CORRESPONDENCE

Vaccination Rates among Younger Siblings of Children with Autism

TO THE EDITOR: Recent outbreaks of illnesses that may be prevented by vaccines have increased public debate about vaccination behaviors (i.e., whether or not and when parents choose to vaccinate a child), and California has been a key affected state. One reason that parents choose not to have their children vaccinated is the perceived link between vaccines and autism spectrum disorder. This reason is particularly relevant for parents of a child who has autism spectrum disorder, since concerns that the disorder will develop in subsequent children may be more pronounced.

Since 2009, we have tracked the development of infants who have a full biologic older sibling with a diagnosis of autism spectrum disorder. The risk of this disorder is increased by a factor of approximately 20 among these "high-risk" infants.[1] Our comparisons of such infants with age-matched "low-risk" infants who have an older sibling without autism spectrum disorder allows for the identification of putative biomarkers of this disorder.[2] Although vaccination behaviors were not our primary focus, studies showing decreased rates of vaccination against measles–mumps–rubella (MMR) among high-risk infants prompted us to analyze available data on vaccination behaviors in our sample of 206 families from southern California (71 of which had a child with autism spectrum disorder and 135 that did not have a child with autism spectrum disorder) (Table 1).[3,4]

Childhood vaccination and autism spectrum disorder continue to be linked in the minds of many people despite overwhelming evidence to the contrary.[5] Adding to this evidence, our data showed no significant difference between rates of vaccination among children with and those without autism (100.0% vs. 98.5%; P=0.30). However, there were two additional interesting findings. Families with children who had autism spectrum disorder were less likely to vaccinate subsequent children. Specifically, the rate of vaccination among full biologic infant siblings of children with autism spectrum disorder was 83.1%, as compared with 97.0% among low-risk infants (Pearson chi-square value with one degree of freedom, 12.62; P<0.001). These findings are consistent with reported rates of MMR vaccination among children at older ages and across broader sampling regions.[3,4]

Our results also suggest that changes in vaccination behavior may relate to adverse reactions to vaccine. In particular, parents who had an older child with autism spectrum disorder retrospectively reported a higher rate of adverse reactions to vaccination among the older child than did those who did not have an older child with autism (22.6% vs. 3.8%; Pearson chi-square value with one degree of freedom, 16.87; P<0.001). Likewise, parents who had an older child with autism retrospectively reported a higher rate of these reactions among the infant sibling than

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Table 1. Demographic Characteristics of Older Siblings, Infants, and Mothers, According to Group.*

Characteristic	Older Siblings		Infants	
	Autism Spectrum Disorder (N=71)	Typically Developing (N=135)	With Older Sibling Who Has Autism Spectrum Disorder (High-Risk) (N=71)	With Typically Developing Older Sibling (Low-Risk) (N=135)
Age (mo)	56.6±3.0	52.4±3.1	5.4±0.5	6.7±0.5
Female sex (%)	11.3	51.1	46.5	43.0
Race or ethnic group (%)†				
White	64.8	65.7	—	—
Hispanic	28.4	18.8	—	—
Black	2.6	0	—	—
Asian	7.0	7.5	—	—
Mixed race or other race	19.7	20.1	—	—
Maternal age (yr)	34.5±0.5	35.4±0.4	—	—
Maternal education (%)				
Less than high school	1.4	0	—	—
High school diploma or equivalent	18.3	10.4	—	—
Some postsecondary education	18.3	14.2	—	—
Bachelor's degree	35.2	37.3	—	—
Master's degree	18.3	30.6	—	—
Professional degree: Ph.D. or M.D.	8.4	7.5	—	—

* Plus–minus values are means ±SE. Older siblings are the closest sibling in age to the infant, with the exception of seven older siblings in the autism spectrum disorder group. Student's t-tests were performed to compare ages across groups, with Welch's correction to adjust for unequal variances in comparisons of older siblings and infants. Categorical data are shown as a percentage for each group, and chi-square analyses were used to investigate differences between the groups. The following data were missing and were therefore excluded from analyses: race (1 child–infant pair in the low-risk group), ethnic group (2 in the low-risk group and 3 in the high-risk group), education (1 in the low-risk group), and maternal age (1 in the high-risk group). In addition, the presence of "0" values in some cells resulted in exclusion of the variables "black" and "less than high school" from group comparisons. Since the sample included only full biologic siblings, categorical data for the older sibling and infant counterpart are identical, except for sex. Older siblings with autism spectrum disorder were more likely to be male than typically developing older siblings ($P<0.001$). $P \geq 0.10$ for all other comparisons.

† Race or ethnic group was reported by the parents, who could report more than one race or ethnic group.

did those who did not have an older child with autism (6.9% vs. 0.8%; Pearson chi-square value with one degree of freedom, 5.87; $P=0.02$). Reported reactions included fever, diarrhea, unusual crying or screaming, and general malaise. These differences in reported reactions may reflect either a true increase or a recall bias, and they warrant larger prospective studies of adverse reactions to vaccine with the use of more objective measures, such as medical records and examination after vaccination, in children in whom autism spectrum disorder ultimately develops.

The relationship between adverse reactions to vaccine and autism spectrum disorder has received little attention in research as of this writing. At the public health level, a better understanding of the relationship between perceived adverse reactions to vaccine and autism spectrum disorder is necessary in order to more effectively address concerns about vaccination.

Gena Glickman, Ph.D.
Elizabeth Harrison, Ph.D.
Karen Dobkins, Ph.D.

University of California, San Diego
La Jolla, CA
glickman@ucsd.edu

Supported by grants from the Congressionally Directed Medical Research Program, Autism Research Program (AR130253, to Drs. Glickman and Dobkins), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health (R01 HD052804-01A2, to Dr. Dobkins).

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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DOI: 10.1056/NEJMc1708223

Head Positioning in Acute Stroke

TO THE EDITOR: Anderson et al. (June 22 issue)[1] report that head positioning did not influence outcome in patients with acute stroke. The lying-flat position theoretically increases cerebral perfusion, which may alleviate acute ischemia through the recruitment of collaterals.[2] However, in the Head Positioning in Acute Stroke Trial (HeadPoST), reported by Anderson et al., many patients had conditions that presumably were not the result of large perfusion defects: specifically, there were patients with stroke mimics (4.9%), lacunar stroke (30.2%), or intracerebral hemorrhage (8.4%). Moreover, the low median scores on the National Institutes of Health Stroke Scale in both study groups[1] suggest that few patients had proximal occlusions of the intracranial arteries, which implies that many patients did not require improvement in their collateral cerebrovascular network during acute stroke. The absence of large ischemic stroke has been proposed as a possible reason for the failure of endovascular therapy to show clinical benefit in some recent trials.[3,4] Head positioning therefore might be evaluated in a more selective population, such as patients with large strokes or large ischemic areas at risk,[5] before we give up on this nonpharmacologic strategy.

Igor Sibon, M.D., Ph.D.
CHU de Bordeaux
Bordeaux, France

Patrick Gérardin, M.D., Ph.D.
Alexandre Gauthier, M.D.
CHU de La Réunion
Saint Pierre, France
agauth05@gmail.com

No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1709517

TO THE EDITOR: We write to request clarification of the consent process used in HeadPoST, in which hospital executives provided institutional consent to implement an intervention and patients provided individual consent only for postintervention data collection and follow-up. Although cluster-randomized trials that expose groups to a common intervention (e.g., community water sanitation) often preclude prospective individual consent, the bed-position intervention in HeadPoST addressed individual patients (which makes it an "individual-cluster" trial).[1] Time constraints[2] seemingly did not preclude consent: interventions were initiated a median of 7 hours after hospital arrival and continued for 24 hours. The investigators describe the study as having "minimal risk," which is generally defined as risk that is similar to the risks involved in daily life (and is distinct from equipoise).[3] But HeadPoST was directed at brain perfusion in acute stroke and was designed to detect effects on disability at 90 days. A final