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Doctoral thesis

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Trondheim, October 2022

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Motoriske og språklige tilleggsvansker og funksjonsnivå hos barn som utredes for autismespekterforstyrrelse (ASD)

Barn med symptomer på autisme og andre utviklingsforstyrrelser representerer en stor gruppe i helsevesen og utdanningssystem. En autismespekterdiagnose forutsetter tilstedeværelse av vansker med sosial kommunikasjon, gjensidighet, og begrensede interesser og aktiviteter som medfører tydelig funksjonsnedsettelse i hverdagen. Tilleggsvansker på andre utviklingsområder er vanlig, viser seg ofte tidligere, og kan påvirke både symptombilde og hverdagsfungering, trolig også hos barn med mindre uttalte autistiske trekk som ikke får en ASD-diagnose. Hovedmålsetningen for avhandlingen var å undersøke forekomst av motoriske og språklige tilleggsvansker hos barn som er utredet for ASD, og om disse tilleggsvanskene har en sammenheng med grad av autismesymptomer og funksjonsnivå. Avhandlingen består av tre delstudier knyttet til den norske BUPgen studien, der barn som utredes i spesialisthelsetjenesten kan delta, enten de får en ASD-diagnose eller vurderes å ikke fylle diagnosekriteriene (non-ASD).

Den første studien undersøkte tidlige motoriske ferdigheter (alder for første selvstendige skritt) blant 490 barn (hvorav 376 med ASD) som var 4 til 18 år gamle ved deltagelse i BUPgen. Gjennomsnittlig gåalder (rapportert av foreldre) var betydelig senere i ASD gruppen sammenlignet med gruppen med bare autistiske trekk (non-ASD). Likevel var gåalder i begge gruppene senere sammenlignet med normer for norske barn. Videre fant vi at senere gåalder var forbundet med mer uttalte autismesymptomer, også når sammenhengen ble kontrollert for intellektuelle ferdigheter. Det var en tendens til at jenter hadde senere gåalder. Den andre studien omfattet 177 barn (hvorav 148 med ASD) i alderen 4-18 år, som hadde gjennomgått en språkkartlegging som ledd i utredningen. Vi undersøkte tidlig språkforsinkelse, nåværende språklige og sosiale ferdigheter (foreldrerapport), og mulige sammenhenger mellom disse. Tidlig språkforsinkelse var mer vanlig hos gutter og forbundet med strukturelle språkvansker (for eks. med grammatikk, språklyder eller ordenes betydning), men det var ingen forskjell i den sosiale bruken av språket (pragmatiske språkferdigheter) eller sosiale ferdigheter mellom barn med og uten tidlig språkforsinkelse. Strukturelle språkvansker var vanlig og sterkt forbundet med dårligere pragmatiske ferdigheter uavhengig av diagnosegruppe, mens de pragmatiske vanskene var mest uttalt hos barn med ASD. Den siste studien omfattet 20 barn i skolealder (hvorav 15 med ASD) som i tillegg til vanlig utredning gjennomgikk en detaljert kartlegging av motoriske, språklige og sosiale ferdigheter, samt hverdagsfungering. Vi fant at de fleste barna hadde motoriske og/eller språklige tilleggsvansker. Bedre motorikk var forbundet med bedre språklige og sosiale ferdigheter. Mange barn deltok ikke i vanlig gym på skolen eller organiserte fritidsaktiviteter.

Samlet tyder funnene våre på at motoriske og språklige tilleggsvansker er vanlig hos barn som utredes for ASD, og kan ha innvirkning på den sosiale fungeringen til barnet. Slike tilleggsvansker debuterer ofte tidlig og kan trolig bidra til å identifisere barn med ASD tidligere, men også barn med risiko for senere motoriske og språklige vansker. De bør derfor kartlegges, slik at tiltak kan tilpasses det enkelte barnets styrker, vansker og funksjonsnivå. Omfanget av slike vansker, og effekt av tiltak rettet mot motoriske og språklige ferdigheter bør undersøkes nærmere i fremtidige studier.

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List of papers

This thesis is based on the following papers, referred to in the text as Papers (studies) I-III.

Paper I (Study I):

Reindal, L., Nærland, T., Weidle, B., Lydersen, S., Andreassen, O. A., & Sund, A. M. (2020). Age of first walking and associations with symptom severity in children with suspected or diagnosed autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *50*(9), 3216–3232. https://doi.org/10.1007/s10803-019-04112-y

Paper II (Study II):

Reindal, L., Nærland, T., Weidle, B., Lydersen, S., Andreassen, O. A., & Sund, A. M. (2021). Structural and pragmatic language impairments in children evaluated for autism spectrum disorder (ASD). *Journal of Autism and Developmental Disorders*. Advance online publication. https://doi.org/10.1007/s10803-020-04853-1

Paper III (Study III):

Reindal, L., Nærland, T., Sund, A. M., Avseth Glimsdal, B., Andreassen, O. A., & Weidle, B. (2022). The co-occurrence of motor and language impairments in children evaluated for autism spectrum disorder. An explorative study from Norway. *Research in Developmental Disabilities*. Advance online publication. https://doi.org/doi:10.1016/j.ridd.2022.104256

Acronyms and abbreviations

ADHD	Attention-deficit/hyperactivity disorder
ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
AOW	Age of onset of independent walking
ASD	Autism spectrum disorder
CAMHS	Child and adolescent mental health services
CCC-2	Children's Communication Checklist Second Edition
CGAS	Children's Global Assessment Scale
DCD	Developmental coordination disorder
DCDQ'07	Developmental Coordination Disorder Questionnaire 2007
DD-CGAS	Developmental Disability-Children's Global Assessment Scale
DSM-III	*Diagnostic and Statistical Manual of Mental Disorders*, 3rd edition
DSM-IV	*Diagnostic and Statistical Manual of Mental Disorders*, 4th edition
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders*, 5th edition
ESSENCE	Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations
GCC	General Communication Composite
ICD-10	*International Classification of Diseases*, 10th Revision
ICD-11	*International Classification of Diseases*, 11th Revision
ID	Intellectual disability
IQ	Intelligence quotient
MABC-2	Movement Assessment Battery for Children – 2
NDD	Neurodevelopmental disorder
NVIQ	Nonverbal intelligence quotient
PDD	Pervasive developmental disorder
PDD-NOS	Pervasive developmental disorder-not otherwise specified
PLI	Pragmatic language impairment
RRBI	Restricted and repetitive behaviour and interests
SCQ	Social Communication Questionnaire
SLI	Specific language impairment

SRS	Social Responsiveness Scale
TD	Typically developing
VABS	Vineland Adaptive Behavior Scales
WHO	World Health Organization

Summary

Autism spectrum disorder (ASD), a common neurodevelopmental disorder (NDD), is characterised by the presence of core symptoms sufficiently severe to cause functional impairment but otherwise highly heterogenous. The core social deficiency is now considered a continuous trait with no natural cut-off between ASD and subthreshold autistic symptoms. Although they do not meet the diagnostic criteria for ASD, such traits are found to overlap with diagnosed ASD genetically and to present with the same comorbidities and functional impairments, including an increased risk for motor and language difficulties. Developing a better understanding of how co-occurring motor and language deficits may interact with core ASD symptoms to impact overall functioning is important for adapting diagnostic and clinical services accordingly. The variable and often early presentations of these symptoms also represent potential markers of subgroups within the autism spectrum.

The overall aim of this thesis was to study co-occurring motor and language impairments and their potential relationship with symptom severity and functional impairment in children with a broad range of autistic symptoms through a dimensional approach, that is, distinguishing the children as diagnosed with ASD or diagnosed with subthreshold autistic symptoms (non-ASD). Participants were recruited from an ongoing large multisite study on NDDs in Norway (BUPgen), in which children were eligible to participate if a suspicion of ASD led to their being evaluated for ASD by public specialist health services. While the first and second studies presented in this thesis (Papers I and II) were based on clinical data from the main study (N = 490 and N = 177, respectively; 4–18 years), the third study (Paper III) was based on an in-depth evaluation of motor, language and overall functioning collected from a local subsample (N = 20; 6–18 years). The categorical approach (ASD/non-ASD) used in recruitment and group comparisons was supplemented by a dimensional approach in assessments and analyses whereby ASD symptomatology, core developmental skills and functional impairment were examined as continuous traits within the whole group of children with autistic symptoms, regardless of diagnostic category. Results for both groups were compared to norms for typically developing Norwegian children.

The first study involved an investigation of early motor skills (age of onset of independent walking [AOW]), as well as the relationship between AOW and severity of autistic symptoms with different measures (Autism Diagnostic Interview-Revised [ADI-R],

Social Communication Questionnaire [SCQ] and Social Responsiveness Scale [SRS]). Potential sex differences were also investigated. While the AOW was found to be more delayed in children diagnosed with ASD compared to children with subthreshold symptoms, significant delays were found in both groups compared to population norms. Moreover, AOW was associated with the severity of core ASD symptoms (ADI-R, SCQ), even after adjustment for cognitive abilities.

The second study investigated the extent of and relationship between early language delay (non-attainment of phrase speech at two years of age), current language deficits (the Children's Communication Checklist Second Edition [CCC-2]) and social impairment (SRS). While early language delays were more common among males and associated with structural language deficits, pragmatic language and social skills did not differ significantly between children with and without language delay. Structural language deficits were common and strongly associated with reduced pragmatic competence regardless of diagnostic group (ASD/non-ASD), while pragmatic impairments were most profound in children with ASD.

The aim of the third study was to provide a more detailed skill profile of school-aged children evaluated for ASD and to explore the co-occurrence and potential impact of motor and language impairments on overall functioning. Therefore, a standard clinical evaluation was extended with measures on current motor (Developmental Coordination Disorder Questionnaire 2007 [DCDQ'07], Movement Assessment Battery for Children – 2 [MABC-2]), language (CCC-2) and social skills (SRS), as well as overall functional impairment (Developmental Disability-Children's Global Assessment Scale [DD-CGAS]). We found that most children had motor and/or structural language deficits in addition to their social impairments. Furthermore, better motor performance was associated with better structural language and social skills. Functional impairment was associated with core ASD symptoms. In addition, limited participation in physical education and out-of-school activities was common.

Taken together, these results suggest that motor and language deficits are common and under-recognised. They often present early and should be anticipated and assessed when evaluating children for suspected ASD. These deficits may need specific interventions that complement those targeting social skill deficits and other ASD core symptoms.

1. Introduction

1.1 Motivation and rationale

> *People don't realize [that] the major problem that nobody ever sees or realizes is how much conscious thinking we have to do just to function. Walking takes thinking. So if I am walking and you ask me a question I could trip or I could mess up the sentence and put the wrong word in. Or have to stop and say, 'what did you say?' I can walk with my girl friend down the street and carry on a conversation as long as she is right there but I have to look down at the sidewalk. I have to keep track of where the sidewalk is and where any obstacles are and all that stuff and sometimes if I have to keep walking and I feel like I am going to blow any second I make sure the path is clear ahead of me and close my eyes and continue walking.*
>
> Female with Asperger syndrome, cited in a study by Robledo et al. (2012, p.9).

In this thesis, the co-occurrence of motor and language impairments in children evaluated for autism spectrum disorder (ASD) was studied to explore their potential relationship to the core ASD characteristics and functional impairment.

My professional journey through paediatrics, general practice and, more recently, child and adolescent psychiatry has provided me with valuable knowledge regarding children's typical development and panorama of medical, neurological and psychiatric disorders. What this journey did not equip me with, however, was a common framework for understanding the complexity of symptoms and impairments present in so many children who have what we now label a 'neurodevelopmental disorder' (NDD; American Psychiatric Association, 2013). As a clinician, I faced a confusing and frustrating overlap of symptoms and behaviours, crossing diagnostic boundaries and levels of service. Hearing families express their apprehensions regarding deviant development and the potential presence of a disorder, as well as the perceived need among these children and their families to be understood and provided with necessary information and support to master their everyday challenges, made a deep impression on me. These experiences also left me with a concern regarding how to organise and tailor assessments and services to fit these children's perceived needs, and more importantly, how to ensure that the right services are available to those who need them, regardless of diagnostic category.

This project was made possible for me by the opportunity to collaborate with BUPgen, a Norwegian multisite study on NDDs, in which children are eligible to participate if a suspicion of ASD has been raised by local or specialist health services. In this study, children diagnosed with ASD, as well as children with symptoms not considered to meet the diagnostic criteria for ASD, are eligible for participation, from both child habilitation services and child and adolescent mental health services (CAMHS). As such, children evaluated for suspected ASD came to be the lens through which to explore the following question: Can the assessment of less prominent co-occurring difficulties, in addition to the core ASD symptoms, provide insight into factors of importance for functional impairment and thereby contribute to earlier identification of and more targeted interventions for those in need of support?

1.2 Theoretical framework

Delayed or deviant development is a major concern for affected children and their families but also represents a significant challenge for those who provide health and educational services. Children's developmental difficulties are at the interface between multiple professions, medical disciplines and services, each of which may adopt unique approaches to conceptualising them and may use different terminology and criteria to decide upon necessary interventions and services.

Child development is considered "a *dynamic* process of growth, transformation, learning and acquisition of abilities to respond and adapt to the environment in a planned, organized and independent manner" (Sharma & Cockerill, 2014, p. 67). This process is driven and refined by interactions between biological and environmental influences, causing considerable variability in children's developmental outcomes (Sharma & Cockerill, 2014). By relating functional activities to chronological age in a child's development, the main domains of development were delineated by Gesell early in the 20th century as gross and fine *motor*, visual–motor problem-solving (*nonverbal cognition*), expressive and receptive *language*, *social* and self-help (*adaptive*) skills (Accardo et al., 2008; Burton & Miller, 1998). While the core aspect of each domain has a distinct neuropsychological basis, these domains overlap and are closely interconnected in their development and functional expression. Variations within and between the different domains over time provide patterns that, at different ages, may suggest or confirm the presence of specific developmental disorders

(Accardo et al., 2008). Developmental milestones reflect the expected 'typical' development within each domain, although the individual milestones "achieve importance only as part of a larger picture" (Accardo et al., 2008, p. 8). Helping families and involved professionals to understand and interpret the overall pattern of deficits and what influences that pattern represents a major goal of *neurodevelopmental paediatrics* (Accardo et al., 2008).

The field of *developmental psychopathology* was formalised by Sroufe and Rutter (1984) and is considered a "conceptual approach that involves a set of research methods that capitalize on developmental and psychopathological variations to ask questions about mechanisms and processes" (Rutter, 2013, p.1201). Developmental psychopathology differs from developmental psychology in its priorities and differs from abnormal psychology and psychiatry in having a broader scope than to describe, differentiate and treat disordered behaviour (Sroufe & Rutter, 1984). Rather than studying any particular age or stage of development, developmental psychopathology is concerned with *how* developmental processes that underlie both continuity and change unfold (Garber & Bradshaw, 2020). Continuity, a central principle of developmental psychopathology, refers to the distinction between normal and abnormal, as well as to recognising the coherence of disorders from early to subsequent development and changes across the lifespan (Garber & Bradshaw, 2020).

The failure to achieve developmental milestones reflects complex developmental interactions (Accardo et al., 2008). While *delay* refers to a significant lag in one or more developmental domains, and *dissociation* to a difference in developmental rates between different domains, *deviance* implies a lack of sequencing or an inversion of the expected developmental pattern (Accardo et al., 2008). The mapping of these processes, as well as of the symptoms of excess, onto the core developmental domains provides a temporal pattern or *neurodevelopmental profile* (Accardo et al., 2008; Moreno-De-Luca et al., 2013). Although the observed pattern may conform to one or more categorical diagnoses, the primary diagnosis is often merely a marker for a larger underlying continuum of central nervous system dysfunction, with co-occurring deficits revealing more information about the severity of the disability and the likelihood of various outcomes (Accardo et al., 2008). Thus, use of a combination of quantitative (dimensional) trait measures that reflect the main developmental skill domains has been suggested to provide a more detailed profile of a child's strengths and difficulties to guide the determination of treatment and interventions (Accardo et al., 2008; Moreno-De-Luca et al., 2013).

Although current medical models, like the biopsychosocial model (Engel, 1977), rely on comprehensive assessments that consider the child's physical, behavioural and developmental status, they still have shortcomings, such as the lack of measures of adaptive and functional skills and the lack of consideration of potential changes across the lifespan. Furthermore, each disorder or deficit is often considered as a separate impairment, not recognising that many children may have an underlying neurodevelopmental impairment (Msall & Msall, 2007). More recently, interest in *functional impairment* has been sparked by an emerging body of literature suggesting that symptoms and functional impairment appear to be separate concepts that both need to be considered when making diagnostic decisions and evaluating treatment responses (Goldstein & Naglieri, 2016).

1.3 Autism spectrum disorder (ASD)

The main topic of this thesis is autism spectrum disorder (ASD). ASD is the collective term for an increasingly more common group of neurodevelopmental conditions characterised by persistent impairments in reciprocal social communication and interaction, along with restricted and repetitive patterns of behaviour and interests (RRBIs; American Psychiatric Association, 2013). Having an ASD diagnosis is associated with substantial and lasting functional impairments in everyday life, poorer lifetime outcomes and increased mortality (Lyall et al., 2017). Children and adolescents with ASD often have service needs in behavioural, educational, health, leisure, family support and other areas (Hyman et al., 2020). Accordingly, the associated burdens, including financial burdens, for affected individuals, their families and society are considerable (Lyall et al., 2017).

1.3.1 History and classification

The term 'autism' was probably first put into formal use in medicine more than 100 years ago by Eugene Bleuler, a Swiss psychiatrist who used the term to describe the tendency of patients with schizophrenia to withdraw into their own world (Bleuler, 1911). The term re-emerged in the first clinical accounts of what we now recognise as ASD, chronicled by Leo Kanner in "Autistic Disturbance of Affective Contact" (Kanner, 1943). Kanner described the characteristics of eight boys and three girls presenting with early onset difficulties relating socially to other people, as well as limited and stereotyped interests and behaviours. Kanner

considered autism as a childhood disorder, distinct from other disorders as well as from typical development. However, his use of the term autism caused confusion, leading many clinicians to view autism as a childhood psychosis or a form of schizophrenia (Jackson & Volkmar, 2019). As research evolved, mounting evidence suggested that autism was a brain-based, strongly genetic disorder, different from childhood schizophrenia in terms of family history, onset, clinical presentation and course (Jackson & Volkmar, 2019).

Autism was included as an official diagnosis (as 'infantile autism') for the first time in the third version of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) published in 1980, under the generic term 'pervasive developmental disorder' (PDD). At this point the concept of autism had changed from the description of a symptom as per Bleuler to the description of a behavioural phenotype broadly matching that of the severe cases described by Kanner in 1943 (Happé & Frith, 2020; Jackson & Volkmar, 2019). Cases of 'idiopathic' autism were commonly viewed as true autism cases and distinct from cases of autism that were 'syndromic', that is, secondary to a known neural or genetic basis (Mazurek, 2016). Scientists searched for a single cause. From the start, however, the behavioural heterogeneity was clearly recognised; even the cases Kanner described showed a wide range of levels of motor, language, intellectual and adaptive functioning (Happé & Frith, 2020).

One year after Kanner published his paper on autism, Hans Asperger (1944) described four boys who resembled those reported by Kanner, except these four boys were more advanced in terms of verbal and cognitive abilities. Asperger's work received little attention until Lorna Wing described the clinical features of a series of cases involving children with Asperger syndrome (Wing, 1981a). Wing also delineated the classical triad of autism (consisting of impairments in social interaction, communication and imagination) and introduced the notion of autism symptomatology as a 'spectrum' (Wing, 1981b). The entrance of Asperger syndrome as a subcategory within the group of pervasive developmental disorders in the *International Classification of Diseases, 10th Revision* (ICD-10; World Health Organization, 1992) and the *DSM-IV* (American Psychiatric Association, 1994) provided a classification for individuals who showed the clinical manifestations of ASD, albeit with a later age of onset and no intellectual or language delay (Mazurek, 2016). Thus, the diagnostic boundaries and the number of individuals to whom an autism spectrum diagnosis applied were broadened.

ASD is currently defined in terms of behaviour. The *International Classification of Diseases* (ICD; World Health Organization) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM; American Psychiatric Association) are the two main diagnostic frameworks that provide definitions of the condition, core symptoms with which to differentiate ASD from other disorders and the threshold for diagnosis. In the most recent revisions of these classification systems – the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (DSM-5; American Psychiatric Association, 2013) and the *International Classification of Diseases, 11th Revision* (ICD-11; World Health Organization, 2019) – the original triad of impairments described by Lorna Wing has been reduced to two core deficits: (1) social communication/social interaction and (2) restricted and repetitive patterns of interests, behaviour or activities. Furthermore, an overarching diagnosis, ASD, has replaced the term pervasive developmental disorder with its subcategories due to their poor inter-rater reliability and instability over time (Lord & Bishop, 2015).

The *DSM-5* is currently used by clinicians and researchers in many parts of the world; the more recently published *ICD-11* is awaiting implementation, so at the time of writing the *ICD-10* is still used when evaluating children for ASD in Norway. The *ICD-10* refers to the same core characteristics of ASD as those identified in the *DSM-5*, although under the term pervasive developmental disorders (ICD-10 code F84), including the subcategories childhood autism (F84.0), atypical autism (F84.1), other childhood disintegrative disorder (F84.3), Asperger syndrome (F84.5) and pervasive developmental disorder-unspecified[1] (F84.9). For consistency with the *DSM-5* and the *ICD-11*, I use the term ASD in this thesis to refer to all these subcategories in the *ICD-10*. For simplicity, and to reflect varying language preferences among affected individuals, the terms 'ASD' and 'autism' are used interchangeably (Kenny et al., 2016). For the same reason, this thesis also includes both identify-first (e.g. autistic person) and person-first (e.g. person with autism) language.

[1] The terminology used for the subcategories in *DSM-IV* and *ICD-10* varies. *DSM-IV* uses the term 'pervasive developmental disorder-not otherwise specified' (PDD-NOS). For simplicity, we also use the term PDD-NOS when referring to F84.9 in *ICD-10*.

1.3.2 Symptom presentation, assessment and diagnosis

As implied by the term spectrum, ASD is a heterogenous disorder, meaning that its clinical presentation or phenotype may vary but converges on the same core characteristics regardless of age, culture, ethnicity or socio-economic group (American Psychiatric Association, 2013; Lord et al., 2018). To meet the diagnostic criteria for ASD, core symptoms must be present to a certain extent from early childhood and must cause clinically significant impairment across functional domains (American Psychiatric Association, 2013).

Individuals with ASD differ in the timing and type of symptom onset (Grzadzinski et al., 2013). Depending on the child's age, cognitive and language abilities, social communication deficits may come to early attention as language deficits, ranging from complete lack of spoken language through language delays, or poor comprehension of speech. Older children may have apparently intact formal language skills, or they may use a limited or overly literal language (American Psychiatric Association, 2013; Jones et al., 2014), while having more pronounced difficulties with the use of spoken language, eye contact or gestures for reciprocal social communication (American Psychiatric Association, 2013). In adolescents with no intellectual disability or language delay, the core social deficits may be evident as difficulties interpreting and responding to more complex social cues or in novel or unsupported situations (American Psychiatric Association, 2013). Individuals with ASD may also have a limited understanding of contextually appropriate behaviour or of the social use of language (e.g. irony, white lies). Sensory sensitivities, inflexible adherence to routines or rituals, resistance to change and limited interests and preoccupations further impede everyday activities and functioning (American Psychiatric Association, 2013; Jones et al., 2014).

A necessary but not sufficient component for assigning an accurate diagnosis involves assessing symptom presentations in relation to prevailing diagnostic criteria as reliably as possible. This has proven difficult for children with ASD (Constantino & Charman, 2016). Although core ASD symptoms typically present early in a child's development, they can be masked in some contexts, or perhaps as a result of other co-occurring medical or neurodevelopmental conditions, compensations and supports (American Psychiatric Association, 2013; Hyman et al., 2020). Thus, some children with milder symptoms may not be identified with impairing symptoms until they reach school age, when increasingly complex social environments expose their underlying challenges (Hyman et al., 2020; Lord et

al., 2018). In addition to heterogeneity across individuals, the severity of autistic symptoms may also be influenced by other comorbidities and contextual factors and may vary according to age (Hus et al., 2013).

As important predictors of outcomes, the *DSM-5* has introduced *specifiers* to be noted along with the diagnosis, of ASD symptom severity, accompanying language impairment, intellectual impairment and determination of whether the disorder is associated with a known medical or genetic condition (American Psychiatric Association, 2013). Another substantial change is the opportunity to assign comorbid diagnoses (e.g. attention-deficit/hyperactivity disorder [ADHD]) when ample evidence for comorbidity exists (Constantino & Charman, 2016). Current best practices recommend that ASD diagnoses are based on expert clinical judgement informed by a comprehensive assessment that includes historical information and accounts of the child's behaviour and functioning obtained from multiple sources, using a combination of semi-structured interviews and direct observations, guided by, for example, the Autism Diagnostic Interview Revised (ADI-R; Lord et al., 1994; Rutter et al., 2003b) and the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) (Constantino & Charman, 2016; Hyman et al., 2020; Lord et al., 2018). A clinician trained to diagnose autism and related conditions integrates all this information to determine whether the criteria for ASD are met and the symptoms are not better explained by another condition. This is a critical part of the diagnostic process that inevitably rests on some personal judgement.

1.3.3 ASD versus subthreshold autistic traits

Already in the earliest descriptions of autism (Asperger, 1944; Kanner, 1943), unusual social behaviour or more subtle autistic traits were noted that extended beyond the diagnosis to close relatives of children diagnosed with ASD. Later, these traits were examined to allow for assessment and estimation of genetic liability, followed by more systematic studies, from which the term 'broader autism phenotype' arose (Pickles et al., 2000; Piven et al., 1997; Rubenstein & Chawla, 2018). The broader autism phenotype refers to the social, language and cognitive characteristics of relatives of an individual diagnosed with ASD (Rubenstein & Chawla, 2018). With the development of continuous measures of these traits, such as the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), the broader autism phenotype profile was further extended beyond close relatives and into the general population, revealing that the core social behaviours of ASD are continuously distributed,

with no evidence of a sharp dividing line between clinical ASD and the broader population (Constantino, 2011; Kamio et al., 2013a). Diagnostic practices employed in clinical cases involving impairing autistic traits when the full diagnostic criteria for ASD are not met likely vary, both within and across countries. The *DSM-IV*'s PDD-not otherwise specified and the *ICD-10*'s atypical autism and PDD-unspecified categories may all have provided a diagnostic home for some children. However, this category was removed from the DSM classifications and, thus, does not appear in the *DSM-5*, emphasising the requirement to meet diagnostic criteria to receive an ASD diagnosis (Volkmar & McPartland, 2014).

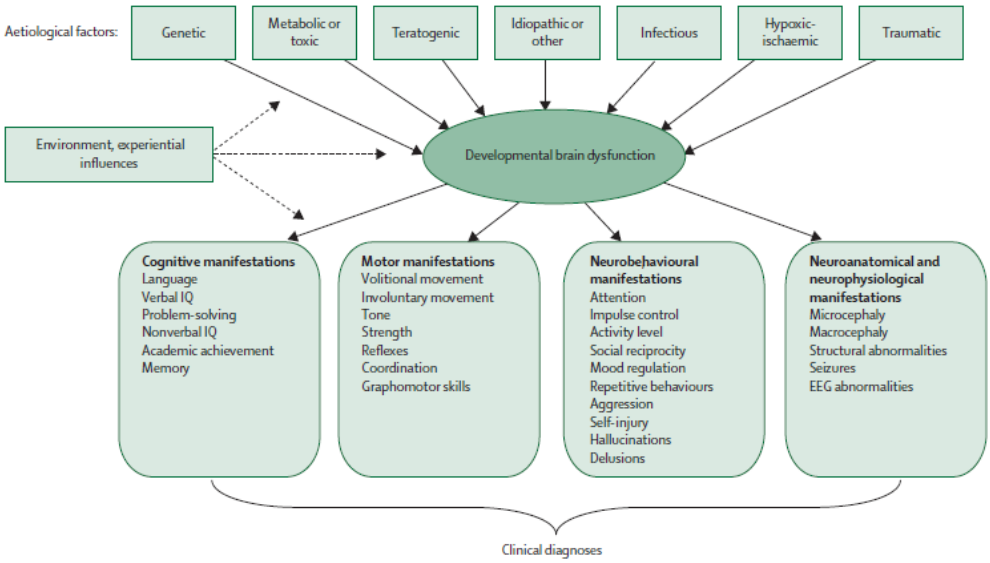
1.3.4 ASD as a neurodevelopmental disorder

The term neurodevelopmental disorder (NDD) was first introduced into the diagnostic classification system with the *DSM-5*, which states that NDDs apply to a group of childhood onset impairments affecting core developmental domains that are associated with altered architecture, maturation and functioning of the developing central nervous system (Thapar et al., 2017). In addition to ASD, the *DSM-5* includes intellectual disabilities (IDs), communication disorders, ADHD, specific learning disorders and motor disorders, such as developmental coordination disorder (DCD) and tic disorders, under this category.

Neurodevelopmental disorders are common childhood problems (Gillberg, 2010; Zablotsky et al., 2019) that share important features, such as being multifactorial in origin, being more common among boys and being associated with impairments that generally last into adult age (Stein et al., 2020). Results from epidemiological as well as genetic studies suggest that NDDs commonly overlap, not only at the symptomatic level but also at the genetic, neurobiological and environmental levels (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2019; Ghirardi et al., 2021; Moreno-De-Luca et al., 2013). Moreno-De-Luca et al. (2013) argued that "rather than being considered as causally and pathophysiologically distinct, neurodevelopmental disorders should be thought of as different patterns of symptoms or impairments of a common underlying neurodevelopmental continuum" (Moreno-De-Luca et al., 2013, p. 406, see Figure 1).

Figure 1

Model of Developmental Brain Dysfunction.



Note. Model of developmental brain dysfunction. Adapted from Myers (2013). Reprinted from *Lancet Neurology, 12*(4), Moreno-De-Luca, A., Myers, S. M., Challman, T. D., Moreno-De-Luca, D., Evans, D. W., & Ledbetter, D. H. "Developmental brain dysfunction: revival and expansion of old concepts based on new genetic evidence", 406-414., Copyright (2013), with permission from Elsevier.

Acknowledging this complexity, particularly in early childhood, Swedish child psychiatrist Christopher Gillberg proposed the acronym ESSENCE (early symptomatic syndromes eliciting neurodevelopmental clinical examinations), an overarching term describing the co-occurrence in early childhood of significant impairments in multiple areas of functioning that encompass many clinical diagnoses (Gillberg, 2010). Although discerning NDDs at the age of presentation is often difficult, evidence has shown that, regardless of the final diagnosis, early intervention for the specific impairments is usually called for as soon as a problem is recognised (Gillberg, 2010). Considering ASD as a NDD emphasises the need to take a broader perspective beyond core ASD symptoms and to anticipate co-occurring, often early presenting deficits in other developmental domains when evaluating children presenting with autistic symptoms (Thapar & Rutter, 2015).

1.3.5 Aetiology and risk factors

Most in the field now agree that ASD is not a single disorder with a single cause. Rather, ASD, or 'the autisms', is considered a group of multifactorially determined conditions that, despite sharing core symptoms, otherwise are extremely heterogenous (Gillberg et al., 2019). While strongly genetic in origin, environmental, developmental and epigenetic factors may act in concert with genetic vulnerabilities to influence both the emergence and subsequent developmental course of ASD (Bourgeron, 2016; Franke et al., 2021; Lyall et al., 2017).

The genetic structure for ASD and autistic traits is shaped by a complex interplay between rare genetic variants of high penetrance and common genetic variants of small effect in a way that likely differs from one individual to another (Bourgeron, 2016; Lyall et al., 2017). Rare variants include inherited and *de novo* mutations and copy number variations identified in a minority (10–25%) of cases, some of which are linked to known genetic syndromes, such as fragile X syndrome and tuberous sclerosis (Bourgeron, 2016; Gillberg et al., 2019; Lyall et al., 2017). The remaining majority of cases are associated with the added effect of numerous common genetic variants, an effect that is currently being extensively studied through *polygenic scores* that seek to operationalise the individual genetic load (Gillberg et al., 2019). These variants are also thought to be shared, at least in part, with other neurodevelopmental and psychiatric disorders (Grove et al., 2019; Lyall et al., 2017).

Systematic reviews and meta-analyses suggest a number of *prenatal* (e.g. parental age), *perinatal* (e.g. preterm birth, small- or large-size-for-gestation, infections), *maternal* (e.g. infections, immune factors, medication, prenatal nutrients, substance use) and *postnatal* (infections) environmental risk factors for ASD (Gillberg et al., 2019; Lyall et al., 2017). Although the neural mechanisms underlying core ASD impairments remain unknown, recent work in genetics, neurobiology, neuroimaging and neuroanatomy has provided some insights. This includes reports of early brain overgrowth, changes in functional connectivity and anatomic differences in brain structures, such as in the cerebral cortex and the cerebellum (Lyall et al., 2017). Different genetic risk variants linked to ASD also seem to converge in a limited number of biological pathways, such as chromatin remodelling, synaptic function and neuronal signalling and development (Bourgeron, 2016; Gillberg et al., 2019; Lyall et al., 2017).

1.3.6 Epidemiology

Originally considered a rare childhood condition with a prevalence estimate of approximately 4 in 10,000 (Lotter, 1966), ASD is now one of the most common childhood onset NDDs (Zwaigenbaum & Penner, 2018). A review published in 2015 estimated the global ASD prevalence to be about 0.8% (Baxter et al., 2015). A more recent estimate of the prevalence in developed countries was 1.5% (Lyall et al., 2017). Over the prior few years, the increase in the reported prevalence has continued, with 1.9% of all U.S. children identified with ASD in 2016 (Maenner et al., 2020).

Not long before this research project started, Surén et al. (2013) had published an overview of the prevalence of ASD and other neurologic and developmental disorders in Norway, providing information that was not previously known. The average nationwide prevalence for ASD in children 6–12 years old was 0.6%, varying between counties from 0.3% to 1.5%. The large difference was considered to reflect variations in diagnostic practices (Surén et al., 2013). In Sweden, an excessive focus on the ASD *diagnosis* rather than on the actual *functioning* of the individual was suggested as possibly having contributed to an observed increase in registered prevalence (Gillberg & Fernell, 2014), while also contributing to the risk of overlooking coexisting disorders that, on their own, may be better predictors of support needs than the autism (Gillberg & Fernell, 2014). Later, increasing prevalence has also been documented in Norway, where the most recent estimates suggest that by the age of eight, 1.1% of boys and 0.3% of girls have been diagnosed with ASD (Surén et al., 2019a). Rather than reflecting a true rise in prevalence, much (or perhaps most) of the increase in ASD prevalence rates are currently assumed to reflect improved awareness and changes in referral, ascertainment and diagnostic practices (Lord et al., 2018; Lundström et al., 2021). While the under-diagnosis of autism has long been a concern, some have cautioned that autism now may be over-diagnosed in some countries (Arvidsson et al., 2018; Lundstrom et al., 2015).

1.3.7 Developmental course

While core ASD symptoms are often recognised during a child's second year of life, they may be evident earlier than 12 months if developmental delays are severe, or they may be noted considerably later than the second year if symptoms are more subtle (American Psychiatric Association, 2013). Prospective studies of high-risk infants during their first year

have suggested the emergence of an *ASD prodrome*, comprising motor deficits, reduced attention and emotional regulation, prior to the development of core ASD symptoms (see Zwaigenbaum & Penner, 2018 for a review). During the second year and after, atypical developmental trajectories with progressive reduction in age-appropriate social behaviours continue to evolve (Zwaigenbaum & Penner, 2018). Recent investigations suggest that regressive forms of onset with declining developmental skills are common but may be under-reported (Ozonoff et al., 2018). While individual trajectories and outcomes are highly variable, learning and compensation typically continue with developmental gains in at least some areas, although not at levels that are commensurate with those of typically developing (TD) peers (American Psychiatric Association, 2013; Howlin, 2021; Klin et al., 2007; Simonoff et al., 2020).

1.3.8 Sex differences

Despite increased recognition of ASD in general, several authors have raised concerns that ASD may present differently in girls, with the risk of under-recognition and more girls failing to receive services from which they may benefit (e.g., Dworzynski et al., 2012; Kopp & Gillberg, 1992). In ASD, the male-to-female ratio is generally considered to be 4–5:1, lower in individuals with ID and higher at the high-functioning end (Lai et al., 2015). As such, when this study was being planned, interest in understanding possible gender and sex differences in ASD was increasing. Reviewing literature current at the time, Dworzynski et al. (2012) found that cognitively able girls with no behavioural problems were less likely than their male counterparts to meet the diagnostic criteria for ASD at equivalently high levels of autistic symptoms or traits. Among girls diagnosed with ASD, Lai et al. (2015) reported more concurrent neurological abnormalities, less RRBIs and poorer cognitive and adaptive functioning than among boys diagnosed with the disorder. This was linked to a greater load of genetic variants associated with autism in these girls, suggesting a genetic 'female protective effect' or an elevated threshold to manifest clinical-level ASD in girls (Kirkovski et al., 2013; Robinson et al., 2013).

Findings suggested that, at the high-functioning end of the spectrum, females with ASD were differently rather than more severely affected compared to males with ASD (Lai et al., 2015). Others described a phenomenon whereby affected females expressed a prominent interest in and imitation of social situations and interactions to an extent reminiscent of

RRBIs that (somewhat counterintuitively) may have masked their social deficits (Kopp & Gillberg, 1992). The high male-to-female ratio in ASD was considered to reflect, at least in part, a gender bias in the diagnostic instruments and criteria used or in the way these criteria were applied to recognise ASD in clinical settings (Kirkovski et al., 2013; Lai et al., 2015). Furthermore, results obtained by directly comparing males and females with ASD may have been clouded by potential normative sex differences, as TD girls and boys may differ across multiple levels (Lai et al., 2015). Reflecting the knowledge base at the time it was published, the *DSM-5* notes gender differences related to autism but does not clearly outline the distinguishing factors (American Psychiatric Association, 2013).

1.3.9 Interventions and services

ASD is now considered a lifelong condition (Happé & Frith, 2020). Known or likely aetiologies are increasingly present (in about 25% of cases), most of which currently cannot be subjected to intervention. Still, a wide range of services and interventions are available that may prove beneficial for affected individuals and their families (Hyman et al., 2020; Lai et al., 2020). Traditionally, these have focused on helping ASD individuals to develop deficient skills and acquire adaptive skills to facilitate their functional independence, reducing unwanted behaviours while implementing autism-friendly environments and promoting communication and daily functioning in school, at work and at home (Hyman et al., 2020). Ideally, treatment strategies should be individualised and developmentally appropriate, meaning they must be tailored to the child's age, developmental level and individual strengths and difficulties (Hyman et al., 2020).

Overall, the evidence base for most ASD interventions is weak, with only a few being sufficiently endorsed (Hyman et al., 2020; Lai et al., 2020). Major methodological challenges remain to identify the key elements of effective interventions, and how to obtain positive distal outcomes outside research settings (Lai et al., 2020; Lord et al., 2022). At present, interventions with the strongest evidence base for preschool- and school-aged children with ASD are behavioural, developmental and/or educational (Hyman et al., 2020; Lai et al., 2020; Lord et al., 2022). Consensus is also developing on the benefits of other intervention techniques, including the use of positive reinforcement, employing visual materials to support behavioural expectations and matching level of difficulty in language and play to the child's ability (Lord et al., 2022). However, considerable variation exists in the availability of

interventions, both in Norway (NOU 2020:1) and internationally (Hyman et al., 2020; Lord et al., 2022).

Although no evidence-based effective pharmacological options are available to alleviate the core deficits of ASD, pharmacological treatment may be indicated in the case of co-occurring ADHD, anxiety/depression disorder or other problem behaviours or symptoms causing significant impairments (e.g. sleep disturbances, aggression) if behavioural interventions are insufficient (Hyman et al., 2020; Lai et al., 2020; Lord et al., 2022). For school-aged children with ASD, several short-term targeted interventions, either directly with the child or with parents, address common co-occurring difficulties (e.g. behavioural problems, anxiety, sleep problems) with proven evidence of efficacy (Lord et al., 2022). Specific therapies, such as speech and language therapy, physical therapy and occupational therapy may also be offered when evidence supports co-occurring language or motor impairments. A variety of techniques are used in such contexts, with at least clinical consensus on the value of many, although the evidence base, particularly for motor interventions in ASD, is currently limited (Lord et al., 2022)

1.4 Co-occurring difficulties and comorbidities

To accurately assess symptoms and differentiate ASD from other conditions, clinicians must be able to distinguish between core ASD symptoms, symptoms solely attributed to other conditions and symptoms that are closely related to but not considered core characteristics of ASD, which may overlap with other conditions (Cervantes & Jang, 2016). “Comorbidity refers to the situation in which two or more separate and independent disorders are present in the same person. This could be either at the same time or it could be sequential over time” (Thapar & Rutter, 2015, p. 33). Notably, this is not the same as the *co-occurrence* of different symptom patterns. Although reasonably sound validity exists for many diagnoses (including ASD), apparent comorbidity may arise if disorders are not independent in terms of risk factors and underlying correlates (Thapar & Rutter, 2015).

ASD is commonly accompanied by other co-occurring difficulties that, although not part of the diagnostic criteria, still may impact everyday functioning and require modifications of intervention strategies (Lord et al., 2018). They may also impact the presentation and recognition of autism symptoms (Havdahl et al., 2016), with the risk of

delaying or masking an ASD diagnosis (Levy et al., 2010). The *DSM-5* has recognised this complexity by allowing multiple diagnoses. Furthermore, clinical specifiers of cognitive and language levels, as well as the presence of medical and genetic conditions that are not specific to ASD, are also noted along with the ASD diagnosis (American Psychiatric Association, 2013). Whether a better characterisation of core symptoms and co-occurring difficulties that are not specific to ASD can identify subgroups within the autism spectrum of importance for earlier recognition or more targeted interventions remains an important but unanswered question in this subject area (Grzadzinski et al., 2013; Mazurek, 2016).

1.4.1 Medical and psychiatric comorbidity

Although estimates of prevalence vary across studies, substantial medical and psychiatric comorbidities have consistently been found in individuals with autism. Epilepsy is reported in a significant minority of affected individuals (12.1%; Lukmanji et al., 2019). Other associated medical problems include gastrointestinal symptoms, constipation, immune conditions, cardiovascular disease, diabetes, obesity and side effects from long-term medication use (Howlin, 2021; Lord et al., 2018). As is now evident, many of these physical health problems continue into old age (Howlin, 2021). This situation, combined with barriers to accessing health care, has been linked to an increased risk of premature mortality in individuals with ASD (Hirvikoski et al., 2016).

In a recent umbrella review, the reported prevalence of psychiatric comorbidity in individuals with ASD varied from 54.8% to 94% (Hossain et al., 2020). The most commonly reported conditions were ADHD (25.7–65%), anxiety (1.5–54%) and depressive disorders (2.5–47.1%; Hossain et al., 2020). Of particular concern, autism has (in some studies) been associated with an increased risk of suicide (Hirvikoski et al., 2016), suicidal ideation or suicide attempts (Cassidy et al., 2014). Prior to publication of the *DSM-5*, co-occurring diagnoses of ASD and ADHD were not permitted, and ADHD symptoms were technically subsumed into the ASD diagnosis. As ADHD is commonly found in children with ASD (e.g., Gjevik et al., 2011) and affects outcomes across the range of cognitive abilities (Hartman et al., 2016), it represents an important and malleable target of intervention when co-occurring with ASD (Lai et al., 2020; Lord et al., 2018).

1.4.2 Motor impairment

Terminology and classification

Historically, terms such as ‘clumsy child syndrome’ and ‘dyspraxia’ have been used to describe children with motor difficulties (Blank et al., 2019; Kirby et al., 2014). As a result of recent efforts to standardise the terminology, *developmental coordination disorder* (DCD) has become the most widely adopted term to reflect the presence of clinical-level motor impairment. DCD is a NDD characterised by poor motor coordination and difficulty learning motor skills (American Psychiatric Association, 2013). The term equates to F82 (specific developmental disorder of motor function) in the *ICD-10*. DCD is common, with a prevalence estimate of 5-6% among school-aged children in Europe (Blank et al., 2019; Lingam et al., 2009). Still, DCD has been described as a hidden problem due to the lack of clinical and community awareness. Children with DCD exhibit slower, less accurate motor performance, achieving lower scores than same-aged, TD children on standardised motor assessments (Kirby et al., 2014). Moreover, affected children frequently experience difficulties performing activities of daily living that their same-aged TD peers perform easily, such as learning to ride a bicycle, tying shoelaces or participating in ballgames or other sports. According to recent European Consensus guidelines, evidence suggests that everyday functioning of individuals with DCD can be improved through effective intervention approaches that target motor skills (Blank et al., 2019; Kirby et al., 2014).

Typical motor development

In typical development, infants advance through a range of gross motor milestones that are attained within certain windows of time, including independent sitting (5–7 months), crawling (7–9 months; a milestone skipped by some infants) and walking (10–15 months; Jones et al., 2014). Fine motor milestones include development of the pincer grip (9–12 months) and the ability to point (8–14 months). Motor development is closely linked to social, cognitive and language development, with attainment of motor milestones often preceding changes in these developmental skills (Jones et al., 2014; West, 2019).

The transition from infancy to toddlerhood is marked by the onset of independent walking at the approximate age of 12 months, which is considered the last of the movement milestones (Burton & Miller, 1998). Compared to other developmental events, the age of onset of independent walking (AOW) is considered a particularly reliable parent-reported milestone (Hus et al., 2011), the timing of which may be used as a marker of atypical

development when attainment occurs at or after 16 months (WHO Multicentre Growth Reference Study Group, 2006b). Fundamental movement skills (e.g. walking, running, jumping, throwing, catching) typically emerge between one and seven years of age (Burton & Miller, 1998). Performance of these skills is more complex, requires greater coordination of the body and is learned primarily through play and imitation of others (Hardy et al., 2010). These skills are also considered the basis for more advanced, or sport specific, movement skills (Burton & Miller, 1998).

Motor impairment in ASD

Although not considered core symptoms of ASD in the same manner as stereotyped and repetitive behaviours (RRBIs), motor difficulties such as clumsiness or atypical gait have been acknowledged as features associated with the ASD phenotype since its earliest descriptions (Asperger, 1944; Kanner, 1943; Wing, 1981a). In the decades that followed these initial reports, several studies documented the pervasiveness of motor deficits in ASD, including delayed attainment of motor milestones and deviant muscle tone, fine and gross motor performance, gait and balance (Fournier et al., 2010; Ming et al., 2007; Van Damme et al., 2015; West, 2019). Depending on sample characteristics, applied measures and criteria, as many as 25–90% of children with ASD are found to meet the diagnostic criteria for DCD (Kopp et al., 2010; Miller et al., 2021).

Longitudinal data suggest that early motor deficits may be a risk factor for later motor impairments but also for language and social communication deficits related to ASD (LeBarton & Landa, 2019; Leonard et al., 2014). Motor performance is variable and can be objectively and reliably measured in children with ASD from an early age, prior to the emergence of core ASD symptoms. Recent studies also suggest that delayed AOW may be an early marker of neurobiological and genetic abnormality in individuals with ASD (Bishop et al., 2017b; Buja et al., 2018). Therefore, motor deficits have been considered potential markers of subgroups within the autism spectrum.

1.4.3 Language impairment

Terminology and classification

The complex and multifaceted nature of language and the lack of agreement about the criteria and terminology used to identify and classify language impairments have presented barriers

to identifying children with intervention or service needs (Bishop et al., 2016a). *Form, content* and *use* of language are three equally important components of communication. Appropriate understanding, production and use of language form (rules for producing and combining speech sounds and for combining words to form complex sentences) and language content (word and text meaning) represent *structural language skills*. Language can be described as receptive (comprehension) or expressive (language production). Appropriate use and interpretation of verbal and nonverbal language in different contexts represent *pragmatic language skills* (e.g., Baird & Norbury, 2016; Geurts & Embrechts, 2008). Language impairments may affect one or more of these components; overlapping problems in several aspects of language are common (Baird & Norbury, 2016).

Notably, the diagnostic classification of language disorders in the *ICD-10* differs to some extent from the same classification in the *DSM-5*, as does the terminology used by many clinicians and researchers (Bishop et al., 2017a). According to a recent consensus study, the term 'language disorder' is now "recommended to refer to a profile of difficulties that causes functional impairment in everyday life and is associated with poor prognosis" (Bishop et al., 2017a, p.1068). The term 'developmental language disorder' is recommended when the language disorder is not associated with a known biomedical aetiology (including ASD) and roughly corresponds to the widely used term 'specific language impairment' (SLI).

Traditionally, the term SLI has been used in reference to the difficulties some children experience with the structural aspects of language in the context of otherwise typical development (Bishop, 2000). Although commonly regarded as secondary to the structural deficits, some of these children also struggle with pragmatic aspects of language. 'Pragmatic language impairment' (PLI) is a term commonly applied to denote children whose difficulties with the pragmatic aspects of language are most prominent, although they do not meet the diagnostic criteria for ASD (Bishop, 2000). Children with PLI have difficulty understanding and using nonverbal cues to convey information during conversation. Furthermore, they often struggle with the rules of conversational exchange and fail to adapt to the conversational partner, which has potential negative effects on the development of peer relations. As such, PLI clearly overlaps with the autism spectrum (Bishop, 2000).

Typical language development

Following the typical course of development, children begin to communicate long before they can talk. By making sounds to get others' attention and maintain interaction, and using

increasingly complex gestures, vocalisation and speech to express various intentions, the child's ability to communicate and respond to others increases during the second half of the first year (Rhea & Simmons, 2019). Typically, a child's first words appear around 12 months of age, with the use of words and word combinations being more frequent than gestures or preverbal vocalisations by 24 months of age (Rhea & Simmons, 2019).

Depending on age, definition and criteria used, prevalence rates for language impairment vary between 3% and 9.5% (e.g., Tomblin et al., 1997; Zambrana et al., 2014). These difficulties may present in a variety of ways. Delayed attainment of language milestones, such as acquisition of first words and first word combinations, are common (American Psychiatric Association, 2013) and easily recognised by adult listeners (Norbury & Paul, 2018), while more subtle deficits in grammatical complexity and language comprehension may go unnoticed (Zhang & Tomblin, 2000). Across time, 3% and 6.5% of Norwegian children are reported to display persisting and late-onset language delay, respectively (Zambrana et al., 2014), with potential negative effects on educational progress and everyday social interactions (Bishop et al., 2017a). Although many 'late talkers' (children with limited expressive vocabulary at 18–24 months) catch up without any help, not having attained phrase speech (two-word combinations) by the age of 24 months has been linked to persisting language difficulties (Bishop et al., 2016a; Bishop et al., 2017a).

Language impairment in ASD

Communication problems are a core diagnostic feature of ASD, albeit with wide variation in functional language (American Psychiatric Association, 2013). Individuals with ASD may show linguistic forms (echolalia, neologisms) to an extent or at a point in development not seen in TD children (Eigsti et al., 2011). Many children with ASD have language deficits, ranging from complete lack of speech through language delays, structural language deficits and poor comprehension of speech (American Psychiatric Association, 2013; Boucher, 2012; Geurts & Embrechts, 2008; Kjelgaard & Tager-Flusberg, 2001). Others learn to produce words and sentences but have difficulty using them for social purposes. While pragmatic deficits are pervasive in this population, larger variability exists in structural language skills (Boucher, 2012).

Delayed language skills are among the most commonly reported initial concerns about children later diagnosed with ASD (Zwaigenbaum & Penner, 2018); when present, they contribute to earlier recognition and diagnosis (Lord et al., 2018). Among verbal children

with ASD, acquisition of phrase speech by 24 months has been found to predict better structural language skills (Kenworthy et al., 2012). Considering the importance of early language as a predictor of long-term outcomes for children with ASD, research addressing the profile of such deficits is scarce, perhaps reflecting a tendency on the part of researchers and clinicians to attribute language delays primarily to the core social deficits of ASD (Eigsti et al., 2011). However, the observed variability of structural language skills, with deficits often presenting early and being associated with persisting impairments, render them a potential target for early identification and intervention in ASD (Boucher, 2012).

At the outset of this research, the shared language impairments of and the nature of the relationship between ASD and SLI had been the subject of a longstanding debate, as had the relationship between PLI and SLI and, thus, the diagnostic status of children who do not meet the criteria for either ASD or SLI. Moreover, research suggested that the different disorders affecting language and communication overlapped (Bishop, 2000; Norbury et al., 2004) and that children with ASD present with structural language deficits similar to those observed in children with SLI (Boucher, 2012). Therefore, this thesis focuses on investigating language impairment and the profile of language deficits among children evaluated for ASD, regardless of whether categorical criteria for a comorbid language disorder are met.

1.4.4 Cognitive impairment

Individuals with ASD display a wide range of cognitive abilities, from intellectual disabilities (IDs) to superior intelligence (Grzadzinski et al., 2013). The recognition of ID in children with ASD is important, as the level of intellectual functioning may affect ASD symptom severity, challenging behaviours, levels of comorbid psychopathology and long-term outcomes (Cervantes & Jang, 2016; Peters-Scheffer et al., 2016). Using a formalised assessment, co-occurring ID is diagnosed based on the presence of deficits in general cognitive abilities (e.g. reasoning, problem-solving, planning, abstract thinking and learning) that impair adaptive functioning in one or more aspects of everyday life (American Psychiatric Association, 2013).

Recent estimates suggest that 70% of individuals with ASD have an intelligence quotient (IQ) in the average range or above (Lyall et al., 2017). Traditionally, the term ‘high-functioning autism’ was used to refer to this group. However, recent data indicate that estimates of intelligence alone are an inaccurate proxy for functional skills when diagnosing

ASD, particularly for those with normal range cognitive abilities (Alvares et al., 2019). Furthermore, divergent subtest score patterns on standardised tests of cognitive abilities are common (Cervantes & Jang, 2016), suggesting that full-scale IQ estimates may not adequately represent the skill profile of the individual (Mazurek, 2016).

1.5 Functional impairment

The broad construct of 'functioning' comprises an assortment of related concepts. In this thesis, focus is limited to the concept of *functional impairment*, or "the extent to which a diagnosed condition results in limitations in daily life, including social experiences and educational opportunities" (Baird & Norbury, 2016, p. 749). While the severity of a disorder refers to the extent to which a disorder is manifested, it does not identify the domains of life in which the individual struggles or how the individual has adapted to the illness (Winters et al., 2005). In contrast to severity, functional impairment indicates how the individual functions across important domains of everyday functioning (e.g. home, school, peer group), capturing any existing "diminished ability to perform at developmentally expected levels" (Fabiano & Pelham, 2016, p.71; Winters et al., 2005).

Understanding impairment is claimed to be the most important challenge facing medical, educational and mental health care providers today (Goldstein & Naglieri, 2016). Traditionally, symptom severity (in terms of the number and intensity of core behaviours) have driven the formulation of clinical diagnoses, with less consideration of whether these symptoms cause actual impairment. However, those in the field have become more aware that symptoms and functional impairment need to be considered separately in making diagnostic decisions and evaluating treatment responses, as they appear to be separate concepts (see Goldstein & Naglieri, 2016, for a review). Importantly, a child may have functional impairment but lack sufficient symptoms to warrant a diagnosis (Angold et al., 1999; Costello et al., 1999). At the same time, many who may meet the symptom criteria for a specific diagnosis may not be significantly impaired.

1.5.1 ASD and the impairment criterion

In the fifth revision of the *DSM*, the severity of core symptoms is included as a specifier and linked to how much support individuals need because of the impairments their ASD

symptoms cause. Another change that appears in the *DSM-5* is the inclusion of a new criterion D: "Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning" (American Psychiatric Association, 2013, p.50). Having made direct observations of the child and gathered adequate information to ascertain current symptomatology sufficient to meet the diagnostic criteria, as well as a developmental history consistent with an ASD diagnosis, the clinician must determine that the clinical-level functional impairment is largely attributable to ASD and not to an alternative psychiatric or developmental disorder (Constantino & Charman, 2016).

The *DSM-5* impairment criterion promotes the view of functional impairment as an important dimension separate from symptomatology, both of which are quantifiable and important to measure in the assessment of and to evaluate interventions for ASD (Constantino & Charman, 2016). Further, this criterion harmonises the *DSM* with the system outlined by the World Health Organization (WHO), in which symptomatology and functioning are separate constructs and treated in different classification systems, documented in the *ICD* and the *International Classification of Functioning, Disability and Health*.

1.5.2 Assessment of functional impairment

Determining the extent to which core ASD symptoms affect daily functions is necessary for diagnosis, functional assessment, treatment planning and evaluation (Hyman et al., 2020). However, the *DSM-5* contains no explicit information clarifying how impairment in children should be defined, operationalised or measured. Neither is the relationship between the severity specifier and the impairment criterion for ASD denoted (Bernier, 2012; Constantino & Charman, 2016).

The repertoire of evidence-based tools for assessing functional impairment is limited (White et al., 2014; Winters et al., 2005). Standardised assessments of adaptive skills such as the Vineland Adaptive Behavior Scales (VABS; Sparrow et al., 1984) are commonly used when evaluating children with suspected ASD and low cognitive abilities, as these measures provide information on adaptive skills across functional domains that may aid in the determination of diagnostic conclusions and further treatment planning. As opposed to time-consuming measures like the VABS that also require training, unidimensional or global impairment scales yield a single score reflecting the individual's overall level of impairment

(Lewandowski et al., 2016). Such scores can easily be assigned in the context of a broader evaluation of the child's symptomatology and functioning, allowing the rater to synthesise the child's current functioning over many domains (Winters et al., 2005). Where comorbidity is common, as is the case for most NDDs, attributing impairment to each of the comorbid disorders may also prove difficult. Hence, focusing more on a child's overall functioning than on core features per se may be more relevant (Thapar et al., 2017). Wagner et al. (2007) modified the Children's Global Assessment Scale (CGAS; Shaffer et al., 1983) for children with developmental disabilities to create the Developmental Disability-Children's Global Assessment Scale (DD-CGAS), a brief, clinician-administered measure of global functioning that is sensitive to change (Wagner et al., 2007).

1.5.3 Controversies related to diagnostic threshold

Given the heterogeneity of ASD, a better understanding of how co-occurring difficulties may interact with core ASD symptoms to impact overall functioning is critical to adapting diagnostic and clinical services accordingly (Bernier, 2012; Mottron & Bzdok, 2020). Although the related literature was scarce when planning for this study began, emerging research suggested that neither the behavioural nor aetiological characteristics of ASD conformed to a categorical diagnostic boundary (Whitehouse, 2017); rather, the core social impairment was considered dimensional, raising issues about whether individuals diagnosed with ASD were quantitatively different rather than categorically distinct from the broader population and about where to set the diagnostic threshold (Constantino & Charman, 2016).

Studies that documented that autistic traits were not rare in school-aged children (Constantino & Todd, 2003; Posserud et al., 2006), that they overlapped with diagnosed ASD aetiologically (Robinson et al., 2011), and that they were linked to the same comorbidities and functional impairments as ASD, including increased risk for motor, language and cognitive difficulties (Christ et al., 2010; Kamio et al., 2013b; Lundstrom et al., 2011; Van Waelvelde et al., 2010), suggested the clinical relevance of these traits. Indeed, it was proposed that the presence of comorbidities leading to functional impairment might move an individual from normal distribution autistic features to the diagnostic status of autism (ASD) (Gillberg & Fernell, 2014). However, the literature provided little guidance on how to establish a clinical threshold for diagnosis or on whether absolute symptom burden or level of functional impairment should dominate the parametrisation of this threshold (Bernier, 2012;

Constantino & Charman, 2016); neither did it contain any guidance on whether thresholds for functional impairment and treatment may be altered in the presence of a clinical-level or subthreshold co-occurring condition (Constantino & Charman, 2016; Thapar et al., 2017).

1.6 Methodological considerations

1.6.1 Dimensional versus categorical approach to study ASD

Traditionally in autism research, categorically defined groups of affected children have been compared to groups of TD children, or other clinical groups, not considering their common overlap or the anticipated level of co-occurring difficulties. The question of whether child and adolescent psychopathology should be regarded as categorical phenomena or as dimensions with psychopathology lying at the extreme end of the distribution has long been debated. Pickles and Angold (2003) argued that the central issue is not the determination of whether psychopathology is dimensional or categorical but, rather, identification of the circumstances under which regarding psychopathology as categorical makes sense, for example, if a decision is needed whether to implement a specific intervention or not. Based on the literature reviewed, we identified a need for research that takes a dimensional approach to study the extent and nature of co-occurring difficulties in children with a broad range of autistic symptoms, regardless of whether they meet the criteria for an ASD diagnosis. This approach aligns with the developmental psychopathology framework (Rutter, 2013). Within developmental psychopathology, an interdisciplinary perspective and multiple levels of analysis (multiple sources of information using reliable and valid age-appropriate measures) provide a comprehensive strategy for studying the full range of variations from normality to psychopathology (Garber & Bradshaw, 2020).

1.6.2 A neurodevelopmental profile of skill strengths and weaknesses

The core social deficiency of ASD is considered a continuously distributed trait across the population, the severity of which can be quantified by continuous measures (Constantino & Charman, 2016). Other developmental skills can also be evaluated using quantitative assessment methods, providing a neurodevelopmental profile of skill strengths and weaknesses that can be used to guide treatment and interventions for individuals with NDDs (Gillberg, 2010; Moreno-De-Luca et al., 2013), regardless of diagnostic category.

Considering the anticipated overlap that creates obstacles to attributing impairments to each potentially comorbid condition, the current study was designed to explore the presence, potential relationships between and impact of deficits in core developmental domains on overall impairment. For the reasons outlined, focus was placed on co-occurring motor and language impairments, while cognitive abilities are included and discussed where relevant.

2. Aims of the thesis

The overall aim of this thesis was to study co-occurring motor and language deficits and their potential relationship with symptom severity and functional impairment in children with a broad range of autistic symptoms through a dimensional approach, that is, differentiating participants into children diagnosed with ASD and children with subthreshold autistic symptoms (non-ASD). More specifically, we aimed to achieve the following:

Paper I

- compare early motor skills as indexed by age of onset of independent walking (AOW), nonverbal cognitive abilities and severity of autistic symptoms between children receiving an ASD diagnosis and children not meeting the diagnostic criteria.
- investigate the associations between AOW and autistic symptom severity independent of ASD diagnosis.
- investigate these questions separately for males and females.

Paper II

- investigate the extent of language deficits based on the Children's Communication Checklist (CCC-2) and parents' retrospective report of early language delay (no phrase speech at two years of age).
- investigate whether current structural language skills are associated with pragmatic competence.
- explore whether early language delay predict current language and social skills.
- explore potential sex differences in language characteristics.

Paper III

- explore the co-occurrence of motor and language impairments, particularly structural language deficits, as measured by parent report and an objective assessment of motor skills.
- explore the relationship between motor, structural language and social skills.
- assess functional impairment and participation and explore potential relationships with motor, structural language and social skills.

3. Methods

3.1 Design and setting

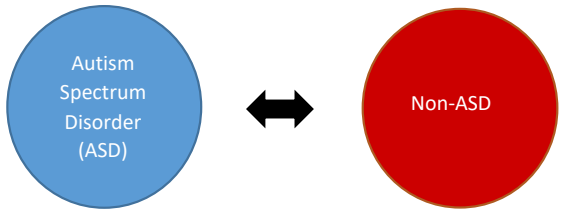
The three studies that form the basis of this thesis were cross-sectional and part of BUPgen, an ongoing large multisite study of NDDs in Norway. The main inclusion criterion in this study was that a suspicion of ASD had been raised by local or specialist health services that prompted a referral for an individual to be evaluated for ASD. Data were collected from two types of sites: 1) child habilitation services and 2) child and adolescent mental health services (CAMHS). These are public specialist health services that receive referrals for assessments for ASD and other NDDs, depending on the presenting symptoms, level of impairment, co-occurring somatic or psychiatric difficulties and local routines. In Norway, assessments are interdisciplinary and provided to citizens free of charge. Local variations in recognition, assessments and diagnostic conclusions have been a concern (Surén et al., 2013). However, during the last decade, substantial resources have been invested to train clinicians in using recommended diagnostic instruments for ASD evaluations. As a result, assessments by the Norwegian specialist health services were recently found to largely adhere to guidelines established by the various health trusts and were also found to provide a high standard of documentation that the diagnostic criteria had been met in 95% of cases (Surén et al., 2019a).

Based on the clinical information collected and data on diagnostics, participants in BUPgen were separated into two main diagnostic groups.

a) Children with autistic symptoms given a clinical diagnosis of ASD according to *ICD-10* formed the ASD group.
b) Children with suspected autistic symptoms who were not given a clinical ASD diagnosis formed the non-ASD (subthreshold autistic symptoms) group.

The categorical approach used in participant recruitment (ASD/non-ASD; see Figure 2a) was supplemented by a dimensional approach in the study assessments and analyses, whereby ASD symptomatology, core developmental skills and functional impairment were also examined as continuous trait variables within the whole group of children with autistic symptoms, regardless of diagnostic category (Figure 2b). In addition, results for both groups were compared to norms for TD Norwegian children, where available.

Figure 2a *Categorical Approach*



Note. Child characteristics (e.g. age, sex), core developmental skills (social, motor, language, cognitive), comorbidities and functional impairment were compared between the two diagnostic groups (ASD/non-ASD).

Figure 2b *Dimensional Approach*

Note. Potential relationships between social skills, other core developmental skills (motor, language, cognitive) and functional impairment were explored within the whole group of children evaluated for suspected ASD, regardless of diagnostic category.

3.2 Procedure

All participating children had undergone a clinical evaluation for ASD by Norwegian specialist health services, during or after which they were invited to participate in the main study (BUPgen) by clinicians at their local site. Thus, many of the assessments and measures included in this research were carried out on an ongoing basis. Diagnostic conclusions were best-estimate clinical diagnoses made by specialist health services, derived from history, test results, interview results and observations. After obtaining informed consent to participate in the main study, retrospective data on type and results of clinical assessments, history and supplementary measures as reported by parents or primary caregivers[2] were collected,

[2] Throughout this thesis the terms 'parent' and '(primary) caregiver' are used interchangeably to refer to the child's guardian

according to the BUPgen Standard Operating Procedure (Papers I, II and III). As we wanted to study a subgroup of children in more detail in a local sub-study (Paper III), supplementary measures of current functional impairment, motor skills, language skills and participation were added to the standard inclusion measures in the main study.

For the local sub-study, school-aged participants from the main study from four outpatient CAMHS in Møre og Romsdal Hospital Trust (Mid-Norway) were invited to participate. After obtaining written informed consent to participate, an appointment for inclusion was made and report forms were sent to the caregiver(s) for completion prior to the assessment. Each child was assessed in one session, conducted at a local CAMHS. The child underwent a standardised motor assessment at the same time or prior to an interview with the child's caregiver(s). During the interview, the child was not present, and caregivers were blind to their child's scores. Primary caregivers were invited to complete the report forms; the same caregiver(s) participating in the interview completed a set of forms for each participant. Only data reported by the interviewed caregiver is included in this thesis.

3.3 Participants

Participants included in the three studies described in this thesis met the main BUPgen criterion of having been referred for evaluation for suspected ASD. Recruitment was ongoing: this thesis includes data from the BUPgen database from 2017 (Paper I), 2019 (Paper II) and 2021 (Paper III). The study documented in Paper I included 490 participants, the study in Paper II involved 177 participants and the study described in Paper III consisted of 20 participants. As inclusion and exclusion criteria differed somewhat between these samples, they are presented separately in the following paragraphs. The main participant characteristics for each sample are summarised in Tables 1–3.

In total, 54 participants in the main study were recruited from Møre og Romsdal Hospital Trust during the project period, 20 of whom were included in the local sub-study (Paper III) between September 2017 and June 2021. Throughout my doctoral studies, I participated in recruiting and including patients from my local unit, I trained and supervised clinicians who performed inclusions from other local units in Møre og Romsdal Hospital Trust, and I completed the additional assessment and inclusion of all participants in the local sub-study (Paper III), with some assistance from a research assistant (physical therapist).

3.3.1 Study sample Paper I

Individuals were eligible to participate in the study documented in Paper I if data on their age (4–18 years) at inclusion in the main study, on their diagnostic classification as either ASD or non-ASD and on their age of onset of independent walking (AOW) were available. A total of 490 children, born between 1992 and 2012, with a mean age at inclusion of 11.1 years (*SD* = 3.7; Table 1), were included in the study sample for Paper I. Comparisons were made with the mean AOW from a TD population, obtained from Storvold et al. (2013).

3.3.2 Study sample Paper II

To be eligible to participate in the study described in Paper II, data on the individual's age (4–18 years) at inclusion in the main study and diagnostic classification as either ASD or non-ASD, as well as their assessment results from the Children's Communication Checklist Second Edition (CCC-2), had to be available. In total, 177 children, born between 1994 and 2012, with a mean age at inclusion of 12.3 years (*SD* = 3.3; Table 2), comprised the study sample for Paper II. The CCC-2 was not a standard inclusion measure in the main study but was completed as part of the clinical evaluation for some children. As the CCC-2 is only completed when the child can speak in at least simple sentences, all participants were verbal.

3.3.3 Study sample Paper III

Children aged 6–18 years at inclusion in the main study from Møre og Romsdal Hospital Trust whose ASD diagnostic status information was available were eligible for participation in the local sub-study highlighted in Paper III. All children were verbal, and children and caregivers were sufficiently fluent to communicate in the Norwegian language, as required. Furthermore, participants' records were reviewed to confirm that they did not have a more severe intellectual impairment or a severe sensory, neurological or muscular impairment that could interfere with motor testing. The final sample consisted of 20 children (14 boys and 6 girls) born between 2000 and 2013, with a mean age at inclusion in the sub-study of 10.7 years (*SD* = 3.4; Table 3).

Table 1 *Sample 1. Paper I. Data Collected and Processed by August 2017*

	ASD (*n* = 376; 76.7%)			Non-ASD (*n* = 114; 23.3%)		
	n	%	M (*SD*)	*n*	%	M (*SD*)
Male	292	77.7		85	74.6	
Verbal language (yes)*	305	92.7		100	100.0	
Age at inclusion	376		11.4 (3.8)	114		10.2 (3.6)
Age at ASD diagnosis	326		9.3 (4.2)			
ASD subgroups (%)						
Childhood autism (F84.0)	112	29.8				
Atypical autism (F84.1)	36	9.6				
Asperger syndrome (F84.5)	134	35.6				
PDD-NOS (F84.9)	86	22.9				
Two or more NDDs	192	51.8		44	41.9	
Nonverbal IQ	254		102.3 (17.7)	85		100.9 (17.5)
Verbal IQ	258		89.1 (17.8)	86		92.9 (18.0)

Note. * Based on information at inclusion, participants were considered nonverbal if (1) they had completed the Autism Diagnostic Observation Schedule Module 1, designed for children who are nonverbal or using single words; (2) they were reported as not combining words and not using sentences (when completing the Social Communication Questionnaire and/or the Autism Diagnostic Interview-Revised; or (3) clinician-reported information at inclusion otherwise indicated that they were nonverbal. The denominator for the reported proportions in this table excludes those with missing data. ASD = autism spectrum disorder; IQ = intelligence quotient; NDD = neurodevelopmental disorder; PDD-NOS = pervasive developmental disorder - not otherwise specified.

Table 2 *Sample 2. Paper II. Data Collected and Processed by April 2019*

	ASD (*n* = 148; 83.6%)			Non-ASD (*n* = 29; 16.4%)		
	n	%	M (*SD*)	*n*	%	M (*SD*)
Male	119	80.4		24	82.8	
Verbal language (yes)**	148	100.0		29	100.0	
Age at inclusion	148		12.5 (3.2)	29		11.0 (3.7)
Age at ASD diagnosis	144		11.5 (3.3)			
ASD subgroups (%)						
Childhood autism (F84.0)	14	9.5				
Atypical autism (F84.1)	7	4.7				
Asperger syndrome (F84.5)	80	54.1				
PDD-NOS (F84.9)	45	30.4				
Two or more NDDs	96	67.1		10	38.5	
Nonverbal IQ	137		102.7 (18.4)	24		101.6 (19.0)
Verbal IQ	138		90.8 (17.0)	25		94.8 (15.9)

Note. ** The Children's Communication Checklist Second Edition (CCC-2), which requires that the child can speak in at least simple sentences was completed. The denominator for the reported proportions in this table excludes those with missing data. ASD = autism spectrum disorder; IQ = intelligence quotient; NDD = neurodevelopmental disorder; PDD-NOS = pervasive developmental disorder - not otherwise specified.

Table 3 *Sample 3. Paper III. Data Collected and Processed by October 2021*

	ASD (*n* = 15; 75.0%)			Non-ASD (*n* = 5; 25.0%)		
	n	%	M (*SD*)	*n*	%	M (*SD*)
Male	11	73.3		3	60.0	
Verbal language (yes)**	15	100.0		5	100.0	
Age at inclusion	15		11.2 (.9)	5		9.6 (1.4)
Age at ASD diagnosis	15		10.2 (3.3)			
ASD subgroups (%)						
Childhood autism (F84.0)	4	26.7				
Atypical autism (F84.1)	1	6.7				
Asperger syndrome (F84.5)	6	40.0				
PDD-NOS (F84.9)	4	26.7				
Two or more NDDs	8	53.3		2	40.0	
Nonverbal IQ	11		108.2 (10.4)	5		86.0 (14.6)
Verbal IQ	12		96.1 (16.2)	5		87.0 (17.9)

Note. ** The Children's Communication Checklist Second Edition (CCC-2), which requires that the child can speak in at least simple sentences was completed. ASD = autism spectrum disorder; IQ = intelligence quotient; NDD = neurodevelopmental disorder; PDD-NOS = pervasive developmental disorder - not otherwise specified.

3.4 Measures

3.4.1 Diagnoses

All main and co-occurring diagnoses were assigned by Norwegian specialist health services using *ICD-10* criteria (World Health Organization, 1992). NDDs were grouped according to *ICD-10* codes into the following categories: ASD (F84), ID (F70–79), ADHD (F90), communication disorder[3] (F80), specific learning disorder (F81 and F83), motor disorders (F82: DCD; F95: tic disorders) and other NDDs (F88, F89 and F94). The presence of previous or current epilepsy and/or cerebral palsy was also registered and included in the total number of NDDs. We also report the number of participants who completed either or both of the recommended diagnostic measures (ADI-R, ADOS) as part of their clinical evaluation for ASD.

3.4.2 Developmental milestones

Age of onset of independent walking

A clinician-rated medical history form that was completed for all participants at inclusion in the main study inquired about age (in months) of onset of independent (unaided) walking (AOW). This form was completed based on the information available in the child's medical record supplemented by information reported by parents when asked to retrospectively recall

[3] To harmonise our description of the NDD categories with the *DSM-5* terminology, we used the heading 'communication disorder' for *ICD-10* code F80. In retrospect, we consider 'language disorder' a more correct descriptor for this category.

this milestone. The AOW was applied as a continuous trait measure of early motor skills. Comparisons were made with the mean AOW from a TD population, obtained from Storvold et al. (2013). These researchers investigated the normal distribution of AOW among Norwegian children (n = 47,515), finding a mean AOW of 12.86 months (SD = 1.88; 95% CI, 12.85 to 12.88). We also created a dichotomised variable to identify children with an AOW ≥ 16 months as 'late walkers', in line with previous reports (Bishop et al., 2016b).

Attainment of phrase speech at two years of age

The medical history obtained also inquired whether the child had attained one spoken word by the age of one and whether the child had expressed their first phrase (a spoken two-word combination) by the age of two. Among children with ASD and normal range cognitive abilities, Kenworthy et al. (2012) found attainment of first phrase speech by two years (24 months) of age to be a useful marker for distinguishing subsequent language trajectories. Therefore, a dichotomous variable was created in order to use the failure to attain first phrase speech by two years of age as a proxy for early language delay (i.e. being a 'late talker').

3.4.3 Autistic symptoms

The Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), with the data collected as part of the main study, was used to reflect current (in the previous six months) parent-reported autistic social impairment. The SRS consists of 65 items rated on a 4-point Likert scale; higher total scores indicate higher degrees of social impairment (Constantino et al., 2003). Designed to ascertain the entire spectrum from unaffected to severely affected, the SRS raw total was applied as a dimensional trait variable, for which previous research has demonstrated strong internal consistency (Cronbach's alpha .97; Constantino & Gruber, 2005). SRS scores are also found to correlate well with ADI-R scores (Constantino et al., 2003) and to be highly preserved over time, with a 5-year test–retest correlation exceeding 0.70 (Constantino et al., 2009).

The Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994; Rutter et al., 2003b) is a clinical diagnostic tool used to guide a comprehensive semi-structured interview with parents or primary caregivers. The scoring algorithm is based on the diagnostic criteria for ASD, yielding separate scores for social, verbal/nonverbal communication and RRBI domains. Although no Norwegian or Scandinavian norms have been established, the inter-

rater reliability for single ADI-R algorithm items and behavioural domain totals and agreement with the diagnostic classification for the Scandinavian versions have been deemed acceptable (Halvorsen & Helverschou, 2017). Following ADI-R conventions as presented by Hus and Lord (2013), and to establish a basis for comparing scores across participants of different ages and language levels, we calculated the ADI-R nonverbal total to reflect severity of core ASD symptoms in the study cited in Paper I. As all participants were verbal, we calculated the ADI-R verbal total reported in Paper III. Higher scores indicate more severe ASD symptoms (Hus & Lord, 2013).

The Social Communication Questionnaire (SCQ) lifetime form (Rutter et al., 2003a) is a 40-item questionnaire used to identify behaviours associated with autism in children older than 4 years. The content parallels that of the ADI-R, with both excellent agreement (Berument et al., 1999; Bishop & Norbury, 2002) and concurrent validity (Rutter et al., 2003a) between the two reported. In cases where the ADI-R had not been administered, the SCQ lifetime form was completed by a parent/primary caregiver at inclusion in the main study if it had not already been completed.

For simplicity, the term ‘symptom severity’ is sometimes used in this thesis to refer to the total score on the different measurements of autistic symptoms (ADI-R, SCQ and SRS), although differing in their content as clarified previously.

3.4.4 Motor skills

The Developmental Coordination Disorder Questionnaire 2007 (DCDQ'07; Wilson et al., 2009) was developed as a screening instrument for DCD among children aged 5–15 years and to confirm the functional consequences of a motor deficit in clinical and research settings (Wilson et al., 2009). The questionnaire, which consists of 15 items scored on a 5-point Likert scale, compares a child’s motor skills with those of their same-aged peers. Raw scores for three subscales (*control during movement*, *fine motor/handwriting* and *general coordination*) are summed into a total score, with a possible value of 15 to 75. We used the DCDQ’07 to ascertain everyday motor skills, as reported by parents. For the local sub-study, an unpublished prefinal Norwegian version of the DCDQ’07 (Wilson et al., 2009; Norwegian cross cultural adaptation by V. Johannesen, H. A. Lillehaug, N. R. Nielsen, G. Skard & S. van Zuiden, 2012) was made available to us by the original author. The original version has a high internal consistency (Cronbach’s alpha = .89) and concurrent validity with the original

Movement Assessment Battery for Children (Wilson et al., 2009). Considering the lack of Norwegian norms, we used the recommended age-appropriate cut-offs to determine the presence of motor difficulties (Wilson et al., 2009).

The Movement Assessment Battery for Children-2 (MABC-2; Henderson et al., 2007) was used for the standardised assessment of fine and gross motor skills. In this evaluation, eight individual test items grouped into three categories (*manual dexterity*, *aiming and catching* and *balance*) are given a raw score and a standard score that translate into a component score. From the three categories, a total test score is derived, and an overall percentile in that child's age band is determined. While total test scores ≤5th percentile are considered representative of a definite motor problem requiring intervention, scores between the 5th and the 15th percentiles suggest a borderline degree of motor difficulties (Henderson et al., 2007). The MABC-2 was published with UK norms and has demonstrated good to excellent inter-rater reliability and test–retest reliability, as well as fair to good validity (Blank et al., 2019). While the specificity seems good at .8 to .9, the sensitivity, at .7 to .8, is somewhat lower ((Blank et al., 2019).

When administering the MABC-2, we used the alternative MABC-2 protocol described in Liu and Breslin (2013), which involved presenting a picture of each task to the child and minimising the verbal instructions to emphasise visual supports. The MABC-2 was administered by the PhD candidate (n = 4) or a research assistant (physical therapist, n = 16), both trained in the assessment. Prior to the study for Paper III, agreement between both examiners was established by separately scoring and afterwards discussing the performance of four healthy children and adolescents. Furthermore, inter-rater agreement was assessed by videotape on 7 (35%) of the 20 assessments in the sub-study, including each age band. Except for one participant whose total test score was invalidated by a technical error on one of the tasks, full agreement was reached on the classification of motor difficulties into *none/borderline/more definite* categories based on the MABC-2 total test score percentile.

Total score at or below the 15th percentile on the MABC-2 and the appropriate cut-off for the child's age on the DCDQ'07 were used to identify 'motor deficits' or 'motor difficulties' (terms used interchangeably) on either measure, while 'motor impairment' refers to being identified with 'motor deficits' on both motor measures.

3.4.5 Language skills

Language skills were assessed using the Children's Communication Checklist Second Edition (CCC-2; Bishop, 2003) − specifically, the Norwegian version (Bishop, 2011) − which was completed by parents. This checklist contains 70 items intended to screen observed language and communicative behaviour. The checklist does not provide a categorical diagnosis but, rather, assesses the presence and profile of language deficits. Items are grouped into 10 subscales that measure different aspects of communication: *language structure* (A–D), *pragmatic language skills* (E–H) and two scales measuring *social aspects* (I and J). The Norwegian version of the CCC-2 is standardised with Norwegian norms based on 731 children in the age range 4:0–16:11 years, with Norwegian as their main language and a parent/caregiver as the informant (Bishop, 2011). Raw scores are converted into scaled scores with a mean of 10 and a standard deviation of 3 based on Norwegian norms, which can also be converted into percentiles for each subscale. In scaled scores, a low score indicates language deficit. The General Communication Composite (GCC) is an overall measure of communication skills, derived by adding the scaled scores of the subscales A–H, with a suggested cut-off <55 to distinguish children with clinically significant language impairments from TD children (Bishop, 2003, 2011). We calculated the Structural Language Score (subscales A–D) and the General Pragmatics Score (subscales E–H) as continuous measures of structural and pragmatic language skills. This specific grouping has been used in other studies (Baixauli-Fortea et al., 2019; Kuijper et al., 2017). The Norwegian version was found to have satisfactory internal consistency (Cronbach's alpha .73 to .89) and inter-rater reliability (Helland et al., 2009).

3.4.6 Cognitive skills

Cognitive function was assessed using the results from prior formal testing of cognitive performance with age-appropriate Wechsler scales (e.g., Wechsler, 1999, 2003, 2008; Wechsler, 2012). These assessments yielded standard scores for nonverbal IQ (NVIQ), verbal IQ and full-scale IQ. To minimise the effect of language in measuring cognitive abilities, we used NVIQ as a trait variable to reflect severity of cognitive impairment.

3.4.7 Functional impairment and participation

The Developmental Disability-Children's Global Assessment Scale (DD-CGAS; Wagner et al., 2007) was employed to obtain a measure of overall functional impairment during the prior month. The DD-CGAS is a revised version of the Children's Global Assessment Scale (CGAS; Shaffer et al., 1983), which was updated to enable a more targeted functional assessment of children with NDDs, such as ASD. The DD-CGAS has previously been translated to Swedish, with good inter-rater reliability in ASD cases (Choque Olsson & Bolte, 2014).

For the present study, the DD-CGAS was translated into Norwegian, which has strong similarity to the Swedish language, with the permission of the original author. No back-translation was performed. As the rater, I was trained according to reliability training procedures as outlined in Wagner et al. (2007). Individual DD-CGAS scores were assigned based on all available information at inclusion, including a semi-structured interview with the caregiver(s) developed for the purpose of the present study (see Appendix I). As part of the DD-CGAS rating, the level of impairment across four domains of everyday functioning (*self-care, communication, social behaviour and school functioning*) is classified as 'not present', 'slight', 'moderate', 'severe' or 'extreme', while considering the child's behaviour in various environments, as well as the accommodations necessary to support the child (Wagner et al., 2007). The DD-CGAS score was chosen to best reflect overall impairment across domains, with possible values from 1 (most impaired) to 100 (superior functioning). A score below 70 was considered to indicate clinically relevant atypical functioning (Wagner et al., 2007).

Supplementary information on participation was collected from the Child Behavior Checklist/6–18 (Achenbach & Rescorla, 2001), which was completed by caregivers at inclusion.

Table 4 *Measures used in Papers I–III*

Measure	Topic	Form	Paper		
			I	II	III
AOW	Early motor skills	Retrospective parent report/ medical record	*		
Attainment of phrase speech by two years	Early language skills	Retrospective parent report/ medical record		*	
SRS	Social skills/autistic traits	Questionnaire	*	*	*
SCQ	Core ASD symptoms	Questionnaire	*		
ADI-R	Core ASD symptoms	Interview	*		(*)
CCC-2	Language skills	Questionnaire		*	*
DCDQ'07	Motor skills	Questionnaire			*
MABC-2	Motor skills	Standardised assessment			*
DD-CGAS	Functional impairment	Rating based on all available information at inclusion, including parent interview			*
CBCL	Participation	Questionnaire			*
Wechsler scales	Cognitive skills	Standardised assessment	*	*	*

Note. ADI-R = Autism Diagnostic Interview-Revised; AOW = age of onset of independent walking; ASD = autism spectrum disorder; CBCL = Child Behavior Checklist; CCC-2 = Children's Communication Checklist Second Edition; DCDQ'07 = Developmental Coordination Disorder Questionnaire 2007; DD-CGAS = Developmental Disability-Children's Global Assessment Scale; MABC-2 = Movement Assessment Battery for Children-2; SCQ = Social Communication Questionnaire; SRS = Social Responsiveness Scale.

3.5 Ethical considerations

The BUPgen study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics (REK Sør-Øst; REK #2012/1967) and the Norwegian Data Inspectorate. A separate approval was obtained for the local sub-study (REK #2016/1954). Both studies were conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all parents and participants (when appropriate due to age) included in the studies.

The BUPgen study relies on collecting data from assessments and tests that are commonly used in clinical practice and are not considered to represent any risk for the participants. In the local sub-study, supplementary measures of functional impairment, motor skills and language skills were added to the standard inclusion measures. At the outset of this research, these skills were not commonly assessed in a systematic and consistent manner as part of the evaluation for ASD in Norway. Consequently, information on these skill domains were not part of the collected information in the BUPgen study. Internationally recommended measures considered feasible and not too time-consuming were chosen to limit the number of additional assessments. As some measures were not validated for use in Norway, test results were not disclosed. However, participants and their parents were offered oral feedback after the assessments, and if serious concerns warranting follow-up were raised regarding the

child's functioning, those concerns were brought to the attention of the service responsible for follow-up, in agreement with the child's caregiver(s). Prior to inclusion, the participant and/or their parents were informed about the purpose of the study, that they could withdraw from the study at any time and that this would not influence their right to treatment or follow-up. Participants were offered a refund of their travel costs.

3.6 Statistical analysis

Descriptive data, such as percentage, central tendency (mean) and variation (standard deviation), are reported for all measures. Variables reflecting core developmental skills (social, motor, language, cognitive) were continuous. Proportions above or below the chosen cut-off to indicate clinical-level deficits were also reported (Papers I, II and III) and compared between groups (Papers I and II) when considered relevant.

Comparisons between the ASD and non-ASD groups were performed using the Pearson's chi-squared test for categorical variables and the independent samples *t*-test for continuous variables (Papers I and II). Analyses of covariance were conducted to compare the main variables of interest between the two diagnostic groups while adjusting for cognitive abilities (NVIQ; Papers I and II). For continuous variables, the assumption of approximate normality was met. Cohen's *d* was computed for effect sizes corresponding to the independent samples *t*-tests (Cohen, 1988; Paper I).

In Papers I and II, relationships between core developmental skills were assessed by performing linear regression analyses with continuous skill measures as dependent variables (Paper I: autistic symptom severity [SRS, ADI-R, SCQ]; Paper II: General Pragmatics Score [CCC-2]) and the developmental skill of primary interest (Paper I: AOW; Paper II: Structural Language Score [CCC-2]) as independent variables. Analyses were carried out unadjusted and adjusted for potential confounding factors, one at a time and simultaneously. Where relevant, we also assessed the unique contribution of the developmental skill of primary interest to predicting the different dependent variables with squared multiple correlation (R^2) in unadjusted and squared semi-partial correlation (sr^2) in adjusted analyses. Analyses were performed for the whole sample, then separately for the two diagnostic groups in Paper II, as well as by sex in Paper I. We also included the interaction between sex and AOW (Paper I)/Structural Language Score (Paper II) as an independent variable. Preliminary analyses

were conducted to ensure no violation of the assumptions of linearity, multicollinearity, independence of errors, homoscedasticity, outliers and normality of residuals. To explore possible sex differences, group comparisons were also repeated for males and females separately in Paper I. Cognitive ability (NVIQ), age at inclusion and sex were included as potential confounding factors in the adjusted regression models conducted as part of the studies described in Papers I and II, and prematurity, ethnicity and maternal and paternal age were used similarly for the study for Paper I.

As the small sample size in Paper III did not allow for multiple linear regression analysis, we used scatter plots and correlations to explore the relationship between current social, motor and structural language skills, as well as overall functional impairment. For these analyses, symptoms were not dichotomised, but the total scores on the respective skill measures were used as dimensional trait variables. As not all variables met the assumption of approximate normality (DD-CGAS and SRS), we used nonparametric analyses. The magnitude of effect sizes was interpreted as small, medium or large as recommended by Cohen (1988).

Two-sided *p*-values < .05 were regarded as statistically significant, and 95% confidence intervals were reported where relevant. In Paper II, we encouraged *p*-values between .01 and .05 to be interpreted with caution to protect against type I errors due to multiple comparisons.

Statistical analyses were performed using IBM SPSS Statistics, version 25.0 (Paper I), 26.0 (Paper II) and 27.0/28.0 (Paper III), except for comparisons with the normative sample in Stata 15 (Paper I), computing the Newcombe hybrid score confidence interval in Stata 16 and the unconditional *z*-pooled test using StatXact11 to compare proportions (Paper II).

Missing data and sensitivity analyses

The BUPgen study relies on clinical data and some supplementary measures completed by parents at inclusion, the completeness of which varies. Some data reported in this thesis reflect information that was not mandatory at inclusion in the BUPgen study and, thus, was not reported to the database for all participants. For previous clinical assessments, such as those evaluating cognitive abilities, complete scores were not always available in the medical records. The number of children with available data on the different measures of autistic symptom severity also varied. In cases where the ADI-R had not been administered as part of the clinical evaluation, the SCQ lifetime form was completed at inclusion, if it had not

already been done. Hence, few children had information from both instruments. The SRS was encouraged to be completed for all participants upon inclusion in the main study, although that was not always feasible. Missing data are problematic because they add to the risk of bias, as individuals with missing data may differ from those with no missing data in terms of the outcomes of interest (Pedersen et al., 2017). Notably, the risk of bias depends on whether data are missing at random, the extent of the data that are missing and the way missing data are handled in the analysis (Pedersen et al., 2017). Usually, missing data are addressed by including in the analysis only individuals who have no missing data in any of the variables required for that analysis (complete cases; Sterne et al., 2009). However, the cumulative effect of missing data across variables often leads to the exclusion of a substantial proportion of the original sample, which affects the statistical power and precision of the estimates (Pedersen et al., 2017; Sterne et al., 2009). Furthermore, the results for such analyses may yield biased estimates because complete cases are assumed to be a random sample of the whole population, which may not be the case after such exclusions are made.

In this thesis we report available case analyses with the corresponding number of missing cases where appropriate. In Paper I, the number of children with available results on the different measures of autistic symptom severity and NVIQ varied considerably. When clinical characteristics of the total study cohort (N = 490) were compared with n = 97 individuals with missing data on all measures of symptom severity, and with n = 393 individuals with available data on one or more measures, missing data tended to be more common among children who were younger, nonverbal and/or had lower cognitive abilities, which is plausible because they may be more difficult to assess using standardised assessments. More children in the group with missing data on all measures of symptom severity had an ASD diagnosis and a later mean AOW. Hence, data were not 'missing completely at random' but, instead, were possibly 'missing at random'. The same pattern was observed among the 151 children with missing data on the NVIQ. We, therefore, handled missing data using multiple imputation. While available case analysis is unbiased only if data are 'missing completely at random', multiple imputation analysis is unbiased under the less restrictive 'missing at random' assumption. All variables used in subsequent analyses were included in the imputation model. In addition, language level (categorical indicator of expressive language), ASD diagnosis and verbal IQ were included as auxiliary variables associated with missingness, increasing the plausibility that the 'missing at random' assumption was a realistic approximation of reality. As recommended by Sterne et al. (2009),

we reported results from available case analyses based on the original dataset and analyses based on multiple imputation.

Sensitivity analyses exploring the potential impact of missing information on AOW (Paper I) and outliers (Paper I) and the potential impact of including individuals with invalid inconsistency check on the CCC-2 (Paper II) on the results are also reported. Generally, these analyses suggested only modest attenuation of the main results. The local sub-study was designed to reduce the amount of missing data on main measures. Still, some values were missing for a few children, the reasons for which are outlined in Paper III.

4. Results

4.1 Paper I: *Age of first walking and associations with symptom severity in children with suspected or diagnosed autism spectrum disorder.*

The aim of the first study was to investigate early motor skills, as well as the relationship between early motor skills and the severity of autistic symptoms, in a large clinical sample of children evaluated for ASD. Potential sex differences were also investigated. The AOW was used as a proxy for early motor skills.

The study included 490 children (aged 4–18 years, 113 females), distinguished as children with ASD (n = 376) and children with non-ASD (n = 114) diagnoses, with varying cognitive abilities. Autistic symptom severity was assessed using total scores from the ADI-R, the SCQ and the SRS. AOW, sex, age, NVIQ and symptom severity were compared between the ASD and non-ASD group. Furthermore, we examined the associations between AOW and symptom severity independent of ASD diagnosis. Available norms for AOW allowed for comparison with TD children.

The mean AOW (in months) was significantly later in children diagnosed with ASD (M = 14.7, SD = 4.3) compared with non-ASD children (M = 13.8, SD = 2.9), p = .005. Significant delays compared with population norms (M = 12.9, SD = 1.9) were found for both groups (p < .001). Furthermore, 31% of children in the ASD and 25% in the non-ASD group were characterised as ‘late walkers’ (AOW ≥ 16 months; see Figure 2 in Paper I). Later AOW was significantly associated with increasing symptom severity. The strongest association was found with the ADI-R nonverbal total score, for which AOW explained 7.0% of the variation after adjusting for potential confounders (p = .02). Contrary to population norms, females had a non-significant tendency towards delayed AOW (M = 15.0, SD = 4.5).

Our findings support that delayed AOW, while not unique to children diagnosed with ASD, is commonly found in affected children and associated with symptom severity. Thus, ASD should be considered an actual differential diagnosis in cases with delayed AOW, perhaps particularly in girls.

4.2 Paper II: *Structural and pragmatic language impairments in children evaluated for autism spectrum disorder (ASD).*

Paper II investigated the extent of early language delay and current language deficits, as well as the relationship between early language delay, current language and social skills, in children with a broad range of autistic symptoms. Potential sex differences in language characteristics were also explored.

The study included 177 children (34 females) aged 4–18 years evaluated for ASD, differentiated into ASD (*n* = 148) and non-ASD (*n* = 29), for whom results were available from the Children's Communication Checklist (CCC-2) assessment. Not having attained first phrase speech at two years of age was used as a proxy for early language delay.

We found that structural language deficits were common and strongly associated with reduced pragmatic competence across the whole sample. Pragmatic language impairments were most profound in children with ASD. Early language delay was more common among males and associated with structural language deficits, whereas pragmatic language and social skills did not differ significantly between children with and without language delay.

Our results lend support to the notion of pragmatic language impairment as a dimensional symptom profile that is closely linked to core ASD symptoms but likely reflects a confluence of risk factors, among them structural language deficits. Further, our findings support the association between early language delay and later language abilities that are distinct from autistic symptoms. We also contribute to recent reports that autistic females may be recognised and diagnosed later than males due to stronger verbal skills and a reduced rate of early language delay. Our results underscore the importance of including language skills assessment in the evaluation of children with suspected ASD, as co-occurring language deficits may represent important targets of intervention, in addition to addressing the core social impairment.

4.3 Paper III: *The co-occurrence of motor and language impairments in children evaluated for autism spectrum disorder. An explorative study from Norway.*

The local sub-study (Paper III) aimed to provide a more detailed developmental skill profile to explore the co-occurrence and potential impact of motor and language impairments on overall functioning and participation among school-aged children evaluated for ASD.

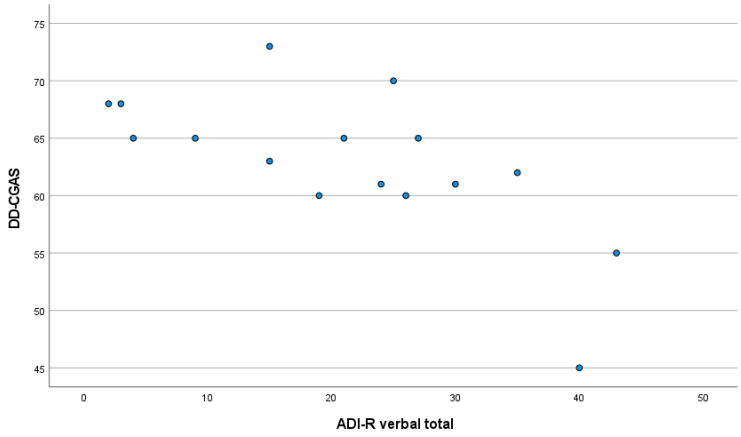
The sample comprised 20 children (6 females) aged 6–18 years evaluated for ASD by CAMHS, differentiated into ASD (*n* = 15) and non-ASD (*n* = 5). Besides clinical evaluation

for ASD, all participants underwent a standardised test of motor performance (MABC-2). Parent report measures of current motor (DCDQ'07), language (CCC-2) and social skills (SRS), as well as a caregiver interview on everyday functioning were completed for each participant. Overall functional impairment was rated (DD-CGAS) based on all available information. The majority (85%) had motor and/or structural language deficits in addition to their current social impairment. All children identified with motor impairment on both measures (39%) also had structural language deficits. Better motor performance on the MABC-2 was strongly correlated with better structural language skills (Spearman's rho = .618, p = .006). Limited participation in ordinary physical education and out-of-school activities was common. No significant correlation was observed between overall impairment and the current skill measures. However, more pronounced core ASD symptoms, as measured by the ADI-R verbal total score (n = 16), were strongly correlated with more severe functional impairment (Spearman's rho = -.657, p = .006; Figure 4).

Although preliminary, our findings suggest that co-occurring motor and structural language deficits should be anticipated and assessed when evaluating school-aged children for ASD. These deficits may need specific interventions that complement those targeting social skill deficits and other ASD core symptoms.

Figure 3

The Relationship Between Functional Impairment and Core ASD Symptoms.



Note. The relationship between functional impairment and core ASD symptoms, illustrated by the distribution of DD-CGAS and ADI-R verbal total scores (n = 16).

5. Discussion

5.1 Summary of findings

This thesis studied children evaluated for ASD by Norwegian specialist health services to examine the extent to which early motor and language delay was reported and current motor and language deficits were present when assessed, as well as their potential relationship with autistic symptom severity, each other and overall functional impairment.

To summarise, delayed walking and failure to attain first phrase speech by two years of age were present in a large minority of the children for whom information on these milestones was available. While later onset of independent walking (AOW) was found among children with ASD compared to children with subthreshold symptoms (non-ASD), significant delays were found for both groups compared with population norms. AOW was associated with the severity of core ASD symptoms across diagnostic groups and cognitive abilities. In the sample of children who had completed a language assessment (CCC-2) as part of their clinical evaluation, early language delay was more common in males and associated with structural language deficits, while pragmatic language and social skills did not differ between children with and without language delay. Structural language deficits were common and strongly associated with reduced pragmatic competence, regardless of diagnostic group. When supplementary measures were added to provide more detailed information on current skill profile and overall functional impairment in a smaller sample of school-aged children, we found that most children had motor and/or structural language deficits in addition to their social impairment. Moreover, better motor performance was strongly associated with better structural language and social skills, and functional impairment was associated with core ASD symptoms.

Taken together, our results suggest that motor and language deficits are common and closely related, with a potential impact on symptom presentation, overall functioning and service needs in children referred for evaluation for ASD.

5.2 General discussion

5.2.1 ASD versus subthreshold autistic traits

By combining the characteristics of children diagnosed with ASD and those of children with subthreshold autistic symptoms with dimensional trait measures applied to the whole group, we provide a profile of skill strengths and deficits among children evaluated for ASD. Our results suggest the presence of clinically important subgroups (not all children had co-occurring motor or structural language deficits) and variations along dimensional symptom profiles (pragmatic competence may vary, despite being closely linked to core ASD symptoms) within the autism spectrum that need to be addressed, regardless of the practical requirements for having diagnostic categories.

More children diagnosed with ASD than as non-ASD were recruited, both in the main study as well as for the local sub-study. The proportion of children in the ASD versus non-ASD group varied across the three samples (ratios ranging from 5:1 to 3:1), as did sample size and participant characteristics. These differences may have affected the extent and profile of deficits observed across the samples. The distinction between ASD and non-ASD inevitably rests on a clinical judgement of where to set the diagnostic threshold. We relied on clinical diagnoses made by specialist health services. The proportion of participants who completed the ADOS, the ADI-R or both as part of their clinical evaluation was generally large and increased throughout the study period. This likely reflects updated clinical guidelines and increased efforts to standardise evaluations for ASD in Norway during the timeframe of this project (NOU 2020:1; Surén et al., 2019a). However, this may also reflect that the children included presented with more severe autistic symptoms, leading to a strong suspicion and thorough evaluation for ASD, whereas children with more subtle autistic symptoms may not have been referred for an ADOS or ADI-R and, thus, may not have been invited to participate in the present study.

Consistent with current diagnostic criteria (American Psychiatric Association, 2013; World Health Organization, 1992), symptom severity was higher in the group of children diagnosed with ASD compared with the non-ASD group. However, there was some overlap between the two groups on all measures, supporting the concept of autistic symptoms as quantitative traits transcending diagnostic categories (Frazier et al., 2015). Such overlaps may be unavoidable, reflecting genetic relationships between ASD and other NDDs (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2019; Grove et al., 2019).

Furthermore, ASD symptom measures are found to capture more than symptoms of ASD; consequently, impairments in other domains, such as cognitive and language deficits and emotional and behaviour problems, may contribute to elevated symptom scores in both groups (Havdahl et al., 2016; Hus & Lord, 2013).

Most children in the non-ASD group were diagnosed with other NDDs, and the proportion of children diagnosed with two or more NDDs was generally large in both groups. Notably, the *ICD-10* does not allow the assignment of a co-occurring diagnosis of ADHD and ASD (World Health Organization, 1992). Still, ADHD was commonly co-diagnosed among ASD children (varying from 33.3% in Paper III to 59.3% in Paper II). This likely reflects a shift of diagnostic practice in the *DSM-5*, where a comorbid ADHD diagnosis is now allowed (American Psychiatric Association, 2013; Surén et al., 2019a). The high percentage may also indicate that clinicians recognise ADHD as an important comorbidity, for which treatment options are available for children with ASD (Lai et al., 2020; Lord et al., 2018).

Nevertheless, the most striking finding was the considerable heterogeneity and variability in skill performance across all domains (social, motor, language, cognitive, functional), even after applying relatively strict inclusion criteria in the local sub-study (verbal, school-aged children without severe cognitive disabilities, evaluated by CAMHS). This variability is important, as it highlights individual differences and the potential presence of important subgroups within the autism spectrum.

5.2.2 Autism symptoms and motor impairment

During the timeframe of this project, the number of publications on the scope, significance and centrality of motor differences in ASD has grown enormously (see Zampella et al. (2021) for a recent review). Thus, our results add to recent meta-analyses, reviews and large-scale studies confirming that motor deficits in individuals with ASD commonly present early and are pervasive across development. However, only a minority of these individuals receive appropriate assessment, a co-occurring diagnosis or specific interventions for their motor difficulties (e.g., Bhat, 2020; Licari et al., 2019; West, 2019; Zampella et al., 2021). By demonstrating that AOW was delayed not only in ASD individuals compared to TD children and the non-ASD group, but also in children with subthreshold symptoms (non-ASD) compared to TD children, we extend these findings to the broader group of children with

autistic symptoms and across a range of cognitive abilities. Although most children did achieve walking by the age of 16 months, almost a third of the ASD group were characterised as ‘late walking’, implying a clinical-level degree of early motor delay that could alert parents and clinicians about potential developmental concerns (Harris, 2017; WHO Multicentre Growth Reference Study Group, 2006b). The observed magnitude of delay – children with ASD walking *on average* almost two months later compared with TD children – is comparable to that reported for previous studies (Lemcke et al., 2013; Ozonoff et al., 2008; West et al., 2017).

Despite increased awareness, knowledge related to the trajectories of motor skills in individuals diagnosed with ASD and their link to other developmental skills, as well as the specificity of motor deficits to ASD versus other diagnoses through childhood, is still limited (Lim et al., 2021; Zampella et al., 2021). In a prospective study of 30 children referred for assessment due to early motor delays or abnormalities, including delayed walking, Hatakenaka et al. (2016) found the majority to have at least one NDD. Thirteen children were later diagnosed with ASD, 92% of whom had two or more NDDs. In a more recent publication from the SPARK study (n = 11,814), the proportion of children with ASD identified at risk for motor impairment by parent report (DCDQ) was significant (87%), and that risk persisted into adolescence (Bhat, 2020). However, only a small segment of the children (32%) were receiving physical therapist services. The proportion of children with current motor deficits reported by parents on the DCDQ’07 in our local sub-study was of the same magnitude (80%), albeit with a considerably lower proportion identified with motor deficits on standardised assessment with the MABC-2 (39%). A recent study examining the psychometric properties of the DCDQ to screen for co-occurring motor deficits in children with ASD (5-15 years) concluded that the DCDQ can be used to exclude a DCD diagnosis as well as to detect motor difficulties in children with ASD, regardless of meeting diagnostic criteria for DCD (Van Damme et al., 2021). Taken together, a significant percentage of the children with ASD were found to have motor deficits of clinical significance when assessed beyond parent report, and an even larger proportion were reported by their parents to possess motor deficits with a likely impact on their everyday functioning (e.g., Bhat, 2021; Hirata et al., 2015), although not clinically recognised. In sum, these motor challenges are at least as prevalent in people with ASD as either intellectual or language impairments, which are both *DSM* specifiers and widely thought to shape the presentation of

core symptoms, functional impairment and treatment needs (De Marchena & Zampella, 2022).

Conceptualising how motor impairments fit within the broader framework of ASD requires disentangling its relationships with core ASD symptoms, other co-occurring deficits and functional impairment to clarify whether they are *domain-specific* (associated with core symptoms of ASD), *domain-general* (associated with general cognitive, language and functional impairments) and/or *transdiagnostic* (increase in severity with co-occurring diagnoses reflecting shared underlying neural mechanisms; Bhat, 2021). Prior to our study on AOW, several studies reported a pattern of increasing motor delay across clinical groups, in which children with ID showed the most delay, followed by ASD subtypes by decreasing severity (Lemcke et al., 2013; Matson et al., 2010; Ozonoff et al., 2008). However, Paper I presents the first study to report that AOW in individuals evaluated for ASD is delayed compared to population norms and is closely associated with ASD symptoms across the broader spectrum of children with autistic symptoms, beyond an ASD diagnosis. Although this relationship held even after adjustment for cognitive abilities, NVIQ contributed somewhat to attenuating the results.

The possibility that motor deficits are more general signs of compromised neurocognitive development, rather than specific to ASD, has been discussed (e.g., Bolton et al., 2012; Ozonoff et al., 2008). Subsequent studies have clarified that motor differences in ASD individuals appear to be associated with *both* core ASD symptoms and cognitive deficits (Buja et al., 2018; Licari et al., 2019). However, AOW is less strongly related to low intellectual ability in children with ASD than in children with other NDDs, both in clinical (Bishop et al., 2016b) and population-based studies (Havdahl et al., 2020). Buja et al. (2018) demonstrated that, among individuals with ASD, lower IQ and measures of impaired motor skills (including AOW and DCDQ) are distinctly associated with damaging mutations and that motor skills are a more sensitive indicator of mutational severity than cognitive abilities. Based on their findings, a combined classification of phenotypic severity was proposed: ‘mild’ (little impairment of either), ‘moderate’ (impairment mainly to motor skills) and ‘severe’ (impairment of both IQ and motor skills).

We report in Paper I that, among children with ASD, where mean AOW was latest, the proportion having two or more NDDs (51.8%) was larger than in the non-ASD group (41.9%), although the difference did not reach a level of statistical significance. Using parent-

report data from the SPARK study, Bhat (2021) recently reported that the risk of motor impairments in children with ASD increased not only with social communication, cognitive and language impairments but also with the presence of comorbid diagnoses, such as ID, DCD and ADHD, underscoring the transdiagnostic nature of motor impairments. Although motor differences are pervasive and associated with both core ASD symptoms and more general functioning across development, the precise nature of these associations and the specificity of motor profiles to ASD remains unestablished (Zampella et al., 2021). A high degree of heterogeneity in motor performance exists within the autism spectrum (Fournier et al., 2010). Indeed, this *variability* at both the group and individual levels may represent an important characteristic of ASD (Wilson et al., 2018b). Thus, it is now commonly argued that motor functioning should be included as a clinical specifier for ASD in the *DSM-5*, in the same manner as intellectual and language impairment, to signal its importance and provide a framework for how motor deficits fit into the diagnostic picture (Bhat, 2021; De Marchena & Zampella, 2022; Licari et al., 2019).

5.2.3 Autism symptoms and language impairment

In the *DSM-IV* and the *ICD-10*, structural language skills (in terms of early language delay and current expressive language skills) have been important to distinguish between ASD subtypes. In currently revised terminology (Delphi consensus study; Bishop et al., 2017a) and diagnostic classification systems (*DSM-5* and *ICD-11*), language impairment is considered a co-occurring deficit or specifier to be noted along with the ASD diagnosis (American Psychiatric Association, 2013; World Health Organization, 2019). The *DSM-5* emphasises that "the current level of verbal functioning should be assessed and described" (American Psychiatric Association, 2013, p. 53). However, little guidance is available for a description beyond broad categories, such as having no intelligible speech (i.e. being nonverbal), using single words only, using phrase speech and speaking in full sentences/fluent speech.

To assess the extent of early language delay and the current profile of language deficits, we used the 'phrases by age two' milestone, as well as the CCC-2, which is designed to provide information on structural and pragmatic language skills that may be difficult to capture in a standardised assessment setting. Notably, our sample in Paper II comprised verbal children evaluated for ASD, a group traditionally considered 'high-functioning' and with verbal strengths. Nevertheless, a large minority (27%) of those with available milestone

information had reported an early language delay. The finding on this proportion is comparable to findings from the Norwegian Mother and Child cohort study (MoBa), a prospective, population-based cohort that includes children all over Norway born from 1999 to 2009 (22%; Surén et al., 2019b). Kenworthy et al. (2012) found retrospectively reported language milestones to predict later structural language skills in children with ASD. We extend their findings to the broader group of children evaluated for ASD and by using the CCC-2 as opposed to a standardised assessment of structural language. Many children in both groups (ASD/non-ASD) had, according to their parents, structural language deficits – such as misinterpreting what has been said (comprehension), mixing pronouns (syntax), mixing up words with similar meanings (semantics), mispronouncing words (speech) and struggling to express a coherent oral narrative (coherence). These deficits obviously may impair social and everyday functioning and may benefit from targeted interventions (Nowell et al., 2021). Although several assessment tools are available for identifying structural language deficits in children, few of them measure the social–pragmatic deficits common in ASD (Nowell et al., 2021). Parent or caregiver reports of the child's communication skills across contexts, such as through the CCC-2, offer one way to collect such information.

Using the CCC-2, we found that most children were classified as 'language impaired', meaning that their general communication skills were rated below the applied cut-off (GCC < 55, corresponding to the 10th percentile in the British normative sample). The observed extent and profile of deficits is consistent with reports from previous studies (Baixauli-Fortea et al., 2019; Boucher, 2012; Helland et al., 2012; Kuijper et al., 2017), although likely representing an underestimate of the true extent. As GCC scores corresponding to the 10th percentile in Norwegian samples are found to be higher, the appropriate GCC cut-off for identification of 'language impairment' in Norwegian samples may be higher, warranting future studies for clarification (Reindal et al., 2022). While pragmatic language impairments were most profound in the ASD group, structural language deficits were common regardless of diagnostic group and were strongly associated with reduced pragmatic competence. Individuals with pragmatic difficulties, such as lacking a response to conversational cues from others and lacking awareness of social expectations during a conversation, may benefit from support that aids them in understanding the social expectations of others (Nowell et al., 2021).

In the sample described in Paper III, several children diagnosed with Asperger syndrome had CCC-2 subscale scores that indicated structural language deficits. Notably, this

diagnose implies no language delay/impairments according to the *ICD-10*, suggesting that such language deficits may be easily overlooked, even in a clinical setting. Our results are consistent with another study that reported that roughly half the children with autism who are verbal manifest with mixed expressive/receptive structural language impairment (Loucas et al., 2008) and underscore the importance of assessing language skills, even in verbal children evaluated for ASD. Notably, the CCC-2 is not a diagnostic tool but designed to identify children with *possible* language disorders and children who should be assessed more closely for ASD. Children with ASD may have good structural language skills while struggling with pragmatics. They may not be identified as 'language impaired' by their GCC score on the CCC-2 but, rather, by a deviant Social Interaction Deviance Composite score, indicating disproportionately affected social and pragmatic skills. As our focus was to describe the extent and profile of language deficits, and not to use the CCC-2 for classification into clinical subgroups, we did not report the Social Interaction Deviance Composite scores. A new diagnosis, Social (Pragmatic) Communication Disorder, was added to the NDD section of the *DSM-5* (American Psychiatric Association, 2013), comprising children who exhibit social communication and pragmatic language impairments, while not meeting the criteria for ASD. This diagnosis, however, is complicated with clear overlaps with the diagnostic criteria for language disorder and ASD, making differential diagnoses particularly challenging (Norbury, 2014). Consequently, Mandy et al. (2017) conceptualised Social (Pragmatic) Communication Disorder as lying "on the borderlands of the autism spectrum, describing those with autistic traits that fall just below the threshold for an ASD diagnosis" (Mandy et al., 2017, p. 1166).

Taken together, structural language deficits are common across diagnostic groups, including those diagnosed with ASD, but vary within the autism spectrum. In the *ICD-11*, *functional language* refers to "the capacity of the individual to use language for instrumental purposes", reflecting primarily structural language deficits and not the pragmatic deficits inherent in the ASD diagnosis (World Health Organization, 2019). Our finding that structural language difficulties were strongly correlated to pragmatic language skills not only in children with ASD but also in children with subthreshold symptoms suggests that deficits in structural language likely will be accompanied by deficits in pragmatic competence. Both need to be addressed in a clinical evaluation. Pragmatic competence requires an understanding of the structural aspects of language but also of how to apply those skills when interacting socially (Eigsti et al., 2011). Thus, although being closely related to the core

symptoms of ASD, pragmatic language skills are not necessarily the same as social communication skills and may be better viewed as a transdiagnostic dimensional trait reflecting a confluence of risk factors, among them deficits in structural language (Norbury, 2014). Factors beyond a child's social and structural language skills may also contribute to pragmatic competence, including cognitive abilities, the presence of co-occurring attention deficits, executive dysfunction and behavioural problems, all of which have been linked to both social and pragmatic deficits (Helland et al., 2014b; Ketelaars et al., 2009).

As with motor skills, conceptualising the role and impact of language impairment within the broader framework of ASD requires an understanding of its relationships with other developmental and functional domains. Notably, children with ASD can have language impairment and normal range cognitive abilities or no language impairment in the presence of nonverbal cognitive deficits (Silleresi et al., 2020). Volden et al. (2009) reported not only that structural language skills predict pragmatic competence in youth with ASD but also that pragmatic language, in turn, uniquely predicted social skills. Thus, although mediated by pragmatic language, structural language skills may influence what we perceive as social skills, underscoring the importance of examining language skill domains separately when evaluating children with suspected ASD.

5.2.4 Early developmental delay and current functioning

The studies included in this thesis were all cross-sectional and do not allow any conclusions to be drawn regarding skill trajectories or causal relationships between these skills. Nevertheless, the combined use of milestone data and current skill measures provides new information on the varying symptoms across the autism spectrum, as well as on potential 'upstream' precursors and 'downstream' developmental consequences of deficits in core developmental domains, all of which may inform our current understanding and future study of underlying developmental processes (Hudry et al., 2020; Sroufe & Rutter, 1984).

The significant variability in symptom presentation and the failure to identify distinct diagnostic markers of ASD has led researchers to focus on broader developmental risk markers for earlier identification that may precede the onset of classic ASD symptoms (Whitehouse, 2017). Duvall et al. (2021) suggested conceptualising the variety of presenting symptoms as 'red flags' (clearly diagnostic, classic symptoms) or 'pink flags' (more subtle associated features and less definitive symptoms) for ASD, depending on their intensity,

atypicality, prevalence and specificity. Although subtle, the latter comprise "potentially diagnostic features of ASD that should raise an evaluator's concern for the diagnosis" (Duvall et al., 2021, p. 3). Some of these associated symptoms may also serve as stratification biomarkers to identify subgroups of individuals within the autism spectrum with different characteristics, such as an underlying genetic abnormality or liability (Bishop et al., 2016b; Hannigan et al., 2020; Havdahl et al., 2020; Satterstrom et al., 2020), prognosis or treatment response (Loth & Evans, 2019).

Traditionally, early motor delay has not been considered a warning sign for ASD. Developmentally, motor skills play a key role in shaping a child's interactions with other people and with their environments; they are also closely intertwined with the development of other skills (De Marchena & Zampella, 2022; Jones et al., 2014; West, 2019). Strides in motor development, such as learning to grab, reach, point, stand and walk, likely alter the landscape in which cognitive, language and social learning occurs (West, 2019). Early motor differences can, therefore, have cascading effects across developmental domains. The reported delay in AOW among children with ASD is consistent with the findings of recent studies documenting that infants who later receive an ASD diagnosis first diverge from their TD peers in the motor domain, a difference that continue to increase with age (Lim et al., 2021; West, 2019). The assessments in Paper I did not include a broader measure of current motor functioning, which would have been useful to examine whether AOW predicts ASD symptom severity over and above general motor ability. Nevertheless, our results support that delayed AOW occurs commonly in ASD and is associated with severity of symptoms that characterise ASD. Exploring the rates of motor difficulties in children (<7 years) from the Australian Autism Biobank and how early motor concern impacted their current functioning, Reynolds et al. (2021) found that more children with delayed walking milestones had motor difficulties based on parent report. Moreover, the likelihood of having difficulties in other non-motor domains (social, communication, daily living) was also greater for children with walking delays. Thus, considering *the possibility of ASD* in infants with delayed AOW may not only enhance the potential for earlier diagnosis but may also improve the chance of targeting and addressing subsequent motor and functional impairments in treatment programmes and may facilitate better prognostic outcomes. Contrary to delayed AOW, early language delay is not found to predict autistic symptom severity in children with ASD (Kenworthy et al., 2012; Loucas et al., 2008). Still, lasting individual differences in language skills seem to be established early (Bornstein et al., 2018). Our finding that early language

delay was associated with later structural language deficits apart from autism symptoms suggests that early language delay may also be an important subgroup marker within the autism spectrum and of importance for targeted interventions.

Typical motor function is considered neither necessary nor sufficient for normative communicative development, yet evidence suggests that early fine and gross motor skills are linked to both concurrent and future communication skills in infants later diagnosed with ASD (West, 2019), as well as in infants with elevated likelihood of ASD (LeBarton & Landa, 2019). Although preliminary, in Paper III we extend previous reports of a similar relationship between motor and language/communication skills in school-aged children (Bhat, 2021; McPhillips et al., 2014) by demonstrating a strong correlation between motor performance and structural language skills in school-aged children evaluated for ASD.

Taken together, our findings highlight a potential relationship between 'late walking' and increased severity of core ASD symptoms, as well as between 'late talking' and current structural language deficits, regardless of being diagnosed with ASD or having subthreshold autistic symptoms. As the attainment of these milestones varies across the broader group of children with autistic symptoms, with delays presenting early (prior to formal diagnosis) and linking to future outcomes, our findings lend strength to the argument that they represent potential stratification biomarkers for ASD. During the last several decades, an increasing number of genetic conditions have been identified that impart risk for ASD and other NDDs. Many of these have been associated with delays in AOW and expressive language (Bishop et al., 2017b; Bishop et al., 2016b; Buja et al., 2018), suggesting that attainment of these milestones may be useful as a marker of potential genetic abnormality in ASD samples. More recently, Wickstrom et al. (2021) compared individuals with one of 16 rare genetic conditions associated with ASD (Simons Searchlight; n = 479) to individuals with idiopathic ASD (absence of known pathogenic findings; SPARK; n = 3,506), finding that individuals with genetic conditions were more likely to display pronounced delays in early gross motor and expressive language milestones. Notably, delays were more common and more severe for the expressive language milestones than for gross motor skills (Wickstrom et al., 2021). By contrast, delays in expressive language milestones were less variable, suggesting that delays in early language for individuals with ASD are not specific to an identifiable genetic condition. Nevertheless, the genetic groups with the largest proportion of expressive language delays also had the largest proportion of gross motor delays. This is consistent with our results reported in Paper III and the results of other studies that suggest that these systems are

strongly related (Bhat, 2021; Libertus & Hauf, 2017). Using polygenic scores from a genotyped subset (N = 25,699) of children in the Norwegian MoBa study, AOW was also found to be associated with genetic liability for ASD in the general population, but only in females (Hannigan et al., 2020). Notably, no robust evidence was found to confirm a similar relationship with language developmental milestones.

An intriguing consideration is whether co-occurring motor and/or language deficits may also affect what we perceive as autistic social impairment. De Marchena and Zampella (2022) argued that because people's movements (including gait, posture and coordination) are highly salient to others in everyday life, motor difficulties can directly influence social interactions and social perceptions of affected individuals. In Paper III we report a significant association between current motor skills (DCDQ'07 and MABC-2) and autistic symptoms in terms of current social impairment (SRS), while *no* significant association was found with core ASD symptoms (ADI-R), indicating the *opposite pattern* of what we found in Paper I (where AOW correlated most strongly with core ASD symptoms as measured by the ADI-R). This may be a consequence of the small sample and lower number of participants with available ADI-R and MABC-2 scores (n = 16). Alternatively, social impairment as *perceived* by parents and reflected by the SRS scores may be influenced by the presence of current motor deficits to a larger extent than as reflected by the ADI-R scores, which instead capture (partly historical) core ASD characteristics. A previous study by Hannant et al. (2016) also reported that MABC-2 scores did not correlate with the ADI-R scores (n = 18 children with ASD), while Hirata et al. (2015) found SRS scores to be strongly associated with both DCDQ and MABC-2 total scores.

5.2.5 Sex-based differences in the pattern of presenting symptoms

The growing awareness of sex-based differences in autism has largely focused on social and behavioural domains rather than on motor and language skills (Sturrock et al., 2021). Contrary to reports of no consistent sex differences in AOW among TD children (Jenni et al., 2013; Storvold et al., 2013; WHO Multicentre Growth Reference Study Group, 2006a), but in line with previous reports that females with ASD exhibit higher rates of delayed AOW (Arabameri & Sotoodeh, 2015; Bishop et al., 2016b), we reported in Paper I that females with autistic symptoms (regardless of ASD diagnosis) were more liable to *delayed* walking compared to males. Females with ASD had the latest AOW among all groups, with a mean

difference of 2.2 months compared to the normative sample, in which no sex difference was found (Storvold et al., 2013).

Consistent with our results reported in Paper I, some studies have shown that motor delays may be an early sign more commonly observed in autistic girls than in autistic boys (Gabis et al., 2020). As mentioned previously, Hannigan et al. (2020) reported autism polygenic scores to be associated with a later AOW, but only in girls. Rare high impact *de novo* risk variants for autism have also been associated both with the female sex and later AOW in ASD samples (Bishop et al., 2017b; Satterstrom et al., 2020). The reason for the observed sex difference in this association remains unknown. Investigating screening-negative infants later diagnosed with ASD in the Norwegian MoBa study, Oien et al. (2018) also found girls to present with less advanced early gross motor skills compared to boys. Along with reports from a large longitudinal population study that a substantial proportion of children with clinically significant autistic social traits did not present with those traits until adolescence, most of whom were girls (Mandy et al., 2018), this may suggest a different phenotype or emerging pattern of symptoms in females with ASD. Whether these girls are genuinely experiencing a later onset of social difficulties or earlier, more subtle pre-existing difficulties are becoming obvious remains to be determined (Mandy et al., 2018).

Studies examining potential sex differences in the structural language of school-aged children with ASD and normal range cognitive abilities are limited. While Solomon et al. (2012) found no sex-differences on the CCC-2 structural language subscales for a group of school-aged children with ASD and normal range cognitive abilities (n = 20 boys and n = 20 girls, matched on IQ), females in the present study generally had higher mean scores (indicating better performance) on most subscales compared to the males, although reaching statistical significance only for the 'syntax' subscale. Notably, the opposite pattern was observed for the pragmatic subscales 'use of context' and 'social relations', where females performed worse (non-significant; see Figure 3 in Paper II). Females also performed better than males on measures of verbal IQ, suggesting somewhat stronger verbal abilities. Consistent with our results, a recent review of the literature has suggested that females with ASD may show better language skills, mirroring normative sex differences and placing females closer to their TD peers and farther away from males with ASD (Lai & Szatmari, 2020). Still, when Burton et al. (2020) compared 18 girls with ASD and normal range cognitive abilities to a matched group of TD girls, they demonstrated age-appropriate structural language but impairments with understanding and using adequate structural

language in context. Despite the relatively subtle presentation of these difficulties (compared to their presentation in autistic males), their impact on social relationships, emotional well-being and functioning seems to be comparable and significant (Sturrock et al., 2021). Furthermore, our findings that only one female (4%) was reported with a language delay compared to the proportion of males (33%) reported with language delays, and that females with ASD received their diagnosis significantly later than males, are consistent with the findings of other studies documenting children with ASD and more advanced language abilities, particularly females, to be diagnosed later than non-verbal and minimally verbal children (McCormick et al., 2020; Salomone et al., 2016).

5.2.6 The relationship between symptom severity and functional impairment

The concept of *multi-morbidity*, which acknowledges the clinical importance of multiple problems (i.e. the presence of two or more chronic conditions) in the same individual, has recently gained awareness in general medicine (Thapar et al., 2017). Our results clearly demonstrate the need to address the common co-occurrence of other developmental issues, not only medical and psychiatric problems, among individuals with ASD and other NDDs, as they may impact both symptom presentation and functional impairment and, thus, have implications for clinical evaluations and treatment planning.

By adding supplementary measures to standard clinical evaluations for ASD for the children participating in the local sub-study, we learned that providing a profile of skill strengths and difficulties and overall impairment was feasible and conveyed valuable information on less prominent co-occurring motor and language deficits, as well as on individual strengths. Notably, co-occurring motor and language deficits and impairments across functional domains were common, even among verbal school-aged children who traditionally have been considered ‘high functioning’. The magnitude of early motor delay and pragmatic difficulties both increased in parallel with autistic symptom severity and were significantly more profound in individuals diagnosed with ASD compared to those with subthreshold autistic symptoms. Still, some children were functioning relatively well, despite deficits across several domains in addition to their current social impairment, perhaps reflecting adequate support and interventions. The observed considerable variability in skill performance underscores how ASD may affect various developing systems and highlights the need for a comprehensive assessment when children are referred for evaluation for ASD.

Clinicians' lack of awareness of this variability in symptom severity and presentation can lead to delayed recognition, misdiagnosis and lack of access to evidence-based treatments and support (Duvall et al., 2021).

Prior to this research, few studies had addressed the relationship between symptom severity and functional impairment in children with ASD or the extent of impairment arising from ASD traits versus co-occurring conditions (Gillberg & Fernell, 2014). Throughout papers I–III, we show that, even when individuals present with subthreshold autistic symptoms, they commonly co-occur with deficits in other developmental domains as well as with significant impairments across important domains of everyday functioning. Given the complex presentation of ASD, clinicians may have difficulty differentiating whether these difficulties impact daily functioning above and beyond the impact of the core impairments associated with ASD. When using the DD-CGAS in Paper III to synthesise the child's level of functioning across multiple domains, independent of main or co-occurring diagnoses, overall impairment mostly varied within the 'upper range', as expected, in a sample of verbal children without severe cognitive disabilities. In line with the results reported by Wagner et al. (2007), we found a strong association between the DD-CGAS score and core ASD symptoms among individuals with available ADI-R scores. Contrary to recent results from the SPARK study (Bhat, 2021), however, we found no significant association between the current skill measures (social, motor, language) and overall impairment. Limited sample size and range of functioning likely contributed to this result.

Using the original MABC and the VABS among school-aged children with ASD (n = 101), Green et al. (2009) discovered that, when the effect of IQ was controlled for, motor impairment was not associated with everyday adaptive behaviour. However, Bremer and Cairney (2018) reported that overall motor coordination was positively related to daily living skills, using the MABC-2 and the VABS-2 in a smaller sample (n = 26) of same-aged children with ASD. Nevertheless, when exploring the contribution of co-occurring problems to impairment and service contact among children with high ASD traits in a total population sample, Posserud et al. (2018) found that both impairment and contact with health services were largely explained by co-occurring problems. As co-occurring motor and language impairments generally have been linked to reduced ability to engage in sports and leisure activities, the acquisition of daily living skills and social and academic challenges, targeting motor and language skill differences may provide an important path for improving functional outcomes (Baird & Norbury, 2016; Duvall et al., 2021; Zampella et al., 2021).

5.3 Strengths and limitations

Traditionally, autism research has focused on studying 'pure' and strictly defined cases. However, such an approach can hinder the generalisation of the results to children seen in clinical settings. Based on the recognition that autism is a relatively common, dimensional and lifelong condition that is usually accompanied by co-occurring difficulties, research approaches have changed, with greater attention to heterogeneity and the increased use of autism trait measures with subclinical groups (Happé & Frith, 2020). At the same time, emphasis on large sample sizes has increased. Still, such big data must be balanced with deep phenotyping (Happé & Frith, 2020).

A major strength of this thesis is the combination of these approaches represented. Papers I and II addressed studies that included relatively large samples of individuals with a broad range of autistic symptoms and cognitive abilities. Contrary to many previous studies on language and motor skills in ASD, we provide information on comorbid diagnoses and children with subthreshold autistic symptoms, which is considered to increase the generalisability of the findings to the broader population of children evaluated for ASD. We used validated instruments, and the nature of our data collection allowed detailed characterisations of the samples, as well as adjustment for covariates and potential confounding factors.

Other strengths of this thesis include the large sample sizes compared to the sample sizes in previous studies on AOW and the CCC-2 in children with ASD, the relatively large number of females included and the availability of Norwegian norms for comparison. Although small and exploratory in nature, a strength of our local sub-study outlined in Paper III is the provision of a more detailed developmental skill profile of school-aged children evaluated for ASD, which is difficult to accomplish within the frame of larger-scale studies.

The cross-sectional study design prevents causal inference and deductions about the developmental trajectories of motor and language skills, their relationship to one another, core ASD symptoms and functional consequences throughout childhood. Nevertheless, by providing a snapshot of children evaluated for suspected ASD by Norwegian specialist health services, the cross-sectional data obtained provide valuable information that may improve our understanding of core symptoms and co-occurring motor, language and functional impairments in line with our research aims. A prerequisite, however, is adequate internal and external validity, which is more thoroughly discussed in the following sections.

5.3.1 Internal validity

Internal validity refers to the degree to which our estimates and inferences are valid (nonbiased, without systematic error) for our sample of participants and not attributable to other factors. Most violations of internal validity can be classified into three categories: *selection bias* (the way in which the participants have been selected), *information bias* (the way the study variables are measured) and *confounding* factors that are not completely controlled (Rothman, 2012).

Selection bias

Participants in all three samples comprised children evaluated for ASD by Norwegian specialist health services, indicating that the referral for assessment was based on a concern. Clinical samples may be highly selective regarding subject characteristics, with factors associated with seeking help or encountering services potentially biasing our conclusions (Verhulst & Koot, 1992). For instance, even referred children may be subject to the effects of gender biases if these are operating in referral sources (e.g. screening instruments or recognition of autistic symptoms in females; Dworzynski et al., 2012). The relatively high proportion of female participants across all samples may indicate that referral and ascertainment bias leading to under recognition of ASD in females was low (Lai et al., 2015).

Generally, co-occurrence rates for problems and disorders are elevated in clinical samples, a phenomenon referred to as Berkson's bias (Rothman et al., 2008). This may have influenced the reported extent of co-occurring deficits, diagnoses and functional impairment. Hence, the participants may not be representative of children with autistic symptoms in the general population. However, a previous Norwegian study on children with high ASD traits found that impairing co-occurring problems were also common in a population-based sample (Posserud et al., 2018).

Information bias

Retrospective information was used related to achievement of developmental milestones (AOW and attainment of phrase speech at two years of age), introducing the possibility of recall bias. The quality of information about developmental milestones from caregivers of children with ASD was examined by Hus et al. (2011), who found AOW to be one of the most reliable parent-reported measures, while phrase speech was reported as occurring significantly later when parents were re-interviewed as the child aged, which is referred to as

forward telescoping (Hus et al., 2011). Similar patterns of telescoping were found for children with other developmental delays, suggesting that these influences on caregiver reporting are not specific to ASD (Hus et al., 2011). The authors suggest the use of records or anchor points to increase the reliability of recall. In the present studies, parent reports on milestone attainment were supplementary to information available in the children's medical records. Notably, we observed a tendency for reported AOW to cluster around typical age markers (e.g. 12, 18 and 24 months). The same tendency is reported with regard to language milestones in a publication by Kenworthy et al. (2012). Although the precision of information regarding AOW and early language delay may have varied, we consider it unlikely to have systematically biased our results. Further, the pattern and magnitude of delay observed is comparable to that found in previous studies.

The BUPgen study relies on archival data, supplemented by a few standard inclusion measures. Hence, clinical diagnoses were obtained from different clinics, which may have introduced variations. Misclassification in both directions for ASD and the non-ASD disorders are considered possible but not very probable. A recent review of patient records showed that 95% of ASD diagnoses provided a high standard of documentation within the Norwegian specialist health service and met the diagnostic criteria (Surén et al., 2019a).

Confounding

Nonverbal cognitive ability (NVIQ), age at inclusion and sex were included as potential confounding factors in the studies documented in Papers I and II, as they may affect both motor and language skills, as well as the severity of autistic symptoms. In the study for Paper I, prematurity, ethnicity and maternal and paternal age were also included due to their potential impact on both autistic symptoms and early motor development. Other confounding factors may not have been adjusted for, thereby biasing our results. For example, both socioeconomic status and the presence of childhood maltreatment may affect the risk of having multiple NDDs (Dinkler et al., 2017; Han et al., 2021). However, we did not have available measures to account for the potential degree of bias introduced by these factors. Mild or moderate deficits in social and communicative competence may also be missed in the context of other co-occurring difficulties, such as ADHD (Skuse et al., 2009), a common NDD across all samples. As the proportion of individuals diagnosed with ADHD did not differ much between the two diagnostic groups, we do not consider their inclusion to have biased our results in one direction. The large proportion with co-occurring ADHD, however,

may have contributed to the observed late age of ASD diagnosis. The limited sample size in Paper III did not allow for adjustment for potential confounding factors.

Children with language impairments may have parents with similar problems, who may find completing questionnaires linguistically demanding, which can put those adults at a disadvantage (Helland et al., 2014a). In Paper II, our sensitivity analyses revealed that 12.6% of parents were inconsistent in their answers when completing the CCC-2. Furthermore, children with parental invalid consistency check had scores indicating larger impairments in general communication and structural language skills. Although excluding individuals with invalid consistency check was not found to affect our main results substantially, our sensitivity analyses suggest that not passing the reliability check may not be a random event, and exclusion of these individuals may bias results on a group level and lead to underestimating the true extent of structural language deficits in research samples.

Reliability and validity of the assessments

The original versions of the instruments used in this thesis are considered to have acceptable reliability and validity to assess social, motor, language and cognitive skills, as well as overall function. However, Norwegian norms were not available for all instruments, or the norm base and information on psychometric properties for the Norwegian version is limited. Thus, we underscore the exploratory nature of some of our results, which should be replicated in larger samples and compared to comparable results for same-aged TD children to confirm their relevance. Where available, training procedures were followed. Where possible, we report Cronbach's alpha and inter-rater reliability. To obtain valid and reliable assessments in the local sub-study, all participants were tested by the same (two) investigators, who were trained in the assessments, and standardised settings were used.

May our results be due to chance?

Having considered systematic errors, what remains are random error or variability in data that cannot readily be explained (Rothman, 2012). The BUPgen study collects clinical data from many participants, providing large datasets. Although reducing the amount of random error, the richness of such datasets can lead to effects that are statistically significant due to chance that do not reflect true differences among groups, i.e. false positive findings (Type I error; Rothman et al., 2008). By limiting our analyses to the variables of primary interest and potential confounding factors, we aimed to reduce the risk of Type I errors. Furthermore, to indicate both the strength of the relationships observed and the precision with which those

relations were measured, we report confidence intervals in addition to our estimates and the corresponding *p*-values. Despite the large samples involved in the studies highlighted in Papers I and II, the relatively small number of females in these samples as well as the limited sample size in Paper III increases the risk of false negative findings (Type II error; Rothman et al., 2008).

5.3.2 External validity

External validity refers to the extent to which the results of a study can be generalised to other settings and individuals outside the study sample. ASD is highly heterogenous in its symptom presentation, aetiology and co-occurring difficulties. This inherently limits the generalisation of studies to similar subgroups within the autism spectrum (Gillberg et al., 2019). Sample sizes and participant characteristics varied across the three samples. The major concern regarding the generalisability of the local sub-study described in Paper III is the small sample size. While a detailed description of each sample was provided, no information was accessible on how many or which children did not get invited in the main study, or on how many of those invited did not participate. Participants mainly comprised verbal school-aged children evaluated for ASD by CAMHS, although some children who were nonverbal, preschool-aged and/or evaluated by child habilitation services did participate. Nevertheless, our estimates may differ for larger, more diverse samples. Furthermore, as we did not have a control group, we cannot know whether the associations reported are specific to children evaluated for ASD or present in other populations as well.

5.4 Ethical reflections

The significant personal and societal burdens associated with ASD and other NDDs call for early attention to a variety of developmental problems and for developing effective interventions to improve future outcomes for affected children (Bhat, 2020). Although clinicians may have difficulty determining whether a child presenting with delayed or deviant development is at risk of being diagnosed with autism, taking a ‘wait-and-see’ approach and not acknowledging a child’s difficulties to avoid causing undue worry for the parents may deprive the child and it’s caregivers from important support and interventions (Coleman & Gillberg, 2012). As reviewed by Happé and Frith (2020), the traditional notion that ASD is defined by deficits inherent to the person has recently been challenged. Instead, many

advocate the position that autism may be considered a difference or *neurodivergence* that "constitutes a disability in the context of the demands of the neurotypical world" (Happé & Frith, 2020, p. 228). As such, our focus on earlier detection and intervention within the broader group of children with autistic symptoms, beyond ASD, may be taken to impose unnecessary concerns and pathologise what some may consider natural variations.

Although eliminating delays in identifying individuals in need of support is critical, Lai et al. (2015) cautioned against pathologising those who manage well and do not meet the functional impairment criteria for a diagnosis, despite presenting above-threshold autistic traits. Important ethical concerns also arise from research on early neurodevelopment and from interventions being developed because of this research (Manzini et al., 2021). "Acknowledging that very early development *influences*, rather than *determines*, autistic individuals' future outcomes is fundamental to oppose certain assumptions that may (and do) harm children and their parents" (Manzini et al., 2021, p.1368). Thus, when interpreting our results and their implications, the observed large variability, despite significant findings on a group level, as well as the lack of specificity regarding ASD, need to be underscored because they do not allow predictions regarding outcomes on an individual level.

5.5 Theoretical implications

Neurodevelopmental disorders are complex conditions that are far from straightforward to conceptualise. While the observed associations with severity of core ASD symptoms highlight the domain-specific nature of motor impairments, the associations with cognitive, language and functional impairments indicate the domain-general nature of motor impairments and support a multisystem view of ASD (Bhat, 2021). Furthermore, associations with other diagnoses highlight the transdiagnostic nature of motor impairments and how motor impairments can be explained by shared neural mechanisms and benefit from shared assessments and treatment approaches across NDDs (Bhat, 2021). Indeed, as Bhat (2021) suggested, "the increasing severity of motor impairment as a function of cognitive, language, and functional impairments in children with ASD shows that motor impairment could be an indicator of how severe the original neuropathology is" (Bhat, 2021, p.213). This is in line with the ESSENCE model (Gillberg, 2010), as well as the developmental brain dysfunction model or conceptual framework launched by Moreno-De-Luca et al. (2013).

Most psychopathological conditions are not associated with a single primary causal pathway. Rather, a variety of developmental pathways may converge on common outcomes (Garber & Bradshaw, 2020). Although the idea of continuous traits underlying ASD and subthreshold autistic traits is appealing, our results clearly support that several traits or developmental skills likely interact with each other in complex ways to provide this heterogenous clinical picture (Lord et al., 2018). Based on the observation that "isolated fragments of the full clinical picture frequently occur", Wing and Wing (1971, p. 256) suggested that autism is best understood as a combination of impairments. More recently, Happé et al. (2006) suggested that the social, communicative and RRBI symptoms that define autism may have separable underpinnings at the genetic, neural and cognitive levels, the so-called *'fractionated triad' hypothesis*. Subsequent studies have documented social and nonsocial autistic traits to correlate only modestly in general population and clinical samples, beyond ASD (Happé & Ronald, 2008; Kim et al., 2018). More recent studies using polygenic scores to demonstrate genetic signals for the social versus nonsocial dimensions of autism have supported this conclusion (Warrier et al., 2017). On the individual level, ASD and co-occurring (non-ASD) impairments, although potentially overlapping, may interact to cause impairment that may be qualitatively more than the sum of its parts and create a unique and distinct condition (Happé & Frith, 2020).

5.6 Clinical implications

5.6.1 Assessment and diagnosis

Given the relatively high prevalence of ASD and autistic traits, clinicians across a range of specialties are likely to see patients who possibly meet the criteria for ASD, regardless of the reasons for referral (Duvall et al., 2021). While not all clinicians are expected to maintain a high level of expertise on ASD, a base knowledge is necessary to support effective identification, intervention and supports for individuals across the lifespan (Duvall et al., 2021; Lord et al., 2022). Knowing and recognising core diagnostic symptoms of ASD ('red flags') as well as more easily missed associated features and symptoms that are suggestive but not definitive of ASD ('pink flags') will improve a clinician's ability to more effectively and accurately confirm or rule out the diagnosis or to know when to refer the child for a more thorough evaluation for ASD (Duvall et al., 2021). To ensure that the diagnostic conceptualisation best captures the individual's symptom presentation, skill profile and

aetiology, the clinician also needs a solid understanding of how comorbidities, the overlap in symptoms across diagnoses, diagnostic overshadowing and individual factors such as age and gender may complicate the diagnostic process (Duvall et al., 2021).

While regarding ASD as a specific disorder is important, our results support that co-occurring difficulties should be highly expected in children with autistic symptoms and that greater emphasis should be placed on multi-domain assessments in the evaluation of children for ASD, to assess their needs beyond diagnosis, and to avoid the possibility of those with subthreshold symptomatology but significant impairment to miss out on vital services (Gillberg, 2010; Lord et al., 2022; Moreno-De-Luca et al., 2013; Thapar et al., 2017). Given the complex nature of NDDs, determining how much of the functional impairment in children with ASD is associated with the primary diagnosis or co-occurring symptoms can be challenging. Therefore, acknowledging the overall burden of core symptoms and co-occurring deficits is important (Thapar et al., 2017).

5.6.2 Early identification

Direct assessment of motor behaviour in the first two years of life has promise for earlier identification of ASD, but also broader developmental vulnerabilities for some children (Licari et al., 2021; Zampella et al., 2021). Motor disruptions may be more easily detected than core ASD symptoms, like social or communicative deficits; for example, recognising that an infant has not yet achieved a motor milestone may be easier than detecting atypical eye gaze or social bids. Whether in health surveillance, low-resource settings or large-scale research projects, AOW and the milestone of using phrases by the age of two may serve to identify subgroups of children with autistic symptoms at increased risk of ASD, motor or structural language impairments that can benefit from a more comprehensive assessment.

5.6.3 Interventions and services

The present findings add to accumulating evidence that motor impairments are clearly under-recognised, under-diagnosed and under-treated in children with ASD (Bhat, 2020; Licari et al., 2019; Zampella et al., 2021). Thus, an urgent call has been raised for clinicians to more routinely incorporate motor skills into ASD screening, evaluation and treatment planning (Zampella et al., 2021). Our findings also suggest a need for increased awareness about co-

occurring language impairments, particularly structural language deficits in verbal children evaluated for ASD, who may benefit from specific interventions targeting these deficits.

Preschool and early school years are a critical period for promoting motor and language skills. For many school-aged children with ASD and lower levels of support need, autism-specific treatments are not as common as those that primarily target comorbidities (Lord et al., 2022; Zampella et al., 2021). Among commonly available motor or language-focused interventions are referral for physical or speech–language therapy. Even if such interventions only yield improvements in motor or language skills, they should still be considered treatment priorities for individuals with ASD evidencing such co-occurring impairments, as they have been strongly linked to functional living skills (Bhat, 2021; Bremer & Cairney, 2018; Licari et al., 2019), indicating an opportunity to meaningfully improve functional outcomes. Although reluctance to engage in physical activity may present an issue, some older children may prefer that treatments focus on mastering everyday motor and language/communication difficulties rather than on changing core autism traits. Also important are efforts to increase society's awareness of individual differences and to encourage participation in activities based on the child's area of interest or competence.

As opposed to the traditional clinical pathway for children with ASD, according to which interventions follow a clinical diagnosis, Whitehouse (2017) proposed an alternative pathway. The key difference within this alternative pathway is the commencement of early and intensive interventions following the identification of 'risk markers' of ASD during the first two years of life, prior to the receipt of a clinical diagnosis. In a recent randomized clinical trial of preemptive intervention versus usual care, Whitehouse et al. (2021) found that receipt of a preemptive social communication intervention from age 9 months among infants showing early behavioural signs of ASD led to improvements in ASD symptom severity, language outcomes, and reduced the odds of an ASD diagnosis at 3 years of age, providing initial evidence of efficacy for such a model. Increased recognition of motor challenges in ASD has led to excitement about the potential development of specific motor-based interventions that can plausibly be delivered from very early in life for children with observed motor impairments and potentially produce broader downstream benefits (Hudry et al., 2020). Offering intervention based on the observation of an identified need rather than awaiting a formal diagnosis represents a transdiagnostic approach. However, the potential role, timing and effect of such interventions need to be clarified in future studies (Hudry et al., 2020).

5.6.4 Future research

Given the range of clinical presentations of children across the autism spectrum presented herein, the outstanding research topics may be how to decide when perceived 'autistic traits' are truly autistic in nature (Mottron & Bzdok, 2020) and "what combination of symptomatology, and at what age, may confer the greatest risk for a later diagnosis of ASD, and what are the best intervention approaches to assist the development of these infants" (Whitehouse, 2017, p.213). Disentangling the nature and complex relationships between different developmental skills and identifying potentially modifiable factors to optimise neurodevelopmental outcomes will require large, longitudinal patient and population-based studies including the entire spectrum of problems, beyond an ASD diagnosis (Thapar et al., 2017; Zampella et al., 2021). Tracking development over time, such studies may reveal the natural history of NDDs across ages, how multi-morbidity affects neurodevelopmental outcomes and the threshold for diagnosis and treatment (Thapar et al., 2017), as well as their relative contributions to functional outcomes (Posserud et al., 2018). Carefully designed intervention studies may provide evidence not only of the effect of targeted interventions but also of directionality, causality and underlying mechanisms (Hudry et al., 2020; Thapar et al., 2017; Zampella et al., 2021).

To uncover the answers to these questions, research participants need to be characterised beyond their primary diagnosis and comparability established across different studies to draw overarching conclusions. A shared measurement tool kit, including a common set of appropriate core developmental skill and functional outcome measures used by clinicians, service providers and researchers, would be extremely helpful (Choque Olsson & Bolte, 2014; Thapar et al., 2017; Wilson et al., 2018a). Although standardised skill measures are currently available, they may not capture more qualitative or subtle differences in overall function (Wilson et al., 2018b). For example, standardised assessments of motor function are valuable in identifying core motor deficits but often fail to capture the variability in motor patterns, such as muscle tone, which should be a priority for future research (Wilson et al., 2018b). Such efforts may be useful to stratify the heterogeneity in motor function across the autism spectrum, perhaps revealing unique endophenotypes (Wilson et al., 2018b). Although continued research on the variability of motor performance as a potential diagnostic and prognostic marker for ASD is encouraged, our results lend strength to the argument that the field may also benefit from studying motor differences as a potential transdiagnostic

symptom domain of relevance for developmental psychopathology more broadly (Hudry et al., 2020; Lim et al., 2021; Zampella et al., 2021).

Autism research has traditionally focused on white males in high-income countries, while current knowledge from underserved groups in low- and middle-income countries is limited (Happé & Frith, 2020). Also lacking is research that specifically asks individuals with ASD how co-occurring difficulties affect their lives and what, if any, supports and interventions would appeal to them (De Marchena & Zampella, 2022). For most non-autistic individuals, everyday functional skills, such as motor performance and combining movement and speech, are performed automatically, smoothly and fluidly. As illustrated in the very beginning of this thesis (section 1.1, first paragraph), first hand accounts may improve our understanding of how co-occurring difficulties may contribute to the differences that we experience as impairments in social interaction, communication and behaviour (Robledo et al., 2012).

6. Conclusions

The studies included in this thesis describe important differences between children diagnosed with ASD and those with subthreshold autistic symptoms; they also suggest the presence of clinically important subgroups and common underlying traits within the broader group of children evaluated for ASD.

Both delayed AOW and failure to attain phrase speech by the age of two were reported in a large minority of participating children. Within the whole group of children evaluated for ASD, later AOW was associated with increased severity of core ASD symptoms, while non-attainment of phrase speech was linked to more pronounced structural language deficits. On a group level, females with autistic symptoms had a liability towards later AOW, while non-attainment of phrase speech was less common in females compared to males. This suggests that early motor and language delays are common and, if present, may lead to earlier identification of children with increased risk for ASD and structural language deficits.

Difficulties with the social use of language (pragmatics) were most profound among children diagnosed with ASD and, thus, closely linked to core ASD symptoms, as expected. However, their presence was also linked to structural language deficits across the range of autistic symptoms. Structural language deficits were more variable and equally common in both diagnostic groups. When assessed simultaneously, both motor and structural language deficits were common and frequently co-occurred. Although they were not found to correlate with overall functional impairment in our sample, better motor and structural language skills were both associated with better social skills reported by parents. Hence, co-occurring motor and language deficits likely make a strong contribution to the overall burden of difficulties among children evaluated for ASD. The extent of this co-occurrence in larger, more diverse samples, as well as the role of specific interventions targeting motor and language skills in children with autistic symptoms, should be addressed in future studies. Meanwhile, motor and language skills assessment should be included in the evaluation of children with suspected ASD so that interventions can be adjusted to the child's profile of strengths, difficulties, demands and level of functioning.

7. References

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Paper I

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ORIGINAL PAPER

Age of First Walking and Associations with Symptom Severity in Children with Suspected or Diagnosed Autism Spectrum Disorder

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Abstract
Age of first walking (AOW) is reported to be later in autism spectrum disorder (ASD) compared with typical development. However, the relationship between AOW and variations in ASD symptoms across different neurodevelopmental disorders is largely unknown. This study investigated AOW and its association with autism symptom severity in a large sample of children ($N = 490$, 23% females) clinically evaluated for suspected ASD, differentiated into ASD ($n = 376$) and non-ASD ($n = 114$) diagnoses. Children with ASD achieved independent walking significantly later than children with non-ASD diagnoses. AOW was significantly associated with ASD symptom severity, and females had a non-significant later AOW. The current findings suggest that in cases with delayed AOW, ASD should be considered as an actual differential diagnosis, perhaps particularly in girls.

Keywords Autism spectrum disorder · Intellectual disability · Motor · Sex differences · Symptom severity · Walking

Neurodevelopmental disorders (NDD) affect 10–15% of children (Gillberg 2010; Boyle et al. 2011), often presenting with early delay in one or more developmental domains. Autism spectrum disorder (ASD) is a childhood onset NDD characterized by persistent deficits in communication skills and social interaction, as well as restricted, repetitive behavior and interests (RRB) (American Psychiatric Association 2013). Autistic symptoms vary widely both across individuals meeting diagnostic criteria and the general population (Constantino and Todd 2003, 2005; Posserud et al. 2006), and clinicians often face the dilemma of assessing children with autistic symptoms who do not meet the diagnostic criteria for ASD. At present, there is a growing dimensional view of ASD symptoms transcending diagnostic categories (Constantino and Charman 2016; Lord et al. 2018; Ryland et al. 2012). However, studies comparing characteristics of children receiving an ASD diagnosis to those who initially display signs of ASD but do not meet diagnostic criteria are needed.

Although motor performance is not part of the diagnostic criteria for ASD, motor deficits are common (Fournier et al. 2010), have been recognized as an associated feature since the earliest descriptions of the phenotype (Asperger 1944; Kanner 1943), and suggested as a cardinal ASD characteristic (Fournier et al. 2010; Staples et al. 2012; Hilton et al. 2012). Motor signs, such as the attainment of motor milestones, may be more easily and reliably observed than core ASD symptoms. This has led researchers to study early motor delays as a potential pathway for early identification and intervention in ASD. Emerging research has documented differences between ASD and typically developing infants, with higher rates of parent reported concerns about motor development and later attainment of motor skills, including walking among children with ASD (West 2018). Longitudinal data suggest these differences amplify

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with age (Landa and Garrett-Mayer 2006), and that early motor difficulties may be a risk factor for impaired social communication and cognition, traits that are related to ASD (Leonard et al. 2014). At present, early motor delays are considered to be a prodromal symptom of ASD (Bhat et al. 2012; Harris 2017), although with low specificity, as they are also associated with intellectual (Lemcke et al. 2013) and other developmental disabilities (Zwaigenbaum et al. 2015; Hatakenaka et al. 2016).

Age for onset of independent walking (AOW) is a fundamental and reliable (Hus et al. 2011) parent-reported milestone. Learning to walk is typically achieved around 12 months of age, and AOW at or after 16 months considered an established marker of atypical development (Onis 2006b). The onset of walking is found to support early language development (West et al. 2017; Walle and Campos 2014) and to affect infants' social interaction (Karasik et al. 2014), suggesting importance not only for later motor skills. Among children with ASD, a deviant pattern of language development following the onset of walking has been reported (West et al. 2017), potentially contributing to the communicative difficulties that characterize ASD. Recently evidence support that delayed AOW may also be an early marker of neurobiological and genetic abnormality in ASD (Bishop et al. 2017; Buja et al. 2018).

Attainment of walking is reported to be later among children with ASD. Estimates vary from 1.1 to 2.5 month delay in mean AOW compared with samples of typically developing children (Ozonoff et al. 2008), children at low risk for ASD (West et al. 2017), and a national birth cohort (Lemcke et al. 2013). Mean AOW has also been reported among different ASD subgroups (Matson et al. 2010; Lemcke et al. 2013; Ozonoff et al. 2008), and for other non-ASD samples with atypical development (Ozonoff et al. 2008; Bishop et al. 2016), intellectual disability (ID) (Lemcke et al. 2013) or language delay (West et al. 2017). Notably, study design, assessment methods, sample sizes and clinical groups used for comparison varied between these studies, hampering comparability and generalization of results. A further methodological limitation has been the lack of normative data regarding AOW. However, this is available in Norway, where the use of both national and regional data (Storvold et al. 2013), as well as comparisons with other countries (Onis 2006b) are considered to increase the external validity and generalizability of the results.

Increased severity of ASD has been related to greater deficits in a multitude of areas. An as yet unanswered question is whether delays in AOW is associated with severity of ASD symptoms across diagnostic categories. Several studies have reported a pattern of slowed motor development across clinical groups (Matson et al. 2010; Ozonoff et al. 2008; Lemcke et al. 2013), where children with ID or general developmental delays show the most delay, followed by ASD subtypes by decreasing severity. Motor skills have also been negatively correlated with symptom severity in autistic children (Hilton et al. 2012) and found to predict autism severity scores in toddlers (MacDonald et al. 2014) and school-age children with ASD (MacDonald et al. 2013), suggesting that motor skills may be related to symptom severity and not just an ASD diagnosis. Because of the high comorbidity of ID in children with ASD, the possible influence of cognitive impairment on early motor delays has been discussed as a limitation of several previous studies. In their sample of 1185 individuals (ASD, $n = 903$; non-ASD, $n = 282$), Bishop et al. (2016) found that lower IQ scores were associated with increased rates of late walking in both ASD and non-ASD groups, but children with low IQ without ASD were more likely to show delayed walking. Among individuals with ASD and nonverbal IQ (NVIQ) above 85, late walking (defined as at or after 16 months) occurred in 13%, against 31% in children with NVIQ less than 70. Female sex was found to heighten risk for delayed walking overall.

ASD is considered to affect males more often than females (Kim et al. 2011). The literature, however, seems biased toward investigating the male profile of ASD (Kirkovski et al. 2013). Given similar levels of ASD symptoms, females appear to require more behavioral/cognitive problems to receive a diagnosis (Dworzynski et al. 2012). Overall, females with ASD are more likely to have neurological abnormalities, less RRB, and worse intellectual and adaptive functioning than males (Lai et al. 2015). Whereas no consistent sex differences in AOW has been observed among typically developing children (Onis 2006a; Jenni et al. 2013; Storvold et al. 2013), there are indications that females with ASD exhibit higher rates of delayed AOW, compared with ASD males (Bishop et al. 2016; Arabameri and Sotoodeh 2015).

Although previous studies have provided useful information regarding AOW as a potential early marker for ASD, whether delays in AOW is associated with severity of ASD symptoms across diagnostic categories remains unclear. We investigated this relationship in a large clinical sample of Norwegian children assessed for suspected ASD by specialist health services, who varied in their severity of symptoms, cognitive abilities, and age at diagnosis. Specifically, we compared AOW, sex, age, NVIQ, and severity of autistic symptoms between children receiving an ASD diagnosis and children not meeting the criteria for diagnosis (non-ASD). Furthermore, we investigated the associations between AOW and symptom severity independent of ASD diagnosis. Finally, we investigated these questions separately for males and females. Available Norwegian population norms for AOW allowed for comparison with typically developing children.

Methods

Study Design

This study involved analyses of data collected and processed by August 31, 2017. The study sample is part of BUPgen, an ongoing large multi-site study of neurodevelopmental disorders in Norway, in which children are eligible for enrollment if a suspicion of ASD has been raised by local or specialist health services. Data are collected from two types of sites: (1) child habilitation services and (2) child and adolescent mental health services. These are public specialist health services receiving referrals for assessment of ASD, depending on the presenting symptoms, level of impairment, co-occurrent somatic or psychiatric difficulties, and according to local routines. After written, informed consent to participate, information from patients' records was extracted by clinicians, following standard procedures.

Participants

Participants were eligible if information on age (4–18 years) at inclusion, diagnostic classification as either ASD or non-ASD, and age of first walking (AOW) was available. A total of $N = 490$ children were included, born between the years 1992 and 2012, with a mean (M) age at inclusion of 11.1 years (standard deviation (SD) = 3.7) (Fig. 1). Data were collected from the clinical evaluation, and included results from present and previous clinical assessments, parent-reported history and supplementary parent-reported measures.

Diagnoses

All diagnoses were clinical diagnoses, assigned by specialist health services, using the International Statistical Classification of Diseases, 10th Revision (ICD-10) criteria (World Health Organization 1992). Participants were separated into two groups: A total of 376 children with a clinical diagnosis of any ASD according to ICD-10 (F84x) formed the ASD group, and 114 children with suspected autistic symptoms but no clinical ASD diagnosis formed the non-ASD group. The majority of ASD (81.6%, $n = 307$) and non-ASD individuals (56.1%, $n = 64$) had completed the Autism Diagnostic Interview-Revised (ADI-R) (Rutter et al. 2003b), the Autism Diagnostic Observation Schedule (Lord et al. 1999), or both as part of their clinical evaluation. Other NDDs were grouped according to ICD-10 codes: Intellectual disability (ID) (F70–79), Attention-deficit/hyperactivity disorder (F90), Communication disorder (F80), Specific learning disorder (F81 and F83), Motor disorder (F82 and F95),

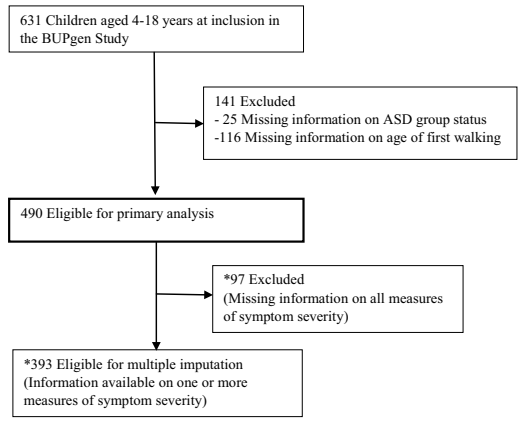

Fig. 1 Study sample recruitment flowchart. **Post hoc* analyses were performed to assess comparability with the total study sample ($N = 490$)

other neurodevelopmental disorder (F88, F89 and F94). The presence of epilepsy or cerebral palsy was also registered.

Measures

Early Motor Impairment

A clinician rated medical history form was filled in for all participants at inclusion, which inquired about age for onset of independent (unaided) walking (in months) (AOW). This form was completed based on available information in the child's medical record supplemented by parent report, asking parents to retrospectively recall AOW. Comparisons were made with mean AOW from a typically developing population, obtained from (Storvold et al. 2013). They investigated the normal distribution of AOW among Norwegian children ($n = 47{,}515$), finding a mean AOW of 12.86 ($SD = 1.88$) months (95% CI 12.85–12.88). In line with previous reports (Bishop et al. 2016), we defined "late walking" as AOW at or after 16 months.

Measures of Autistic Symptoms

The Autism Diagnostic Interview-Revised (ADI-R) (Rutter et al. 2003b; Lord et al. 1994) is a semi-structured caregiver interview consisting of items relevant to the core domains of ASD. The scoring algorithm is based on DSM-IV and ICD-10 criteria, yielding separate scores for social, verbal/nonverbal communication, and RRB domains. The ADI-R has demonstrated high sensitivity and moderate specificity (Lord et al. 1994), with a Cronbach's α of .69 for the RRB and .95 for the social domain. In our sample, the Cronbach's α ranged from .49 for the RRB to .82 for

the social domain. There are no Norwegian or Scandinavian norms available for the ADI-R, but the inter-rater reliability for single ADI-R algorithm items, behavioral domains totals and agreement for diagnostic classification for the Scandinavian versions is reported to be good (Halvorsen and Helverschou 2017). Following ADI-R conventions as presented by Hus and Lord (2013), and to make scores comparable across participants of different ages and language levels, the ADI-R nonverbal total included totals from the social, nonverbal communication, and RRB domains, leaving 27 items (totals ranged from 9 to 54). Mean age at administration of ADI-R was 9.8 years ($SD = 3.9$).

The Social Communication Questionnaire (SCQ) (Rutter et al. 2003a) comprises 40 yes/no questions, and is completed by caregiver to identify behaviors associated with autism across the lifespan. The SCQ content parallels that of the ADI-R, and excellent agreement (Berument et al. 1999; Bishop and Norbury 2002) and concurrent validity (Rutter et al. 2003a) has been reported. Cronbach's α for SCQ total lifetime score in the present sample was .89, comparable to previous reports (Rutter et al. 2003a).

The Social Responsiveness Scale (SRS) (Constantino and Gruber 2005) is a 65-item, ordinal-scaled caregiver-report questionnaire examining a child's ability to engage in reciprocal social interactions. The total score is a valid measure of autistic social impairment, with higher scores indicating greater severity (Constantino and Todd 2003; Constantino et al. 2003). We applied SRS raw total as a dimensional trait variable, for which the Cronbach's α was .94 in the present sample, comparable to previous reports (Constantino and Gruber 2005).

For simplicity, we use the term "symptom severity" as a proxy for total score on the different measurements of autistic symptoms (ADI-R, SCQ and SRS).

Measures of Cognitive Abilities

Cognitive function was assessed using results from previously administered, age-appropriate Wechsler scales: the Wechsler Preschool and Primary Scale of Intelligence (Wechsler 2012; 9.2%), Wechsler Intelligence Scale for Children (Wechsler 2003; 77.8%), Wechsler Abbreviated Scale of Intelligence (Wechsler 1999; 9.2%), and Wechsler Adult Intelligence Scale (Wechsler 2008; 3.7%). These assessments yield standard scores for nonverbal IQ (NVIQ), verbal IQ, and full scale IQ. To minimize the effect of language in measuring cognitive abilities, we used NVIQ as a trait variable, reflecting severity of cognitive impairment. Mean age at assessment of cognitive abilities was 10.2 years ($SD = 3.4$).

Statistical Analyses

We used the independent samples t-test and Pearson's Chi squared to compare sample characteristics between ASD and non-ASD individuals. AOW was compared with a Norwegian normative sample, for which the mean AOW was 12.86 months ($SD = 1.88$) (Storvold et al. 2013). Cohen's d was computed for effect sizes corresponding to the independent samples t-tests (Cohen 1988). A post hoc analysis of covariance was conducted to compare mean AOW between the two diagnostic groups after controlling for NVIQ. We assessed whether AOW was associated with severity of autistic symptoms by performing linear regression analyses with total scores on the ADI-R, SCQ, and SRS as dependent variables, one at a time. Analyses were carried out unadjusted and adjusted for potential confounders, one at a time and simultaneously. The unique contribution of AOW to predicting the different dependent variables was assessed with squared multiple correlation (R^2) in unadjusted, and squared semipartial correlation (sr^2) in adjusted analyses. Potential confounding factors included were cognitive ability (NVIQ) (Levy et al. 2010), prematurity, maternal and paternal age (Lord et al. 2018), which are known risk factors for ASD and may influence AOW. In addition, age at inclusion (years), sex, and ethnicity (both parents of Caucasian ethnicity or not) were included in the adjusted regression models. To explore possible sex differences, group comparisons were repeated for males and females separately. Possible sex differences in the associations between AOW and symptom severity were explored in subsequent regression analyses including an interaction term between sex and AOW, and in separate analyses for each sex.

The number of children who completed the different measures of ASD symptom severity varied from 141 to 335, and 97 children had missing data on all three measures. 151 children did not have available data on NVIQ. Missing values were handled by multiple imputation (MI) on the sample of $n = 393$ individuals with available data on one or more measures of ASD symptom severity, as described in Appendix 1. We report both available case analyses based on the original dataset, and analyses based on MI. Two-sided p-values < 5% were regarded as statistically significant. IBM SPSS 25 software was used for statistical analyses, except for comparisons with the normative sample in Stata 15.

Results

Among the 376 children with ASD, common subtypes included Asperger syndrome (35.6%), Childhood Autism (29.8%), Pervasive Developmental Disorder Not Otherwise Specified (22.9%), and Atypical Autism (9.6%). Mean age at ASD diagnosis was 9.3 years ($SD = 4.2$). The majority

of the children in the non-ASD group (92.4%) had one or more NDDs. Having two or more NDDs was more common in the ASD group (192/371, 51.8%) than in the non-ASD group (44/105, 41.9%), although not reaching statistical significance ($p = .075$). All children had achieved independent walking. AOW ranged from eight to 48 months, with a mean of 14.5 months ($SD = 4.0$) (Fig. 2).

Differences Between ASD and Non-ASD

The main sample ($N = 490$) included 377 males, with a male to female ratio of 3.5:1 in the ASD and 2.9:1 in the non-ASD group (Table 1). Mean NVIQ was in the normal range and did not differ significantly between these groups ($p = .54$). Non-ASD individuals were younger at inclusion, 10.2 years ($SD = 3.6$) versus 11.4 years ($SD = 3.8$) in the ASD group (t (194) = 2.99, $p = .003$). However, mean age at administration of ADI-R did not differ significantly between the diagnostic groups ($p = .77$). ASD individuals had higher scores on all measures of symptom severity compared with non-ASD (p < .001, all) (Table 2).

Figure 3 illustrates the proportion for having attained independent walking at increasing ages in both groups. A widening gap appears from age 12–13 months, reaching a maximum at 18–19 months, at which time more non-ASD individuals had attained walking. Applying a "cut off" for AOW at 16 months, the extent of "late walkers" was found to be somewhat higher in the ASD group (117/376, 31%) compared with the non-ASD group (28/114, 25%), although not statistically significant ($p = .22$).

Mean AOW among ASD children, however, was later compared with non-ASD, 14.7 ($SD = 4.3$) versus 13.8 ($SD = 2.9$) months, respectively (t (278) = 2.80, $p = .005$; $d = 0.34$). Compared with the normative sample (Storvold et al. 2013) (stippled line in Fig. 2), mean AOW was later among ASD (mean difference 1.9 months, t (376) = 8.51, $p < .001$; $d = 0.55$), as well as non-ASD individuals (mean difference 0.9 months, t (113) = 3.33, $p < .001$; $d = 0.38$). When adjusting for NVIQ in a post hoc analysis of covariance, mean AOW remained significantly later in the ASD group compared with non-ASD in the imputed dataset (mean difference 0.9 months, $p = .04$). In available case analysis (n = 339 due to missing information on NVIQ) mean AOW did not differ significantly between the ASD and non-ASD group: 14.0 ($SD = 3.0$) versus 13.7 ($SD = 2.9$) months, respectively ($p = .33$). This finding can be explained by the result that the 151 children with missing data on NVIQ had a later AOW (mean of 15.8, $SD = 5.5$ months) and 80% were diagnosed with ASD, as further discussed in the Appendix.

A proportion of children in the non-ASD group (29% vs 11% in the ASD group, $p < .001$) were diagnosed with motor disorder, all of which were Tic disorders. Four children were also diagnosed with F82 (i.e. they had both F82 and F95). Within the non-ASD group, mean AOW among children diagnosed with motor disorder was earlier, however not significant ($p = .35$), compared with those not diagnosed with a motor disorder (n = 66); 13.4 months ($SD = 2.6$) versus 14.0 ($SD = 2.8$), respectively.

AOW and Autistic Symptom Severity

Delays in AOW was associated with increasing symptom severity (Table 3). The strongest association was found between AOW and ADI-R, with AOW explaining

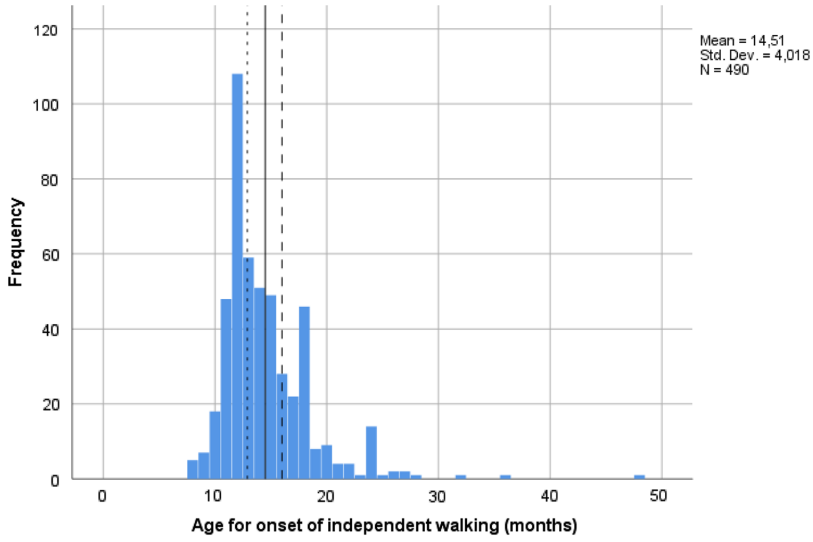

Fig. 2 Distribution of age for onset of independent walking (AOW) in the total study sample ($N = 490$). Small and larger stippled lines represent mean AOW among Norwegian children (Storvold et al. 2013) and cutoff for "late walking" (≥ 16 months), respectively; solid line represents mean AOW in the present sample

Table 1 Participant characteristics ($N = 490$)

	ASD ($n = 376$)			Non-ASD ($n = 114$)		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)
Sex						
Male	292	(77.7)		85	(74.6)	
Early motor development						
AOW (months)	376		14.7 (4.3)	114		13.8 (2.9)
"Late walking" (≥ 16 months)	117	(31.1)		28	(24.6)	
Diagnoses						
ASD (F84)	376	(100.0)		0	0	
Former ASD	0	0		6	(5.5)	
Intellectual Disability (F70–79)	49	(15.1)		9	(9.8)	
ADHD (F90)	114	(36.2)		52	(55.9)	
Communication disorder (F80)	12	(3.8)		23	(23.0)	
Specific learning disorder (F81 + F83)	18	(5.7)		22	(23.4)	
Motor disorders (F82 + F95)	35	(11.1)		27	(29.0)	
Epilepsy	25	(6.6)		8	(7.0)	
Cerebral Palsy	1	(.3)		1	(.9)	
Other NDD (F88 + F89 + F94)	4	(1.3)		8	(8.4)	
No of NDDs						
0	0	0		8	(7.6)	
1	179	(48.2)		53	(50.5)	
2–3	182	(49.1)		40	(38.1)	
≥ 4	10	(2.7)		4	(3.8)	
Verbal language	305	(92.7)		100	(100.0)	
Age (years) at inclusion	376		11.4 (3.8)	114		10.2 (3.6)
Age (years) at ASD diagnosis	326		9.3 (4.2)			
Nonverbal IQ	254		102.3 (17.7)	85		100.9 (17.5)
Verbal IQ	258		89.1 (17.8)	86		92.9 (18.0)
Paternal age (years)	213		32.5 (6.3)	69		32.9 (6.5)
Maternal age (years)	231		30.3 (5.0)	73		30.8 (5.5)
Prematurity	50	(14.8)		15	(15.5)	
Ethnicity						
European (Caucasian)	281	(81.2)		98	(89.1)	

AOW age for onset of independent walking, *ASD* autism spectrum disorder, *ADHD* attention-deficit/hyperactivity disorder, *NDD* neurodevelopmental disorder. Data are expressed as *n* (%) or mean (SD). The denominator for the reported proportions in this table excludes those with missing data: 151 participants for nonverbal IQ; 146 for verbal IQ; 61 for language level; 56 for prematurity; 34 for ethnicity; 208 for paternal age; 186 for maternal age; 14 for number of NDDs, and 52 ASD cases for age at diagnosis. IQ was obtained from various age-appropriate standardized tests

5.4% of the variance in ADI-R nonverbal total score ($R^2 = .054$, $p = .005$) in unadjusted analyses. After adjustment with potentially confounding variables, the association remained significant, with AOW explaining 7.0% of the total variance ($sr^2 = 0.070$, $p = .02$). The association between AOW and SCQ lost its significance after adjustment in the available case analysis, but remained significant ($p = .02$) after adjustment in the imputed dataset. Otherwise, there were no major changes in the significance of parameter estimates between the original and imputed data. The association between AOW and SRS was non-significant and therefore not subject to further analyses.

Sex Differences

AOW, NVIQ, and symptom scores, as well as between-group comparisons within each sex, are presented in Table 4. Among all children with suspected ASD, AOW was later among females ($M = 15.0$, $SD = 4.5$) than males ($M = 14.4$, $SD = 3.9$), but at a non-significant level ($p = .16$). Mean

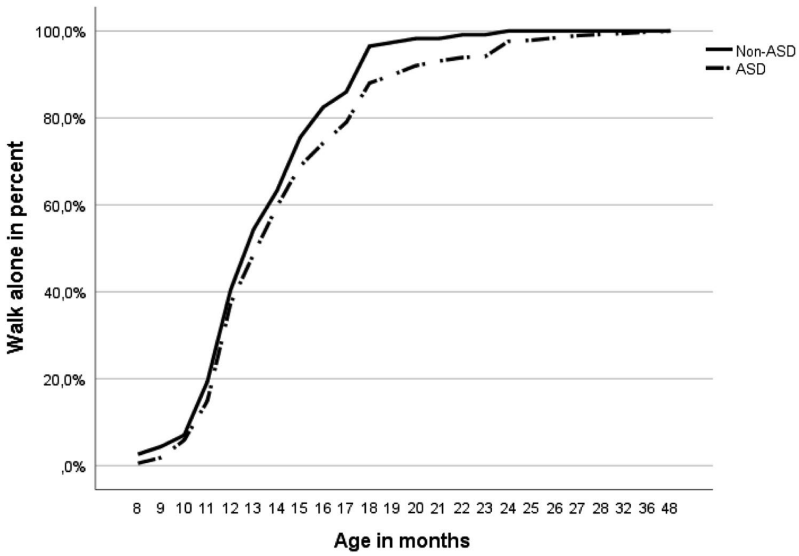

Fig. 3 Cumulative proportion of children having attained independent walking at increasing ages (per parent report), based on ASD group status ($N = 490$). Information is included through age 48 months. ASD = autism spectrum disorder, Non-ASD = assessed for autistic symptoms, but without ASD diagnosis

Table 2 Mean score on measures of autistic symptom severity and comparisons between diagnostic groups

	ASD			Non-ASD			95% CI for the difference
	n	Range	Mean (SD)	*n*	Range	Mean (SD)	
Available case analysis ($n \leq 490$)							
SCQ total	143	2–34	16.2 (7.2)	72	0–24	8.1 (5.6)	(6.4 to 9.9)***
ADI-R nonverbal total	118	0–45	22.0 (8.9)	23	0–38	11.9 (9.8)	(6.0 to 14.2)***
SRS total	247	7–168	86.8 (28.6)	88	19–130	64.5 (25.2)	(15.5 to 29.1)***
Multiple-imputation ($n = 393$)							
SCQ total	296		15.0 (6.4)	97		9.4 (5.9)	(4.2 to 7.0)***
ADI-R nonverbal total	296		22.3 (16.5)	97		12.5 (22.0)	(4.8 to 14.9)***
SRS total	296		85.9 (26.4)	97		66.1 (24.5)	(14.1 to 25.6)***

Measures of autistic symptom severity: *SCQ* Social Communication Questionnaire, *ADI-R* Autism Diagnostic Interview-Revised, *SRS* Social Responsiveness Scale. Results based on available case analyses of the main sample and multiple imputation of $n = 393$ participants with data on at least one measure of autistic symptom severity. *SD* standard deviation, *CI* confidence interval, *p* *p*-value

*$p < .05$; **$p < .01$; ***$p < .001$ for independent samples t-tests

AOW was later among males with ASD compared with males in the non-ASD group-14.6 ($SD = 4.2$) versus 13.4 ($SD = 2.4$) months, respectively (t (238) = 3.50, $p = .001$; $d = 0.53$)-but did not differ between groups in females. Females with ASD exhibited the latest AOW among all groups ($M = 15.1$, $SD = 4.7$), with a mean difference of 2.2 months (t (83) = 4.37, $p < .001$; $d = 0.62$), compared with the normative sample, in which no sex difference was found (Storvold et al. 2013). Adjusting for NVIQ in separate post hoc analyses for each sex did not alter the significance of observed group differences in mean AOW.

The interactions between sex and AOW were not significant in analyses predicting symptom severity. In separate analyses for each sex, associations remained significant among males but not females (Table 5). Looking at the regression coefficients, however, they were of the same magnitude in females and males in both datasets in unadjusted analyses, indicating that for each month increase in AOW, the burden of autistic symptoms as measured by ADI-R increased approximately as much in each sex.

Table 3 Linear regression with measures of autistic symptom severity as dependent variables and AOW as primary covariate

Available case analysis (n ≤ 490)	SRS total				SCQ total				ADI-R nonverbal total			
	n	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*
Unadjusted												
AOW (months)	335	.72	(−.15 to 1.59)	.10	215	.55	(.24 to .86)	.001	141	.69	(.21 to 1.18)	.005
Adjusted separately for												
Sex (female)					215	.57	(.26 to .89)	< .001	141	.66	(.18 to 1.15)	.007
Age (years)					215	.56	(.24 to .87)	.001	141	.69	(.21 to 1.18)	.005
Nonverbal IQ					178	.15	(−.24 to .53)	.44	123	.48	(−.10 to 1.06)	.11
Prematurity					199	.61	(.29 to .92)	< .001	129	.81	(.30 to, 1.33)	.002
Ethnicity (non-Caucasian)					209	.52	(.20 to .84)	.001	137	.72	(.24 to 1.21)	.004
Paternal age (years)					130	.47	(.05 to .89)	.03	98	.95	(.39 to 1.50)	.001
Maternal age (years)					146	.46	(.08 to .83)	.02	102	.85	(.30 to 1.40)	.003
Adjusted for all	151	−.37	(−1.82 to 1.09)	.62	103	.23	(−.25 to .70)	.35	75	.88	(.14 to 1.62)	.02
Multiple imputation (n = 393)	SRS total				SCQ total				ADI-R nonverbal total			
	n	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*
Unadjusted												
AOW (months)	393	.61	(−.13 to 1.35)	.11	393	.25	(.07 to. 43)	.007	393	.93	(.39 to 1.46)	.001
Adjusted separately for												
Sex (female)					393	.26	(.07 to .44)	.006	393	.94	(.41 to 1.47)	.001
Age (years)					393	.25	(.07 to .44)	.007	393	.93	(.40 to 1.46)	.001
Nonverbal IQ					393	.23	(.04 to .42)	.02	393	.84	(.29 to 1.39)	.003
Prematurity					393	.24	(.05 to .42)	.01	393	.94	(.41 to 1.47)	.001
Ethnicity (non-Caucasian)					393	.25	(.07 to .43)	.008	393	.92	(.39 to 1.46)	.001
Paternal age (years)					393	.25	(.07 to .44)	.007	393	.92	(.39 to 1.45)	.001
Maternal age (years)					393	.25	(.07 to .43)	.007	393	.93	(.39 to 1.46)	.001
Adjusted for all	393	.48	(−.30 to 1.27)	.23	393	.24	(.05 to .44)	.02	393	.83	(.29 to 1.37)	.003

AOW age for onset of independent walking. Dependent variables: *SCQ* Social Communication Questionnaire, *ADI-R* Autism Diagnostic Interview-Revised, *SR*S Social Responsiveness Scale. Results based on available case analysis of the main sample and multiple-imputation analysis of *n* = 393 participants with data on at least one dependent variable. *B* unstandardized regression coefficient, *CI* 95% confidence interval, *p* *p*-value

Discussion

In this study of AOW in a large sample of Norwegian children assessed for suspected ASD by specialist health services, we found that mean AOW was later among children with ASD compared to their typically developing peers, consistent with previous reports (Ozonoff et al. 2008; Lemcke et al. 2013; West et al. 2017). AOW was associated with severity of core autistic symptoms, even after adjustment for potential confounders. Whereas AOW was significantly later in males with ASD compared with non-ASD diagnosis, females with autistic symptoms seem to have a liability toward later AOW, regardless of ASD diagnosis.

To our knowledge, this is the first study of AOW among children evaluated for suspected ASD, and directly aimed at investigating associations with symptom severity and possible sex differences. Applying a dimensional approach, we found that among children who displayed signs of ASD without meeting the criteria for diagnosis (non-ASD), AOW was significantly later compared with norms for typically developing children, but to a less extent than in children with ASD. Consistent with our results, Lane et al. (2012) found that in a small sample (n = 30) of young children referred for possible ASD, those who received an ASD diagnosis tended to have greater delays in fine and gross motor domains, although not statistical significant, compared with children not diagnosed as ASD.

In the present study, symptom severity was higher in the ASD group compared with non-ASD, but with some overlap on all measures. Such overlap may be unavoidable, reflecting genetic relationships between ASD and other developmental disorders (Lichtenstein et al. 2010; Lundstrom et al. 2011). Our findings support the concept of autistic symptoms as quantitative traits transcending diagnostic categories (Frazier et al. 2015). Further, a pattern emerged, where AOW

Table 4 AOW, nonverbal IQ, and symptom scores in ASD versus non-ASD, as well as between-groups comparisons

	ASD females		Non-ASD females		95% CI for the difference	ASD males		Non-ASD males		95% CI for the difference
	n	Mean (SD)	*n*	Mean (SD)		*n*	Mean (SD)	*n*	Mean (SD)	
Available case analysis ($n \leq 490$)										
AOW (mo)	84	15.1 (4.7)	29	14.9 (3.8)	(−1.7 to 2.1)	292	14.6 (4.2)	85	13.4 (2.4)	(0.6 to 2.0) **
Nonverbal IQ	53	99.4 (13.9)	23	98.2 (14.7)	(−5.9 to 8.2)	201	103.0 (18.6)	62	101.9 (18.4)	(−4.2 to 6.4)
SCQ total	32	15.6 (7.5)	17	7.0 (6.3)	(4.3 to 12.9) ***	111	16.4 (7.2)	55	8.4 (5.3)	(6.0 to 10.0) ***
ADI-R nonverbal total	28	20.7 (9.7)	8	7.4 (7.1)	(5.8 to 20.8) **	90	22.4 (8.7)	15	14.3 (10.4)	(3.2 to 13.1) **
SRS total	51	93.5 (26.4)	21	61.0 (26.5)	(18.9 to 46.2) ***	196	85.1 (29.0)	67	65.7 (24.8)	(11.7 to 27.2) ***
Multiple-imputation analysis ($n = 393$)										
AOW (mo)	63	14.7 (4.6)	24	15.0 (3.7)	(−2.5 to 1.7)	233	14.6 (3.6)	73	13.3 (2.3)	(0.6 to 2.0) ***
Nonverbal IQ	63	99.6 (17.8)	24	98.6 (15.2)	(−6.6 to 8.6)	233	102.2 (25.9)	73	103.0 (19.9)	(−6.5 to 5.0)
SCQ total	63	14.5 (7.2)	24	8.4 (6.9)	(2.8 to 9.4) ***	233	15.1 (6.1)	73	9.7 (5.6)	(3.9 to 6.9) ***
ADI-R nonverbal total	63	21.5 (19.7)	24	9.2 (22.1)	(1.5 to 23.1) *	233	22.5 (16.0)	73	13.5 (20.9)	(3.5 to 14.5) **
SRS total	63	91.7 (24.2)	24	63.7 (25.9)	(16.3 to 39.5) ***	233	84.3 (26.8)	73	66.8 (24.2)	(10.6 to 24.4) ***

ASD autism spectrum disorder, *AOW* age for onset of independent walking. Measures of autistic symptom severity: *SCQ* Social Communication Questionnaire, *ADI-R* Autism Diagnostic Interview-Revised, *SRS* Social Responsiveness Scale. Results based on available case analysis of the main sample and multiple imputation of $n = 393$ participants with data on at least one measure of symptom severity. *SD* standard deviation, *CI* confidence interval, *p* *p*-value

*$p < .05$; **$p < .01$; ***$p < .001$ for independent samples t-tests

Table 5 Linear regression among females and males with measures of symptom severity as dependent variables and AOW as the primary covariate

Available case analysis ($n \leq 490$)	Females								Males							
	SCQ total				ADI-R nonverbal total				SCQ total				ADI-R nonverbal total			
AOW (mo)	*n*	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*
Unadjusted	49	.31	(−.27 to .88)	.29	36	.64	(−.59 to 1.87)	.30	166	.72	(.34 to 1.11)	< .001	105	.67	(.15 to 1.19)	.01
Adjusted for all*	23	−.52	(−1.44 to .39)	.24	22	1.15	(−.91 to 3.21)	.25	80	.51	(−.10 to 1.12)	.10	53	.37	(−.487 to 1.22)	.39
Multiple imputation ($n = 393$)	SCQ total				ADI-R nonverbal total				SCQ total				ADI-R nonverbal total			
AOW (mo)	*n*	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*	*n*	B	CI	*p*
Unadjusted	87	.21	(−.16 to .57)	.27	87	.87	(−.30 to 2.04)	.15	306	.28	(.07 to .49)	.008	306	.98	(.41 to 1.54)	.001
Adjusted for all*	87	.16	(−.22 to .54)	.40	87	1.02	(−.17 to 2.21)	.09	306	.31	(.09 to .54)	.007	306	.78	(.18 to 1.37)	.01

AOW age for onset of independent walking. Dependent variables: *SCQ* Social Communication Questionnaire, *ADI-R* Autism Diagnostic Interview-Revised. Results based on available case analysis of the main sample, and multiple imputation of $n = 393$ participants with data on at least one dependent variable. *B* unstandardized regression coefficient, *CI* 95% confidence interval, *p* *p*-value

*Adjusted for the covariates: age, nonverbal IQ, prematurity, ethnicity, maternal and paternal age

seems to represent a continuum along which children with ASD show the most delay, followed by those with fewer autistic symptoms. This is in line with previous findings indicating that the more severe the autistic symptoms, the greater the likelihood of co-occurring conditions (Lundstrom et al. 2011) and functional difficulties (Skuse et al. 2009), including motor difficulties (Matson et al. 2010; Green et al. 2009; Hilton et al. 2012; MacDonald et al. 2013, 2014). Regarding AOW, a similar pattern of observed delay has been reported in retrospective (Ozonoff et al. 2008) as well as prospective (Lemcke et al. 2013) studies. The latter, a Danish national birth cohort study, reported increasing delay in AOW across different conditions, with the longest delay among children with ID and not ASD, followed by childhood autism and then any ASD diagnosis, including childhood autism. Extending previous studies, we included children with autistic symptoms without an ASD diagnosis. The lack of a control group was mitigated by using normative AOW data from the same population (Storvold et al. 2013). While significant differences in mean AOW between groups and compared to norms was found, most children in both groups did attain walking within 16 months. The proportion of children characterized as "late walking" (i.e., AOW at or after 16 months) was smaller but considerable; 31% of the ASD and 25% of the non-ASD group. Our findings contrast somewhat with a recent study by Bishop et al. (2016), in which 22% of 903 children with ASD were "late walking", with mean AOW 14.00 (4.73) months.

Children with ASD are reported to have high frequencies of one or more co-occurring neurodevelopmental, psychiatric, and possibly causative medical diagnoses (Levy et al. 2010; Lord et al. 2018). Other diagnoses or symptoms may be present before all the symptoms of ASD are evident. In a prospective study of 30 children referred for early motor delays or abnormalities, including delayed walking (Hatakenaka et al. 2016), the majority were found to have at least one NDD. Thirteen children were later diagnosed with ASD, of which 92% had two or more NDDs. Also in the present sample NDDs were common; 52% in the ASD and 42% in the non-ASD group had two or more NDDs. Moreno-De-Luca et al. (2013) have argued that "neurodevelopmental disorders should be thought of as different patterns of symptoms or impairments of a common underlying neurodevelopmental continuum". As such, the possibility that the observed common co-occurrence of NDDs in the present sample may represent a common etiology or underlying issues affecting also the motor domain, should be considered. In the present sample, 29% in the non-ASD and 11% in the ASD group were diagnosed with 'motor disorder'. This category comprised ICD-10 diagnoses F82 (Specific developmental disorder of motor function) and F95 [Tic disorders, including Tourette's disorder (F95.2)], see Table 1,

the majority of which were Tic disorders. The inclusion of motor disorder had a negligible effect on the main results.

Although it is possible to make a diagnosis of ASD before 24 months age in some cases, the majority of children with ASD in northern Europe are diagnosed by early school age (Lord et al. 2018). In the present sample, mean age at ASD diagnosis was 9.3 years. Our results are consistent with Suren et al. (2012) who used nationwide Norwegian register data and found that the proportions with ASD from 2008 to 2010 increased by age and was 0.7% in 11-year-olds. This suggests that ASD is often not diagnosed until late childhood or early adolescence in Norway. Later diagnoses are reported to occur in the context of co-occurring problems and other factors (e.g. female sex, more advanced language) that might have either exacerbated or masked the ASD (Lord et al. 2018). The present study included children from both child habilitation services and child and adolescent mental health services evaluated for suspected ASD. This enabled the inclusion of individuals with a broad range of autistic symptoms and cognitive abilities. We consider this to strengthen the representativity of our results for the broader population of individuals assessed for suspected ASD in the health care system.

Taken together, the relatively high number of females, individuals with ASD subtypes without language delay (36% had Asperger syndrome) and the high proportion with co-occurring NDDs may have contributed to the relatively late age at ASD diagnosis in our sample. In terms of cognitive functioning, individuals with ASD display a wide range of abilities, from severe ID to superior intelligence, with prevalence rates for ID in different studies between 15 and 65% (Lord et al. 2018). In our sample, 15.1% of ASD and 9.8% of non-ASD individuals were diagnosed with ID, further indicating a more 'high functioning' sample. Applying a dimensional approach, we included children with a broad range of autistic symptoms despite having other co-occurring disorders. In our sample, 27 children with ASD and seven in the non-ASD group had known genetic conditions, some of which may have contributed to later AOW in both groups, and later AOW compared to other ASD samples with more strict exclusion criteria. Further, Norwegian children are *on average* older at AOW, compared with other countries (Storvold et al. 2013; Onis 2006b).

Our finding of mean AOW at 14.7 months in the ASD group is later compared with some earlier reports (Lemcke et al. 2013; Bishop et al. 2016). The magnitude of delay, however—children with ASD walking *on average* almost 2 months later compared with typically developing children—is comparable to previous studies (Lemcke et al. 2013; Ozonoff et al. 2008; West et al. 2017). This highlights the need to assess AOW in relation to autistic symptoms. The strongest association between AOW and symptom severity was found for ADI-R, with AOW making a unique contribution in explaining ADI-R total score. This held after adjusting for potential confounders. The association between AOW and SCQ was lost following adjustment in available case analyses, but remained significant after adjustment in the MI sample, which is considered less biased and to strengthen our results. A weaker association between AOW and SCQ may be reasonable, however, given that SCQ is a short parent-report questionnaire allowing only yes/no answers, whereas ADI-R is a semi-structured interview requiring trained examiners, which may perform better in eliciting parental concerns and capturing current and historical ASD symptoms. Further, the SCQ is found to be more similar to the ADI-R total score in differentiating ASD from non-ASD in the older (8-10, > 11) than younger age groups (Corsello et al. 2007). Contrary to our finding that AOW was associated with symptom severity, as measured by the ADI-R and SCQ, and previous reports of correlations between SRS and motor skills (Hilton et al. 2007, 2012), we found no significant association between AOW and SRS. This may indicate that SRS captures other aspects of social impairment that are not as strongly associated with AOW, compared with measures of core autistic symptoms.

When assessing relationships between ASD symptoms and other behavioral or neurobiological variables, taking into account phenotypic characteristics, such as age, IQ or co-occurring difficulties is important. ASD symptom measures such as the SRS and ADI-R are reported to capture more than symptoms of ASD, with elevating scores potentially reflecting impairments in dimensions other than the core characteristics of ASD (Havdahl et al. 2016). The possibility that early motor delays are more general signs of compromised neurocognitive development, rather than specific to ASD, has also been discussed (Bolton et al. 2012; Ozonoff et al. 2008). Of the covariates included in the regression model in the present sample, NVIQ was making the strongest contribution to attenuating the relation between AOW and severity of core ASD symptoms. Significant associations remained, however, as did the difference in mean AOW between the ASD and non-ASD groups after adjusting for NVIQ. Thus, in our sample AOW was related to ASD symptom severity, even after adjusting for NVIQ. In order to examine whether AOW predicts ASD symptom severity over and above general motor ability, results from broader measures of motor functioning would have been useful. Unfortunately, such a measure was not included in the present study.

Because of potential typical sex differences, it is important to compare how males and females with ASD differ from typically developing males and females (Lai et al. 2015). The WHO Multicentre Growth Reference Study (MGRS) found no significant, consistent sex differences in motor milestone achievement ages among typically developing children (Onis 2006a). However, "girls in the MGRS tended to achieve milestones at earlier ages than did boys"

(p. 71). Contrary to this, but in line with previous reports (Bishop et al. 2016; Arabameri and Sotoodeh 2015), we found that females with autistic symptoms (regardless of ASD diagnosis) are more liable to *delayed* walking compared with males. Findings from screening-negative infants later diagnosed with ASD (Oien et al. 2018) have highlighted the discrepancy between categorical criteria for ASD and developmental signs of an emerging or subthreshold autism phenotype (Oien et al. 2018). Specifically, girls had less advanced early gross motor skills compared with boys. Along with a recent report from a large population study that autistic social traits in females tend to increase towards adolescence (Mandy et al. 2018), these results may indicate a different phenotype or emerging pattern of symptoms in females with ASD.

Strengths of our study include the sample size and inclusion of individuals with a broad range of autistic symptoms and cognitive abilities. In addition, we used validated instruments, and the nature of data collection allowed adjustment for covariates and potential confounding factors. Study limitations are the retrospective nature of some of the information collected in the study, varying measures of autistic symptoms, and missing data (se Appendix for further discussion). We used clinical diagnoses obtained from different clinics, which may have introduced variation. Misclassification (in both directions) is possible, but not very probable for ASD and the non-ASD disorders, and is unlikely to be related to AOW assessment. ASD diagnoses assigned by Norwegian specialist health services have previously shown high overall validity (Suren et al. 2012). Further, the relatively high number of females in our sample may indicate that referral and ascertainment bias leading to under recognition of ASD in females (Lai et al. 2015) was low. For some analyses regarding sex differences our sample may have been underpowered. Otherwise, we do not consider type I errors to be likely. Nevertheless, these findings should be replicated in independent samples. Finally, the lack of control group was overcome by using normative AOW data from the Norwegian study by Storvold et al. (2013). In that study, information on AOW was collected by parent report when children were 18 months of age, whereas we used retrospective information on AOW collected at inclusion (age from 4 to 18 years), introducing the possibility of recall bias. The quality of information about developmental milestones from caregivers has been examined by Hus et al. (2011), who found AOW to be one of the most reliable parent report measures (Hus et al. 2011). Although the precision of information regarding AOW may have varied, it is unlikely to have systematically biased our results. Further, the pattern and magnitude of delay observed is in accordance with results from previous studies.

Children with ASD share common features with children with other developmental delays, which may contribute to difficulties of accurate diagnosis. Although delayed onset of walking is not unique to ASD, the present study supports previous reports that it occurs commonly in ASD, and further demonstrate associations with severity of symptoms in other diagnostic criterion domains that characterize ASD. Recognizing that autistic symptoms may be difficult to interpret at an early age, assessing early motor delays and specifically AOW may have the potential to improve earlier identification of some cases with ASD, and perhaps particularly in females. Considering the possibility of ASD in infants with motor delays may not only enhance the potential for earlier diagnosis, but also improve the chance of targeting and addressing these delays in treatment programs and facilitate better prognostic outcomes.

Conclusion

Our results showing later onset of independent walking among children with ASD compared to children who display symptoms of ASD without meeting diagnostic criteria, highlight the importance of assessing AOW in relation to autistic symptoms. The current findings suggest that AOW may constitute a continuum parallel to the continuum of autistic symptoms, with potential sex effects. In cases with delayed AOW, ASD should be considered as an actual differential diagnosis, taking particular notice of females. The underlying mechanisms and clinical implications should be investigated in prospective studies.

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Author Contributions OAA and AMS have contributed equally to this work. LR and AMS conceptualized and designed the study, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. BW, TN and OAA contributed in conceptualizing and designing the study, interpreted the findings and critically reviewed the manuscript and its analyses. SL performed the multiple imputation, supervised and critically reviewed the analyses and reviewed the manuscript. All authors approved the final manuscript as submitted and are accountable for all aspects of the work.

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Compliance with Ethical Standards

Conflict of interest AMS and OAA declares no direct conflict of interest related to this article. AMS discloses that she received travel sup-

port for conference attendance from Medice in 2018. OAA discloses that he has received speakers honorarium from Lundbeck. All other authors declare that they have no conflicts of interest.

Ethical Approval The BUPgen study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (REK#2012/1967) and the Norwegian Data Inspectorate and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent Informed consent was obtained from all individual participants (and/or parents when necessary due to age) included in the study.

Appendix: Missing Data, Multiple Imputation and Sensitivity Analyses

The number of children with available data on the different measures of symptom severity varied. For ADI-R, subscales that sum to the ADI-R nonverbal total (social, nonverbal communication, and RRB domains) were complete for 141 subjects, 329 subjects were missing all subscales, and 20 were missing one or more subscales. For SCQ, subscales were complete for 210 subjects, five subjects had a total value available but no subscales, and 275 were missing all data. For SRS, subscales were complete for 335 subjects, one was missing one or more subscales, and 154 were missing all data. SRS raw scores were based on caregiver report. For three participants, a teacher was the informant. Clinician-reported data were missing for 151 participants for nonverbal IQ, 146 for verbal IQ, 61 for language level, 56 for prematurity, 34 for ethnicity, 208 for paternal age, 186 for maternal age, 74 for ID diagnose, and 52 ASD cases for age at diagnosis. Information on age at administration of ADI-R was available for 188 children.

Primary demographic and clinical characteristics of the total study cohort ($N = 490$) were compared with $n = 97$ individuals with missing data on all measures of symptom severity, and $n = 393$ individuals with available data on one or more measures (Tables 6, 7). Levels of missing data tended to be comparable for males and females but more common among those who where younger, nonverbal, and/or with lower cognitive performance. More members of the sample with data missing for all measures of symptom severity had an ASD diagnosis, and mean AOW was later. The same pattern was observed among the 151 children with missing data on NVIQ, where mean AOW was 15.8 ($SD = 5.5$), and 80% were diagnosed with ASD. Hence, data were not missing completely at random (MCAR), but possibly missing at random (MAR). As such, estimates of symptom scores in the available case analyses may be biased toward higher functioning (in the ASD group), making group comparisons and estimates of associations more conservative.

Missing data were handled using multiple imputation (MI), creating m = 100 imputed data sets as recommended by Van Buuren (2018). Available case analysis is unbiased only if data are MCAR, while multiple imputation analysis is unbiased under the less restrictive MAR assumption.

Table 6 Participant characteristics across samples

	$n = 490$ Main sample			$n = 97$ Missing data on symptom severity			$n = 393$ Multiple imputation sample		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)	*n*	(%)	Mean (SD)
Sex									
Male	377	(76.9)		71	(73.2)		306	(77.9)	
AOW (months)	490		14.5 (4.0)	97		15.1 (5.2)	393		14.4 (3.7)
Age (years) at inclusion	490		11.1 (3.7)	97		9.3 (4.1)	393		11.5 (3.5)
Verbal language	405	(94.4)		30	(76.9)		375	(96.2)	
Nonverbal IQ	339		101.9 (17.7)	14		94.4 (16.8)	325		102.2 (17.6)
Verbal IQ	344		90.1 (17.9)	15		82.2 (14.2)	329		90.4 (18.0)
Paternal age (years)	282		32.6 (6.3)	28		32.7 (6.6)	254		32.6 (6.3)
Prematurity	65	(15.0)		18	(23.1)		47	(13.2)	
Ethnicity									
European (Caucasian)	379	(83.1)		56	(60.2)		323	(89.0)	

Data are expressed as *n* (%) or mean (SD). The denominator for proportions reported in this table excludes those with missing data. Nonverbal IQ was obtained from various age-appropriate standardized tests

AOW age for onset of independent walking, *ASD* autism spectrum disorder

Table 7 Characteristics of participants with missing data on symptom severity ($n=97$)

	ASD ($n=80$)			Non-ASD ($n=17$)		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)
Sex						
Male	59	(73.8)		12	(70.6)	
AOW (months)	80		15.3 (5.5)	17		14.1 (3.4)
Age (years) at inclusion	80		9.5 (4.1)	17		7.9 (3.5)
Verbal language	27	(75.0)		3	(100.0)	
Nonverbal IQ	12		96.9 (14.5)	2		79.5 (29.0)
Verbal IQ	13		85.1 (13.0)	2		63.5 (3.5)
Paternal age (years)	25		32.8 (5.8)	3		31.7 (13.3)
Prematurity	16	(23.9)		2	(18.2)	
Ethnicity						
European (Caucasian)	45	(59.2)		11	(64.7)	

Data are expressed as *n* (%) or mean (SD). The denominator for proportions reported in this table excludes those with missing data. Nonverbal IQ was obtained from various age-appropriate standardized tests

AOW age for onset of independent walking, *ASD* autism spectrum disorder

The wealth of data collected through BUPgen allowed multiple imputation to include auxiliary variables associated with missingness, increasing the plausibility that the MAR assumption is a realistic approximation of reality. All variables used in subsequent analyses were included in the imputation model, with the following modifications: For ADI-R the four subscales (social, verbal communication, nonverbal communication, and RRB domains) were used in imputation. For SCQ, we included the total and the four subscales that summed to the total, without constraints. For SRS, we included the five subscales and the total. The variable ADI-R nonverbal total was computed after imputation. In addition, language level, ASD diagnosis and verbal IQ were also included in the imputation model. To accommodate interactions with sex, we imputed files separately for males and females, and merged the imputed files, as described by Van Buuren (2018, pp. 175, 176). We did not restrict the imputed values to the scale range, as recommended by Rodwell et al. (2014).

The variable language level was dichotomized as verbal or nonverbal based on information at inclusion. Individuals were considered to be nonverbal if: (1) they had received ADOS Module 1 as part of their clinical evaluation, designed for children who are nonverbal or using single words; (2) they were reported to not combine words and use sentences (question 1 in the SCQ and/or question 30 in the ADI-R); or (3) clinician-reported information at inclusion otherwise indicated that they were nonverbal. Information on language level was used as a categorical indicator of expressive language to help explain data missingness in the imputation model, but was not included as a covariate in further analyses. The variables verbal IQ and nonverbal IQ were obtained from previously administered age-appropriate measures of cognitive ability.

Due to missing information on AOW, 116 children were not eligible for the present sample. Primary demographic and clinical characteristics for these children, however, was comparable to those of the total study cohort ($N=490$). To assess the potential impact of outliers on mean AOW of the total study sample, as well as estimates of group differences and associations with symptom severity, we used z-scores, finding 5 observations (1.0%) with z-scores > 2.58, and 15 observations (3.1%) with z-scores > 1.96. Thus, the number of potential outliers did not deviate much from what expected within a normal distribution. Further, main analyses were repeated after removing first the most extreme, thereafter the two most extreme values (AOW ≥ 36 months), resulting in a modest attenuation of the results, not affecting the statistical significance of the difference between groups.

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Paper II

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ORIGINAL PAPER

Structural and Pragmatic Language Impairments in Children Evaluated for Autism Spectrum Disorder (ASD)

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Abstract
Pragmatic language impairments are common in neurodevelopmental disorders, especially in autism spectrum disorder (ASD). The relationship between structural language skills and pragmatic competence in children with autistic symptoms, however, is largely unknown. We investigated this relationship based on the Children's Communication Checklist-2 and early language delay among children ($N = 177$, 19% females) clinically evaluated for ASD, differentiated into ASD ($n = 148$) and non-ASD ($n = 29$). Structural language deficits were common and associated with reduced pragmatic competence in both groups. Pragmatic language impairments were most profound in children with ASD. Early language delay and structural language deficits were less common in females. Our findings suggest that assessment of structural language skills should be included in the evaluation of children with suspected ASD.

Keywords Autism spectrum disorder · Language impairment · Structural language skills · Pragmatic language skills · Language milestones · Sex differences

Introduction

Neurodevelopmental disorders (NDDs) are characterized by impairments in one or more developmental domains, such as cognition, communication, social, and motor functioning, as a result of atypical brain development (American Psychiatric Association 2013; Moreno-De-Luca et al. 2013). Autism spectrum disorder (ASD) is a childhood onset NDD characterized by persistent deficits in social communication and interaction, as well as restricted, repetitive behavior and interests (American Psychiatric Association 2013; World Health Organization 1992). The common co-occurrence of different NDDs and the dimensional nature of their symptom profiles represent major challenges to the recognition, as well as the classification of these disorders (Baird and Norbury 2016). Many children with NDDs have language difficulties, particularly using language in social communication. In a clinical setting, however, language impairments are often unnoticed due to other, more prominent symptoms, and frequently remain undiagnosed (Cohen et al. 1998). Although a neglected area in current research, language impairment is suggested as an associated feature, independent from core ASD features in some aspects, with great importance for outcome in individuals on the autism spectrum (Happé and Frith 2020).

Within communication the *form, content* and *use* of language are all essential components. Language *form* (e.g. phonology, morphology, syntax) and *content* (semantics) represent *structural language skills*, while appropriate *use* of language in social or situational contexts represent *pragmatic language skills* (e.g. Geurts and Embrechts 2008; Baird and Norbury 2016). Language impairments reflect

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deficits in one or more of these skills, and vary depending on the individual's age, intellectual level, as well as co-occurring difficulties in other developmental domains (Lord et al. 2018; Boucher 2012).

Impairments in pragmatic language are observed in a broad range of NDDs, including ASD (e.g. Bishop 1998; Norbury et al. 2004; Gilmour et al. 2004; Geurts and Embrechts 2008). Although not required for meeting diagnostic criteria, pragmatic impairments are a recognized feature of ASD regardless of language level or age (e.g., Baird and Norbury 2016; La Valle et al. 2020). Still, these impairments are often less emphasized than the social communication impairments inherent in the ASD diagnosis (Norbury 2014). Pragmatic skills require use of both the language and the social context to reach intended meaning. As such, they stand at the intersection of structural language and social skills (Volden et al. 2009). Norbury (2014) has argued that pragmatic language skills are closely associated with structural aspects of language, and not necessarily the same as social communication skills.

Although receiving less attention than pragmatic language deficits, structural language is also commonly affected in ASD. Preschool children with ASD show structural as well as pragmatic language impairments, resembling the language profile in children with specific language impairment (Geurts and Embrechts 2008; Boucher 2012). By school-age, however, structural deficits are reported to improve, while pragmatic language deficits become more prominent (Rapin and Dunn 2003; Geurts and Embrechts 2008). Moreover, an ASD-typical profile is reported to emerge in school-age, with articulation and syntax least affected, and comprehension, semantics and morphology most affected, as reviewed by Boucher (2012). Notably, children with ASD often evidence variability in skills across specific language domains, which appear to differentially relate to other aspects of functioning (Levinson et al. 2020). While previous work is limited and has disproportionately focused on the association between pragmatic language and social skill deficits, there are reports suggesting a link between structural language deficits and social skills in ASD, that is mediated by reduced pragmatic competence and may be at play for children without ASD as well (Volden et al. 2009; Levinson et al. 2020). Concomitant deficits in structural language may represent a potential target of intervention, separate from the social communication impairments characteristic of ASD. Therefore, investigating structural language skills and their potential influence on pragmatic competence in referred children with autistic symptoms is of importance.

ASD symptoms vary widely across individuals meeting diagnostic criteria for ASD and are also present in the general population to a minor degree (Constantino and Todd 2003, 2005; Posserud et al. 2006). For clinicians evaluating children with autistic symptoms, it may be challenging to disentangle core ASD symptoms from more specific language impairments that disturb social communication (Levy et al. 2010; Baird and Norbury 2016). It has been argued that the association between the different disorders affecting language and communication may best be understood dimensionally (Bishop and Norbury 2002; Bishop 2000). The individual differences in social communication and pragmatic language seen across various NDDs may then reflect a confluence of risk factors such as deficits in structural language, social and cognitive skills, with ASD at "the extreme end of the distribution" (Norbury 2014, p. 212), but without a disorder-specific profile. Investigating language impairments in a broader clinical population of children with autistic symptoms, beyond those receiving an ASD diagnosis, can offer an important complementary insight into the nature of these impairments and their extent in both ASD and non-ASD individuals.

The Children's Communication Checklist (CCC-2) (Bishop 2011, 2003) is designed to identify structural and pragmatic language deficits that may be difficult to elicit in a test situation, and is to be completed by an adult who knows the child well (Norbury et al. 2004). Previous efforts to distinguish different NDDs based on their CCC-2 language profile have largely failed, but significant deficits in structural language in children with ASD compared to typically developing children are documented (Kuijper et al. 2017; Baixauli-Fortea et al. 2019; Geurts and Embrechts 2008). In addition pragmatic language impairments were evident in children across a range of NDDs, many of them had structural language deficits as well (Norbury et al. 2004; Geurts and Embrechts 2008). Recently, Baixauli-Fortea et al. (2019) reported an association between more advanced structural language skills and greater pragmatic competence in children with ASD, as measured by the CCC-2. On a continuum of communication impairment, ASD and specific language impairment are found on the opposite endpoints, with comparable structural language skills but more profound pragmatic impairments in children with ASD (Oi et al. 2017). However, design, measures, and comparison groups varied between these studies, limiting comparability and generalization of their results. Further, the ASD groups in many of these studies were relatively small. Thus, an unanswered question is whether pragmatic language impairment represents a dimensional trait that is associated with structural language deficits across the range of autistic symptoms.

While language milestones and current language skills have been important for distinction between ASD subtypes (e.g. World Health Organization 1992), they are not found to predict autistic symptom severity in children with ASD (Loucas et al. 2008; Kenworthy et al. 2012). Still, lasting individual differences in language skills seem to be established early, underscoring the importance of identifying lagging language skills early in life (Bornstein et al. 2018).

Being a "late talker" (i.e. delayed attainment of first words and/or first word combinations) is considered a hallmark of specific language impairment (Conti-Ramsden and Durkin 2015), a condition characterized by structural language deficits. Delays in language milestones are also common in children later diagnosed with ASD, and represent early signs of the condition, although with low specificity (Tager-Flusberg 2016). Measured by a sentence repetition task, retrospectively reported language milestones were predictive of later structural language skills in children with ASD (Kenworthy et al. 2012). Whether milestone data can be useful markers of later language performance also across the broader range of autistic symptoms, as measured by the CCC-2, remains to be resolved.

Females demonstrated better pragmatic language skills on the CCC (Ketelaars et al. 2010; Geurts et al. 2009) and its successor, the CCC-2 (Ash et al. 2017) in community-based samples. However, no significant sex differences were found in a Norwegian normative sample (Hollund-Møllerhaug 2010). Regarding ASD, females may present with a different profile of symptoms than males, and therefore be under- or misdiagnosed, or diagnosed with delay (Green et al. 2019; Kreiser and White 2014; Van Wijngaarden-Cremers et al. 2014). At present, studies exploring potential sex differences in language characteristics within the broader group of children with autistic symptoms are lacking.

While originally autism was conceptualized as distinct from typical development, a more recent conception is the dimensional, with ASD as a spectrum of manifestations and no natural cut-off point between high autism traits and ASD (Happé and Frith 2020). The same authors argue that an unintended consequence of focusing on 'pure' autism has been the neglect of language impairment in recent research (Happé and Frith 2020). By including a large group of children evaluated for ASD by specialist health services, some not fulfilling the criteria for such a diagnosis (non-ASD), we aimed to use a dimensional approach and study language impairment across the broader range of autistic symptoms. Four specific objectives were addressed:

(i) To investigate the extent of language deficits based on the CCC-2 (composite and subscale scores) and parents retrospective report of early language delay.
(ii) To investigate whether current structural language skills are associated with pragmatic competence (as measured by CCC-2 composite scores).
(iii) To explore whether parent reported early language delay predict current language and social skills as measured by CCC-2 composite scores and Social Responsiveness Scale (SRS) total score.
(iv) To explore potential sex differences in language characteristics.

Methods

Study Design

The present study is part of BUPgen, an ongoing large multi-site study of neurodevelopmental disorders in Norway, in which children are eligible for enrollment if a suspicion of ASD has been raised by local or specialist health services. This study involved analyses of data collected and processed by April 2019. Data are collected from two types of sites: (1) child habilitation services and (2) child and adolescent mental health services, i.e. public specialist health services receiving referrals for assessment of ASD. After written, informed consent to participate, information from patients' records was extracted by clinicians, following standard procedures.

Participants

Participants were eligible if information on age (4–18 years) at inclusion, diagnostic classification as either ASD or non-ASD, and results from assessment with the Children's Communication Checklist Second Edition (CCC-2) was available. In total, $N = 177$ children were included, born between 1994 and 2012, with a mean age at inclusion of 12.3 years (standard deviation (SD) = 3.3). As the CCC-2 is only completed when the child can speak in at least simple sentences, all participants were verbal. Children were not excluded from participation if they were bilingual speakers of Norwegian ($n = 6$), if they had histories of impaired hearing ($n = 14$) or receiving services from a speech therapist ($n = 21$). Data included results from present and previous clinical assessments, parent-reported history and supplementary parent-reported measures.

Participants consisted of 148 children (83.6%) with a clinical diagnosis of any ASD according to ICD-10 (F84x) and 29 children (16.4%) with suspected ASD, but no clinical ASD diagnosis (non-ASD). Common ASD subtypes included Asperger syndrome (AS) (80/148, 54.1%), Pervasive developmental disorder not otherwise specified (45/148, 30.4%), Childhood autism (14/148, 9.5%) and Atypical autism (7/148, 4.7%), whereas the majority of non-ASD children had one or more NDDs (21/26, 80.8%). Other NDDs were grouped according to ICD-10 codes into the following categories: intellectual disability (F70-79), attention-deficit/hyperactivity disorder (ADHD) (F90), communication disorder (F80), specific learning disorder (F81 and F83), motor disorder (F82 and F95), other NDD (F88, F89 and F94). The presence of epilepsy or cerebral palsy was also registered and included in the total number of NDDs.

Assessments

Diagnoses

All diagnoses were assigned by Norwegian specialist health services, using the *International Statistical Classification of Diseases, 10th Revision* (ICD-10) criteria (World Health Organization 1992). The majority of ASD (121/148, 81.8%) and non-ASD individuals (20/28, 71.4%) had completed the Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 1999), or the Autism Diagnostic Interview-Revised (ADI-R) (Rutter et al. 2003b), or both as part of the clinical evaluation. In cases where ADI-R had not been administered, the Social Communication Questionnaire (SCQ), Lifetime form (Rutter et al. 2003a) was completed at inclusion—if not performed earlier.

Early Language Development

A clinician rated medical history form was obtained for all participants at inclusion, which inquired whether the child had attained one spoken word at 1 years' age, and whether the child had attained its first phrase (a spoken two-word combination) at 2 years' age. This assessment was completed based on the child's medical record supplemented by parent report, asking parents to retrospectively recall this information. Among children with ASD and normal range cognitive abilities, Kenworthy et al. (2012) found attainment of first phrase speech by 2 years' (24 months) age to be a useful marker for distinguishing later language trajectories. For simplicity, therefore, not having attained first phrase at 2 years' age was used as a proxy for early language delay in the present study.

Current Language and Communication Skills

The Children's Communication Checklist Second Edition (CCC-2) (Bishop 2003; Norwegian version: Bishop 2011) is a caregiver reported measure that identifies children with language impairment in both clinical (Norbury et al. 2004) and community contexts (Ketelaars et al. 2009). The CCC-2 consists of 70 items grouped into 10 subscales that measure different aspects of communication: language structure (A: speech, B: syntax, C: semantics, D: coherence), pragmatic language skills (E: inappropriate initiation, F: stereotyped language, G: use of context, H: nonverbal communication), and two scales measuring social aspects (I: social relations and J: interests). The raw scores are converted into scaled scores with a mean of 10 and an SD of 3 based on Norwegian norms, that can also be converted into percentiles for each subscale. The Norwegian version of the CCC-2 has satisfactory internal consistency (Cronbach alpha ranging from 0.73 to 0.89) and inter-rater reliability (Spearman's rho ranging from 0.44 to 0.76) (Helland et al. 2009). The checklist does not provide a categorical diagnosis, but subscales may be combined as composites. The General Communication Composite (GCC) is an overall measure of communication skills, derived by adding the scaled scores of the subscales A-H. In scaled scores a high score indicates language strength and a low score language deficit. A GCC below 55 is considered the cut-off for distinguishing children with clinically significant language impairment from typically developing (TD) children (Bishop 2011). We calculated the Structural Language Score, obtained by adding together the scores on the structural scales (A-D) and the General Pragmatics Score by adding together the scores on the four pragmatic scales (E–H), without the two social nonlinguistic scales (I, J). This specific grouping has been used in other studies (Baixauli-Fortea et al. 2019; Kuijper et al. 2017). Contrary to these, we report scaled scores (see Appendix for further discussion).

Current Social Impairment

The Social Responsiveness Scale (SRS) (Constantino and Gruber 2005) is a 65-item caregiver questionnaire that examines a child's ability to engage in reciprocal social interaction. The SRS total score is a valid quantitative measure of autistic social impairment or traits, with higher scores indicating greater severity (Constantino et al. 2003). Previous reports indicate excellent internal consistency of the SRS, with a Cronbach alpha coefficient of .97 (Constantino and Gruber 2005). In the present study, we applied SRS raw total as a dimensional trait variable reflecting current (last 6 months) level of social impairment.

Cognitive Abilities

Cognitive function was assessed using results from age-appropriate Wechsler scales ($n = 169$): the Wechsler Preschool and Primary Scale of Intelligence (Wechsler 2012; 12.4%), Wechsler Intelligence Scale for Children (Wechsler 2003; 81.7%), Wechsler Abbreviated Scale of Intelligence (Wechsler 1999; 3.0%), and Wechsler Adult Intelligence Scale (Wechsler 2008; 3.0%). These assessments yield standard scores for nonverbal IQ (NVIQ), verbal IQ, and full-scale IQ. Mean age at assessment of cognitive abilities in the present sample ($n = 168$) was 10.0 ($SD = 3.4$) years. To minimize the effect of language in measuring cognitive abilities, we used NVIQ as a trait variable, reflecting severity of cognitive impairment.

Statistical Analyses

Descriptive statistics are presented as *n* (%) and mean (*SD*). First, we report the extent of language deficits by the mean

(SD) for the CCC-2 composite and subscale scores. We also assessed the proportion of children with scores below the chosen cut-off to indicate significant deficits (i.e. GCC < 55 or subscale score ≤ 5th percentile compared to the Norwegian norms, respectively). Second, we investigated whether current structural language skills were associated with pragmatic competence across the whole sample by performing a linear regression analysis with the General Pragmatics Score as dependent variable. The analysis was carried out unadjusted and adjusted for potential confounders, one at a time, and simultaneously. Potential confounding factors included were NVIQ, age at inclusion, and sex. Third, we divided the sample into two groups based on early language delay (i.e. not having attained first phrase at 2 years' age) and compared current language and social skills between these groups. We used independent sample *t*-test and Pearson's chi-squared for between-group comparisons. Mean CCC-2 composite scores were compared using linear regression, adjusting for cognitive ability (NVIQ) and age at inclusion (years). To compare proportions, we computed the Newcombe hybrid score confidence interval as recommended by Fagerland et al. (2015) using Stata 16, and the unconditional z-pooled test as recommended by Lydersen et al. (2012) using StatXact 11. Finally, to explore possible sex differences, group comparisons were repeated for males and females within the whole sample. Possible sex differences in the association between structural and pragmatic language skills were explored in a subsequent regression analysis including an interaction term between sex and the Structural Language Score.

We report available case analyses with the corresponding number of missing cases where appropriate. Following the example of Geurts and Embrechts (2008) we conducted these analyses with ($n = 177$) and without ($n = 153$) the inclusion of participants with invalid consistency check on the CCC-2. As the results in general were the same, the values in tables and figures include all children ($n = 177$). Two-sided p values < 0.05 were regarded as statistically significant. In order to protect against type I error due to multiple hypotheses, however, we recommend p-values between .01 and.05 to be interpreted with caution. Except otherwise noted, we used SPSS 26 for statistical analyses.

Results

Sample Characteristics

The main sample ($N = 177$) included 143 males (80.8%) with a male to female ratio of approximately 4:1 (Table 1). Most children (148/177, 83.6%) had an ASD diagnosis. The majority of children that did not meet the criteria for an ASD diagnosis (non-ASD) were diagnosed with one or more NDDs, mainly ADHD (17/27, 63.0%), specific learning disorders (6/27, 22.2%), and motor disorders (5/27, 18.5%). Co-occurrent ADHD was equally frequent among children with ASD (86/145, 59.3%) and did not differ between groups. Within the whole sample, participating females ($n = 34$) were older at inclusion compared with males (13.5 ($SD = 3.2$) versus 12.0 ($SD = 3.3$) years), and females with ASD had received their diagnosis later (13.6 ($SD = 2.8$) versus 11.0 ($SD = 3.3$) years among ASD males).

Mean age at ASD diagnosis was 11.5 years ($SD = 3.3$). Children with ASD had higher mean scores on diagnostic measures as well as the measure of current social skills (SRS) compared with non-ASD ($p < .01$, all). Non-ASD individuals were younger at inclusion (11.0 years ($SD = 3.7$) versus 12.5 years ($SD = 3.2$) in the ASD group). Mean age at assessment of cognitive abilities and at administration of ADI-R, however, did not differ between the groups. Lastly,

Table 1 Participant characteristics ($N = 177$)

	n	(%)	Range	Mean (SD)
Male sex	143	80.8		
Age (years) at inclusion	177		4–18	12.3 (3.3)
Age (years) at ASD diagnosis	144			11.5 (3.3)
Current social impairment (SRS total)	162		9–153	83.4 (29.8)
Age (years) at cognitive testing	168		4–18	10.0 (3.4)
Nonverbal IQ	161		59–142	102.5 (18.4)
Verbal IQ	163		53–124	91.4 (16.9)
Early language milestones				
One word 1 year (no)	32	22.2		
Two words 2 year (no)	38	27.1		
Diagnoses				
ASD (F84)	148	83.6		
Intellectual Disability (F70-79)	8	4.6		
ADHD (F90)	103	59.9		
Communication disorder (F80)	7	4.1		
Specific learning disorder (F81 + F83)	18	10.5		
Motor disorders (F82 + F95)	27	15.7		
Epilepsy	10	5.6		
Cerebral Palsy	2	1.1		
Other NDD (F94)	1	0.6		
No of NDDs				
0	5	2.8		
1	58	32.8		
≥ 2	106	59.9		
Ethnicity				
European (Caucasian)	157	88.7		

Data are expressed as *n* (%) or mean (SD). The denominator for the reported proportions in this table excludes those with missing data. IQ was obtained from various age-appropriate standardized tests

ASD autism spectrum disorder, *SRS* Social Responsiveness Scale, *NDD* neurodevelopmental disorder

mean values of nonverbal and verbal cognitive abilities were in the normal range and without significant group differences (see Appendix for details on characteristics in both groups).

Extent of Language Deficits Across the Range of Autistic Symptoms

Most children (144/177, 81%) were classified as language impaired, by the CCC-2 (GCC < 55) (Table 2). In general, pragmatic language deficits were more common than structural deficits. Among the structural language skills, 'syntax' was least affected. Still, 27% of children had significant deficits on this subscale (≤ 5th percentile). Moreover, 66% had significant deficits on the 'coherence' subscale, which was the most affected structural scale. For all subscales measuring pragmatic aspects of language, more than half of the sample presented with significant deficits. The most affected pragmatic skill in both groups was nonverbal communication. However, in children with ASD, the deficits on the 'nonverbal communication' subscale were more profound (4.2 (*SD* = 2.7)) than in the non-ASD group (5.6 (*SD* = 2.9); $p = .01$). The ASD group also performed worse on the General Pragmatics Score compared to the non-ASD group (16.3 (*SD* = 9.2) versus 21.1 (*SD* = 11.3); $p = .01$). Both groups performed equally on the GCC and the Structural Language Score. Adjusting for NVIQ and age at inclusion did not alter these findings substantially. Notably, language impairment was not universal. Within the whole sample, 33 children (19%) did not have any language impairment as measured by the CCC-2. A minority (38/140, 27%) had reported early language delay, i.e. not having attained first phrase at 2 years' age (Table 1). Analyses comparing characteristics between individuals with ($n = 153$) and without ($n = 22$) valid consistency check on the CCC-2 are presented in the Appendix.

The Relationship Between Current Structural Language Skills and Pragmatic Competence

The Structural Language Score was strongly associated with the General Pragmatics Score with a regression coefficient 0.56 (CI 0.45 to 0.68), $p < .001$, and explained 35.9% of the variance in the General Pragmatics Score. After adjustment for potentially confounding variables, the association remained substantially unchanged (Table 3). The potential influence of diagnostic group on the observed association was also explored. As illustrated in Fig. 1, current structural and pragmatic language skills, as measured by the CCC-2, were highly correlated regardless of diagnostic group.

Table 2 CCC-2 subscale and composite scores (a high score indicates better language ability): means, standard deviations, proportion below 'cut-off' indicating significant deficits for the whole sample, the ASD and the non-ASD group

	Whole sample			ASD			Non-ASD		
	N = 177			*n* = 148			*n* = 29		
	Mean	SD	Below 'cut-off' (%)	Mean	SD	Below 'cut-off' (%)	Mean	SD	Below 'cut-off' (%)
CCC-2 subscale scores			≤ 5 percentile*			≤ 5 percentile*			≤ 5 percentile*
A. Speech	6.5	3.9	35.0	6.6	4.0	35.1	5.9	3.6	34.5
B. Syntax	6.5	3.6	27.1	6.6	3.6	27.0	6.4	3.6	27.6
C. Semantics	5.0	3.1	34.5	4.8	3.0	35.8	5.9	3.4	27.6
D. Coherence	4.0	3.0	66.1	3.9	2.9	67.6	4.7	3.5	58.6
E. Inappropriate initiation	4.5	2.6	55.4	4.3	2.4	58.1	5.6	3.2	41.3
F. Stereotyped language	4.8	3.0	50.8	4.6	3.0	52.0	5.7	3.0	44.8
G. Use of context	3.4	3.0	57.1	3.2	2.9	60.1	4.3	3.4	41.4
H. Nonverbal communication	4.4	2.8	71.8	4.2	2.7	75.7	5.6	2.9	51.7
I. Social relations	3.3	2.9	73.4	3.0	2.6	77.7	5.1	3.6	51.7
J. Interests	3.3	2.3	60.5	3.1	2.2	66.2	4.7	2.5	31.0
CCC-2 composite scores			GCC < 55			GCC < 55			GCC < 55
GCC (sum scales A–H)	39.1	17.9	81.4	38.1	17.2	83.8	44.2	20.9	69.0
Structural Language Score (sum scales A–D)	22.0	10.3	n.a	21.8	10.0	n.a	22.9	11.9	n.a
General Pragmatics Score (sum scales E–H)	17.1	9.7	n.a	16.3	9.2	n.a	21.1	11.3	n.a

ASD autism spectrum disorder, *CCC-2* Children's Communication Checklist Second Edition, *SD* standard deviation, *n.a.* not applicable

*Proportion (%) of individuals with subscale score at or below the 5th percentile compared to Norwegian norms

Table 3 Linear regression with General Pragmatics Score as dependent variable and Structural Language Score as primary covariate (scaled scores)

	Correlation coefficient			*p*
	n	B	95% CI	
Unadjusted				
Structural Language Score	177	.56	(.45 to .68)	< .001
Adjusted separately for				
Sex (female)	177	.57	(.45 to .68)	< .001
Age (years)	177	.57	(.46 to .68)	< .001
Nonverbal IQ	161	.60	(.48 to .72)	< .001
Adjusted for all	161	.60	(.48 to .72)	< .001

Results based on available case analysis of the main sample

B unstandardized regression coefficient, *CI* confidence interval, *p* *p*-value

Early Language Delay and Current Language and Social Skills

Within the whole sample, the 38 children with reported language delay performed worse on current measures of general communication (GCC; 34.1 (*SD* = 18.8) versus 40.9 (*SD* = 16.8); $p = .04$) and structural language skills (Structural Language Score; 17.0 (SD = 10.4) versus 23.9 (SD = 9.5); $p < .001$) compared with the 102 children without language delay. No significant difference was found regarding pragmatic skills (Fig. 2). Adjusting for NVIQ and age at inclusion did not alter the findings substantially, except that the difference in GCC no longer was significant ($p = .20$). Children in the language delayed group also performed worse on measures of verbal IQ (80.8 (*SD* = 16.2) versus 94.9 (*SD* = 15.1), respectively; $p < .001$), while no difference was found regarding current social skills (SRS total raw score), when compared with the group without language delay. Children receiving an ASD diagnosis were diagnosed earlier if they had early language delay (10.1 years (*SD* = 4.0) versus 11.9 years (*SD* = 2.9); $p = .03$).

Sex Differences

The majority of both males (117/143, 82%) and females (27/34, 79%) was identified as language impaired (GCC < 55), and the overall extent and profile of language impairments, as measured by the CCC-2 composite scores, did not differ by sex (unadjusted and adjusted for potential confounders) (Table 4). Generally, females had higher mean scores (indicating better performance) on most subscales, although reaching statistical significance only for the 'syntax' subscale ($p = .02$) (Fig. 3). There was no significant interaction between sex and Structural Language Score on

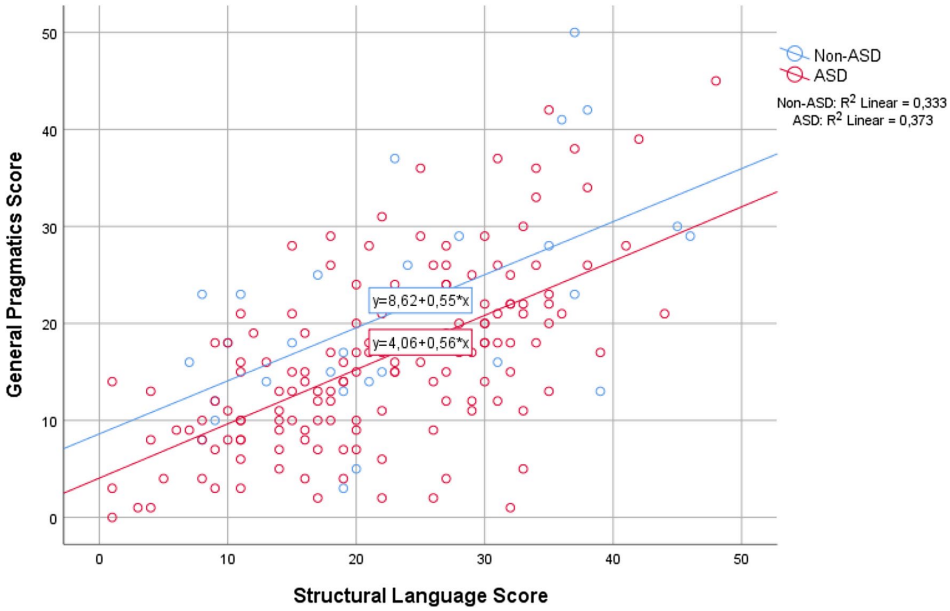

Fig. 1 Distribution of Structural Language and General Pragmatics composite scores across the study sample ($N = 177$), and their linear associations in the group with and without diagnosed autism spectrum disorder (ASD; $n = 148$ and non-ASD; $n = 29$)

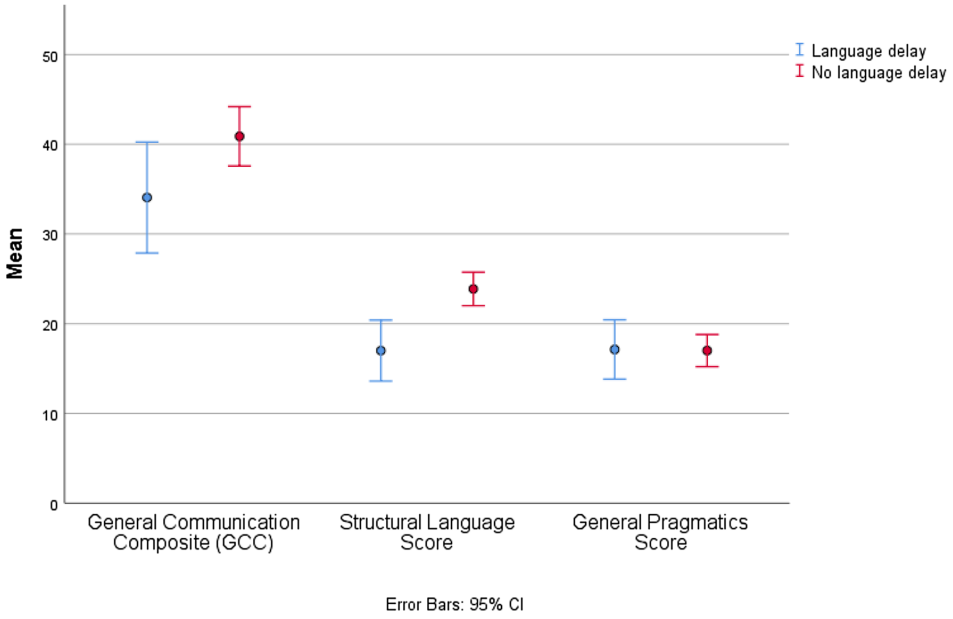

Fig. 2 Clustered error bar mean of CCC-2 composite scores of children ($n = 140$) with parent report on early language delay, separated into children with ($n = 38$) and without ($n = 102$) early language delay (i.e. not having attained first phrase at 2 years' age). Means and 95% CI

Table 4 Participant and language characteristics by sex ($N = 177$)

	Males ($n = 143$)			Females ($n = 34$)			Difference		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)	Estimate	95% CI	*p*
ASD	119	83.2		29	85.3		−2.1	(−12.9 to 14.2)	.79
Age (years) at inclusion	143		12.0 (3.3)	34		13.5 (3.2)	−1.5	(−2.8 to −.3)	.02
Age (years) at ASD diagnosis	118		11.0 (3.2)	26		13.6 (2.8)	−2.6	(−4.0 to −1.2)	< .001
Age (years) at cognitive testing	135		9.8 (3.4)	33		10.9 (3.2)	−1.1	(−2.4 to .15)	.08
Nonverbal IQ	128		102.7 (19.6)	33		101.8 (12.9)	1.0	(−4.7 to 6.6)	.74
Verbal IQ	130		90.1 (16.8)	33		96.5 (16.2)	−6.4	(−12.8 to .1)	.05
Early language milestones									
One word 1 year (no)	30	25.6		2	7.4		18.3	(.8 to 28.4)	.04
Two words 2 year (no)	37	32.7		1	3.7		29.0	(12.4 to 38.6)	.003
Language impaired (GCC < 55) CCC-2 composite scores	117	81.8		27	79.4		2.4	(−10.1 to 19.5)	.7 7
GCC (sum scales A–H)	143		38.2 (18.4)	34		42.9 (15.7)	−4.7	(−11.4 to 2.1)	.17
Structural Language Score (sum scales A–D)	143		21.4 (10.5)	34		24.7 (9.0)	−3.3	(−7.2 to .6)	.09
General Pragmatics Score (sum scales E–H)	143		16.8 (10.0)	34		18.2	−1.3	(−5.0 to 2.3)	.47

Data are expressed as *n* (%) or mean (SD). The denominator for the reported proportions in this table excludes those with missing data. IQ was obtained from various age-appropriate standardized tests

ASD autism spectrum disorder, *NDD* neurodevelopmental disorder

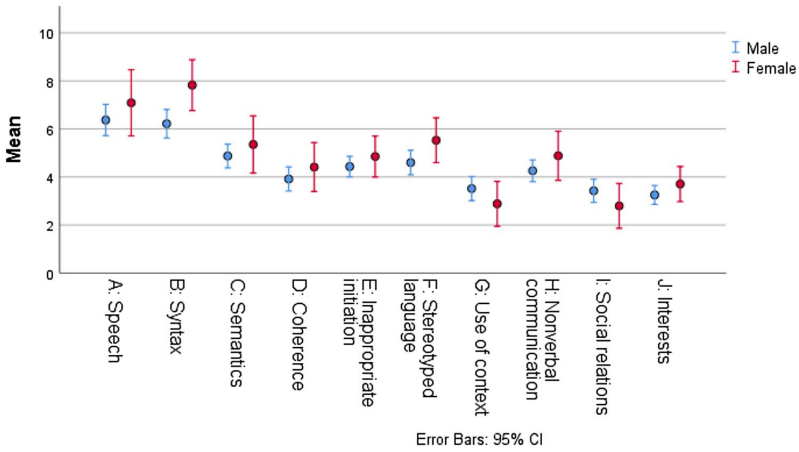

Fig. 3 Clustered error bar mean of CCC-2 subscale scores in the total study sample ($N = 177$), by sex. Means and 95% CI

the General Pragmatics Score. Females, however, performed better than males on measures of verbal IQ (96.5 ($SD = 16.2$) versus 90.1 ($SD = 16.8$), respectively, $p = .05$). Only one female (1/27, 4%) was reported with language delay compared with males (37/113, 33%), $p = .003$.

Discussion

In this study of language characteristics in a sample of children evaluated for ASD by specialist health services we found that the majority had language impairment, i.e. general communication skills below the CCC-2 cut-off (GCC < 55). Structural language deficits were common and strongly associated with pragmatic competence across the whole sample. Pragmatic language impairments were most profound in children with ASD. Early language delay was more common among males and associated with structural language deficits, whereas pragmatic language and social skills did not differ significantly among children with and without language delay. Our findings support that pragmatic language impairment as a dimensional symptom profile probably reflect a confluence of risk factors, among them structural language deficits. Further, they support that early language delay is associated with later language abilities that are distinct from autistic symptoms. Lastly, we contribute to recent reports that females with ASD may be recognized and diagnosed later than males probably due to stronger verbal skills and a reduced rate of early language delay.

Structural and Pragmatic Language Deficits Across the Range of Autistic Symptoms

Existing research on language impairment often overlooks differences in autism severity (Levinson et al. 2020). As a result, little is known about how distinct language skills may present differently across the autism spectrum. In the present study, we applied a dimensional approach and studied language skills in a sample of children evaluated for ASD, with and without ASD diagnoses. We found a large extent of language impairment across the whole sample, as measured by the CCC-2 (GCC < 55), that did not differ significantly between children diagnosed with ASD (84%) and children not fulfilling the diagnostic criteria (non-ASD; 69%). The observed extent of language impairment is comparable to previous findings among children with Asperger syndrome and children with ADHD (Helland et al. 2012), both of which were common diagnoses in the present sample.

Although both structural and pragmatic language skills were widely distributed across both groups, pragmatic aspects (the *use*) of language were most affected. This is in line with previous results among school-aged children with ASD (Geurts and Embrechts 2008; Boucher 2012). As expected, the ASD and non-ASD group differed significantly on the subscales that map social deficits characteristic of ASD ('social relations' and 'interests', $p = .004$ and $p = .001$, respectively). Although our non-ASD group was small ($n = 29$), significant pragmatic deficits were found compared to Norwegian norms, albeit less profound than in the ASD group. These results support the concept of pragmatic language impairment as a dimensional symptom profile present across a range of NDDs, with ASD "at the extreme end", as suggested by Norbury (2014, p. 212). Pragmatic skills include a child's ability to initiate and maintain a mutual conversation, to flexibly adapt the use of language to the social context and resolve ambiguities, as well as nonverbal aspects of communication. Our findings coincide with previous studies using the CCC-2 that have reported more profound pragmatic impairments among children with ASD compared to typically developing children (e.g. Geurts and

Embrechts 2008; Oi et al. 2017; Helland et al. 2012), but also compared to children with other NDDs, such as specific language impairment (Oi et al. 2017; Geurts and Embrechts 2008; Norbury et al. 2004), and ADHD (Geurts and Embrechts 2008; Kuijper et al. 2017; Helland et al. 2012). With the exception of Oi et al. (2017) who investigated whether aspects of communicative impairment were continuously distributed in a population-based sample, these studies compared categorically defined clinical groups, which were also considerably smaller than the ASD group in the present sample. Applying a dimensional approach, we extend their findings to a larger clinical population of children with autistic symptoms.

Together, the CCC-2 structural scales ('speech', 'syntax', 'semantics', 'coherence') assess language functions apart from pragmatics that are commonly affected in children with specific language impairment (Norbury et al. 2004), including vocabulary and articulatory issues. By combining these subscales, we were able to assess structural aspects of the child's language, as assessed by their caregivers. This includes the ability to apply rules for producing and combining speech sounds and combinations of words to form phrases and sentences, as well as the ability to understand and use the meaning of words and sentences, and to use a coherent language. We found that structural language deficits are common (compared to Norwegian norms) in children evaluated for suspected ASD, with deficits in 'syntax' being relatively infrequent, and 'coherence' being the most affected subscale. The overall extent and profile of structural language deficits did not differ between children with and without an ASD diagnosis, and is consistent with the language profile reported from previous studies in school-aged children with ASD, as reviewed by Boucher (2012). Further, the observed extent of deficits is comparable to previous studies in school-aged children with ASD (Helland et al. 2012; Kuijper et al. 2017; Baixauli-Fortea et al. 2019). Clinicians and researchers have long been aware of the high comorbidity between ASD and other NDDs (Lord et al. 2018), as well as their potential impact on specific aspects of language and communication. Still, studies on language skills in ASD rarely provide information on these comorbid diagnoses (Levinson et al. 2020). In the present study the proportion of children diagnosed with (co-occurrent) ADHD was high in both the ASD and the non-ASD group. Our finding that structural language skills were equally impaired in both groups are consistent with previous reports that children with ASD and ADHD are not possible to distinguish from each other on CCC-2 structural scales, while on pragmatic scales they can (Kuijper et al. 2017; Geurts and Embrechts 2008; Helland et al. 2012).

Co-occurring language impairment may influence the presentation of ASD symptoms, as well as the functional impairment of the child. Therefore, assessment of language skills is recommended as part of the diagnostic evaluation for ASD (Hyman et al. 2020). In line with Kjelgaard and Tager-Flusberg (2001) we report considerable heterogeneity in the language skills of children with ASD, but a somewhat smaller proportion of children with no language impairment. In our sample, only 16% (24/148) of children with ASD had no language impairment (GCC > 55). Suren et al. (2019a) reviewed patients records obtained from the specialist health service for 503 children with ASD in Norway, finding that the assessments largely were conducted in accordance with local guidelines. Notably, however, only a minority of children in their study underwent a formal assessment of language as part of their clinical evaluation (33%). Although the present sample consist of children who underwent an assessment using the CCC-2, our findings underscore that structural language deficits are frequent across the range of autistic symptoms and important to assess also in verbal children evaluated for ASD.

High Correlation Between Current Structural and Pragmatic Language Skills

Previous work that has examined the relationship between specific language domains and other aspects of functioning has largely focused on the association between pragmatic language and social skills deficits in ASD. The expression of pragmatic competence often relies on verbal skills. As such, the close relationship between structural and pragmatic language skills observed in the present sample is expected, and consistent with previous reports of an association between structural and pragmatic language skills in children with specific language impairment (Ketelaars et al. 2009) as well as children with ASD (Volden et al. 2009; Baixauli-Fortea et al. 2019; Levinson et al. 2020). We replicate and extend their findings to a large group of children with a broad range of autistic symptoms. By investigating this relationship in a broader clinical population, we found that structural and pragmatic language skills, as measured by the CCC-2, were highly correlated regardless of diagnostic group. This suggests that the close relationship between structural and pragmatic language skills is present not only in children with ASD, but also in children with autistic symptoms seen across various NDDs. Further, our finding that pragmatic competence was statistically not solely explained by structural language skills is compatible with the notion that pragmatic language impairments might reflect a confluence of risk factors, among them deficits in structural language (Norbury 2014). Volden et al. (2009) not only reported structural language skills to predict performance on a standardized measure of pragmatic language in youth with ASD, but also that pragmatic language in turn uniquely predicted social skills. Taken together, these and the present findings suggest that although mediated by pragmatic language, structural

language skills may influence social skills, and demonstrate the necessity of examining language skill domains separately when evaluating children with suspected ASD.

Notably, both composites used in the present analyses include various aspects of structural and pragmatic skills. The Structural Language Score include both *form* ('speech' and 'syntax') and *content* ('semantics' and 'coherence') skills, that may also tap into vocabulary knowledge and discourse. Although a strong correlation was found, it is likely that some aspects of structural language bear a stronger significance on pragmatic competence than others. Further, some aspects of pragmatic competence may be stronger related to structural language than others. In a CCC-2 validation study, Norbury et al. (2004) reported no group differences between children with specific language impairment and groups thought to have more severe pragmatic difficulties on the 'stereotyped language' and 'use of context' subscales, suggesting that structural language difficulties may influence ratings on these subscales. For instance, a child with limited expressive skills may rely on a few phrases that might appear stereotyped. Moreover, children with specific language impairment demonstrated strengths in 'nonverbal communication', suggesting that their structural deficits did not impact this aspect of pragmatic competence (Norbury et al. 2004).

The profile of language impairments in children with ASD is reported to change with pragmatic impairments becoming more prominent relative to structural deficits by school-age (Rapin and Dunn 2003; Geurts and Embrechts 2008). Such changes may be related to maturity, interventions, the interplay of developmental risk factors to cause more profound impairments over time (Geurts and Embrechts 2008), as well the pervasiveness of pragmatic language impairment becoming more apparent with increasing demands. The present sample mainly comprised school-aged children, and the cross-sectional design does not allow conclusions regarding language trajectories. Importantly, however, we report structural language deficits to be common in school-age children evaluated for suspected ASD, and to be strongly associated with pragmatic competence across the range of autistic symptoms.

Early Language Delay and Current Language and Social Impairment

Deficits in pragmatic language and social communication may not become fully manifest until demands exceed limited capacity (Baird and Norbury 2016). As young children with clear developmental disabilities are likely to be referred earlier for specialist assessment than those without, it has been cautioned against overlooking young children with ASD and no language delay (Lord et al. 2018). As expected in a sample of verbal children, the proportion of children with language delay in the present study was relatively low, but comparable to findings from the Norwegian MoBa cohort (Suren et al. 2019b). While children with language delay had more structural language deficits compared to children without language delay, they did not differ in pragmatic language and social skills. In an earlier study Kenworthy et al. (2012) reported age of first phrases among verbal children with ASD to predict later structural language, but not other social communicative impairments characteristic of ASD. Moreover Loucas et al. (2008) found phrase speech to be acquired significantly later in ASD children with co-occurrent language impairment compared to those without, while current autistic symptoms and pragmatic language impairment did not differ. Although caution when interpreting retrospectively reported language milestone data is recommended (Hus et al. 2011; Ozonoff et al. 2018), these and the present findings suggest that early language delay represents an important predictor of later language ability that is distinct from autism symptoms. Further, they lend support to the recent revisions of *the Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) and *the International classification of diseases* (ICD-11), where delayed or impaired language is no longer included as a core symptom of ASD, but should be specified as co-occurrent language impairment (American Psychiatric Association 2013; World Health Organization 2018).

Sex-Based Differences in Language Profile

Assessing male and female language profiles separately may contribute to a better understanding of the female ASD phenotype. Consistent with findings in clinically-referred children with ASD (Solomon et al. 2012) we found no significant sex differences on the CCC-2 composite scores. We did, however, find that females presented with a relative strength in their structural language skills, performing better than males on the 'syntax' subscale. Consistent with our results, a recent review by Lai and Szatmari (2020) suggest that females with ASD may show higher linguistic abilities, mirroring normative sex differences and placing them closer to typically developing peers and away from males with ASD. However, these linguistic strengths may mask their real struggles with social communication, and complicate or delay the detection of their ASD symptoms (Parish-Morris et al. 2017; Lai and Szatmari 2020). The presence of early language delay has been related to earlier diagnosis of ASD (Goodwin et al. 2017; Lord et al. 2018). Early language delay was rare among females in the present sample, whose mean age at ASD diagnosis was higher compared with males. Although our findings may not seem surprising, they contrast with several studies that did not find significant sex differences in language and communication among ASD individuals (Tillmann et al. 2018; Solomon et al. 2012;

Lawson et al. 2018). Due to the limited number of female participants in our study ($n = 34$), it is not possible to draw firm conclusions on potential sex differences. However, two large studies recently reported that children with ASD and more advanced language abilities, particularly females, were diagnosed later than non-verbal and minimally verbal children (McCormick et al. 2020; Salomone et al. 2016).

Strengths and Limitations

A major strength of our study is the dimensional approach which enabled us to study language skills in a sample of children assessed for ASD with and without ASD diagnoses, increasing generalizability to the broader population of children evaluated for ASD. The large sample size compared to previous studies of CCC-2 in children with ASD, including a relatively large number of females, is another strength. Further, available data on age at inclusion and cognitive abilities allowed adjustment for these potential confounding factors.

Limitations include a potential selection bias, as referral for assessment in the present sample was based on concern. The participants may not be representative for children with autistic symptoms in the general population. Further, we relied upon parent report of structural and pragmatic language skills in everyday contexts as measured by the Norwegian version of the CCC-2. As this checklist is only suitable for verbal children who speak Norwegian, our results may be less applicable to younger children, children with no verbal language, as well as other languages. A small number of children with a *history* of hearing impairment were not excluded, as they were considered verbal and had completed the CCC-2. We used retrospective parent report on early language delay collected at inclusion (age from 4 to 18 years), introducing the possibility of recall bias. This information, however, was supplementary to available information in the child's medical record. Although the precision of information regarding attainment of phrase speech at 2 years' age may have varied, we do not consider it likely to have biased our results systematically. Further, the proportion of children with early language delay observed in the present study is comparable to a previous Norwegian study by Suren et al. (2019b). Mild or moderate deficits in social and communicative competence may be missed in the context of co-occurring difficulties, such as ADHD (Skuse et al. 2009), a common NDD in the present sample. As the proportion of individuals diagnosed with ADHD did not differ between the two diagnostic groups, we do not consider their inclusion to have biased our results in one direction. The large proportion with co-occurring ADHD, however, may have contributed to the observed late age at ASD diagnosis (11.5 years). Finally, the use of clinical diagnoses obtained from different clinics is a potential source of bias. Misclassification in both directions for ASD and the non-ASD disorders are considered possible, but not very probable. A recent review of patient records show that 95% of ASD diagnoses provided a high standard of documentation within the Norwegian specialist health service and meet the diagnostic criteria (Suren et al. 2019a).

Clinical Implications

Language and communication skills are critical to the cognitive and social development of children, and highly predictive of academic and employment outcomes, regardless of the primary diagnosis (Norbury and Paul 2018; Conti-Ramsden and Durkin 2015). Children evaluated for suspected ASD commonly present with structural as well as pragmatic language impairments, that are likely to persist and to require on-going support as the child gets older. These impairments represent an important target of intervention. In a clinical setting, such interventions should be centered on the child's age and profile of strength and needs, rather than the diagnostic category alone. They should be multifaceted, incorporating techniques for improving structural language skills, social communication and interaction, as well as using linguistic context to improve comprehension (Norbury 2014). Our results suggest that both language milestones and the CCC-2 may be helpful for identifying children with increased risk for structural language impairments, which needs to be managed separately from the presenting ASD symptoms.

Conclusion

We found a large extent of structural as well as pragmatic language deficits in children evaluated for suspected ASD. Structural language deficits were associated with reduced pragmatic competence across the whole sample and more common among children with early language delay, while pragmatic language impairments were most profound in children with diagnosed ASD. Our results support the notion of pragmatic language impairment as a dimensional symptom profile potentially linked to several developmental risk factors, among them structural language deficits. This underscores the importance of including language skills assessment in the diagnostic evaluation of children with suspected ASD. Applied both in clinical and research settings language milestones have the potential for identifying a subgroup of children with increased risk for structural language impairments. These children may benefit from specific language interventions in addition to management of the core ASD symptoms.

Appendix

Supplementary Material and Sensitivity Analyses

For the purpose of comparison with previous samples we have included information on participant characteristics by ASD group status (Table 5). The Norwegian CCC-2 manual (Bishop 2011, p. 72) provides a description on how to assess the internal consistency of the parents' answers. In cases of invalid consistency check, it is recommended not to interpret the individuals' test result. In the present sample, we compared participant characteristics between individuals with valid consistency check on the CCC-2 ($n = 153$) and $n = 22$ individuals with invalid CCC-2 scores not passing the instruments' consistency check (Table 6). Participant characteristics did not differ substantially between these two groups, except that a larger proportion of children not passing the consistency check were diagnosed with two or more neurodevelopmental disorders ($p = .007$). Children with invalid consistency check, however, had lower scores on the General Communication and Structural Language composites, indicating larger impairment in general communication and structural language skills. Further, the group with invalid consistency check also had lower pragmatic scores, that were more proportionate to their structural language skills. In the present study, analyses with and without exclusion of individuals with invalid consistency check did not affect the main outcomes substantially. The proportion of parents ($n = 22/175$; 12.6%) that were inconsistent in their answers on the CCC-2 in the present study is in line with findings by Geurts and Embrechts (2008) (9.3–22.8%), and most likely due to the change in questions types throughout the CCC-2. During the first part of the CCC-2 questions focusing on difficulties are negatively formulated, whereas the last 20 questions focusing on strengths are positively formulated. Although instructions clearly state that there is a change in question type, answers to the last questions may be given as if they were still negatively formulated. Consequently, the scaled scores of each subscale will be higher (indicating less difficulties) than if the questions were answered consistently, underestimating the difficulties a child encounter. Considering results on the consistency check is important when using the CCC-2 in individual assessment of the communication pattern of a child in a clinical setting, where an invalid consistency check should elicit careful consideration of possible reasons for the invalid result. However, our results indicate that not passing the reliability check may not be a random event, and that exclusion of these individuals may bias results on a group level and underestimate the true extent of structural language deficits in research samples.

In order to assess the potential impact of including children with intellectual disability ($n = 8$) on CCC-2 composite scores in the present study, as well as estimates of group differences and associations between structural and pragmatic language skills, we checked whether these children represented outliers in the distribution of CCC-2 scores (Fig. 4). Further, main analyses were repeated with these individuals excluded, resulting in a modest attenuation of the results, not affecting the statistical significance of our findings.

In the present study we have chosen to present scaled scores from the CCC-2 as recommended in the CCC-2 manual. Further, we have chosen to use the Structural Language and the General Pragmatics composite scores, although not described in the manual. No Norwegian norms are available for these composite scores. However, since 10 is the average of the scaled scores on each of the four subscales for both indexes, a putative mean value of 40 is expected for each. Previous studies reporting these composites have presented their results as raw totals (Kuijper et al. 2017; Baixauli-Fortea et al. 2019), while we have chosen to report scaled scores. We therefore present some of our results as CCC-2 raw scores for comparison (Fig. 5 and Table 7). Kuijper et al. (2017) reported a mean (SD) Structural Language Score in the ASD group of 20.4 (9.0), and a mean (SD) General Pragmatic Score of 37.4 (13.1), both of which are higher (indicating larger deficits) compared with the present sample. In a more recent study, Baixauli-Fortea et al. (2019) report a mean (SD) Structural Language Score in the ASD group of 19.0 (9.4), which is close to the observed value in the present sample. There are, however, important differences between these two and the present study; smaller sample sizes ($n = 36$ and $n = 52$), the inclusion of only participants with normal range cognitive abilities, as well as a more limited age range under study (6–12 and 7–11 years), which may limit comparability.

Table 5 Participant characteristics by diagnostic group ($N = 177$)

	ASD ($n = 148$)			Non-ASD ($n = 29$)		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)
Male sex	119	80.4		24	82.8	
Age (years) at inclusion	148		12.5 (3.2)	29		11.0 (3.7)
Age (years) at ASD diagnosis	144		11.5 (3.3)			
Autistic symptom severity						
ADI-R nonverbal total	66		22.2 (9.5)	10		10.0 (10.6)
SCQ total	94		15.8 (7.5)	20		10.3 (8.2)
SRS raw total	136		86.7 (27.7)	26		66.2 (34.8)
Age (years) at cognitive testing	142		10.0 (3.3)	26		10.0 (3.7)
Nonverbal IQ	137		102.7(18.4)	24		101.6(19.0)
Verbal IQ	138		90.8 (17.0)	25		94.8 (15.9)
Early language milestones						
One word 1 year (no)	30	24.0		2	10.5	
Two words 2 year (no)	31	25.6		7	36.8	
Diagnoses						
Intellectual disability (F70-79)	7	4.8		1	3.4	
ADHD (F90)	86	59.3		17	63.0	
Communication disorder (F80)	5	3.4		2	7.4	
Specific learning disorder (F81 + F83)	12	8.3		6	22.2	
Motor disorders (F82 + F95)	22	15.2		5	18.5	
Epilepsy	8	5.4		2	6.9	
Cerebral palsy	1	0.7		1	3.6	
Other NDD (F94)	1	0.7		0	0	
Motor disorders (F82 + F95)	22	15.2		5	18.5	
Epilepsy	8	5.4		2	6.9	
Cerebral Palsy	1	0.7		1	3.6	
Other NDD (F94)	1	0.7		0	0	
No of NDDs						
0	0			5	19.2	
1	47	32.9		11	42.3	
≥ 2	96	67.1		10	38.5	
Prematurity (yes)	19	14.3		7	25.9	
Paternal age (years)	97		32.3 (5.9)	21		33.2 (6.3)
Maternal age (years)	106		29.8 (5.2)	25		29.4 (5.3)
Ethnicity						
European (Caucasian)	129	89.0		28	100.0	

Data are expressed as *n* (%) or mean (SD). The denominator for the reported proportions in this table excludes those with missing data. IQ was obtained from various age-appropriate standardized tests

ADI-R Autism Diagnostic Interview-Revised, *ASD* autism spectrum disorder, *SCQ* Social Communication Questionnaire, *SRS* Social Responsiveness Scale, *NDD* neurodevelopmental disorder

Table 6 Participant characteristics by CCC-2 consistency check ($n=175$)

	Valid ($n=153$)			Not valid ($n=22$)		
	n	(%)	Mean (SD)	*n*	(%)	Mean (SD)
Male sex	123	80.4		18	81.8	
ASD	127	83.0		20	90.9	
Age (years) at inclusion	153		12.3 (3.4)	22		12.3 (2.7)
Age (years) at ASD diagnosis	123		11.4 (3.4)	20		11.6 (2.7)
Nonverbal IQ	138		102.8 (18.8)	21		100.2 (15.3)
No of NDDs						
0	4	2.7		0	0	
1	56	38.1		2	10.0	
≥2	87	59.2		18	90.0	
Early language development						
One word 1 year (no)	26	21.0		6	31.6	
Two words 2 year (no)	33	27.5		5	26.3	
CCC-2 composite scores						
GCC (sum scales A–H)	153		40.2 (18.3)	22		30.0 (9.8)
Structural Language Score (sum scales A–D)	153		22.7 (10.4)	22		15.6 (6.3)
General Pragmatics Score (sum scales E–H)	153		17.5 (10.1)	22		14.3 (4.9)
Ethnicity						
European (Caucasian)	135	90.0		21	95.5	

Data are expressed as *n* (%) or mean (SD). The denominator for the reported proportions in this table excludes those with missing data. IQ was obtained from various age-appropriate standardized tests. 2 participants had missing information on results of the consistency check

ASD autism spectrum disorder, *CCC-2* Children's Communication Checklist Second Edition, *NDD* neurodevelopmental disorder

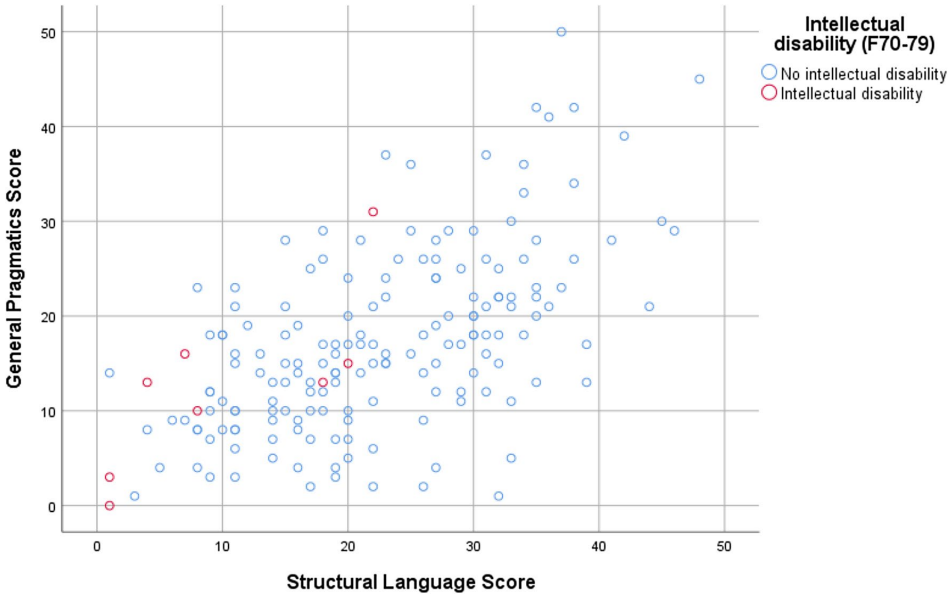

Fig. 4 Distribution of Structural Language and General Pragmatics composite scores, in the group with ($n=8$) and without ($n=169$) co-occurrent intellectual disability

Fig. 5 Distribution of Structural Language and General Pragmatics composite scores (raw scores) across the study sample, and their linear associations in the group with and without diagnosed autism spectrum disorder (ASD; $n = 147$ and non-ASD; $n = 28$)

Table 7 CCC-2 raw scores (a low score indicates better language ability): means, standard deviations, and comparisons between diagnostic groups

	Groups				Difference		
	ASD		Non-ASD				
	$n = 147$		$n = 28$				
	Mean	SD	Mean	SD	Estimate	95% CI	*p*
CCC-2 subscale scores							
A. Speech	2.4	3.2	3.5	4.1	−1.2	(−2.5 to .2)	.09
B. Syntax	2.3	2.7	2.8	3.1	−.5	(−1.6 to .6)	.36
C. Semantics	5.7	3.4	5.5	4.4	.1	(−1.3 to 1.6)	.85
D. Coherence	6.8	4.3	6.6	4.1	.2	(−1.5 to 2.0)	.79
E. Inappropriate initiation	8.5	4.6	8.3	5.4	.3	(−1.7 to 2.2)	.79
F. Stereotyped language	4.4	3.4	3.6	3.0	.8	(−.6 to 2.1)	.28
G. Use of context	7.3	4.4	6.9	4.3	.4	(−1.3 to 2.2)	.63
H. Nonverbal communication	7.7	4.5	5.9	4.0	1.8	(.9 to −.005)	.05
I. Social relations	7.6	4.0	5.7	4.2	2.0	(.3 to 3.6)	.02
J. Interests	9.6	4.6	7.3	3.8	2.3	(.5 to 4.1)	.01
CCC-2 composite scores							
Structural Language Score (sum scales A–D)	17.1	10.7	18.4	13.2	−1.3	(−5.9 to 3.2)	.57
General Pragmatics Score (sum scales E–H)	27.9	14.3	24.7	14.3	3.2	(−2.6 to 9.1)	.28

ASD autism spectrum disorder, *CCC-2* Children's Communication Checklist Second Edition, *SD* = standard deviation, *CI* confidence interval, *p* *p*-value for independent samples t-test

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Author Contributions LR and TN conceptualized and designed the study, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. AMS, BW, and OAA contributed in conceptualizing and designing the study, interpreted the findings and critically reviewed the manuscript and its analyses. SL reviewed the analyses and reviewed and revised parts of the manuscript. All authors approved the final manuscript as submitted and are accountable for all aspects of the work.

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Compliance with Ethical Standards

Conflict of interest AMS and OAA declares no direct conflict of interest related to this article. AMS discloses that she received travel support for conference attendance from Medice in 2018. OAA discloses that he has received speaker's honorarium from Lundbeck. All other authors declare that they have no conflicts of interest.

Ethical Approval The BUPgen study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (REK#2012/1967) and the Norwegian Data Inspectorate and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent Informed consent was obtained from all individual participants (and/or parents when necessary due to age) included in the study.

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Paper III

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The co-occurrence of motor and language impairments in children evaluated for autism spectrum disorder. An explorative study from Norway.

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ABSTRACT

Background: Current research suggest that motor and language impairments are common and closely related in infants with autism spectrum disorder (ASD). In older children, less is known about how these impairments are related to each other.
Aims: The current study explored the co-occurrence and potential impact of motor and language impairments in a sample of school-aged children evaluated for ASD by Norwegian specialist health services.
Methods: Besides clinical evaluation for ASD, all participants (N = 20, mean age 10.7 (SD = 3.4) years) underwent a standardized test of motor performance (MABC-2), parent report measures of current motor (DCDQ'07), language (CCC-2), and social (SRS) skills, and a caregiver interview on everyday functioning, providing an overall impairment score (DD-CGAS).
Results: The majority (85%) had motor and/or structural language deficits in addition to their social impairment. All children identified with motor impairment on both measures (39%) also had structural language deficits. Better motor performance was strongly correlated with better structural language skills ($r = .618$, $p = .006$).
Conclusions: Our findings suggest that co-occurring motor and structural language deficits should be anticipated and assessed when evaluating children for ASD. These deficits may need specific interventions that complement those targeting social skills deficits and other ASD core symptoms.

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1. Introduction

Autism spectrum disorder (ASD) is a common and highly heterogenous neurodevelopmental disorder (NDD). Assigning an ASD diagnosis requires persistent deficits in social communication and interaction, alongside atypical and restricted patterns of behavior sufficiently severe to cause functional impairment (American Psychiatric Association, 2013). Yet, there is considerable variation in the clinical presentation of children with ASD. The core social deficiency of ASD is now considered a continuous trait with no natural cut-off between ASD and subthreshold autistic traits (Happé and Frith, 2020).

The revised Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) has recognized the complex presentations of ASD. Acknowledging the need to interpret core symptoms within a broader developmental context, cognitive and language level specifiers to be noted alongside the diagnosis have been included (American Psychiatric Association, 2013). It is now recommended that common comorbidities are investigated and treated in children with ASD (Fuentes, Hervás, & Howlin, 2020; Hyman, Levy, & Myers, 2020). Furthermore, that evaluation includes assessment of potential needs beyond diagnosis, to avoid children with subthreshold symptoms but significant impairment missing out on vital services (Thapar, Cooper, & Rutter, 2017). While motor and language impairments (beyond not having a functional language) are common in children with autistic symptoms, current evidence suggest they are often poorly recognized and triaged behind core ASD symptoms in both evaluation and treatment planning (Bhat, 2020; Boucher, 2012; Licari et al., 2019; Suren et al., 2019). Thus, many children evaluated for suspected ASD potentially miss out on available interventions. Motor and language impairments often present at an early age, prior to formal diagnosis (Hyman et al., 2020). Early fine- and gross motor skills have been linked to concurrent and future communication in infants with ASD (West, 2019), including expressive language (LeBarton & Landa, 2019). Whether the same co-occurrence and close relationship between motor and language impairments seen in infants with ASD are also present in school-aged children evaluated for ASD is currently unknown but of great interest as it could inform potential targets for earlier identification and intervention for affected children.

1.1. Motor and language impairments in children with autistic symptoms

Although not universal or specific to the disorder, motor deficits are common in children with ASD, even within the first year of life (West, 2019), and across the range of autistic symptoms and cognitive abilities (Fournier, Hass, Naik, Lodha, & Cauraugh, 2010; Licari et al., 2019; Reindal et al., 2020). Possible deficits include delayed attainment of motor milestones, deviant muscle tone, balance, gait, fine and gross motor coordination (Fournier et al., 2010; West, 2019), some of which may be captured by parent report or standardized assessment of motor skills. Depending on age, criteria, and measures applied, as many as 25–90% of children with ASD may have co-occurring developmental coordination disorder (DCD) (Kopp, Beckung, & Gillberg, 2010; Miller et al., 2021). Still, motor deficits were recognized by clinicians at a low rate (1.34%) relative to their prevalence (35.4%)(Licari et al., 2019), indicating the need for more knowledge.

Social communication difficulties are a core diagnostic feature of ASD, albeit with wide variation in functional language (American Psychiatric Association, 2013). Comprehension and expression of language *form* and *content* (structural language skills), as well as appropriate *use* of verbal and nonverbal language in social contexts (pragmatic language skills) may all be affected alone or in combination to cause *language impairments* (Baird & Norbury, 2016). Although of importance for specifying language in ASD, the extent and role of structural language deficits has received less attention than the more prominent pragmatic difficulties (Boucher, 2012; Reindal et al., 2021). However, their reported variability with deficits often presenting early and being associated with persisting impairments, render them a potential target of early identification and intervention for subgroups within the autism spectrum (Boucher, 2012; Reindal et al., 2021).

1.2. The relationship between motor, language, and social communication impairments

Longitudinal data suggest that early motor deficits may be a risk factor for later motor difficulties, but also for the development of language and social communication difficulties related to ASD (LeBarton & Landa, 2019; Leonard, Bedford et al., 2014). Developing motor skills enables the infant to interact with other people and their surroundings, and are considered to assist the development of language and communication (West, 2019). Early motor disruptions could therefore have downstream effects that further compromise language and social development in children with ASD. In a recent meta-analysis West (2019) aggregated data from 890 infants with ASD (age 6.0–42.9 months) across nine studies. A significant association between motor and language/communication skills was found ($r = .35$, $p < .001$), that held for both fine and gross motor skills. In school-aged children with ASD, motor and language impairments have mostly been studied separately, not addressing their potential co-occurrence or additive impact. An exception is the cross-syndrome study by McPhillips, Finlay, Bejerot, and Hanley (2014), where an association between motor performance (standardized assessment) and general communication skills (teacher report) among children with ASD (n = 28; mean age 9 years 11 months) was reported. More recently, Bhat (2021) analyzed parent reported motor skills from 13,887 children with ASD in the SPARK study. An increasing risk for motor impairment was found with greater language, social communication, cognitive, and functional impairments. However, none of these studies investigated language deficits beyond general communication or language functioning.

1.3. Theoretical and clinical importance of co-occurring motor and language impairments

Despite efforts to improve earlier diagnosis, many children are school-aged when they receive their ASD diagnosis (Lord,

Elsabbagh, Baird, & Veenstra-Vanderweele, 2018). Levy et al. (2010) found that children with ASD and co-occurring diagnoses were diagnosed later, indicating that the ASD was masked by other problems. Compared to a decade ago many individuals referred for ASD assessment are now more language-abled, display milder symptoms, and are diagnosed with ASD based on fewer symptoms (Arvidsson, Gillberg, Lichtenstein, & Lundström, 2018; Avlund, Thomsen, Schendel, Jørgensen, & Clausen, 2021). However, perceived impairment has increased, and most in individuals with autistic symptoms that previously were considered subthreshold (Lundström et al., 2021), suggesting that overall impairment might reflect overlooked co-occurring problems that may be better predictors of support need than the ASD diagnosis alone (Gillberg & Fernell, 2014).

Functional impairment refers to the extent to which a diagnosed condition results in limitations in daily life and is found to predict future adolescent problems (Costello, Angold, & Keeler, 1999) and adult outcomes (Copeland, Wolke, Shanahan, & Costello, 2015). In children with ASD, motor impairments may affect participation in leisure activities, sports, or interactive play "beyond the effect of their social skills alone" (Hyman et al., 2020, p.27). Language impairments may further limit social learning opportunities. In school-aged children with ASD or high autistic traits, co-occurring language and motor difficulties have been linked to reduced daily living skills, participation in physical education and out-of-school activities, overall impairment and contact with services (Bhat, 2021; Hilton, Crouch, & Israel, 2008; Kopp, Beckung, & Gillberg, 2010; Licari et al., 2019; Posserud, Hysing, Helland, Gillberg, & Lundervold, 2018). However, few studies have investigated the co-occurrence of motor and language impairments, their relationship to each other and to overall functioning in school-aged children evaluated for ASD.

1.4. Aims of the current study

In this exploratory study we assessed the co-occurrence of motor and language impairments in a sample of school-aged children evaluated for ASD by specialist health services. We further explored relationships between motor, language, social, and overall functional impairment, regardless of meeting the diagnostic criteria for ASD or having subthreshold autistic symptoms. The following objectives were addressed:

1. To explore the co-occurrence of motor and language impairments, in particular structural language deficits, as measured by parent report and standardized assessment of motor skills.
2. To explore the relationship between motor, structural language, and social skills.
3. To assess overall functional impairment and participation, and explore potential relationships with motor, structural language, and social skills.

2. Materials and methods

2.1. Study design and participants

The study has a cross-sectional design including children referred for evaluation of ASD at four outpatient clinics, providing public specialist child and adolescent mental health services (CAMHS) in Mid-Norway.

We invited children participating in an ongoing large multi-site study on NDDs in Norway, in which children are eligible for enrollment if a suspicion of ASD has been raised by local or specialist health services (BUPgen, see Reindal et al., 2020). Children aged 6–18 years with available information on ASD diagnostic status were eligible for participation in the present study. Medical records were reviewed to ensure that the participants did not have moderate or severe intellectual impairment, severe sensory, neurological, or muscular impairments that could interfere with motor testing. As one of the assessments required that the child could speak in at least simple sentences, all participants were verbal. Children and their caregivers also had to be sufficiently fluent in Norwegian language. A total of 20 children and adolescents with mean age 10.7 (SD = 3.4, range 6–17) years at inclusion were eligible, of which 15 had been diagnosed with ASD. For simplicity, we use the term 'children' or 'school-aged children' to refer to the whole group. Retrospective data on clinical assessments, parent-reported history, and supplementary parent-reported measures, as well as data from the additional assessment in the present study were collected.

Written informed consent was obtained from all parents and participants (when appropriate due to age) before inclusion in the study. The study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics South East (REK#2016/1954; REK#2012/1967), and the Norwegian Data Inspectorate. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

2.2. Measures

2.2.1. Diagnoses

All diagnoses were assigned by Norwegian specialist health services, using the *International Classification of Diseases, 10th Revision* (ICD-10) criteria (World Health Organization, 1992). All participants had completed either the Autism Diagnostic Interview-Revised (ADI-R; n = 1) (Rutter, Le Couteur, & Lord, 2003), the Autism Diagnostic Observation Schedule (ADOS; n = 2) (Lord, Rutter, DiLavore, & Risi, 1999), or both (n = 17) as part of their clinical evaluation. NDDs were grouped according to ICD-10 codes into the following categories: ASD (F84), intellectual disability (F70–79), attention-deficit/hyperactivity disorder (ADHD) (F90), communication disorder (F80), specific learning disorder (F81 and F83), motor disorder (F82: DCD and F95: tic disorders), other NDD (F88, F89 and F94). The presence of previous or currently active epilepsy was also included in the total number of NDDs.

2.2.2. Motor skills

The Developmental Coordination Disorder Questionnaire 2007 (DCDQ'07) (Wilson et al., 2009) was used to ascertain everyday motor skills, as reported by parents. The DCDQ'07 is a 15-item questionnaire to screen for DCD and to confirm the functional consequences of a motor deficit in clinical and research settings (Wilson et al., 2009). Raw scores for three subscales (*control during movement*, *fine motor/handwriting*, and *general coordination*) are summarized into a total score, with possible values from 15 to 75. The original version has a high internal consistency (Cronbach's alpha = .89) and concurrent validity with the original Movement Assessment Battery for Children (MABC; $r = -.55$) (Wilson et al., 2009). For the present study an unpublished prefinal Norwegian version of the DCDQ'07 (Wilson et al., 2009); Norwegian cross cultural adaptation by V. Johannesen, H. A. Lillehaug, N. R. Nielsen, G. Skard & S. van Zuiden, 2012), was used with the recommended age-appropriate cut-offs to indicate the presence of motor difficulties (Wilson et al., 2009). Cronbach alpha was .86 (DCDQ'07 total).

The Movement Assessment Battery for Children-2 (MABC-2) (Henderson, Sugden, & Barnett, 2007) is a standardized assessment of fine and gross motor skills frequently used to identify children with motor difficulties for clinical or research purposes. Eight individual test items grouped into three categories (*manual dexterity*, *aiming and catching*, and *balance*) are given a raw score and a standard score, that translate to a component score. From the three categories, a total test score is derived and an overall percentile in that child's age band. While total test score $\leq$ 5th percentile is considered to represent a definite motor problem requiring motor intervention, scores between the 5th and the 15th percentile suggest a borderline degree of motor difficulties (Henderson et al., 2007).

The MABC-2 was administered by either the fourth (n = 16) or the first author (n = 4), both trained in the assessment. The 15th percentile on the MABC-2 and the appropriate cut-off for the child's age on the DCDQ'07 was used to identify *'motor deficits'* or *'motor difficulties'* (these terms are used interchangeably). *'Motor impairment'* refers to being identified with *'motor deficits'* on both measures. Notably, the MABC-2 protocol, as described in Liu and Breslin (2013), was modified by showing a picture of each task to the child and minimizing the verbal instructions to emphasize visual supports.

2.2.3. Language skills

Language skills were assessed using *the Children's Communication Checklist Second Edition (CCC-2)* (Bishop, 2003; Norwegian version: Bishop, 2011), completed by parents. This checklist consists of 70 items to screen for the presence and profile of language deficits in children who can speak in at least simple sentences. Items are grouped into 10 subscales (A-J) that measure different aspects of communication: *language structure* (A-D), *pragmatic language skills* (E-H), and two scales measuring *social aspects* (I, J). The Cronbach alpha in the present sample was .97 (total alpha, based on raw scores), comparable to previous reports (e.g., Helland, Biringer, Helland, & Heimann, 2009). We report the General Communication Composite (GCC), an overall measure of communication skills (sum A-H), with a suggested cut-off < 55 to identify *'language impairment'* (Bishop, 2003, 2011). Further, we used the Structural Language Score (sum A-D) and the General Pragmatics Score (sum E-H) (see Reindal et al., 2021) as continuous measures of structural and pragmatic language skills. *'Structural language deficits'* were defined as having a score $\leq$ 5th percentile on two or more of the structural subscales, comprising 'speech' (A), 'syntax' (B), 'semantics' (C), and 'coherence' (D).

2.2.4. Social and cognitive skills

The Social Responsiveness Scale (SRS) (Constantino & Gruber, 2005) was collected to reflect parent reported current (last 6 months) social impairment. This 65-item questionnaire ascertains autistic symptoms across the spectrum of difficulties, with higher scores indicating greater social impairment (Constantino et al., 2003). SRS raw total score was applied as a dimensional trait variable, for which the Cronbach alpha was .95. To assess clinical-level social impairment we converted raw scores to T scores ($M = 50$, $SD = 10$), according to the SRS manual, finding that all participants had *T*-score $\geq$ 60 (clinical range).

All children had completed formal testing of cognitive abilities with age-appropriate Wechsler scales as part of their clinical evaluation. Standard scores for nonverbal and verbal IQ were available for 16 children, for one child only verbal IQ was available, and for three others the IQ scores were not available. Mean age at assessment (n = 19) was 8.8 ($SD = 2.6$) years.

2.2.5. Functional impairment and participation

The Developmental Disability-Children's Global Assessment Scale (DD-CGAS) (Wagner et al., 2007) was rated to provide a measure of overall functional impairment during the previous month. The DD-CGAS is a revised version of the Children's Global Assessment Scale (CGAS) (Shaffer et al., 1983). In the DD-CGAS, text revisions are introduced to enable a more targeted functional assessment of children with NDDs such as ASD. The instrument focuses on four domains: *self-care, communication, social behavior,* and *school functioning* (Wagner et al., 2007). Scores range from 1 (most impaired) to 100 (superior functioning), with scores < 70 indicating clinically relevant atypical functioning (Wagner et al., 2007). The DD-CGAS has been translated to Swedish, with good inter-rater reliability in ASD cases (Choque Olsson & Bolte, 2014). Convergent validity with measures of adaptive functioning and autistic symptom severity have been reported for the original version (Wagner et al., 2007).

The DD-CGAS was translated into Norwegian for this study, after permission from the original author. Individual DD-CGAS scores were assigned by the same rater (first author), based on all available information at inclusion, including a semi-structured interview with the caregiver(s). During this interview, caregivers were asked to compare their child's functioning and participation, as well as necessary environmental accommodations and level of support, to same-aged peers across functional domains. As part of the DD-CGAS rating, the level of impairment across four domains (self-care, communication, social behavior, and school functioning) was classified as 'not present', 'slight', 'moderate', 'severe', or 'extreme', while considering the child's behavior across environments, and the accommodations necessary to support the child. The DD-CGAS score was chosen to best reflect overall impairment across domains. Supplementary information on participation was collected from the *Child Behavior Checklist/6–18* (Achenbach & Rescorla, 2001),

completed by caregiver(s) at inclusion.

2.3. Procedure

After consent to participate, an appointment for inclusion was made and report forms were sent to the caregiver(s) for completion prior to the assessment. Each child was assessed in one session. Both caregivers were invited to complete report forms, while ensuring that the same caregiver(s) participating in the interview completed a set of forms for each participant. In the following, only data reported by the interviewed caregiver (85.0% mother, 5.0% father, 10.0% both parents) are included.

2.4. Statistical analyses

Descriptive statistics are presented as n (%) and mean *(SD)*. First, we report the proportion of children with scores to indicate motor (DCDQ'07, MABC-2) and language (CCC-2) impairment or deficits, as well as their co-occurrence. Second, scatter plots and correlations were used to explore the relationship between motor, structural language, and social skills. For these analyses symptoms were not dichotomized, but the total scores on the respective skill measures were used as dimensional trait variables. Lastly, we report functional impairment by the mean DD-CGAS, the proportion of children with a moderate to severe level of impairment across functional domains, and overall impairment in the clinical range. Relationships with motor, structural language, and social skills were explored. Spearman's rank correlation was used to analyze the relationship between the different measures, because of non-normality of some of the continuous variables. The magnitude of effect sizes was interpreted as small (r = .10 to .29), medium (r = .30 to .49), or large (r = .50 to 1.0) (Cohen, 1992). Two-sided p values $< .05$ were regarded as statistically significant. IBM SPSS 27/28 was used for statistical analyses.

3. Results

3.1. Participant characteristics

The sample included 20 children (6 girls), born between 2000 and 2013, with a mean (*M*) age of 10.7 (SD = 3.4) years. Of these, 15 children (75.0%) were diagnosed with ASD, while 5 children did not receive an ASD diagnosis (non-ASD). ASD subtypes included childhood autism (26.7%), atypical autism (6.7%), Asperger syndrome (40.0%) and pervasive developmental disorder not otherwise specified (26.7%). Mean age at ASD diagnosis was 10.2 (SD = 3.3) years. All children in the non-ASD group were diagnosed with one or more NDDs, most commonly ADHD (n = 4). Within the whole sample, frequent NDDs beyond ASD were ADHD (n = 9), tic disorders (n = 3), and epilepsy (n = 3). Average cognitive abilities were in the normal range (Table 1).

Most parents were Norwegian or European in origin (97.5%). All participants were followed-up by municipal services and/or specialist health services. All participants attended mainstream schools, albeit with 85.0% receiving special adaptations (e.g., support teaching, own curriculum, daily schedule, social skills training, own assistant).

Table 1
Participant characteristics.

	n	%	Mean	*SD*
Age at inclusion (years)	20		10.7	3.4
SRS raw total	20		88.3	29.3
DCDQ'07 total	20		48.0	11.3
MABC-2 total	18		8.1	2.7
Manual Dexterity	19		8.4	2.4
Aiming & Catching	19		7.5	3.5
Balance	18		9.1	3.2
CCC-2				
General Communication Composite (GCC)	20		36.1	21.5
Structural Language Score	20		18.6	12.4
General Pragmatics Score	20		17.5	9.8
Nonverbal IQ	16		101.3	15.6
Verbal IQ	17		93.4	16.7
DD-CGAS	20		61.1	8.4
Comorbidity				
≥ 2 NDDs	10	50.0		
≥ 1 psychiatric disorder	5	25.0		
≥ 1 somatic disorder	9	45.0		
Current medication	15	75.0		

CCC-2 = Children's Communication Checklist Second Edition; DCDQ'07 = Developmental Coordination Disorder Questionnaire 2007; DD-CGAS = Developmental Disability-Children's Global Assessment Scale; IQ = intelligence quotient; MABC-2 = Movement Assessment Battery for Children-2; NDD = neurodevelopmental disorder; *SD* = standard deviation; SRS = Social Responsiveness Scale.

3.2. Co-occurring motor and/or language impairment

Most children (80.0%) were rated by their caregivers as having motor deficits on the DCDQ'07. Limitations in all aspects of motor functioning (*control during movement, fine motor/handwriting, general coordination)* were reported. On standardized assessment with the MABC-2, seven of 18 children with valid results (38.9%) had total scores indicating motor deficits. Although all subdomains were affected, composite scores indicated most difficulties with *manual dexterity* and *aiming & catching* (36.8% for each subdomain). Due to a technical error on one task, total test score could not be calculated for one child, and MABC-2 results for another child were not valid because of intercurrent illness.

The distribution of DCDQ'07 and MABC-2 total scores are shown in Fig. 1. All cases identified with motor deficits on the MABC-2 (n = 7) were also captured by the DCDQ'07. The DCDQ'07 total was positively correlated with the MABC-2 total score, with Spearman's rho = .211, although not significant and with a small effect size.

The proportion of children with scores below cut-off to indicate language impairment on the CCC-2 was also large (75.0%) (Table 2). A smaller proportion (55.0%) had structural language deficits, i.e., they had subscale scores at or below the 5th percentile on two or more of the structural subscales ('speech', 'syntax', 'semantics', 'coherence'). Deficits were observed across all subscales, albeit with 'syntax' being relatively spared. Taken together, co-occurring motor and structural language deficits were common, with all but three children (85.0%) having deficits in one or both developmental domains (Table 2). All children identified with *motor impairment* also had structural language deficits. The three children with no co-occurring deficits had all been diagnosed with ASD.

3.3. The relationship between motor, structural language, and social skills

Motor performance and structural language skills varied both among children diagnosed with ASD and children with subthreshold autistic symptoms (non-ASD) (Fig. 2). Within the whole sample, a strong, positive correlation was found between MABC-2 total and the Structural Language Score (Spearman's rho = .618, $p = .006$) (Table 3), indicating that better motor performance on standardized assessment was associated with more advanced structural language. A strong, negative association was also found between the MABC-2 and the SRS total (Spearman's rho = –.521, $p = .027$), as well as between the Structural Language Score and the SRS total (Spearman's rho = –.691, $p < .001$). Thus, better motor and structural language skills were both associated with less social impairment, as reported by parents on the SRS.

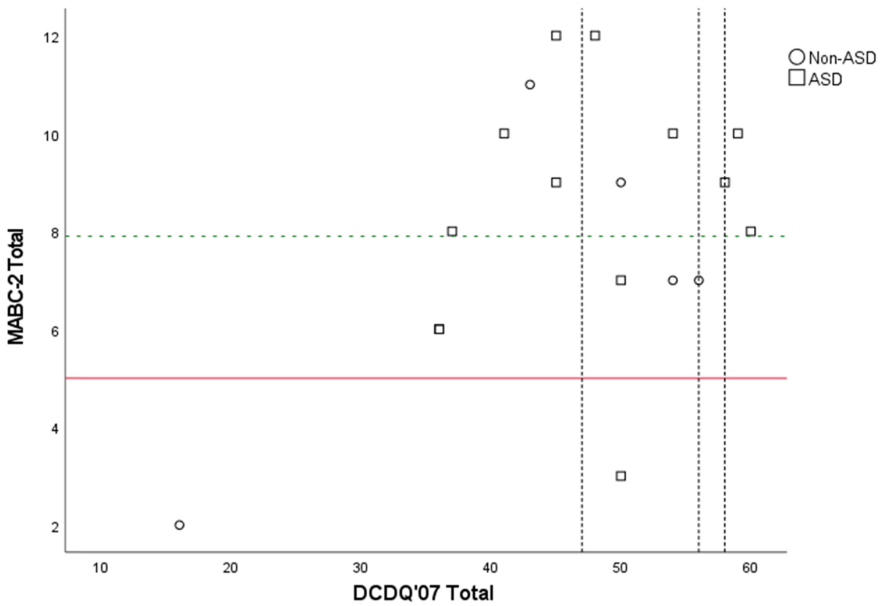

Fig. 1. Distribution of DCDQ'07 and MABC-2 total scores (n = 18), by diagnostic group. Horizontal lines indicate the MABC-2 cut-off for motor difficulties (at or below the 15th percentile; green dashed line) and more definite motor problems (at or below the 5th percentile; red solid line). Dashed vertical lines indicate the DCDQ'07 cut-off for motor difficulties at ages 5:0–7:11 (<47), 8:0–9:11 (<56) and 10:0 and older (<58). 2 participants are not represented on this graph as they did not have valid MABC-2 total scores. 2 children had identical scores on both measures and appear as a single point in the distribution. ASD = autism spectrum disorder; DCDQ'07 = Developmental Coordination Disorder Questionnaire 2007; MABC-2 = Movement Assessment Battery for Children-2.

Table 2
Frequencies and percentages for classifications of functional motor and language performance.

Measure	Classification	Whole sample *n* (%)
DCDQ'07 (n = 20)	Motor deficits*	16 (80.0)
MABC-2 (n = 18)	Motor deficits*	7 (38.9)
MABC-2 and DCDQ'07 (n = 18)	Motor impairment**	7 (38.9)
CCC-2 (n = 20)	Language impairment (GCC<55)	15 (75.0)
	Structural language deficits***	11 (55.0)
MABC-2 and DCDQ'07 and CCC-2 (n = 18 to 20)	Motor impairment** *and* structural language deficits***	7 (38.9)
	Motor deficits* *and* structural language deficits**	3 (15.0)
	Motor deficits* *only*	6 (30.0)
	Structural language deficits*** *only*	1 (5.0)
	None	3 (15.0)

*Total scores below cut-off to indicate motor deficits on either the DCDQ'07 or the MABC-2.
**Total scores below cut-off to indicate motor deficits on both the DCDQ'07 and the MABC-2.
*** ≤5th percentile on two or more structural subscales on the CCC-2 (A-D).
CCC-2 = Children's Communication Checklist Second Edition; DCDQ'07 = Developmental Coordination Disorder Questionnaire 2007; MABC-2 = Movement Assessment Battery for Children-2

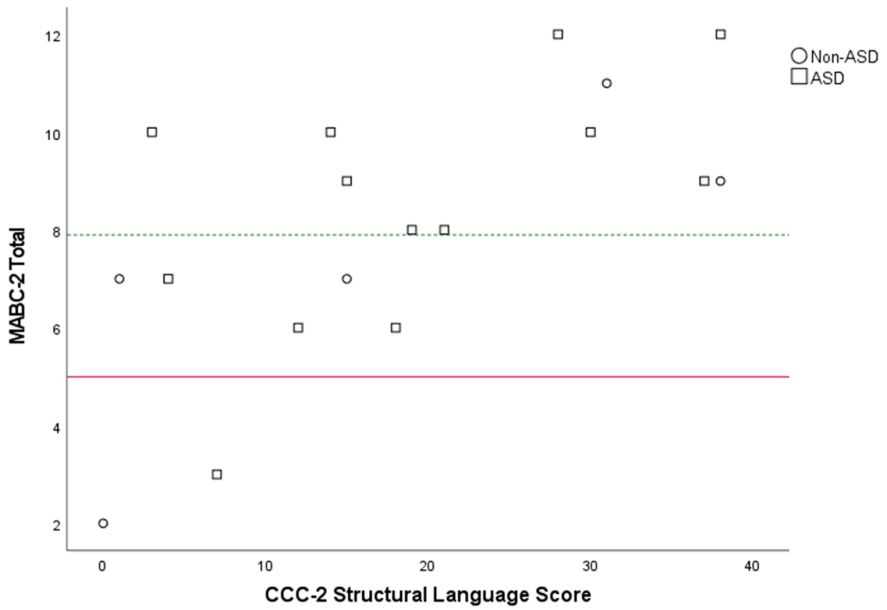

Fig. 2. The relationship between structural language and motor skills, illustrated by the distribution of scores on the Children's Communication Checklist-Second Edition (CCC-2 Structural Language Score) and the Movement Assessment Battery for Children-2 (MABC-2 Total), by diagnostic group. Horizontal lines indicate the MABC-2 cut-off for motor difficulties (at or below the 15th percentile; green dashed line) and more definite motor problems (at or below the 5th percentile; red solid line). ASD = autism spectrum disorder.

3.4. Functional impairment and participation

DD-CGAS scores ranged from 43 to 73, implying considerable variations in overall functioning during the last month. Two children had scores indicating overall functioning consistent with that of same-aged peers (DD-CGAS>70). The rest (90.0%) had scores in the clinical range, although mostly varying within the "upper half" of the scale. The DD-CGAS was negatively correlated with SRS total score, with a large effect size, albeit not reaching statistical significance (Table 3). Notably, all children with childhood autism (n = 4) had DD-CGAS ≤ 61, while children with other ASD subtypes (n = 11) had DD-CGAS ≥ 61. In the non-ASD group, DD-CGAS ranged from 44 to 68. To assess whether DD-CGAS scores were associated with core ASD symptoms, we performed an additional correlation analysis between DD-CGAS and ADI-R verbal total among individuals with available scores (n = 16). A strong negative correlation was found (Spearman's rho= −.657, 95% CI [−.873 to −.224], $p = .006$), suggesting that less prominent core ASD symptoms were associated with better overall functioning.

None of the participants presented with an extreme level of impairment regarding *self-care, communication, social behavior,* or *school*

Table 3
Nonparametric correlations between functional impairment, structural language, motor, and social skills.

	n	Mean	*SD*	Spearman's *rho* / 95% *CI* / *p*-value				
				1	2	3	4	5
1. DD-CGAS	20	61.1	8.4	1				
2. CCC2-SLS	20	18.6	12.4	.276 (−.204 to .648) $p = .24$	1			
3. DCDQ'07	20	48.0	11.3	.061 (−.404 to .501) $p = .80$	.238 (−.241 to .625) $p = .31$	1		
4. MABC-2 total	18	8.1	2.7	-.015 (−.490 to .467) $p = .95$	.618 (.198 to .846) $p = .006$	.211 (−.297 to .627) $p = .40$	1	
5. SRS total	20	88.3	29.3	-.369 (−.705 to .101) $p = .11$	-.691 (−.871 to −.345) $p < .001$	-.525 (−.790 to −.094) $p = .017$	-.521 (−.800 to −.057) $p = .027$	1

CCC-2 = Children's Communication Checklist Second Edition; *CI* = confidence interval; DD-CGAS = Developmental Disability-Children's Global Assessment Scale; DCDQ'07 = Developmental Coordination Disorder Questionnaire 2007; MABC-2 = Movement Assessment Battery for Children-2; *SD* = standard deviation; SRS = Social Responsiveness Scale.

functioning. The most affected functional domain was social behavior, where level of impairment was moderate (90.0%) or severe (10.0%) for all participants. School functioning was moderately or severely affected for 13 children (65.0%), and communication was slightly (30.0%) to moderately (70.0%) affected for all participants. Twelve children (60.0%) participated in ordinary physical education (PE), while three did not participate at all, and five (25.0%) participated with some level of accommodation or alternative activity. Nine children (45.0%) participated in one or two organized leisure activities. Five children (25.0%) did not have any close friends.

4. Discussion

In this study we explored the co-occurrence of motor and language impairments, as well as their potential relationship to each other, current social, and functional impairment in a clinical sample of school-aged children evaluated for suspected ASD.

4.1. Extent of motor impairments

The majority (80%) of participating children had deficits on one or both measures of motor performance, a proportion close to reports from a recent large study using the DCDQ among children with ASD and normal range cognitive abilities (Bhat, 2020). The larger proportion with motor deficits on parent report (80%) compared to standardized assessment (39%) is plausible, as these measures capture different aspects of motor ability (Wilson et al., 2009). The DCDQ'07 was designed to screen for possible motor difficulties and is more likely to over-identify than to miss such deficits (Wilson et al., 2009). Contrary to parent report based on observations over time, standardized test results represent a "snap-shot" of motor performance, which may be impacted by other non-motor factors (Licari et al., 2019). The well-structured, one-to-one assessment setting may also allow some children to perform better than when faced with the demands of everyday life.

Although recommended to confirm more definite motor impairments or a diagnosis of DCD (Wilson et al., 2009), only a few studies have combined the MABC-2 and the DCDQ'07 when investigating motor skills in ASD. Comparable to the present study, Hirata et al. (2015) found that while 47% of 19 children with ASD (7–15 years) had motor deficits on the MABC-2, all were identified with motor deficits on the DCDQ'07. Methodological differences likely have contributed to some discrepancies observed. The present sample comprised children with a broader spectrum of autistic symptoms. While mean MABC-2 total was comparable to Hirata et al. (2015), mean DCDQ'07 total was higher, indicating that parents in the present sample reported their children to have less motor difficulties. As there are no Norwegian norms for the DCDQ'07, our results should be interpreted with caution. The distribution of scores may differ between cultures. Furthermore, we applied a modified MABC-2 protocol (Liu & Breslin, 2013), which may have elicited better motor performance in our study.

4.2. Extent of language impairments and co-occurrence with motor impairments

The extent of language impairment as measured by the CCC-2 was substantial (75%), and consistent with previous results among preschool and school-aged children with ASD, ADHD, and subthreshold autistic symptoms (Helland, Biringer, Helland, & Heimann, 2012; Reindal et al., 2021). More than half the sample had difficulties with structural language (e.g., language sounds, articulation, grammar, understanding the meaning of words). While pragmatic difficulties (the appropriate use of language in social contexts) are closely related to the core social communication impairment in ASD, structural language deficits have traditionally been considered a characteristic of specific language impairment (developmental language disorder). Although being less closely related to core ASD symptoms, such deficits are also commonly reported in children with ASD and subthreshold autistic symptoms (Boucher, 2012; Reindal et al., 2021). Notably, CCC-2 is not a diagnostic tool. Rather this checklist was developed to screen for language impairment in clinical and community contexts, as well as to identify structural and pragmatic language deficits that may be difficult to elicit in a test situation (Bishop, 2011). In line with previous findings, neither motor nor language impairments were universal among children with

ASD (Boucher, 2012; West, 2019).

Nevertheless, the most striking finding was the common co-occurrence of structural language *and* motor deficits in the present sample. While motor deficits were reported in isolation for some children, structural language deficits were mostly found in children also identified with motor deficits, and in *all* children identified with *motor impairment*. These findings are consistent with recent reports from the SPARK study that the risk of motor impairment increased with increasing language impairment (Bhat, 2021).

4.3. The relationship between motor, structural language, and social skills

Our finding that better motor performance on standardized assessment was strongly associated with better structural language skills as reported by parents is consistent with the observed association between motor performance and general communication skills (teacher report) among school-aged children with ASD reported by McPhillips et al. (2014). Notably, both composites used in the present analyses (MABC-2 total and CCC-2 Structural Language Score) include various aspects of motor and structural language skills. Although a strong correlation was found, it is likely that some aspects of motor performance (e.g., fine- or gross motor skills) bear a stronger significance on structural language skills, and vice versa. While the correlation between parent reported motor skills (DCDQ'07 total) and structural language skills in the present sample did not reach statistical significance (spearman's rho .238, $p = .31$, Table 3), the effect size of this correlation is of the same magnitude as the significant relationship found between the DCDQ total and language function in the SPARK study (Bhat, 2021). Taken together, these findings highlight not only the pervasiveness of motor impairments, but also the close association with language impairments in school-aged children with a broad spectrum of autistic symptoms.

Strong associations between social impairment (SRS total) and both measures of motor skills were also found, suggesting a clear relationship between these factors. These results build on and extend previous reports among children with ASD (e.g., Bhat, 2021; Ohara, Kanejima, Kitamura, & Izawa, 2019). While reasons for the apparent relationship between motor skills and social skills currently remain unclear, a commonly suggested mechanism includes shared neural correlates between these skill domains (Ohara et al., 2019). West (2019) suggested that motor and communicative ability may also have overlapping neural correlates, which could disrupt both domains. Several postmortem and brain imaging studies have consistently identified the cerebellum as one of the most abnormal brain regions associated with ASD (see Wang, Kloth, & Badura, 2014 for a review). The cerebellum is considered to play an important role not only for motor coordination and movement control but also for higher functions such as cognition and language/communication, both of which are linked to an individual's social interactions (Ohara et al., 2019; Wang et al., 2014). Another possible mechanism has been suggested through the cascading effects of early motor deficits on other developmental domains (e.g., Leonard & Hill, 2014). Importantly, these potential mechanisms are not mutually exclusive. Even if motor and social communication skills are both affected by atypical neural development, the resulting motor deficits may further impact a developing child's social interaction and experiences, with potential down-stream effects on other developmental skills and overall functioning. Much remains to be understood about the developmental consequences of early motor deficits, as well as their role as potential intervention targets for cross-domain impact (Hudry, Chetcuti, & Hocking, 2020). Prospective longitudinal studies of at-risk infants tracking developmental skills across several domains, as well as employing randomized controlled trials to test the utility of specific motor interventions whilst also testing hypotheses about their causal role has been suggested as a way forward (Hudry et al., 2020).

4.4. Functional impairment and participation

While current guidelines generally converge on a set of well-established tools for assessing core ASD symptoms, evidence-based assessment tools addressing functional impairment are limited (Choque Olsson & Bolte, 2014; Winters, Collett, & Myers, 2005). We used the DD-CGAS, allowing us to synthesize the child's level of functioning across multiple domains (Winters et al., 2005), independent of main or co-occurring diagnoses. DD-CGAS scores mostly varied within the "upper range", as expected in a sample of verbal children without severe cognitive disabilities. Consistent with the fact that all participants were evaluated for ASD, social impairment was most affected, albeit with limitations seen across all functional domains. Klin et al. (2007) reported a similar profile using the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cichetti, 1984), a more general standardized measure of adaptive functioning which is found to correlate with the DD-CGAS (Wagner et al., 2007). Thus, although being less resource-demanding, DD-CGAS is considered to capture a related construct. Contrary to recent results from the SPARK study (Bhat, 2021), we found no significant association between motor and language skills and overall impairment, as measured by the DD-CGAS. Limited sample size and range of functioning, as well as contextual and methodic factors may have contributed to this result. Together with previous findings by Wagner et al. (2007) our results indicate that the DD-CGAS may align better with measures of core ASD symptoms, such as the ADI-R, instead of co-occurring language and motor difficulties.

Our finding that several children did not participate in organized sports/leisure activities and had no close friends are consistent with a previous study by Hilton et al. (2008) among children with ASD. In their study, physical activities showed the greatest differences, both in terms of the number of activities and the frequency of participation. The authors point to the potential importance of motor skills for participation, and of motor skills interventions for children with ASD (Hilton et al., 2008). Similar concerns have been expressed by Kopp et al. (2010). While participation was limited, our results highlight school as *the* arena where many children *do* participate. Thus, well-tailored physical education for children with NDDs may represent a potential intervention to promote both motor skills and social skills training. Tailored efforts to integrate children with social and other functional impairments in out-of-school activities may also be beneficial, acknowledging each child's individual capacities, and modifying the demands of school and daily life to a level the child can cope with.

4.5. Strengths and limitations

The present study was cross-sectional, small, and exploratory in nature. Therefore, it can only be used to illuminate potential relationships, not to make any causal inferences. Nevertheless, we consider the provision of a detailed developmental skill profile of school-aged children evaluated for suspected ASD a major strength of our study. By using validated instruments, complementary parent reports, and a standardized measure of motor skills we provide valuable information that is difficult to accomplish in larger-scale studies. Still, the relationships found here may differ in larger, more diverse samples. The relatively large number of girls may be considered a strength. Nevertheless, it is possible that the larger proportion of girls may be due to a selection bias, where individuals with co-occurring motor and language impairments were more prone to participate. Referral bias may also have influenced the reported extent of co-occurring deficits and functional impairment. However, a previous Norwegian study on children with high ASD traits found that co-occurring problems were also common in a population-based sample (Posserud et al., 2018). While some of the applied measures are validated and well-established in other countries, the Norwegian norm base is limited. Thus, we underscore the exploratory nature of our results, which should be replicated in larger samples, and compared to same-aged, typically developing children to confirm their relevance.

4.6. Clinical implications

Although preliminary, our results suggest that co-occurring difficulties beyond the core social impairment should be anticipated and planned for when evaluating children for ASD, considering more specific motor and language assessments and interventions. Where available and indicated, guided interventions from physical and/or speech-language therapists may prove useful (Fuentes et al., 2020). Motor interventions may focus on building strength, coordination, or acquisition of adaptive skills such as handwriting, safer mobility and play (Hyman et al., 2020). Acknowledging the child's difficulties, it may be wise to encourage participation in activities based on the child's area of interest or competence, and to ensure structured settings with available support to promote mastering. Whether specific interventions delivered to children presenting with early motor deficits could also mitigate downstream effects on social and language skills should be addressed in future studies (Hudry et al., 2020).

5. Conclusion

Results from the present study suggest that co-occurring motor and structural language deficits are common and closely related in school-aged children referred for evaluation of ASD. The extent of this co-occurrence, as well as the potential role and timing of specific interventions targeting motor and language skills in children with autistic symptoms should be addressed in future studies. Meanwhile, assessment should be broad to tailor interventions to the child's profile of strengths and difficulties and adjust demands to the child's level of functioning.

CRediT authorship contribution statement

Lise Reindal: Conceptualization, Methodology, Investigation, Formal analysis, Writing-Original Draft, Funding acquisition. **Terje Nærland:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Funding acquisition. **Anne Mari Sund:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Project administration. **Birgit Avseth Glimsdal:** Investigation, Writing-Review & Editing. **Ole A. Andreassen:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Funding acquisition. **Bernhard Weidle:** Conceptualization, Methodology, Writing-Review & Editing, Supervision, Project administration.

What this paper adds?

Co-occurring motor and language impairments are common and closely related in infants with autism spectrum disorder (ASD), with potential downstream effects on other developmental domains. Thus, they represent potential targets for earlier identification and intervention for subgroups of children. In school-aged children with ASD, motor and language deficits have mostly been studied separately, not considering their potential co-occurrence and additive impact on overall functioning. This study provides new information suggesting that the co-occurrence of motor and structural language deficits is common also in school-aged children evaluated for ASD, with the majority having deficits in one or both domains when assessed with a combination of parent report measures and a standardized test of motor performance. Furthermore, motor, and structural language deficits seem to be closely related, with potential impact on symptom presentation, overall functioning, and service needs. The extent of this co-occurrence, as well as the potential role and timing of specific interventions targeting motor and language skills in children with autistic symptoms should be addressed in future studies. Meanwhile, assessments should be broad and consider co-occurring motor and language impairments when evaluating children for ASD, so that interventions can be tailored to the child's profile of strengths and difficulties and demands adjusted to the child's level of functioning.

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Appendix I

Versjon 13/02-2019 (Revidert etter REK 081118)

Fylles ut av intervjuer ved inklusjon

Utfylt dato*:* _____

Reg. nr: _____

Intervjuer: _____

Dato for inklusjon: _____

Instruksjon til intervjuer

Prosjektet ønsker i størst mulig grad at intervjuet skal være utført uten fokus på om og evt hvilken diagnose barnet/ungdommen har fått innen autismespekteret (ASD). Intervjuet er *semistrukturert.* Det er ikke nødvendig at spørsmålene i intervjuet siteres ordrett – de er veiledende for å vise hvordan man kan få frem nødvendige opplysninger for skåring av de ulike punktene. Intervjueren står fritt til å tilpasse spørsmålene til barnets utviklingsnivå og bruke de ord og uttrykk som foresatte selv bruker når de intervjues.

Skåringene gjøres etter de instruksjonene som er gitt for hvert instrument.

CGAS og DD-CGAS skal skåres i forhold til personens faktiske generelle funksjonsnivå den siste mnd, uten hensyn til behandling eller prognose. Skåringen av **CGAS** og **DD-CGAS** gjøres på grunnlag av informasjon fremkommet i intervjuet **og** all annen informasjon som er tilgjengelig etter inklusjon og gjennomgang av de andre instrumentene. Dette betyr at skåringen av **CGAS** og **DD-CGAS** gjøres helt til slutt.

Intervju med foresatt som basis for vurdering av nåværende vansker og funksjonsnivå

Du/dere har fått tilsendt og fylt ut noen spørreskjema, som vi nå har sett over sammen,
(se over utfylling og avklar evt spørsmål/misforståelser før intervjuet starter).

jeg vil nå spørre deg/dere litt nærmere om hvilke vansker barnet/ungdommen har hatt eller fått behandling for, og om dette er vansker du tenker er til stede nå og påvirker fungering i hverdagen på ulike områder.*

Intervjuet med deg vil vare omtrent like lenge som den motoriske undersøkelsen av barnet/ungdommen.
(*I intervjumalen brukes av praktiske grunner «barnet» om prosjektdeltaker. Dette kan med fordel erstattes med «ungdommen» i intervjusituasjonen der alderen tilsier det).

Barnets fødselsår/alder/klassetrinn:

_____ / _____ år og _____mnd / _____ klasse.

Hvem blir intervjuet (relasjon til barnet)?

Hvem bor barnet sammen med? (sett kryss for det som passer, evt flere kryss)

	Nei	Ja
Biologisk mor _____	□	□
Biologisk far _____	□	□
Stemor _____	□	□
Stefar _____	□	□
Adoptiv-/fosterforeldre _____	□	□
Søsken _____	□	□
Besteforeldre _____	□	□
Andre slektninger _____	□	□
Andre, ikke slektninger _____	□	□
Institusjon _____	□	□
Annet, spesifiser _____	□	□

Lever begge foreldre? □ Nei □ Ja □ Vet ikke

Er foreldre skilte? □ Nei □ Ja

Hvis **ja**, hvor lenge er det siden samlivsbruddet? _____ år _____ mnd

Er barnet adoptert? □ Nei □ Ja

Hvilket land kommer biologisk mor fra *(se også utfylt CBCL)?* _____

Hvilket land kommer biologisk far fra *(se også utfylt CBCL)?* _____

Hvis **annen** etnisk bakgrunn enn norsk:

Har barnet alltid bodd i Norge? □ Nei □ Ja

Hvis **Nei**, evt hvor mange år har barnet bodd i Norge? _____

Søsken (regn også med halvsøsken og stesøsken)

Antall eldre søsken _____ Hvor mange bor sammen med barnet til daglig? _____

Antall yngre søsken _____ Hvor mange bor sammen med barnet til daglig? _____

Har barnet oppfølging av spesialisthelsetjeneste eller kommunalt hjelpeapparat nå?

□ Ja, kommunale instanser (Fastlege, PPT, helsesøster, psyk.helsetjeneste, barneverntjeneste, logoped, fysioterapeut, annet):

(spesifiser) _____

□ Ja, spesialisthelsetjeneste (BUP, Habilitering, Somatisk barneavdeling, annet):

(spesifiser) _____

□ Nei, ingen oppfølging

Er det opprettet ansvarsgruppe?

□ Ja

□ Nei

□ Vet ikke

Er det opprettet individuell plan?

□ Ja

□ Nei

□ Vet ikke

Er det tidligere gjennomført diagnostisk screeningintervju for psykiske vansker (Kiddie-SADS PL) som ledd i utredning?

□ Ja, med foreldre/foresatte

□ Ja, med barnet/ungdommen

Spesifiser tidspunkt for gjennomført intervju: _____ / _____ / _____ og evt _____ / _____ / _____

□ Nei

Dere er invitert med i dette prosjektet fordi barnet har vært vurdert for sosiale vansker/symptomer på en autismespekterforstyrrelse. Har barnet ditt fått en (ASD) diagnose?

□ Ja, spesifiser hvilken _____ Tidspunkt for diagnose _____

□ Ja, tidligere. Diagnose fjernet etter revurdering.

□ Nei

□ Uavklart /Under fortsatt utredning, spesifiser _____

Når var det første gang mistanke om symptomer innen autismespekteret? _____*(alder)*

Hva tenker du var de første symptomene? _____

Innenfor hvilke av disse områdene tenker du at barnet ditt har vansker nå (se også utfylt SRS og ASSQ)?
(Spørsmålene gjelder uavhengig av diagnose ASD eller ikke, og ses i sammenheng med vurdering av funksjonsnivå på ulike områder senere i intervjuet).

ASD symptomer	Ingenting	Litt	Moderat	Alvorlig	Ekstrem
Sosiale vansker					
Kommunikasjons-vansker					
Stereotyp og repetitiv atferd					
Begrensede «smale» interesser					
Rigiditet					
Sensoriske vansker					
Andre atferdsvansker					

Har barnet noen gang hatt en eller flere av følgende tilstander eller mottatt behandling for slike vansker?

Med **nåværende** menes det i løpet av den siste mnd.

Med **tidligere** menes det at slike vansker var til stede tidligere, men ikke i løpet av de siste 3 mnd.

- *Oppmerksomhets-/konsentrasjonsvansker eller ADHD:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Angstlidelse:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Depresjon:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Tvangstanker eller tvangshandlinger:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Lese-/skrivevansker eller andre lærevansker:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Motoriske vansker (klosset, koordineringsvansker, etc):*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Språkvansker:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Søvnvansker:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Psykoselidelse:*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Har barnet annen psykisk lidelse ?*
  □ Ja, nåværende (spesifiser evt diagnose): _____
  □ Ja, tidligere (spesifiser evt diagnose): _____
  □ Nei, men tenker slike vansker kan være til stede nå (mulig diagnose).
  □ Nei
  □ Vet ikke

- *Har barnet annen kjent sykdom eller medisinsk tilstand som har vart over 3 måneder ?*
  □ Ja, **tidligere** (spesifiser evt diagnose): □ Ja, **nåværende** (spesifiser evt diagnose):

  1. _____ 1. _____
  2. _____ 2. _____
  3. _____ 3. _____

  □ Nei, men tenker slike vansker kan være til stede nå.
  □ Nei
  □ Vet ikke

- *Bruker barnet noen medisiner nå?*
  □ Nei

  □ Ja (spesifiser medikamentnavn, startdato og aktuell dosering):

  1. _____

  2. _____

  3. _____

- *Har barnet tatt noen medisiner i dag?*

  □ Ja, følgende medikament(er) og dosering er tatt i dag:

  _____

  _____

  □ Nei
  □ Vet ikke

Så vil jeg gjerne spørre deg litt om hvordan du opplever barnets fungering på ulike områder. Jeg vil da at du skal tenke på barnet sammenlignet med andre barn på samme alder, og ikke legge spesielt vekt på noen av de symptomene eller vanskene vi nå har snakket om, men den generelle fungeringen sammenlignet med jevnaldrende.

- *Skole (jobb), skoleferdigheter (se også utfylt CBCL for bakgrunnsinformasjon til skåring):*

Hvordan fungerer barnet på skolen (evt. jobben)?

Har barnet tilrettelagt undervisning?

I hvilken grad følger barnet klassens pensum?

Har barnet mye skolefravær? Hva tenker du evt. er årsaken til dette?

Deltar barnet i gym/kroppsøving på skolen?

□ Deltar i gym/kroppsøving på linje med jevnaldrende

□ Deltar i gym/kroppsøving med tilrettelagt opplegg

□ Deltar ikke i gym/kroppsøving

□ Annet, spesifiser:

I hvilken grad er det behov for annen tilrettelegging, hjelp og tilsyn på skolen for at hverdagen skal fungere?

- *Venner og fritid (se også utfylt CBCL for bakgrunnsinformasjon til skåring):*

Deltar barnet i noen fritidsaktiviteter?

Er barnet sammen med andre jevnaldrende utenom skoletiden (regn ikke med søsken, kartlegg ensomhet)?

I hvor stor grad er det behov for tilrettelegging, hjelp og tilsyn for at barnet skal kunne være sammen med andre?

- *Hjem/familie/daglige rutiner:*

Hvordan opplever du at det går hjemme for tiden (se også utfylt KINDL)?

I hvilken grad opplever du at barnet er selvhjulpet ifht daglige rutiner (påkledning, mat/spising, søvn, hygiene, etc)?

I hvor stor grad er det behov for tilrettelegging, hjelp og tilsyn hjemme for at hverdagen skal fungere?

Hvordan opplever du at barnets vansker påvirker familielivet (forholdet til foresatte, søsken)?

- *Annet:*

Bruker barnet mye tid på plager, krangler, engstelse eller lignende?

Opplever du at barnet forstår og kan gjøre seg forstått i kommunikasjon og sosial samhandling med andre?

I hvor stor grad er det behov for tilrettelegging og hjelp i kommunikasjon og samhandling med andre?

Hva tenker du er barnets største utfordringer i forhold til fungering i hverdagen?

(For utfylling/oppsummering av intervjuer i etterkant):

- *Vurdering av selvhjelpsferdigheter, skoleferdigheter, kommunikasjon/forståelse, sosial atferd, nødvendig grad av tilsyn og tilrettelegging fra omgivelsene:*

Grad av funksjonsnedsettelse						
Funksjons-område		Ingen	Lett	Moderat	Alvorlig	Ekstrem
	Selvhjelps-ferdigheter					
	Kommunikasjon					
	Sosial atferd					
	Skoleferdigheter					

GLOBAL VURDERINGSSKALA FOR BARN

(CGAS – Children's Global Assessment Scale)

Bruk mellomliggende tall når det passer (f.eks. 35, 58, 62). Det er den faktiske funksjonsevne som skal skåres, uten hensyn til behandling eller prognose. Atferdseksemplene tjener kun til illustrasjonsformål; de behøver ikke å foreligge som grunnlag for en gitt skåre.

100 – 91	Utmerket funksjon på alle områder (hjemme, på skolen og med venner); engasjert i et bredt spekter av aktiviteter og har mange interesser (f.eks. har hobbier eller deltar i aktiviteter utenom skolen eller tilhører en organisert gruppe som speider'n el.l.) likandes, tillitsfull; "daglidagse" bekymringer tar aldri overhånd; gjør det godt på skolen; ingen symptomer.
90 – 81	God funksjon på alle områder; trygg i familie, skole, og med venner; det kan være forbigående vansker og "dagligdagse" bekymringer som av og til tar overhånd (f.eks. lett angst forbundet med en eksamen, hendelige "utblåsninger" overfor søsken, foreldre eller venner).
80 – 71	Lett forstyrrelse av funksjonen hjemme, på skolen eller blant venner; noe forstyrrelse av atferd eller følelsesmessig lidelse kan forkomme som svar på livsbelastninger (f.eks. foreldreseparasjon, dødsfall, fødsel av søsken) men disse er korte og påvirkningen av funksjon er forbigående; slike barn er bare minimalt forstyrrende for andre og blir ikke betraktet som avvikende av dem som kjenner dem.
70 – 61	Noen vansker på ett enkelt område, men fungerer generelt temmelig bra (f.eks. sporadisk eller isolert antisosiale handlinger slik som av og til skoleskulk eller småtyveri; mindre skolevansker, kortvarige stemningsforandringer, frykt eller angst som ikke fører til alvorlig unngåelsesatferd eller tvil på seg selv). Har noen meningsfylte mellommenneskelige relasjoner; de fleste mennesker som ikke kjenner barnet godt vil ikke se på han eller henne som avvikende, men de som kjenner ham/henne godt kan uttrykke bekymring.
60 – 51	Variabel funksjon med sporadiske vansker eller symptomer på flere, men ikke alle sosiale områder; forstyrrelsen er synlig for de som møter barnet i en dysfunksjonell sammenheng eller tidsperiode, men ikke for dem som ser barnet i en annen sammenheng.
50 – 41	Moderat påvirket funksjon på de fleste sosiale områder eller alvorlig forstyrrelse av funksjon på ett område, kan opptre på bakgrunn av f.eks. suicidal opptatthet eller grubling, skolenekting eller andre former for angst, tvangsmessige ritualer, alvorlige konversjonssymptomer, hyppige angstanfall, dårlige eller upassende sosiale ferdigheter, hyppige episoder av aggressiv eller annen antisosial atferd med noen meningsfylte sosiale relasjoner bevart.
40 – 31	Alvorlig svekket funksjon på flere områder. Ute av stand til å fungere på ett av disse områdene; dvs. Forstyrret hjemme, på skolen, med venner, eller i samfunnet, f.eks. vedvarende aggresjon uten klar bakgrunn; markert tilbaketrekning eller isolasjon på grunn av stemnings – eller tankeforstyrrelse, suicidalforsøk med klar dødelig intensjon; slike barn trenger sannsynligvis spesialskole og /eller hospitalisering eller å bli tatt ut av skolen. (Dette er imidlertidig ikke et tilstrekkelig kriterium for å inkluderes i denne kategorien)
30 – 21	Ute av stand til å fungere på nesten alle områder, f.eks. oppholder seg i hjemmet, på avdeling, eller i sengen hele dagen uten å ta del i sosiale aktiviteter eller alvorlige forstyrrelse i virkelighetsforståelse eller alvorlig forstyrrelse i kommunikasjon (f.eks. av og til usammenhengende eller upassende tale)
20 – 11	Trenger betydelig tilsyn og omsorg for å hindre skade av andre eller seg selv. (f.eks. ofte voldsom, gjentatte suicidalforsøk) eller for å ivareta personlig hygiene, eller alvorlig forstyrrelse av alle former for kommunikasjon, f.eks.alvorlige avvik i verbal eller non-verbal kommunikasjon, markert sosial reserverthet, stupor, etc.
10 – 1	Trenger konstant tilsyn (24-timers omsorg) på grunn av alvorlig aggressiv eller selvdestruktiv atferd eller grov forstyrrelse i virkelighetsoppfatning, kommunikasjon, kognisjon, følelser eller personlig hygiene.

Shaffer, D, M. Gould, J. Brasic, P. Ambrosini, P. Fischer, H. Bird, S. Aluwahlia: «A Children's Global Assessment Scale (CGAS)», *Psychopharmacology Bulletin 1985,21,747-48. Oversatt av I.H. Vandvik*

Children's Global Assessment Scale for Developmental Disabilities (DD-CGAS)

Vurder personens funksjonsnivå innen de viktigste områdene som a) **selvhjelpsferdigheter, mat, påkledning, søvn**; b) **kommunikasjon**; c) **sosial atferd**; d) **skoleferdigheter**, og på de ulike arenaene (**hjemme, på skolen og i andre sosiale fellesskap**).
Skår personens samlede funksjonsnivå ved å velge den overskriften nedenfor som best beskriver funksjon sammenlignet med vanlig utvikling for barn på samme alder. Bruk mellomliggende tall når det passer (f. eks. 35,38,62). Det er det faktiske funksjonsnivået som skal skåres, uten hensyn til behandling eller prognose. Fokuser på endring av funksjon som følge av psykopatologi, mer enn symptomer i seg selv.
Eksemplene nedenfor tjener kun til illustrasjonsformål; de behøver ikke å foreligge som grunnlag for en gitt skåre.

Spesifisert tidsperiode: 1 måned

100-91 Svært god funksjon på alle områder (hjemme, på skolen og med venner). Svært gode ferdigheter sammenlignet med jevnaldrende, deltar i fritidsaktiviteter og kan opprettholde interesser over tid. Gode skoleprestasjoner, kan selvstendig gjennomføre daglige aktiviteter og mestrer forventede selvhjelpsferdigheter for alderen.

90-81 God funksjon på alle områder (hjemme, på skolen og med venner). Det kan være forbigående endring av atferd eller emosjonelt ubehag som respons på påkjenninger i hverdagen (f. eks. uforutsette endringer i daglige rutiner eller det fysiske miljøet), men uten at dette påvirker funksjon. Adaptive ferdigheter som forventet i forhold til alder, på alle områder.

80-71 Lett forstyrrelse av funksjonen. For det meste aldersadekvate ferdigheter, men kan ha behov for påminning og struktur for å mestre daglige gjøremål. Mindre endringer i daglige rutiner eller miljø kan forårsake forbigående funksjonsnedsettelse. Sosial samhandling kan være ensidig og basert på interesser og aktiviteter mer enn genuin interesse for nære, gjensidige relasjoner. Språket er aldersadekvat, men en samtale kan oppleves ensidig og/eller fokusert på særinteresser. Barnet/ungdommen kan fremstå mer umoden enn jevnaldrende, men ikke tydelig avvikende.

70-61 Lett forstyrrelse av funksjonen og moderat påvirket funksjon på minst et område. Tilsynelatende sosiale vansker i de fleste situasjoner. Lærer seg egnede sosiale ferdigheter, men kan være rigid og mangle evne til å generalisere. Umodne adaptive/selvhjelpsferdigheter på de fleste områder. Tydelig avvikende atferd i enkelte situasjoner (f. eks. i sosiale grupper, lite strukturerte situasjoner) som påvirker sosiale relasjoner negativt og kan begrense deltagelse i aldersadekvate aktiviteter på et eller to områder, eller i en bestemt situasjon.

60-51 Moderat påvirket funksjon på de fleste områder. Stort behov for struktur og tilsyn for å gjennomføre daglige gjøremål/rutiner. Adaptive/selvhjelpsferdigheter er under forventet nivå for alder. Kommuniserer sine behov, responderer på enkle forespørsler (verbalt eller nonverbalt). Det verbale språket (hvis til stede) er forsinket og lite fleksibelt. Sosiale vansker og/eller uvanlig atferd er tydelig i de fleste situasjoner og medvirker til et lavere funksjonsnivå enn forventet for alderen.

50-41 Moderat påvirket funksjon på de fleste områder og alvorlig svekket funksjon på minst et område (f. eks. dagliglivsferdigheter eller kommunikasjon). Sosiale tilnærmelser og/eller responser er tydelig fraværende eller upassende. Dagliglivsferdigheter er betydelig forsinket (f. eks. påkledning, hygiene, spise). Stereotyp og/eller annen vedvarende og uvanlig atferd er merkbart for en tilfeldig observatør og hindrer funksjon.

40-31 Alvorlig svekket funksjon på enkelte områder. Ikke utviklede eller instrumentelle (ikke sosiale) kommunikasjonsferdigheter. Repetitiv atferd som forstyrrer adaptiv funksjon. Markert sosial tilbaketrekning i de fleste situasjoner. Adaptiv atferd er betydelig svekket sammenlignet med jevnaldrende. Behov for betydelig tilrettelegging fra omgivelsene på enkelte områder. Umoden tilpasningsevne og selvhjelpsferdigheter på minst to funksjonsområder.

30-21 Alvorlig svekket funksjon på alle områder og arenaer, (f. eks. hjemme og på skolen). Tydelig tilbaketrekning og isoleringsatferd. Krever omfattende tilrettelegging fra omgivelsene (f. eks. 1:1 tilsyn for atferd, tilpasset bolig, låse skap, fjerne farlige gjenstander fra rommet). Avhengig av hjelp fra andre i alle aspekter av hverdagen både hjemme og på skolen (f. eks. påkledning, bad, toalettbesøk), og i større grad enn forventet for alderen. Kan fremvise grunnleggende reguleringsvansker (f. eks. i forhold til søvn, mat).

20-11 Ekstreme funksjonsvansker på minst ett område (trenger betydelig tilsyn og omsorg). Trenger kontinuerlig tilsyn eller omfattende tilrettelegging fra omgivelsene på grunn av sikkerhet eller for å ivareta basale behov (f. eks. mat, hygiene, toalettbesøk). Kan trenge institusjonsplass/omsorgsbolig. Kommuniserer ikke grunnleggende behov. Samhandler ikke med andre. Tydelig forstyrrelse av grunnleggende regulering (f.eks. i forhold til søvn, mat).

10-1 Ekstreme og gjennomgripende funksjonsvansker (trenger konstant tilsyn og omsorg). Utgjør en fare for seg selv og/eller andre. Trenger konstant tilsyn (f. eks. 24-timers omsorg utenfor hjemmet) på grunn av sikkerhet eller total avhengighet av hjelp til å ivareta basale behov (f. eks. hygiene, mat/næring, toalettbesøk). Tydelig forstyrrelse av grunnleggende regulering. Behov krever spesialisert omsorg (f. eks. medisinsk behandling, atferdsregulering) utover det som kan gis av polikliniske eller hjemmebaserte tjenester.

Lise Reindal (2017) etter Wagner et al. (2007) BIOL PSYCHIATRY; 61:504-511; DD-CGAS som er basert på/omarbeidet fra Children's Global Assessment Scale (Shaffer et al, 1983) og Global Assessment Scale (GAS; Endicott et al, 1976).

Instruksjon for skåring
Children's Global Assessment Scale for Developmental Disabilities (DD-CGAS)

Områder som skal vurderes ved skåring inkluderer:

- Samlet funksjonsnivå på de viktigste funksjonsområdene:
  - Selvhjelpsferdigheter: daglige rutiner, mat/spising, påkledning, søvn
  - Kommunikasjon
  - Sosial atferd
  - Skoleferdigheter, nivå og miljø
- Samsvar eller manglende samsvar i funksjon på ulike arenaer: hjemme, på skolen og i andre sosiale fellesskap.
  - Nødvendig grad av tilrettelegging fra omgivelsene
  - Nødvendig grad av tilsyn

1. Bruk tabellen nedenfor til å organisere din vurdering av funksjonsnedsettelse på de fire funksjonsområdene.

2. Velg den overskriften/kategorien som best beskriver det generelle funksjonsnivået (f. eks. *«Moderat påvirket funksjon på de fleste områder»*). Kategorien bør gi en god beskrivelse av det generelle funksjonsnivået til barnet, uavhengig av om funksjonsnedsettelsen skyldes kognitive, atferdsmessige eller andre vansker. **Du sammenligner beskrivelsen av adaptiv funksjon hos det aktuelle barnet med det som forventes av et barn med upåfallende utvikling, uavhengig av om funksjonsnedsettelsen skyldes en utviklingsforstyrrelse, atferdsvansker, miljømessige eller andre forhold.** Vær forsiktig med å legge for stor vekt på standardskårer; variasjon i funksjon kan «jevnes ut» i standardskåren. Legg i stedet mer vekt på beskrivelsen av funksjonsnivået i vignettene.

3. Sjekk detaljer i kategorien for å bekrefte at den generelle beskrivelsen passer, men vær oppmerksom på at de fleste barn ikke vil passe helt inn i noen spesiell kategori. Du ønsker å finne den kategorien som passer best.

4. Når du mener at du har funnet den kategorien som passer best skal du vurdere de to nærliggende kategoriene. Vurder om barnet har noen karakteristika som passer inn i kategorien over eller under den du har valgt. Dette vil hjelpe deg til å justere skåren. Hvis for eksempel barnet passer best i kategorien «*60-51 Moderat påvirket funksjon på de fleste områder»*, men har noen likheter med 41-50, så vil du velge en skåre i nedre del av skalaen (51-55). Hvis barnet i motsatt fall passer best i 60-51, men har noen styrker som samsvarer med neste kategori over, så vil du velge en skåre i øvre halvdel av kategorien (55-60).

Grad av funksjonsnedsettelse						
Funksjons-område		Ingen	Lett	Moderat	Alvorlig	Ekstrem
	Selvhjelps-ferdigheter					
	Kommunikasjon					
	Sosial atferd					
	Skoleferdigheter					

Wagner A, Lecavalier L, Arnold LE, Aman MG, Scahill L, Stigler KA, Johnson CR, McDougle CJ, Vitiello B. Developmental disabilities modification of the Children's Global Assessment Scale. *Biol Psychiatry* 61:504-511.

GLOBAL VURDERINGSSKALA FOR BARN (CGAS og DD-CGAS)

Bruk skåringsskalaene på de forutgående sidene. Sett en skåre for barnets generelle funksjonsnivå den siste mnd. Skåringen av CGAS gjøres først, deretter DD-CGAS.

Begge skåringene skal først gjøres etter at de øvrige instrumentene er skåret og intervjuet med foresatte er ferdig gjennomført.

CGAS (den siste mnd):_____

DD-CGAS (den siste mnd): _____

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