What's Going On? The Question of Time Trends in Autism

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SYNOPSIS

Increases in the reported prevalence of autism and autistic spectrum disorders in recent years have fueled concern over possible environmental causes. The author reviews the available survey literature and finds evidence of large increases in prevalence in both the United States and the United Kingdom that cannot be explained by changes in diagnostic criteria or improvements in case ascertainment. Incomplete ascertainment of autism cases in young child populations is the largest source of predictable bias in prevalence surveys; however, this bias has, if anything, worked against the detection of an upward trend in recent surveys. Comparison of autism rates by year of birth for specific geographies provides the strongest basis for trend assessment. Such comparisons show large recent increases in rates of autism and autistic spectrum disorders in both the U.S. and the U.K. Reported rates of autism in the United States increased from <3 per 10,000 children in the 1970s to >30 per 10,000 children in the 1990s, a 10-fold increase. In the United Kingdom, autism rates rose from <10 per 10,000 in the 1980s to roughly 30 per 10,000 in the 1990s. Reported rates for the full spectrum of autistic disorders rose from the 5 to 10 per 10,000 range to the 50 to 80 per 10,000 range in the two countries. A precautionary approach suggests that the rising incidence of autism should be a matter of urgent public concern.

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Since the 1960s, autism researchers have published more than 50 surveys that provide estimates of the frequency of autism in defined populations. This survey base provides a significant opportunity for analysis, but also poses many difficulties with respect to interpretation. In recent years, these difficulties have come into sharp relief as reports of higher and rising prevalence rates have fueled concern over possible environmental causes.[1,2] This survey literature has been the subject of several reviews and commentaries,[3–11] many of them by a single author.[3–8] This small set of reviewers have shared a common interpretation regarding the trend evidence, emphasizing the notion that autism is "not an extremely rare disorder,"[10] while arguing that there is no evidence for an increase over time in the prevalence of autism.[5]

In order to reconcile the full body of evidence with this interpretation, several authors have suggested mechanisms that might explain the reported increases in the apparent absence of a secular trend, including diagnostic substitution,[12–15] changing diagnostic standards,[16] and improved detection.[17]

The controversy over the true rates of autism might appear a simple matter, one that is best resolved prospectively, with improvements in reporting procedures. In reality, the persistence of the trend controversy reflects a vigorous debate over causality in the broadest sense. Is autism primarily a genetic disorder, as many would claim,[18] or do environmental factors play a stronger role than previously acknowledged? In comparison to the methodological hypotheses, the search for possible environmental causes has generated far greater controversy, particularly as iatrogenic hypotheses have been advanced and challenged.[19–24]

In the context of these controversies, a careful review of the available literature is essential. Assessment of trend evidence bears directly on the relative explanatory power of environmental and genetic theories. Causal theories that emphasize genetic inheritance carry greater weight if disease frequency is unchanged over time, whereas rising incidence demands environmental explanations. Reliable trend assessment requires a comprehensive synthesis of the best available evidence.[25,26]

This article reviews the available survey evidence on the prevalence of autism in order to demonstrate that the underlying rates—and not merely the reported rates—of autism have risen sharply in the U.S. and the U.K. This discussion is divided into two sections. The first section provides an analysis of the impact of survey design choices on frequency and trend estimates. The second section offers an in-depth quantitative and qualitative comparison of 11 U.K. and eight U.S. surveys published since the mid-1960s (see Table 1).

IMPACT OF DIFFERENCES IN SURVEY DESIGN

Definitions

The determination of disease frequency requires, first, a definition of the disease event. In the case of autism, this determination has long been based on subjective psychological assessments. Because autism has no well-defined biological markers, the condition itself is an hypothesis, "a suggestion that behind the behavioral description [lies] a disease entity."[27] Not surprisingly, over the six decades since Leo Kanner first described the condition,[28] the standard definition has been updated many times (see Table 2), incorporating changes in nomenclature, diagnostic criteria, age of onset, and disease categories. While the general intent has been to make diagnostic decisions more consistent, these revisions complicate the challenge of comparing findings across and within studies.

Nomenclature. The word *autism* has remained in constant use since Kanner adopted the term to describe *early infantile autism* or *infantile autism* in 1943,[28] yet the accompanying modifiers have changed with time. In Rutter's influential modernization of the definition in 1978,[27] three related terms—*autism*, *infantile autism*, and *childhood autism*—were used somewhat interchangeably. The third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III)[29] used *infantile autism* as the core descriptor, but also placed autism in the context of the *pervasive developmental disorders* (PDDs) for the first time. In 1987, a revised edition, DSM-III-R,[30] abandoned the term *infantile autism*, in part to recognize cases in which the onset of symptoms did not occur in early infancy; DSM-III-R distinguished between *autistic disorder* and *pervasive developmental disorder, not otherwise specified* (PDD-NOS). In 1993, the World Health Organization published the *International Classification of Diseases, 10th revision* (ICD-10) definitions,[31] which used the term *childhood autism*. One year later, the fourth DSM edition,[32] in most respects identical to ICD-10, used the term *autistic disorder*.

Diagnostic criteria. Kanner and Eisenberg provided the first formal set of criteria for the diagnosis of autism in 1956; the criteria focused on two dimensions of the condition: "a profound lack of affective contact" and "repetitive, ritualistic behavior, which must be of an elaborate kind."[33] Practitioners found these criteria somewhat problematic over the years, in particular because they omitted the unusual language and communication patterns that seemed to many a core element of the disease. Rutter's refinement introduced the concept of simultaneous deficits in three behavioral domains: impaired social relationships, impaired language and communication skills, and "insistence on sameness."[27] In one form or another, these three domains have determined the operational definition of autism ever since.

Some evidence suggests that the shift away from the Kanner criteria may have effectively broadened the scope of the diagnosis. One group of investigators in Finland applied both the Kanner criteria and the ICD-10 criteria in a population survey.[34] These researchers interpreted the Kanner criteria as more restrictive and reported a lower rate for what they called *classic autism* of 5.6 per 10,000, compared with 12.2 per 10,000 for *childhood autism*. The mean prevalence rate for 11 studies using the Kanner criteria was two per 10,000.[35–45] This compares to a mean of seven per 10,000 for 13 surveys of *infantile autism* that applied either the Rutter or DSM-III criteria or similar "post-Kanner" clinical criteria.[46–58]

Age of onset is the one criterion that has changed most measurably over time. Kanner and Eisenberg implied an age assumption by using the term *early infantile autism*. Rutter[27] (followed by DSM-III) set a specific age of onset limit of earlier than 30 months. The DSM III-R criteria relaxed this limit, requiring only that the age of onset occur "during

Table 1. Overview of 54 published reports of studies that provide disease frequency statistics on autism, autistic spectrum disorders (ASDs), and related disorders.

Author(s)	*Location*	*Year of publication*	*Number of cases per 10,000 children*
Lotter[35]	England	1966	4.1
Treffert[36]	U.S.	1970	0.7
Yamazaki et al.[37]	Japan	1971	2.6
Tanino[38]	Japan	1971	1.1
Haga and Miyamoto[39]	Japan	1971	1.1
Nakai[40]	Japan	1971	1.7
Brask[41]	Denmark	1972	4.3
Wing and Gould[42]	England	1979	4.9
Bohman et al.[46]	Sweden	1981	6.1
Hoshino et al.[43]	Japan	1982	2.3
Ishii and Takahashi[47]	Japan	1983	16.0
McCarthy et al.[44]	Ireland	1984	4.3
Gillberg[48]	Sweden	1984	2.0
Steinhausen et al.[49]	Germany	1986	5.8
Steffenburg and Gillberg[50]	Sweden	1986	4.6
Burd et al.[45,a]	U.S.	1987	1.2
Matsuishi et al.[51]	Japan	1987	15.5
Tanoue et al.[52]	Japan	1988	13.9
Bryson et al.[86]	Canada	1988	10.1
Ritvo et al.[53]	U.S.	1989	2.5
Aussilloux et al.[54]	France	1989	4.7
Sugiyama and Abe[55]	Japan	1989	13.0
Cialdella and Mamelle[56]	France	1989	5.1
Gillberg et al.[60]	Sweden	1991	5.8
Fombonne and du Mazaubrun[57]	France	1992	4.9
Herder[88]	Norway	1993	5.5
Rumeau-Rusquette et al.[58,79]	France	1994	3.1
Deb and Prasad[82]	U.K.	1994	9.0
Honda et al.[66]	Japan	1996	21.1
Fombonne et al.[79]	France	1997	5.4
Wignyosumarto et al.[87]	Indonesia	1997	11.7
Webb et al.[89]	U.K.	1997	7.2
Arvidsson et al.[93]	Sweden	1997	10.0
Sponheim and Skejdal[94]	Norway	1998	3.8
California Department of Developmental Services[2,b]	U.S.	1999/2003	31.2 (peak)
Taylor et al.[20]	U.K.	1999	5.3
Kadesjo et al.[85]	Sweden	1999	24.0
Irie[90]	Japan	1999	10.4
Kielinen et al.[34]	Finland	2000	5.6
Baird et al.[78,c]	U.K.	2000	30.8
Hillman et al.[84]	US	2000	—
Chakrabarti and Fombonne[61]	U.K.	2001	16.8
Fombonne et al.[62]	U.K.	2001	26.1 (ASDs)
Powell et al.[67]	U.K.	2001	—
Kaye et al.[68]	U.K.	2001	16.3
Bertrand et al.[80]	U.S.	2001	40.0
Sturmey and James[83]	U.S.	2001	16.0
Davidovitch et al.[91]	Israel	2001	9.9
Magnusson and Saemundsen[92]	Iceland	2001	8.6
Croen et al.[12]	U.S.	2002	11.0
Scott et al.[95]	U.K.	2002	57.0 (ASDs)
Lingam et al.[63]	U.K.	2003	14.9
Gurney et al.[73]	U.S.	2003	3.0–52.0 (ASDs)
Yeargin-Allsopp et al.[75]	U.S.	2003	34 (ASDs)

[a]A later survey[77] examined the same population. The authors consider that the findings of the second survey confirm the original findings.

[b]An earlier survey[1] examined the same population. The authors consider the later report to contain the more accurate estimates.

[c]An earlier survey[74] examined the same population. The authors consider the later report to contain the more accurate estimates

Table 2. Changes in nomenclature and major shifts in diagnostic criteria in widely accepted definitions of autism

	Kanner and Eisenberg[33]	*Rutter*[27]	*DSM-III*[29]	*DSM-III-R*[30]	*ICD-10*[31]/*DSM-IV*[32]
Date published	1956	1978	1980	1987	1994
Larger category	—	—	PDD	PDD	PDD
Autism					
Nomenclature	Early infantile autism; infantile autism	Infantile autism; autism; childhood autism	Infantile autism	Autistic disorder	Autistic disorder
Age at onset of symptoms	None specified	By 30 months	By 30 months	During infancy or childhood	By 36 months
Related disorders[a]	—	Other infantile psychoses	Infantile autism/ residual state; atypical PDD	PDD-NOS	PDD-NOS; Asperger's syndrome; Rett's syndrome; childhood onset disintegrative disorder

[a]A number of studies based on the diagnostic criteria outlined in DSM-III and DSM-III-R used the term "autistic-like condition" to refer to certain related disorders, although this term was not included in the official definition of pervasive developmental disorders.

PDD = pervasive developmental disorder

NOS = not otherwise specified

infancy or childhood." ICD-10 and DSM-IV set an age limit at 36 months, in part a reaction to the problem posed by the expanded definition introduced in DSM-III-R.[59]

Other autistic spectrum diagnoses. DSM-III introduced, in a broad sense, the concept of a spectrum of autistic disorders through PDDs, and specifically introduced the term *atypical PDD*, which some found useful,[45,77] while others applied the term *autistic-like condition*.[50,60] DSM-III-R introduced the term PDD-NOS, which was retained in DSM-IV. By contrast, ICD-10 opted to use the term *atypical autism*.

In recent years, researchers have begun adopting the phrase *autistic spectrum disorders* (ASDs), used interchangeably with PDDs. The ASDs include autism and PDD-NOS, as well as a larger list of related disorders, including *Asperger's syndrome, childhood disintegrative disorder, and Rett's syndrome*. Asperger's cases represent approximately 14% to 19% of the ASD population,[20,61–63] while reported rates are very low for childhood disintegrative disorder[64] and Rett's syndrome (a well-characterized genetic disorder).[65]

Methodological issues: nomenclature and diagnostic criteria.

- The core definition of autism has remained relatively stable since Rutter's introduction of the three main behavioral domains in 1978,[27] facilitating comparison of rate estimates over time.
- Early surveys that applied the Kanner criteria may have reported lower autism rates than later studies because the Kanner criteria were more restrictive. This modest effect may contribute to a perception of an increasing trend over time.
- The three sets of DSM criteria for autism have varied modestly in breadth. Some have argued that the move from DSM-III to DSM-III-R broadened the concept of autism, contributing to an apparent increase in prevalence over time; however, in the shift from the DSM-III-R criteria to the DSM-IV/ICD-10 criteria, "a corrective narrowing occurred."[59] Thus, differences over time in the breadth of the diagnostic criteria are unlikely to have had a meaningful effect on reported disease frequency.
- Any comparison of surveys must take into account differences in disease definitions, in particular whether PDD-NOS and Asperger's syndrome are included in the definition of autism.

Measurements of disease frequency

The overwhelming majority of autism surveys have used prevalence rates as the primary measure of disease frequency. A small minority of studies have reported "incidence" rates of various kinds,[20,66–68] but the actual differences in assumptions, data sources, and methods make these "incidence" calculations little different from reported prevalence rates. The emphasis on prevalence reporting fits well with the historical consensus among autism researchers that autism is largely (if not exclusively) genetic in origin, unlikely to vary in disease frequency over time, and unlikely to demonstrate secular changes in incidence.[3]

In principle, incidence calculations are essential for trend assessment. But developing incidence measures for autism presents special difficulties. Measuring incidence *rates* requires clearly identifiable incidence *times*. With respect to autism, many researchers have conflated time of onset with time of detection, due to both theoretical and practical complexities. In practice, most researchers opt for simplicity and report prevalence rates. Those few studies that report incidence rates have used a wide range of incidence times,

including age at diagnosis,[20,67,68] year of birth,[66,68] age at onset of symptoms (sometimes called "age at parental concern"),[20] and (although this measure is also used in calculating prevalence rates) age at entry into a services system.[1,2]

Prevalence calculations can vary from cumulative incidence rates in numerous ways. First, they may underestimate cumulative incidence by failing to count cases in which the disease condition has lapsed. In autism, since the presence of the disease condition is defined by its onset at a certain stage of development, this concern is irrelevant in principle. In practice, since the few follow-up studies have shown the condition to be persistent,[69,70] it may be unimportant. Second, prevalence calculations may underestimate older populations if excess case mortality increases with age. Studies in California have found excess mortality among autistic children (largely due to accidental drowning deaths),[71,72] but not in autistic adults. In addition, this excess mortality was extremely small relative to the population size. Third, most prevalence surveys fail to adjust for net migration effects, i.e., the effect of children with autism moving in and out of the study area. These three issues have concerned some reviewers,[10,21] but there is little evidence in the literature for a systematic large effect on either disease frequency or trend. Finally, prevalence rates can vary from true disease rates when case ascertainment is incomplete. This is an important issue addressed further in the following section on case finding.

The studies reviewed for the purposes of this article have used four main approaches to reporting disease frequency:

1. Point prevalence with no stratification by age or birth year. This common approach was used in 23 of the 54 studies listed in Table 1.
2. Point prevalence with stratification by birth year and/or age. This approach has been used most frequently, with 28 of 54 studies employing some form of stratification. Studies reporting stratified prevalence rates provide potentially useful trend information.
3. Cumulative incidence, defined by many autism researchers as the number of cases diagnosed within a specified age-at-diagnosis window divided by the total population at risk.[20,53,68,73] These studies are most reliably informative with respect to trend, but they are few in number.
4. Incidence. Only one study claimed to measure incidence.[67] The authors gathered data on age at diagnosis but did not provide any data on birth years, making comparison to other studies impossible.

Methodological issues: measurement of disease frequency.

- The common practice of using point prevalence measures facilitates the collection and comparison of survey data. Point prevalence measures that have been stratified by age and/or birth year provide additional information for trend assessment by allowing for the comparison of frequencies and trends within as well as across studies.
- Comparisons of prevalence estimates across studies must take into account differences in study design that affect frequency assessment, especially differences in the scope of the autism definition. Comparisons of birth cohort disease prevalence estimates within studies must take into account specific design choices that affect trend assessment.

Case-finding: ascertainment issues

There are many practical obstacles to recognizing autism in a young child. These problems start in the home, where delays in recognition will produce ascertainment failures under any survey method. The three behavioral domains of autism are not medical problems and can be overlooked for substantial periods of time: social interaction problems can be interpreted as due to hearing impairments, and delays in language development can be explained by the phenomenon of "late-talking children." Paradoxically, the "insistence on sameness" of autistic children can also make them appear to be "easy" children, since they may make few demands. Further delays can occur once concerned parents have recognized that their child has serious developmental issues; the process of scheduling a formal clinical assessment can take many months.

While definitions of autism have generally specified the time for the onset of symptoms as 30 to 36 months, the age of diagnosis carries no similar requirement. Diagnoses can come as early as 18 months with specialized methods,[74,78] or as late as 10 years of age. A number of autism surveys report mean or median ages at diagnosis (see Table 3), with a wide variation across the populations measured. A few surveys reporting lower ages at diagnosis have based their calculations on truncated samples, removing later ages at diagnosis from their calculations.[20,61,67] Other studies report median ages at diagnosis ranging from 3 to 6 years of age,[1,2,63,68] or means ranging from 3.9 to 6.9 years of age.[8,36,75,76] This wide variation and relatively late average age at diagnosis argues for caution in interpreting surveys based on young children and especially those based on survey populations that include children younger than 5 years of age.

Several recent surveys using administrative data have demonstrated the disproportionate effect of ascertainment bias on younger birth cohorts. Reports from states that have updated their case files over a period of several years demonstrate clearly the way in which young children can enter a survey population gradually over time. This effect has been described in Minnesota and California.[2,73] Recent experience with California survey data has revealed how misinterpretation of trends based on mixed age groups in a survey population can lead to erroneous conclusions.[12–15]

Arguably, however, ascertainment bias can be reduced with aggressive case-finding methods, which accelerate the age of diagnosis. One useful test of the impact of ascertainment is to compare findings from repeated case-finding efforts, i.e., pairs of surveys that cover identical geographic areas and birth populations but in different time frames. Three such pairs of surveys have been published (Table 4). One such pair was initiated in North Dakota,[45,77] where two PDD prevalence surveys (neither stratified by age) were conducted more than a decade apart by the same research group. The first survey identified 98% of the cases found 12 years later; this high case ascertainment rate was likely due to a high median age in the earlier survey, a wide age range,

Table 3. Age of autism diagnosis in selected U.K. and U.S. studies

Author(s)	*Age at diagnosis*	*Time period*
United Kingdom		
Taylor et al. 1999[20]	3.1 years[a] (median)	1979–1982 (birth year)
Powell et al. 2000[67]	3.1 years[a] (median)	1991–1996 (birth year)
Chakrabarti and Fombonne 2001[61]	3.4 years[b] (mean)	1998–1999 (year diagnosed)
Kaye et al. 2001[68]	4.6 years (median); 4.0–6.0 range	1989–1999 (birth year)
Lingam et al. 2003[63]	3.3 years (median)	1984–1995 (birth year)
United States		
Treffert 1970[36]	5.1 years (mean)	1962–1967 (year diagnosed)
California Department of Developmental Services 1999[1]	5–9 years (median)	Up to 1987 (year entered services system)
Croen et al. 2002[12]	6.9 years (mean)	1987–1994 (birth year)
Mandell et al. 2002[76]	6.3 years (mean)	1993–1999 (claim year)
California Department of Developmental Services 2003[2]	<4 years (median)	Up to 2002 (year entered services system)
Yeargin-Allsopp et al. 2003[75]	3.9 years (mean)	1986–1993 (birth year)

[a]Case collection in this study was truncated to exclude children who were diagnosed after 60 months of age. This exclusion makes the median age at diagnosis a low estimate of eventual age of diagnosis in this case population.

[b]Case collection in this study was truncated to exclude children who were diagnosed after 78 months of age. This exclusion makes the mean age at diagnosis a low estimate of eventual age of diagnosis in this case population.

and low overall prevalence in the survey population. A second pair of surveys (with stratified age cohorts) was conducted four years apart in a region in Sweden that includes the city of Goteburg and the rural Bohuslan area.[50,60] The first survey found a wide variation in prevalence rates across age cohorts, ranging from two per 10,000 to 11 per 10,000. These researchers reported complete ascertainment after an interval of four years for the cohort aged 8 to 10 years in the original survey. For the cohort aged 4 to 6 years, the ascertainment rate declined to 73%, and for children younger than age 4, the ascertainment rate was only 23%. In this survey pair, what appeared to be a declining time trend in the first survey population was not replicated in the second survey. Finally, a third pair of surveys was initiated in the

Table 4. Description of three survey pairs: identical geographic areas and populations

Location, description, and findings	*Earlier study*	*Later study*	*Case ascertainment rate in earlier study*
North Dakota	Burd et al. 1987[45]	Burd et al. 2000[77]	
Age range at time of study	2–18 years	14–30 years	
Number of cases	59	60	98%
Prevalence of PDDs	3.26 per 10,000	3.51 per 10,000	
Goteburg/Bohuslan, Sweden	Steffenburg and Gillberg, 1986[50]	Gillberg et al. 1991[60]	
1975–1977			
Age range at time of study	7–10 years	11–13 years	
Number of cases	27	26[a]	100%[a]
1978–1980			
Age range at time of study	4–6 years	8–10 years	
Number of cases	19	26	73%
1981–1984			
Age range at time of study	≤3 years	4–7 years	
Number of cases	6	22	27%
Prevalence of PDDs	6.6 per 10,000	9.5 per 10,000	
South East Thames Health Region, U.K.	Baron-Cohen et al. 1996[74]	Baird et al. 2000[78]	
Age at time of study	18 months	7 years	
Number of cases	10	50	20%
Prevalence of autism	6.3 per 10,000	30.8 per 10,000	

[a]Lower number of cases in later study due to one child having moved out of study region.

PDD = pervasive developmental disorder

South East Thames Health Region in England to test the efficacy of a newly designed Checklist for Autism in Toddlers (CHAT).[74,78] The researchers first carried out a careful survey of 18-month-old children to see if the CHAT could predict autism at an early age. Although the CHAT checklist showed a high specificity rate (98%) for childhood autism, the first survey failed to ascertain the majority of cases found in the same population six years later. The autism ascertainment rate for the combined medium and high risk groups from the first survey was only 20%.

This pattern of ascertainment bias can also be detected in the seven single surveys that provide annual birth cohort prevalence estimates across wide age ranges.[2,43,56,63,75,79,80] (Personal communication, Ron Huff, PhD, California Department of Developmental Services, February 2003). Birth cohort prevalence rates for children ages 6 or older show a wide range of trends, from declining to flat to sharply increasing, across the seven surveys. Yet each study shows a pronounced and rapid decline in prevalence rates with decreasing age in age cohorts younger than 6 years. Interestingly, these declines are comparable in administrative surveys and active case-finding surveys.

If ascertainment lags in autism surveys have a predictable effect on trend assessments, then this effect can only be more pronounced for other autism spectrum diagnoses with later median ages at diagnosis. One recent U.K. survey reporting age at diagnosis for the full autism spectrum reported a median age at diagnosis for Asperger's syndrome of 8.1 years, compared with a median age of 4.3 years for atypical autism (PDD-NOS), and 3.3 years for childhood autism.[63] This pattern suggests that any survey reporting trend evidence for populations of children younger than 10 years of age may understate both the ASD trend and the relative proportion of core autism cases vs. cases of less severe ASDs.

Methodological issues: ascertainment.

- Obstacles to recognizing autism in children younger than 5 years of age can lead to ascertainment bias, distorting trend evidence in surveys that do not control for age effects, either reducing a positive trend or suggesting a negative trend where reported rates are stable.
- Survey populations that have high proportions of young children may yield reported prevalence significantly below actual disease frequency.
- Aggressive case-finding may reduce ascertainment bias by accelerating diagnoses in small populations, but appears not to eliminate it. The ascertainment effect holds with comparable strength in administrative surveys and in surveys using aggressive case-finding methods.
- The later age at diagnosis for Asperger's syndrome and PDD-NOS increases the risk of misinterpretation of trend evidence in surveys that attempt to measure disease frequency of all ASDs.

Case finding: population restrictions, case identification, and case validation methods

Population restrictions. Some autism researchers have made specific choices that restrict their surveys' population coverage. These include the following: limiting case finding to mentally retarded children or children in special schools,[81,82] a choice likely to downwardly bias reported rates; focusing on males only,[68] a choice likely to yield higher rates based on the high male/female ratio in autism; or truncating the case-finding period at an early age,[61,68] a choice likely to downwardly bias reported rates.

Case identification. Increasingly, autism surveys have been conducted using cases identified entirely from centralized databases. These databases are generally designed to facilitate the administration of service delivery and may be more or less reliable as epidemiological resources. Often called administrative surveys, efforts relying on central databases are less costly to conduct than surveys that rely on independent identification and validation of cases, often from multiple sources, especially when the former do not require individual interviews for case validation. In the United States, special education benefits are administered at the state level, so several recent administrative surveys have been undertaken at the state level.[2,73,83,84] In the United Kingdom, health care services databases have provided the case identification for similar administrative surveys.[20,63,68]

When researchers rely on service providers rather than a central database to identify potential cases, cases may be missed through non-cooperation at many stages. Concerns regarding the effectiveness of case-finding in such surveys have been extensively reviewed elsewhere;[3,4] issues include institutional coverage and response rates, parent refusal rates, diagnostic interview completion rates, and the quality of diagnostic instruments.

One recent review has hypothesized that rising rates of autism have resulted in part from improved case identification in recent surveys based on small survey populations (<50,000).[11] These authors argue that small surveys have generated a disproportionately high number of reports of prevalence in excess of 10 per 10,000. Arguing against this hypothesis is the observation that surveys of large populations in the U.S. and the U.K. have yielded ASD and autism rates consistently greater than 10 per 10,000 and have also reported upward trends during their survey periods.[2,63,73,83]

The same review also suggests that close coordination with a "routine developmental check" in preschool children can explain high levels of case identification, pointing for support to several Japanese surveys that have found prevalence rates greater than 10 per 10,000.[51,52,55,66] Arguing against this suggestion are numerous earlier Japanese surveys that reported lower autism rates,[37–40,43,47] given no evidence of changing practices in Japan. Additionally, none of the published Japanese surveys has ever reported a rate of autism greater than 25 per 10,000, the range of concern for recent surveys in the U.S. and U.K.

Case validation. Methodological features of both administrative and intensive case-recruitment surveys can affect the quality of diagnoses and the accuracy of disease rates. These include choice of screening instruments and instruments for intensive assessment and/or record review, numbers of informants, and methods to ensure inter-rater reliability. These methods are reviewed in depth elsewhere.[3,4]

Recent experience has shown that surveys with aggressive case validation methods can uncover more cases of autism

and PDD than surveys that work entirely from administrative records. But even these experiences can provide support for the usefulness of administrative databases. One recent study in Atlanta estimated that only 41% of children with PDDs had been given an autism diagnosis by school administrators,[75] but the survey's definition of PDDs included Asperger's syndrome, whereas the school system may have applied a more restrictive definition of autism. School sources were the main source for case identification: only 3% of the children in the sample who were classified by the researchers as having PDDs were identified through databases other than school records. This low percentage of missed cases underscores the value of central databases in identifying cases and also the importance of specifying PDD categories for validation purposes.

Methodological issues: population restrictions, case identification, and case validation method.

- Use of restricted populations based on age or receipt of services may lead to underestimating true disease frequency by reducing the potential for case identification; alternatively, restricting the study population to males may lead to overestimating the true frequency.
- Administrative surveys based on central databases may provide lower estimates of disease frequency than surveys that rely on independent case-finding and validation. The impact of this effect is hard to assess based on current data and is influenced by the quality and coverage of specific databases.
- Smaller survey populations may allow for better case identification rates.
- Differences in case validation methods may explain disease frequency differences across surveys.

REVIEW OF U.S. AND U.K. STUDIES

Previous autism reviews have consistently concluded that autism incidence rates show no clear time trend.[3–11] These reviews, however, have shared three major flaws: use of flawed meta-analytic methods, limited survey evidence, and inadequate correction for ascertainment bias.

Critical examination of methods for cross-survey comparisons

A single author, Fombonne, has been the most active reviewer and interpreter of autism surveys.[3–8] This reviewer has conducted three meta-analyses of autism time trends.[3,4,6] In these cross-survey comparisons, he has correlated reported prevalence estimates with the years in which the selected surveys were published. The first meta-analysis showed an increase in autism rates over time, but the correlation was not statistically significant.[3] The later analyses showed a rising trend that reached statistical significance.[4,6] In each case, however, the author attributed any positive trend in reported prevalence rates to methodological changes. Other reviewers have supported him in this opinion.[10,11]

Until recently, this was a reasonable inference to draw from the literature. Reviewers have emphasized the difficulty of assessing trends against a background of regular changes in diagnostic criteria. When dates of publication are used in a meta-analysis, an analysis of time trends will reveal little beyond an apparent effect of changes in diagnostic standards. An assessment (not shown) of all published prevalence studies by diagnostic criteria set (Kanner,[35–45] Rutter/DSM-III,[46–58] DSM-III-R,[60,82,85–92] and DSM-IV through 2001[2,12,20,34,61–63,66–68,73,75,78–80,92–96]) reveals that prevalence was relatively stable until the most recent set of diagnostic criteria was introduced.

Relying on the date of publication can obscure large differences in the study populations observed. For example, three Scandinavian studies published in a three-year period used markedly different populations: a Swedish study published in 1997 measured the prevalence of autism in a 3- to 6-year-old population born from 1988 through 1991[93]; another Swedish study published two years later, in 1999, focused on 7-year-olds who were born in 1985, several years before the children in the first group[85]; while a Norwegian study published between the two covered a wide range of age cohorts and measured prevalence rates going back as far as 1978.[94]

In addition, combining surveys from locations as widely separated as Yokohama, California, and Goteburg greatly increases the potential for non-comparability. None of the three meta-analyses chose surveys based on country groupings, therefore risking the introduction of confounding environmental factors that are geographically specific. With the publication since 1999 of six U.S. studies and seven U.K. studies, the opportunity for useful geographic comparison has improved greatly.

An alternative approach is to synthesize evidence from autism surveys using the following methods:

- Analyze surveys from a single country separately instead of grouping separate regions together.
- Use the most common measure of disease frequency: point prevalence.
- Compare prevalence reports based on birth dates of children in the survey population, not the publication date.
- Highlight differences in diagnoses, distinguishing (using DSM-IV nomenclature) autistic disorder from PDD-NOS and Asperger's syndrome.
- Identify all possible sources of bias resulting from specific survey design choices.

Cross-survey comparisons: U.K. and U.S. studies

Tables 5 and 6 show how factors likely to affect comparisons across surveys (factors affecting frequency estimates) and within surveys (factors affecting trend estimates) impact 11 U.K. studies and eight U.S. studies that provide usable autism rate data.

Frequency factors include the following: use of the Kanner criteria, reliance on administrative databases, early age truncation of the survey population, restrictions of the survey population based on school or mental status, and gender restrictions. Surveys applying one of these factors may report lower autism rates than other surveys; however, in the case of gender restrictions, relative rates will be higher when only males are included. Although scant evidence supports a population effect, the sizes of the survey populations are

Table 5. Description of 11 U.K. surveys of autism prevalence, with factors affecting the assessment of disease frequency and time trends

	Lotter 1966[35]	*Wing and Gould 1979*[42]	*Deb and Prasad 1994*[83]	*Webb et al. 1997*[89]	*Taylor et al. 1999*[20]	*Fombonne et al. 2001*[62]
Geographic area	Middlesex	Camberwell	Northeastern Scotland	Wales	North Thames area	Multiple
Birth year range	1953–1955	1955–1970	1969–1983	1977–1989	1979–1992	1984–1994
Survey population	78,000	35,000▲	101,814	73,301	490,000	10,438▲
Number of cases per 10,000 children						
Autism	4.1 (95% CI 2.7, 5.5)	4.9 (95% CI 2.9, 7.8)	9 (95% CI 7.2, 11)	7.2 (95% CI 5.3, 9.3)	5.3	—
PDD, not including Asperger's	6.9[a]	—	—	—	8.7	21.1
ASD, including Asperger's	—	—	—	—	10.1	26.1 (95% CI 16.2, 36.0)
Factors affecting prevalence						
Diagnostic criteria	Kanner[33]▼	Kanner[33]▼	DSM-III-R[30]	DSM-III-R[30]	ICD-10[31]	ICD-10[31]
Central database	No	No	No	No	Yes	No
Age truncation	No	No	No	No	No	No
Population restriction	No	No	Yes	No	No	No
Gender restriction	No	No	No	No	No	No
Factors affecting trend						
Year of birth breakdowns	No[b]	No[b]	Yes[b]	Yes[c]	Yes, but NA[b]	Yes[b]
Age variation (range)	No (8–10)	No (≤15)	Yes (5–19)▼	Yes (3–15)▼	Yes (5–16)	Yes (5–15)▼
Ages <5 years	No	Yes	No	Yes▼	No	No
Asperger's included	No	No	No	No	Yes	Yes▼

continued on p. 545

Table 5 (continued). Description of 11 U.K. surveys of autism prevalence, with factors affecting the assessment of disease frequency and time trends

	Lingam et al. 2003[63]	*Kaye et al 2001*[68]	*Scott et al 2002*[95]	*Chakrabarti and Fombonne 2001*[61]	*Baird et al. 2000*[78]
Geographic area	North London	U.K.	Cambridgeshire	Staffordshire	South East Thames Health Region
Birth year range	1985–1994	1988–1993	1988–1994	1992–1995	1993
Survey population	186,206	70,000	43,472	15,500▲	16,235▲
Number of cases per 10,000 children					
Autism	14.9	16.3	—	16.8 (95% CI 11.0, 24.6)	30.8 (95% CI 22.9, 40.6)
PDD, not including Asperger's	25.4	—	—	52.9	57.9 (95% CI 46.8, 70.9)
ASD, including Asperger's	30.5	—	57 (95% 49.5, 65.8)	62.6 (95% CI 50.8, 76.3)	—
Factors affecting prevalence					
Diagnostic criteria	ICD-10[31]	ICD-10[31]	ICD-10[31]	ICD-10[31]	ICD-10[31]
Central database	Yes▼	Yes▼	No	No	No
Age truncation	No	Yes (2–5)▼	No	Yes (2.5–6.5)▼	No
Population restriction	No	No	No	No	No
Gender restriction	No	Yes (male)▲	No	No	No
Factors affecting trend					
Year of birth breakdowns	Yes[d]	Yes[d]	No[b]	No[b]	No[b]
Age variation (range)	Yes (1–16)▼	No	No (5–11)	No (2–6)	No (7)
Ages <5 years	Yes▼	NA	No	Yes	No
Asperger's included	Yes▼	No	Yes	Yes	No

NOTE: Arrows indicate study design features with potential impact on reported outcomes, with downward-pointing arrows indicating a possible downward effect on frequency or trend estimates and upward-pointing arrows indicating a possible upward impact.

[a]Combined prevalence of 6.9 per 10,000 for "autistic" children and children with "similar but less marked features."

[b]Autism rates by age cohort and times of data collection provided by authors, allowing alignment of age cohort with birth years.

[c]Autism rates by year of birth provided by authors.

[d]Autism rates by year of birth provided by authors graphically.

CI = confidence interval

PDD = pervasive developmental disorder

ASD = autistic spectrum disorder

NA = not applicable

Table 6. Description of eight U.S. surveys of autism prevalence, with factors affecting the assessment of disease frequency and time trends

	Treffert 1970[36]	*Ritvo et al. 1989*[53]	*Burd et al. 1987*[45]	*California Department of Developmental Services 2003*[2]	*Sturmey and James 2001*[83]	*Yeargin-Allsopp et al. 2003*[75]	*Bertrand et al. 2001*[80]	*Gurney et al. 2003*[73]
Geographic area	Wisconsin	Utah	North Dakota	California	Texas	Atlanta, GA	Brick Township, NJ	Minnesota
Birth year range	1949–1969	1960–1984	1967–1991	1970–1997	1983–1994	1986–1993	1988–1995	1989–1993
Survey population	899,750	769,620	180,986	14,200,000	3,565,000	289,456	8,896	1,600,000
Number of cases per 10,000 children								
Autism	0.7 (95% CI 0.6, 0.9)	2.47 (95% CI 2.1, 2.8)	1.16	12.6	16	—	40 (95% CI 28, 56)	—
PDD, not including Asperger's	3.1	—	3.26 (95% CI 2.5, 4.2)	—	—	—	—	—
ASD, including Asperger's	—	—	—	—	—	34 (95% CI 32, 36)	67 (95% CI 51, 88)	20-66
Factors affecting prevalence								
Diagnostic criteria	Kanner[33]▼	DSM-III[29]	Kanner[33]▼	DSM-IV[32]	—	DSM-IV[32]	DSM-IV[32]	DSM-IV[32]
Central database	Yes▼	No	No	Yes▼	Yes▼	No	No	Yes▼
Age truncation	No	No	No	No	No	No	No	No
Population restriction	No	No	No	No	No	No	No	No
Gender restriction	No	No	No	No	No	No	No	No
Factors affecting trend								
Year of birth breakdowns	No[a]	Yes[c]	Yes[b]	Yes[c]	Yes, but NA[a]	Yes[d]	Yes[a]	Yes[c]
Age variation (range)	No (3–12)	3–27▼	1–1▼	Yes (5–32)	Yes (6–17)▼	Yes (3–10)▼	Yes (3–10)▼	No
Ages <5 years	Yes	Yes▼	Yes▼	No	No	Yes▼	Yes▼	No
Asperger's included	No	No	No	No	No	Yes▼	Yes/No	Yes▼

NOTE: Arrows indicate study design features with potential impact on reported outcomes, with downward-pointing arrows indicating a possible downward effect on frequency or trend estimates and upward-pointing arrows indicating a possible upward impact.

[a]Autism rates by age cohort and times of data collection provided by authors, allowing alignment of age cohort with birth years.

[b]Number of autism cases by year of birth provided by authors graphically, allowing calculation of rates using state census of live births.[96]

[c]Autism rates by year of birth provided by authors.

[d]Autism rates by year of birth provided by authors graphically.

CI = confidence interval

PDD = pervasive developmental disorder

ASD = autistic spectrum disorder

NA = not applicable

shown in the Tables and may also be a factor affecting frequency.

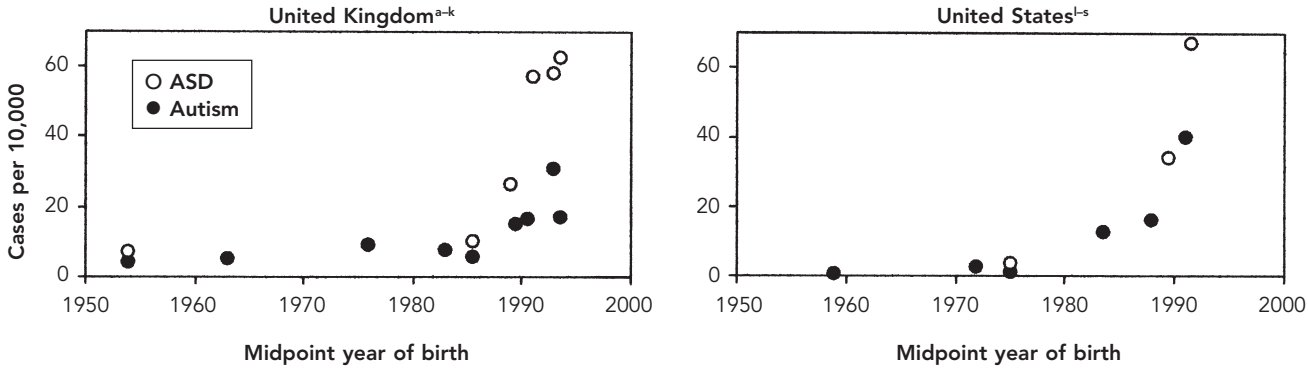
Factors affecting trend assessment relate to ascertainment bias and include the following: the availability of trend information for the survey period, the inclusion of a range of age groups in the survey population, the inclusion of children younger than 5 years of age in the survey population, and the inclusion of Asperger's syndrome in the survey scope. Each of the last three factors may depress evidence of an underlying trend. A large trend effect may also affect comparisons across surveys.

Figure 1 shows a comparison of reported prevalence rates across surveys from the U.K. and U.S., using the mid-point year of birth as the basis for comparing survey populations. This comparison demonstrates that reported autism rates in the U.K. rose from <10 per 10,000[19,35,42,83,89] to the 17 to 31 per 10,000 range[61,78] over 40 years and that reported PDD rates rose to approximately 60 per 10,000 in the same period.[61,78,95] According to the reported confidence intervals (CIs), these changes are statistically significant. The magnitude of the increase appears larger in the U.S. than in the U.K. The U.K. data show a strong inflection point around 1990, whereas autism rates in the U.S. appear to have begun their rise in the 1980s.

The amount of useful comparative information expands when one examines details of the published reports (Figure 2). In the U.K., starting with the earliest surveys based on children born before 1990 in Middlesex,[35] Camberwell,[42] Scotland,[82] and Wales,[89] the prevalence rates for autism were generally well below 10 per 10,000. In surveys including children born after 1990, reported autism rates were both higher[20] and rising.[20,68,78] Each of these surveys had unique features. A survey in the North Thames health region showed a remarkable rising trend in numbers of autism cases by birth year.[20] An administrative survey with one of the most credible trend reports (this design controlled for age-at-ascertainment bias) found a clear increase using a measure of cumulative incidence by birth year.[68] This result is difficult to compare to those of other surveys since this study used data on boys only (introducing an upward bias) and administrative data truncated to 2- to 5-year-olds (introducing a downward bias). The South East Thames survey provided a well-supported and high estimate of autism prevalence—30.8 per 10,000—in a single age cohort with a small population and effective case-finding.[78] One survey in Staffordshire stands out as an exception;[61] the reported autism rate is modestly lower than in other recent surveys, while the reported PDD rate (including Asperger's syndrome) is the highest ever reported in the U.K.

Evidence from U.K. surveys of the full range of ASDs also supports an increasing trend. A survey that sampled multiple areas showed a rising trend from approximately 1990.[62] Four recent surveys found similarly high rates,[61,63,78,95] three with rates of approximately 60 per 10,000[61,78,95] and a fourth

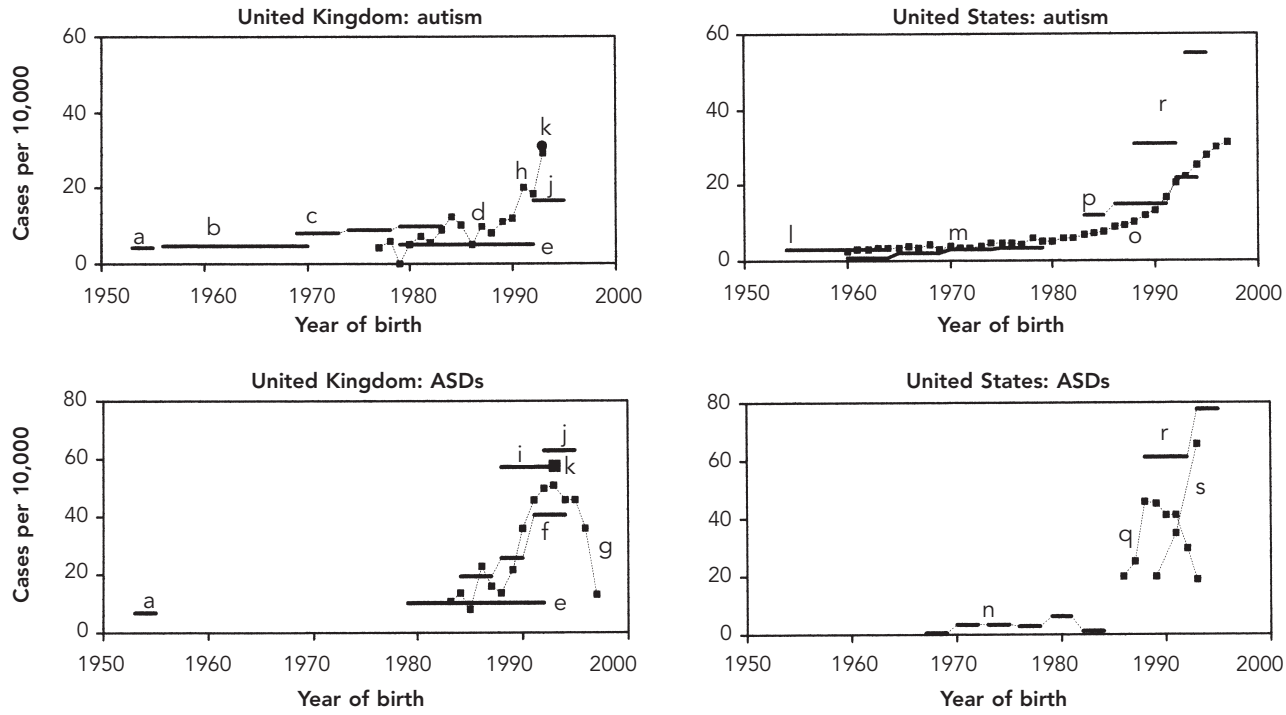
Figure 1. Reported prevalence of autism and autistic spectrum disorders (ASDs), by midpoint year of birth, United Kingdom and United States, 1954–1994



NOTE: These graphs show prevalence estimates from 11 U.K. and 8 U.S. studies. For studies with survey populations spanning a range of birth years, the midpoint of the birth year range is used.

[a]Lotter 1966[35]
[b]Wing and Gould 1979[42]
[c]Deb and Prasad 1994[82]
[d]Webb et al. 1997[89]
[e]Taylor et al. 1999[20]
[f]Fombonne et al. 2001[62]
[g]Lingam et al. 2003[63]
[h]Kaye et al. 2001[68]
[i]Scott et al. 2002[95]
[j]Chakrabarti and Fombonne 2001[61]
[k]Baird et al. 2000[78]
[l]Treffert 1970[36]
[m]Ritvo et al. 1989[53]
[n]Burd et al. 1987[45]
[o]California Department of Developmental Services 2003[2]
[p]Sturmey and James 2001[83]
[q]Yeargin-Allsopp et al. 2003[75]
[r]Bertrand et al. 2001[80]
[s]Gurney et al. 2003[73]

Figure 2. Reported prevalence of autism and autistic spectrum disorders (ASDs), by year of birth, United Kingdom and United States, 1953–1997



NOTE: These graphs show prevalence estimates from 11 U.K. and 8 U.S. studies. Horizontal lines represent estimates for multi-year birth cohorts. Squares represent estimates for single-year birth cohorts. Broken lines are used to link multiple estimates from the same study.

[a]Lotter 1966[35]
[b]Wing and Gould 1979[42]
[c]Deb and Prasad 1994[82]
[d]Webb et al. 1997[89]
[e]Taylor et al. 1999[20]
[f]Fombonne et al. 2001[62]
[g]Lingam et al. 2003[63]
[h]Kaye et al. 2001[68]
[i]Scott et al. 2002[95]
[j]Chakrabarti and Fombonne 2001[61]
[k]Baird et al. 2000[78]
[l]Treffert 1970[36]
[m]Ritvo et al. 1989[53]
[n]Burd et al. 1987[45]
[o]California Department of Developmental Services 2003[2]
[p]Sturmey and James 2001[83]
[q]Yeargin-Allsopp et al. 2003[75]
[r]Bertrand et al. 2001[80]
[s]Gurney et al. 2003[73]

with rates peaking at >50 per 10,000.[63] These recent survey reports can be compared with two earlier reports.[20,35] A survey of children born in the 1950s found a low prevalence rate of only 2.8 per 10,000 for children who had "similar but less marked features" than children diagnosed with autism.[35] A survey of children born from 1979 through 1992 found a rate of 3.4 per 10,000 for atypical autism.[20]

The results of seven U.S. surveys are also shown in Figure 2. These surveys support conclusions similar to those for the U.K. The early autism surveys show a clear convergence in disease frequency from the 1950s through 1980, with four different studies reporting rates consistently lower than three per 10,000.[2,36,45,53] Such low rates held in administrative surveys and active case-finding surveys and across four states. More recent data show a marked (if gradual) increase for autism in California[2] and also in New Jersey,[80] to levels >30 per 10,000. This 10-fold increase holds both within[2] and across surveys. An increasing trend was also reported in a survey of Missouri children.[84]

Three U.S. surveys report rates for ASDs of 43 per 10,000,[75] 66 per 10,000,[73] and 80 per 10,000.[80] These rates are both considerably higher than the earliest PDD rates reported in North Dakota,[45] which peaked at <7 per 10,000 around 1980, and all three survey populations showed higher frequency in later birth cohorts during survey periods. The Minnesota survey was well controlled with respect to ascertainment, and reported rising prevalence rates among 8-year-olds over a five-year period; the authors attributed the three-fold rate increase to changing administrative practices.[73] Surveys of 3- to 10-year-old populations in Georgia[75] and New Jersey[80] shared nearly identical ascertainment bias problems, with likely higher rates of Asperger's syndrome in the

older age cohorts and likely incomplete ascertainment of all PDDs in the 3 to 5 year age group.[75,80] These biases may have the effect of dampening evidence of rising rates while also skewing the shape of the trend. (This skew may be especially relevant in the Georgia study, in which a large number of children who had not received a prior autism diagnosis were reclassified into the PDD category.[75]) Like the autism evidence, the data for PDDs point to roughly a 10-fold increase for all ASDs from the 1970s to the early-to-mid 1990s.[45,73,75,79]

CONCLUSIONS

The evidence supporting an increasing rate of autism in the U.K. and the U.S. has gathered strength. Although both the nomenclature and the criteria set used to define autism have changed over the years, these changes are not so great as to prevent comparative analysis and do not explain major differences in reported prevalence over time. The largest stable source of variability in reported autism rates comes from incomplete ascertainment in young age cohorts, which limits the ability to detect an underlying and rising secular trend. Reviews that have downplayed the rising trend have overemphasized unimportant methodological problems, employed flawed meta-analytic methods, and failed to take into account the most relevant biases in survey methodologies. Point prevalence comparisons made within and across surveys conducted in specific geographic areas, using year of birth as a reference for trend assessment, provide the best basis for inferring disease frequency trends from multiple surveys. A comparison of U.K. and U.S. surveys, taking into consideration changing definitions, ascertainment bias, and case-finding methods, provides strong support for a conclusion of rising disease frequency. The rate of autism in the U.S., once reported as <3 per 10,000, has now risen to >30 per 10,000, a 10-fold increase. The rate of autism in the U.K., once reported as <10 per 10,000, has risen to roughly 30 per 10,000. Reported rates for ASDs in both countries have risen from the 5 to 10 per 10,000 range to the 50 to 80 per 10,000 range. This review has found little evidence that systematic changes in survey methods can explain these increases, although better ascertainment may still account for part of the observed changes. A precautionary approach therefore suggests that increased rates of autism and related disorders be accepted as an urgent public health concern.

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