Epidemiology of Autistic Disorder and Other Pervasive Developmental Disorders

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Is the incidence of autistic disorder and other pervasive developmental disorders (PDDs) increasing? Recent epidemiological surveys of autistic disorder and other PDDs have heightened awareness of and concern about the prevalence of these disorders; however, differences in survey methodology, particularly changes in case definition and case identification over time, have made comparisons between surveys difficult to perform and interpret. Recent surveys suggest that the rate of all PDDs is about 60 per 10,000. The prevalence of autism today is estimated at 13 per 10,000, Asperger's disorder is approximately 3 per 10,000, and childhood disintegrative disorder is very rare at about 0.2 per 10,000. The assessment process, sample size, publication year, and geographic location of studies all have an effect on prevalence estimates. In addition, data from many of these surveys indicate correlates of autistic disorder and other PDDs with IQ, gender, and other medical disorders.

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Epidemiological surveys of autistic disorder and other pervasive developmental disorders (PDDs) have been conducted for nearly 40 years, but the number of studies has increased in recent years. This review covers the 34 surveys[1–34] reporting data on the prevalence of autistic disorder and 6 others providing data on the whole spectrum of PDDs[35–38] or on Asperger's disorder[39,40] that have been conducted in 14 countries and published in English-language journals to date. The median population was 65,000 (range, 1941–4,950,333) and primarily included school-aged children (median age = 8.0 years; range, 0–20 years). The assessment process varied from study to study, but overall, the number of subjects determined to have autistic disorder ranged from 6 children[18] to 5038 children[32] across studies (median = 50; mean = 220).

METHODOLOGY

Differing methods of identifying cases of possible autism or related disorders were used in the surveys, but most incorporated a screening stage and a diagnostic stage.

Screening methods used to identify possible cases of autism varied from study to study. Some investigators relied on existing databases[32,38] while others sent brief letters or checklists to speech therapists, teachers, health care professionals, and family members. Some surveys[3,17,20,24,32] included only cases already identified by education or health care professionals, while others[1,13,19,22,31,34,40] included the entire population of a given geographic area. Other screening variables, such as whether or not health care professionals were trained to detect PDDs during systematic health visits, whether parental permission to participate was denied, and what types of information were requested, added to the variety of methods used to discern suspected PDDs. Because the sensitivity of the screening method used is difficult to determine in autism surveys, it is probable that children who have a PDD may screen negatively. Estimations of false negatives were not performed in the surveys because the low frequency of autism would render estimates of sensitivity imprecise and costly to perform. The implication is that some children with a PDD are not detected, so the prevalence estimates derived from each survey must be considered to be underestimates of the actual prevalence rate.

In a second phase, the diagnostic stage, children who screened positively in the first stage enter a confirmatory phase whereby investigators determine whether or not these children meet criteria for a diagnosis of autism or other kinds of PDDs. The assessment process used in this stage also varies from survey to survey. Some investigators review the medical record and the information at hand and make a judgment about a particular child. In other, more comprehensive surveys, a specialist team directly assesses the child, interviews the parents, and employs a structured diagnostic tool such as the Autism Diagnostic Interview (ADI)[41] or the Autism Diagnostic Observation Schedule (ADOS).[42]

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Table 1. Asperger's Disorder in Recent Autism Surveys[a]

	Autistic Disorder		Asperger's Disorder		
Study (year)	N	Prevalence Rate/10,000	N	Prevalence Rate/10,000	Autism/Asperger's Ratio
Sponheim and Skjeldal[23] (1998)	32	4.9	2	0.3	16.0
Kadesjö et al[40] (1999)	6	72.6	4	48.4	1.5
Powell et al[26] (2000)	54	…	16	…	3.4
Baird et al[25] (2000)	45	30.8	5	3.1	9.9
Chakrabarti and Fombonne[30] (2001)	26	16.8	13	8.4	2.0
Overall	163		40		4.1

[a]Adapted with permission from Fombonne.[52]

Diagnostic criteria have changed over time according to changes in the classification system. Cases of PDDs reported in the 1960s were primarily assessed using Kanner's criteria.[43] Lotter's[44] and Rutter's[45] definitions and the ICD-9,[46] used in the 1970s, were replaced by the DSM-III[47] and DSM-III-R[48] in the 1980s. Over the last 15 years, new cases have been defined by the DSM-IV[49] and ICD-10.[50] Evolving case definitions and differing diagnostic criteria are important factors that affect the epidemiology of autism and other PDDs. Most surveys, however, have relied on the clinical judgment of experts to determine case groupings.

PREVALENCE ESTIMATES OF AUTISTIC DISORDER

The median prevalence for autistic disorder across the 34 autism surveys was 8.7 per 10,000 (range, 0.7[3] to 46.4[22]). A wide confidence interval indicated a large variability in the precision of estimates across surveys, i.e., a negative correlation existed between the sample size and the prevalence rate. Studies based in large populations appeared to be more precise than those in smaller populations. Studies with a limited sample size tended to have the largest prevalence rates, while large studies tended to have lower prevalence rates on average.

Another correlate of the prevalence of autism is the publication year. Surveys published between the mid-1960s and mid-1970s[1,2,4] estimated that 4 children per 10,000 had autism, while prevalence estimates of autism in more recent surveys have been much higher. By excluding studies that were imprecise,[18,22] had a limited sample size, and were conducted prior to 1987,[3,5–8] the range of prevalence of autistic disorder in the remaining studies that reported data on the prevalence of autistic disorder[9–17,19–21,23–34] and 6 others providing data on the whole spectrum of PDDs[35–40] varied from 11 to 18 per 10,000. On the basis of these data, a conservative estimate of the prevalence of autism today is 13 per 10,000 (a true estimate would be higher because some children have been missed).

ATYPICAL FORMS OF AUTISM

Beginning with the earliest surveys, investigators tried to apply strict diagnostic criteria to delineate children who had autistic disorder. In the course of their investigations, researchers met many children who had developmental problems similar to those identified in children with autism but who failed to meet full diagnostic criteria for the disorder. These children were not studied extensively in the first surveys, but were eventually described as having "other psychoses"[2] and were labeled "the socially impaired"[4] or "autistic-like."[5,9] The number of children so labeled was sometimes as high as or higher than the number of children identified as having autistic disorder. Recent studies[28,30,33,34] confirm that atypical forms of autism are more frequent than instances of children meeting strict criteria for autism.

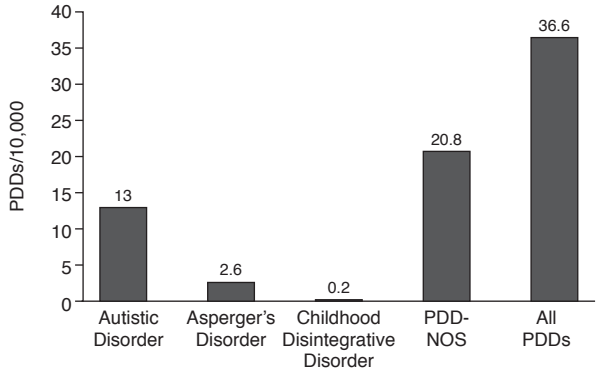
Another atypical form of PDD—childhood disintegrative disorder (CDD)—is rare. Only 6 surveys[9,23,29,30,34,51] have reported children meeting criteria for CDD. These children developed normally up to the age of about 3 years and then regressed profoundly, culminating in severe autism with severe mental retardation. On the basis of these surveys, the rate of CDD is estimated to be about 1 or 2 per 100,000 children. The lack of diagnosed cases makes this rare condition difficult to study.

Asperger's disorder was introduced in the ICD-10 in 1992 and in the DSM-IV in 1994. Two Scandinavia-based epidemiological surveys[39,40] were conducted on small populations in the 1990s, and each survey described 4 cases of Asperger's disorder. Because of the small sample size, however, the confidence interval was so wide that it is very difficult to draw any meaningful inferences from these 2 surveys. By contrast, a comparison[52] of recent surveys that classified children as having either autism or Asperger's disorder showed that the number of children meeting criteria for Asperger's disorder was consistently lower than that of those meeting criteria for autistic disorder in the same survey (Table 1). Overall, these surveys suggested a prevalence of Asperger's disorder about one fourth that of autism. More studies are required on the epidemiology of Asperger's disorder to support this estimate.

PREVALENCE ESTIMATES OF ALL PDDS

Overall prevalence estimates for autistic disorder, Asperger's disorder, CDD, PDD-NOS, and all PDDs are

Figure 1. Prevalence of Pervasive Developmental Disorders (PDDs)/10,000[a]



[a]Data from Fombonne.[53]
Abbreviation: NOS = not otherwise specified.

shown in Figure 1.[53] Reviewed individually, the prevalence rate for each disorder is relatively low (CDD is negligible). However, reviewed in total, the resulting 37 PDDs per 10,000 are substantial, especially when one considers that many children have been missed in these surveys. Newer surveys[25,28,30,34,36] converge in estimating the prevalence of the whole spectrum of PDD as being substantially higher, around 60 or 65 per 10,000 (although the rates of autism, PDD-NOS, and Asperger's disorder vary widely within each survey).

CHARACTERISTICS OF AUTISTIC DISORDER SAMPLES

Nineteen studies* have reported an assessment of intellectual function. Despite differences between instruments used and the bands of intellectual level reported by investigators, about 30% of the children scored in the normal range of intelligence, about 30% scored in the mild-to-moderate mental retardation range, and about 40% scored in the serious-to-profound mental retardation range.[55]

Thirty studies† reported male:female ratio among children with autism. The male:female ratio varied from 1.33[7] to 16.0,[4] with a mean male:female ratio of 4:1. No epidemiological survey has identified more girls than boys with autism, a finding that confirms gender differences found in clinically referred children.[56] The constant preponderance of male subjects in all autism surveys, however, indicates an association that has not yet been explained.

Among children with a PDD and mental retardation, the preponderance of boys is less pronounced. The more profoundly retarded the children, the less differentiation by sex (2 boys for 1 girl, typically),[20,53] whereas, in the high-functioning children with autism, the preponderance of males is even more pronounced (6 to 8 boys for 1 girl).[53]

Epilepsy, fragile X syndrome, tuberous sclerosis, cerebral palsy, phenylketonuria, neurofibromatosis, Down syndrome, congenital rubella, and hearing and visual impairments are among the medical conditions associated with autism in children.[55] Epilepsy rates are high among children with autism and higher among children reported to have autism and severe mental retardation.[16,17,20] Both fragile X syndrome and tuberous sclerosis are genetic disorders associated with increased risk of autism. Although the rate of 0.3 children with autism who also have fragile X syndrome is well documented,[15–17,20] the rate is probably an underestimate because of varying methods of collecting information (today's rate is closer to 2% to 4%[57]). Tuberous sclerosis is one of the most robust associations of a medical disorder known to be associated with autism (consistently about 1.2% of 100 children).[1,15–17,20,23] Compared with the rate of tuberous sclerosis in the general population (1 in 10,000 children), the prevalence of tuberous sclerosis in autism represents a 100-fold increase.

Between 6% and 10% of children with autism[20,55] have a medical disorder that might have led to autism. Therefore, in more than 90% of the cases, one would not find any medical explanations for the autistic disorder. These cases of idiopathic autism are eligible for genetic research in many ongoing molecular genetics studies.

Early epidemiological surveys suggested a correlation between social class, ethnicity or immigrant status, or geographic variation and autism. Surveys prior to 1980[1–4] suggested an association between autism and higher social class or parental educational level. This finding is likely a reflection of bias in accessing services at that time. Autism and PDDs are found across the social classes with similar frequencies.[55]

An association between autism and various ethnic or immigrant groups and higher social class has also been theorized.[16,58–60] Reports of this nature often rely on a very small sample size and are not supported by empirical results. Recently, a large group of African American children were studied,[37] and no differences in the rates of autism or PDDs were found when compared with white children.

Occasional reports of geographical clustering of cases have also raised concern about the possibility of environmental factors increasing the risk of autism or PDDs. In one report,[61] 7 children living near each other in the United Kingdom were diagnosed with either autism or PDD-NOS, but a closer examination revealed methodological variation and preselection bias that led to inappropriate comparison between clustering and population incidence.[55] Cluster reports require confirmation, and epidemiological and statistical methods must be employed to test whether or not clusters are a true clustering of cases or just occurring by chance. No evidence so far has indicated that significant clusters exist in particular regions.

*References 1, 4, 6, 8, 12, 15–17, 19, 20, 22, 23, 25, 27–30, 32, 54.
†References 1–12, 14–23, 25, 27–32, 54.

Table 2. Study Design Impact on Prevalence[a]

Study (year)	Location	Population	Age Group (y)	Method	PDD Rate/10,000
United Kingdom Surveys[b]					
Baird et al[25] (2000)	Southeast Thames	16,235	7	Early screening and follow-up identification	57.9
Chakrabarti and Fombonne[30] (2001)	Stafford	15,500	2.5–6.5	Intense screening and assessment	62.6
Fombonne et al[35] (2001)	England and Wales	10,438	5–15	Household survey of psychiatric disorders	26.1
Taylor et al[24] (1999)	North Thames	490,000	0–16	Administrative records	10.1
United States Surveys[c]					
Bertrand et al[28] (2001)	New Jersey	8,896	3–10	Multiple sources of ascertainment	67
Department of Developmental Services[62] (1999)	California	3,215,000	4–9	Educational services	15
Sturmey and Vernon[63] (2001)	Texas	3,564,577	6–18	Educational services	16
Hillman et al[64] (2000)	Missouri	…	5–9	Educational services	4.8

[a]Reprinted with permission from Fombonne.[55]
[b]The prevalence of pervasive developmental disorder in 4 studies in the United Kingdom reflects a 6-fold variation in estimates.
[c]The prevalence of pervasive developmental disorder in 4 studies in the United States reflects a 14-fold variation in estimates.
Abbreviation: PDD = pervasive developmental disorder.

TIME TRENDS

While cross-sectional surveys conducted at a given point in time determine prevalence rates, they do not measure incidence (the number of new cases occurring over time) and therefore limit our ability to draw inferences about an epidemic of autism. Furthermore, over time a broadening of diagnostic criteria used to define autism, changes in how autism is identified in surveys, and heightened public awareness and more available services have had an effect on reported prevalence.

Changes in case definition and diagnostic criteria have had an impact on the accuracy of prevalence rates. Kanner's autism criteria[43] were narrow and studies that relied on these criteria had a mean rate of autism of 3.8. By contrast, DSM-IV[49] and ICD-10[50] criteria include broader definitions and led to a mean rate of 20 per 10,000 cases in recent surveys. The effect of changes in diagnostic criteria is illustrated by a Finnish survey[27] that applied different diagnostic criteria to the same group of children in the same survey (N = 39,216). Using Kanner's criteria, the rate of autism was 2.3 per 10,000. By contrast, ICD-10 and DSM-IV autism criteria further increased the rate to 6.1 per 10,000, and ICD-10 autism spectrum criteria further increased the rate to 7.6 per 10,000. These data demonstrate a 3-fold variation in prevalence rate based on diagnostic criteria.

Estimates of prevalence are also affected by study design. Methods vary widely and may include early screening and follow-up,[25] intense screening and assessment,[30] household surveys about psychiatric disorders,[35] review of administrative records,[24] ascertainment from multiple sources,[28] and assessment from educational services.[62–64] Despite similarities in time frame and age group studied, a comparison[55] of study design among surveys conducted in the United Kingdom and in the United States produced a 6-fold variation in prevalence among the United Kingdom surveys and a 14-fold variation in rates in surveys conducted in the United States (Table 2). These differences in prevalence rates appeared to be related to differences in study method.

Referral statistics are another approach to assessing trends over time. However, referral data must be used with caution because availability of services, heightened awareness by a population, and legislative and social policies contribute to the increasing number of cases reported. The reporting of autistic disorder in California is a good example of misinterpretation of referral data because of these confounding factors. More than 40 years of data have been collected in California using the Client Development Evaluation Report (CDER). The CDER data set summarizes how many children in California visit public centers and have accessed early intervention programs. According to a report to the California legislature in 1999,[62] the number of children who have accessed services since the early 1980s has steadily increased. Some interpret this upward trend as an epidemic of autism, but in fact, this is far from being the case. From December 1998 through December 2002, more than 20,000 cases of autism had been reported through CDER services in California.[65] According to the 2003 census,[66] about 10.5 million people between the ages of 0 and 19 years of age lived in California. The epidemiology of PDDs derived from international and U.S. surveys, as stated earlier, would indicate a prevalence of PDDs of 37 per 10,000, a conservative estimate, or about 38,850 subjects in this age group in California. On the basis of the more realistic estimate of 60 per 10,000, one would expect 63,000 diagnosed cases of a PDD in California in this age group in 2003. Therefore, the 20,000 cases among 10.5 million youths recorded

in the CDER database do not suggest an epidemic but rather suggest that the number of children accessing services has grown. There is no indication that there is an epidemic of autistic disorder or other PDDs.

A similar trend toward more children being diagnosed with a PDD was reported in Minnesota[38] in 2003. Gurney et al. showed that after 1990, the number of children being diagnosed with PDDs in the same growth cohort increased 16-fold. Children were earning a diagnosis of autism between the ages of 12 and 14 years, which is not consistent with autism, which is defined by onset before age 3. But, as social policies changed, children not previously diagnosed with autism changed status and had more access to support services in the educational system. Gurney et al.[38] argued that changes in the national Individuals With Disabilities Education Act (IDEA) in 1990 may account for some of the rise in the numbers of children earning a diagnosis of autism in U.S. school systems.

Another approach to determine trends over time has been to compare surveys done in the same areas at different times. Two surveys[30,34] were conducted in the region of Stafford, Great Britain. The first comprised children who were born between 1992 and 1995; the rate of PDDs was 62 per 10,000. The second study comprised children born between 1996 and 1998 in the same region using the same methods for identifying cases in the community and for diagnosing them. The rate of PDDs was 59 per 10,000. No significant differences in the rates of PDDs or the rates of any specific subtypes of PDDs were found. These findings suggest that there is no trend toward increasing prevalence rates in a given region over time.

Using a large electronic database of patients of general practitioners, Smeeth et al.[67] showed an increase in incidence of PDDs from 1988 to 2001. The increase, however, could not be attributed to a true change in the incidence of PDDs as opposed to increased awareness and a broadening of diagnostic criteria at the same time.

CONCLUSION

Most of the studies of the epidemiology of autism are not informative to gauge trends over time. A few informative studies are available, but generally they do not control for changes in case definition and diagnostic criteria, which are alternative explanations for the upward trend in autism rates. Nevertheless, the prevalence rates for autism and PDDs have increased and are in the vicinity of 60 per 10,000 or 0.6%, making PDDs, particularly autistic disorder, among the most prevalent medical conditions of childhood. This increase in prevalence, however, cannot be interpreted as a secular change in the incidence or an epidemic of autism. Most of the upward trend in prevalence can be accounted for by methodological factors such as change in the diagnostic criteria. Can we say for sure that there is no increase in the incidence of autism and PDDs? No. No data definitively support this hypothesis, but it cannot be ruled out. Researchers must be vigilant and test this hypothesis further with adequate epidemiological data acquired during the next 5 or 10 years.

For the United States, the implications of recent prevalence figures are straightforward. If the conservative rate of 37 per 10,000 children were applied to today's population of the United States under the age of 20 years (based on census 2002 estimates),[66] approximately 300,000 individuals in the United States would have a PDD diagnosis. If the less conservative but perhaps more realistic estimate of 60 per 10,000 were applied, approximately 486,000 individuals under age 20 currently living in the United States would have a PDD diagnosis. Decision makers who plan services for this needy group of patients should use the less conservative figure.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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