



Vaccine Hesitancy and Low Immunization Rates in Children with Down Syndrome

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Objectives To determine the prevalence of vaccine hesitancy and refusal among parents of children with Down syndrome and to determine how well the Parent Attitudes about Childhood Vaccines Survey (PACV) is associated with vaccine receipt among children with Down syndrome.

Study design We mailed the PACV to parents of children with Down syndrome who attend the Down Syndrome Clinic at Akron Children's Hospital and examined associations between PACV scores and immunization status at 19 months of age.

Results Of 120 surveys sent, 63 parents completed the PACV (52% response rate) of which 60 were linked to vaccination records. Of these 60 respondents, 55 children were ≥ 19 months old. PACV scores were significantly correlated with days of underimmunization at 19 months of age. All parents who refused all vaccines had PACV scores of ≥ 50 . Only 58% of children were up to date for the combined 7 vaccine series at 19 months of age.

Conclusions The PACV may be a valuable tool to identify vaccine hesitancy among parents of young children with Down syndrome. Special emphasis is needed to increase adherence with on-time vaccine recommendations for children with Down syndrome to optimize their health and to potentially avoid hospitalizations. (*J Pediatr* 2020;223:64-7).

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Immunizations are regarded as one of the greatest public health interventions and have been associated with a marked reduction in morbidity and mortality due to a number of infectious diseases. Over the past 10-20 years, parental acceptance of childhood immunizations has decreased sharply. The World Health Organization ranked vaccine hesitancy as one of the top 10 public health threats in the world for 2019.¹ Research about vaccine hesitancy and vaccine refusal has focused largely on the general pediatric population and little is known about vaccine hesitancy and refusal in children with Down syndrome. The American Academy of Pediatrics Guidelines for Health Supervision of Children with Down Syndrome recommends immunizing children with Down syndrome by the same schedule, including influenza vaccine, as healthy children unless specifically contraindicated.²

Children with Down syndrome are at increased risk for physical disorders, including congenital heart disease, hypothyroidism, and lower respiratory tract infection and are at greater risk of developing autoimmune disorders than typically developing children.³ Down syndrome also is the most common recognizable genetic syndrome associated with immunologic abnormalities, including reduced T-lymphocyte counts, reduced B-lymphocyte counts, small thymus size, and suboptimal antibody responses to immunization.^{4,5} The relationship between the immunologic differences in Down syndrome and the increased frequency and severity of infections is not clear. Other relevant medical and anatomic differences, including hypotonia of the upper airway, gastroesophageal reflux, and cardiopulmonary conditions, also contribute to infection burden in children with Down syndrome.⁵ Young children with Down syndrome are more frequently hospitalized with pneumonia and sepsis than typical children.^{6,7} Although many of the respiratory tract infections experienced by children with Down syndrome are due to viruses or *Mycoplasma*, for which there are no vaccines currently, influenza and many bacterial infections are vaccine preventable.

The Parent Attitudes about Childhood Vaccines Survey (PACV) assesses vaccine hesitancy.⁸ It has been used retrospectively and prospectively in multiple general pediatric settings and the score correlates strongly with days of underimmunization (days of under immunization) in young children. We sought to use the PACV to determine the prevalence of vaccine hesitancy and refusal among parents of children with Down syndrome and to determine the association of

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PACV	Parent Attitudes about Childhood Vaccines Survey
UTD	Up-to-date

parents' responses on a survey about attitudes toward vaccines with underimmunization of children with Down syndrome at 19 months of age.

Methods

The PACV was used to assess vaccine hesitancy among parents of children with Down syndrome. The PACV is a brief, self-administered questionnaire with 15 items about vaccine hesitancy and 7 demographic questions (parental age, parental educational level, marital status, race or ethnicity, relationship to child, number of children in the household, and household income). It was developed to identify vaccine-hesitant parents who have underimmunized children. The questionnaire asks about routine childhood immunizations, excluding the seasonal influenza vaccine. The PACV is a reliable, valid survey developed for use in the general pediatric population. In the present study, 1 question was added to ask about the current age of the child with Down syndrome. Each of the 15 survey questions are scored as 2 for the hesitant response, 1 for don't know or not sure, and 0 for the nonhesitant response. The total raw PACV score was calculated by summing the score from each item and converting the raw score to a 0-100 scale using a simple linear transformation accounting for items with missing values as described by Opel et al.⁸ A higher score on the PACV is associated with a higher percentage of days of under immunization. Days of under immunization and percent days of under immunization were calculated at 19 months of age following the protocol developed by Opel et al.⁸ If a parent gave the hesitant answer on 5 questions, don't know or not sure response on 5 questions, and the nonhesitant response on the remaining PACV questions with no missing values, the final score would be 50. In a general pediatric population, 71.9% of children were up-to-date (UTD) at 19 months if the PACV score was 0-49, only 42.4% were UTD if the score was 50-69, and 14.2% were UTD if the score was 70-100.⁹

In November 2017, an introductory letter explaining the study and the PACV was mailed to the parent/legal guardian of patients <8 years old who had been seen in the Down Syndrome Clinic at Akron Children's Hospital in the preceding 3 years. In the mailed survey, the parent/guardian was asked for permission to access the child's immunization record to determine the child's current immunization status and to correlate it to the PACV score. A release of information form to obtain the child's immunization record from the primary care physician and an addressed, stamped return envelope were included with the mailed survey. Immunization records were obtained from the child's primary care physician. Parents were asked to identify all primary care providers who administered vaccines to the child through 5 years of age. The release of information form signed by the parent was mailed to the primary care physician(s) with an introductory letter asking them to mail or fax the child's immunization record to us. A second mailing was sent 8 weeks

later to parents who had not responded. Upon return of a completed PACV, a \$10 gift card was mailed to responding parents as an incentive to participate. The study was approved by the Akron Children's Hospital Institutional Review Board. Parents/legal guardians who were non-English speaking and children who were in foster care were excluded. Children who had not reached 19 months of age were also excluded.

The Down Syndrome Clinic provides comprehensive developmental evaluations and coordination of care of children with Down syndrome from birth to age 21 years. The Down Syndrome Clinic does not provide primary care or immunizations. The primary outcome of interest was days of under immunization for 8 vaccines at 19 months of age. We included the following vaccines: hepatitis A, hepatitis B, DTaP (diphtheria, tetanus, and pertussis), inactivated polio vaccine, *Haemophilus influenzae* type b, conjugate pneumococcal vaccine (PCV7 or PCV13), MMR (measles, mumps, and rubella), and varicella vaccine. Rotavirus vaccine was excluded. For each dose of vaccine assessed, the study evaluated those given on time by using the latest age recommended by the Advisory Committee on Immunization Practices Recommended Immunization Schedule.¹⁰ A dose was considered to be late if it was received >30 days beyond the latest age (if there was a recommended age range) for that dose in the recommended schedule. UTD status for each child was calculated at 19 months of age.

Statistical Analyses

Normally distributed continuous variables were expressed as mean (SD), and non-normally distributed continuous variables as median (IQR; 25th-75th percentile). Categorical variables were shown as frequencies (%). The normality of variables was analyzed by the Kolmogorov-Smirnov test. The Pearson χ^2 or Fisher exact tests were used to analyze categorical variables. Spearman correlation analysis was used to establish the association between continuous variables, specifically between total PACV score and days of under immunization as well as total PACV scores and percent days of under immunization. A *P* value of <.05 was considered statistically significant. The analysis was performed using SAS (version 9.4; SAS Institute Inc, Cary, North Carolina).

Results

Of the 120 surveys sent, 63 parents completed and returned the PACV (52% response rate), of which 60 were linked to immunization records. Of these, 55 children were ≥ 19 months old and were included in the analyses. The respondents were mostly middle class, well-educated, older white parents (**Table I**).

In bivariate analyses, no demographic factors, including patient sex, parent marital status, parent education, race, family income, or number of children in the family, were associated with PACV scores. Likewise, no demographic

Table I. Characteristics of respondents to the PACV survey (n = 55)

Characteristics	
Child age, mo	52 ± 24
Child male sex	28 (51)
Relationship of respondent–mother	52 (95)
Age of respondent, y	
21-25	1 (2)
26-30	6 (11)
31-35	17 (31)
>35	30 (54)
Did not answer	1 (2)
Race of respondent–Caucasian	50 (91)
Marital status of respondent–married	38 (69)
Educational level of respondent	
High school graduate, general education degree or less	7 (13)
Some college	17 (31)
≥4 years of college	31 (56)
Household annual income, US\$	
<30 000	9 (16)
30 000-49 999	6 (11)
50 000-74 999	13 (24)
≥75 000	22 (40)
Don't know/did not answer	5 (9)
No. of children in household <19 years old	
1	7 (13)
2 or 3	40 (73)
≥4	8 (14)

Values are mean ± standard deviation or number (%).

characteristics were associated with days of under immunization. Demographic factors did not differ significantly between parents whose children were UTD in their vaccines and those who were not UTD. Among parents who were married, there was a trend ($P = .07$) toward a greater percentage of children who were not UTD (63% vs 37%).

Table II (available at www.jpeds.com) presents the parents' responses to the PACV questions. Although 25% of parents indicated that they had delayed having their child get a shot for reasons other than illness or allergy and 18% endorsed that they had ever decided not to have their child get a shot for reasons other than illness or allergy, only 18% of respondents considered themselves to be vaccine hesitant. More than one-half of the parents stated that it is better for children to receive fewer vaccines at the same time. Among the respondents, 42% of parents reported concern that their child with Down syndrome might have a serious side effect from ≥1 vaccines and 35% replied that they feared that ≥1 vaccines might not be safe. Almost all parents reported they were able to discuss their concerns about shots openly with their child's doctor.

At 19 months, 32 children (58%) were UTD for all 8 vaccines and 7% of parents refused all vaccines. However, only 17 children (31%) were UTD for all 8 vaccines and had had no delays in immunization before 19 months of age. The median number of days of under immunization was 64 (IQR, 0-238) at 19 months. No vaccine was significantly refused or delayed more than other vaccines. UTD status for individual vaccines ranged from 76% for DTaP (4 doses) to 93% for polio (3 doses) at 19 months.

Analyses revealed a fair to modest correlation between PACV scores and days of under immunization as well as PACV scores and percent days of under immunization at 19 months of age ($r = 0.36$ for each; P values = .007; **Figure 1** [available at www.jpeds.com]). In addition, all parents who refused all vaccines had PACV scores of ≥50. The percentage of UTD children declined with higher PACV scores (**Figure 2**; available at www.jpeds.com).

Discussion

Little information is available about vaccine hesitancy and refusal in children with chronic conditions.^{11,12} Some chronic conditions may make children more susceptible to vaccine-preventable infections and complications of these infections. In a study of 3 rare genetic diseases (Rubinstein-Taybi syndrome, Sotos syndrome, and Beckwith-Wiedemann syndrome), Esposito et al found lower rates of on-time vaccination among children with these disorders compared with typical controls.¹¹ In particular, MMR vaccination rates were significantly lower among children with these conditions (40% in Rubinstein-Taybi syndrome, 50% in Sotos syndrome, and 46% in Beckwith-Wiedemann syndrome compared with 91% in healthy controls). Esposito et al reported that most parents who refused vaccines were concerned about side effects of the vaccine or worsening of the child's underlying condition. Pandolfi et al found lower rates of vaccination among Italian children with chronic conditions, including type 1 diabetes, cystic fibrosis, Down syndrome, and neurologic disorders, compared with healthy children.¹² However, among those with chronic disorders, Pandolfi reported that children with Down syndrome had the highest vaccination rates. Our study's novelty is its focus on children with Down syndrome and the application of the PACV to parents of children with Down syndrome. In the current study, higher scores on the PACV were associated with more days of under immunization among children with Down syndrome at 19 months of age.

Our results show a higher rate of vaccine refusal and a lower rate of UTD status in our sample compared with rates in the general population. Using data from the 2017 National Immunization Survey-Child, Hill et al demonstrated that 1.3% of all children born in the US in 2015 had no immunizations at 24 months of age. The same report stated that, among US children 19-35 months of age, 70.7% were UTD for the combined 7-vaccine series.¹³ Among children with Down syndrome, we found 7% vaccine refusal and 58% UTD rate for the combined 7-vaccine series at 19 months of age. (The National Immunization Survey-Child does not include hepatitis A vaccine, although we had included hepatitis A vaccine in our study.)

Timely immunization is critical for children with Down syndrome because they are at increased risk of lower respiratory tract infections, are hospitalized more frequently owing to infectious diseases, and have a higher mortality rate owing to respiratory tract infections and sepsis than typical

children.^{7,14,15} In particular, children with Down syndrome have been reported to have higher complication rates, including death owing to some vaccine-preventable diseases such as varicella.^{16,17} Much of the increased life span experienced by people with Down syndrome in recent decades has been attributed to changes in the care of children with Down syndrome who have congenital heart disease. However, the leading causes of mortality in childhood for individuals with Down syndrome include congenital heart disease and respiratory disorders, specifically respiratory infections and pneumonia.¹⁸ In the future, more attention should focus on the causes of respiratory infection, some of which may represent vaccine-preventable diseases.

Limitations of our study include a modest rate of response to the survey, thus introducing the risk of response bias. Parents of children with Down syndrome who have strong opinions about vaccination may have been more likely to respond to our survey, thus introducing response bias, but the lower level of UTD status at 19 months in our Down syndrome sample is substantially different than that reported in the general population. Immunization records were obtained from the child's primary care physician(s). In some cases, immunization records may have been incomplete if the child received immunizations in >1 setting and not all sources of immunization were identified. The sample is small and from 1 geographic area, so the results may not be generalizable. In addition, the sample included English-speaking, mostly white, well-educated, middle class, older parents whose attitudes may differ from those of other parents. Furthermore, parents were asked to recall decisions that they made as many as 8 years earlier, so their responses may reflect current attitudes and understanding rather than those at the time the child received immunizations.

Although increasing attention has been focused on adherence to specific guidelines for health supervision for Down syndrome, completion of the recommended vaccination schedule for children with Down syndrome should receive special emphasis.¹⁹ Addressing the factors contributing to vaccine hesitancy and improving vaccination coverage among children with Down syndrome may contribute to increased life expectancy and decreased hospitalization rates owing to infectious illnesses. ■

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Table II. PACV survey responses (n = 55)

Questions	Response	Percent
1. Have you ever delayed having your child get a shot for reasons other than illness or allergy?	Yes	25
	No	73
	Don't know	2
2. Have you ever decided not to have your child get a shot for reasons other than illness or allergy?	Yes	18
	No	82
3. If you had another infant today would you want him/her to get all the recommended shots?	Yes	75
	No	15
	Don't know	10
4. Children get more shots than are good for them.	Agree	17
	Disagree	44
	Not sure	39
5. I believe that many of the illnesses shots prevent are severe.	Agree	87
	Disagree	4
	Not sure	9
6. It is better for my child to develop immunity by getting sick than to get a shot.	Agree	9
	Disagree	64
	Not sure	27
7. It is better for children to get fewer vaccines at the same time.	Agree	53
	Disagree	11
	Not sure	36
8. How concerned are you that your child might have a serious side effect from a shot?	Concerned	42
	Not concerned	51
	Not sure	7
9. How concerned are you that any one of the childhood shots might not be safe?	Concerned	35
	Not Concerned	54
	Not Sure	11
10. How concerned are you that a shot might not prevent the disease?	Concerned	22
	Not concerned	65
	Not sure	13
11. Overall, how hesitant about childhood shots would you consider yourself to be?	Hesitant	18
	Not hesitant	73
	Not sure	9
12. I trust the information I receive about shots.	Agree	78
	Disagree	9
	Not Sure	13
13. I am able to openly discuss my concerns about shots with my child's doctor.	Agree	93
	Disagree	5
	Not sure	2
The following questions use a Likert scale		
14. All things considered, how much do you trust your child's doctor? [0 (= do not trust at all) to 10 (= completely trust)]	≤5	2
	6 or 7	7
	≥8	91
15. How sure are you that following the recommended shot schedule is a good idea for your child? [0 (= not at all sure) to 10 (= completely sure)]	≤5	24
	6 or 7	7
	≥8	69

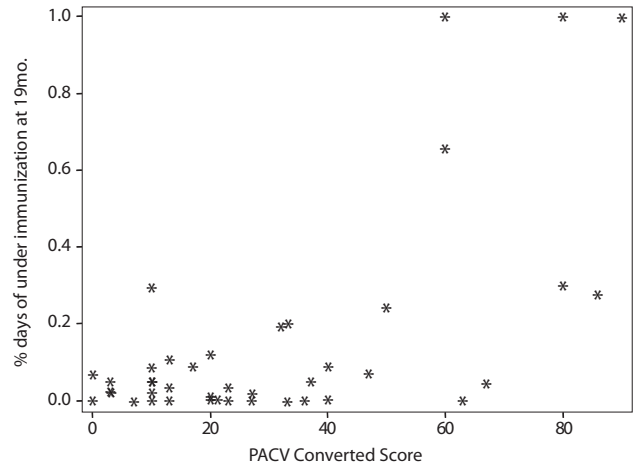


Figure 1. Correlation between individual converted PACV scores and days of under immunization at 19 months in children with Down syndrome.

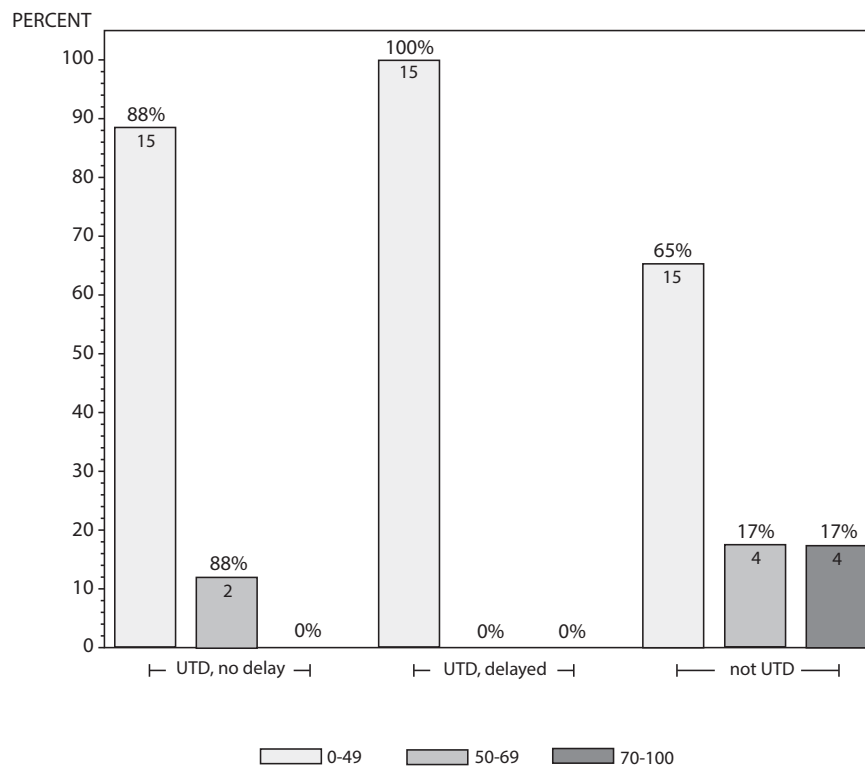


Figure 2. PACV converted score categories by UTD categories at 19 months in children with Down syndrome.