

Conclusion

.....

The rise in the number of autism cases in California has been a cause for much concern. How to respond to these increasing numbers has been a point of major debate. Increases of the magnitude that have been reported challenge our limited understanding of the cause or causes of autism. It is natural to discount that which we do not understand or force it to fit a paradigm with which we are comfortable. This study has been an attempt to determine whether or not the increased numbers are due to a real epidemic, or if the rise in autism cases can be explained by factors that have artificially created that increase.

Has there been a loosening in the criteria used to diagnose autism, qualifying more children for Regional Center services and increasing the number of autism cases? We did not find this to be the case.

These results show that approximately 90% of children reported by the Regional Center System as having CDER status 1 autism met DSM-IV criteria for autism. More importantly, this close correspondence did not differ between the two birth cohorts. Our results, based on ADI-R interviews with families, are similar to the findings of a recently published study that evaluated Regional Center records³⁵. This study by Croen and colleagues, using the birth cohorts 1983-85 and 1993-95, found that 85% of children with CDER status 1 autism in the older cohort and 84% of the younger cohort met DSM-IV criteria for autism. Using the same birth cohorts, our study found that 88% and 89% met DSM-IV criteria for autism. Although Croen and colleagues did not conduct independent confirmation of the autism diagnosis (as was performed in this study with the ADI-R), nonetheless both studies concluded that the diagnosis of autism was reliable for most children in the Regional Center system.

The Autism Epidemiology Study required that families consent to participate, and our response rate was low (18% and 24% in the two age cohorts). One must consider the effects of unmeasurable biases that may have influenced a family's willingness to respond to our letter and participate in the study. This influence on participation would have to affect one birth cohort differently than the other to alter the overall results. Our findings on the percentage of autism cases meeting DSM-IV criteria were comparable in both birth cohorts. The Croen study, which was not subject to participation biases, had results similar to our own. This replication of findings gives added weight to our results.

Has the increase in cases of autism been created artificially by having "missed" the diagnosis in the past, and instead reporting autistic children as "mentally retarded?" This explanation was not supported by our data.

In our sample of children with mental retardation (MR) we did find that 18%-19% met DSM-IV criteria for autism. However, this percentage was consistent in the two birth cohorts. So, while misclassification occurs, children were not disproportionately misclassified in the past compared with the present. We might have attributed some percentage of the rise in autism cases to misclassification if we had found a difference between the two age groups, but we did not find a difference. In the aforementioned Regional Center record review study, the researchers found misclassification in 10% of the older MR cohort but in only 3.9% of the younger MR cohort. They interpreted

these results to mean that the reliability of the CDER diagnosis of MR for children qualifying for Regional Center services had changed during the study period. However, the Regional Center record would have documentation of autism only when an autism diagnosis is considered. In our study, there were some cases of children in the MR group who met DSM-IV criteria for autism even though their CDER records did not record a CDER status 1 autism diagnosis. There were other children in this study group who met DSM-IV criteria for autism whose Regional Center record would not have supported this diagnosis. Thus, a record review alone may result in an undercount of misclassification compared with active screening. Our findings, based on screening for autistic spectrum disorders with the SCQ and verifying an autism diagnosis with the ADI-R, are in contrast to their results.

In the Autism Epidemiology Study, the response rate was especially low for families whose children had a primary diagnosis of MR and not autism (10% for the older cohort and 15% for the younger cohort). As with Study Aim 1, we must assess this low participation rate and how it may have affected our results and conclusions. Examining our enrolled subjects with the CDER data, we found that parents of children with MR were more likely to enroll if their child had been reported with an autism spectrum disorder (CDER status 2, 4, or 9). However the odds of enrollment for an MR subject with an autism spectrum disorder were consistent in the two birth cohorts (odds ratio 1.42 in the older cohort and 1.44 in the younger cohort), so this enrollment bias did not differentially affect the MR group. The overall effect of this bias, where families whose child may have an autism spectrum disorder were somewhat more willing to participate, is to assume that the rate of misclassification for the whole group of children with MR in the Regional Center system is lower than the 18% estimate that we calculated.

It is worth considering what these misclassification numbers mean. Because the number of children in the MR group has historically been much larger than the autism group, even a modest rate of misclassification significantly increases the number of children who meet criteria for autism. For example, if the rate were 10% in the older cohort as reported by Croen et al, that translates to an additional 1,214 children with autism in the 1983-85 birth cohort ($0.10 * 12,139$). That would raise the total for that birth cohort from 991 to 2,205, more than doubling the number of children identified with full syndrome autism. There were fewer children reported with MR and not autism in the younger cohort, so the increase in autism cases would be less dramatic. The low enrollment rate in the MR groups and the bias in enrollment do limit our ability to state what the exact amount of misclassification appears to be. We can assume it is no higher than 18% and similar in the two birth cohorts. Universal autism screening of children with mental retardation by the California Regional Center System would definitively answer this important question. Such systematic screening could be done as part of the annual reassessment of children receiving Regional Center services and would likely further increase the number of autism cases reported.

Can the observed increase be accounted for an increase in the overall State population during the time period or by children with autism moving into California? No, increases in the State population account for less than 10% of the rise in case reports, and most children with autism served by the Regional Center System were born in

California. Based on parental report, 93% of children in the younger cohort and 87% of children in the older cohort were born in the State. To attribute some of the increase in autism cases to children with autism moving into California, we would have expected to see a greater proportion of out-of-California births among the younger children with autism. The finding that a greater proportion of older children are born out-of-state is not unexpected, given that the older group has had more time to move into California.

One additional issue regarding mobility should be mentioned. We found 57 instances where a child reported with autism in California and counted in the CDER database was no longer residing in the State. The cumulative total of cases in California probably represents an overestimation of known Regional Center clients, although not significantly so, based on our observations. Out-migration would be more likely to decrease prevalent cases in the older age cohort, as the greater period of time would increase the likelihood of a change in residence. Adjusting for out-migration then would decrease the number of cases in the older cohort and create a steeper increase in cases than has been reported.

In this study we asked many questions of parents. We compared the responses between the two birth cohorts, searching for differences in the hope of explaining what changing factors might have caused this increase in autism. No single factor investigated could explain the tripling in cases. Differences that were noted between the two groups include reports of more gastrointestinal symptoms during infancy in the younger group; and less mental retardation in the younger group. Regression of developmental milestones, as reported during the ADI-R, had not significantly increased in the younger group. On a more hopeful note, most parents reported improvements in their child's autism. Improvements were noted especially by parents of the younger children with autism.

What do parents think caused their child's autism? The data showed that participants in the study have a range of beliefs as to what causes autism. Most parents said that they "don't know" or they did not respond. Genetics and pregnancy- or birth-related events were frequently reported by parents. Immunization concerns ranked among the top responses. There is a high level of concern about immunizations and their association with autism. Unfortunately, this report was unable to evaluate the association of immunizations with autism recurrence in families due to our low number of unvaccinated younger siblings (Study Aim 6).

The Autism Epidemiology Study did not find evidence that the rise in autism cases can be attributed to artificial factors, such as loosening of the diagnostic criteria for autism; more misclassification of autism cases as mentally retarded in the past; or an increase in in-migration of children with autism to California. Without evidence for an artificial increase in autism cases, we conclude that some, if not all, of the observed increase represents a true increase in cases of autism in California, and the number of cases presenting to the Regional Center system is not an overestimation of the number of children with autism in California.