*, *41*(12), 1635-1645. https://doi.org/10.1007/s10803-011-1191-3

Andrews, G., Anderson, T. M., Slade, T., & Sunderland, M. (2008). Classification of anxiety and depressive disorders: problems and solutions. *Depression and Anxiety*, *25*(4), 274-281. https://doi.org/10.1002/da.20489

Arvidsson, O., Gillberg, C., Lichtenstein, P., & Lundström, S. (2018). Secular changes in the symptom level of clinically diagnosed autism. *Journal of Child Psychology and Psychiatry*, *59*(7), 744-751. https://doi.org/10.1111/jcpp.12864

Ashwood, K. L., Gillan, N., Horder, J., Hayward, H., Woodhouse, E., McEwen, F. S., Findon, J., Eklund, H., Spain, D., Wilson, C. E., Cadman, T., Young, S., Stoencheva, V., Murphy, C. M., Robertson, D., Charman, T., Bolton, P., Glaser, K., Asherson, P., . . . Murphy, D. G. (2016). Predicting the diagnosis of autism in adults using the Autism-Spectrum Quotient (AQ) questionnaire. *Psychological Medicine*, *46*(12), 2595-2604. https://doi.org/10.1017/S0033291716001082

Asperger, H. (1938). Das psychisch abnorme Kind. *Wiener Klinische Wochenschrift, 49*, 1314-1317.

Asperger, H. (1944). Die "Autistischen Psychopathen" im Kindesalter. *Archiv für psychiatrie und Nervenkrankheiten*, *117*, 76-136.

Atladottir, H. O., Gyllenberg, D., Langridge, A., Sandin, S., Hansen, S. N., Leonard, H., Gissler, M., Reichenberg, A., Schendel, D. E., Bourke, J., Hultman, C. M., Grice, D. E., Buxbaum, J. D., & Parner, E. T. (2015). The increasing prevalence of reported diagnoses of childhood psychiatric disorders: a descriptive multinational comparison. *European Child and Adolescent Psychiatry*, *24*(2), 173-183. https://doi.org/10.1007/s00787-014-0553-8

Bailey, A., Le Couteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., & Rutter, M. (1995). Autism as a strongly genetic disorder: evidence from a British twin study. *Psychological Medicine*, *25*(1), 63-77. https://doi.org/10.1017/s0033291700028099

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): evidence from Asperger Syndrome/high functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders*, *31*(1), 5-17. https://doi.org/10.1023/a:1005653411471

Bejerot, S., & Nylander, L. (2022). An overestimation of the prevalence of ASD among psychiatric patients. *Journal of Autism and Developmental Disorders*, *52*(9), 4204-4205. https://doi.org/10.1007/s10803-022-05568-1

Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2005). Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *European Addiction Research*, *11*(1), 22-31. https://doi.org/10.1159/000081413

Billstedt, E., Gillberg, I. C., & Gillberg, C. (2005). Autism after adolescence: population-based 13- to 22-year follow-up study of 120 individuals with autism diagnosed in childhood. *Journal of Autism and Developmental Disorders*, *35*(3), 351-360. https://doi.org/10.1007/s10803-005-3302-5

Billstedt, E., Gillberg, I. C., & Gillberg, C. (2011). Aspects of quality of life in adults diagnosed with autism in childhood: a population-based study. *Autism*, *15*(1), 7-20. https://doi.org/10.1177/1362361309346066

Bishop, S. L., Richler, J., & Lord, C. (2006). Association between restricted and repetitive behaviors and nonverbal IQ in children with autism spectrum disorders. *Child Neuropsychology*, *12*(4-5), 247-267. https://doi.org/10.1080/09297040600630288

Bleuler, E. (1924). *Textbook of psychiatry*. Macmillan & Co.

Bolton, D., & Gillett, G. (2019). *The biopsychosocial model of health and disease: New philosophical and scientific developments*. Springer Nature.

Booth, T., Murray, A. L., McKenzie, K., Kuenssberg, R., O'Donnell, M., & Burnett, H. (2013). Brief report: an evaluation of the AQ-10 as a brief screening instrument for ASD in adults. *Journal of Autism and Developmental Disorders*, *43*(12), 2997-3000. https://doi.org/10.1007/s10803-013-1844-5

Brugha, T. S., Tyrer, F., Leaver, A., Lewis, S., Seaton, S., Morgan, Z., Tromans, S., & van Rensburg, K. (2020). Testing adults by questionnaire for social and communication disorders, including autism spectrum disorders, in an adult mental health service population. *International Journal of Methods in Psychiatric Research*, *29*(1), e1814. https://doi.org/10.1002/mpr.1814

Brugha, T. S., McManus, S., Smith, J., Scott, F. J., Meltzer, H., Purdon, S., Berney, T., Tantam, D., Robinson, J., Radley, J., & Bankart, J. (2012). Validating two survey methods for identifying cases of autism spectrum disorder among adults in the community. *Psychological Medicine*, *42*(3), 647-656. https://doi.org/10.1017/S0033291711001292

Brugha, T. S., McManus, S., Bankart, J., Scott, F., Purdon, S., Smith, J., Bebbingtons, P., Jenkins, R., & Meltzer, H. (2011). Epidemiology of autism spectrum disorders in adults in the community in England. *Archives of General Psychiatry*, *68*(5), 459-466. https://doi.org/https://doi.org/10.1001/archgenpsychiatry.2011.38

Brugha, T. S., Spiers, N., Bankart, J., Cooper, S. A., McManus, S., Scott, F. J., Smith, J., & Tyrer, F. (2016). Epidemiology of autism in adults across age groups and ability levels. *The British Journal of Psychiatry*, *209*(6), 498-503. https://doi.org/10.1192/bjp.bp.115.174649

Buck, T. R., Viskochil, J., Farley, M., Coon, H., McMahon, W. M., Morgan, J., & Bilder, D. A. (2014). Psychiatric comorbidity and medication use in adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *44*(12), 3063-3071. https://doi.org/10.1007/s10803-014-2170-2

Cassidy, S., Au-Yeung, S., Robertson, A., Cogger-Ward, H., Richards, G., Allison, C., Bradley, L., Kenny, R., O'Connor, R., Mosse, D., Rodgers, J., & Baron-Cohen, S. (2022). Autism and autistic traits in those who died by suicide in England. *The British Journal of Psychiatry*, *221*(5), 683-691. https://doi.org/10.1192/bjp.2022.21

Cassidy, S., Bradley, L., Shaw, R., & Baron-Cohen, S. (2018). Risk markers for suicidality in autistic adults. *Molecular Autism*, *9*, 42. https://doi.org/10.1186/s13229-018-0226-4

Chatham, C. H., Taylor, K. I., Charman, T., Liogier D'ardhuy, X., Eule, E., Fedele, A., Hardan, A. Y., Loth, E., Murtagh, L., Del Valle Rubido, M., San Jose Caceres, A., Sevigny, J., Sikich, L., Snyder, L., Tillmann, J. E., Ventola, P. E., Walton-Bowen, K. L., Wang, P. P., Willgoss, T., & Bolognani, F. (2018). Adaptive behavior in autism: Minimal clinically important differences on the Vineland-II. *Autism Research*, *11*(2), 270-283. https://doi.org/10.1002/aur.1874

Chiarotti, F., & Venerosi, A. (2020). Epidemiology of Autism Spectrum Disorders: A Review of Worldwide Prevalence Estimates Since 2014. *Brain Sciences*, *10*(5), 274. https://doi.org/10.3390/brainsci10050274

Coleman, M., & Gillberg, C. (2012). *The Autisms* (4th ed.). Oxford University Press.

Constantino, J. N., & Gruber, C. P. (2012). *The social responsiveness scale* (2nd ed.). Western Psychological Services.

Creak, M. (1961). Schizophrenic syndrome in childhood. *British Medical Journal, 2*, 889-890.

Creak, M. E. A. (1964). Schizophrenic syndrome in childhood: further progress report of a working party (April 1961). *Developmental Medicine and Child Neurology, 6*, 530-535. https://doi.org/10.1111/j.1469-8749.1964.tb10828.x

Culpin, I., Mars, B., Pearson, R. M., Golding, J., Heron, J., Bubak, I., Carpenter, P., Magnusson, C., Gunnell, D., & Rai, D. (2018). Autistic traits and suicidal thoughts, plans, and self-harm in late adolescence: population-based cohort study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *57*(5), 313-320 e316. https://doi.org/10.1016/j.jaac.2018.01.023

Dawson, G. (1996). Brief Report: Neuropsychology of autism: a report on the state of the science. *Journal of Autism and Developmental Disorders*, *26*(2), 179-184. https://doi.org/10.1007/BF02172008

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan executive function system: examiner's manual*. Psychological Corporation.

Eberhard, D., Billstedt, E., & Gillberg, C. (2022). Neurodevelopmental disorders and comorbidity in young adults attending a psychiatric outpatient clinic. *Psychiatry Research*, *313*, 114638. https://doi.org/10.1016/j.psychres.2022.114638

Engel, G. L. (1981). The clinical application of the biopsychosocial model. *The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine*, *6*(2), 101-124. https://doi.org/https://doi.org/10.1093/jmp/6.2.101

Eriksson, J. M., Andersen, L. M. J., & Bejerot, S. (2013). RAADS-14 Screen: validity of a screening tool for autism spectrum disorder in an adult psychiatric population. *Molecular Autism*, *4*(49). https://doi.org/doi:10.1186/2040-2392-4-49

Fombonne, E. (2003). Epidemiological surveys of autism and other pervasive developmental disorders: an update. *Journal of Autism and Developmental Disorders*, *33*(4), 365-382. https://doi.org/10.1023/A:1025054610557

Fombonne, E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric Research*, *65*(6), 591-598. https://doi.org/10.1203/PDR.0b013e31819e7203

Fombonne, E., Green Snyder, L., Daniels, A., Feliciano, P., Chung, W., & Consortium, S. (2020). Psychiatric and Medical Profiles of Autistic Adults in the SPARK Cohort. *Journal of Autism and Developmental Disorders*, *50*(10), 3679-3698. https://doi.org/10.1007/s10803-020-04414-6

Frith, U. (1989). Autism and "theory of mind". In C. Gillberg (Ed.), *Diagnosis and Treatment of Autism* (pp. 33-52). Plenum Press.

Fusar-Poli, L., Brondino, N., Rocchetti, M., Panisi, C., Provenzani, U., Damiani, S., & Politi, P. (2017). Diagnosing ASD in Adults Without ID: Accuracy of the ADOS-2 and the ADI-R. *Journal of Autism and Developmental Disorders*, *47*(11), 3370-3379. https://doi.org/10.1007/s10803-017-3258-2

Gajwani, R., & Minnis, H. (2023). Double jeopardy: implications of neurodevelopmental conditions and adverse childhood experiences for child health. *European Child and Adolescent Psychiatry*, *32*(1), 1-4. https://doi.org/10.1007/s00787-022-02081-9

Gaus, V. L. (2018). *Cognitive-Behavioral Therapy for Adults with Autism Spectrum Disorder* (2nd ed.). The Guilford Press.

Geurts, H. M., Corbett, B., & Solomon, M. (2009). The paradox of cognitive flexibility in autism. *Trends in Cognitive Sciences*, *13*(2), 74-82. https://doi.org/10.1016/j.tics.2008.11.006

Ghaziuddin, M., & Ghaziuddin, N. (2020). Bipolar Disorder and Psychosis in Autism. *Child and Adolescent Psychiatry Clinics of North America*, *29*(3), 433-441. https://doi.org/10.1016/j.chc.2020.02.004

Gillberg, C. (1984). Infantile autism and other childhood psychoses in a Swedish urban region. Epidemiological aspects. *Journal of Child Psychology and Psychiatry, 25*(1), 35-43. https://doi.org/10.1111/j.1469-7610.1984.tb01717.x

Gillberg, C. L. (1992). The Emanuel Miller Memorial Lecture 1991. Autism and autistic-like conditions: subclasses among disorders of empathy. *Journal of Child Psychology and Psychiatry, 33*(5), 813-842. https://doi.org/10.1111/j.1469-7610.1992.tb01959.x

Gillberg, C. (2010). The ESSENCE in child psychiatry: Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations. *Research in Developmental Disabilities*, *31*(6), 1543-1551. https://doi.org/10.1016/j.ridd.2010.06.002

Gillberg, C. (2021). *The ESSENCE of autism and other neurodevelopmental conditions*. Jessica Kingsley Publishers.

Gillberg, C., & Fernell, E. (2014). Autism plus versus autism pure. *Journal of Autism and Developmental Disorders*, *44*(12), 3274-3276. https://doi.org/10.1007/s10803-014-2163-1

Gillberg, C., Gillberg, I. C., Råstam, M., & Wentz, E. . (2001). The Asperger Syndrome (and high-functioning autism) Diagnostic Interview (ASDI): a preliminary study of a new structured clinical interview *Autism*, *5*(1), 57-66. https://doi.org/10.1177/1362361301005001006

Gillberg, C., Steffenburg, S., & Schaumann, H. (1991). Is autism more common now than ten years ago? *The British Journal of Psychiatry*, *158*, 403-409. https://doi.org/10.1192/bjp.158.3.403

Gillberg, C., & Wing, L. (1999). Autism: not an extremely rare disorder. *Acta Psychiatrica Scandinavica, 99*(6), 399-406. https://doi.org/10.1111/j.1600-0447.1999.tb00984.x

Gillberg, I. C., & Gillberg, C. (1989). Asperger syndrome - some epidemiological considerations: a research note. *Journal of Child Psychology and Psychiatry*, *30*, 631-638. https://doi.org/10.1111/j.1469-7610.1989.tb00275.x

Gillberg, I. C., Helles, A., Billstedt, E., & Gillberg, C. (2016). Boys with Asperger Syndrome Grow Up: Psychiatric and Neurodevelopmental Disorders 20 Years After Initial Diagnosis. *Journal of Autism and Developmental Disorders*, *46*(1), 74-82. https://doi.org/10.1007/s10803-015-2544-0

Girard, T. A., Axelrod, B. N., Patel, R., & Crawfors, J. R. (2015). Wechsler Adult Intelligence Scale – IV dyads for estimating global intelligence. *Assessment*, *22*(4), 441-448. https://doi.org/http://dx.doi.org/10.1177/1073191114551551

Graham Holmes, L., Zampella, C. J., Clements, C., McCleery, J. P., Maddox, B. B., Parish-Morris, J., Udhnani, M. D., Schultz, R. T., & Miller, J. S. (2020). A Lifespan Approach to Patient-Reported Outcomes and Quality of Life for People on the Autism Spectrum. *Autism Research*, *13*(6), 970-987. https://doi.org/10.1002/aur.2275

Guastella, A. J., & Hickie, I. B. (2016). Oxytocin Treatment, Circuitry, and Autism: A Critical Review of the Literature Placing Oxytocin Into the Autism Context. *Biological Psychiatry*, *79*(3), 234-242. https://doi.org/10.1016/j.biopsych.2015.06.028

Hadjikhani, N., Zurcher, N. R., Rogier, O., Ruest, T., Hippolyte, L., Ben-Ari, Y., & Lemonnier, E. (2015). Improving emotional face perception in autism with diuretic bumetanide: a proof-of-concept behavioral and functional brain imaging pilot study. *Autism*, *19*(2), 149-157. https://doi.org/10.1177/1362361313514141

Happe, F., & Frith, U. (2006). The weak coherence account: detail-focused cognitive style in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *36*(1), 5-25. https://doi.org/10.1007/s10803-005-0039-0

Harrison, P. L., & Oakland, T. (2008). *ABAS-II manual*. Pearson Assessment and Information AB.

Helles, A., Gillberg, C. I., Gillberg, C., & Billstedt, E. (2015). Asperger syndrome in males over two decades: stability and predictors of diagnosis. *Journal of Child Psychology and Psychiatry*, *56*(6), 711-718. https://doi.org/10.1111/jcpp.12334

Helles, A., Gillberg, I. C., Gillberg, C., & Billstedt, E. (2017). Asperger syndrome in males over two decades: Quality of life in relation to diagnostic stability and psychiatric comorbidity. *Autism*, *21*(4), 458-469. https://doi.org/10.1177/1362361316650090

Hirvikoski, T., Boman, M., Chen, Q., D'Onofrio, B. M., Mittendorfer-Rutz, E., Lichtenstein, P., Bolte, S., & Larsson, H. (2020). Individual risk and familial liability for suicide attempt and suicide in autism: a population-based study. *Psychological Medicine*, *50*(9), 1463-1474. https://doi.org/10.1017/S0033291719001405

Hirvikoski, T., Lajic, S., Jokinen, J., Renhorn, E., Trillingsgaard, A., Kadesjo, B., Gillberg, C., Borg, J., & the F. T. F. working group. (2021). Using the Five to Fifteen-collateral informant questionnaire for retrospective assessment of childhood symptoms in adults with and without autism or ADHD. *European Child and Adolescent Psychiatry*, *30*(9), 1367-1381. https://doi.org/10.1007/s00787-020-01600-w

Hirvikoski, T., Mittendorfer-Rutz, E., Boman, M., Larsson, H., Lichtenstein, P., & Bolte, S. (2016). Premature mortality in autism spectrum disorder. *The British Journal of Psychiatry*, *208*(3), 232-238. https://doi.org/10.1192/bjp.bp.114.160192

Hofvander, B., Delorme, R., Chaste, P., Nyden, A., Wentz, E., Stahlberg, O., Herbrecht, E., Stopin, A., Anckarsater, H., Gillberg, C., Råstam, M., & Leboyer, M. (2009). Psychiatric and psychosocial problems in adults with normal-intelligence autism spectrum disorders. *BMC Psychiatry*, *9*, 35. https://doi.org/10.1186/1471-244X-9-35

Hollocks, M. J., Lerh, J. W., Magiati, I., Meiser-Stedman, R., & Brugha, T. S. (2019). Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. *Psychological Medicine*, *49*(4), 559-572. https://doi.org/10.1017/S0033291718002283

Howlin, P., & Magiati, I. (2017). Autism spectrum disorder: outcomes in adulthood. *Current Opinion in Psychiatry*, *30*(2), 69-76. https://doi.org/10.1097/YCO.0000000000000308

Huang, J. S., Yang, F. C., Chien, W. C., Yeh, T. C., Chung, C. H., Tsai, C. K., Tsai, S. J., Yang, S. S., Tzeng, N. S., Chen, M. H., & Liang, C. S. (2021). Risk of substance use disorder and its associations with comorbidities and psychotropic agents in patients with autism. *JAMA Pediatrics*, *175*(2), e205371. https://doi.org/10.1001/jamapediatrics.2020.5371

Huke, V., Turk, J., Saeidi, S., Kent, A., & Morgan, J. F. (2013). Autism spectrum disorders in eating disorder populations: a systematic review. *European Eating Disorders Review*, *21*(5), 345-351. https://doi.org/10.1002/erv.2244

Johansson, R., Carlbring, P., Heedman, A., Paxling, B., & Andersson, G. (2013). Depression, anxiety and their comorbidity in the Swedish general population: point prevalence and the effect on health-related quality of life. *PeerJ – the Journal of Life & Environmental Sciences*, *1*, e98. https://doi.org/10.7717/peerj.98

Joon, P., Kumar, A., & Parle, M. (2021). What is autism? *Pharmacological Reports*, *73*(5), 1255-1264. https://doi.org/10.1007/s43440-021-00244-0

Joshi, G., Wozniak, J., Petty, C., Martelon, M. K., Fried, R., Bolfek, A., Kotte, A., Stevens, J., Furtak, S. L., Bourgeois, M., Caruso, J., Caron, A., & Biederman, J. (2013). Psychiatric comorbidity and functioning in a clinically referred population of adults with autism spectrum disorders: a comparative study. *Journal of Autism and Developmental Disorders*, *43*(6), 1314-1325. https://doi.org/10.1007/s10803-012-1679-5

Kadesjö, B., Janols, L. O., Korkman, M., Mickelsson, K., Strand, G., Trillingsgaard, A., & Gillberg, C. (2004). The FTF (Five to Fifteen): the development of a parent questionnaire for the assessment of ADHD and comorbid conditions. *European Child and Adolescent Psychiatry*, *13 Suppl 3*, 3-13. https://doi.org/10.1007/s00787-004-3002-2

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child*, *2*, 217-250.

Kendler, K. S. (2016). Phenomenology of schizophrenia and the representativeness of modern diagnostic criteria. *JAMA Psychiatry*, *73*(10), 1082-1092. https://doi.org/10.1001/jamapsychiatry.2016.1976

Kendler, K. S. (2019). The genealogy of dementia praecox I: signs and symptoms of delusional psychoses from 1880 to 1900. *Schizophrenia Bulletin*, *45*(2), 296-304. https://doi.org/10.1093/schbul/sbx147

Kendler, K. S., & Mishara, A. (2019). The prehistory of Schneider's first-rank symptoms: texts from 1810 to 1932. *Schizophrenia Bulletin*, *45*(5), 971-990. https://doi.org/10.1093/schbul/sbz047

Kent, R. G., Carrington, S. J., Le Couteur, A., Gould, J., Wing, L., Maljaars, J., Noens, I., van Berckelaer-Onnes, I., & Leekam, S. R. (2013). Diagnosing autism spectrum disorder: who will get a DSM-5 diagnosis? *Journal of Child Psychology and Psychiatry*, *54*(11), 1242-1250. https://doi.org/10.1111/jcpp.12085

Kenworthy, L., Yerys, B. E., Anthony, L. G., & Wallace, G. L. (2008). Understanding executive control in autism spectrum disorders in the lab and in the real world. *Neuropsychology Review*, *18*(4), 320-338. https://doi.org/10.1007/s11065-008-9077-7

Kincaid, D. L., Doris, M., Shannon, C., & Mulholland, C. (2017). What is the prevalence of autism spectrum disorder and ASD traits in psychosis? A systematic review. *Psychiatry Research*, *250*, 99-105. https://doi.org/10.1016/j.psychres.2017.01.017

King, M., & Bearman, P. (2009). Diagnostic change and the increased prevalence of autism. *International Journal of Epidemiology*, *38*(5), 1224-1234. https://doi.org/10.1093/ije/dyp261

Klonsky, E. D. (2011). Non-suicidal self-injury in United States adults: prevalence, sociodemographics, topography and functions. *Psychological Medicine*, *41*(9), 1981-1986. https://doi.org/10.1017/S0033291710002497

Kočovská, E., Billstedt, E., Ellefsen, A., Kampmann, H., Gillberg, I. C., Biskupstø, R., Andorsdóttir, G., Stóra, T., Minnis, H., & Gillberg, C. (2013). Autism in the Faroe Islands: diagnostic stability from childhood to early adult life. *The Scientific World Journal*, *2013*, 592371. https://doi.org/10.1155/2013/592371

Kosidou, K., Edwin, V., Magnusson, C., & Dalman, C. (2017). *Autism spectrum disorder and ADHD among children and youth in Stockholm county: prevalence in the population and those seeking care during 2011 to 2016.* Region Stockholm. https://www.ces.regionstockholm.se/globalassets/verksamheter/forskning-och-utveckling/centrum-for-epidemiologi-och-samhallsmedicin/folkhalsoguiden/rapporter-och-faktablad/ast-och-adhd-bland-barn-och-unga-i-stockholms-lan-faktablad-2017.1.pdf

Kraepelin, E. (1899). *Psychiatrie: Ein Lehrbuch für Studierende und Arzte* (6th ed., vol. 2.). von Barth Verlag.

Kranzler, H. R., Kadden, R. M., Babor, T. F., & Rounsaville, B. J. (1994). Longtitudinal, expert, all data procedure for psychiatric diagnosis in patients with psychoactive substance use disorders. *The Journal of Nervous and Mental Disease*, *182*(5), 277-283. https://doi.org/10.1097/00005053-199405000-00005

Kraper, C. K., Kenworthy, L., Popal, H., Martin, A., & Wallace, G. L. (2017). The gap between adaptive behavior and intelligence in autism persists into young adulthood and is linked to psychiatric co-morbidities. *Journal of Autism and Developmental Disorders*, *47*(10), 3007-3017. https://doi.org/10.1007/s10803-017-3213-2

Kuo, S. S., & Eack, S. M. (2020). Meta-analysis of cognitive performance in neurodevelopmental disorders during adulthood: comparisons between autism spectrum disorder and schizophrenia on the Wechsler Adult Intelligence Scales. *Frontiers in Psychiatry*, *11*, 187. https://doi.org/10.3389/fpsyt.2020.00187

Lai, M. C., Kassee, C., Besney, R., Bonato, S., Hull, L., Mandy, W., Szatmari, P., & Ameis, S. H. (2019). Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. *The Lancet Psychiatry*, *6*(10), 819-829. https://doi.org/10.1016/S2215-0366(19)30289-5

Leonard, H. C., Bernardi, M., Hill, E. L., & Henry, L. A. (2015). Executive functioning, motor difficulties, and developmental coordination disorder. *Developmental Neuropsychology*, *40*(4), 201-215. https://doi.org/10.1080/87565641.2014.997933

Lever, A. G., & Geurts, H. M. (2016). Psychiatric co-occurring symptoms and disorders in young, middle-aged, and older adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *46*(6), 1916-1930. https://doi.org/10.1007/s10803-016-2722-8

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel, D. (2012). *Neuropsychological Assessment* (5th ed.). Oxford University Press.

Linnenbank, M., Feldmann, R., Schulte-Körne, G., Beimdiek, S., & Strittmatter, E. (2021). Children with autism spectrum disorder of all ages, levels of symptom severity and general cognitive ability display low processing speed index scores warranting special educational assistance. *Journal of Autism and Developmental Disorders*, *52*(8), 3668-3675. https://doi.org/10.1007/s10803-021-05249-5

Lloyd-Richardson, E. E., Perrine, N., Dierker, L., & Kelley, M. L. (2007). Characteristics and functions of non-suicidal self-injury in a community sample of adolescents. *Psychological Medicine*, *37*(8), 1183-1192. https://doi.org/10.1017/S003329170700027X

Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S. (2012). *Autism diagnostic observation schedule: ADOS-2*. Western Psychological Services.

Lotter, V. (1966). Epidemiology of autistic conditions in young children: 1. Prevalence. *Social Psychiatry*, *1*(3), 124-135.

Lugnegård, T., Unenge Hallerbäck, M., & Gillberg, C. (2011). Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome. *Research in Developmental Disabilities*, *32*(5), 1910-1917. https://doi.org/10.1016/j.ridd.2011.03.025

Lugnegård, T., Ungenge Hallerbäck, M., & Gillberg, C. (2012). Personality disorders and autism spectrum disorders: what are the connections? *Comprehensive Psychiatry*, *53*(4), 333-340. https://doi.org/10.1016/j.comppsych.2011.05.014

Lugnegård, T., Ungenge Hallerbäck, M., & Gillberg, C. (2015). Asperger syndrome and schizophrenia: overlap of self-reported autistic traits using the Autism-spectrum Quotient (AQ). *Nordic Journal of Psychiatry*, *69*(4), 268-274. https://doi.org/10.3109/08039488.2014.972452

Lugo-Marín, J., Magán-Maganto, M., Rivero-Santana, A., Cuellar-Pompa, L., Alviani, M., Jenaro-Rio, C., Díez, E., & Canal-Bedia, R. (2019). Prevalence of psychiatric disorders in adults with autism spectrum disorder: A systematic review and meta-analysis. *Research in Autism Spectrum Disorders*, *59*, 22-33. https://doi.org/10.1016/j.rasd.2018.12.004

Lundström, S., Chang, Z., Kerekes, N., Gumpert, C. H., Råstam, M., Gillberg, C., Lichtenstein, P., & Anckarsater, H. (2011). Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults. *Psychological Medicine*, *41*(11), 2423-2433. https://doi.org/10.1017/S0033291711000377

Lundström, S. (2011). *Autistic-like traits* [Doctoral thesis, Lund University]. https://lup.lub.lu.se/record/1897931

Maddox, B. B., Trubanova, A., & White, S. W. (2017). Untended wounds: non-suicidal self-injury in adults with autism spectrum disorder. *Autism*, *21*(4), 412-422. https://doi.org/10.1177/1362361316644731

Maiano, C., Normand, C. L., Salvas, M. C., Moullec, G., & Aime, A. (2016). Prevalence of school bullying among youth with autism spectrum disorders: a systematic review and meta-analysis. *Autism Research*, *9*(6), 601-615. https://doi.org/10.1002/aur.1568

Makary, A. T., Testa, R., Tonge, B. J., Einfeld, S. L., Mohr, C., & Gray, K. M. (2015). Association between adaptive behaviour and age in adults with Down syndrome without dementia: examining the range and severity of adaptive behaviour problems. *Journal of Intellectual Disability Research*, *59*(8), 689-702. https://doi.org/10.1111/jir.12172

Marcus, L. M., Lansing, M., Andrews, C. E., & Schopler, E. (1978). Improvement of teaching effectiveness in parents of autistic children. *Journal of the American Academy of Child Psychiatry*, *17*(4), 625-639. https://doi.org/10.1016/s0002-7138(09)61016-5

McDonnell, C. G., Boan, A. D., Bradley, C. C., Seay, K. D., Charles, J. M., & Carpenter, L. A. (2019). Child maltreatment in autism spectrum disorder and intellectual disability: results from a population-based sample. *Journal of Child Psychology and Psychiatry*, *60*(5), 576-584. https://doi.org/10.1111/jcpp.12993

Mesibov, G. B., & Schopler, E. (1983). The development of community-based programs for autistic adolescents. *Children's Health Care*, *12*(1), 20-24. https://doi.org/10.1207/s15326888chc1201_3

Modabbernia, A., Velthorst, E., & Reichenberg, A. (2017). Environmental risk factors for autism: an evidence-based review of systematic reviews and meta-analyses. *Molecular Autism*, *8*, 13. https://doi.org/10.1186/s13229-017-0121-4

Moseley, R. L., Gregory, N. J., Smith, P., Allison, C., Cassidy, S., & Baron-Cohen, S. (2022). Non-suicidal self-injury and its relation to suicide through acquired capability: investigating this causal mechanism in a mainly late-diagnosed autistic sample. *Molecular Autism*, *13*(1), 45. https://doi.org/10.1186/s13229-022-00522-5

Muskens, J. B., Velders, F. P., & Staal, W. G. (2017). Medical comorbidities in children and adolescents with autism spectrum disorders and attention deficit hyperactivity disorders: a systematic review. *European Child and Adolescent Psychiatry*, *26*(9), 1093-1103. https://doi.org/10.1007/s00787-017-1020-0

National Institute for Health and Care Excellence. (2021). *Autism spectrum disorder in adults: diagnosis and management*. National Institute for Health and Care Excellence. http://www.nice.org.uk/guidance/cg142

Nishiyama, T., Suzuki, M., Adachi, K., Sumi, S., Okada, K., Kishino, H., Sakai, S., Kamio, Y., Kojima, M., Suzuki, S., & Kanne, S. M. (2014). Comprehensive comparison of self-administered questionnaires for measuring quantitative autistic traits in adults. *Journal of Autism and Developmental Disorders*, *44*(5), 993-1007. https://doi.org/10.1007/s10803-013-2020-7

Nylander, L., & Gillberg, C. (2001). Screening for autism spectrum disorders in adult psychiatric out-patients: a preliminary report. *Acta Psychiatrica Scandinavica*, *103*, 428-434. https://doi.org/10.1034/j.1600-0447.2001.00175.x

Paykel, E. S., Myers, J. K., Lindenthal, J. J., & Tanner, J. (1974). Suicidal feelings in the general population: a prevalence study. *The British Journal of Psychiatry*, *124*(582), 460-469. https://doi.org/10.1192/bjp.124.5.460

Peeters, T. (1997). *Autism: from theoretical understanding to educational intervention*. Wiley.

Posserud, M. B., Lundervold, A. J., & Gillberg, C. (2006). Autistic features in a total population of 7-9-year-old children assessed by the ASSQ (Autism Spectrum Screening Questionnaire). *Journal of Child Psychology and Psychiatry*, *47*(2), 167-175. https://doi.org/10.1111/j.1469-7610.2005.01462.x

Påhlman, M., Gillberg, C., & Himmelmann, K. (2021). Autism and attention-deficit/hyperactivity disorder in children with cerebral palsy: high prevalence rates in a population-based study. *Developmental Medicine & Child Neurology, 63*(3), 320-327. https://doi.org/10.1111/dmcn.14736

Ritvo, R. A., Ritvo, E. R., Guthrie, D., Ritvo, M. J., Hufnagel, D. H., McMahon, W., Tonge, B., Mataix-Cols, D., Jassi, A., Attwood, T., & Eloff, J. (2011). The Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R): a scale to assist the diagnosis of autism spectrum disorder in adults: an international validation study. *Journal of Autism and Developmental Disorders*, *41*(8), 1076-1089. https://doi.org/10.1007/s10803-010-1133-5

Roth, M., Isquith, P. K., & Gioia, G. A. (2005). *Behavior Rating Inventory of Executive Function - Adult version (BRIEF-A)*. Psychological Assessment Resources.

Roux, A. M., Tao, S., Marcus, S., Lushin, V., & Shea, L. L. (2022). A national profile of substance use disorder among Medicaid enrollees on the autism spectrum or with intellectual disability. *Disability and Health Journal*, *15*(2), 101289. https://doi.org/10.1016/j.dhjo.2022.101289

Roy, M., Prox-Vagedes, V., Ohlmeier, M. D., & Dillo, W. (2015). Beyond childhood: psychiatric comorbidities and social background of adults with Asperger Syndrome. *Psychiatria Danubina*, *27*(1), 50-59.

Rutter, M., Le Couteur, A., & Lord, C. (2003). *Autism Diagnostic Interview - Revised*. Western Psycholgical Services.

Ruzich, E., Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H., & Baron-Cohen, S. (2015). Measuring autistic traits in the general population: a systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*, *6*(2). https://doi.org/https://doi.org/doi:10.1186/2040-2392-6-2

Ryden, E., & Bejerot, S. (2008). Autism spectrum disorders in an adult psychiatric population. A naturalistic cross-sectional controlled study. *Clinical Neuropsychiatry*, *5*(1), 13-21.

Rydzewska, E., Hughes-McCormack, L. A., Gillberg, C., Henderson, A., MacIntyre, C., Rintoul, J., & Cooper, S. A. (2019). Prevalence of sensory impairments, physical and intellectual disabilities, and mental health in children and young people with self/proxy-reported autism: observational study of a whole country population. *Autism*, *23*(5), 1201-1209. https://doi.org/10.1177/1362361318791279

Sarovic, D. (2021). A unifying theory for autism: the pathogenetic triad as a theoretical framework. *Frontiers in Psychiatry*, *12*, 767075. https://doi.org/10.3389/fpsyt.2021.767075

Saunders, J. B., Aasland, O. G., Babor, T. F., De La Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption - II. *Addiction*, *88*, 791-804. https://doi.org/https://doi.org/10.1111/j.1360-0443.1993.tb02093.x

Schneider, K. (1939). *Psychischer Befund und Psychiatrische Diagnose*. Thieme.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G.C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry*, *59*(20).

Sparrow, S. S., Cicchetti, D., & Balla, D. A. (2005). *Vineland Adaptive Behavior Scales* (2nd ed.). NCS Pearson Inc.

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, *18*(6), 643-662. https://doi.org/10.1037/h0054651

Swedish National Board of Health and Welfare. (2022). *Guidelines for care and support for adhd and autism*. Swedish National Board of Health and Welfare. https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2022-10-8100.pdf

Takara, K., & Kondo, T. (2014). Autism spectrum disorder among first-visit depressed adult patients: diagnostic clues from backgrounds and past history. *General Hospital Psychiatry*, *36*(6), 737-742. https://doi.org/10.1016/j.genhosppsych.2014.08.004

Takei, R., Matsuo, J., Takahashi, H., Uchiyama, T., Kunugi, H., & Kamio, Y. (2014). Verification of the utility of the social responsiveness scale for adults in non-clinical and clinical adult populations in Japan. *BMC Psychiatry*, *14*, 302. https://doi.org/10.1186/s12888-014-0302-z

Taylor, M. J., Rosenqvist, M. A., Larsson, H., Gillberg, C., D'Onofrio, B. M., Lichtenstein, P., & Lundström, S. (2020). Etiology of autism spectrum disorders and autistic traits over time. *JAMA Psychiatry*, *77*(9), 936-943. https://doi.org/10.1001/jamapsychiatry.2020.0680

Tillmann, J., San Jose Caceres, A., Chatham, C. H., Crawley, D., Holt, R., Oakley, B., Banaschewski, T., Baron-Cohen, S., Bolte, S., Buitelaar, J. K., Durston, S., Ham, L., Loth, E., Simonoff, E., Spooren, W., Murphy, D. G., Charman, T., & group, E.-A. L. (2019). Investigating the factors underlying adaptive functioning in autism in the EU-AIMS Longitudinal European Autism Project. *Autism Research*, *12*(4), 645-657. https://doi.org/10.1002/aur.2081

Tromans, S., & Brugha, T. (2022). Autism epidemiology: distinguishing between identification and prevalence. *Progress in Neurology and Psychiatry*, *26*(1), 4-6. https://doi.org/10.1002/pnp.732

Tromans, S., Chester, V., Kiani, R., Alexander, R., & Brugha, T. (2018). The prevalence of autism spectrum disorders in adult psychiatric inpatients: a systematic review. *Clinical Practice & Epidemiology in Mental Health*, *14*, 177-187. https://doi.org/10.2174/1745017901814010177

Ustun, T. B., Kostanjesek, N., Chatterji, S., Rehm, J., & World Health Organization. (2010). *Measuring health and disability : manual for WHO Disability Assessment Schedule (WHODAS 2.0)*. https://apps.who.int/iris/handle/10665/43974

Van Naarden Braun, K., Christensen, D., Doernberg, N., Schieve, L., Rice, C., Wiggins, L., Schendel, D., & Yeargin-Allsopp, M. (2015). Trends in the prevalence of autism spectrum disorder, cerebral palsy, hearing loss, intellectual disability, and vision impairment, metropolitan atlanta, 1991-2010. *PLoS One*, *10*(4), e0124120. https://doi.org/10.1371/journal.pone.0124120

Velikonja, T., Fett, A. K., & Velthorst, E. (2019). Patterns of nonsocial and social cognitive functioning in adults with autism spectrum disorder: a systematic review and meta-analysis. *JAMA Psychiatry*, *76*(2), 135-151. https://doi.org/10.1001/jamapsychiatry.2018.3645

Volkmar, F. R., & McPartland, J. C. (2014). From Kanner to DSM-5: autism as an evolving diagnostic concept. *Annual Review of Clinical Psychology*, *10*, 193-212. https://doi.org/10.1146/annurev-clinpsy-032813-153710

Waern, M., Stromsten, L., Wiktorsson, S., Runeson, B., & Renberg, E. S. (2022). Overlapping patterns of suicide attempts and non-suicidal self-injuries in adults: a prospective clinical cohort study. *The Journal of Clinical Psychiatry*, *83*(6). https://doi.org/10.4088/JCP.21m14330

Wallace, G. L., Kenworthy, L., Pugliese, C. E., Popal, H. S., White, E. I., Brodsky, E., & Martin, A. (2016). Real-world executive functions in adults with autism spectrum disorder: profiles of impairment and associations with adaptive functioning and co-morbid anxiety and depression. *Journal of Autism and Developmental Disorders*, *46*(3), 1071-1083. https://doi.org/10.1007/s10803-015-2655-7

Wang, T., Shan, L., Miao, C., Xu, Z., & Jia, F. (2021). Treatment effect of Bumetanide in children with autism spectrum disorder: a systematic review and meta-analysis. *Frontiers in Psychiatry*, *12*, 751575. https://doi.org/10.3389/fpsyt.2021.751575

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale (WAIS-III)* (3rd ed.). Psychological Corporation.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale (WAIS-IV)* (4th ed.). Psychological Corporation.

Wechsler, D., Coalson, R. D., & Railford, S. E. (2008). *WAIS-IV technical and interpretive manual*. Psychological Corporation.

Weiss, J. A., Thomson, K., & Chan, L. (2014). A systematic literature review of emotion regulation measurement in individuals with autism spectrum disorder. *Autism Research*, *7*(6), 629-648. https://doi.org/10.1002/aur.1426

Wigham, S., Rodgers, J., Berney, T., Le Couteur, A., Ingham, B., & Parr, J. R. (2019). Psychometric properties of questionnaires and diagnostic measures for autism spectrum disorders in adults: a systematic review. *Autism*, *23*(2), 287-305. https://doi.org/10.1177/1362361317748245

Wing, L. (2006). *Diagnostic Interview for Social and COmmunication disorders, 11th edition (DISCO-11)*. Centre for Social and Communicative Disorders.

Wing, L., & Gould, J. (1979). Severe impairments of social and associated abnormalities in children: epidemiology and classification. *Journal of Autism and Developmental Disorders*, *9*(1), 11-29. https://doi.org/ 10.1007/BF01531288

Wolff, S. (1996). The first account of the syndrome Asperger described?. *European Child and Adolescent Psychiatry*, *5*, 119-132. https://doi.org/10.1007/BF00571671

Wolff, S. (2004). The history of autism. *European Child and Adolescent Psychiatry*, *13*(4), 201-208. https://doi.org/10.1007/s00787-004-0363-5

World Health Organization. (2004). *ICD-10: international statistical classification of diseases and related health problems: tenth revision* (2nd ed.). World Health Organization.

Xie, S., Heuvelman, H., Magnusson, C., Rai, D., Lyall, K., Newschaffer, C. J., Dalman, C., Lee, B. K., & Abel, K. (2017). Prevalence of autism spectrum disorders with and without intellectual disability by gestational age at birth in the Stockholm Youth Cohort: a register linkage study. *Paediatric and Perinatal Epidemiology*, *31*(6), 586-594. https://doi.org/10.1111/ppe.12413

Zeidan, J., Fombonne, E., Scorah, J., Ibrahim, A., Durkin, M. S., Saxena, S., Yusuf, A., Shih, A., & Elsabbagh, M. (2022). Global prevalence of autism: a systematic review update. *Autism Research, 15*(5), 778-790. https://doi.org/10.1002/aur.2696

Zimmerman, M., McDermut, W., & Mattia, J. I. (2000). Frequency of anxiety disorders in psychiatric outpatients with major depressive disorder. *American Journal of Psychiatry*, *157*(8), 1337-1340. https://doi.org/10.1176/appi.ajp.157.8.1337

Zubin, J., & Spring, B. (1977). Vulnerability - a new view of schizophrenia. *Journal of Abnormal Psychology*, *86*(2), 103-126. https://doi.org/10.1037/0021-843X.86.2.103

Åsberg Johnels, J., Yngvesson, P., Billstedt, E., Gillberg, C., Halldner, L., Råstam, M., Gustafsson, P., Selinus, E. N., Lichtenstein, P., Hellner, C., Anckarsater, H., & Lundström, S. (2021). The relationship between intelligence and global adaptive functioning in young people with or without neurodevelopmental disorders. *Psychiatry Research*, *303*, 114076. https://doi.org/10.1016/j.psychres.2021.114076