Study Aim 1 Results

Autism Diagnostic Interviews were conducted on the majority (94% and 93%) of children in the autism groups. The results of the ADI-R were considered positive if scores in each of three domains (Qualitative Impairments in Reciprocal Social Interaction, Communication Impairments, and Repetitive Behaviors and Stereotyped Patterns) met criteria matching DSM-IV criteria for autism, and the age of onset of symptoms (age < 36 months) was consistent with a diagnosis of autism. The results of comparison between the two age cohorts of children with CDER status 1 autism are presented in Table 2.

Table 2. *Comparison of ADI-R results for children with CDER status 1 autism, by age group, Autism Epidemiology Study.*

	Birth Year 1983-85	Birth Year 1993-95	p-value
Enrolled	143	232	
ADI-R Completed	135	216	
Proportion ADI-R Completed	94.4%	93.1%	0.78
Positive ADI-R	120	193	
Proportion Positive ADI-R (Unweighted and unadjusted)	88.9%	89.4%	0.97
Proportion Positive ADI-R (Weighted, adjusted for the staged sampling design)	88.2%	88.7%	0.90
Standard Error	0.0289	0.0215	
Design Effect	1.08	0.99	

The main finding is that the vast majority of children with CDER status 1 autism met DSM-IV criteria for autism and that this close correlation differs little between the two age cohorts. Using unadjusted numbers, 88.9% of children in the 1983-85 group met DSM-IV criteria, compared to 89.4% in the 1993-95 group. The results change very little when applying a weighting factor and accounting for differences in sampling and response by Regional Center and by age cohort (88.2% and 88.7%). The design effect of nearly 1 shows that the complex sampling employed in the analysis approximates a simple random sample. This means that simple comparisons of the results closely match results from a more precise weighted and adjusted analysis. Results from both simple comparisons and the more complex, but more accurate, analyses are presented for the first three study aims to assure readers that the results presented in this report are real and not just a fabrication based on complex statistical modeling.

Thirty-eight children (15 from Cohort 1 and 23 from Cohort 2) had a negative ADI-R despite having a CDER status 1 autism designation. For Cohort 1, study questionnaires were returned for 13 of these 15 children; nine parents reported that their child had autism, two reported PDD, one reported Asperger's Disorder, and one reported Rett's Disorder. In the two remaining children whose ADI-R scores did not meet DSM-IV criteria for autism, parents had reported autism in one and PDD in the other based on answers given during the ADI-R. For Cohort 2, study questionnaires were returned for 20 of the 23 children with a negative ADI-R; 18 parents reported their child as having autism, one reported PDD, and one reported Childhood Disinte-

grative Disorder. For the remaining three children in this cohort without questionnaire responses, two parents reported their child's diagnosis as autism; the remaining parent reported attention deficit disorder, but did not specifically refute their child's diagnosis of autism. Thus, most of the children in the autism groups whose ADI-R score did not meet DSM-IV criteria for autism were somewhere on the autism spectrum.

Scores on the three main components and the age criteria were compared for the two age cohorts to test whether or not the number of criteria used to determine the diagnosis of autism differs by age cohort. Differences in mean scores would suggest that the threshold for making a designation of CDER status 1 autism had changed between the two age cohorts. The results (shown in Table 3) indicate that the threshold for making the diagnosis of autism changed little between the two age cohorts. There was a statistically significant difference in the score for age criteria with the younger cohort, but this difference of a quarter point is of little clinical significance and not likely to result in major changes in the diagnosis of autism. Likewise, the three-quarter point difference between scores for the Repetitive/Stereotypic Behaviors Section is not likely to be associated with significant changes in the diagnosis of autism. Furthermore, these two differences would exert an opposing influence on any overall change in autism diagnostic thresholds.

Table 3. *Comparisons of component scores on ADI-R for children with CDER status 1 autism who were ADI-R positive, by age group, Autism Epidemiology Study.*
(Results of weighted and adjusted analyses)

	# ADI-R Positive	Mean Score	Standard Error	Design Effect	p-value
Age criteria					
AD1 (1983-85)	120	3.26	0.11	1.27	0.03
AD2 (1993-95)	193	3.50	0.07	0.98	
Social Impairments					
AD1 (1983-85)	120	22.86	0.34	1.03	0.31
AD2 (1993-95)	193	23.33	0.31	0.87	
Repetitive/Stereotypic Behaviors					
AD1 (1983-85)	120	6.84	0.23	1.23	0.01
AD2 (1993-95)	193	6.07	0.16	0.98	
Communication Impairment — Overall					
AD1 (1983-85)	120	16.66	0.32	1.05	0.12
AD2 (1993-95)	193	16.02	0.26	0.94	
Communication Impairment — Verbal Children					
AD1 (1983-85)	93	17.88	0.32	1.03	0.20
AD2 (1993-95)	144	17.33	0.28	0.97	
Communication Impairment — Non-Verbal Children					
AD1 (1983-85)	27	13.07	0.25	0.84	0.053
AD2 (1993-95)	49	12.41	0.22	0.88	

Study Aim 2 Results

A portion of children categorized as having mental retardation by the Regional Center system met DSM-IV criteria for autism, representing an undercounting of cases of autism. Of the 1983-85 cohort, 17% met criteria for autism, compared to 21% of children in the 1993-95 cohort. When the results were weighted and the analyses adjusted for the complex sampling design, these proportions are approximately 18% for both groups. These results, shown in Table 4, demonstrate that there is not a significant difference in misclassification between the two age cohorts. For this type of misclassification to contribute to an apparent increase in autism cases, the misclassification rate would have to be greater for the older cohort. We found similar rates of misclassification in both age cohorts.

Table 4. *Autism screening and ADI-R results among children determined to have mental retardation without CDER status 1 autism, by age group, Autism Epidemiology Study.*

	Birth Year 1983-85	Birth Year 1993-95	p-value
Enrolled	124	185	
SCQ's Completed	106	153	
Completion Rate	85.5%	82.7%	0.62
SCQ Positive (score ≥ 22)	34	54	
Proportion of Positive SCQ's (unweighted and unadjusted)	32.1%	35.3%	0.71
Proportion of Positive SCQ's (Analysis weighted, adjusted)	32.9%	33.5%	0.93
Number of Follow-up ADI-R's (among the positive SCQ's)	24	37	
Number of Positive ADI-R's	16	28	
Rate of Positive ADI-R's (among the positive SCQ's)	66.7%	75.7%	0.64
Rate of Positive ADI-R's (excluding positive SCQ without a follow-up ADI-R)	16.7%	20.6%	0.56
Rate of Positive ADI-R's (excluding positive SCQ without a follow-up ADI-R) (Analysis weighted, adjusted)	18.4%	18.7%	0.96

Our estimate that 18% of children with mental retardation meet DSM-IV criteria for autism is likely to be an overestimation of the actual percentage. Parents of children in the MR groups might have been more likely to respond and enroll if they believed their child had autistic features. The low response rate in this group also increased the likelihood of a differential response ("bias") among the parental respondents. We tested whether parents of children in the MR group were more likely to respond if the CDER record indicated the child may have an autism spectrum disorder (ASD). If the CDER record was marked for Autism Status 2, 4, or 9 (defined previously) we considered this evidence for ASD. The odds ratio for enrollment given a listing of an ASD condition was 1.50, but this was not significantly different from an odds ration of 1.0 (95% confidence interval 0.82-2.75). This slight bias of enrollment

for children with ASD conditions was similar in both cohorts (odds ratios of 1.42 and 1.44).

There was a high rate of positive ADI-R's among the children whose SCQ was positive. Unfortunately, not all of these families completed an ADI-R interview. We tested for potential bias in the completion of the ADI-R's by comparing the average total SCQ score for those who completed an ADI-R with those who did not. There were 88 children with MR who scored positively on the SCQ; an ADI-R was completed on 61 and not on 27. The mean SCQ score for ADI-R completers was 25.48 ±3.01, and for those lacking ADI-R follow-up, the mean score was 25.30 ±2.80 (p=.79).

Among the 44 children in the MR group who met DSM-IV criteria for autism based on the ADI-R, some parents reported an autism diagnosis while most did not.

If all of the positive SCQ results were followed up with an ADI-R interview, it is likely that more children in the MR group would have been found to meet DSM-IV criteria for autism. However, there are many potential problems with these data which limit our ability to produce an accurate estimate of the misclassification of autism among children reported with mental retardation. Misclassification would have to occur more frequently in the past and less frequently currently to produce an apparent rise in autism. We found no evidence that such a difference exists.

Among the 44 children in the MR group who met DSM-IV criteria for autism based on the ADI-R, some parents reported an autism diagnosis while most did not. In Cohort 1, study questionnaires were completed on 14 of the 16 children with a positive ADI-R. Autism was reported by three parents and was not reported by 11. Of these 11, one child was reported to have Childhood Disintegrative Disorder, two were reported to have PDD, one was reported to have Prader-Willi syndrome, six had no autism spectrum disorder, and one had an unknown condition. Families for two children in Cohort 1 did not complete the questionnaire, but did report fragile X syndrome with autistic tendencies (1) and a duplication on the X chromosome (1) during the ADI-R interview. In Cohort 2, questionnaire data were available for 27 of 28 study subjects. Autism was noted on the study questionnaire by eight parents and PDD by seven parents. The other 12 parents did not report an autism spectrum disorder diagnosis. The one remaining study subject was reported to have cerebral palsy and microcephaly.

Study Aim 3 Results

Place of birth was compared for each age cohort among children with CDER status 1 autism to determine whether the apparent increase in autism numbers can be attributed in part to large numbers of children with autism moving into California. Table 5 shows the results of these place-of-birth analyses. The vast majority of children with autism were born in California. The trend for a greater proportion of California births among the younger children with autism is the opposite that would be necessary for increased numbers of autism cases to be due to children with autism moving into California. The finding that a greater proportion of older children are born out-of-state would be expected with the older group having more time to be comprised of children born elsewhere and then move into the State.

Table 5. *Place of birth comparisons for children with CDER status 1 autism, by age group and ADI-R status, Autism Epidemiology Study.*

CDER Status 1 Autism	**Birth Year 1983-85**	**Birth Year 1993-95**	**p-value**
Enrolled	143	232	
Study Surveys completed	117	189	
California birth	105	178	
Proportion of CA Births (unweighted and unadjusted)	89.7%	94.2%	0.23
Proportion of CA Births (Analysis weighted, adjusted)	88.5%	93.0%	0.25
CDER Status 1 Autism and +ADI-R	**Birth Year 1983-85**	**Birth Year 1993-95**	**p-value**
Positive ADI-R	100	161	
California birth among +ADI-R	89	152	
Proportion of CA Births (unweighted and unadjusted)	89.0%	94.4%	0.17
Proportion of CA Births (Analysis weighted, adjusted)	87.3%	92.9%	0.22

In summary, mobility of children with autism does not account for any of the observed increase in autism in the Regional Center System.