

Chapter 2

Epidemiology of Autism Spectrum Disorders

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Abstract In this chapter, we review existing prevalence estimates for autism spectrum disorders (ASDs) since 2000 and discuss methodological factors impacting the estimation of prevalence and the interpretation of changes in prevalence estimates over time. Possible explanations for an increase in the prevalence of ASD within and across populations are considered. Increases in ASD diagnostic rates cannot currently be attributed to a true increase in the incidence of ASD due to multiple confounding factors. It remains to be seen how changes to diagnostic criteria introduced in the *DSM-5* will impact estimates of ASD prevalence going forward.

Keywords Epidemiology · Prevalence · Autism

2.1 Introduction

Epidemiological surveys of autism were first initiated in the mid-1960s in England (Lotter 1966, 1967) and have since been conducted in over 20 countries. In this chapter, we provide a comprehensive review of the findings and methodological features of published epidemiological surveys about the prevalence of autism spectrum disorders (ASDs¹). This chapter builds upon previous reviews (Elsabbagh et al. 2012; Fombonne 2003a, 2005; Fombonne et al. 2011; French et al. 2013; Hill et al. 2014; Williams et al. 2006) and includes the results of pertinent studies since published. The specific questions addressed are: (1) What is the range of prevalence

¹ Autism spectrum disorder (ASD) is the modern term that replaces the former pervasive developmental delay (PDD).

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estimates for ASDs?, and (2) How should the time trends observed in the current prevalence rates of ASDs be interpreted?

2.1.1 Study Design and Methodological Issues

Epidemiologists use several measures of disease occurrence including incidence, cumulative incidence, and prevalence. Prevalence is a measure used in cross-sectional surveys (in which there is no passage of time) and reflects the proportion of subjects in a given population who suffer from the disease at that point in time. Most epidemiological studies of ASDs have assessed prevalence (point prevalence or period prevalence) as a cross-sectional approach is more appropriate for disorders where timing of diagnosis lags behind the onset of symptoms and is likely to be influenced by a range of factors unrelated to risk. In designing a prevalence study, three elements are critical: case definition, case identification (or case ascertainment), and case evaluation methods (Fombonne 2007).

2.1.1.1 Case Definition

The definition and diagnostic criteria of autism has changed over time. Starting with Kanner's definition of autism (1943), case definitions have progressively broadened to include criteria proposed by Rutter (1970), and subsequently the International Classification of Diseases, ninth revision (ICD-9; World Health Organization 1977); the *Diagnostic and Statistical Manual of Mental Disorders*, third edition (*DSM-III*; American Psychiatric Association 1980; *DSM-III-R*, American Psychiatric Association 1987), until two recent nosographies were adopted worldwide; ICD-10 (World Health Organization 1992) and the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (*DSM-IV*, American Psychiatric Association 1994; *DSM-IV-TR*, American Psychiatric Association 2000).

Early diagnostic criteria reflected the more qualitatively severe behavioral phenotypes, usually associated with severe delays in language and cognitive skills. In the 1980s less severe forms of autism were recognized, either as a qualifier for autism occurring without intellectual disability (i.e., high-functioning autism), or as separate diagnostic categories (e.g., pervasive developmental disorders not otherwise specified [PDD-NOS], or ASD). Asperger's disorder appeared in the 1990s, with unclear validity, particularly with respect to its differentiation from high-functioning autism. Some ASD subtypes that were described in *DSM-III* subsequently disappeared (e.g., Autism-Residual State); however, other nomenclatures have since added new diagnostic categories, such as "atypical autism" and "PDD unspecified" (ICD-10).

The changes now occurring with the introduction of *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*; American Psychiatric Association 2013), may impact prevalence estimates in the future. *DSM-5* proposes a single new category of ASDs, conceptually equivalent to the previous diagnostic class of

PDDs. However, fewer diagnostic criteria have been retained that are combined in two clusters of social communication deficits, and restricted patterns of behaviors and interests. The removal of the loosely defined PDD-NOS that was in *DSM-IV-TR* (American Psychiatric Association 2000) will likely increase the specificity of the ASD diagnostic category, and the removal of Asperger disorder as a separate category is consistent with the research that has generally failed to provide evidence for the discriminant validity of this diagnostic concept vis-à-vis the forms of autistic disorder that are not associated with severe language impairments or intellectual deficits.

The impact of *DSM-5* changes remains to be fully assessed in the context of epidemiological surveys. Two recent population-based surveys have addressed this issue. Maenner and colleagues (2014) retrospectively applied the new diagnostic criteria to a previously obtained population-based sample from the Centers for Disease Control and Prevention (CDC) 2006 and 2008 surveillance years. They found that 81.2% of children classified as having ASD according to *DSM-IV-TR* (American Psychiatric Association 2000) also met *DSM-5* criteria (American Psychiatric Association 2013), resulting in a *DSM-5* based prevalence of 100/10,000—an estimate lower than the CDC 2006 and 2008 estimates. In addition, 304 children met *DSM-5* but not *DSM-IV-TR*. In a similar study, Kim and colleagues (2014) reported that 92% of children with ASD according to *DSM-IV-TR* also met *DSM-5* criteria. However, when *DSM-5* ASD and social communication disorder (SCD; a new diagnostic category in *DSM-5*) were considered together, there was no significant change in the prevalence estimate (Kim et al. 2014). It is important to note that new diagnostic information required in *DSM-5* (e.g., emphasis on sensory processing deficits) is generally not available in prior studies, leading to potentially biased estimates. Additionally, previous studies are often constrained in sampling children with a *DSM-IV* PDD diagnosis and cannot therefore accurately estimate the proportion of children who did not meet the criteria for *DSM-IV* yet would have met those for *DSM-5*.

While there is currently high reliability overall regarding diagnosis of ASDs and commonality of concepts across experts, differences still persist between nomenclatures about the terminology and operationalized criteria of ASDs. It is unclear to what extent the changing nomenclature of ASDs plays a role in prevalence estimates described in epidemiological studies. More studies are on their way that will provide further examination of the impact on prevalence estimates of narrowing the ASD definition in *DSM-5*.

2.1.1.2 Case Identification/Ascertainment

When a population is identified for a survey, different strategies are employed to find individuals matching the study's case definition. Some studies rely solely on service provider databases (Chien et al. 2011; Croen et al. 2002; Davidovitch et al. 2013), special education databases (Fombonne et al. 2006; Gurney et al. 2003; Lazoff et al. 2010; Maenner and Durkin 2010), or national registers (Al-Farsi et al. 2011; Parner et al. 2012; Samadi et al. 2011) for case identification. These studies

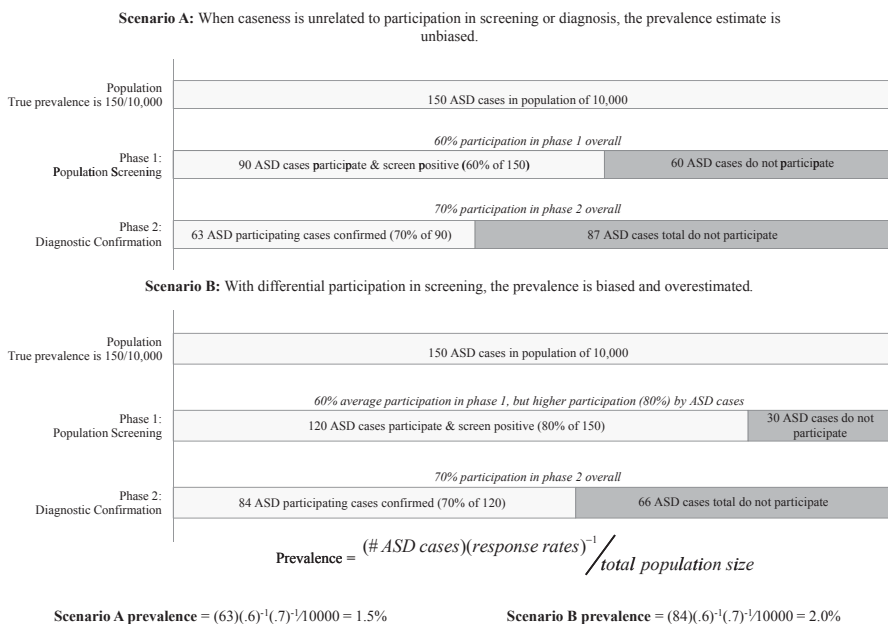


Fig. 2.1 Assuming a true ASD prevalence of 150/10,000 and a sensitivity of 100% for the screening process and total accuracy in the diagnostic confirmation, weighting back phase 2 data results in an unbiased prevalence estimate when caseness is unrelated to participation in screening (Scenario A), but when participation in screening is more likely for ASD cases than for non-cases (Scenario B), prevalence will be overestimated (see discussion in text)

have the common limitation of relying on a population group that was readily accessible, rather than sampling from the population at large. As a result, individuals with the disorder who are not in contact with services are not included as cases, leading to an underestimation of prevalence. This limitation is particularly problematic in communities with recognized limitations in available services.

Other investigations have relied on a multistage approach to identify cases in underlying populations (Centers for Disease Control and Prevention 2012; Idring et al. 2012; Kim et al. 2011). In these studies' first screening stage, a wide net is cast to identify subjects possibly affected with ASD, with the final diagnostic status being determined at subsequent stages. This process often consists of sending letters or screeners to school and health professionals, searching for the possible cases of autism. Few such investigations rely on systematic sampling techniques that would ensure a near complete coverage of the target population, and screening often varies substantially in ascertainment of all relevant data sources. Additionally, surveyed areas often differ in terms of specific educational or health care systems available, and inclusion information sent often varies in reliability and validity. Finally, uneven participation rates in the screening stage can lead to variation in the screening efficiency of surveys.

To illustrate how differential participation in the screening stage affect prevalence estimates, two hypothetical scenarios are illustrated in Fig. 2.1, both of which are based on a true ASD prevalence of 150/10,000 and a sensitivity of 100% for

the screening process and total accuracy in the diagnostic confirmation. In Scenario A, we assume 60% participation for ASD and non-ASD cases in the first screening stage, resulting in 90 participating ASD cases that screen positive. With 70% participation for both ASD and non-ASD cases in the diagnostic stage, we would identify and confirm 63 ASD cases in the second phase. Weighting back phase 2 data, we would obtain an unbiased prevalence estimate of 1.5% (or 150/10,000) in this scenario. In Scenario B, we also assume 60% overall participation, but with an 80% participation rate for ASD cases, reflecting a scenario in which individuals with ASD are more likely to participate in the first screening stage than non-ASD cases. Thus, with the same participation rates in the first screening (60%) and final diagnostic stages (70%), we identify 84 ASD cases and calculate a biased prevalence estimate of 2% (200/10,000), an estimate that is 0.5% higher than true prevalence. The bias arises for two reasons: (1) participation in screening is associated with case status (here, with ASD cases more likely to participate than non-cases); and (2) as investigators typically have no such information, weights used for prevalence estimation were not adjusted correspondingly, resulting in the upward bias.

It is also possible that individuals with ASD participate less than non-cases, which would result in underestimates of prevalence. For example, Posserud and colleagues (2010) reported the ASD prevalence of 72/10,000 in their identified sample and estimated a prevalence of 128/10,000 in no responders (based on teacher ratings during the screening phase), indicating increased refusal rates among those with more ASD symptoms. Unfortunately, few studies have been able to estimate the extent to which willingness or refusal to participate is associated with final caseness, so it is not known what effect differential participation rates at different phases in population surveys may have on prevalence estimates.

The sensitivity of the screening methodology is difficult to gauge in autism surveys, as the proportion of children truly affected with the disorder but not identified in the screening stage (false negatives) remains generally unmeasured. Few studies provided an estimate of the reliability of the screening procedure. The usual approach, which consists of randomly sampling screen-negative subjects to adjust estimates, has not been generally used, mainly due to the relatively low frequency of ASD, which makes such a strategy both imprecise and costly.

As an example, the surveys conducted by US CDC (2007a, 2007b, 2009, 2012, 2014) rely, for case ascertainment, on scrutinizing educational and medical records. Children not accessing such services cannot be identified. Although some recent surveys that systematically screen the normal school population might detect a large pool of unidentified cases (Kim et al. 2011), it remains to be seen if this applies to most populations and requires change in sampling approaches for surveying autism. Of note, the CDC methodology identifies ASD cases without prior official ASD diagnosis (21% of identified cases in 2008; Centers for Disease Control and Prevention 2012), suggesting that underidentification is a widespread phenomenon.

Since more recent prevalence studies suggest that autism can no longer be regarded as rare, screening for false negatives may become a more common strategy. Currently, however, prevalence estimates must be understood as underestimates of “true” prevalence rates, with the magnitude of this underestimation unknown in each survey.

2.1.1.3 Case Evaluation

When the screening phase is completed, subjects identified as positive go through a more in-depth diagnostic evaluation to confirm case status. Similar considerations about methodological variability across studies apply in more intensive assessment phases. The information used to determine diagnosis usually involves a combination of data from informants (parents, teachers, pediatricians, other health professionals, etc.) and data sources (medical records, educational sources), with a direct assessment of the person with autism being offered in some but not all studies. When subjects are directly examined, assessments typically use various diagnostic instruments, ranging from a typical unstructured examination by a clinical expert (but without demonstrated psychometric properties) to the use of batteries of standardized measures by trained research staff. The Autism Diagnostic Interview-Revised (ADI-R; Lord et al. 1994) and/or the Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000) have been increasingly used in the most recent surveys (Table 2.1).

Obviously, surveys of large populations, such as those conducted by the CDC (2007a, 2007b, 2009, 2012) or in national registers (Idring et al. 2012), cannot include direct diagnostic assessment of all subjects by researchers. However, investigators generally improve the accuracy of caseness determinations by undertaking, on a randomly selected subsample, a more complete diagnostic workup (Rice et al. 2007). The CDC surveys have established a methodology for surveys of large populations based on the screening of the population using multiple data sources, standardized records abstraction, and systematic review and scoring of the data gathered in the screening phase. In the less obvious cases, this information is combined with input from experienced clinicians with known reliability and validity. This methodology is adequate for large samples, and is likely to be used in the future for surveillance efforts.

2.2 Systematic Review of Prevalence Estimates

2.2.1 Search Strategies

Keeping in mind the range and limitations of case definition, identification, and evaluation methods employed in epidemiological surveys, we present the results of epidemiological reports conducted since 2000 in Table 2.1. These reports were identified from previous reviews of epidemiological surveys (Elsabbagh et al. 2012; Fombonne 2003b, 2003a, 2005, 2009a; Fombonne et al. 2011; French et al. 2013; Williams et al. 2006) and through systematic searches using major scientific literature databases (Medline, PsycINFO, Embase, PubMed). Where multiple surveys based on the same or overlapping populations were evident, the publication listed is the most detailed and comprehensive account. For example, surveys conducted by

Table 2.1 Prevalence surveys of ASDs since 2000.

Year	Authors	Country	Area	Population	Age	Number Affected	Diagnostic Criteria	% with Normal IQ	Gender Ratio (M:F)	Prevalence /10,000	95% CI
2000	Baird et al.	UK	South East Thames	16,235	7	94	ICD-10	60	15.7 (83:11)	57.9	46.8; 70.9
2000	Powell et al.	UK	West Midlands	58,654 ^a	1–5	122	Clinical, ICD-10, DSM-IV	–	–	20.8	17.3; 24.9
2001	Bertrand et al.	USA	New Jersey	8896	3–10	60	DSM-IV	51	2.7 (44:16)	67.4	51.5; 86.7
2001	Chakrabarti and Fombonne	UK	Stafford	15,500	2.5–6.5	96	ICD-10	74.2	3.8 (77:20)	61.9	50.2; 75.6
2001	Fombonne et al.	UK	England and Wales	10,438	5–15	27	DSM-IV, ICD-10	55.5	8.0 (24:3)	26.1	16.2; 36.0
2002	Scott et al.	UK	Cambridge	33,598	5–11	196	ICD-10	–	4.0 (–)	58.3 ^a	50.7; 67.1 ^a
2003	Yeargin-Allsopp et al.	USA	Atlanta, GA	289,456	3–10	987	DSM-IV	31.8	4.0 (787:197)	34.0	32; 36
2003	Gurney et al.	USA	Minnesota (2001–2002)	787,308 ^a	6–11	4094	Receipt of MN special education services	–	–	52.0 ^a	50.4; 53.6 ^a
2003	Lingam et al.	UK	North East London	186,206	5–14	567	ICD-10	–	4.8 (469 :98)	30.5 ^a	27.9; 32.9 ^a
2004	Icasiano et al.	Australia	Barwon	45,153 ^a	2–17	177	DSM-IV	53.4	8.3 (158:19)	39.2	33.8; 45.4 ^a
2005	Chakrabarti and Fombonne	UK	Stafford	10,903	4–6	64	ICD-10	70.2	6.1 (55:9)	58.7	45.2; 74.9

Table 2.1 (continued)

Year	Authors	Country	Area	Population	Age	Number Affected	Diagnostic Criteria	% with Normal IQ	Gender Ratio (M:F)	Prevalence /10,000	95% CI
2006	Baird et al.	UK	South Thames (1990–1991)	56,946	9–10	158	ICD-10	45	3.3 (121:37)	116.1	90.4; 141.8
2006	Fombonne et al.	Canada	Montreal	27,749	5–17	180	DSM-IV	–	4.8 (149:31)	64.9	55.8; 75.0
2006	Harrison et al.	UK	Scotland	134,661	0–15	443b	ICD-10, DSM-IV	–	7.0 (369:53)	44.2	39.5; 48.9
2006	Gillberg et al.	Sweden	Göteborg	32,568	7–12	262	DSM-III, DSM-IV, Gillberg's criteria for AS	–	3.6 (205:57)	80.4	71.3; 90.3
2006	Ouellette-Kuntz et al.	Canada	Manitoba and Prince Edward Island	227,526	1–14	657	DSM-IV	–	4.1 (527:130)	28.9 ^a	26.8; 31.2 ^a
2007	Croen et al.	USA	Northern California (1995–1999)	132,844	5–10	593	ICD-9-CM	–	5.5 (501:92)	45	41.2; 48.4 ^a
2007 ^b	CDC	USA	6 states	187,761	8	1252	DSM-IV-TR	38 to 60 ^d	2.8 to 5.5	67.0	63.1; 70.5 ^a
2007 ^c	CDC	USA	14 states	407,578	8	2685	DSM-IV-TR	55.4 ^e	3.4 to 6.5	66.0	63; 68
2007	Latif and Williams	UK	South Wales	39,220	0–17	240	ICD-10, DSM-IV, Kanner's and Gillberg's criteria	–	6.8 (–)	61.2	53.9; 69.4 ^a

Table 2.1 (continued)

Year	Authors	Country	Area	Population	Age	Number Affected	Diagnostic Criteria	% with Normal IQ	Gender Ratio (M:F)	Prevalence /10,000	95% CI
2008	Wong and Hui	China	Hong Kong Registry	4,247,206	0–14	682	DSM-IV	30	6.6 (592:90)	16.1	14.9; 17.3 ^a
2008	Montiel-Nava and Pena	Venezuela	Maracaibo	254,905	3–9	430	DSM-IV-TR	–	3.3 (329:101)	17	13; 20
2008	Kawamura et al.	Japan	Toyota	12,589	5–8	228	DSM-IV	66.4	2.8 (168:60)	181.1	159.2; 205.9 ^a
2008	Williams et al.	UK	Avon	14,062	11	86	ICD-10	85.3	6.8 (75:11)	61.9	48.8; 74.9
2009	Baron-Cohen et al.	UK	Cambridgeshire	8824	5–9	83	ICD-10	–	–	94 ^f	75; 116
2009	Nicholas et al.	USA	South Carolina	8156	4	65	DSM-IV-TR	44.2	4.7	80	61; 99
2009	van Balkom et al.	Netherlands	Aruba	13,109	0–13	69	DSM-IV	58.8	6.7 (60:9)	52.6	41.0; 66.6
2009	CDC	USA	11 states	308,038	8	2,757	DSM-IV-TR	59	4.5	90	86; 93
2010	Fernell and Gillberg	Sweden	Stockholm	24,084	6	147	DSM-IV, DSM-IV-TR, ICD-10	33	5.1 (123:24)	62	52; 72
2010	Lazoff et al.	Canada	Montreal	23,635	5–17	187	DSM-IV	–	5.4 (158:29)	79.1	67.8; 90.4
2010	Barnevik-Olsson et al.	Sweden	Stockholm	113,391	6–10	250	DSM-IV	0	–	22	19.4; 25.0 ^a

Table 2.1 (continued)

Year	Authors	Country	Area	Population	Age	Number Affected	Diagnostic Criteria	% with Normal IQ	Gender Ratio (M:F)	Prevalence /10,000	95% CI
2010	Maenner and Durkin	USA	Wisconsin	428,030	Elementary school-aged	3831	DSM-IV like criteria for WI special education services (by school district)	–	–	90	86.7; 92.4 ^a
2010	Posserud et al.	Norway	Bergen	9,430	7–9	16	DSM-IV, ICD-10 Included DAWBA and DISCO	–	7 (14:2)	87 ^g	–
2011	Al-Farsi et al.	Oman	National Register	528,335	0–14	113	DSM-IV-TR	–	2.9 (84:29)	1.4	1.2; 1.7
2011	Brugha et al.	UK	England	7333	16–98	72	ADOS	100	3.8	98.2	30; 165
2011	Kim et al.	S. Korea	Goyang City	55,266	7–12	201	DSM-IV	31.5	3.8	264	191; 337
2011	Mattila et al.	Finland	Northern Ostrobothnia County	5484	8	37	DSM-IV-TR included ADOS-G and ADI-R	65	1.8	84	61; 115
2011	Parner et al. ^h	Australia	Western Australia (1994–1999)	152,060	0–10	678	DSM-IV, DSM-IV-TR	–	4.1	51	47; 55.3
2011	Samadi et al.	Iran	National Register	1,320,334	5	826	ADI-R	–	4.3	6.4	5.84; 6.70

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