

## Executive Summary

### Introduction and Study Objectives

The National Institute of Mental Health (NIMH) contracted with The Lewin Group to conduct a two-year study from September 2010 to September 2012 entitled “The Study of Health Outcomes in Children with Autism and their Families.” This study seeks to address a significant gap in the empirical knowledge base about the trajectories of health conditions, health outcomes and utilization of health care services among children with autism spectrum disorders (ASD), their siblings, and their parents. The ability to study a very large and heterogeneous group of children with ASD using claims data and the ability to link to information about family members is unprecedented and holds promise to advance clinical and health services knowledge about ASD substantially.

The overall purpose of Task B was to compare the health conditions of children with ASD and their siblings and parents to children without ASD and their siblings and parents. This study first examined the occurrence of a broad set of groups of health conditions and then addressed targeted research questions for three specific conditions. The goals of the three specific subtasks were to:

- Compare the prevalence of gastrointestinal conditions in children with ASD to children without ASD;
- Compare the rates of injury in children with ASD to children without ASD; and
- Compare the prevalence of stress-related conditions in parents of children with ASD to parents of children without ASD.

Thus the overall goals of the Task B of the Health Outcomes Study are to:

- Report the proportions and the associated odds ratios of the samples with evidence of eight groups of health conditions and overall comorbidity controlling only for length of continuous enrollment to examine the broad association between ASD and the co-occurring health conditions.
- Calculate odds ratios for gastrointestinal conditions among children with and without ASD; hazard ratios for injuries among children with and without ASD; and the odds ratios for stress-related conditions among parents of children with and without ASD.

### Study Design and Analytic Strategy

This retrospective claims data study used medical data, pharmacy data, and enrollment information from the OptumInsight research database containing claims from the large health plan affiliated with OptumInsight. Claims data for the period 01 January 2001 to 31 December 2009 were linked to a consumer database for select socioeconomic information. All study subjects were identified among commercial enrollees who have medical, pharmacy, and behavioral health coverage. Six main samples were selected: children with ASD, a comparison group of children without ASD, parents of children with and without ASD, and siblings of children with and without ASD.

Based on the results of the Task A: Chart Study, children with at least 2 ASD claims were defined as having ASD and were included in the Task B study. In the chart study, the positive predictive value increased from 74.2% to 87.4% when children with only 1 ASD claim were excluded from the case definition, increasing our confidence that the children with ASD in Task B are true cases. However, exclusion of children with only 1 ASD claim from both the case and control groups likely increases the differences between children with ASD and their family members when compared to controls. Also, two additional sample subgroups were identified for select analyses to address the research questions identified for Task B. The first was a subset of children with ASD for whom we estimated their initial diagnosis occurred during the study observation period. The second was the parents of these children initially diagnosed with ASD during the enrollment period.

To address the research questions concerning the associations between ASD and selected groups of co-occurring health conditions, we adjusted for enrollment time and demographic variables. Specifically, for binary dependent variables indicating whether a study subject had evidence of a particular group of conditions (e.g., infectious diseases, autoimmune conditions), we utilized logistic regression to produce enrollment-adjusted proportions and odds ratios (OR) for the outcomes of interest. Logistic regression models were fitted including the primary independent dichotomous variable capturing the samples of interest (e.g., subjects with ASD vs. comparison group) and the total enrollment time. The odds ratios were produced comparing the two samples of interest.

In addition to using a binary indicator for injuries, we measured the count of injury episodes. For these count measures, enrollment-adjusted rates were calculated as the count of episodes across a sample divided by the total person-time for that sample. Rate ratios (RR) comparing the rates between the ASD and non-ASD samples along with the associated p-values were then generated.

## Results

Among 33,565 children with ASD and their 99,970 family members, we found the following results about health outcomes:

- After controlling for varying enrollment time during study, a higher proportion of children with ASD than children without ASD have all eight groups of health conditions examined, including neurological/neurodevelopmental disorders, mental health conditions, gastrointestinal/nutritional conditions, autoimmune conditions, congenital/genetic disorders, and metabolic dysfunction and common childhood conditions including infectious diseases and injuries.
- Specifically, 70.8% of children with ASD had evidence of co-occurring neurological/neurodevelopmental disorders; 70.1% had evidence of mental health conditions; and 19.5% had evidence of gastrointestinal/nutritional conditions. Substantially fewer children without ASD had evidence of these conditions (9.2%, 8.7%, and 5.1%, respectively).
- Siblings of children with ASD also experience higher rates of all eight groups of physical and mental health conditions. For example, more siblings of children with ASD had evidence of neurological/neurodevelopmental disorders (17.3% vs. 9.0%), mental health

conditions (17.9% vs. 8.6%), and gastrointestinal/ nutritional conditions (7.4% vs. 4.2%) than siblings of children without ASD.

- The unadjusted results showed children with ASD to be at a slightly greater risk for injuries overall, but this increase in risk diminished (and actually reversed) after controlling for demographic, socioeconomic variables and co-occurring conditions. However, analyses exploring injury risk separately by age period indicated that during younger ages (<6 years old), those with ASD were at increased risk for injury compared to those without ASD, while during older ages (>10 years old) those with ASD were at decreased risk of injury compared to those without ASD.
- Interactions between sample group (with ASD vs. not) and gender and co-occurring conditions were also modeled to examine whether the effect of ASD differs across subgroups defined by these variables. While these interaction terms (with the exception of seizures) were statistically significant at conventional alpha error tolerance ( $p < 0.05$ ), the statistical significance was driven by the large sample size. The heterogeneity of the ASD effects across subgroups, unlike in the case of age, was not large.
- Children with ASD had substantially higher odds of a GI condition than children without ASD (OR=3.94,  $p < 0.001$ ). Our attempts to control for surveillance bias did not change the effect estimates at all. Stronger ASD effects on GI occurrence were seen in subjects without seizure or autoimmune disease, respectively, (OR=4.01 and 4.12) compared to subjects with seizure or autoimmune disease (OR=1.83 and OR=3.07, respectively).
- Among children with ASD, girls, younger children, and children with seizures or an autoimmune condition had increased odds of a GI condition.
- The odds of having a GI condition were 40% higher in the 12 month period following, compared to the 12 month period before, a child's initial ASD diagnosis (OR = 1.397,  $p < 0.001$ ).
- Parents of children with ASD had higher odds of a stress-related condition than parents of children without ASD (OR=1.48,  $p < 0.001$ ). Controlling for surveillance bias in the model did not alter the ASD effect on having a stress-related condition (ASD OR=1.50,  $p < 0.001$ ), meaning that the observed increase in stress-related conditions was not due to greater exposure to the health care system among parents of children with ASD.
- Both the odds of a stress-related condition and costs associated with stress-related conditions were higher in the 12 month period following, compared to the 12 month period before, their child's initial ASD diagnosis (OR = 1.322,  $p < 0.001$ ; Cost ratio = 1.246,  $p < 0.001$ ).

## Implications and Recommendations

In summary, we found that children with ASD and their families were at greater risk for many different types of health conditions than were children without ASD and their families. Specifically, our results lead to the following implications:

- Overall injury risk associated with ASD appeared to be age dependent. We saw approximately 30% higher injury rates in ASD than in the comparison groups at younger

ages (<6 years) - but that effect reversed at higher ages (>10 years) where the children with ASD had injury rates approximately 35% lower than comparably aged children without ASD after adjusting for socio-demographic variables and co-occurring conditions. In the U.S., the distribution of injury type (particularly nonfatal injury) is known to vary greatly by age. Consequently, further investigation of injury risk in children with ASD should focus on distinct age subgroups and consider the varying determinants of different injury types.

- Our findings indicate that, in the community, children with ASD are more frequently recognized with, and presumably treated for, GI conditions. This strongly supports the need for further research into the relationship between ASD and the gastrointestinal system.
- Our finding that parents of children with ASD were more likely to experience a stress-related condition than parents of children without ASD demonstrate that support for both parents as well as children is essential to caring for children with ASD and helping families live a high quality life.

Because we have the ability to include a large and heterogeneous group of children with ASD and to compare to children and families without ASD, our estimates of risk may be more precise and objective than previously available. These findings, along with our results concerning the poorer physical and mental health among parents and siblings, demonstrate that the health of the child both reflects and impacts the health of the whole family, which may potentially threaten family resources and points to a need for supportive interventions for the family as a whole rather than each individual separately in order to most improve the health and quality of life of children with ASD and their families. The family associations also raise questions about potentially shared etiologic pathways that could be the grounds for future research.