

babies in Norway constitutes one good example of what is needed in that connection.⁵

It should be added that the factor responsible for a real rise in autism (if that truly has occurred) need not necessarily be a specific environmental hazard. The trigger could be a rising age of parenthood, given the evidence that high paternal age is associated with an increased rate of autism in the offspring.⁶ How might that operate? One possibility is that it increases the rate of developmental perturbations such as copy number variation (i.e. submicroscopic substitutions or deletion)⁷ or minor congenital anomalies or chromosomal anomalies, all of which have been found to be more common in autism.

Whilst there is value in considering the role of changing concepts and better ascertainment in the observed rise in the rate of diagnosed autism, and there is still uncertainty on whether or not there has been a true rise in incidence, the greater the need is for hypothesis-testing focused research on possible causal mechanisms that could lead to changes in incidence.

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Commentary: Diagnostic change and the increased prevalence of autism

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Parsing increases in autism diagnoses into the proportion arising from changes in criteria, awareness, diagnostic practices and methodology, versus the fraction representing a true rise in incidence, is not easy. Recently, we found three artefacts—younger age at diagnosis, change in the accepted criteria and inclusion of milder cases—accounted for about one-third of a 12-year rise in incidence in California.¹ We did not tackle other factors.

King and Bearman² undertook a daunting task to quantitatively estimate the contribution of diagnostic substitution to the rise in autism. The challenge is to determine how today's children would have been viewed through the eyes of diagnosticians over 20 years ago. Their approach was to fit a predictive model to the California DDS population of persons born before 1987, prior to the major rise in the autism caseload, in order to estimate the odds that a child with an autism diagnosis between 1992 and 2005 previously had a diagnosis of mental retardation (MR). This model was adjusted for demographic and behavioural characteristics. The estimated probabilities of change, either replacement of the original MR diagnosis or accretion of the autism diagnosis

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while maintaining the MR diagnosis, were then derived and used for calculating annual and cumulative probability that persons of any age diagnosed with autism during this period would have been diagnosed with MR, had the diagnostic practices been those of earlier years. This counterfactual probability was applied to all birth years, including prior to 1987.

In a supplemental analysis, they modelled the odds that a person with MR would acquire an autism diagnosis, and applied the derived probabilities to the DDS MR population.² This analysis projected 31.4% [7410/(28 046–4446)] of the 2005 autism caseload would have initially had an MR diagnosis by 1992 standards, compared with 26.4% when conditioning on those who ended with an AU diagnosis.

Validity of these projections rests on correct estimation of 'period' effects from years during which practice changes occurred. Certain features of the analysis, however, are puzzling. First, severity of MR was included as a predictive factor, the referent group being those without MR, yet the model's outcome was whether or not they entered the DDS system with an MR diagnosis: hence the right side of the equation includes a variable that closely resembles the left side. This was not the case for their supplemental analysis, in which the outcome was acquisition of an autism diagnosis among those with MR. Secondly, the authors made the assumption, admitting it could not be verified but strongly influenced the results, that throughout the period, 8% of the MR cases also had autism. Might this vary by age, and hence affect generalizability to the post-1987 births? Thirdly, figure 2 in their paper shows cumulative probability of change with values quite similar to the column of probabilities of change (not cumulative) in the supplemental analysis. If they are cumulative probabilities, then they should not be multiplied times the at-risk population; if they are not cumulative probabilities, then the steep rise in rate of change requires explanation, given roughly similar odds ratios (ORs) for later and earlier years. Finally, the method by which they 'netted out' the effects of other factors seems unusual (it could have produced a negative probability for years when $OR < 1$). Since the model is multiplicative, internal coherence would imply that the subtraction be carried out on the log scale.

Another concern surrounds the authors' focus on years when documents were published or events occurred that they deemed likely to have increased autism diagnoses in California. The story they tell is far from consistent with their data. For example, conversions spiked in 1994, the year DSM IV was adopted, yet in 1995 the number dropped back to the level of 1993. Since clinicians rarely adopt new practices immediately, one might expect 1995 to be closer to 1994, or higher, as DSM IV would continue to be applied in 1995, and not all persons with MR meeting the new criteria for autism would have been immediately identified. Moreover, some events

presumed to cause an increase could have had the opposite effect. Whether the report issued jointly with the California Department of Education³ would have resulted in a net increase or decrease was considered as debatable by DDS staff (Dr Ron Huff, personal communication). The 2001 Best Practices Guidelines⁴ advocated eligibility evaluations formally document which DSM IV criteria were met, potentially restricting diagnoses. Additionally, King and Bearman omitted the 2003 change requiring three rather than one functional limitation, which might have had the effect of excluding some previously eligible persons.

Despite serious concerns about methodology, their results are not implausible. In the CHARGE (Childhood Autism Risks from Genetics and the Environment) Study,⁵ which recruits pre-school children from the DDS system, 71% of those who meet criteria for autism on both the Autism Diagnostic Observation Schedule (ADOS)^{6,7} and Autism Diagnostic Inventory-Revised (ADI-R)⁸ also met criteria for MR based on scoring below the cut points on both the Mullen's Scale of Early Development (MSEL)⁹ and the Vineland Adaptive Behavior Scales (VABS).¹⁰ Among those meeting criteria for ASD but not autism on both ADOS and ADI-R, 45% would be classified as MR using scores on both the MSEL and VABS. However, these percentages were lower at the age of 4 years than at 2 years, reflecting delays in language development and suggesting that, at older ages, fewer display cognitive impairment. The conundrum is that children with autism may not be interested in entering the social contract of taking a test. As one teacher explained: 'Just because they don't do it doesn't mean they can't'.

Reasonable or not, the estimates of King and Bearman require verification. If proven valid, cautious interpretation must take account the overlap of diagnostic substitution and accretion with the impacts of earlier age at diagnosis, changing definitions and inclusion of milder cases, already quantified elsewhere.¹ For now, whether the conversion proportions from MR to autism for births after 1987 is higher or lower than predicted remains unknown.

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Commentary: On King and Bearman

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Much has been speculated about the origin of increased numbers of children receiving a diagnosis of autism spectrum disorder (ASD) in the last 20 years. This phenomenon has been observed worldwide, in countries where repeated epidemiological surveys or surveillance systems could capture these trends upwards. Interestingly, this acceleration occurred at around the same time in the late 1980s or early 1990s. As these trends were recorded in countries as far apart as the USA, the UK, Denmark, Sweden and Japan, it made it less likely that increases were due to exposure to environmental risk factors that would operate simultaneously in such disparate and contrasting settings. Observers also noted that changes started to occur in the 1980s (the term ‘pervasive developmental disorder’ was used for the first time in 1980, in the DSM-III nosography), at a time when the conceptualization of autism was broadened, more ‘high-functioning’ children with good language and intellectual skills were recognized, and when the view of autism as a severe, qualitatively deviant, disorder was progressively replaced by a continuum of combinations of

more or less severe deficits. A new dimensional view of the ASD phenotype has emerged, the boundaries of which with other developmental problems or psychopathological syndromes, and with normal development, have become progressively more difficult to establish. Clinical practice changed with increasing demands for standardization of clinical evaluations embodied by the development of semi-structured diagnostic tools such as the Autism Diagnostic Interview (ADI) or the Autism Diagnostic Observational Schedule (ADOS).

Diagnostic changes or substitution were among factors incriminated to account for increased prevalence rates. This phenomenon is not new in medicine, and it made perfect sense to postulate that, when autism became increasingly recognized with corollary improvements in funding and educational policies, a flow from previous diagnoses such as mental retardation (MR) to the new broadened concept of ASD would be observed. New studies suggestive of efficacy of early intensive behavioural intervention added to this momentum.¹ Practitioners’ and consumers’ views changed as developmental trajectories of young children diagnosed with ASD were no longer equated with fixed, lifelong, deficits that could not be overcome. The introduction of the 1990 Individual Disabilities Educational Act (IDEA) in the USA was followed by diagnostic practice changes,² whereby

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