CHILDREN WITH AUTISM GROW UP

Use of the DISCO (Diagnostic Interview for Social and COmmunication disorders) in population cohorts

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Abstract

Objectives: Examine the prevalence and outcome of autism in child and adult population cohorts using the Diagnostic Interview for Social and COmmunication disorders (DISCO). **Method**: The Faroe Islands school population aged 7-18 years (n=7689) was screened for autism and cases raising suspicion were examined and tested. Parents were interviewed using the DISCO. Clinical diagnoses were established on the basis of all available information. Prevalence rates for autistic disorder, atypical autism and Asperger syndrome were calculated. The autism outcome was looked at in 3 partly overlapping population cohorts of individuals (n=120) diagnosed in childhood as suffering from autism or atypical autism from the region of Göteborg, Sweden. They were re-examined at ages 17-40 years, 13-22 years after diagnosis. Parents and carers were interviewed using the DISCO. Strict operationalised criteria for outcome were used. Diagnostic stability over time was analysed. Symptom profiles on the basis of the DISCO were reviewed and background factors contributing to outcome in adult age were assessed. Aspects of Quality of Life were examined. **Results**: The prevalence of autism, atypical autism, and Asperger syndrome in the Faroe Islands child population was 0.56%. The boy:girl ratio was 4.8:1. The DISCO was very useful in eliciting the information needed for a correct clinical diagnosis. The overall outcome of autism in the Göteborg population was psychosocially poor with few adults leading independent lives. Mortality was high (5%) and seemed to be associated with medical disorders including epilepsy. All but one of the individuals included in the follow-up study (n=108) still met criteria for autism or atypical autism. A small subgroup showed better psychosocial outcomes. They had all had some spoken language at age 3 years. Those with a childhood diagnosis of atypical autism tended to be diagnosed with autism at follow-up. The correspondence between clinical diagnoses and DISCO algorithm diagnoses was very good. The level of intellectual functioning showed a significant shift downwards. A subgroup deteriorated in adolescence. According to DISCO results, social, communication, and sensory impairment problems typical of the childhood period were still present at very high rates in late adolescence and adult life. Quality of Life seemed to be relatively good in some cases in spite of the poor overall psychosocial outcome. Early communication skills and IQ predicted aspects of outcome. **Discussion**: The DISCO is a useful instrument for diagnosis and follow-up of individuals with autism spectrum conditions. Combined with clinical examination of the individuals themselves, the DISCO yields important diagnostic and symptom information needed for appropriate diagnosis in childhood and for clinical review of diagnosis and symptom load in adolescence and adult life. The prevalence of autism in the Faroe Islands was very similar to that reported for autism in other parts of the world. The outcome of autism in the Göteborg cohort was psychosocially very poor, but life quality did not generally appear to be at a correspondingly low level. However, an important minority had very poor quality of life. The Faroe Islands cohort included relatively much higher functioning individuals than did the Göteborg group, which included cases diagnosed 15-30 years ago. The Faroe Islands cohort may have a very different prognosis, and the outcome findings from the Göteborg study can only be generalized, if at all, to other populations with autism diagnosed before the 1990s, when diagnostic concepts and criteria were more narrow than they are today. **Conclusions**: Autism is not a very rare disorder. Outcome in severe cases with intellectual impairment is psychosocially poor (with little or no independence in adult life), but life quality can be good even in such cases. The DISCO is a very helpful instrument for diagnosis in childhood and in adult life and can be used for follow-up of symptom profiles and problem assessment before and after adolescence.

Key words: DISCO, autism, Asperger syndrome, diagnosis, prevalence, outcome, quality of life
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To Fanny, Love and John

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- Billstedt, E., Gillberg, I.C. & Gillberg, C. (2005). Autism after adolescence: Population-based 13-22-year follow-up study of 120 individuals with autism diagnosed in childhood. *Journal of Autism and Developmental Disorders,* 35:351-60.

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ABBREVIATIONS USED IN THIS THESIS

A	Average intelligence
ADD	Attention Deficit Disorder
ADHD	Attention-Deficit/Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview-Revised
ADOS	Autism Diagnostic Observation Schedule
APA	American Psychiatric Association
ASD	Autism Spectrum Disorder
ASSQ	Autism Spectrum Screening Questionnaire
DISCO	Diagnostic Interview for Social and COmmunication Disorders
DSM-III	Diagnostic and Statistical Manual of Mental Disorders. Third Edition
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders. Third Edition Revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders. Fourth Text Revision
HBS	Handicaps, Behaviours and Skills schedule
ICD-10	International Classification of Diseases. Tenth Edition
LD	Learning Disability
MMR	Mild Mental Retardation (IQ 50-70)
MR	Mental Retardation
NA	Near Average intelligence (IQ 71-84)
PDD	Pervasive Developmental Disorder
PDD-NOS	Pervasive Developmental Disorder Not Otherwise Specified
QOL	Quality Of Life
SMR	Severe Mental Retardation (IQ<50)
VABS	Vineland Adaptive Behavior Scales
WAIS-R	Wechsler Adult Intelligence Scale-Revised
WHO	World Health Organisation
WISC-III	Wechsler Intelligence Scale for Children-Third Revision
WISC-R	Wechsler Intelligence Scale for Children-Revised
WPPSI	Wechsler Preschool and Primary Scale of Intelligence

INTRODUCTION

Autism (APA, 2000) is currently conceptualized as a neurodevelopmental/neuropsychiatric disorder with early childhood onset and a variable but usually chronic course. It was long considered a very rare condition that affected no more than a fraction of 0.1 per cent of the general population of children (Lord & Rutter, 1994). However, Gillberg (Gillberg, Schaumann & Steffenburg, 1991, Gillberg, 1992) suggested, more than 15 years ago, that autism might be much more common than generally believed, and Wing proposed that the spectrum of conditions now included under the diagnostic label of autism could affect as many as 0.5-1.0 per cent of all children (Wing & Potter, 2002). The most recent estimates of the prevalence of disorders included in the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) as belonging in the autism spectrum are close to 1 per cent (or a little over) (e.g. Baird, Simonoff, Pickles, Chandler, Loucas, Meldrum et al, 2006), but it is still unclear whether or not autism prevalence might vary considerably across regions, countries and cultures. The outcome of autism has been assumed to be psychosocially poor (Lotter, 1978; Nordin & Gillberg, 1998), but few studies have included very long-term and detailed follow-up of representative population cohorts of cases with autism followed prospectively from childhood into their twenties and thirties. There is a need for such studies as a basis for planning assessment services, interventions and long term care. This thesis deals with both the prevalence and long-term outcome of autism in general population cohorts screened for autism in schools and registers and using individual clinical assessments and the Diagnostic Interview for Social and COmmunication Disorders (DISCO) in those individuals raising suspicion of suffering from a disorder in the autism spectrum.

Autism: brief review of past and current concepts

John Haslam and Jean Itard, independently of each other reported on “wild” boys “living” in the forest and described characteristic autistic symptoms possibly for the first time in the literature around 1800 (Horston & Frith, 2000). The concept of autism was mentioned for the first time in 1911 by Eugen Bleuler, and was used to refer to the type of egocentric thinking that, at the time, was felt to be a core feature of schizophrenia.

It was not until 1943, when Leo Kanner of the Johns Hopkins Hospital in Baltimore, USA described a group of 11 children (8 boys, 3 girls) with abnormalities in social behaviour, that autism came to be regarded as a disorder with specific features and very early childhood onset. Kanner (1943) introduced the term early infantile autism when referring to “his” condition, which is now subsumed under labels such as “autistic disorder”, “childhood autism” and “autistic syndrome”.

Independently of Kanner, Hans Asperger in Vienna, Austria studied and published on boys with a similar but milder form of the disorder (Asperger, 1944) that later became known as Asperger syndrome (Wing, 1981; Gillberg & Gillberg, 1989). It has gradually become clear that both Kanner´s variant of autism and Asperger´s variant of the condition he himself referred to “autistic psychopathy” had been described by other researchers already in the 1920s and 1930s (Critchley & Earl, 1932; Ssucharewa, 1926; Ssucharewa & Wolff, 1996).

Autistic disorder and Asperger´s disorder/Asperger syndrome are now listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV, APA, 1994), and in the International Classification of Diseases and Disorders 10 (ICD-10, WHO, 1993) as two of

five “pervasive developmental disorders” (PDD). In clinical practice, and in some research, the PDD concept is often equated with Autism Spectrum Disorder (ASD). The other three “PDDs” are Rett syndrome, disintegrative disorder (rare and very severe disorders) and pervasive developmental disorder not otherwise specified (PDD-NOS) which is often used synonymously with the ICD-10 concept of atypical autism - and that of “autistic-like condition” launched by Gillberg (Steffenburg & Gillberg, 1986) and included in current Swedish legislation regarding “autism and autistic-like conditions” (LSS, 1993:387). All these ASDs – except some cases of Rett syndrome, which, for unclear reasons, has been defined as a specific variant of PDD, when, in fact it is a neurological disorder which can be associated with PDD - have in common varying degrees of impairment in reciprocal social interaction, communications skills, and restricted and repetitive patterns of behaviour.

The concept of autism and its classification has changed over the years. The general trend has been for a widening of the criteria that were suggested by Kanner, who emphasised social aloofness and indifference (“autistic aloneness”) and elaborate rituals as crucial features (Kanner & Eisenberg, 1956). The current triad (social, communication, behaviour impairments) concept was launched by Lorna Wing (Wing & Gould, 1979) after her influential epidemiological study of disabled children in south-east London. It has pervaded all the available diagnostic systems to the extent that it has become difficult to even ask the question: What is autism (really)?

Table 1 reviews, in overview format, some of the most salient changes in terminology and diagnostic practice in the field of ASD over the past 65 years.

Autism: diagnosis and diagnostic instruments

There is, at present, little debate regarding the core concept of autistic disorder, which seems to have become generally accepted as a recognizable condition across medical and psychological disciplines. There is much more controversy in respect of Asperger syndrome, which has been reported to be virtually non-existent when portrayed the way it is in the DSM-IV/ICD-10 (Miller & Ozonoff, 1997; Leekam, Libby, Wing, Gould & Gillberg, 2000), and for which the criteria by Gillberg (1991) are probably the ones most used in international clinical practice. These criteria have been based on Asperger´s original case descriptions. There is also considerable debate regarding the delineation of PDD-NOS and atypical autism, neither of which has any specific operationalized diagnostic criteria or algorithms in the DSM-IV-TR or ICD-10 (Njardvik, Matson & Cherry, 1999; Filipek, Accardo, Baranek, Cook, Dawson, Gordon et al, 1999; Walker, Thompson, Zwaigenbaum, Goldberg, Bryson, Mahoney et al, 2004; Volkmar, Lord, Bailey, Schultz & Klin, 2004). Some authors (e.g. our own group, see Billstedt, Gillberg & Gillberg, 2005) have suggested specific diagnostic criteria and an algorithm for this diagnosis (Table 2), as it is important to have some degree of “common ground” when comparing data across research groups.

The “gold standard” for diagnostics in the field of autism remains the clinical diagnosis (which nowadays is based on diagnostic criteria and clinical judgment, whereas in the past a diagnosis was made almost exclusively on the “gestalt” of the disorder perceived by the experienced clinician). During the last decades, an increasing number of diagnostic instruments have been developed. Systematic interviews and observation scales have been introduced and adopted in clinics and research. Different diagnostic instruments have been proved to be of great value for assuring a more detailed account of symptomatology, but they cannot be more valid for diagnosis than the clinical judgement of an experienced clinician, given that the instruments have always been validated against such judgment.

Table 1. Changes in the classification of autism over the past 65 years

Originator/ Classification system	Year	Overall classification	Subgroup Autistic disorder/ infantile autism	Subgroup Atypical autism/ autisticlike condition	Subgroup Asperger syndrome	General outline
Leo Kanner	1943		Early infantile autism			Description
Hans Asperger	1944				Autistic psychopathy	Description
WHO, Manual of the int. statistical classification of diseases, injuries and causes of death	1967	Schizophrenia	Infantile autism			Description
ICD-8 WHO	1974	Behaviour disorders of childhood	Infantile autism			Description
ICD-9 WHO	1977	Psychoses with origin specific to childhood	Infantile autism	Other unspecified psychosis in childhood		General outline of clinical presentation, no diagnostic criteria or algorithm
DSM-III APA	1980	PDD	Infantile autism	Childhood onset PDD		General outline of clinical presentation, diagnostic criteria but no algorithm
DSM-III-R APA	1987	PDD	Autistic disorder	PDD-NOS		Operationalized diagnostic criteria, PDD-NOS description
Gillberg & Gillberg	1989				Asperger syndrome	Operationalized diagnostic criteria
Gillberg	1991				Asperger syndrome	Elaborated operational diagnostic criteria and algorithm
ICD-10 WHO, criteria for research	1993	PDD	Childhood autism	Atypical autism	Asperger´s syndrome	Operationalized diagnostic criteria and algorithm for autism and Asperger syndrome, no diagnostic criteria or algorithm for atypical autism
DSM-IV APA	1994	PDD	Autistic disorder	PDD-NOS	Asperger´s disorder	Operationalized diagnostic criteria and algorithm for autism and Asperger syndrome, no diagnostic criteria or algorithm for PDD-NOS
DSM-IV-TR APA	2000	PDD	Autistic disorder	PDD-NOS	Asperger´s disorder	Operationalized diagnostic criteria, PDD-NOS description

Table 2. Diagnostic criteria for DSM-IV autistic disorder, DSM-IV PDD-NOS, and Gillberg´s atypical autism

DSM-IV Autistic disorder (similar to ICD-10)	A. A total of six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3): **(1) qualitative impairment in social interaction** (a) marked impairment in the use of multiple nonverbal behaviours such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction (b) failure to develop peer relationships appropriate to developmental level (c) a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest) (d) lack of social and emotional reciprocity **(2) qualitative impairments in communication** (a) delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime) (b) in individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others (c) stereotyped and repetitive use of language or idiosyncratic language (d) lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level **(3) restricted repetitive and stereotyped patterns of behaviour, interests, and activities** (a) encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus (b) apparently inflexible adherence to specific, non-functional routines and rituals (c) stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, or complex whole-body movements) (d) persistent preoccupation with parts of objects **B.** Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years: (1) social interaction, (2) language as used in social communication, or (3) symbolic or imaginative play. **C.** The disturbance is not better accounted for by Rett´s Disorder or Childhood Disintegrative Disorder.
DSM-IV criteria for PDD-NOS	This category should be used when there is a severe and pervasive impairment in the development of reciprocal social interaction or verbal and nonverbal communication skills, or when stereotyped behaviour, interests, and activities are present, but the criteria are not met for a specific Pervasive Developmental Disorder, Schizophrenia, Schizotypal Personality Disorder or Avoidant Personality Disorder.
Gillberg´s proposed criteria for atypical autism	Autistic disorder's social interaction met plus a total of at least 4 symptoms but not full criteria for Autistic disorder or Gillberg's Asperger syndrome met

Table 3. Diagnostic criteria for Gillberg's Asperger syndrome

Gillberg´s Asperger syndrome criteria	All six criteria must be met for confirmation of diagnosis: **1.Severe impairment in reciprocal social interaction (at least two of the following)** -inability to interact with peers -lack of desire to interact with peers -lack of appreciation of social cues -socially and emotionally inappropriate behaviour **2.All-absorbing narrow interest (at least one of the following)** **-**exclusion of other activities -repetitive adherence more rote than meaning **3. Imposition of routines and interests (at least one of the following)** **-**on self, in aspects of life -on others **4. Speech and language problems (at least three of the following)** -delayed development -superficially perfect expressive language -formal, pedantic language -odd prosody, peculiar voice characteristics -impairment of comprehension including misinterpretations of literal/implied meanings **5. Non-verbal communication problems (at least one of the following)** -limited use of gestures -clumsy/gauche body language -limited facial expression -inappropriate expression -peculiar, stiff gaze **6. Motor clumsiness** **-** poor performance on neuro-developmental examination

The four most widely used diagnostic instruments in the field of ASD are the CARS, ADI-R, the ADOS and the DISCO (see below). More recently, two new instruments have been developed specifically for people with autism, the 3-di (Skuse, Warrington, Bishop, Chowdhury, Hau, Mandy et al, 2004) for ASD at all levels of intellectual functioning, and the ComFor (Noens, van Berckelaer-Onnes, Verpoorten & van Duijn, 2006) for individuals with severe cognitive impairments.

Childhood Autism Rating Scale (CARS)

The CARS (Schopler, Reichler, DeVellis & Daly, 1980; Schopler, Reichler & Renner, 1988) is the best validated autism diagnostic instrument for individuals with autism who have some degree of intellectual impairment. It is a mixture of observation and interview and takes about 45 minutes to complete for an expert clinician. It yields a summary score ranging from 15-60, scores of 30-35.5 indicating "mild" autism and scores of 36 and above indicating "severe autism".

Autism Diagnostic Interview-Revised (ADI-R)

The ADI-R (Lord, Rutter & Le Couteur, 1994) is a revised version of The Autism Diagnostic Interview (ADI; Le Couteur, Rutter, Lord, Rios, Robertson, Holdgrafer et al, 1989). The ADI-R is a standardised, semi-structured, investigator-based interview for caregivers of individuals

with autism, which provides a diagnostic algorithm for ICD-10 and DSM-IV definitions of autism. It takes 2-3 hours to complete for a trained rater.

Autism Diagnostic Observation Schedule (ADOS)
The ADOS (Lord, Risi, Lambrecht, Cook, Leventahal & DiLavore, 2000) is a standardised protocol for observation of social and communicative behaviour associated with autism. The ADOS consists of several structured or semi-structured situations for interaction, accompanied by coding of specific target behaviours in connection with particular tasks and by general ratings of the quality communication and social interaction. It takes about 45 minutes to complete and requires two trained examiners.

The DISCO (Diagnostic Interview for Social and COmmunication disorders)
The DISCO (used in the present study and reviewed in more detail in the Methods section) is a semi-structured investigator-based interview intended for use with a person (often a parent) who knows the individual with a suspected autism spectrum disorder from early childhood. The DISCO was developed from the "Handicaps, Behaviours and Skills (HBS) schedule" (Wing & Gould, 1978) and designed to function both in clinical work (to compile a clinical history and present clinical picture, to be a help in the diagnostic classification, and a guide for educational/environmental recommendation) and in research. It takes about 2-4 hours to complete for a trained rater.

Autism: prevalence

Up until about 1990, autistic disorder was considered a rare condition. The studies by Lotter (1966) and by Brask (1967) yielded prevalence figures for autism of 4-5 per 10,000 children. Later studies (Wing, 1979; Gillberg, 1984) gave closely comparable results. However, in 1991, Gillberg, Schaumann and Steffenburg asked the question "Is autism more common now than 10 years ago?" and reported rising prevalence rates in Gothenburg, Sweden from 1980 through 1988 (Gillberg et al, 1991). In a review study by Gillberg and Wing (1999) of prevalence studies published between 1966 and 1997, they found that early studies yielded prevalence rates of under 0.5 in 1000 children whereas the later ones showed a mean rate of about 1 in 1000. Several recent studies have reported an overall prevalence for autism spectrum disorder (including childhood autism, Asperger syndrome, and atypical autism (PDD-NOS) of more than 0.5% of the general population of children (Arvidsson, Danielsson, Forsberg, Gillberg, Johansson & Kjellgren, 1997; Kadesjö, Gillberg & Hagberg, 1999; Bertrand, Mars, Boyle, Bove, Yeargin-Allsopp & Decoufle, 2001; Chakrabarti & Fombonne, 2001; Charman, 2002; Fombonne, 2003; Merrick, Kande & Morad, 2004; Fombonne, 2005; Williams, Glasson, Wray, Tuck, Helmer, Bover et al, 2005; Chakrabarti & Fombonne, 2005; Barbaresi, Katusic, Colligan, Weaver & Jacobsen, 2005; Fombonne, Zakarian, Bennet, Meng & McLean-Heywood, 2006; Gillberg, Cederlund, Lamberg & Zeijlon, 2006; Reading, 2006). In a recent study of prevalence of autism spectrum disorder conducted in a population cohort in South Thames, UK, the total prevalence of Autism spectrum disorder was 1.16% (Baird et al, 2006). It is now generally accepted that in many parts of the world the ASD prevalence is in the range of 0.5 through 1.2 per cent and that rates, of course, depend on exactly where you draw the line for impairment and how much symptomatology is required for diagnosis.

Boy:girl ratios have been reported to be extremely high in ASD. Most studies have reported male:female ratios of 3-5 to 1 (e.g. Wing, 1996; Bartley, 2006), even though some authors (e.g. Kopp & Gillberg, 2007) have suggested that many girls and young women with ASD remain undiagnosed and so contribute to the mistaken notion that male:female ratios are extremely high in autism. There can be no doubt that autism (and other ASDs) are much more

common in boys than in girls, but it is still unclear as to what the "true" ratio is. Clinical experience and new evidence from studies of girls and women with social deficits, suggest that ratios of 2-3 males:females will become a more likely gender ratio in ASD within the next several years.

The association of ASD and learning disability/mental retardation (MR) has recently emerged as an area of some debate. In the past, most authors reported that about 75% of all individuals with autism had concomitant MR (e.g. Rutter, 1978). However, with the inclusion of Asperger syndrome and other atypical autism cases in the broader spectrum of autism, it has become clear that the proportion of individuals with autism and concomitant MR is much smaller than previously held, probably amounting to 20-40% rather than double these rates or more. The reduction in number of ASD cases with concomitant MR stems from the extremely low prevalence of MR in individuals diagnosed with Asperger syndrome.

Autism: outcome

Classic autism usually persists into adulthood, and the majority of cases diagnosed in childhood probably continue to meet criteria for the disorder in early adult life (Rutter, Greenfeld & Lockyer, 1967; Gillberg & Steffenburg 1987; von Knorring & Hägglöf, 1993; Nordin et al, 1998; Seltzer, Krauss, Shattuck, Orsmond, Swe & Lord 2003; Howlin, Goode, Hutton & Rutter 2004; McGovern & Sigman 2005; Rutter, Kim-Cohen & Maughan, 2006). Individuals with autism continue to show impairments in the typical autism triad domains of reciprocal social interaction, reciprocal communication, and restricted behaviour patterns (Rumsey, Rapoport & Sceery, 1985; Ballaban-Gil, Rapin, Tuchman & Shinnar, 1996; Kobayashi & Murata, 1998; Howlin, 2003). Outcome is known to be poor for those with autism and an IQ below 50. Almost all of those with an IQ below 50 are likely to have a poor or very poor prognosis in regard to social functioning, and almost no one can be expected to live independently (Nordin et al, 1998). Those with an IQ above 50 have a considerable better outcome, although many in this latter group remain dependent on others for support (Venter, Lord & Schopler, 1992; Larsen & Mouridsen, 1997; Szatmari, Bartolucci, Bremner, Bond & Rich, 1989; Starr, Szatmari, Bryson & Zwaigenbaum, 2003; Howlin et al, 2004), and a variety of psychiatric problems can occur (Frith, 2004; Bradley & Bolton, 2006).

Another predictor of outcome, possibly independently of level of IQ, is the ability to use speech communicatively (Lotter, 1974) and to have this ability before 5-6 years of age (Gillberg et al, 1987; Howlin, 2000).

Several studies have shown the occurrence of deterioration or aggravation of symptoms in puberty for people with autism. About 22 % of children with autism can be expected to show behavioral and cognitive deterioration during this period, accompanied by a regression and reappearance of typical pre-school symptoms, and aggravated behavior, such as self-destructiveness, aggressiveness and hyperactivity, might be observed in about 50 % of all cases with autism (Nordin et al, 1998).

Recognition of the persistence and complexity of the problem associated with autism has led to a continuing search for interventions in autism. Recent research suggests that the most effective results stem from early intensive behavioral interventions, although many questions remain concerning the optimal age at which intervention should begin, the intensity of intervention and the many other variables that may affect outcome (Howlin, 2005).

AIMS OF THE PRESENT THESIS

The purpose of the study was to gain further insight into autism across the life-span. More specifically, the aims were:

- to examine the current prevalence of autism in children in a population-based study using the DISCO, an investigator-based collateral interview for diagnosing autism spectrum disorders;

- to examine, prospectively, the outcome of autism after puberty in a population based cohort representative of autism as diagnosed in the 1970s and 1980s;

- to examine the diagnostic stability of autism over time and to establish the validity of DISCO algorithm diagnoses against gold standard clinical diagnoses;

- to describe distinctive DISCO symptoms and symptom patterns (included associated background factors) within the broader autism spectrum in post-pubertal people diagnosed in childhood;

- to study outcome with specific reference to social aspects/quality of life in these post-pubertal individuals with autism.

METHODS

Subjects

An overview of all subjects participating in the studies of the present thesis is given in Table 4. The different substudies will be referred to using Roman numerals. The target group of study I is those school age children in the Faroe Islands who, after screening of the whole school population, raised suspicion of suffering from ASD. The target group of studies II, III and IV is the same group of individuals with autism/atypical autism identified in three different, but partly overlapping population studies in Göteborg, Sweden (Gillberg, 1984; Steffenburg & Gillberg, 1986; Gillberg et al, 1991).

Table 4. Study groups and methods used in study I-IV

Study	I	II	III	IV
Object of study	Prevalence	Overall outcome	Symptoms	Quality of life
Target group	43	120	120	120
Attrition	2	6	9	6
Dead	0	6	6	6
Group examined	41	108	105	108
Male: female	35:6	77:31	75:30	77:31
Age range years	8-17	17-40	17-40	17-40
Mental development level	A 22 NA 6 MMR 2 SMR 11	A 4 NA 10 MMR 38 SMR 56	A 3 NA 10 MMR 36 SMR 56	A 4 NA 10 MMR 38 SMR 56
Diagnostic criteria	ICD-10 DSM-IV Gillberg´s Asperger syndrome	ICD-10 DSM-IV Gillberg´s Asperger syndrome	ICD-10 DSM-IV Gillberg´s Asperger syndrome	ICD-10 DSM-IV Gillberg´s Asperger syndrome
Measurements	DISCO ASSQ Wechsler scales Psychiatric- medical examination	DISCO VABS Wechsler scales Psychiatric-medical examination GAF score Lotter´s criteria for outcome	DISCO	DISCO VABS QOL1 QOL2 Social outcome interview

DISCO prevalence study in the Faroe Islands (I)

All children living in the Faroe Islands on December 31 2002, and born in the 10-year period from 1985 through 1994, comprised the target population. Of the total population of the Faroe Islands (47,704) 7689 children (3895 boys, 3794 girls) met these criteria. The central population register in Torshavn provided census population figures for the Faroe Islands. All schools and registers pertaining to this 8-17 year-old Faroe Islands population of children and

adolescents were screened for ASD. Cases raising suspicion of suffering from ASD (or who had already been diagnosed with ASD) were examined individually and their parents were interviewed using the DISCO. A total of 43 cases (36 boys, 7 girls) with ASD were identified.

DISCO outcome study (II, III, IV)

The participants of the studies comprised all individuals included in three partly overlapping population-based studies of children diagnosed with autism in childhood from the region of Gothenburg, Sweden (Gillberg, 1984; Steffenburg et al, 1986; Gillberg et al, 1991). A total of 120 individuals with autism or atypical autism were included in this cohort. They were now targeted for follow-up in late adolescence – adult life (Billstedt et al, 2005). The original study group was followed prospectively for a period of 13-22 years (mean age 17.8 years, 3.6 SD) and re-evaluated at ages 17-40 years (mean age 25.5 years, 6.4 SD).

Original study 1

The first study (Gillberg, 1984) included 51 children, 26 of whom met the 1978 criteria by Rutter (1978) and the DSM-III-criteria (American Psychiatric Association, 1980) for infantile autism – later shown to meet also the DSM-III-R-criteria (American Psychiatric Association, 1987) for autistic disorder, and 25 of whom met criteria for other childhood psychosis. Infantile autism was diagnosed if onset was before 30 months of age (onset documented in medical record data). All cases in this group showed aloofness and elaborate repetitive routines. They also showed severe impairment of social relationships (failure to establish peer relations and signs of aloofness) and speech-language impairment (echolalia and pronominal reversals and/or extremely delayed speech development and/or lack of communicative speech) in combination with behaviour problems dominated by stereotyped movements, repetitive routines and/or insistence on sameness. Other childhood psychosis was diagnosed in cases with similar symptomatology but for whom onset before 30 months could not be unequivocally documented in medical records. The upper limit for inclusion was onset at 10 years of age. The majority of this group has been followed-up once before (in the 1980s) at ages 16-23 years (Gillberg et al, 1987).

Original study 2

The second study (Steffenburg et al, 1986) included 52 children, 35 of whom met criteria for DSM-III and DSM-III-R infantile disorder/autistic disorder and 17 of whom met criteria for autistic-like condition. What was referred to other childhood psychosis in study 1 was referred to as autistic-like condition in study 2. Six children in study 2 had also been included in study 1, meaning that the total number remaining after pooling the two cohorts was 97.

Original study 3

In the third study (Gillberg et al, 1991) the term autistic disorder was used instead of infantile autism. The third study included 75 children, 55 of whom met criteria for DSM-III-R autistic disorder and 20 of who met criteria for autistic-like condition. All 52 cases included in study 2 were also included in study 3. Thus, when pooling the cohorts of all three studies, we were left with 120 individuals.

Final outcome study target cohort (II, III, IV)

The 120 individuals (78 with DSM-III-R autistic disorder and 42 with autistic-like conditions) from studies 1, 2, and 3 were fairly representative of all children with autistic disorder/autistic-like conditions (as conceptualized in the 1980s) born in 1962-1984 and living in the Gothenburg region at the time of the original diagnostic studies. Nevertheless, there are some caveats. The Gothenburg region was slightly differently delineated at the three census

dates. Also, differently from those born in 1975-1984, the population of children born in 1962-1974 was not re-screened in 1988. Finally, it was discovered in a later epidemiological study of severe mental retardation and epilepsy, that a small, but significant number of autistic disorder cases had been missed by the original screening procedures (Steffenburg, Gillberg & Steffenburg, 1996). There is also a possibility that some autism cases might have been missed in the population with Down syndrome (Rasmussen, Borjesson, Wentz & Gillberg, 2001; Zafeiriou, Ververi & Vargiami, 2006).

The overall outcome study (II, IV)
Out of the 120 individuals (84 males, 36 females) with autistic disorder/infantile autism (61 males, 17 females) or autistic-like conditions/atypical autism (23 males, 19 females) who were included in the original studies 1-3, 108 individuals were included in the overall outcome study (Table 4). Six of the 120 (5%) had died at follow-up (causes of death reported under Results) and 6 had relatives who declined participation.

The DISCO symptoms outcome study (III)
One hundred and five individuals participated in study III. Those 3 of the 108 individuals (see previous section) who did not participate in the DISCO symptoms study (III) failed to do so for the following reasons: (i) one man with an autistic-like condition would not give permission for his parents to be DISCO-interviewed, (ii) one parent agreed to meet the researchers together with his daughter with autism but declined to have the DISCO interview, and (iii) one parent failed to show up at the interview because of a sudden family crisis.

Age range (I-IV)
All children in the DISCO prevalence study (Table 4) were 8 to 17 years old. In the DISCO outcome studies participants´ ages ranged from 17 to 40 years.

Mental development level (I-IV)
Mental development was divided into 4 broad categories: (i) average intellectual-developmental capacity (A, IQ≥ 85), (ii) near average intellectual-developmental capacity (NA, IQ=71-84), (iii) mild mental retardation (MMR, IQ=70-50), and (iv) severe mental retardation (SMR, IQ<50). Twenty-seven percent in the DISCO prevalence study (I) belonged in the SMR category, 5 % in the MMR category, and the remaining 68 % in the NA or A category. In the DISCO outcome studies (II, III, IV) these proportions were rather different with 52% belonging in the SMR category, 35 % in the MMR category, and 13 % in the NA or A category.

Diagnostic criteria used (I-IV)
In the DISCO prevalence and DISCO outcome study (I, II), ICD-10 criteria for childhood autism and atypical autism, DSM-IV criteria for autistic disorder, and Gillberg´s criteria for Asperger syndrome (1989, 1991) were used. The Gillberg´s criteria were chosen in favour of the ICD-10/DSM-IV criteria for Asperger syndrome/Asperger´s disorder because they have been shown to be unrealistic for clinical purposes (Leekam et al, 2000). Very few, if any , individuals really meet ICD-10/DSM-IV criteria due to the insistence in these manuals on normal development in the first three years of life, including not only normal intellectual and language development but also normal curiosity about the environment.

Clinical best-estimate “gold standard” diagnoses were made by the clinicians after personal examination of the children and interviews with parents (and staff in many cases). Separate

DISCO algorithm diagnoses were made by the computer. The results of the DISCO algorithm procedure were not known when the clinical diagnoses were made.

Instruments

The instruments used in the different studies were briefly reviewed in Table 4.

Diagnostic Interview for Social and COmmunication Disorders (DISCO) (II-VI)

The DISCO is 2-4 hour investigator-based interview intended for use with a person (often a parent) who knew the individual with a suspected ASD from early childhood. The DISCO is highly valid for assigning diagnoses (including common comorbidity diagnoses) in the autism spectrum and the inter-rater and re-test reliability are excellent (Wing, Leekam, Libby, Gould & Larcombe, 2002; Nygren, Billstedt, Hagberg, Gillberg & Johansson, 2007). Because of the DISCO design with its inclusion of a range of items intended to detect milder forms of ASD, it was chosen rather than the Autism Diagnostic Interview - ADI, (LeCouteur et al, 1989) - which is a similar interview widely used. Other reasons for choosing the DISCO include the fact that it has a developmental perspective, is specifically intended for use throughout the person's lifespan, has computerized algorithms for diagnoses of a wide variety of operationalized ASD categories, and that it covers a number of symptoms often encountered in ASD but which are not necessarily part of the core diagnostic triad. The DISCO algorithm enables decision to be made whether the criteria necessary for the following diagnoses are present: Pervasive Developmental Disorders (ICD-10 (WHO, 1993), DSM-III-R (APA, 1987), DSM-IV (APA, 1994)), Kanner's Early Infantile Autism (Kanner et al, 1956), Asperger syndrome (Gillberg et al, 1989), Autistic Spectrum Disorder (Wing et al, 1979) and social impairment (Wing et al, 1979).

The (first) forerunner of the DISCO was the "Childhood Behaviour Schedule" which was designed for use in a study comparing children with autism with those who had Down's syndrome, developmental receptive language disorders, developmental expressive language disorders, and children with partial sight/partial hearing. This schedule contained information concerning behaviour and symptoms encountered in autism including the social, language, imaginative and motor impairments and the odd responses to sensory input and stereotyped behaviour (Wing, 1969; Wing & Wing, 1971).

This schedule was then reorganized and expanded to include items on developmental skills and was renamed the "Handicaps, Behaviours and Skills (HBS) Schedule" (Wing et al, 1978). The HBS was used in an epidemiological study of ASD in Camberwell (Wing, 1980, 1981; Wing et al, 1979) in the Southeast of London. It was also used in a follow-up study of children into adult life (Wing, 1988), and in several diagnostic studies of autism in Gothenburg (e.g. Steffenburg et al, 1996).

The DISCO is a further development of the HBS, and is now in widespread international clinic and research use. Its psychometric properties have been shown to be very good in studies in the UK (Wing et al, 2002), Sweden (Nygren et al, 2007) and the Netherlands (van Berckelaer-Onnes et al, 2007, personal communication).

The authorized Swedish translation of the DISCO by Maria Johansson and Christopher Gillberg was used in the present study.

The Wechsler scales (I, II)
The Wechsler intelligence scales for adults (WAIS-R) (Wechsler, 1981) and for children (WISC-R and WISC-III) (Wechsler, 1981, Wechsler, 1992) are well-established IQ-tests, including full-scale IQ (FSIQ), and subtests for verbal IQ (VIQ) and performance IQ (PIQ). In the Faroese prevalence study the WISC-III was given to 26 children (by the Faroese psychologists). In the follow-up study one of these tests was given to 25 individuals (WAIS-R n=17, WISC-III n=8) (by the author).

The Vineland Adaptive Behavior Scales (VABS) (II, IV)
All individuals participating in study II, III and IV, including those taking the WAIS-R or the WISC-III, were given the VABS (Sparrow, Balla & Cicchetti, 1984). The VABS is an informant-based measure of adaptive behaviour with four major domains that are assessed: communication, daily living skills, socialization and motor skills. These domains yield an adaptive composite score and an age-equivalent. Since the motor domain is not administered for ages older than 6 years, this domain was excluded in the present study. Among many other things, the VABS yields a reasonable estimate of whether or not an individual belongs in the SMR category.

Psychiatric medical examination (II-IV)
In the DISCO prevalence study (I) additional expert psychiatric-medical assessments were done in children where there was any degree of uncertainty regarding ASD category classification (n=5). In the DISCO outcome study (II) psychiatric-medical examinations comprising observation and a semi-structured interview with verbal subjects or with a parent (or another person close to the individual with autism), were performed in all cases. This interview covered - among other things - problem behaviours, hyperactivity, violent and self-injurious behaviours, and medical history.

Global Assessment of Functioning scale (GAF) (II)
The DSM-III-R Global Assessment of Functioning scale (GAF) (American Psychiatric Association, 1987) was used in all cases in study II. This measure yields scores ranging from 0-100, 70 and above indicating good functioning or only mildly abnormal psychosocial situation.

Criteria for poor and good outcome (II)
A set of criteria was used in study II for the classification of outcomes, similar to those employed in the original study 1 at 16-23 years by Gillberg and Steffenburg (1987). This classification, in turn, was based on the outcome criteria published by Lotter (1978). Reliability studies – to our knowledge – have not been performed. The classifications were made by the first and second author conjointly and were based on all available information (including that from the DISCO) at the time of examination. The outcome criteria were:
Good outcome: (a) being employed or in higher education/vocational training, and, (b) if over the age of 23 years, living independently, if 22 years or younger, having two or more friends/a steady relationship;
Fair outcome: either (a) or (b) under very good outcome;
Restricted but acceptable outcome: neither (a) nor (b) under good outcome, and not meeting criteria for a major psychiatric disorder other than autistic disorder or another autism spectrum disorder. This category refers to a group of people with the characteristics of poor outcome but who have been accepted by a group of peers or personnel to such an extent that their handicaps are not so readily obvious;

Poor outcome: Obvious severe handicap, no independent social progress, some clear verbal or non-verbal communicative skills;
Very poor outcome: Obvious very severe handicap, unable to lead any kind of independent existence, no clear verbal or non-verbal communication.

Two dimensions of Quality Of Life (IV)
Quality Of Life measure 1 (QOL1):"Autism-friendly environment"
A "level of fit" five-item scale was developed so as to provide an overall measure of quality of life for the individuals in our follow-up study. Each of the five items on the scale is for global assessment (based on all available information) of a category, and is rated on a 1-5 scale (1= very good, 2= good, 3= medium, 4= poor, 5= very poor). The item categories are:
(a) Staff and caregivers have specific "autism-knowledge", i.e. they are aware of the core features, including communication problems, associated with ASD;
(b) Applied structured education implemented;
(c) Individual specific treatment/training plan for the person with autism implemented;
(d) Occupation or everyday life activity corresponding to his/her level of capacity implemented;
(e) Overall quality of life level.
The ratings were based on a combination of information provided by the (i) general impression, (ii) observations made during visits at group-homes, schools and other occupational settings, and (iii) information from interviews with staff, caregivers and with the individuals themselves.

Quality Of Life measure 2 (QOL2): "Parent/carer-rating of individual's well-being"
Parents/caregivers were asked to estimate how the individual with autism enjoyed/liked his/her residential conditions. They were asked to rate this on the same type of 1-5 scale as used for QOL1. A rating of 1 indicated very good, and a rating of 5 very poor well-being in the residential setting.

Ethics
The epidemiological study in the Faroe Islands was approved by the Scientific Ethics Committee of the Faroe Islands. The Medical Ethical Committee of Gothenburg University approved the Swedish follow-up study.

Statistical analyses
In the DISCO prevalence study (I) Poisson-distributed 95% confidence intervals (CI) were calculated for population absolute rates and overall prevalence rates. In the DISCO outcome studies (II, III, IV), group differences were examined using chi-square tests, with Yates´s correction whenever appropriate. Means were compared using Fischer's non-parametric permutation test (II), and Fischer´s exact test was used when comparing group frequencies (IV). In the outcome studies, stepwise regression techniques were used in the analysis of background factors and their contribution to DISCO symptomatology (III) and to QOL1 (IV). Pearson correlation was used to investigate the relationship between DISCO items for ASD (Wing et al, 1979) and symptoms (III). Inter-rater reliability was examined using intra-class correlation (ICC).

RESULTS

Prevalence of autism (I)

Forty-one children in the target population were found to have an ASD. Seventeen individuals (41%) had been diagnosed clinically as suffering from ASD before the study took place. Two further children had been diagnosed (by an independent child psychiatrist) to have an ASD before the study began, but their parents declined participation (Table 5, Table 6).

Including these two individuals in the estimation of overall prevalence, the rate of ASD in the group of children aged between 8 and 17 years was 0.56% (CI 0.38-0.73%). Another 4 children were suspected of suffering from Asperger syndrome in the screening part of the study, but were not included in the study because the families refused further participation (and hence refused to take the DISCO).

Childhood autism accounted for 29%, Asperger syndrome for 49% and atypical autism for 22% of all ASD cases.

Only 7 girls were found to have a clinical ASD diagnosis, corresponding to a total population girl prevalence rate of 0.19% (7/3794), and a total population boy prevalence rate of 0.92% (36/3895). The overall population-adjusted male:female ratio was 4.8:1.

Table 5. Rates of clinical diagnoses of ASD in the Faroe Islands (based on 41 examined cases)

Clincal diagnosis	Boys *n*	Boys population prevalence (%)	Girls *n*	Girls population prevalence (%)	Total *n*	Total population prevalence (%)	CI lower	CI upper
Childhood autism	9	0.23	3	0.08	12	0.16	0.07	0.25
Asperger syndrome	17	0.44	3	0.08	20	0.26	0.14	0.38
Atypical autism	9	0.23	0	0.0	9	0.12	0.04	0.20
ASD total	35	0.90	6	0.16	41	0.53	0.36	0.70

95% confidence interval (CI) calculated from exact Poisson distribution

The prevalence rates of childhood autism in younger children appeared to be higher than in older children, but the trend was not statistically significant. In the other diagnostic subgroups there were no trends either way.

Table 6. Number of cases with ASD in the Faroe Islands: year of birth

Year of birth (n of birth cohort)	Childhood autism	Asperger syndrome	Atypical autism	All ASD	CI lower	CI upper
1985 (683)	1	3	0	4	0	8
1986 (658)	2	2	0	4	0	8
1987 (746)	0	1	0	1	0	3
1988 (799)	0	4	0	4	0	8
1989 (838)	0	2	2	4	0	8
1990 (884)	2	2	3	7	1	13
1991 (818)	0	2	1	3	3	7
1992 (771)	2	2	1	5	1	10
1993 (740)	3	0	0	3	0	7
1994 (716)	2	2	2	6	1	11
1985-1994 (7689)	**12**	**20**	**9**	**41**	**28**	**54**

Diagnostic aspects: clinical diagnoses in the child population (I)

The target study group in the prevalence study from the Faroe Islands comprised 43 children (two of whom did not take part in the DISCO part of the study but had received expert diagnoses of childhood autism in one case and Asperger syndrome in another). As already mentioned, about 30% of these had ICD-10 childhood autism, 50% had Gillberg's Asperger syndrome and 20% had ICD-10 atypical autism. No cases of disintegrative disorder were identified in this population.

The population adjusted male:female ratios in the ASD diagnostic subgroups were 2.9:1 in the childhood autism/autistic disorder group, and 5.5:1 in the Asperger syndrome group. No girl was found with atypical autism.

Diagnostic aspects: stability of clinical diagnoses from childhood through adolescence and into adult age (II)

In the DISCO outcome study, the majority of individuals with an original diagnosis of autistic disorder (62 out of 73) in childhood, still met clinical diagnostic criteria for this condition at follow-up, while 10 individuals with an original autistic disorder diagnosis met criteria for atypical autism/autistic like condition. One man, with autistic disorder and normal IQ in childhood, did not meet any criteria for ASD in adulthood.

The majority of those with atypical autism in childhood, met criteria for autistic disorder at follow-up, 29 of 35 (83%) examined individuals. The remaining 6 individuals still met criteria for atypical autism at follow-up.

The overall male: female ratio was 2.5:1. The male:female ratios in the ASD diagnostic subgroups were 2.6:1 in the autistic disorder, and 2.2:1 in the atypical autism group.

Diagnostic aspects: clinical versus DISCO diagnoses (I, III)

DISCO diagnoses in the prevalence study in the Faroe Islands (I)

In the prevalence study in the Faroe Islands (I), DISCO algorithm criteria for ICD-10 childhood autism were met by 11 out of 12 cases (91%) in the clinical autism group (Table 5, Table 7). The child with childhood autism who did not receive an ICD-10 diagnosis according to the DISCO algorithm met the DISCO algorithm criteria for PDD-NOS (DSM-IV). All in this group also met Wings and Gould´s criteria for social impairment. Only one child, a child with a clinical childhood autism/autistic disorder, met DISCO algorithm for Kanner´s autism (corresponding to a prevalence rate of 1.3 in 10,000 children). None of the children with a clinical diagnosis of autistic disorder/childhood autism met DISCO algorithm criteria for ICD-10 atypical autism, ICD-10 Asperger syndrome or Gillberg´s Asperger syndrome. The girls (n=3) with clinical childhood autism all met DISCO algorithm for ICD-10 childhood autism.

Six of 9 (67%) in the clinical atypical autism group met DISCO algorithm criteria for ICD-10 atypical autism, whereas only 2 met DISCO algorithm criteria for DSM-IV PDD-NOS. Two individuals in the atypical autism subgroup met the DISCO algorithm criteria for ICD-10 Asperger syndrome. Nobody in the clinical atypical autism group met DISCO algorithm criteria for ICD-10 childhood autism. Only 3 of those with a diagnosis of "atypical autism" met Wing and Gould´s algorithm criterion for " social impairment", which is based on one single (albeit important) item. In the DISCO criteria for atypical autism and Asperger syndrome, this item is but one among several social impairment items. Thus, the individual might be socially impaired (as was the case in all 9 cases with a diagnosis of atypical autism in this study) even though Wing and Gould´s specific algorithm criterion for " social impairment" may not be met.

Table 7. DISCO-10 diagnoses in DISCO prevalence study and DISCO outcome study

DISCO diagnosis	Clinical diagnosis study I			Clinical diagnosis study III		
	AU *n*=12	Atyp *n*=9	AS *n*=20	AU *n*=89	Atyp *n*=15	AT *n*=1
Childhood autism (ICD-10)	11	0	10	82	3	0
Atypical autism (ICD-10)	0	6	0	7	12	0
Asperger´s syndrome (ICD-10)	0	2	7	0	0	0
Asperger syndrome (Gillberg & Gillberg)	0	0	16	13	1	0
PDD-NOS (DSM-IV)	1	2	4	8	8	0
social impairment (Wing & Gould)	12	3	20	89	15	1
Early infantile autism (Kanner)	1	0	0	15	0	0

AU=autism, Atyp=atypical autism, AS=Asperger syndrome, AT=autistic traits

In the clinical Asperger syndrome group, 16 of 20 (80%) met DISCO algorithm for Gillberg´s criteria for Asperger syndrome and 7 individuals (35%) met DISCO algorithm for ICD-10 criteria for Asperger syndrome. Half the group (50%) with a clinical Asperger diagnosis also met DISCO algorithm criteria for ICD-10 childhood autism. Four individuals in the clinical Asperger group met DISCO algorithm criteria for DSM-IV PDD-NOS. All individuals (100%) in the clinical Asperger syndrome group met DISCO algorithm criteria for Wing and Gould's social impairment.

DISCO diagnoses in the DISCO outcome study (II, III)
Eighty-two of 89 (92%) in the clinical autistic disorder group (follow-up diagnosis), met DISCO algorithm criteria for ICD-10 childhood autism and the remaining 7 individuals in this group (8%), met DISCO algorithm criteria for ICD-10 atypical autism. All individuals met criteria for social impairment. Fifteen individuals (17%) met Kanner´s criteria for early infantile autism, and another 13 individuals (17%) met Gillberg & Gillberg´s criteria for Asperger syndrome. No one met DISCO algorithm criteria for ICD-10 Asperger syndrome.

In the clinical atypical autism group, 3 of 15 individuals (20%) met the DISCO algorithm criteria for autistic disorder and 12 individuals (80%) met the DISCO algorithm criteria for atypical autism. DISCO algorithm criteria for DSM-IV PDD-NOS were met by 53% (n=8) in this group. All individuals in the group (n=15) met criteria for social impairment. One man (7%) met the criteria for Asperger syndrome according to Gillberg & Gillberg, and none in this group met Kanner´s criteria for early infantile autism.

The individual with a diagnosis of childhood autism in childhood and with no clinical diagnosis of childhood autism or atypical autism at follow up, though still exhibiting some autistic traits, met DISCO algorithm for social impairment.

Mortality (II)
At follow-up, 6 of the 120 individuals with autism/atypical autism (5%) had died. They were 7, 10, 15, 18 and 19 years at the time of their death. The cause and time of death could not be determined in one case. The causes of death in the other five cases were (1) status epilepticus (a girl with "idiopathic" autistic disorder), (2) unknown but occurring during sleep and suspected of being associated with status epilepticus (a girl with autistic disorder diagnosed in early childhood, many years later shown to be suffering from Rett syndrome), (3) accidental major fire in one case (a boy with autistic disorder/fragile X syndrome), (4) complications after major heart surgery in one case (a boy with autistic disorder, trisomy 13, and a major heart malformation), and (5) brain tumour in one case (a girl with atypical autism).

Epilepsy (II)
At least 40% of the total cohort of 120 in the DISCO outcome study had/had had epilepsy. Forty-three per cent of the 108 individuals examined had had epileptic seizures in the past or continued to have epilepsy at the time of the follow-up study. At least two of the remaining 12 who did not take part in the follow-up, had had epilepsy in the past and one of these had died from status epilepticus. The epilepsy subgroup was included in a study by Danielsson, Gillberg, Billstedt, Gillberg, and Ohlsson (2005) performed one year later than the DISCO outcome study. In this epilepsy study one further individual had been diagnosed as suffering from a seizure disorder with an onset after 30 years of age.

Medical conditions (II)

A "syndromal" medical disorder was present in 27 individuals (23%) (which was already known in the original diagnostic studies). The medical disorders were the following: tuberous sclerosis (1), neurofibromatosis (4), fragile X syndrome (9), Moebius syndrome (3), Rett syndrome (3), Williams syndrome (1), operated hydrocephalus (1), or another named/known syndrome (5).

The fragile X syndrome group constituted a relatively large subgroup. This subgroup tended to do a little better at follow-up than the others who had an associated medical disorder. In the subgroup of 9 individuals with fragile X syndrome, there was one death, but the mean GAF-score in those 8 living at the time of follow-up was 33.2 (SD 19.3, range 12-62) to be compared with 11.7 (SD 6.2, range 3-26) in the remainder with a medical disorder (Fisher non-parametric permutation test, $p<0.001$).

Medical problems as part of one or other of the mentioned medical disorders were quite common. In addition, two women and one man suffered severe attacks of "migraine". Two men had chronic nocturnal enuresis. Two men had severe atopic dermatitis. One young man had a stricture of the oesophagus after eating dishwashing powder. Another man had recently suffered severe anaemia and had had to be transfused after regurgitation and chronic oesophageal bleeding. One of the young women with psychosis had developed diabetes mellitus. Several individuals had been operated on because of epilepsy (2), heart conditions (2, of whom 1 had a chromosomal disorder), scoliosis (3, of whom 1 had Rett syndrome), or shortening of the Achilles tendon (5, of whom 2 had Rett syndrome). Except for one woman with chronic eye-infections due to faecal smearing, and one man with chronic skin infections due to auto-mutilation, severe infections were not reported in any of the 108 individuals examined.

Although these individuals had a high rate of medical problems, the general impression from the interviews with parents/carers was that a many were very rarely ill with common colds, flu or other infections.

The course of intellectual/general level of functioning (II-III)

In the DISCO outcome studies, both the autism group and the atypical autism group had been tested before age 10 years with an age- and ability-appropriate neuropsychological, developmental, or social developmental test. At follow-up 25 individuals included in the study were able to take a complete IQ-test. However, 108 were assessed using VABS allowing us to make reasonable clinical assessments regarding whether or not an individual should be diagnosed as belonging in the SMR category (Table 8).

SMR at follow-up was found in 68% in the autistic disorder group and in 77% in the atypical autism group (n.s.). The corresponding rates at original diagnostic study had been 46% and 48% (n.s). Correspondingly, MMR was found in 25% and 20% of the groups (n.s.), NA in 3% and 0% of the groups (n.s.), and A in 4% and 3% of the groups (n.s.).

Of those 25 individuals who were tested with an IQ-test (not just the Vineland) both in childhood and at follow-up, 7 had a drop in IQ of 15 points or more, 2 had a drop of 10-14 points, and the remainder had no a major downward shift of IQ (<10 points).

Table 8. The course of intellectual level of functioning in the outcome study

The course of intellectual/ developmental level of functioning	Level of functioning in the autism/atypical autism group at follow-up				
	SMR	MMR	NA	A	Total
Improved level	0	1	0	0	1
No change	54	17	2	4	77
Deteriorated level	23	7	0	0	30
Total	77	25	2	4	108

Overall, collapsing the autistic disorder and atypical autism groups, there was a downward shift of IQ-level from the diagnostic study to the follow-up evaluation. Fifty-six of the original 120 children had been diagnosed as having SMR in the first study. At follow-up, 77 of 108 (71%) were diagnosed in this category ($p<0.001$, $X^2=14.2$, df 1).

In the analysis of the VABS scores, uneven profiles of adaptive behaviour were found. Particularly low scores in the areas of socialization, and, to a lesser degree, in communication were found independent of IQ-level.

Puberty/adolescence (II)

All the participants in the study were postpubertal or (in a few instances) late pubertal. In the DISCO outcome study, 38% had had a remarkably problem-free adolescent period. However 31% had shown major problems and more than half of these had deteriorated significantly in puberty. Altogether 17% of the 108 examined were reported to have had a clear setback in puberty and half of these never really recovered. Data on pubertal onset was available in 98 cases (parents report). In 22 cases (20%) onset was ”late” (n=8) or reported to have occurred at or after age 16 years (n=14). In 3 cases onset of puberty was reported to have occurred at or under 10 years of age.

Overall outcome (II-IV)

When using the Lotter criteria for outcome in the DISCO outcome study II, 57% had a very poor outcome with no statistically significant differences across the subgroups (autistic disorder vs. atypical autism), 21% had poor outcome, 13% had restricted but acceptable outcome, 8% had fair outcome, and none had good outcome.

More than half of the group had a very poor outcome with a very severe handicap, a very high level of support and no clear verbal or non-verbal communication. Childhood IQ-level was positively correlated with better adult outcome.

The GAF-score correlated to the outcome criteria. The mean GAF-score for the whole group was 21.1 (SD 16.4, range 4-67). Thirteen individuals (12%) of the 108 examined at follow-up had GAF-scores of 50-69 indicating moderate or mild psychiatric problems or functional impairment. Of these, 6 had had an IQ of 70 or above, whereas the remaining 7 tested in the MMR range.

Improvement in a small subgroup
A subgroup, in the group of individuals who originally received an autistic disorder diagnosis, was diagnosed as having atypical autism/autistic traits at follow-up. This subgroup consisted of three men who, in spite of still showing autistic features had better outcomes in terms of independency, occupation and social relations. The only denominator found in this subgroup was that all three had had some communicative speech at age 3 years. Only three further individuals in the whole study had similar speech development (information missing in one of the 108 cases) as the three with relatively better outcomes. These three did not have an outcome as good as the three men in the subgroup, concerning independency, occupational and social relations. The latter group of three comprised one woman, and one man, who developed epilepsy which influenced their language development and general outcome, and one man who developed psychosis that had an effect on his general condition and outcome. - Of course, no definite conclusions can be drawn on the basis of findings from just three individuals but it is remarkable that all three (100%) with the best outcomes in the study had some communicative spoken language at age 3 years and that only 3 % of those who did not have similarly good outcomes did.

Psychosocial outcome
A large majority in the DISCO outcome study group had been, and still were, very dependent on others for support during school years, in their occupational and residential situation.

Educational background
A majority of the group attended school for individuals with learning disabilities (93%). Of the 8 who had attended a mainstream school, 5 had received assistance in school and 3 individuals did not receive any specific assistance. Four individuals completed the mainstream high school and one of these obtained an academic degree from a regular university.

Residential situation
A majority of the study group lived in community based group homes (49%) or in their parents home (38%). The minority who lived in their own apartments had some support, either from the community (8%) or from their relatives (4%). Only one man lived in his own apartment (with his girlfriend) without any community/parent help (1%).

The occupational situation
The occupational situation corresponded to educational history and residential situation in regard of a high level of support. Twenty seven percent were still in high school, but for the group who had finished school, work activity centres for people with disabilities dominated (48%). There was a small group (7%) who had supported employment at regular place of work. Sadly, there was a large minority who had no daytime occupation except for some daily routines, e.g., taking a stroll daily or to leave the daily newspaper in a recycling container once a day (18%).

Access to medical services
Forty-nine percent of the individuals in the DISCO outcome study had a major medical problem (whether related to an underlying medical disorder possibly directly associated with autism or not) needing regular medical attention. Seventy individuals (65%) had access to a doctor for their psychiatric or neurological problems demanding medical treatment. The need for medical services was expressed for another 4 individuals (4%) who had not received the

proper services that they should be getting. Thirty individuals (28%) required no regular access to medical services (missing information in 2 cases).

Two dimensions of Quality Of Life (IV)

QOL1

The results from the two quality of life scales, QOL1 and QOL2 were remarkably positive. On the QOL1, based on the items concerning staff/professionals knowledge in autism, applied structured education, existence of specific treatment/training plan, and an adjusted everyday occupation, received all relatively high scores but with somewhat lower scores on the item concerning everyday occupation. In the estimation of the overall quality of life, 62 % had a good or very good quality of life, 26% had a medium quality of life and 12% had a poor or very poor quality of life.

QOL2

The results from QOL1 were supported by QOL2 on which 91 of 100 were reported to have a high or very high quality of life. Five individuals were reported to have a medium quality of life, and only 4 had a poor or very poor quality of life on QOL2.

Further aspects of quality of life

Leisure activities

Regular recreational activities involved one third of the study group (33%), often arranged by the group home. Having a friend was not common in this group (12%), but 11% were reported to wanting friends but not having the capacity to form friendships.

Sexuality

Sexual interests were reported in sixty-four of 95 individuals (67%, missing information in 13 cases) and 31 (33%) as having no evident sexual interest. Of the 64 individuals who had an obvious sexual interest, 43 (73%) had sexual behaviours that appeared to be intentional and person-oriented whereas 16 (27%) individuals had sexual behaviours that appeared to lack sexual intent (missing information in 5 individuals). Inappropriate sexual behaviours including masturbation in public or indecent exposure were reported in 15 (16%) individuals. An additional 7 (6%) individuals had prior a history of such inappropriate sexual behaviour. Seventy-nine individuals (84%) out of 94 (missing information in 14 cases) were reported to not have been engaging in inappropriate sexual behaviours**.**

Co-occurrence with other problems (II)

Psychiatric disorder

Psychosis

Psychosis had been diagnosed by independent adult psychiatrists in 8 individuals (5 males, 3 females). One of these (a man) had been diagnosed as having schizophrenia, and one other (also male) had been diagnosed as suffering from bipolar disorder. The medical histories of four further individuals suggested the presence of bipolar disorder, but the psychiatric diagnosis in their medical records was unspecified “psychosis”.

Tics

Simple or complex motor or vocal tics were reported in 23% of the group and one further individual had a severe form of Tourette syndrome.

Catatonia, catatonic features
The child psychiatrist in the outcome study had made clinical diagnoses of catatonia in 13 individuals with severe motor initiations problems. According to the results obtained at DISCO interview, 4 further individuals had catatonic features. Fourteen of these 17 individuals (82%) were 25 years or older. No one in this group had been diagnosed as having psychosis by independent psychiatrist. Six of the 17 individuals (35%) had no speech at follow-up. The male: female ratio in the group with catatonia/catatonic features was 1.7:1.

Hyperactivity and self-injurious acts
Hyperactivity was reported in 36 individuals (33%) at follow-up. Twenty-three of those 36 who showed persistent hyperactivity were also engaging in self-injurious acts. According to the results from the DISCO, a total of 54 individuals (51%) hade engaged in moderate or severe degrees of self-injurious behaviour at some point during their development.

Medication
All individuals with a diagnosis of "psychosis" were on lithium medication, possibly indicating an important quality of mood swings in the "psychotic" condition.

Thirty-five individuals (32%) were prescribed neuroleptic medication by independent psychiatrists. The reasons given for medication were "behavioural problems", often dominated by impulsive and violent outbursts, self-injury, and sometimes also because of hyperactivity.

Thirty-one percent in the total group (n=108) used antiepileptic medication for epilepsy and another 14 % were given antiepileptic medication for major behavioural problems.

There was a significant correlation between the use of antiepileptic and neuroleptic medication ($p<0.01$). There was also a correlation between neuroleptic medication and depression ($p<0.01$), self-injurious behaviours ($p<0.05$) and obsessive behaviours ($p<0.05$). IQ ($P<0.05$), and violent behaviours ($p<0.05$) were correlated with antiepileptic medication. There was also a, rather unexpected, correlation between antiepileptic medication and good or very good quality of life (according to QOL1) ($p<0.05$).

No correlation was found between medication (antiepileptic or neuroleptic) and catatonia, gender, social phobia, hyperactivity, or tics.

Manifestations of autism in adulthood – symptoms according to DISCO-interview (III)
Social interaction
Overall rates of abnormal social behaviour were high in adulthood. The quality of the interaction was, when it occurred, inappropriate (92%), and social approaches were often one-sided (90%). Interaction with age peers was uncommon and often reported to be led by others (90%), or avoided (78%), and lack or inappropriate emotional response to age peers was often reported (84%). No or inappropriate sharing of interest and enjoyment (80%) and no adequate giving of comfort (79%) or not seeking comfort in an adequate way when in pain or in stress (72%) were reported in a large majority. Reaction/response to physical affection was often inappropriate or missing (70%), and there was a lack of behaviours indicating awareness of feelings of others (77%). In the study group there was often reported an inappropriate or missing reaction to other's happiness (58%). The response to visitors was reported to be

inadequate in 50 % of the group. Eye contact was reported to be poor or missing in half of the group (50%) and to be blank and unfocused (51%).

Communication
Lack of reciprocity in communication was a common problem (83%). Inability to smile on request (74%), limited or odd facial expression (67%) and abnormal tone of voice (53%) were also often reported. Autism communication problems typical of early childhood, such as immediate echolalia (32%) and delayed echolalia (37%) were not as prevalent in adulthood.

Maladaptive behaviours, repetitive stereotyped activities, and odd responses to sensory stimuli
Maladaptive behaviours often mentioned included laughing for no reason (67%), needing constant supervision (59%), lacking co-operation (59%) and lacking psychological barriers (55%). Temper tantrums were reported in 50% of the group.

According to the results from the DISCO-interviews, a large majority of the group was very limited in the number of their activities On the matter of self-chosen activities; repetitive activities were the only choice or a prominent part in the majority of the group (87%). The need for maintaining the sameness in routines was recognized as a common feature (62%).

A total of 98 out of the 105 (93%) who had a completed DISCO were reported to have some kind of impairing sensory abnormality. Various types of abnormal responses to touch were most common, affecting 88% of the study group. Sixty-six percent of the study group reported to have abnormal responses to auditory stimuli, and 45% showed abnormal responses to visual stimuli. A large proportion of the study group reacted with dislike to firm touch (60%) (and almost half of all individuals reacted in unexpected ways to gentle touch, 49%). Indifference to pain, heat and cold (58%) and acuteness of hearing (53%) were reported to occur in more than half of the study group.

As reported above, about half the study group (51%) had been engaging in moderate or severe degrees of self-injurious behaviours at some point during development, according to the result from the DISCO interviews. Other aspects that were reported in more than half of the study group were the lack of awareness of suitability in clothing (75%), poor co-ordination in physical education and games (67%) and immature gait when walking (56%).

Background factors

Background factors, documented prospectively in the records from the original studies, were correlated to 3 core items of Wing and Gould´s DISCO-algorithm for autistic spectrum disorder. The items concerned the quality of social interaction (aloof, passive, active but odd, over-formal, shy, electively mute, chatty/friendly (typical of Williams syndrome), vs. appropriate), individual's style of communication (communicating only needs, one-sided and repetitive, vs. truly reciprocal) and the overall pattern of activities (narrow and repetitive, vs. varied and flexible). The 4 remaining items (concerning imagination and pretend play) in this algorithm were omitted because many parents/caregivers were able to provide only partial information for these items. The ASD items were related to the following background factors derived from the original studies: gender, childhood IQ-level, presence of some communicative speech before 5 years of age, early onset epilepsy (onset before 5 years of age), later onset epilepsy (onset after 5 years of age up until one year before the date of follow-up) (data on epilepsy onset as evidenced by recording in childhood files), medical disorders regardless of presence or not of epilepsy (as detailed in medical records at the time

of the early childhood population studies), and immigrant parents (at least one parent born in a foreign country). Whether or not there had been some degree of intelligible communicative speech present before age 5 years had been recorded systematically in the original childhood case records held for all individuals included in the study.

Childhood predictors of adult quality of social interaction
Speech before 5 years of age, and childhood IQ each showed a strong correlation with the DISCO-ASD-algorithm item for quality of social interaction at follow-up. Early onset epilepsy and female gender correlated, but to a lesser degree, to more abnormality as regards quality of social interaction. In the stepwise regression analysis, speech before 5 years of age and female gender emerged as predictors, together accounting for 45% of the variance.

Childhood predictors of adult reciprocal communication
Speech before 5 years of age, and childhood IQ were the strongest single childhood predictors of outcome as regards the DISCO-ASD-algorithm item for reciprocal communication. Early onset epilepsy also correlated (negatively) with more abnormality on this item but to a lesser degree. In the stepwise analysis of background factors, speech before 5 years of age, and childhood medical disorders accounted for 39% of the variance.

Childhood predictors of limited adult pattern of self-chosen activities
Speech before 5 years of age, and childhood IQ were also the factors that correlated most strongly with the item concerning limited pattern of self-chosen activities. In the stepwise analysis of background factors, they accounted for 43% of the variance.

Reported regression

Two individuals with the early childhood clinical presentation of childhood disintegrative disorder were reported by their parents to have shown regression of skills (one or more of speech, social interaction or play) at ages 3-4 years. Of the remaining 106 individuals in the study, 16 (15%) were reported by parents to have shown some degree of regression in development before 3 years of age.

In puberty, loss of skills was reported in 26/108 (24%) individuals. No significant correlation was found between early regression and regression in puberty.

Gender aspects

The overall male:female ratio in the DISCO prevalence study was 4.8:1 compared to 2.5:1 in the DISCO outcome study. There was no significant difference between the male:female ratio in the ASD diagnostic subgroups in the outcome study (2.6:1 in the autistic disorder, and 2.2:1 in the atypical autism group), as opposed to in the prevalence study where the male:female ratio for autistic disorder was 3:1 and 5.7:1 in the Asperger syndrome group. No girl was found with atypical autism in the DISCO prevalence study.

There was no statistically significant association between female gender and overall outcome, GAF-scores (a non-significant trend for better outcomes in females was noted for this variable), or detoriation in adolescence, in the DISCO outcome study. The only association that was found as regards behavioural/psychiatric symptoms was between female gender and obsessive behaviour ($p<0.05$). However, no correlations were found between gender and medication (neuroleptic or antiepileptic medication), aggressive behaviour, depression, self-destructivity, overactivity, tics, IQ, catatonic behaviour (even though the male:female ratio in

this category is more even in the overall male:female) or estimation of quality of life (according to QOL1).

An association was found between female gender, SMR and epilepsy. In the group with epilepsy and SMR the male:female ratio was 1:1.8, and in the group with no epilepsy and SMR the male:female ratio was 4.8:1 (<0.05). All except one of the females in the study who had epilepsy also had SMR. Fifty-five percent of the female study group and 28% of the male study group had epilepsy with SMR ($p<0.05$).

DISCUSSION

Implications of the present study findings

The prevalence study yielded findings comparable to those of the majority of recent studies reporting on autism prevalence. The concept of ASD used in that study included the various categories subsumed in most current diagnostic systems, i.e. not only autistic disorder and atypical autism/PDD-NOS, but Asperger syndrome as well. The findings in our outcome study group are similar to those reported in the older literature on long-term prognosis in autism. Unlike the prevalence study ASD cohort, the outcome study group represented the older conceptualisation of autism as a condition that is commonly associated with mental retardation and occurs three times more frequently in boys than in girls. Asperger syndrome cases were not included at all in this substudy. In other words, the outcome study relates to individuals diagnosed as having typical or atypical autism 15-30 years ago and this sample is probably not representative of all individuals currently diagnosed as having ASD. The sample followed up is certainly not typical of high-functioning individuals with autism or Asperger syndrome. Our results can probably only be generalised to low and middle-functioning groups with autism/atypical autism. Nonetheless, the outcome was relatively poor even for those, admittedly few, individuals with autism with relatively higher levels of IQ. None of all the 120 individuals from the population-based groups of individuals included had a good outcome, in spite of the fact that almost 10% had normal (or low-normal) IQ in the original study.

Prevalence

Our finding of 0.56% ASD in the Faroe Islands child population is very similar to the mean prevalence of ASD of about 0.6% recently reported by Fombonne (2003). Some more recent prevalence studies (e.g. Baird et al, 2006) indicate even higher prevalence rates, above 1% ASD in the general population, with a rather wide range of minimum and maximum rates, partly depending on exactly how diagnostic algorithms are applied. The much higher rate than reported in early studies of autism is associated with the broadening of diagnostic criteria over time. At the time of the original studies in the DISCO outcome study the autism prevalence rate was estimated to be about 4 in 10.000. The findings of the DISCO outcome study – in spite of including a sample of almost only more severely affected individuals with autism/atypical autism (and some degree of learning disability in the vast majority) - actually supports the theory that the higher prevalence rates are associated with the broadening of the criteria. What was diagnosed as atypical autism a couple of decades ago are now diagnosed, under the diagnostic systems currently in widespread use, as typical autism.

Outcome

Eighty-five percent of both original diagnostic groups (typical and atypical autism) met clinical DSM-IV diagnostic criteria for autistic disorder at follow-up. This could be interpreted to mean that subdividing cases in early childhood into atypical and typical autism has little or no meaning for later outcome in terms of ability to predict diagnostic status, and that, therefore such attempts at more finely tuned diagnosis are futile. However, differences between the two original diagnostic groups have been demonstrated on biological measures in childhood, adolescence, and in early adult life (Steffenburg, 1991; Gillberg & Steffenburg, 1992; Billstedt et al, 2005) arguing in favour of subgrouping. Nevertheless, in terms of psychosocial outcome (e.g. the need for support) (Billstedt, Gillberg & Gillberg, 2007) and symptom load, the two groups were remarkably similar at follow-up.

A large subgroup in our study showed a decline in intellectual/functional ability over time. Sigman and McGovern (2005) found a similar development in a group of 48 adolescents and adults with autism who had previously been assessed at pre-school age and mid-school period. In contrast to the earlier follow-up when one-third of the children had made dramatic improvements, cognitive and language skills tended to remain stable or decline from childhood to adulthood.

The importance of speech before 5 years of age (and even before 3 years of age) is interesting regarding the accumulating evidence of a closer relationship between specific language impairment and autism (Contin-Ramsden, Simkin & Botting, 2006).

DISCO as a diagnostic instrument in childhood

The correspondence between clinical gold standard diagnoses and DISCO-algorithm diagnoses was very good in a vast majority of cases in the Faroe Islands prevalence study. However, given that the same two psychologists who made the gold standard clinical diagnosis of autism, atypical autism and Asperger syndrome, were also those who performed the DISCO-interviews, one cannot conclude that the validity of the DISCO for diagnosing autism is good or excellent in cases clinically diagnosed by completely independent clinicians.

DISCO as a diagnostic instrument in adulthood

The correspondence between clinical gold standard diagnoses and DISCO-algorithm diagnoses was good or very good in a large majority of the cases included in the Göteborg outcome study. In this study, an independent child psychiatrist and the author of this thesis made conjoint clinical diagnoses after reviewing all available information except the DISCO. Therefore, the good correspondence between clinical and DISCO algorithm diagnoses should be generalisable to other groups of low to middle functioning cases with autism/atypical autism. Furthermore, the good agreement between the childhood diagnosis made up to 20 years before the study and the current DISCO algorithm diagnosis argues strongly in favour of the validity of the DISCO in diagnosing autism in adults. Nevertheless, the DISCO only cannot be used as the sole basis for making diagnoses in the field of autism in adults. There is always a need to observe and psychiatrically examine the individual affected, even though the DISCO will usually be "correct" in its clinical prediction. A recommended diagnostic procedure would be one that included both independent clinical "gold standard" diagnosis *and* interview using the DISCO.

DISCO as an outcome measure

The findings of the outcome study yielded very detailed results as regards current symptomatology. This argues in favour of the DISCO as an instrument with good face validity for use in outcome studies, just as has been demonstrated to be the case for its forerunner, the HBS (Beadle-Brown, Murphy & Wing, 2005) However, we have not used the DISCO in a longitudinal prospective fashion (even though we plan to follow-up the Faroe Islands cohort after adolescence using the DISCO again) and so cannot vouch for its power when it comes to measure longitudinal "change" over long periods of time.

Quality of life

Publications on adult outcome in people with autism spectrum disorders have mainly concentrated on crude and "objective" outcome domains, such as descriptive information regarding psychiatric functioning, academic functioning, comorbidity or on the value of predictive variables related to outcome. Subjective variables, such as satisfaction and subjective well-being, have almost always been neglected in the area of autism research,

especially in the low-moderate functioning autism group. The main reason for this state of affairs is likely to be the fact that most traditional measures for quality of life are not appropriate for use in a population with severe communicative impairments (and sometimes with no obvious communicative skills at all).

In the future, scales assessing outcome in autism will need to look at new aspects of quality of life for middle and low functioning individuals in the autism spectrum. Ruble and Dalrymple (1996) have stated the need for new frameworks to characterize "good outcome" for this group and have proposed that "good outcome" might best be conceptualised within a framework that takes account of the interaction between the environment and the person with autism. This is supported by Renty and Royer´s study (2006), which showed that environment and support characteristics explained a significant amount of variance in quality of life in a group of adults with autism spectrum disorder, whereas disability characteristics per se did not. The autism-friendly environment scale developed for the present study (QOL1) has the necessary focus on the environment in which the person with autism lives. The QOL2, and the VABS also provide more information on the perceived quality of life for individuals with autism (be it through the eyes of others rather than the individuals themselves).

VABS

The VABS has been used in many other studies of individuals with autism in the past and has a good track record of being broadly applicable across the board of intellectual functioning in such groups (deBildt, Sytema, Kraijer, Sparrow Minderaa, 2005). In our study, VABS was useful in estimating the overall level of functioning and findings generally corresponded to the overall assessment made by the clinicians. The uneven and variable profiles of adaptive behaviour that were found in the groups with identical clinical diagnoses in the outcome study suggest that the VABS might contribute to the more refined diagnostic process and identification of behavioural subgroups. However, the present study did not attempt systematic evaluation of this aspect meaning that the findings can only indicate an area of more in-depth research.

QOL1 and QOL2

Our newly developed life quality measure, QOL1, relating to "autism-friendly environment" showed considerable promise. It demonstrated good-excellent inter-rater reliability for the general outcome measure, and good validity when compared to the other quality of life scale that was used (QOL2). It is important to understand that our measure has its limitation, and also raises some questions. Is it not almost impossible to assess personal "suffering" in a population with severe communicative impairments? Is it really possible to state that there is "good quality of life" in a population that sometimes engages in self-injurious behaviours? In the present state of our knowledge we have very few means of validating personal quality of life other than the information provided by the persons who know the individuals best in daily life situations (i.e. parents and other close careers).

Other instruments

Several of the IQ-tests were inappropriate, and only a minority of low and middle functioning individuals could take any of the Wechsler tests. However, in the generally much higher functioning group with ASD in the Faroe Islands, the vast majority completed such tests without major problems.

The outcome criteria used

The outcome criteria suggested by Lotter and slightly modified by Gillberg et al, (1987) seemed adequate for the purpose of following up the severely handicapped group of the DISCO outcome study. However, these criteria do not reflect the indications we had of widely variable life quality across the individuals in the study. They probably would not be well suited for the study of more high-functioning individuals with ASD, such as many of those included in the DISCO prevalence study. The Lotter criteria may be too focused on the very severely impaired group of people with ASD and possibly would not allow a differential rating of outcome in higher functioning people. It appears that there is a great need for developing new instruments for studying outcome, incorporating the "classic" outcome criteria published by Lotter, but with added items reflecting the very considerable variation in outcome and quality of life that is likely to be typical of individuals with the more broadly defined ASD that is used today. Even in relatively lower functioning cases there is possibly very variable outcomes. There is a need to separate out the effects of cognitive impairment and autism on the outcome measure of independence, which is, in essence, the main focus of the Lotter criteria. It is unlikely that individuals with autism and mental retardation should be able to achieve a very high level of independence in adult life, but this could be equally be said of individuals with mental retardation without autism.

Symptom patterns in young adult life in the outcome study

There was considerable stability of the social and communication problems from childhood to adolescence and young adult life, whereas a number of childhood type behaviour problems were reported at DISCO interview to be at moderate to low rather than high to pervasive rates. Given that there are very few studies – if any – available for head-to-head comparison, it is difficult to draw any firm conclusions in this respect on the basis of the findings reported here, but it is suggested that it is the social and communication deficits of autism that are at the root of the syndrome and that the behaviour problems are a much more variable (and perhaps not necessary) component of the core condition.

Wing and her group have reported high stability of sensory abnormalities in autism over time (Leekam, Nieto, Libby, Wing & Gould, 2006). The results from my study support their findings of an extremely high proportion in the ASD group still showing abnormal responses to sensory stimuli in adult life. It is possible that abnormal responses to sensory stimuli rather than other behaviours considered diagnostically crucial for the syndrome of autism might be part of the core condition of autism.

Background factors

In previous studies of the outcome of autism, the most consistently identified predictors of adult functioning have been early communication skills and the level of intellectual functioning (Lotter, 1974; Gillberg et al, 1987; Nordin et al, 1998; Howlin, 2000). The symptom study confirmed the importance of both of these factors.

Another background factor that correlated to outcome in the area of quality of social interaction and reciprocal communication was onset of epilepsy before 5 years of age. However, in the stepwise procedure, this factor "disappeared" and did not account for a significant proportion of the total outcome variance. Instead, in the stepwise analysis, "medical disorder" (often associated with epilepsy) was found to account for a significant proportion of the variable in terms of poor outcome of reciprocal communication in early adult life. This would seem to indicate that, at least in our group, the epilepsy per se did not

appear to contribute to poorer outcome, unless encountered in the presence of another diagnosable medical disorder (such as tuberous sclerosis or fragile X syndrome).

Psychiatric "comorbidity"

There was a relatively high rate of associated psychiatric non ASD-problems in the adolescents and adults in the outcome study. Catatonia was seen in more than one in ten individuals in the sample, which is similar to rates previously reported by Wing and Shah (2000) and Shah and Wing (2006). A small number of individuals in the study had been diagnosed as suffering from "psychosis" by adult psychiatrists, although, judging from the clinical reports, these were mostly confusional states and possible bipolar disorder rather than schizophrenia or schizophrenia-like conditions. This is also in line with findings cited by Wing (1996). The rate of other specific reported conditions – including diagnosed ADHD and tic disorders – was low, but this, at least according to the symptoms review on the basis of DISCO-reported problems – could be accounted for by the failure to diagnose such conditions by adult psychiatrists or other adult specialists, even in the presence of full blown clinical syndrome presentations of ADHD or Tourette syndrome.

The relatively high rate of associated psychiatric problems together with the high rate of epilepsy in the adult participant group probably accounted for the rather high proportion in the group who had access to a doctor for subscriptions of medicine, and for other medical procedures. Also, most of the group homes, where almost half of the participants lived, had a doctor "linked" to the group home, which, of course, is another factor that promotes easy access to medical services.

Gender aspects

The overall ASD male:female ratio was considerably higher in the Faroe Islands prevalence study than in the Göteborg outcome study. This could be taken to indicate a general difference in gender ratio across regional sites or across time. However, when broken down into diagnostic subgroups, the male:female ratio in the autistic disorder subgroups at the two sites (and at the different times of original diagnostic studies) was very similar. Much of the difference across the two studies was accounted for by the inclusion of Asperger syndrome cases in the ASD group from the Faroe Islands, a diagnostic subcategory that was not included at all in the Göteborg sample.

The relationship with gender and outcome is ambiguous in the DISCO outcome study. No association between female gender and overall outcome, GAF-scores, psychiatric coexistence (except for obsessive behaviour) or detoriation in adolescence were found. However, substantially more females than males were found to have epilepsy and SMR, suggesting that SMR and female gender might predict the development of epilepsy in autism.

Intervention/"treatments"

Many different treatment methods and interventions have been promoted to be effective, and sometimes even to provide a cure for autism. These methods have seldom been involved in controlled studies of any kind and have not been proved to be as effective as promised (Howlin, 2005). Several of the adult participants and their families in the follow-up study had experienced family therapy, holding therapy, and auditory integration training when they were younger, as an intervention for autism. The TEACCH model has had an increasing influence on the care and intervention for many of the adult participants in the study over the past ten years in Sweden. Interventions based on TEACCH guidelines have proved to be the most effective intervention so far in clinical practice, in both children and adults (Ozonoff &

Cathcart, 1998; Persson, 2000; Van Bourgondien, Reichle & Schopler, 2003). This model emphasizes structure and individualised programming. Recent research suggests that early intensive behavioural intervention, particularly focused on language skills, and on improving communication in a more general sense (Szatmari, Bryson, Boyle, Streiner & Duku, 2003) might also be effective but there is still not enough data to prove this unequivocally (Howlin, 2005).

SUMMARY

The prevalence of autism, atypical autism and Asperger syndrome in the Faroe Islands child population was 0.56%. The boy:girl ratio in the autistic disorder subgroup was 3:1 and very similar to that of autistic disorder in the outcome study. The DISCO was very useful in eliciting the information needed for a correct clinical diagnosis in the child population. The finding of this relatively high rate of ASD in the genetic isolate of the Faroe Islands is important. On the one hand, it accords well with recent estimates of ASD prevalence in other regions of the world. On the other hand, one might have expected a somewhat higher rate in the Faroe Islands, given the high rate of inbreeding. Nevertheless, it is also possible that a much smaller "autism gene-pool" exists in the isolate, and this could explain a lower than "average" rate of the disorders. Maybe both types of factors are in operation and outweigh each other.

It seems likely that some girls with ASD may have been missed by the screening procedure both in the DISCO prevalence study in the Faroe Islands and in the original diagnostic autism studies in Göteborg.

The overall outcome of autism in the Göteborg population was psychosocially poor with very few adults leading independent lives. Mortality was high (5%) and seemed to be associated with severe complicating medical disorders including epilepsy. All but one of the individuals included in the follow-up study (n=108) still met criteria for autism or atypical autism. A small subgroup showed better psychosocial outcomes. All individuals in this subgroup had some spoken language at age 3 years. Early communication skills and higher intellectual functioning were the most consistently identified predictors of better outcome. Those with a childhood diagnosis of atypical autism tended to be diagnosed with autism at follow-up. The correspondence between clinical diagnoses and DISCO algorithm diagnoses was very good both in the child and the adult population. In the outcome study, the level of intellectual functioning showed a significant shift downwards from childhood to adulthood. A subgroup deteriorated in adolescence. The rate of epilepsy increased even after adolescence (with new cases emerging at age 30 years). Females were considerably more likely than males to develop epilepsy, and the combination of autism, SMR and female gender was a particularly strong predictor of epilepsy. According to DISCO results, social and non-verbal communication problems (and perceptual abnormalities) typical of the childhood period were still present at very high rates in late adolescence and adult life. Some spoken language problems and certain behaviour problems, such as echolalia and hyperactivity, appeared to be less problematic in adult life. Quality of life seemed to be relatively good, in spite of the poor overall psychosocial outcome.

Summing up, the DISCO is a useful instrument for child and adult diagnosis of the full range of autism spectrum conditions. In addition, it appears to be helpful in systematic follow-up studies of individuals with autism spectrum conditions. When combined with clinical examination of the individuals themselves, this collateral interview yields important diagnostic and symptom/problem information needed for appropriate diagnosis in childhood and for clinical review of diagnosis and symptom load in adolescence and adult life. The prevalence of autism in the Faroe Islands was very similar to that reported for autism in other parts of the world. Some cases of girls with ASD may have been missed both in the child and adult study. Based on the DISCO-findings, the outcome of autism in the Göteborg cohort was

psychosocially very poor (including mortality and regression in adolescence), but life quality did not generally appear to be at a correspondingly low level. However, an important minority had very poor quality of life. The Faroe Islands cohort included relatively much higher functioning individuals than did the Göteborg group, which included cases diagnosed 15-30 years ago. The Faroe Islands cohort may have a very different prognosis, and the outcome findings from the Göteborg study can only be generalized, if at all, to other populations with autism diagnosed before the 1990s, when diagnostic concepts and criteria were more narrow than they are today.

Strengths and limitations

These studies are population-based and individuals have been clinically examined in some detail. Attrition rates are low. The results obtained are therefore of particular interest for clinicians and researchers alike. The prevalence study is unique in that no previous autism epidemiological study of a similar in-depth character has ever been performed in the Faroe Islands. The outcome study is the largest, longest and most comprehensive epidemiological follow-up study of autism ever performed.

Nevertheless, there are limitations in both sets of studies. The prevalence study did not include medical examination of all individuals, the number of cases included was limited (for obvious reasons given the small overall population), and autism knowledge in the Faroe Islands was not generally at a very high level at the time of the launch of the study, meaning that estimates regarding prevalence and co-occurring conditions have to be regarded with some caution (caseness has probably been underestimated). The long-term follow-up study did not include many high-functioning individuals, and so conclusions regarding outcome can only be generalized to fairly typical cases of autism in the low- and middle-functioning range.

Concluding remarks

In conclusion, then, autism is *not*, as was long believed, a very rare disorder. Outcome in severe cases with intellectual impairment is psychosocially poor (with little or no independence in adult life), but life quality can often be good even in such cases. The DISCO is a very helpful instrument for diagnosis in childhood and in adult life and can be used for follow-up of symptom profiles and problem assessment before and after adolescence.

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REFERENCES

American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders. Third Edition.* Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1987). *Diagnostic and Statistical Manual of Mental Disorder. Third Edition Revised.* Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. Text Revision*. Washington, DC: American Psychiatric Association.

Arvidsson, T., Danielsson, B., Forsberg, P., Gillberg, C., Johansson, M. & Kjellgren, G. (1997). Autism in 3-6 year-old children in a suburb of Goteborg, Sweden. *Autism,* 2, 163-73.

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

Baird, G., Simonoff,E., Pickles, A., Chandler, S., Loucas T., Meldrum, D. & Charman T. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). *Lancet*, 368, 210-15.

Ballaban-Gil, K., Rapin, I., Tuchman, R. & Shinnar, S. (1996). Longitudinal examination of the behavioural, language, and social changes in a population of adolescents and young adults with autistic disorder. *Pediatric Neurology*, 15, 217-23.

Barbaresi, W.J., Katusic, S.K., Colligan, R.C., Weaver, A.L. & Jacobsen, S.J. (2005). The incidence of autism in Olmsted County, Minnesota, 1976-1997. *Archives of Pediatrics and Adolescent Medicine*, 159, 37-44.

Bartley, J.J. (2006). An update on autism: science, gender, and the law. *Gender Medicine*, 3, 73-8.

Beadle-Brown, J., Murphy, G. & Wing, L. (2005). Long-term outcome for people with severe intellectual disabilities: impact of social impairment. *American Journal of Mental Retardation,* 110, 1-12.

Bertrand, J., Mars, A., Boyle, C., Bove, F., Yeargin-Allsopp, M. & Decoufle, P. (2001). Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. *Pediatrics*, 108, 1155-61.

Billstedt, E., Gillberg, I.C. & Gillberg, C. (2005). Autism After Adolescence: Population-based 13-22-year follow-up Study of 120 Individuals with autism Diagnosed in Childhood. *Journal of Autism and Developmental Disorders,* 35:351-60.

Billstedt, E., Gillberg, I.C. & Gillberg, C. (2007). Adults with autism diagnosed in childhood. Aspects of quality of life in a sample of individuals from the general population (submitted).
Bradley, E. & Bolton, P. (2006). Episodic psychiatric disorders in teenagers with learning disabilities with and without autism. *British Journal of Psychiatry*, 189, 361-66.

Brask, B.H. (1967). On the need for hospital beds for psychotic children. An analysis based on a prevalence investigation in the county of Aarhus. *Ugeskift for Laeger,* 16, 1560-70.

Chakrabarti, S. & Fombonne, E. (2001). Pervasive developmental disorders in preschool children. *Journal of the American Medical Association*, 285, 3093-99.

Chakrabarti, S. & Fombonne, E. (2005). Pervasive developmental disorders in preschool children: confirmation of high prevalence. *American Journal of Psychiatry*, 162, 1133-41.

Charman, T. (2002). The prevalence of autism spectrum disorders. Recent evidence and future challenges. *European Child and Adolescent Psychiatry,* 11, 249-56.

Contin-Ramseden, G., Simkin, Z. & Botting, N. (2006). The prevalence of autistic spectrum disorders in adolescents with a history of specific language impairments (SLD). *Journal of Child Psychology and Psychiatry,* 47, 621-8.

Critchley, M. & Earl, CJC. (1932). Tuberous sclerosis and allied conditions. *Brain,* 55, 311-46.

Danielsson, S., Gillberg, I.C., Billstedt, E., Gillberg, C. & Olsson, I. (2005). Epilepsy in young adults with autism: a prospective population-based follow-up study of 120 individuals diagnosed in childhood. *Epilepsia*, 46, 918-23.

de Bildt, A., Sytema, S., Kraijer, D., Sparrow, S. & Minderaa, R. (2005). Adaptive functioning and behaviour problems in relation to level of education in children and adolescents with intellectual disability. *Journal of Intellectual Disability Research*, 49, 672-81.

Filipek, P.A., Accardo, P.J., Baranek, G.T., Cook, E.H., Dawson, G., Gordon, B., Gravel, S.E., Johnson, C.P., Kallen, R.J., Levy, S.E., Minshew, N.J., Prizant, B.M., Rapin, I., Rogers, S.J., Stone, W.L., Teplin, S., Tuchman, R.F. & Volkmar, F.R. (1999). The screening and diagnosis of autistic spectrum disorders. *Journal of Autism and Developmental Disorders*, 29, 439-84.

Fombonne, E. (2003). Epidemiological Surveys of autism and other pervasive developmental disorder: an update. *Journal of Autism and Developmental Disorders*, 33, 365-82.

Fombonne, E. (2005). Epidemiology of autistic disorders and other pervasive developmental disorders. *Journal of Clinical Psychiatry*, 66, 3-8.

Fombonne, E., Zakarian, R., Bennet, A., Meng, L. & McLean-Heywood, D. (2006). Pervasive developmental disorders in Montreal, Quebec, Canada: prevalence and links with immunization. *Pediatrics*, 118, 139-50.

Frith, U. (2004). Emanuel Miller lecture: confusions and controversies about Asperger syndrome. *Journal of Child Psychology and Psychiatry,* 45, 672-86.
Gillberg, C. (1984). Infantile autism and other childhood psychoses in a Swedish urban region. Epidemiological aspects. *Journal of Child Psychology and Psychiatry*, *25*, 35-43.

Gillberg, C. & Steffenburg, S. (1987). Outcome and prognostic factors in infantile autism and similar conditions: a population-based study of 46 cases followed through puberty. *Journal of Autism and Developmental Disorders,* 17, 273-88.

Gillberg, C. & Gillberg, I.C. (1989). Asperger syndrome – some epidemiological considerations: a research note. *Journal of Child Psychology and Psychiatry,* 30, 631-38.

Gillberg, C. (1991). *Clinical and neurobiological aspects of Asperger syndrome in six family studies*. In U.Frith (Ed).) Autism and Asperger Syndrome. (pp. 122-146). Cambridge: Cambridge University Press.

Gillberg, C., Schaumann, H. & Steffenburg, S. (1991). Is autism more common now than 10 years age? *British Journal of Psychiatry*, 158, 403-09.

Gillberg, C. (1992). The Emanuel Miller Memorial Lecture 1991. Autism and autistic-like conditions: subclasses of disorders of empathy. *Journal of Child Psychology and Psychiatry,* 33*,* 813-42.

Gillberg, C., Gillberg, I.C. & Steffenburg, S. (1992). Siblings and parents of children with autism: a controlled population-based study. *Developmental Medicine and Child Neurology*, 34, 389-98.

Gillberg C. & Wing L. (1999). Autism: not an extremely rare disorder, *Acta Psychiatrica Scandinavica,* 6, 399-406.

Gillberg, C., Cederlund, M., Lamberg, K. & Zeijlon, L. (2006) Brief report: "the autism epidemic". The registered prevalence of autism in a Swedish urban area. *Journal of Autism and Developmental Disorders*, 36, 429-35.

Horston, R. & Frith, U. (2000). *Autism in History. The Case of Hugh Blair of Bourge*. Blackwell Publisher Ltd. UK.

Howlin, P. (2000). Outcome in adult life for more able individuals with autism or Asperger syndrome, *Autism,* 4, 63-83.

Howlin, P. (2003). Outcome in high-functioning adults with autism with and without early language delays: implications for the differentiation between autism and Asperger syndrome. *Journal of Autism and Developmental Disorder*, 33, 3-13.

Howlin, P., Goode, S., Hutton, J. & Rutter, M. (2004). Adult outcome for children with autism. *Journal of Child Psychology and Psychiatry,* 45, 212-29.

Howlin, P. (2005). The effectiveness of interventions for children with autism. *Journal of Neural Transmission.* Supplementum*,* 101-19.

Kadesjö, B., Gillberg,C. & Hagberg, B. (1999) Brief report: Autism and Asperger syndrome in seven-year-old children: a total population study. *Journal of Autism and Developmental Disorders*, 29, 327-31.

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child*, 2, 217-50.

Kanner, L. & Eisenberg, L. (1956). Child psychiatry: mental deficiency. *American Journal of Psychiatry,* 112, 531-4.

Kopp, S. & Gillberg, G. (2007). 100 girls with social and attention deficits (in progress).

Kobayashi, R. & Murata, T. (1998). Setback phenomenon in autism and long-term prognosis. *Acta Psychiatrica Scandinavica,* 4, 296-303.

Larsen, F.W. & Mouridsen, S.E. (1997). The outcome in children with childhood autism and Asperger syndrome originally diagnosed as psychotic. A 30-year follow-up study of subjects hospitalized as children. *European Child and Adolescent Psychiatry,* 6, 181-90.

Le Couteur, A., Rutter, M., Lord, C., Rios, P., Robertson, S., Holdgrafer, M. & McLennan, J. (1989). Autism diagnostic interview: a standardized investigator-based instrument. *Journal of Autism and Developmental Disorders*, 19, 363-87.

Leekam, S., Libby, S., Wing, L., Gould, J. & Gillberg, C. (2000). Comparison of ICD-10 and Gillberg's criteria for Asperger syndrome. *Autism,* 4, 11-28.

Leekam, SR., Nieto, C., Libby, S.J., Wing, L. & Gould, J. (2006). Describing the Sensory Abnormalities in Children and Adults with Autism. *Journal of Autism and Developmental Disorders* (Epub ahead of print).

Lord, C. & Rutter, M. (1994). Autism and pervasive developmental disorders. In M. Rutter, E. Taylor & L. Hersov (Eds.) *Child and Adolescent Psychiatry: Modern Approaches,* 3rd Edition, pp. 569-93. Oxford. Blackwell Science Inc.

Lord, C., Rutter, M. & LeCouteur, A. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, 24, 659-85.

Lord, C., Risi, S., Lambrecht, L., Cook, E.H., Leventahal, B.L. & DiLavore, P.C. (2000). The Autism Diagnostic Observation Schedule-Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders,* 30, 205-23.

Lotter, V. (1966). Epidemiology of autistic conditions in young children – I. Prevalence. *Social Psychiatry,* 1, 124-37.

Lotter V. (1974). Factors related to outcome in autistic children. *Journal of Autism and Childhood Schizophrenia,* 4, 263-77.

Lotter, V. (1978). Follow-up studies. In: Rutter M, Schopler E, ed. *Autism. A Reappraisal of Concepts and Treatments.* New York: Plenum Press, 475 –95.

LSS (1993). Lag om stöd och service till vissa funktionshindrade. *Socialdepartementet*, 1993:387.

McGovern, C.V. & Sigman, M. (2005). Continuity and change from early childhood to adolescence in autism. *Journal of Child Psychology and Psychiatry,* 46, 401-08.

Merrick, K., Kande, I. & Morad, M. (2004). Trends in autism. *International Journal of Adolescent Medical Health,* 16, 75-8.

Miller, J.N. & Ozonoff, S. (1997). Did Asperger's cases have Asperger disorder? A research note. *Journal of Child Psychology and Psychiatry*, 38, 247-51.

Njardvik, U., Matson, J.L. & Cherry, K.E. (1999). A comparison of social skills in adults with autistic disorder, pervasive developmental disorder not otherwise specified, and mental retardation. *Journal of Autism and Developmental Disorders*, 29, 287-95.

Noens, I., van Berckelaer-Onnes, I., Verpoorten, R. & van Duijn, G. (2006). The ComFor: an instrument for the indication of augmentative communication in people with autism and intellectual disability. *Journal of Intellectual Disability Research*, 50, 621-32.

Nordin, V. & Gillberg, C. (1998). The long-term outcome of autistic disorders. *European Child and Adolescent Psychiatry,* 97, 99-108.

Nygren, G., Billstedt. E., Hagberg, B., Gillberg, C. & Johansson, M. (2007). The Swedish Interview for Social and COmmunication disorders (DISCO-10) in patients with autism spectrum conditions. Psychometric properties. (In progress).

Ozonoff, S. & Cathcart, K. (1998). Effectiveness of a home program intervention for young children with autism. *Journal of Autism and Developmental Disorders*, 28, 25-32.

Persson, B. (2000). Brief Report: A longitudinal study of quality of life and independence among adult men with autism. *Journal of Autism and Developmental Disorders*, 30, 61-66.

Rasmussen, P., Borjesson, O., Wentz, E. & Gillberg, C. (2001). Autistic disorders in Down syndrome: background factors and clinical correlates. *Developmental Medicine and Child Neurology*, 43, 750-4.

Renty, J. & Roeyers, H. (2006). Quality of life in high-functioning adults with autism spectrum disorder: The predictive value of disability and support characteristics. *Autism,* 10, 511-24.

Reading, R. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP). *Child: Care, Health and Development*, 32, 752-3.

Ruble, L.A. & Dalrymple, NJ. (1993). Social/sexual awareness of persons with autism: a parental perspective. *Archives of Sexual Behaviour,* 22, 229-40.

Rumsey, J.M., Rapoport, J.L. & Sceery, W.R. (1985). Autistic children as adults: Psychiatric social and behavioral outcomes. *Journal of the American Academy of Child Psychiatry,* 24, 465-73.

Rutter, M., Greenfeld, D. & Lockyer, L. (1967). A five to fifteen year follow-up study of infantile psychosis: 1. Description of sample. *British Journal of Psychiatry*, 113, 1169-82.

Rutter, M. (1978). Diagnosis and definition of childhood autism. *Journal of Autism and Child Schizophrenia*, 8, 139-61.

Rutter, M., Kim-Cohen, J. & Maughan, B. (2006). Continuities and discontinuities in psychopathology between childhood and adult life. *Journal of Child Psychology and Psychiatry*, 47, 276-95.

Schopler, E., Reichler, R.J., DeVellis, R. & Daly K. (1980). Towards objective classification of childhood autism: Childhood Autism Rating Scale (CARS). *Journal of Autism and Developmental Disorders,* 10, 91-103.

Schopler, E., Reichler, R.J. & Renner, B.R. (1988). *The Childhood Autism Rating Scale (CARS).* Los Angeles: Western Psychological Services.

Seltzer, M.M., Krauss, M.W., Shattuck, P.T., Orsmond, G., Swe, A. & Lord, C. (2003). The symptoms of Autism Spectrum Disorders in Adolescence and Adulthood. *Journal of Autism and Developmental Disorders*, 33, 565-81.

Shah, A. & Wing, L. (2006). Psychological approaches to chronic catatonia-like deterioration in autism spectrum disorders. *International Review of Neurobiology*, 72, 245-64.

Sigman, M. & McGovern, C. (2005) Improvement in Cognitive and Language Skills from Preschool to Adolescence in Autism. *Journal of Autism and Developmental Disorders*, 35, 15-23.

Skuse, D., Warrington, R., Bishop, B., Chowdhury, U., Lau, J., Mandy, W. & Place, M. (2004). The Developmental, Dimensional and Diagnostic Interview (3di): A Novel Computerized Assessment for Autism Spectrum Disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, 43, 548-58.

Sparrow, S., Balla, D. & Cicchetti, D. (1984). *Vineland Adaptive Behavior Scales*. Circle Pines, MN: American Guidance Service.

Ssucharewa, G.E. (1926). Die schizoiden Psychopathien im Kindesalter. *Monatsschrift für Psychiatrie und Neurologie,* 60, 235-61.

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

Starr, E., Szatmari, P., Bryson, S. & Zwaigenbaum, L. (2003). Stability and change among high-functioning children with pervasive developmental disorders: a 2-year outcome study. *Journal of Autism and Developmental Disorders,* 33, 15-22.

Steffenburg, S. & Gillberg, C. (1986). Autism and autistic-like condition in Swedish rural and urban areas: a population study. *British Journal of Psychiatry*, 149, 81-87.

Steffenburg, S. (1991). Neuropsychiatric assessment of children with autism: a population-based study. *Developmental Medicine and Child Neurology*, 33, 495-511.

Steffenburg, S., Gillberg, C. & Steffenburg, U. (1996). Psychiatric disorders in children with adolescents with mental retardation and active epilepsy. *Archives of Neurology*, 53, 904-12.

Szatmari, P., Bartolucci, R., Bremner, R., Bond, S. & Rich, S. (1989). A follow-up study of high functioning autistic children. *Journal of Autism and Developmental Disorders,* 19, 213-25.

Szatmari, P., Bryson, S.E., Boyle, M.H., Streiner, D.L. & Duku, E. (2003). Predictors of outcome among high functioning children with autism and Asperger syndrome. *Journal of Child Psychology and Psychiatry*, 44, 520-28.

Walker, D.R., Thompson, A., Zwaigenbaum, L., Goldberg, J., Bryson, S.E., Mahoney, W.J., Strawbridge, C.P. & Szatmari, P. (2004). Specifying PDD-NOS: a comparison of PDD-NOS, Asperger syndrome, and autism. *Journal of the American Academy of Child and Adolescent Psychiatry,* 43, 172-80.

Van Bourgondien, M.E., Reichle, N.C. & Schopler, E. (2003). Effects of a model treatment approach on adults with autism. *Journal of Autism and Developmental Disorders,* 33, 131-40.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised*. San Antonio. TX: Psychological Corporation.

Wechsler, D. (1992). *Wechsler Intelligence Scale for Children-Third edition*. UK. London: Psychological Corporation.

Venter, A., Lord, C. & Schopler, E. (1992). A follow-up study of high functioning autistic children. *Journal of Child Psychology and Psychiatry*, 33, 489-507.

Williams, K., Glasson, E.J., Wray, J., Tuck, M., Helmer, M., Bover, C.I. & Mellis C.M. (2005). Incidence of autism spectrum disorders in children in two Australian states. *Medical Journal of Australia*, 7, 108-11.

Wing, L. (1969). The handicaps of autistic children – A comparative study. *Journal of Child Psychology and Psychiatry*, 10, 1-40.

Wing, L. & Wing, J.K. (1971). Multiple impairment in early childhood autism. *Journal of Autism and Childhood Schizophrenia*, 1, 256-66.

Wing, L. & Gould, J. (1978). Systematic recording of behaviours and skills of retarded and psychotic children. *Journal of Autism and Childhood Schizophrenia,* 8, 79-97.

Wing, L. & Gould, J. (1979). Severe impairments of social interaction and associated abnormalities in children: epidemiology and classification. *Journal of Autism and Developmental Disorders*, 9, 11-29.

Wing, L. (1979). The current status of childhood autism. *Psychological Medicine*, 9, 9-12.

Wing, L. (1980). The MRC Handicaps, Behaviour and Skills (HBS) schedule. *Acta Psychiatrica Scandinavica,* supplementum, 285, 62, 241-7.

Wing, L. (1981) A schedule for deriving profiles of handicaps in mentally retarded children. In B. Cooper (ED.) *Assessing the Handicaps and Needs of Mentally Retarded Children.* London: Academic Press.

Wing, L. (1981). Asperger's syndrome: a clinical account. *Psychological Medicine*, 11, 115-29.

Wing, L. (1988). The continuum of autistic characteristics. In E. Schopler & G, Mesibov (Eds.) *Diagnosis and Assessment in Autism*. New York: Plenum.

Wing, L. (1996). Autistic spectrum disorders. *British Medical Journal,* 10, 327-8.

Wing, L. & Shah, A. (2000). Catatonia in autistic spectrum disorders. *British Journal of Psychiatry,* 176:357-62.

Wing, L., Leekam, S., Libby, S., Gould, J. & Larcombe, M. (2002). The Diagnostic Interview for Social and Communication Disorders: background, inter-rater reliability and clinical use. *Journal of Child Psychology and Psychiatry,* 43, 307-25.

Wing, L. & Potter, D. (2002). The epidemiology of autistic spectrum disorders: Is the prevalence rising? *Mental Retardation and Developmental Disability Research Review*, 8, 151-61.

Volkmar, F.R., Lord, C., Bailey, A., Schultz, R.T. & Klin, A. (2004). Autism and pervasive developmental disorders. *Journal of Child Psychology and Psychiatry,* 45, 135-70.

von Knorring, A-L. & Hägglöf, B. (1993). Autism in northern Sweden: a population-based follow-up study: psychopathology. *European Child and Adolescent Psychiatry*, 2, 91-97.

World Health Organisation (1993). The ICD-10 Classification of Mental and Behavioural Disorders. Diagnostic Criteria for Research. Geneva: World Health Organisation.

Zafeririou, D.I., Ververi, A. & Vargiami, E. (2006). Childhood autism and associated comorbidities. *Brain and Development* (Epub ahead of print).