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Epidemiological Surveys of Autism and Other Pervasive Developmental Disorders: An Update

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This paper was commissioned by the committee on the Effectiveness of Early Education in Autism of the National Research Council (NRC). It provides a review of epidemiological studies of pervasive developmental disorders (PDD) which updates a previously published article (The epidemiology of autism: a review. Psychological Medicine 1999; 29: 769–786). The design, sample characteristics of 32 surveys published between 1966 and 2001 are described. Recent surveys suggest that the rate for all forms of PDDs are around 30/10,000 but more recent surveys suggest that the estimate might be as high as 60/10,000. The rate for Asperger disorder is not well established, and a conservative figure is 2.5/10,000. Childhood disintegrative disorder is extremely rare with a pooled estimate across studies of 0.2/10,000. A detailed discussion of the possible interpretations of trends over time in prevalence rates is provided. There is evidence that changes in case definition and improved awareness explain much of the upward trend of rates in recent decades. However, available epidemiological surveys do not provide an adequate test of the hypothesis of a changing incidence of PDDs.

KEY WORDS: Autism; pervasive developmental disorder; epidemiology; prevalence; incidence; childhood disintegrative disorder; Asperger disorder.

INTRODUCTION

Epidemiological surveys of autism started in the mid-sixties in England (Lotter, 1966) and have since then been conducted in many countries. All epidemiological surveys have focused on a categorical-diagnostic approach to autism that has relied over time on different sets of criteria; however, all surveys used a definition of autism which comprised severe impairments in communication and language, social interactions, and play and behavior. This paper is therefore concerned with autism defined as a severe developmental disorder and not with more subtle autistic features or symptoms which occur as part of other, more specific, developmental disorders, as unusual personality traits, or as components of the lesser variant of autism thought to index genetic liability to autism in relatives. With the exception of recent studies, other pervasive developmental disorders (PDD) falling short of diagnostic criteria for autism (PDD-NOS, Asperger syndrome) were generally not included in the definition used in the earlier surveys although several epidemiological investigations yielded useful information on the rates of these particular types of PDDs. These data are summarized separately. The aims of this article are to provide an up-to-date review of the methodological features and substantive results of published epidemiological surveys. This article updates our previous review (Fombonne, 1999) with the inclusion of 9 new studies made available since then. A key feature of the review was to rely on summary statistics throughout in order to derive quantitative estimates for rates and correlates of autism-spectrum disorders. The specific questions addressed in this review update are: a) what is the range of prevalence estimates for autism, and related disorders? b) what proportion of autism

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cases is attributable to specific associated medical disorders? c) is the incidence of autism increasing? d) what are the other correlates of autistic-spectrum disorders, particularly with respect to race and ethnicity? e) what is the role, if any, of cluster reports in causal investigations of autism?; what are the directions for future epidemiological studies?

SELECTION OF STUDIES

The studies were identified through systematic searches from the major scientific literature databases (MEDLINE, PSYCINFO) and from prior reviews (Wing, 1993; Zahner & Pauls, 1987; Fombonne, 1998, 1999). Only studies published in the English language were included in this review. This led to the exclusion of several questionnaire-based studies and of small-scale investigations published in the national literature of the relevant countries (Aussilloux *et al.,* 1989; Haga & Miyamoya, 1971; Herder, 1993; Ishii & Takahashi, 1983; Nakai, 1971) and, most certainly, of other similar studies unknown to the author. Overall, 32 studies published between 1966 and 2001 were selected which surveyed autism in clearly demarcated, non-overlapping samples. They are listed in Table I by order of their appearance in the literature. Studies are numbered from 1 to 32, and these numbers are used subsequently to index each study. For several studies, the publication listed in Table I is the most detailed account or the earliest one; however, other published articles were used to extract relevant information from the same study, when appropriate.

SURVEY DESCRIPTIONS

The surveys were conducted in 13 countries and half of the results have been published during the last decade (Table I). Details on the precise socio-demographic composition and economical activities of the area surveyed in each study were generally lacking; most studies were, however, conducted in predominantly urban or mixed areas, with only 2 (studies 6 and 11) surveys carried out in predominantly rural areas. The proportion of children from immigrant families was generally not available and very low in 5 surveyed populations (studies 11, 12, 19, 23, and 26); only in study 4 was there a substantial minority of children with an immigrant West-Indian background living in the area. The age range of the population included in the surveys is spread from birth to early adult life, with an overall median age of 8.0 across the 32 studies. Similarly, there is huge variation in the size of the population surveyed (range: 826–899,750), with a median population size of 65,300 subjects (mean = 153,700) and about half of the studies relying on targeted populations ranging in size from 15,000 to 152,000. The total number of children surveyed is just approaching the 5 million figure (N = 4,918,000).

STUDY DESIGNS

Most investigations have relied on a two-stage or multi-stage approach to identify cases in underlying populations. The first screening stage of these studies often consisted of sending letters or brief screening scales requesting school and health professionals to identify possible cases of autism. Each investigation varied in several key aspects of this screening stage. First, the coverage of the population varied enormously from one study to another. In some (i.e., studies 3, 17, 20, and 24), only cases already known from educational or medical authorities could be identified, whereas in other surveys an extensive coverage of the entire population, including children attending normal schools (studies 1 and 25) or children undergoing systematic developmental checks (studies 13, 19, 22, and 32) was achieved. In addition, the surveyed areas varied in terms of service development as a function of the specific educational or health care systems of each country and of the year of investigation. Secondly, the type of information sent out to professionals invited to identify children varied from simple letters including a few clinical descriptors of autism-related symptoms or diagnostic checklists re-phrased in non-technical terms, to more systematic screening based on questionnaires or rating scales of known reliability and validity. Thirdly, participation rates in the first screening stages provide another source of variation in the screening efficiency of surveys. Refusal rates were available for 11 studies (studies 1, 5, 6, 9, 12, 14, 19, 20, 23, 25, and 30); the rate of refusal ranged from 0% (study 25) to 29.4% (study 5), with a median value of 10%. Fewer studies could examine the extent to which refusal to participate or uncooperativeness in surveys is associated with the likelihood that the corresponding children have autism. Bryson *et al.* (1988), however, provided some evidence that those families who refused cooperation in the intensive assessment phase had children with ABC scores similar to other false positives in their study, thereby suggesting that these children were unlikely

Table I. Prevalence Surveys of Autism

No.	Year of publication	Authors	Country	Area	Size of target population	Number of subjects with autism	Diagnostic Criteria	Percent with normal IQ	Gender ratio (M:F)	Prevalence Rate /10,000	95% CI
1	1966	Lotter	UK	Middlesex	78,000	32	Rating scale	15.6	2.6 (23/9)	4.1	2.7; 5.5
2	1970	Brask	Denmark	Aarhus County	46,500	20	Clinical	—	1.4 (12/7)	4.3	2.4; 6.2
3	1970	Treffert	USA	Wisconsin	899,750	69	Kanner	—	3.06 (52/17)	0.7	0.6; 0.9
4	1976	Wing *et al.*	UK	Camberwell	25,000	17[a]	24 Items rating scale of Lotter	30	16 (16/1)	4.8[b]	2.1; 7.5
5	1982	Hoshino *et al.*	Japan	Fukushima-Ken	609,848	142	Kanner's criteria	—	9.9 (129/13)	2.33	1.9; 2.7
6	1983	Bohman *et al.*	Sweden	County of Västerbotten	69,000	39	Rutter criteria	20.5	1.6 (24/15)	5.6	3.9; 7.4
7	1984	McCarthy *et al.*	Ireland	East	65,000	28	Kanner	—	1.33 (16/12)	4.3	2.7; 5.9
8	1986	Steinhausen *et al.*	Germany	West Berlin	279,616	52	Rutter	55.8	2.25 (36/16)	1.9	1.4; 2.4
9	1987	Burd *et al.*	USA	North Dakota	180,986	59	DSM-III	—	2.7 (43/16)	3.26	2.4; 4.1
10	1987	Matsuishi *et al.*	Japan	Kurume City	32,834	51	DSM-III	—	4.7 (42/9)	15.5	11.3; 19.8
11	1988	Tanoue *et al.*	Japan	Southern Ibaraki	95,394	132	DSM-III	—	4.07 (106/26)	13.8	11.5; 16.2
12	1988	Bryson *et al.*	Canada	Part of Nova-Scotia	20,800	21	New RDC	23.8	2.5 (15/6)	10.1	5.8; 14.4
13	1989	Sugiyama et Abe	Japan	Nagoya	12,263	16	DSM-III	—	—	13.0	6.7; 19.4
14	1989	Cialdella et Mamelle	France	1 département (Rhône)	135,180	61	DSM-III like	—	2.3	4.5	3.4; 5.6
15	1989	Ritvo *et al.*	USA	Utah	769,620	241	DSM-III	34	3.73 (190/51)	2.47	2.1; 2.8
16	1991	Gillberg *et al.*[d]	Sweden	South-West Gothenburg + Bohuslän County	78,106	74	DSM-III-R	18	2.7 (54/20)	9.5	7.3; 11.6
17	1992	Fombonne et du Mazaubrun	France	4 régions 14 départements	274,816	154	Clinical-ICD-10 like	13.3	2.1 (105/49)	4.9	4.1; 5.7
18	1992	Wignyosumarto *et al.*	Indonesia	Yogyakarita (SE of Jakarta)	5,120	6	CARS	0	2.0 (4/2)	11.7	2.3; 21.1

(*Continued*)

Table I. (*Continued*)

No.	Year of publication	Authors	Country	Area	Size of target population	Number of subjects with autism	Diagnostic Criteria	Percent with normal IQ	Gender ratio (M:F)	Prevalence Rate/10,000	95% CI
19	1996	Honda *et al.*	Japan	Yokohama	8,537	18	ICD-10	50.0	2.6 (13.5)	21.08	11.4; 30.8
20	1997	Fombonne *et al.*	France	3 départements	325,347	174	Clinical ICD-10-like	12.1	1.81 (112/62)	5.35	4.6; 6.1
21	1997	Webb *et al.*	UK	South Glamorgan, Wales	73,301	53	DSM-III-R	—	6.57 (46/7)	7.2	5.3; 9.3
22	1997	Arvidsson *et al.*	Sweden (West coast)	Mölnlycke	1,941	9	ICD-10	22.2	3.5 (7/2)	46.4	16.1; 76.6
23	1998	Sponheim and Skjeldal	Norway	Akershus County	65,688	34	ICD-10	47.1[c]	2.09 (23/11)	5.2	3.4; 6.9
24	1999	Taylor *et al.*	UK	North Thames	490,000	427	ICD-10	—	—	8.7	7.9; 9.5
25	1999	Kadesjö *et al.*	Sweden (Central)	Karlstad	826	6	DSM-III-R/ICD-10 Gillberg's criteria (Asperger syndrome)	50.0	5.0 (5/1)	72.6	14.7; 130.6
26	2000	Baird *et al.*	UK	South-East Thames	16,235	50	ICD-10	60	15.7 (47/3)	30.8	22.9; 40.6
27	2000	Powell *et al.*	UK	West Midlands	25,377	62	Clinical/ ICD10/ DSM-IV	—	—	7.8	5.8; 10.5
28	2000	Kielinen *et al.*	Finland	North (Oulu & Lapland)	152,732	187	ICD-8/ ICD-9/ ICD-10	49.8	4.12 (156/50)	12.2	10.5; 14.0
29	2001	Bertrand *et al.*	USA	Brick Township, New Jersey	8,896	36	DSM-IV	36.7	2.2 (25/11)	40.5	28.0; 56.0
30	2001	Fombonne *et al.*	UK	Angleterre & Pays de Galles	10,438	27	DSM-IV/ ICD-10	55.5	8.0 (24/3)	26.1	16.2; 36.0
31	2001	Magnússon and Saemundsen	Iceland	Whole Island	43,153	57	Mostly ICD-10	15.8	4.2 (46/11)	13.2	9.8; 16.6
32	2001	Chakrabarti et Fombonne	UK (Midlands)	Staffordshire	15,500	26	ICD10/ DSM-IV	29.2	3.3 (20/6)	16.8	10.3; 23.2

[a] This number corresponds to the sample described in Wing et Gould (1979).
[b] This rate corresponds to the first published paper on this survey and is based on 12 subjects amongst children aged 5 to 14 years.
[c] In this study, mild mental retardation was combined with normal IQ, whereas moderate and severe mental retardation were grouped together.
[d] For the Goteborg surveys by Gillberg *et al.* (Gillberg, 1984; Steffenburg & Gillberg, 1986; Gillberg *et al.,* 1991) a detailed examination showed that there was overlap between the samples included in the 3 surveys; consequently only the last survey has been included in this table.

to have autism. By contrast, in a Japanese study (Sugiyama & Abe, 1989; study 13) where 17.3% of parents refused further investigations for their 18-month old children who had failed a developmental check, follow-up data at age 3 suggested that half of these children still displayed developmental problems. Whether or not these problems were connected to autism is unknown, but this study points to the possibility of having higher rates of developmental disorders among non-participants to surveys. Similarly, in Lotter's study (1966; study 1), 58 questionnaires covering schools for handicapped children were returned out of the 76 forms sent out, and an independent review of the records showed that 4 of the 18 missing forms corresponded to autistic children. Therefore, it is difficult to draw firm conclusions from these different accounts. Although there is no consistent evidence that parental refusal to co-operate is associated with autism in their offspring, it appears that a small proportion of cases may be missed in some surveys as a consequence of non-cooperation at the screening stage. No survey included a weighting procedure to compensate for non-response.

Only two studies (studies 1 and 30) provided an estimate of the reliability of the screening procedure. The sensitivity of the screening methodology is also difficult to gauge in autism surveys. The usual epidemiological approach which consists of sampling at random screened negative subjects in order to estimate the proportion of false negatives, has not been used in these surveys for the obvious reason that, due to the very low frequency of the disorder, it would be both imprecise and very costly to undertake such estimations. The consequence of these remarks is that prevalence estimates must be seen as underestimates of 'true' prevalence rates because cases are being missed due either to lack of cooperation or to imperfect sensitivity of the screening procedure. The magnitude of this underestimation is unknown in each survey.

Similar considerations about the methodological variability across studies apply to the intensive assessment phases. Participation rates in these second stage assessments were not always available, either because they had simply not been calculated, or because the design and/or method of data collection did not lead easily to their estimation. When available (studies 1, 5, 8, 12, 13, 15, 22, 23, 25, 29, 30, 32), they were generally high, ranging from 76.1% (study 12) to 98.6% (study 25). The source of information used to determine caseness usually involved a combination of informants and data sources, with a direct assessment of the person with autism in 19 studies.

The assessments were conducted with various diagnostic instruments, ranging from a classical clinical examination to the use of batteries of standardized measures. The Autism Diagnostic Interview (Le Couteur *et al.,* 1989) was used in 5 of the most recent surveys. The precise diagnostic criteria retained to define caseness vary according to the study and, to a large extent, reflect historical changes in classification systems. Thus, Kanner's criteria, Lotter's and Rutter's definitions were used in the first 8 surveys (all conducted before 1982), whereas DSM-based definitions took over thereafter as well as ICD-10 since 1990. Some studies have relaxed partially some diagnostic criteria such as the requirement of an age of onset before 30 months (study 6) or that of the absence of schizophrenic-like symptoms (studies 13 and 14). However, most surveys have relied on the clinical judgment of experts to arrive at the final case groupings. It is worth underlining that field trials for recent classifications such as DSM-III-R (Spitzer & Siegel, 1990) or DSM-IV/ICD-10 (Volkmar *et al.,* 1994) have also relied upon the judgment of clinical experts, taken as a gold standard to diagnose autism. Therefore, the heterogeneity of diagnostic criteria used across surveys is somewhat mitigated by reliance on expert clinical judgment to determine final caseness. It is furthermore difficult to assess the impact of a specific diagnostic scheme or of a particular diagnostic criterion on the estimate of prevalence since other powerful method factors confound between-studies comparisons of rates. Surprisingly, few studies have built in a reliability assessment of the diagnostic procedure; reliability during the intensive assessment phase was high in 6 surveys (studies 4, 13, 16, 23, 24, and 32) and moderate in another one (study 14).

CHARACTERISTICS OF IDENTIFIED SAMPLES

A total number of 2,380 subjects assessed in the second stage of the 32 surveys were considered to suffer from autism, this number ranging from 6 to 427 across studies (median: 51). An assessment of intellectual function was obtained in 20 studies. These assessments were conducted with various tests and instruments; furthermore, results were pooled together in broad bands of intellectual level which did not share the same boundaries across studies. As a consequence, differences in rates of cognitive impairment between studies should be interpreted with caution. With these caveats in mind, some general conclusions can

nevertheless be reached (Table I). The median proportion of subjects without intellectual impairment is 30% (range: 0%–60%).[1] The corresponding figures are 30% (range: 6.6%–100%) for mild to moderate intellectual impairments, and 40% (range: 0%–81.3%) for severe to profound level of mental retardation. Gender repartition among subjects with autism was reported in 29 studies and the male/female sex ratio varied from 1.33 (study 7) to 16.0 (study 4), with a mean sex ratio of 4.3. Thus, no epidemiological study ever identified more girls than boys with autism, a finding which parallels the gender differences found in clinically referred samples (Lord *et al.,* 1982). Gender differences were more pronounced when autism was not associated with mental retardation. In 12 studies (841 subjects) where the sex ratio was available within the normal band of intellectual functioning, the median sex ratio was 5.75:1. Conversely, in 11 studies (789 subjects), the median sex ratio was 1.9:1 in the group with autism and moderate to severe mental retardation.

PREVALENCE ESTIMATIONS FOR AUTISTIC DISORDER

Prevalence estimates ranged from 0.7/10,000 to 72.6/10,000 (Table I). Confidence intervals were computed for each estimate; their width (difference between the upper and lower limit of the 95% confidence interval) indicates the variation in sample sizes and in the precision achieved in each study (range: 0.3–115.9; mean = 12.0). Prevalence rates were negatively correlated with sample size (Spearman $r = -0.77$; $p < 0.01$); small-scale studies tended to report higher prevalence rates.

When surveys were combined in two groups according to the median year of publication, the median prevalence rate for 16 surveys published in the period 1966–1991 was 4.4/10,000, and the median rate for the 16 surveys published in the period 1992–2001 was 12.7/10,000. Indeed, the correlation between prevalence rate and year of publication reached statistical significance (Spearman $r = 0.70$; $p < 0.01$); and the results of the 18 surveys with prevalence rates over 7/10,000 were all published since 1987. These findings point towards an increase in prevalence estimates in the last 15 years. In order to derive a best estimate of the current prevalence of autism, it was therefore deemed appropriate to restrict the analysis to the 21 most recent surveys, i.e., those published since 1987. We decided to further exclude 2 studies with a target population of less than 10,000 children as estimates deriving from smaller size studies were associated with excessively large confidence intervals and were influencing unduly the results. For the 19 remaining studies, the prevalence estimates ranged from 2.5 to 30.8/10,000 (average 95% CI width: 6.4), with an average rate of 11.1/10,000 and a median rate of 9.5/10,000. Similar values were obtained when slightly different rules and time cutpoints were used. From these results, the best estimate for the current prevalence of autism is most consistent with values lying somewhere between 9/10,000 and 11/10,000. For further calculations, we arbitrarily adopted the mid-point of this interval as the working rate for autism prevalence, i.e., the value of 10/10,000.

ASSOCIATED MEDICAL CONDITIONS

Rates of medical conditions associated with autism were reported in 15 surveys and the findings are summarized in Table II. It will be appreciated that these medical conditions were investigated by very different means ranging from questionnaires to full medical work-ups.

Conditions such as congenital rubella, and PKU account for almost no cases of autism. Prior studies suggesting an association of congenital rubella (Chess, 1971) and PKU (Knobloch & Pasamanick, 1975; Lowe *et al.,* 1980) with autism were conducted before implementation of systematic prevention measures. Likewise, our nil estimate of 0% for autism and neurofibromatosis is comparable to the 0.3% rate found in a large series of 341 referred cases (Mouridsen *et al.,* 1992) and, contrary to earlier claims (Gillberg & Forsell, 1984), it does not exceed the rate expected under the assumption of independence of the two

Table II. Medical Disorders Associated with Autism in Recent Epidemiological Surveys

	No. of studies	Median rate	Range
Cerebral palsy	6	2.0	0–4.8
Fragile X	8	0.3	0–8.1
Tuberous sclerosis	10	1.2	0–3.8
Phenylketonuria	7	0	0–0
Neurofibromatosis	6	0	0–1.4
Congenital rubella	10	0.3	0–5.9
Down Syndrome	11	1.3	0–16.7
At least one disorder	***14***	***6.4***	***0–16.7***
Epilepsy	11	16.8	0–26.4
Hearing deficits	7	1.7	0–5.9
Visual deficits	5	1.3	0–11.1

[1]Study 23 which relied upon different IQ groupings has been excluded.

disorders. Similarly, bearing in mind the high rate of mental retardation among samples of autistic subjects, the rates found for cerebral palsy and Down's syndrome equally suggest no particular association. The recognition that Down's syndrome and autism co-occur in some individuals has been the focus of attention in recent reports (Bregman & Volkmar, 1988; Ghazziudin *et al.,* 1992; Howlin *et al.,* 1995); the epidemiological findings give further support to the validity of these clinical descriptions (i.e., that the 2 conditions co-occur in some children), although they do not suggest that the rate of comorbidity is higher than that expected by chance once the effects of mental retardation are taken into account. For fragile X, the low rate available in epidemiological studies is most certainly an underestimate due to the fact that fragile X was not recognized until relatively recently and that, in the most recent surveys, systematic screening for fragile X was not always undertaken. In line with prior reports (Smalley *et al.,* 1992), tuberous sclerosis (TS) has a consistently high frequency among autistic samples. Assuming a population prevalence of 1/10,000 for TS (Shepherd *et al.,* 1991; Hunt & Lindenbaum, 1984; Ahlsen *et al.,* 1994), it appears that the rate of TS is about 100 times higher than that expected under the hypothesis of no association. The rate of TS in autistic samples is, however, much lower in these epidemiological studies than the 9% minimum rate claimed in a recent study (Gillberg *et al.,* 1994). Whether or not the association between TS and autism is mediated by epilepsy, localized brain lesions or direct genetic effects is a matter for future research (Smalley, 1998).

The overall proportion of cases of autism which could be causally attributed to known medical disorders therefore remains low. From the 14 surveys where rates of one of 7 clear-cut medical disorders potentially causally associated with autism (cerebral palsy, fragile X, TS, PKU, neurofibromatosis, congenital rubella, and Down's syndrome) were available, we computed the proportion of subjects with at least one of these recognizable disorders. Because the overlap between these conditions is expected to be low and because the information about multiply-handicapped subjects was not available, this overall rate was obtained by summing directly the rates for each individual condition within each study; the resulting rate might, therefore, be slightly overestimated. The fraction of cases of autism with a known medical condition potentially etiologically significant ranged from 0% to 16.7%, with a median and mean values of 6.4% and 6.0% respectively. Even if some adjustment was made to account for the underestimation of the rate of fragile X in epidemiological surveys of autism, the attributable proportion of cases of autism would not exceed the 10% figure for any medical disorder (excluding epilepsy and sensory impairments). Although this figure does not incorporate other medical events of potential etiological significance, such as encephalitis, congenital anomalies, and other rare medical syndromes, it is similar to that reported in a recent review of the question (Rutter *et al.,* 1994). It is worth noting that epidemiological surveys of autism in very large samples (i.e., studies 15, 17, and 20) provided estimates in line with our conservative summary statistics. By contrast, claims of average rates of medical conditions as high as 24% appear to apply to studies of smaller size and relying on a broadened definition of autism (Gillberg & Coleman, 1996).

Rates of epilepsy are high among autism samples. The proportion suffering from epilepsy tends also to be higher in those studies which have higher rates of severe mental retardation (as in studies 16, 17, and 20). Age-specific rates for the prevalence of epilepsy were not available. The samples where high rates of epilepsy were reported tended to have a higher median age, although these rates seemed mostly to apply to school-aged children. Thus, in light of the increased incidence of seizures during adolescence among subjects with autism (Rutter, 1970; Deykin & MacMahon, 1979), the epidemiological rates should be regarded as underestimates of the lifetime risk of epilepsy in autism. These rates are nonetheless high and support the findings of a bimodal peak of incidence of epilepsy in autistic samples, with a first peak of incidence in the first years of life (Volkmar & Nelson, 1990).

RATES OF OTHER PERVASIVE DEVELOPMENTAL DISORDERS

Unspecified PDDs—PDD-NOS

Several studies have provided useful information on rates of syndromes similar to autism but falling short of strict diagnostic criteria (Table III). Because the screening procedures and subsequent diagnostic assessments differed from one study to another, these groups of disorders are not strictly comparable across studies. In addition, as they were not the group on which the attention was focused, details are often lacking on their phenomenological features in the available reports. Different labels (see Table III) have been used to characterize them such as the triad of impairments involving impairments in reciprocal social interaction, communication and imagination (Wing & Gould, 1979). These groups would be overlapping with current

Table III. Informative Studies on Rates of Nonautism Pervasive Developmental Disorders

No. Study	Rates of Autism	Prevalence rate of other PDD	Combined rate autism + other PDD's	Prevalence rate ratio[c]	Case definition for other PDD's
1. Lotter (1966)	4.1	3.3	7.8	0.90	Children with some behaviour similar to autistic children
2. Brask (1970)	4.3	1.9	6.2	0.44	Children with "other psychoses" or "borderline psychotic"
4. Wing *et al.* (1976)	4.9	16.3	21.2	3.33	Socially impaired (triad of impairments)
5. Hoshino *et al.* (1982)	2.33	2.92	5.25	1.25	Autistic mental retardation
9. Burd *et al.* (1987)	3.26	>7.79[a]	>11.05[a]	2.39	Children referred by professionals with "autistic-like" symptoms, not meeting DSM-III criteria for IA, COPDD or atypical PDD.
14. Cialdella and Mamelle (1989)	4.5	4.7	9.2	1.04	Children meeting criteria for other forms of "infantile psychosis" than autism, or a broadened definition of DSM III.
17. Fombonne and du Mazaubrun (1992)[b]	4.6	6.6	11.2	1.43	Children with mixed developmental disorders
20. Fombonne *et al.* (1997)	5.3	10.94	16.3	2.05	Children with mixed developmental disorders
26. Baird *et al.* (2000)	30.8	27.1	57.9	0.9	Children with other PDD's
27. Powell *et al.* (2000)	7.8	13.0	20.8	1.7	Children with other PDD's
29. Bertrand *et al.* (2001)	40.5	27.0	67.4	0.7	Children with PDD-NOS and Asperger Disorder
32. Chakrabarti and Fombonne (2001)	16.8	36.1	52.9	2.15	Children with PDD-NOS

[a] Computed by the author.
[b] These rates are derived from the complete results of the survey of 3 birth cohorts of French children (*Rumeau-Rouquette et al. 1994*).
[c] Other PDD rate divided by autism rate.

diagnostic labels such as atypical autism and PDDNOS, which does little to understand their relationship with a narrower definition of autism. Twelve of the 32 surveys yielded estimates of the prevalence of these developmental disorders, with 8 studies showing higher rates for the non-autism disorders than the rates for autism. The ratio of the rate of non autistic PDD to the rate of autism varied between from 0.44 to 3.33 (Table III) with a mean value of 1.5, which translates into an average prevalence estimate of 15/10,000. In other words, for 2 children with autism assessed in epidemiological surveys, 3 children were found to have severe impairments of a similar nature but falling short of strict diagnostic criteria for autism. This group has been much less studied in epidemiological studies but it should be clear from these figures that they represent a very substantial group of children whose treatment needs are likely to be as important as those of children with autism.

Asperger Syndrome and Childhood Disintegrative Disorder

The reader is referred to recent epidemiological reviews for these two conditions (Fombonne, 2001a; Fombonne, 2002). In brief, epidemiological studies of Asperger syndrome (AS) are sparse, probably due to the fact that it was acknowledged as a separate diagnostic category only recently in both ICD-10 and DSM-IV. Only two epidemiological surveys have been conducted which specifically investigated its prevalence (Ehlers & Gillberg, 1993; Kadesjö *et al.,* 1999). However, only a handful ($N < 5$) of cases were identified in these surveys, with the resulting estimates of 28 and 48/10,000 being extremely imprecise. By contrast, other recent autism surveys have consistently identified smaller numbers of children with AS than those with autism within the same survey. In 6 such surveys (studies 23–27, 32), the ratio of autism to AS rates in each survey was above unity, suggesting that the rate of AS was consistently lower than that for autism. How much lower is difficult to establish from existing data, but a ratio of 4 to 1 would appear an acceptable, albeit conservative, conclusion based on this limited available evidence. This translates into a rate for AS which would be one fourth that of autism. We therefore used for subsequent calculations an estimate of 2.5/10,000 for AS.

Few surveys have provided data on childhood disintegrative disorder (CDD), also known as Heller syndrome, disintegrative psychosis (ICD-9) or late-onset autism (see Volkmar, 1992). In 4 studies (studies 9, 23, 31, 32), prevalence estimates ranged from 11.1 to 64.5 per million (Fombonne, 2002). Most of the upper limits of the 95% confidence intervals were consistent with an upper bound limit of 1/10,000, and the pooled estimate was 1.7/100,000. As cases of CDD were both rare and already included in the numerator alongside autism cases in most surveys, we do not provide separate estimates of the numbers of subjects suffering from CDD in subsequent calculations.

PREVALENCE FOR COMBINED PDDs

Taking the aforementioned conservative estimates, the prevalence for all PDDs is at least 27.5/10,000 (i.e., the sum of estimates for autism (10/10,000), PDDNOS (15/10,000), and AS (2.5/10,000)). This global estimate is derived from a conservative analysis of existing data.

However, 3 recent epidemiological surveys yielded rates about twice as high (Table IV). The common features in the design of these epidemiological enquiries are worth noting. First, the case definition chosen for these investigations was that of a pervasive developmental disorder (PDD) as opposed to a narrower approach focusing on autistic disorder. Investigators were concerned with any combination of severe developmental abnormalities occurring in one or more of the 3 symptomatic domains defining PDD and autism. Second, case finding techniques employed in these surveys were proactive, relying on multiple and repeated screening phases, involving both different

Table IV. Newer Epidemiological Surveys of PDDs

		Autism			PDDNOS + AS			All PDDs
	Age	Rate/ 10,000	M/F ratio	% IQ normal	Rate/ 10,000	M/F ratio	% IQ normal	Rate/ 10,000
Bertrand *et al.,* 2001	3–10	40.5	2.2	37	27.0	3.7	51	67.5
Baird *et al.,* 2000	7	30.8	15.7	60	27.1	4.5	—	57.9
Chakrabarti and Fombonne 2001	4–7	16.8	3.3	29	44.5	4.3	94	61.3

informants at each phase and surveying the same cohorts at different ages, which certainly maximized the sensitivity of case identification. Third, assessment were performed with standardized diagnostic measures (i.e., ADI-R and ADOS) which match well the dimensional approach retained for case definition. Finally, these samples comprised young children around their fifth birthday, thereby optimizing sensitivity of case finding procedures. Furthermore, the size of targeted populations was reasonably small (between 9,000 and 16,000), probably allowing for the most efficient use of research resources. Conducted in different regions and countries by different teams, the convergence of estimates (Table IV: right-hand column) is striking. Two further results are worth noting. First, in sharp contrast with the prevalence for combined PDDs, the separate estimates for autistic disorder and PDDNOS vary widely across studies, as if the reliability of the differentiation between autistic disorder and PDDNOS was mediocre at that young age, despite the use of up-to-date standardized measures. Second, the rate of mental retardation was, overall, much lower than in previous surveys of autism. While this should not be a surprise for children in the PDDNOS/AS groups, this trend was also noticeable within the samples diagnosed with autistic disorder. To what extent this trend reflects the previously mentioned differential classification issues between autism and PDDNOS or a genuine trend over time towards decreased rate of mental retardation within children with autistic disorder (possibly as a result as earlier diagnosis and intervention) remains to be established.

TIME TRENDS

The debate on the hypothesis of a secular increase in rates of autism has been obscured by a lack of clarity in the measures of disease occurrence used by investigators, or rather in their interpretation. In particular, it is crucial to differentiate prevalence (the proportion of individuals in a population who suffer from a defined disorder) from incidence (the number of new cases occurring in a population over a period of time). Prevalence is useful to estimate needs and plan services; only incidence rates can be used for causal research. Both prevalence and incidence estimates will be inflated when case definition is broadened and case ascertainment is improved. Time trends in rates can therefore only be gauged in investigations which hold these parameters under strict control over time. These methodological requirements must be borne in mind whilst reviewing the evidence for a secular increase in rates of PDDs.

Five approaches to assess this question have been used in the literature.

Referral Statistics

Increasing numbers of children referred to specialist services or known to special education registers have been taken as evidence for an increased incidence of autism-spectrum disorders. However, trends over time in referred samples are confounded by many factors such as referral patterns, availability of services, heightened public awareness, decreasing age at diagnosis and changes over time in diagnostic concepts and practices, to name only a few. Failure to control for these confounding factors is obvious in some recent reports, such as the widely quoted report from California educational services (Department of Developmental Services, 1999; Fombonne, 2001b). First, these reports apply to numbers rather than rates, and failure to relate these numbers to meaningful denominators leave these figures vulnerable to changes in the composition of the underlying population. Second, no attempt was made to adjust the trends for changes in diagnostic concepts and definitions. However, major nosographical modifications were introduced during the corresponding years with a general tendency in most classifications to broaden the concept of autism (as embodied in the terms ‘autism spectrum’ or ‘pervasive developmental disorder’). Third, age characteristics of the subjects recorded in official statistics were portrayed in a confusing manner where the preponderance of young subjects was presented as evidence of increasing rates in successive birth cohorts. The problems associated with disentangling age from period and cohort effects in such observational data are well known in the epidemiological literature and deserve a better statistical handling. Fourth, the decreasing age at diagnosis leads in itself to increasing numbers of young children being identified in official statistics or referred to already busy specialist services. Earlier identification of children from the prevalence pool may result in increased service activity; however, it does not mean increased incidence. Fifth, upward trends were also reported for other disorders (such as cerebral palsy, epilepsy or mental retardation), therefore casting doubts on the specificity of the trends for autism. Evidence from these referral statistics is therefore very weak (Fombonne, 2001b). Accordingly, proper epidemiological studies are needed in order to assess secular changes in the incidence of a disorder.

Comparison of Cross-sectional Epidemiological Surveys

Due to their cross-sectional methodology, most epidemiological investigations of autism have all been concerned with prevalence estimation of autism. As shown earlier, epidemiological surveys of autism each possess unique design features which could account almost entirely for between-studies variations in rates, and time trends in rates of autism are therefore difficult to gauge from published prevalence rates. The significant correlation previously mentioned between prevalence rate and year of publication could merely reflect increased efficiency over time in case identification methods used in surveys as well as changes in diagnostic practices. Thus, changes in diagnostic practices were reported in Magnusson and Saemundsen's study (2001) where ICD-9 rates for the oldest cohorts born in the years 1964–1983 were lower than the ICD-10 rates of the most recent 1984–1992 birth cohorts. Similarly, lower rates in the oldest birth cohorts were thought to reflect changes in diagnostic practices and boundaries in Webb *et al.*'s study (1997). One large survey recently conducted in the UK (study 24) also documented a steep rise in the number of cases diagnosed with autism or atypical autism, and a similar trend for AS. The interpretation of these trends is, however, unclear since there was no control of drift over time in diagnostic practices nor of changes in service development.

The most convincing evidence that method factors could account for most of the variability in published prevalence estimates comes from a direct comparison of 8 recent surveys conducted in the UK and the USA (Table V). In each country, the 4 surveys were conducted around the same year and with similar age groups. As there is no reason to expect huge between-area differences in rates, prevalence estimates should therefore be comparable within each country. However, an inspection of estimates obtained in each set of studies (Table V: right-hand column) shows a six-fold variation in rates for UK surveys, and a fourteen-fold variation in US rates. In each set of studies, high rates derive from surveys where intensive population-based screening techniques were employed whereas lower rates were obtained from studies relying on administrative methods for case finding. Since no passage of time was involved, the magnitude of these gradients in rates can therefore be attributed to differences in case identification methods across surveys, and the replication of the pattern in two countries provides even more confidence in this interpretation. Thus, following this analysis of recent and contemporaneous studies, it should become obvious that no inference on trends in the incidence of PDDs can be derived from a simple comparison of prevalence rates over time, since studies conducted at different periods are likely to differ even more with respect to their methodology.

The next two approaches are in essence comparable to this one although specific attempts are made to maintain some design features of surveys constant.

Repeat Surveys in Defined Geographical Areas

Repeated surveys, using the same methodology and conducted in the same geographical area at different points in time, can potentially yield useful information on time trends provided that methods are kept relatively constant. The Göteborg studies (Gillberg, 1984; Gillberg *et al.,* 1991) provided 3 prevalence

Table V. Study Design Impact on Prevalence

	Location	Size	Age group	Method	PDD rate/10,000
UK studies					
Chakrabarti & Fombonne, 2001	Staffordshire	15,500	2½–6½	intense screening + assessment	62.6
Baird *et al.,* 2000	South-East Thames	16,235	7	early screening + follow-up identification	57.9
Fombonne *et al.,* 2001	England & Wales	10,438	5–15	national household survey of psychiatric disorders	26.1
Taylor *et al.,* 1999	North Thames	490,000	0–16	administrative records	10.1
US studies					
Bertrand *et al.,* 2001	Brick Township, NJ	8,896	3–10	multiple sources of ascertainment	67
Sturmey & James	Texas	3,564,577	6–18	educational services	16
CDER, 1999	California	3,215,000	4–9	educational services	15
Hillman *et al.,* 2000	Missouri	—	5–9	educational services	4.8

estimates which increased over a short period of time from 4.0 (1980) to 6.6 (1984) and 9.5/10,000 (1988), the gradient being even steeper if rates for the urban area alone are considered (4.0, 7.5 and 11.6/10,000) (Gillberg *et al.,* 1991). However, comparisons of these rates is not straightforward as different age groups were included in each survey. For example, the rate in the first survey for the youngest age group (which resembles more closely the children included in the 2 other surveys) was 5.1/10,000. Second, the increased prevalence in the second survey was explained by improved detection among the mentally retarded, and that of the third survey by cases born to immigrant parents. That the majority of the latter group was born abroad suggests that migration into the area could be a key explanation. Taken in conjunction with a change in local services and a progressive broadening of the definition of autism over time acknowledged by the authors (Gillberg *et al.,* 1991), these findings do not provide solid evidence for an increased incidence in the rate of autism.

Successive Birth Cohorts

In large surveys encompassing a wide age range, increasing prevalence rates among the most recent birth cohorts could be interpreted as indicating a secular increase in the incidence of the disorder, provided that alternative explanations can confidently be ruled out. This analysis was used in two French surveys (studies 17 and 20) which derived from large sample sizes. In the first study (study 17), prevalence estimates were available for the two birth cohorts of children born in 1972 and 1976 surveyed in 1985–86. The rates were similar (5.1 and 4.9/10,000) and not statistically different (Fombonne & du Mazaubrun, 1992). Furthermore, in a subsequent investigation conducted in 1989–90 in exactly the same areas, the age-specific rate of autism for the 1981 birth cohort was slightly lower (3.1/10,000) (Rumeau-Rouquette *et al.,* 1994). In any instance, the findings were not suggestive of increasing rates in the most recent cohorts. Another survey conducted with the same methodology but in different French regions a few years later (study 20) led to a similar overall prevalence estimate as compared to the first survey (Table I). The latter survey included consecutive birth cohorts from 1976 to 1985, and, pooling the data of both surveys, age-specific rates showed no upward trend (Fombonne *et al.,* 1997). Some weight should be given to these results as they derive from a total target population of 735,000 children, 389 of whom had autism. However, the most retarded children with autism were reflected in these studies and, as a consequence, any upward trend which would apply specifically to high-functioning subjects might have gone undetected.

Incidence Studies

Only two studies provided recent incidence estimates (Powell *et al.,* 2000; Kaye *et al.,* 2001). Both studies showed an upward trend in incidence over short periods of time, but no attempt was made in both investigations to assess changes over the corresponding periods in diagnostic criteria and sensitivity of case detection methodology.

Conclusion on Time Trends

The available epidemiological evidence does not strongly support the hypothesis that the incidence of autism has increased, and several other reasons could easily account for an artefactual impression of an increase (Fombonne, 1996). As it stands now, the recent upward trend in rates of *prevalence* cannot be directly attributed to an increase in the *incidence* of the disorder. Most of the existing epidemiological data are however inadequate to properly test hypotheses on changes in the incidence of autism in human populations. Moreover, due to the relative rarity of autism and PDDs, power is seriously limited in each investigation and variations of small magnitude in the incidence of the disorder are very likely to go on undetected. Future investigations should aim at setting up surveillance programs which will allow to estimate the incidence of PDDs (as opposed to autism only) and to monitor its changes over time. It will be crucial to set up parallel investigations in different geographical areas in order to replicate findings across areas as a validating tool. Such programs should focus on age groups where the identification and diagnosis of the range of PDDs is less likely to fluctuate over time. Rapid changes in the age at first diagnosis and concerns about the validity and stability of diagnostic assessments amongst preschool samples require us to focus on older age groups. On the other hand, changes in the autistic symptomatology in adolescence and difficulties in service delivery to teenagers (and therefore in case identification) suggest focusing on rather younger children. The school age years (7–12 years) should therefore be selected for efficient monitoring. Mandatory education at that age would facilitate identification, and potential difficulties in diagnosing high-functioning subjects would be minimized at the upper end of this age range. Diagnostic assessments should rely on standardized measures of known reliability and validity. Furthermore, developmental and phenomenological data should be

collected at a symptomatic level, and uniformly across the whole spectrum of PDDs, and remaining free of particular nosological contingencies. Secondary application of diagnostic algorithms (current and/or future) on datasets containing detailed developmental and symptomatic data will then allow for meaningful comparisons over time to be performed, with diagnostic groupings being held constant. Finally, good psychometric data on cognitive functioning will also be needed to assess trends in various subgroups in light of the preliminary evidence that patterns of mental retardation in autism may be changing. Obviously, measures of risk factors hypothesized to exert causal influences for this group of disorders should also be incorporated in surveillance programs.

OTHER CORRELATES

Autism, Race, and Immigrant Status

Some investigators have mentioned the possibility that rates of autism might be higher among immigrants (Wing, 1980; Gillberg *et al.,* 1991, 1995; Gillberg, 1987). Five of the 17 children with autism identified in the Camberwell study were from Caribbean origin (study 4; Wing, 1980) and the estimated rate of autism was 6.3/10,000 for this group as compared to 4.4/10,000 for the rest of the population (Wing, 1993). However, the wide confidence intervals associated with rates from this study (Table I) indicate no statistically significant difference. In addition, this area of London had received a large proportion of immigrants from the Caribbean region in the 1960's and, under circumstances where migration flux in and out of an area are happening, estimation of population rates should be viewed with much caution. Yet, Afro-Caribbean children referred from the same area were recently found to have higher rates of autism than referred controls (Goodman and Richards, 1995); however, the sample was again very small (N = 18) and differential referral patterns to a tertiary center also providing services for the local area could not be ruled out. It is worth noting that only one child was born from British-born Afro-Caribbean parents in a recent UK survey (study 21; Webb *et al.,* 1997), providing little support to this particular hypothesis. Similarly, the findings from the Göteborg studies paralleled an increased migration flux in the early 1980s in this area (Gillberg, 1987); they, too, were based on relatively small numbers (19 children from immigrant parents). In the same geographical area, Arvidsson *et al.* (1997; study 22) had 5 children out of 9 in their sample with either both parents (N = 2) or 1 parent (N = 3) having immigrated to Sweden; however, there were no systematic comparisons with rates of immigrants in the population. It is worth noting that a positive family history for developmental disorders was reported in 3 such cases and a chromosomal abnormality in 1 further case. In the Icelandic survey (study 31), 2.5% of the autism parents were from non-European origin compared to a 0.5% corresponding rate in the whole population, but it was unclear if this represented a significant difference. In study 23, the proportion of children with autism and a non-European origin was marginally but not significantly raised as compared to the population rate of immigrants (8% versus 2.3%) but this was based on a very small sample (2 children on non-European origin). A recent UK survey found comparables rates in areas contrasting for their ethnic composition (Powell *et al.,* 2000). Taken altogether, the combined results of these reports should be interpreted in the specific methodological context of these investigations. All studies had low numbers of identified cases, and especially small numbers of autistic children born from immigrant parents, and many authors in these studies relied upon broadened definitions of autism. Statistical testing was not rigorously conducted and doubts could be raised in several studies about the appropriateness of the comparison data which were used. Thus, the overall proportion of immigrants in the population is an inappropriate figure to which to compare observed rates of children from immigrant parents amongst autistic series; fertility rates of immigrant families are likely to be different from those in the host populations and call for strictly age-adjusted comparisons of individuals at risk for the disorder. The proportion of immigrants in the entire population might seriously underestimate that for younger age groups, and, in turn, this could have given rise to false positive results. Finally, studies were generally poor in their definition of immigrant status, with some unclear amalgamation of information on country of origin, citizenship, immigrant status, race and ethnicity. In the Utah survey, where a clear breakdown by race was achieved (Ritvo *et al.,* 1989; study 15), the autism parents showed no deviation as compared to the racial distribution of this state; the proportion of non-whites in this study and state was, however, noticeably low, providing little power to detect departures from the null hypothesis. Unfortunately, other studies have not systematically reported the proportion of immigrant groups in the areas surveyed. However, in four studies where the proportions of immigrant groups were low (studies 11, 12, 19 and 21), rates of autism were in the upper range of rates. Conversely, in other populations where immigrants contributed

substantially to the denominators (studies 14, 17 and 20), rates were in the rather low band. Finally, it is unclear what common mechanism could explain the putative association between immigrant status and autism, since the origins of the immigrant parents (especially in study 16; see also Gillberg & Gillberg, 1996) were very diverse and represented in fact all continents. With this heterogeneity in mind, what common biological features might be shared by these immigrant families and what would be a plausible mechanism explaining the putative association between autism and immigrant status? The possibility of an increased vulnerability to intrauterine infections in non-immunized immigrant mothers was raised but not supported in a detailed analysis of 15 autistic children from immigrant parents (Gillberg & Gillberg, 1996). These authors instead posited that parents, and in particular fathers, affected with autistic traits would be inclined to travel abroad in order to find female partners more naïve to their social difficulties. This speculation was based, however, on 3 observations only, and assessment of the autistic traits in two parents was clearly not independently obtained.

The hypothesis of an association between immigrant status or race and autism, therefore, remains largely unsupported by the empirical results. Most of the claims about these possible correlates of autism derived from *post-hoc* observations of very small samples and were not subjected to rigorous statistical testing.

Autism and Social Class

Twelve studies provided information on the social class of the families of autistic children. Of these, 4 studies (1, 2, 3 and 5) suggested an association between autism and social class or parental education. The year of data collection for these four investigations was before 1980 (Table l), and all studies conducted thereafter provided no evidence for the association. Thus, the epidemiological results suggest that the earlier findings were probably due to artefacts in the availability of services and in the case finding methods, as already shown in other samples (Wing, 1980; Schopler *et al.,* 1979).

CLUSTER REPORTS

Occasional reports of space or time clustering of cases of autism have raised concerns in the general public. In fact, only one such report has been published in the professional literature (Baron-Cohen *et al.,* 1999) which described 7 children with either autism or PDD-NOS living within a few streets from each other in a small town of the Midlands (UK). The cluster was first identified by a parent and the subsequent analysis was uninformed with proper statistical procedures and inconclusive as to whether or not this cluster could have occurred by chance only. The comparison of the incidence or prevalence rate within the cluster to that of the general population (as performed by Baron-Cohen *et al.,* 1999) is an inappropriate technique to assess cluster alarms since, by definition, a pre-selection bias occurs in the delineation of the cluster boundaries (Kulldorf, 1999). Thus, finding an increased incidence or prevalence rate ratio in a cluster does *not* prove anything; this erroneous approach has been referred to in the literature as the Texan sharpshooter effect, referring to the gunman who shot first and then painted a target around the bullet hole. On the other hand, a negative finding would certainly suggest a random phenomenon.

When cluster alarms are associated to a possible causal mechanism, it is recommended to perform focused tests of clustering at other suspected sources of risk exposure. For example, the cluster alarms for childhood leukemia occurring near a nuclear plant in England were followed by investigations of disease incidence at other nuclear plants, which proved to be negative (Hoffmann & Schlatmann, 1999). However, the potential source of the cluster alarm is not always identified and, in these instances, it is suggested to monitor the incidence of future cases in the area of first alarm. Chen *et al.* (1993) have outlined post-alarm monitoring techniques which allow to confirm or reject alarms, based on the observation of the time intervals preceding each of the first 5 cases diagnosed subsequent to the alarm. The approach is a confirmatory technique which ignores the cluster alarm data and thus avoids the aforementioned preselection bias. Other techniques, such as space-time scan statistics (Kulldorf, 1999) exist which can confirm or reject a cluster alarm by extending the investigation to a larger area whilst avoiding selection biases, adjusting for population density, confounding variables and multiple testing, and allowing for the precise location of clusters. They do require however the availability of regional or national geocoded data which are usually not available for autism. Other general statistical techniques to assess time and space clustering are reviewed in specialist journals (Marshall, 1991; see also special issues of the Journal of the Royal Statistical Society, Series A (1989); of the American Journal of Epidemiology (1990); and of Statistics in Medicine (1993, 1995, 1996)).

Cluster alarms are likely to represent random occurrence in most instances, as illustrated by several recent investigations of cluster alarms for other rare

disorders of childhood. Cluster alarms in autism have not been investigated with scientific rigor whereas research strategies and ad hoc statistical procedures exist for that purpose. The approach to such cluster alarms should be to confirm the alarm in the first place, using the available techniques to assess the significance of clusters and to exclude random noise in spatial and time distribution of the disorder. It is only when an alarm has been confirmed that more complex epidemiological investigations should be set up to investigate risk factors and causal mechanisms.

CONCLUSION

Epidemiological surveys of autism have now been carried out in several countries. Methodological differences in case definition and case finding procedures make between survey comparisons difficult to perform. Nevertheless, in spite of these differences, some common characteristics of autism and PDDs in population surveys have emerged with some consistency. Autism is associated with mental retardation in about 70% of the cases and is overrepresented amongst males (with a male/female ratio of 4.3:1). Autism is found in association with some rare and genetically determined medical conditions, such as tuberous sclerosis. Overall, the median value of about 6% for combined rate of medical disorders in autism derived from this review is consistent with the 5% (Tuchman *et al.,* 1991) to 10% (Rutter *et al.,* 1994) figures available from other investigations.

A majority of surveys has ruled out social class as a risk factor for autism, a result once supported by studies of clinical, i.e., less representative, samples. The putative association of autism with immigrant status or race is, so far, not borne out by epidemiological studies. The conclusion of a lack of variation in the incidence of autism according to race or ethnicity is reached, however, from a weak empirical base and future studies might address this issue more efficiently. In fact, epidemiological studies of autism and PDDs have generally been lacking sophistication in their investigation of most other risk factors.

The same considerations apply to the issue of secular changes in the incidence of autism. The little evidence which exists does not support this hypothesis but power to detect time trends is seriously limited in existing datasets. The debate has been largely confounded by a confusion between prevalence and incidence. Whilst it appears that prevalence estimates have gone up over time, this increase most likely represents changes in the concepts, definitions and awareness of autistic-spectrum disorders in both the lay and professional public. To assess whether or not the incidence has increased, method factors which account for an important proportion of the variability in rates must be tightly controlled.

Taking 10/10,000 as the base rate for autism, a rate of 27.5/10,000 for the combination of all PDDs can be derived. It could well be that, because these surveys were not focusing primarily on the non autistic group, the actual rate of combined pervasive developmental disorders could be even higher, in the neighbourhood of 60 to 70/10,000 as suggested by 3 recent surveys. Using population estimates for the USA in year 2000 and estimates of 27.5/10,000 (or 60/10,000 respectively), it can be estimated that about 221,000 (483,000) subjects under the age of 20 suffer from a PDD in the USA, which include 53,000 (114,000) children under five (Table VI). Based on the projections of the Census Bureau, it is forecasted that there will be a 42.7% increase in the number of under fives in the US

Table VI. U.S. Estimates of the Number of Persons with a PDD[a]

	Age group				
	0–4	5–9	10–14	15–19	<20
Population size	19,175,798	20,549,505	20,528,072	20,219,890	80,473,265
Expected numbers with					
Autism	19,175	20,549	20,528	20,219	80,473
Asperger disorder	4794	5137	5132	5055	20,118
PDD-NOS	28,762	30,823	30,792	30,328	120,710
Any PDD	52,731	56,510	56,452	55,602	221,301[b]

[a]Based on an estimate of 27.5/10,000 (see text) and on population estimates for 2000 (US Census Bureau, Census 2000).

[b]If prevalence estimates for all PDDs are taken from newer surveys (60/10,000), the number of subjects under 20 with any PDD would be about 483,000.

population in year 2050. Everything else being constant, this will translate into 76,000 (163,000) children under five suffering from a PDD. These figures carry straightforward implications for current and future needs in services and early educational intervention programs.

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