Prevalence of autism spectrum disorders in an Icelandic birth cohort

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ABSTRACT

Objectives: A steady increase in the prevalence of autism spectrum disorders (ASD) has been reported in studies based on different methods, requiring adjustment for participation and missing data. Recent studies with high ASD prevalence rates rarely report on co-occurring medical conditions. The aim of the study was to describe the prevalence of clinically confirmed cases of ASD in Iceland and concomitant medical conditions.

Design: The cohort is based on a nationwide database on ASD among children born during 1994–1998.

Participants: A total of 267 children were diagnosed with ASD, 197 boys and 70 girls. Only clinically confirmed cases were included. All received physical and neurological examination, standardised diagnostic workup for ASD, as well as cognitive testing. ASD diagnosis was established by interdisciplinary teams. Information on medical conditions and chromosomal testing was obtained by record linkage with hospital registers.

Setting: Two tertiary institutions in Iceland. The population registry recorded 22 229 children in the birth cohort.

Results: Prevalence of all ASD was 120.1/10 000 (95% CI 106.6 to 135.3), for boys 172.4/10 000 (95% CI 150.1 to 198.0) and for girls 64.8/10 000 (95% CI 51.3 to 81.8). Prevalence of all medical conditions was 17.2% (95% CI 13.2 to 22.2), including epilepsy of 7.1% (95% CI 4.6 to 10.8). The proportion of ASD cases with cognitive impairment (intellectual quotient <70) was 45.3%, but only 34.1% were diagnosed with intellectual disability (ID). Children diagnosed earlier or later did not differ on mean total score on a standardised interview for autism.

Conclusions: The number of clinically verified cases is larger than in previous studies, yielding a prevalence of ASD on a similar level as found in recent non-clinical studies. The prevalence of co-occurring medical conditions was high, considering the low proportion of ASD cases that also had ID. Earlier detection is clearly desirable in order to provide counselling and treatment.

INTRODUCTION

The earliest epidemiological studies on the prevalence of autism-reported figures are in

ARTICLE SUMMARY

Article focus

- Information on the prevalence of autism spectrum disorders (ASD) is important for effective service planning.
- Increases in the prevalence of ASD have been found by different methods, and the procedures have required adjustments for low response rate or missing data. High rates of ASD need to be confirmed in studies based on clinical cases in well-defined populations.

Key messages

- A high prevalence rate based on clinically verified cases of ASD was found in a nationwide birth cohort and is, on average, comparable to that in recent studies.
- Hospital registries ensured accurate rates of co-occurring medical conditions and chromosomal aberrations.
- Although the service and health care system diagnosed a fair number of autism cases, earlier detection is needed in order to provide counselling and treatment.

Strengths and limitations of this study

- The population is well defined and relatively homogenous. Good record keeping, easy access to healthcare, education free of charge and the comprehensive social system have all ensured efficient case finding at tertiary institutions.
- Case finding was based on the presence of ASD in the records at tertiary level services. Thus, the prevalence found should be regarded as the minimum figures.

the range of 3–5/10 000. In the 1980s, there was some evidence of an increased prevalence of autism, but since the early 90s a steady increase has been apparent.¹ In a recent review of 43 studies, which provided estimates for the prevalence of autism and pervasive developmental disorders (PDDs), 19 were classified as newer epidemiological surveys of PDDs.² These were published between 2000 and 2008 and covered the ages 0–17 years. The prevalence figures were in the range of 30.0–67.4/10 000 except in two studies, one

in South Thames (UK) with a prevalence of 116.1/10 000³ and another from Toyota (Japan) with a prevalence of 181.1/10 000.⁴ More recent studies have reported an even higher prevalence, 157/10 000 and 260/10 000.^{5 6} Whether this increase in prevalence over the decades reflects a true increase in incidence or is due to different methodological factors is a matter of debate.^{2 5}

From the first prevalence studies on autism to the present, few studies have dealt with co-occurring medical conditions, some of which have been reviewed recently.⁷ In studies involving the whole autism spectrum, medical conditions are rarely reported.²

In this study, we present the prevalence of autism spectrum disorders (ASD) in a birth cohort of an entire nation with a clinical ascertainment of all cases at a tertiary institute. Co-occurring medical conditions of neurodevelopmental origin obtained from hospital registers are reported.

METHODS

This prevalence study was performed at the State Diagnostic and Counselling Centre (SDCC), which is a tertiary institute, serving children with serious neurodevelopmental disorders in Iceland, and has had the responsibility of ASD diagnostics and services since 1997. For the purpose of this study, a database on ASD was kept at SDCC.

The healthcare system, the educational system and social services in Iceland are financed by governmental taxes and all residents are covered by national health insurance schemes and these services have an important role in case finding and referrals. Primary healthcare centres manage a comprehensive maternity and child-care plan. The child health and developmental surveillance includes 11 visits during the preschool years to a general practitioner/paediatrician or a nurse where the children are vaccinated and clinically evaluated. The vaccination schedule includes the pertussis/diphtheria/tetanus immunisation, which covers 97% of the children and the first measles/mumps/rubella immunisation at the age of 18 months, which covers more than 92% according to the Chief Epidemiologist.⁸ The first contact with the educational system is through preschool services, which are attended by approximately 90% of children.⁹ Education is compulsory for children aged 6–16 years, and includes special educational needs. The social services provide financial support to parents of children with serious developmental disorders or long-term illnesses, based on medical certificate.

Two specialised tertiary centres formally diagnose autism and ASD: the SDCC and the Department of Child and Adolescent Psychiatry at the Landspítali University Hospital (LUH), and records from the latter are included in the database of ASD at SDCC. An interdisciplinary team consisting of paediatricians or child psychiatrists, clinical child psychologists and social

workers reach consensus on the clinical diagnoses. Other professionals involved in the diagnostic workup include speech and language pathologists, special teachers and occupational therapists.

All the children in the study underwent a physical examination and a neurological evaluation. The Autism Diagnostic Interview-Revised (ADI-R)¹⁰ and the Autism Diagnostic Observation Schedule (ADOS)¹¹ were administered, as well as cognitive tests and tests evaluating adaptive behaviour. Of the children classified as ASD cases, 94% received ADI-R and 87.6%, ADOS. All received either ADI-R or ADOS. The intellectual quotient (IQ) or developmental quotient data, henceforth both referred to as IQ, were available for all the children and assessment of adaptive behaviour for 88.3% of children. The diagnoses were based on the above information as well as other information from hospitals, schools and the referral services. The majority of children diagnosed early during the preschool years were reassessed before beginning elementary school at 6 years of age.¹²

The classification of autism and ASD was based on the International Classification of Diseases (ICD)-10.¹³ To facilitate comparison with DSM-IV,¹⁴ three diagnostic categories are reported: childhood autism (CA) ICD-10 F84.0 (DSM-IV Autistic Disorder), Asperger's Syndrome (AS) ICD-10 F84.5 (DSM-IV Asperger's Disorder) and other ASD including ICD-10 F84.1, F84.8 and F84.9 (DSM-IV PDD, not otherwise specified). The ICD-10 F84.4 code was not used.

Cognitive ability was classified into three levels, IQ<50, 50–69, 70+, and cognitive impairment was defined as IQ<70. The diagnosis of intellectual disability (ID) was established according to ICD-10 criteria, taking into account the total score on standardised intellectual or developmental tests,^{15–19} the pattern of abilities, as well as measures of adaptive behaviour^{20 21} and other relevant information. Diagnosis of ID was made only after two successive cognitive tests.

As ASD is thought to result from a neurological abnormality, co-occurring medical conditions with neurodevelopmental underpinnings were collected. Based on the personal identifier, a record linkage was made between the ASD database and the electronic database containing all discharge diagnoses at LUH, thus obtaining access to all medical diagnoses of these children up to the end of 2009. For increased precision of the medical data, we double-checked information regarding genetic testing by linking the personal identifier of the ASD cases to the records of the Department of Cytogenetics, LUH. The genetic testing and the related results were a product of different routine tests used for clinical evaluation over the years. A paediatrician (IG) selected the medical conditions to be reported from diagnoses obtained by record linkage with the hospital registry and the records at SDCC. This was carried out by taking into consideration neurological abnormalities, neurodevelopmental conditions, genetic and congenital syndromes, and epilepsy without assuming an aetiological role

between the condition and ASD for the individual case.⁷ The definition of epilepsy was two unprovoked seizures.

For the calculation of prevalence, the numerator was children pertaining to the 1994–1998 cohort diagnosed with ASD, while the denominator was all children born in Iceland during this period and residing in Iceland at the end of 2009, in total 22 229, 11 424 males and 10 805 females according to the National Registry.²² A calculation of 95% CI was based on a method proposed by Wilson.²³ A comparison was made between the group diagnosed by the end of 2005 and the group diagnosed during 2006 and 2009. A χ^2 test was used to compare groups for categorical variables and a *t* test for differences in means. All *p* values were two tailed and considered statistically significant at a *p* value less than 0.05.

The study was approved by the Data Protection Authority, the National Bioethics Committee (VSNb2009100017/03.1) and the Scientific Committee of LUH.

RESULTS

Among the birth cohort 1994–1998, a total of 267 children were diagnosed with ASD, 197 males and 70 females. Table 1 shows the prevalence of ASD diagnoses, as well as the male/female ratio, cognitive level and the number of children with medical conditions. The overall prevalence was 120.1 (95% CI 106.6 to 135.3); the prevalence for boys was 172.4/10 000 (95% CI 150.1 to 198.0) and for girls it was 64.8/10 000 (95% CI 51.3 to 81.8).

Of the cases, 17.2% tested below IQ 50, 28.1% in the 50–69 range, and 54.7% tested ≥ 70 . The mean IQ for all ASD cases was 72.84 (SD=23.90, range<20–134), for boys 74.44 (SD=23.74), and for girls 68.31 (SD=23.91), *t*(265)=1.85, *p*=0.065. The male/female ratio was 2.1 for children with cognitive impairment (IQ<70) and 3.7 for those without such impairment, $\chi^2(1, N=267)=4.14$, *p*=0.042. The proportion of children with cognitive impairment using the IQ<70 classification was 45.3%, but only 34.1% of the ASD cases were formally diagnosed with ID. The proportion of children with ID in the CA group was 64%, and 29.9% for the other ASDs group. ID is by definition excluded in AS. The male/female ratio among those with ID was 1.8.

Chromosomal analyses were performed in 122 children (45.7%), and of these 78 were tested for fragile X. None of those tested was positive for fragile X. The prevalence

Table 2 Medical conditions in children (n=46) with childhood autism, Asperger's syndrome and other autism spectrum disorders in an Icelandic cohort born during 1994–1998*

	CA	AS	Other ASD	All ASD (%)
Genetic and congenital syndromes†	8	2	4	14 (5.2)
Chromosomal aberrations‡	3	0	3	6 (2.2)
Congenital CNS malformations§	3	1	2	6 (2.2)
Other neurological conditions¶	6	1	9	16 (6.0)
Epilepsy**	10	0	9	19 (7.1)

*Some children had more than one condition.

Figures in brackets indicate the number of cases:

†Down syndrome [3], Arnold-Chiari malformation [2], Ehlers-Danlos syndrome [1], homocystinuria [1], neurofibromatosis [1], Prader-Willi syndrome [1], Saethre-Chotzen syndrome [1], Smith-Magenis syndrome [1], Sotos syndrome [1], Sturge-Weber syndrome [1], Turner syndrome [1].

‡inv.9 [p11q12] [2], balanced autosomal rearrangements t4;14 [p11;q11] [1], microdeletion 3 [p26.3-pter] [1], partial duplication 8 [q1–q22] [1], partial duplication 20 [q12–q13.13] [1]. §Microcephaly [3], agenesis of the corpus callosum [1], macrogyria [1], cerebral cyst [1].

¶Cerebral palsy [5], asphyxia/intracranial haemorrhage [3], CNS infections [3], hearing impairment [2], CNS tumour [1], extrapyramidal motor disorder [1], vision impairment [1].

**Six children had seizure onset in the first year of life.

AS, Asperger's syndrome; ASD, autism spectrum disorder; CA, childhood autism; CNS, central nervous system.

of all medical conditions was 17.2% (95% CI 13.2 to 22.2), including epilepsy. Of the 46 children with a medical condition, 29 (63%) also had ID. The different medical conditions are shown in table 2. The prevalence of epilepsy for all ASD was 7.1% (95% CI 4.6 to 10.8). Fourteen (73.7%) of those with epilepsy also had ID. The male/female ratio among those with medical conditions was 2.3, and among those with epilepsy it was 1.4.

The prevalence of ASD for the 1994–1998 birth cohort at the end of 2005 was 56.7/10 000 (95% CI 47.6 to 67.4). During the 4-year interval from 2006 to the end of 2009, more than twice as many children were diagnosed and the prevalence of ASD doubled. The comparison of the characteristics within the ASD group in the two time points (2005 and 2009) is shown in table 3. The children diagnosed earlier were more often diagnosed with CA, while those diagnosed later were more often diagnosed with AS. No difference was found

Table 1 Prevalence of childhood autism, Asperger's syndrome, other autism spectrum disorders and all autism spectrum disorders, 95% CIs, male/female ratio, cognitive level and medical conditions in an Icelandic cohort born during 1994–1998

ASD diagnoses	Number of cases	Rate/10 000	95% CI lower/upper	Male/female ratio	IQ ≥ 70 (%)	MC (%)
CA	75	33.7	26.9 to 42.3	2.1	21 (28.0)	22 (29.3)
AS	48	21.6	16.3 to 28.6	3	48 (100)	4 (8.3)
Other ASD	144	64.8	55.1 to 76.2	3.2	77 (53.5)	20 (13.9)
All ASD	267	120.1	106.6 to 135.3	2.8	146 (54.7)	46 (17.2)

AS, Asperger's syndrome; ASD, autism spectrum disorder; CA, childhood autism; MC, medical conditions.

Table 3 Icelandic children born during 1994–1998 with autism spectrum disorders diagnosed until the end of 2005 compared with those diagnosed during 2006–2009 with respect to diagnostic subtypes, gender, cognitive level, medical conditions and epilepsy

	2005 n=126 (%)	2009 n=141 (%)	Rate ratio	95% CI lower/upper	p Value
CA	49 (38.9)	26 (18.4)	2.11	1.40 to 3.18	0.0002
AS	13 (10.3)	35 (24.8)	0.42	0.23 to 0.75	0.002
Other ASD	64 (50.8)	80 (56.7)	0.90	0.72 to 1.12	0.331
Males	96 (76.2)	101 (71.6)	1.06	0.92 to 1.23	0.398
IQ ≥ 70	60 (47.6)	86 (61.0)	0.78	0.62 to 0.98	0.028
All MCs	26 (20.6)	20 (14.2)	1.45	0.86 to 2.47	0.163
Epilepsy*	13 (10.3)	6 (4.3)	2.42	0.95 to 6.19	0.054

*Subcategory of MCs.

AS, Asperger's syndrome; ASD, autism spectrum disorders; CA, childhood autism; MCs, medical conditions.

in the frequency of other ASD whether diagnosed earlier or later. However, the mean total score on ADI-R based on verbal cases (n=213) did not differ between groups, $t(211)=0.63$, $p=0.53$, not shown in table 3. More children diagnosed earlier had an IQ below 70 than those diagnosed later. This difference was also evident when comparing mean IQ scores between groups, $t(264)=-3.37$, $p=0.001$, not shown in the table. However, the proportion of children with a formal diagnosis of ID did not decrease significantly over time ($\chi^2(1, N=267)=2.45$, $p=0.117$, not shown in the table). Medical conditions were not more common among children diagnosed earlier than later in the study period.

DISCUSSION

In the present study, the prevalence of all ASD was 1.2%. This prevalence is in concordance with the higher end of the range (0.3–1.8%) reported in the 19 newer surveys published during 2000–2008, according to the review of Fombonne.² However, when considering more recent studies with ASD prevalence of approximately 1% or higher, our prevalence figure is at the lower end of the range from 0.9% to 2.6% (see table 4).^{3–6 24 25} The highest prevalences reported, 1.8% and 2.6%, are from Japan⁴ and South Korea,⁶ respectively. It is notable that the gender ratio in these two studies is relatively low

(2.5–2.8) and similar to the ratio reported in some of the other studies in table 4.

In the discussion of these studies, care must be taken as there are considerable differences in the methods used as well as geographical, cultural and ethnic differences. The studies from South Thames UK,³ Cambridgeshire UK,⁵ Goyang City South Korea⁶ and Bergen City Norway²⁴ were based on screening for ASD among children with special educational needs or those who were on a disability registry, and/or screening among children in elementary schools, and/or among local clinicians. In these studies, different adjustments had to be made to estimate the prevalence due to sampling procedures and different responses and missing data. In the Autism and Developmental Disabilities Monitoring Network USA surveillance,²⁵ the prevalence of ASD was estimated at 0.90% in children aged 8 years, through a systematic retrospective review by examining records from areas of 11 states. The prevalence of 1.81% in the study from Toyota, Japan⁴ was based on screening and advice to parents to consult, while the diagnosis was founded on a clinical interview with parents and observation of the child.

In the present study, the diagnostic category of CA represented a relatively small proportion (28%) of the total number of cases, even if the prevalence is high (0.34%). This prevalence is 7.7 times higher than that

Table 4 Recent studies on the prevalence of autism spectrum disorders in children estimated at approximately 1% or higher

Study and location	Age groups	Method	Number of clinically verified cases	Target population	Prevalence %	Male/female ratio
Baird (2006) ³ UK	9–10	Records/Survey	158	56 946	1.16*	3.3
Kawamura (2008) ⁴ Japan	1–7	Clinical	228	12 589	1.81†	2.8
ADDM (2009) ²⁵ USA	8	Records	NA	307 790	0.90‡	3.2–7.6
Baron-Cohen (2009) ⁵ UK	5–9	Records/Survey	NA	8824	1.57*	Not reported
Posserud (2010) ²⁴ Norway	7–9	Survey	14	6609	0.87*	Not reported
Kim (2011) ⁶ South-Korea	7–12	Records/Survey	201	55 266	2.64*	2.5
Present study Iceland	11–15	Clinical	267	22 229	1.20†	2.8

*Estimated prevalence taking non-responders into consideration.

†Calculated from raw numbers.

‡An overall average across 11 ADDM sites.

ADDM, Autism and Developmental Disabilities Monitoring Network, USA; NA, not applicable.

reported in the first study on autism published in Iceland²⁶ and almost four times that reported in a more recent study.²⁷

None of the 19 studies selected by Fombonne² were included in a review on medical condition in ASD population samples,⁷ and none of the studies in table 4 reported on medical conditions, except for the present one. In the above review, the rate of medical conditions varied from 8% to 25% in studies published between 1996 and 2007.⁷ A comparison of the proportion of medical conditions found in the present study with the findings of other studies is difficult because a generally accepted definition of the phenomenon is lacking.⁷ Our estimate of 17.2% may seem high, considering how a large proportion (65.9%) of our ASD cases did not have diagnosed ID.²⁸ No case with fragile X was identified, although the literature predicts fragile X to be in the range of 2–8% with autism when DNA testing is utilised.²⁹

Epilepsy in our ASD group was associated with ID and the female gender, as demonstrated in a meta-analysis.³⁰ The lifetime prevalence of epilepsy for all ASD in the present study was 7.1%, which is low compared with other studies on the subject.^{31–32} It should be noted that the follow-up in the hospital registry, and thus the registration of medical conditions, was up to the end of 2009 when the children were 11–15 years old. In this context, it is of paramount importance to distinguish between studies on autism in adulthood on the one hand³¹ and studies on all ASD in childhood on the other.³² In fact, the literature on the incidence and prevalence of epilepsy is sparse in relation to high ASD prevalence.

In a 4-year period, from the end of 2005 to the end of 2009, the prevalence of ASD in the cohort studied doubled, moving from 0.6% to 1.2%. This increase cannot be explained by immigration to Iceland, confirmed by the National Registry,²² and migration of people from one part of the country to another is irrelevant since the area studied and the whole country are the same. As expected, children diagnosed earlier (by 2005) were more likely to have CA than AS and were generally more impaired than those diagnosed later (2006–2009), although the groups did not differ regarding the frequency of ID and medical conditions. In order to examine symptom severity from another angle than diagnostic classification, we compared the earlier and later diagnosed groups on ADI-R total score. This comparison did not reveal differences between groups. High scores on ADI-R for those diagnosed later indicate serious autistic symptoms, possibly in association with co-occurring developmental and psychiatric disorders. Another point of interest is that the number of boys did not increase, contrary to what is suggested by some investigators.³³ One interpretation of these results is simply that as the cohort studied grows older, more girls are identified with ASD,³⁴ and because girls with ASD are more likely to be cognitively impaired, it would counteract the predicted trend for fewer children with co-occurring ID as the prevalence

of ASD increases. Comparing the distribution of boys and girls in the group of children with ID (n=91) diagnosed earlier or later with ASD revealed some support for this hypothesis, as the gender ratio was 2.8 and 1.2, respectively, although this difference fell short of statistical significance.

Of our ASD cases, 54.7% were classified with an IQ of 70 or above. This proportion ranged from 30% to 74.2% in the studies selected by Fombonne,² where IQ data were reported (13/19). The studies in table 4, which present comparable data, show this proportion to be from 44% to 66.4%.^{3–4} These figures indicate that as the prevalence of ASD increases, the proportion of children with cognitive impairment decreases. However, important as the classification of cognitive level above or below IQ 70 may be for comparing epidemiological samples with ASD, it should not be overlooked that IQ<70 simply serves as a proxy for ID. For instance, it is possible to arrive at a full-scale score on a Wechsler test of IQ below 70 in various ways, notably when severe language impairments or non-verbal learning disabilities are present. From this perspective, there is a notable difference between the proportion of children with IQ<70 (45.3%) and the proportion receiving a formal diagnosis of ID (34.1%) in the present study. Thus, the IQ<70 classification may provide an inaccurate estimate of how many individuals actually have ID in addition to ASD.

In the present study, case finding was based on the presence of ASD in the records at tertiary level services, and hence prospective screening identifying potential cases followed by clinical examination did not take place. Thus, the clinical source of the data indicates that the prevalence reported should be regarded as the minimum figures. However, the prevalence of ASD found is based on the exact number of clinically confirmed cases and definite number of the population derived from a population register of a whole nation. Also, based on record linkage, co-occurring medical conditions were obtained for ASD cases from electronic hospital records. Nevertheless, this follow-up ended when the children were 11–15 years of age and other conditions, for example, epilepsy, may be diagnosed later during their lifetime. The population is well defined and relatively homogeneous. Good record keeping, easy access to healthcare, education free of charge, and the comprehensive social system have all ensured efficient case finding at tertiary institutions, whose purpose is to serve the diagnostic and counselling needs of children with serious developmental disorders. The referral and diagnostic process in the country has been fairly standardised and is relatively transparent, compared with larger societies where a multitude of record sources is to be expected, behind which there may be widely different diagnostic practices. Only two tertiary instances offered diagnostic services for ASD and these have worked in close cooperation regarding diagnostic procedures. ADI-R was used for 94% of

children by qualified clinicians; all had formal cognitive or developmental testing and consensus diagnoses were reached within an interdisciplinary team. In addition, the majority of children diagnosed during their early preschool years were reassessed before entering elementary school.

CONCLUSION

The number of clinically verified cases is larger than in previous studies, yielding a prevalence rate of ASD on a similar level as found in recent non-clinical studies. The tertiary level of services diagnosed a fair number of ASD cases; however, it may be considered a public-health issue of how many children are diagnosed after they enter the elementary school system.

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Contributors ES, VR and PM designed the study. ES and PM oversaw the data entry. IG and VR oversaw the gathering of data on medical conditions. EE assisted with quality control regarding data entry and the statistical analysis with ES and VR. ES did the literature review and wrote the first draft with the assistance of VR. All authors read and commented on the content of the manuscript and agreed on the final version and approved its submission.

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REFERENCES

- McDonald M, Paul J. Timing of increased autistic disorder cumulative incidence. *Environ Sci Technol* 2010;44:2112–18.
- Fombonne E. Epidemiology of pervasive developmental disorders. *Pediatr Res* 2009;65:591–8.
- Baird G, Simonoff E, Pickles A, et al. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the special needs and autism project (SNAP). *Lancet* 2006;368:210–15.
- Kawamura Y, Takahashi O, Ishii T. Re-evaluating the incidence of developmental disorders: impact of elevated rates of detection through implementation of an integrated system of screening in Toyota, Japan. *Psychiat Clin Neurosci* 2008;62:152–9.
- Baron-Cohen S, Scott FJ, Allison C, et al. Prevalence of autism spectrum conditions: UK school-based population study. *Br J Psychiatry* 2009;194:500–9.
- Kim YS, Leventhal BL, Koh YJ, et al. Prevalence of autism spectrum disorders in a total population sample. *Am J Psychiatry* 2011;168:904–12.
- Bolton P. Medical conditions in autism spectrum disorders. *J Neurodev Disord* 2009;1:102–13.
- World Health Organization. Global Health Observatory Data Repository, Countries. <http://apps.who.int/ghodata/?vid=10300&theme=country> (accessed 26 Nov 2012).
- Statistics Iceland. Children in pre-primary institutions by sex, age and regions 1998–2011. <http://www.statice.is/Statistics/Education/Pre-primary-institutions>. (accessed 2 Jan 2011).
- Rutter M, Le Couteur A, Lord C. *Autism Diagnostic Interview-Revised (ADI-R)*. Los Angeles, CA: Western Psychological Services, 2003.
- Lord C, Rutter M, DiLavore PC, et al. *The Autism Diagnostic Observational Schedule (ADOS)*. Los Angeles, CA: Western Psychological Services, 2001.
- Jónsdóttir SL, Saemundsen E, Ásmundsdóttir G, et al. Follow-up of children diagnosed with pervasive developmental disorders: stability and change during the preschool years. *J Autism Dev Disord* 2007;37:1361–74.
- World Health Organization. *The ICD-10 classification of mental and behavioural disorders. Diagnostic criteria for research*. Geneva, Switzerland: World Health Organization, 1993.
- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders* 4th edn. Washington, DC: American Psychiatric Association, 1994.
- Bayley N. *Manual for the Bayley scales of infant development* 2nd edn. New York: Psychological Corporation, 1993.
- Wechsler D. *Manual for the Wechsler preschool and primary scale of intelligence—revised*. Antonio, TX: The Psychological Corporation, 1989.
- Wechsler D. *Wechsler intelligence scale for children* 3rd edn. London, UK: Psychological Corporation Europe, 1992.
- Gudmundsson E, Ólafsdóttir H. *Manual for Wechsler preschool and primary scale of intelligence-revised WPPSI-R [Greindarpróf David Wechsler handa börnum á leikskóla- og grunnskólaaldri. Handbók]*. Reykjavík: Námsmatsstofnun, 2003.
- Salvarsdóttir K, Skúlason S. *Icelandic standardization of Wechsler intelligence scale for children-fourth edition [Íslensk stöðlun á greindarprófi Wechslers fyrir 6–16 ára börn. Handbók. Fyrirlögn og mat]*. Reykjavík: Námsmatsstofnun, 2006.
- Sparrow S, Balla D, Cicchetti D. *Vineland Adaptive Behavior Scales, survey form*. Circle Pines, MN: American Guidance Service, 1984.
- Sparrow S, Cicchetti D, Balla D. *Vineland Adaptive Behavior Scales: Second edition (Vineland II) survey/interview form*. Livonia, MN: Pearson Assessments, 2005.
- Statistics Iceland. Population by sex and age 1841–2010. <http://www.statice.is/Statistics/Population/Overview> (accessed 11 Aug 2010).
- Newcombe R, Altman D. Proportions and their differences. In: Altman D, Machin D, Bryant T, Gardner M, eds. *Statistics with confidence*. Bristol, UK: BMJ Books, 2003:105–19.
- Posserud M, Lundervold AJ, Lie SA, et al. The prevalence of autism spectrum disorders: impact of diagnostic instrument and non-response bias. *Soc Psych Psych Epid* 2010;45:319–27.
- Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders—Autism and Developmental Disabilities Monitoring Network, United States, 2006. *MMWR Surveill Summ* 2009;58:1–20.
- Magnússon GT. Athugun á geðveikum börnum á Íslandi: Börn fædd 1964–1973. (An investigation of psychotic children in Iceland: children born 1964–1973). *Laeknabladid* 1977;63:237–43.
- Magnússon P, Saemundsen E. Prevalence of autism in Iceland. *J Autism Dev Disord* 2001;31:153–63.
- Cohen D, Pichard N, Tordjman S, et al. Specific genetic disorders and autism: clinical contribution towards their identification. *J Autism Dev Disord* 2005;35:103–16.
- Harris SW, Hessel D, Goodlin-Jones B, et al. Autism profiles of males with fragile X syndrome. *Am J Ment Retard* 2008;113:427–38.
- Amiet C, Gourfinkel-An I, Bouzamondo A, et al. Epilepsy in autism is associated with intellectual disability and gender: evidence from a meta-analysis. *Biol Psychiatry* 2008;64:577–82.
- Bolton P, Carcani-Rathwell I, Hutton J, et al. Epilepsy in autism: features and correlates. *Brit J Psychiatry* 2011;198:289–94.
- Spence S, Schneider M. The role of epilepsy and epileptiform EEGs in autism spectrum disorders. *Pediatr Res* 2009;65:599–606.
- Whiteley P, Todd L, Carr K, et al. Gender ratios in autism, Asperger syndrome and autism spectrum disorder. *Autism In* 2010;2:17–24.
- Kočovská E, Biskupstø R, Gillberg IC, et al. The rising prevalence of autism: a prospective longitudinal study in the Faroe Islands. *J Autism Dev Disord* 2012;42:1959–66.