

RESEARCH PAPER



Vaccine hesitancy and influenza beliefs among parents of children requiring a second dose of influenza vaccine in a season: An American Academy of Pediatrics (AAP) Pediatric Research in Office Settings (PROS) study

Ekaterina Nekrasova^a, Melissa S. Stockwell^b, Russell Localio^c, Justine Shults^c, Chelsea Wynn^d, Laura P. Shone^e, Lindsay Berrigan^a, Chelsea Kolff^b, Miranda Griffith^e, Andrew Johnson^a, Alessandra Torres^e, Douglas J. Opel^f, and Alexander G. Fiks^a

^aDepartment of Pediatrics, Center for Pediatric Clinical Effectiveness & PolicyLab, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; ^bDepartment of Pediatrics, Department of Population and Family Health, Columbia University, New York, NY, USA; ^cDepartment of Biostatistics, Epidemiology & Informatics, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA; ^dDepartment of Pediatrics, Columbia University, New York, NY, USA; ^eDepartment of Research, American Academy of Pediatrics, Itasca, IL, USA; ^fUniversity of Washington School of Medicine and Center for Clinical and Translational Research, Seattle Children's Research Institute, Seattle, WA, USA

ABSTRACT

To receive adequate protection against influenza, some children 6 months through 8 y old need two doses of influenza vaccine in a given season. Currently, only half of those receiving the first dose receive a second. Our objective was to assess vaccine hesitancy and influenza disease and vaccine knowledge, attitudes, and beliefs among caregivers of children who received the first of their two needed doses. As part of a national-randomized control trial of second dose text-message influenza vaccine reminders (2017–2018 season), a telephone survey collected caregiver and index child demographic information. Each child had received the first of two needed influenza vaccine doses. Caregivers completed a measure of general vaccine hesitancy – the five-question Parent Attitudes About Childhood Vaccines Survey Tool (PACV-5) – and questions about influenza infection and vaccine. We assessed associations between participant demographic characteristics, vaccine hesitancy, and influenza beliefs and calculated the standardized proportion of caregivers endorsing each outcome using logistic regression. Analyses included responses from 256 participants from 36 primary care practices in 24 states. Some caregivers (11.7%) reported moderate/high vaccine hesitancy and many had misperceptions about influenza disease and vaccine. In multivariable models, no single variable was consistently associated with inaccurate knowledge, attitudes, and beliefs. These results demonstrate that caregivers whose children received the first dose of influenza vaccine may still be vaccine hesitant and have inaccurate influenza beliefs. Pediatricians should consider broadly addressing inaccurate beliefs and promoting vaccination even after caregivers agree to the first dose.

ARTICLE HISTORY

Received 19 September 2019
Revised 10 December 2019
Accepted 14 December 2019

KEYWORDS

Influenza; influenza vaccine; vaccine hesitancy; primary care; childhood vaccination; parent attitudes

Introduction

Influenza infection in the United States annually results in high morbidity, mortality, and cost burden from direct medical expenses and days lost from work and school.^{1–3} The 2017–2018 influenza season alone accounted for estimated 48.8 million symptomatic illnesses, 959,000 hospitalizations, and 79,400 deaths.⁴

Young children are at higher risk for hospitalization and severe influenza complications including pneumonia and neurological outcomes like seizures and encephalopathy.^{5–11} They are also a source of transmission to other household members.^{5–12} The influenza vaccine can protect against influenza infection and significantly reduce the risk of influenza-associated hospitalizations and deaths in children.^{12–14} Children of 6 months through 8 y old, who were never vaccinated against influenza before or who have previously received only one dose of the influenza vaccine, need two doses in a season, given at least 4 weeks apart, to receive

adequate protection.^{7,15–20} Only 40 to 60% of those who receive the first dose get their second needed dose.^{21–23} According to the Center for Disease Control and Prevention, less than half of children 6 months through 8 y old who needed two doses during the 2017–2018 influenza season received both (6 to 23 months old: 47.2%, 2 to 4 years old: 37.8%, and 5 to 8 years old: 33.5%).^{15,24}

Caregiver vaccine hesitancy can contribute to childhood influenza vaccine refusal, delayed vaccination, or missed vaccine doses.^{25–29} Limited information and misperceptions about influenza severity among caregivers can also negatively affect their confidence in childhood vaccine safety and reduce influenza vaccine uptake.^{28,30} However, prior research has not examined caregiver vaccine hesitancy and influenza knowledge after caregivers have agreed to the first of the two required influenza vaccine doses. It is important to examine this question because many children do not receive two

needed doses which put them at risk of potentially life-threatening influenza disease.²¹⁻²³ We aim to close this knowledge gap and also investigate whether, in this subset of caregivers, child and caregiver demographic characteristics are associated with caregiver vaccine hesitancy and influenza disease and vaccine knowledge, attitudes, and beliefs.

Methods

Study design, setting, and population

As part of a National Institutes of Health (NIH) funded randomized controlled trial of text-message vaccine reminders for the second dose of influenza vaccine, “Flu2Text,” (2017–2018 season), caregiver-child dyads were recruited from 36 primary care practices across 24 states. All sites belong to the American Academy of Pediatrics (AAP) Pediatric Research in Office Settings (PROS) primary care research network. All enrolled caregivers had a child 6 months through 8 y old who received the first dose of the influenza vaccine and needed a second dose, spoke English or Spanish, and had a cell phone with a text messaging plan. At enrollment, a questionnaire was verbally administered over the phone. Institutional Review Boards of the Children’s Hospital of Philadelphia (CHOP), Columbia University, and the AAP approved this study.

Measures and analyses: vaccine hesitancy

Caregivers completed the PACV-5, a 5-item version of the validated 15-item Parent Attitudes About Childhood Vaccines Survey Tool.^{26,31,32} The PACV-5 has been used in prior studies.^{31,32} The PACV-5 includes the following items: (1) “I trust the information I receive about shots”; (2) “It is better for my child to develop immunity by getting sick than to get a shot”; (3) “It is better for children to get fewer shots at the same time”; (4) “Children get more shots than are good for them”; (5) “Overall, how hesitant about childhood shots would you consider yourself to be?” Participants responded to PACV-5 items on a 5-point Likert scale.³² Consistent with previous studies, we assigned a numeric score of 0–2 to each item, with non-hesitant responses receiving a score of 0, responses of “not sure” and “I don’t know” receiving a score of 1, and hesitant responses receiving a score of 2 (Table 2).^{31,33} Responses from the five items were then summed with scores ranging from 0 (non-hesitant) to 10 (most hesitant) per person.³¹ We categorized PACV-5 total scores corresponding to levels of hesitancy as low (0–4), moderate (5–6), and high (7–10). For logistic regression analyses, we collapsed moderate and high vaccine hesitancy groups into one category.³²

Influenza disease and vaccine beliefs

Caregivers also responded to four items that captured their knowledge, attitudes, and beliefs about influenza infection and vaccine, measured with a 5-point Likert scale. Items and response categories are shown in Table 3. We dichotomized responses to these items into accurate and inaccurate beliefs. For the question “How well do you think your child will be protected if he/she only gets one flu shot this season?”, responses “very unprotected,” “somewhat unprotected,” and “somewhat protected” were considered accurate, as only two doses provided adequate protection for this cohort.^{15,16,19} Responses “very protected” and “don’t

know” were coded as inaccurate beliefs.^{15,16,19} Parents were also asked their level of agreement with the following statements: “Children can die from the flu,” “The flu is just a bad cold,” and “The flu shot can cause the flu.” The item “children can die from the flu,” was reverse coded as “children cannot die from the flu” for analyses in order to match the coding for other inaccurate beliefs. After re-coding, and for all the remaining questions, the only response considered accurate was “strongly disagree”. All other responses (strongly agree, somewhat agree, somewhat disagree, don’t know) were coded as inaccurate beliefs.

Demographic variables

Demographic information was self-reported by caregivers (age, English proficiency, highest level of education, and relationship to a child) and children (age, gender, ethnicity, race, health insurance/coverage status, and caregiver-reported child health status). Table 1 details how each variable was captured in caregiver surveys.

Statistical analyses

We performed a series of separate multivariable logistic regression models to calculate standardized (adjusted) proportions and risk differences of covariates associated with high/moderate vaccine hesitancy and the four inaccurate influenza disease and vaccine beliefs. All demographic variables were included as they were *a priori* identified as having a potential impact on the outcomes.

Table 1. Participant demographic characteristics.

	% ^a (N = 257)
Caregiver English Proficiency	
Excellent English	91.8 (236)
Less Than Excellent	8.2 (21)
Caregiver Education	
High School or Less	23.7 (61)
Some College or Above	76.3 (196)
Caregiver Age	
<30 years old	32.3 (83)
30-39	59.9 (154)
40+	7.8 (20)
Relationship to the Child	
Mother	84.1 (216)
Other	16.0 (41)
Child Age	
6–23 months	91.8 (236)
2–8 years	8.2 (21)
Child Gender	
Male	52.1 (134)
Female	47.9 (123)
Child Insurance Type	
Public Insurance/No Insurance ^b	30.4 (78)
Commercial ^c	69.7 (179)
Child Race	
White	70.0 (180)
Black	18.3 (47)
Asian	7.0 (18)
Other	4.7 (12)
Child Ethnicity	
Hispanic/Latino/Spanish	16.0 (41)
Non-Hispanic/Latino/Spanish	84.1 (216)
Child Health	
Excellent	79.8 (205)
Less Than Excellent	20.2 (52)

^aAll percentages were rounded up. Due to rounding, the total percentages may not equal 100%.

^b3 participants had no insurance and were categorized into Public Insurance/No Insurance.

^c3 participants had Tricare insurance and were categorized into Commercial.

Table 2. Response distribution and score assignment (0–2) to a measure of caregiver vaccine hesitancy: PACV-5 survey tool.

PACV-5 Survey Items	PACV-5 Responses % (n) ^a (total N=256)				
	Strongly Agree (Score 0)	Somewhat Agree (Score 0)	Not Sure/I don't Know (Score 1)	Somewhat Disagree (Score 2)	Strongly Disagree (Score 2)
1. I trust the information I receive about shots	70.7% (181)	23.8% (61)	4.7% (12)	0.39% (1)	0.39% (1)
2. It is better for my child to develop immunity by getting sick than to get a shot	3.1% (8)	5.5% (14)	14.1% (36)	33.2% (85)	44.1% (113)
3. It is better for children to get fewer shots at the same time	10.2% (26)	25.4% (65)	27.7% (71)	25.4% (65)	11.3% (29)
4. Children get more shots than are good for them	9.4% (24)	17.6% (45)	11.3% (29)	34.8% (89)	27% (69)
5. Overall, how hesitant about childhood shots would you consider yourself to be?	58.6% (150)	27.3% (70)	4.7% (12)	7.4% (19)	2% (5)

^aDue to rounding, the total percentages may not equal 100%.

Among 257 enrolled participants, only one was excluded from multivariable logistic regression analyses due to missing data, leaving a final sample of 256 participants. All statistical analyses were conducted using Stata 15.1 (StataCorp, College Station, TX, 2018).

To arrive at adjusted estimates of the association of variable level (e.g., male sex) and outcome on the probability rather than the odds scale, we implemented marginal standardization (“margins” commands in Stata).³⁴ We then estimated differences in response probabilities by variable levels. Owing to the sparse nature of the data (small cells counts), we estimated 95% confidence intervals using the percentile approach to bootstrap resampling. This method of estimating confidence bounds permitted the use of logistic regression to express effect estimates and their uncertainty on the probability (or absolute percent) scale. This bootstrap resampling process accounted for the clustering of responses by practice site. Our reporting conventions follow the guidelines announced by the American Statistical Associations.³⁵

Results

Caregiver and child demographic characteristics

Of the full sample of 257 caregivers, all (100%) completed a telephone demographic survey. The majority of participants were 30 to 39 years old (59.9%), completed at least some college (76.3%), were of excellent English proficiency (91.8%), and were mothers of the index child (84.1%) (Table 1). Most children were 6 to 23 months old (91.8%), White (70%), of non-Hispanic, Latino or Spanish origin (84.1%), covered by commercial insurance (69.7%), and were reported to be in excellent health (79.8%).

Caregiver vaccine hesitancy

Although they had already agreed for their child to receive the first dose of influenza vaccine, according to the PACV-5 8.2% (N = 21) of caregivers reported moderate vaccine hesitancy (general, not specific to influenza vaccine) and 3.5% (N = 9) had high general

Table 3. Caregiver knowledge, attitudes, and beliefs about influenza disease and vaccine.

Survey Items	Knowledge, Attitudes and Beliefs Responses % (n) ^a (total N=256)					
	Inaccurate			Accurate		
	Very Protected	Don't Know	Total (all 2 categories combined)	Somewhat Protected	Somewhat Unprotected	Very Unprotected
How well do you think your child will be protected if he/she only gets one flu shot this season?	12.1% (31)	3.1% (8)	15.2% (39)	48.8% (125)	29.7% (76)	6.3% (16)
	Strongly Agree	Somewhat Agree	Somewhat Disagree	Don't Know	Total (all 4 categories combined)	Accurate Strongly Disagree
The flu shot can cause the flu	4.3% (11)	24.6% (63)	26.6% (68)	1.6% (4)	57.0% (146)	43% (110)
The flu is just a bad cold.	7% (18)	12.1% (31)	20.3% (52)	0.8% (2)	40.2% (103)	59.8% (153)
Children cannot die from the flu ^b	5.5% (14)	5.5% (14)	19.9% (51)	1.2% (3)	32.0% (82)	68% (174)

^aAll percentages were rounded up. Due to rounding, the total percentages may not equal 100%.

^bThe original statement was “Children can die from the flu.” It was reversely coded to “children cannot die from the flu” to match other inaccurate beliefs. After recoding, the only response considered accurate was “strongly disagree”. All other responses (strongly agree, somewhat agree, somewhat disagree, & don't know) were summarized under inaccurate beliefs.

Table 4. Caregiver vaccine hesitancy: PACV-5 score distribution and categorization.

PACV-5 Score	Responses % (n) ^a (total N=256)	PACV-5 Vaccine Hesitancy Category	PACV-5 Vaccine Hesitancy Category Combined
0	22.7% (58)		
1	16.8% (43)		
2	22.7% (58)	Low: 88.3% (226)	Low: 88.3% (226)
3	14.5% (37)		
4	11.7% (30)		
5	3.5% (9)	Moderate: 8.2% (21)	
6	4.7% (12)		
7	1.6% (4)	High: 3.5% (9)	Moderate/High: 11.7% (30)
8	1.6% (4)		
9	0.4% (1)		
10	0		

^aDue to rounding, the total percentages may not equal 100%.

vaccine hesitancy (Table 4). In a multivariable model, caregiver lower English proficiency was an important predictor of moderate/high vaccine hesitancy (lower English proficiency-standardized risk difference = 19.0% points, 95% confidence interval = 5.5% to 48.3) (Table 5). Nearly a third (28.5%) of caregivers with limited English proficiency were vaccine hesitant compared to 9.6% of those who reported themselves to be fluent speakers.

Caregiver beliefs about influenza disease and vaccine

A high proportion of caregivers reported the following beliefs about influenza disease and vaccination (Table 3): “the flu shot can cause the flu” (57.0%); “the flu is just a bad cold” (40.2%); and, children cannot “die from the flu” (32.0%). About 15.2% of caregivers did not know their child will not be very well protected with “only one flu shot this season” (Table 3). In multivariable models, although certain child and caregiver demographic characteristics had an association with general vaccine hesitancy and inaccurate knowledge, attitudes, or beliefs about influenza disease and vaccine, no single variable was consistently associated with these outcomes (Table 5).

Discussion

In this study, we found that approximately 1 in 10 parents who agreed to the first dose of influenza vaccine for their child had moderate to high general vaccine hesitancy. Vaccine hesitancy has been documented as a barrier to complete childhood vaccination and may represent a serious public health threat.³⁶⁻³⁸ It is important to note that even if caregivers are not hesitant per the PACV-5 results, they may still express hesitancy about influenza vaccines, as this tool was not adapted specifically for influenza vaccines. In addition, even after agreeing to vaccinate their child with the first dose of influenza vaccine, many parents still reported inaccurate knowledge, attitudes, or beliefs about influenza vaccination and infection. Although knowledge, attitudes, and beliefs are likely important, other factors such as convenience (time and ability to schedule a follow-up appointment) may also influence a caregiver’s decision to ultimately receive the second influenza vaccine dose.

While there is an increasing number of studies on influenza vaccine attitudes, knowledge, and beliefs among the general public, parents of children 6 to 59 months are not as well studied.³⁸ We also lack studies that examine caregiver beliefs

after the receipt of the first of two required doses of influenza vaccine. The study cohort is distinct in that caregivers have already accepted the influenza vaccine; thus, the findings should be considered in this context. One of the concerning findings of our study was that 12.1% of the caregivers enrolled in a study of text-message reminders for the second dose of influenza vaccine thought their child will be “very protected” with “only one flu shot” this season and 3.1% did not know the answer to this question. These results underscore the importance of explaining the need to return for the second influenza dose to all families.

Several previous studies provide context for our results. In an Italian study that used the 15-item PACV, 7.7% of parents of kindergartners aged 1 to 5 y were vaccine hesitant.³⁹ Another non-U.S.-based study used the 15-item PACV among multi-ethnic Malaysian parents and found 11.6% of parents were vaccine hesitant. These findings are consistent with the level of caregiver vaccine hesitancy found in our population (11.7%). Similar general vaccine hesitancy levels (8.9%) were found among caregivers of infants who are 2 weeks old in a private urban pediatric office in Tennessee,⁴⁰ and in a study of primarily Latino patients, the PACV-5 indicated that 14.5% of respondents had moderate to high hesitancy.³²

Determinants of vaccine hesitancy have been previously examined, including psychological, physical, contextual, and sociodemographic; however, the results were mixed.^{38,39,41,42} We focused on sociodemographic characteristics, and although the number of participants with lower English proficiency was small, we found that caregiver limited English proficiency was associated with moderate/high vaccine hesitancy. Caregiver limited English proficiency may represent larger issues of language barriers or low health literacy impeding understanding of vaccine-related information.⁴³⁻⁴⁵

Despite increased public health efforts to promote accurate information about vaccination, myths about influenza disease and vaccine among caregivers remain common.⁴⁶⁻⁵³ While prior research focused on influenza knowledge in targeted populations, such as caregivers of children with chronic conditions, little is known about caregiver knowledge, attitudes, and beliefs about influenza disease and influenza vaccine after the receipt of the first of the two required influenza vaccine doses in a season.^{49,50} Perceptions about the severity of influenza disease can influence the intent to vaccinate.^{51,53} In our study, a third of caregivers believed that children “cannot die from the flu,” and almost half thought that “the flu is just a bad cold,” suggesting that not all caregivers were aware of the seriousness of influenza infection. In a study of caregivers of children 6 to 23 months, 7.2% of caregivers reported “flu is not serious” as the primary driver of the decision not to have their child receive the influenza vaccine.⁴⁶ This number may be lower than what was found in our study since it reflected the proportion of parents for whom that was their primary concern – not one of the several concerns as in our study.

Prior studies have also examined the question of whether caregivers believe that influenza vaccine causes disease. In a study of English-speaking caregivers of children 6 to 23 months, 49% of participants believed that the vaccine could cause influenza disease and for 20% it was the primary concern for influenza vaccination.⁴⁶ Fitch & Racine have examined the belief that the influenza vaccine could itself make a child sick in a racially diverse group of inner-city caregivers

Table 5. No one variable was consistently associated with vaccine hesitancy and inaccurate influenza disease and vaccine knowledge, attitudes and beliefs.^a

Caregiver and Child Characteristics	PACV-5 Score (N=256)									
	Moderate or High Vaccine Hesitancy (5-10)		Your Child is Protected with "Only 1 Flu Shot"		"Flu Shot Can Cause the Flu"		"Flu is Just a Bad Cold"		Children Cannot "Die from the Flu"	
	%	Risk Difference (95% CI)	%	Risk Difference (95% CI)	%	Risk Difference (95% CI)	%	Risk Difference (95% CI)	%	Risk Difference (95% CI)
Caregiver English Proficiency										
Excellent English	9.6	Ref	12.2	Ref	56.8	Ref	36.7	Ref	30.5	Ref
Less Than Excellent	28.5	19.0% (5.5, 48.3) ^b	43.2	31.0% (9.5, 66.2) ^b	61.4	4.7% (-24.1, 28.2)	92.2	55.5% (18.5, 62.7) ^b	50.9	20.4% (-7.2, 37.5)
Caregiver Education										
Some College or Above	9.7	Ref	12.5	Ref	54.4	Ref	35.7	Ref	27.7	Ref
High School or Less	15.9	6.2% (-2.6, 18.8)	20.9	8.4% (-2.6, 24.7)	67.7	13.3% (-2.9, 31.0)	56.7	21.0% (0.9, 38.5) ^b	45.5	17.8% (1.5, 38.3) ^b
Relationship to a Child										
Mother	11.4	Ref	14.3	Ref	58.2	Ref	42.9	Ref	31.7	Ref
Other	13.2	1.8% (-12.8, 13.3)	20.8	6.5% (-9.5, 20.4)	51.1	-7.1% (-31.4, 12.7)	26.6	-16.3% (-28.1, -4.4) ^b	33.6	1.9% (-13.5, 15.9)
Caregiver Age										
<30 years old	12.5	Ref	18.3	Ref	58.1	Ref	41.9	Ref	33.0	Ref
30-39	9.6	-2.9% (-9.8, 6.1)	12.1	-6.1% (-14.4, 0.8)	57.0	-1.1% (-10.0, 9.7)	37.0	-4.9% (-18.3, 10.2)	28.7	-4.4% (-18.6, 15.5)
40+	21.5	8.9% (-6.3, 30.6)	20.1	1.8% (-11.0, 16.8)	53.4	-4.7% (-28.6, 20.8)	59.8	17.9% (0.3, 38.9) ^b	54.6	21.5% (7.9, 46.9) ^b
Child Insurance Type										
Commercial	11.0	Ref	12.9	Ref	51.8	Ref	40.6	Ref	32.5	Ref
Public Insurance/No Insurance	12.6	1.6% (-10.2, 17.0)	18.2	5.3% (-7.6, 18.1)	70.7	18.9% (3.3, 33.3) ^b	39.4	-1.2% (-13.0, 12.2)	31.2	-1.3% (-17.1, 11.9)
Child Race										
White	10.5	Ref	13.1	Ref	56.7	Ref	40.2	Ref	29.6	Ref
Black	13.1	2.6% (-3.4, 16.3)	20.5	7.4% (-4.8, 20.8)	54.2	-2.5% (-19.4, 13.1)	44.3	4.1% (-11.6, 17.7)	39.2	9.5% (-7.4, 24.4)
Asian	14.8	4.3% (-3.9, 32.8)	14.5	1.4% (-10.7, 33.6)	76.9	20.2% (-10.5, 37.1)	35.3	-4.9% (-28.0, 30.8)	58.2	28.6% (4.1, 44.0) ^b
Other	15.0	4.5% (-5.7, 39.9)	19.3	6.2% (-5.0, 42.2)	35.2	-21.5% (-41.3, -0.9) ^b	27.0	-13.3% (-29.2, 17.6)	12.6	-17.0% (-25.1, -1.2) ^b
Child Gender										
Female	12.3	Ref	19.1	Ref	59.1	Ref	46.2	Ref	31.8	Ref
Male	11.2	-1.2% (-10.2, 8.9)	11.6	-7.5% (-16.0, -0.7) ^b	55.0	-4.1% (-16.3, 8.6)	34.7	-11.5% (-21.7, -1.5) ^b	32.2	0.4% (-10.7, 11.9)
Child Ethnicity										
Non-Hispanic/Latino/Spanish	10.3	Ref	13.9	Ref	53.8	Ref	38.5	Ref	30.2	Ref
Hispanic/Latino/Spanish	16.3	6.0% (-9.3, 31.9)	19.8	5.9% (-9.2, 23.9)	76.3	22.5% (0.8, 42.5) ^b	51.0	12.5% (-6.4, 36.2)	41.3	11.1% (-5.5, 30.9)

^aStandardized proportions of demographic characteristics that showed associations in at least one study outcome model are shown. All models were adjusted for child age and child health. ^b95% confidence intervals do not cross zero.

and found that 48% of the participants thought it was true.⁴⁷ In our sample, the belief “influenza vaccine can cause influenza” was similarly common, even in a population that had accepted the first of the two vaccine doses for the season. In our study, no demographic variable was consistently associated with inaccurate knowledge, attitudes, and beliefs about influenza vaccine and disease. Other studies had similar findings and came to the conclusion that erroneous beliefs should be addressed for all families, regardless of specific caregiver and child sociodemographic characteristics.^{46,47}

Given that general vaccine hesitancy and inaccurate beliefs about influenza persist even in the cohort of caregivers that already accepted the first dose of influenza vaccination, mitigation strategies are warranted. A systematic review of strategies to address vaccine hesitancy revealed that there is no single intervention strategy that would best combat vaccine hesitancy.^{54,55} Rather, multicomponent interventions tailored to a specific population and reasons for vaccine hesitancy are most effective.^{54,55} Pediatricians and other health-care professionals are among the most trusted sources of health-care information for parents, affording them opportunities to address vaccine hesitancy early and often and to provide accurate information about the influenza vaccine.^{51,56,57} In our cohort, caregivers accepted the first dose of the influenza vaccine despite having a high prevalence of misperceptions about influenza. This suggested that caregiver trust may outweigh other factors in acceptance of the first dose of influenza vaccine. Decision-drivers for accepting the first dose of influenza vaccine in the presence of vaccine hesitancy and inaccurate beliefs should be examined in future studies. Future analyses from the original study may also provide insights on the impact of hesitancy and beliefs on actual receipt of the second influenza vaccine dose. Additionally, specific provider-parent communication strategies need to be further investigated. Nyhan & Reifler found that while correcting a myth that “flu vaccine can cause flu” reduced the belief in this myth, it also reduced vaccination intent among those with higher levels of vaccine hesitancy.⁵⁸ A pediatric clinical study in New York City among parents of children 6 months and older found that providing educational handouts about the influenza vaccine and disease in the waiting room before the visit increased child influenza vaccine receipt by the end of the season.³² Other studies, focused on patient-provider communication strategies, suggest that starting parental vaccine education early on, building trust, and addressing questions about vaccines with scientific facts and personal stories can reduce vaccine hesitancy.^{32,46,57}

Limitations

This was a cross-sectional study with a modest sample size, so all associations should be interpreted with caution and be confirmed by larger cohort studies. This study included only caregivers who already accepted the first of the two needed doses of influenza vaccine for their children, potentially not capturing the most vaccine-hesitant caregivers. We measured general vaccine hesitancy but did not measure hesitancy

specific to influenza vaccine. We also did not ask caregivers about potential motivators for influenza vaccination. All survey items, including those addressing demographics, vaccine hesitancy, and influenza knowledge, attitudes, and beliefs were self-reported by study participants. The convenience sample of participants was collected from a diverse group of primary care pediatric practices from around the US, but we are unable to assess the representativeness of their responses compared to the larger U.S. population. Caregiver participation was voluntary and all practices self-selected to participate in a larger trial of text-message reminders for the second dose of influenza vaccine. Parents who refused an initial dose or did not participate in the study are not represented. Additionally, all caregivers were identified as eligible during their child’s health supervision visit, and those with barriers to scheduling/attending an appointment were not included in this study.

Conclusions

Even caregivers whose children receive the first dose of influenza vaccine may be vaccine hesitant and have misperceptions about influenza vaccine and disease. Since no single variable was consistently associated with influenza disease and vaccine knowledge, attitudes, and beliefs across all outcomes, pediatricians and other health-care professionals may benefit from the awareness that hesitancy can persist even after caregivers agree to the first dose. It also may be helpful to broadly address misperceptions and promote vaccination regardless of previous doses. Future studies should examine interventions that can help mitigate caregiver vaccine hesitancy and inaccurate influenza beliefs even after caregivers agree to the first dose.

Acknowledgments

The authors thank all Flu2Text practices (see list of below), pediatricians, nurse practitioners, other physicians, staff, parents, and families who participated in our study, and the University of South Carolina Institute for Public Service and Policy Research, Survey Research Lab. This work was supported by the National Institutes of Health (NIH) National Institute of Child Health and Health Development (NICHD) grant number R01HD086045 (PI: Stockwell, Fiks). Additional infrastructure funding was provided by the American Academy of Pediatrics and the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under UA6MC15585 – National Research Network to Improve Children’s Health. The information, content and/or conclusions are those of the author(s) and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government. Flu2Text practices participating in this study, who agreed to be acknowledged included ABC Pediatrics, PC; Advanced Pediatrics, PC; All Pediatrics, PC; Altru Health System; Anaconda Pediatrics; Anchorage Pediatric Group; Ashley Clinic; A to Z Pediatrics, PLLC; Bethesda Pediatrics; Building Blocks Pediatrics; Burlington Pediatrics; Cambridge Pediatrics; Child Health Partners, PC; Childhood Health Associates of Salem; Elmwood Pediatric Group, LLP; Fishing Bay Family Practice; Goshen – Columbus Pediatrics & Adolescent Care; Hirsch Pediatrics, LLC; Ivancic Pediatric Clinic, PA; Mesa Pediatrics; One Hanson Place Pediatrics, PC; OHSU Doernbecher Pediatrics – Westside Clinic; Pediatric Associates of Davidson County, PA; Pediatric Associates of Medford; Pediatrics by the Sea; Pennridge Pediatric Associates; Prattville Pediatrics; Priority Care Pediatrics; Purohit Pediatric Clinic; Quality Kids Kare, PC; Scarano & Taylor Pediatrics; Southeastern Pediatric Associates; Springfield Pediatrics;

Sunset Park Family Health Center at NYU Langone; The Child & Teen Wellness Center; Zaheer Pediatrics & Associates, SC; Zimble & Reinstein Pediatrics.

Disclosure of potential conflicts of interest

Dr. Fiks reported receiving an independent research grant from Pfizer for work unrelated to this project and unrelated to vaccination. He also received grants from the National Institutes of Health; grants and personal fees from the Patient-Centered Outcomes Research Institute and the Academic Pediatric Association; personal fees from the American Academy of Pediatrics, Boston Medical Center, Children's Specialized Hospital, Columbia University, PRIME, and Washington University; and conference travel support from Children and Screens outside the submitted work. Additionally, Dr. Stockwell was an unremunerated coinvestigator for an unrelated, investigator-initiated grant from the Pfizer Medical Education Group. No other disclosures were reported.

Funding

This work was supported by the American Academy of Pediatrics and the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) [UA6MC15585]; National Institutes of Health (NIH) National Institute of Child Health and Health Development (NICHD) [R01HD086045].

References

- Centers for Disease Control and Prevention (CDC). Estimates of deaths associated with seasonal influenza — United States, 1976–2007. *MMWR Morb Mortal Wkly Rep.* 2010;59(33):1057–62.
- Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, Fukuda K. Influenza-Associated Hospitalizations in the United States. *JAMA.* 2004;292(11):1333–40. doi:10.1001/jama.292.11.1333
- Molinari N-AM, Ortega-Sanchez IR, Messonnier ML, Thompson WW, Wortley PM, Weintraub E, Bridges CB. The annual impact of seasonal influenza in the US: measuring disease burden and costs. *Vaccine.* 2007;25(27):5086–96. doi:10.1016/j.vaccine.2007.03.046.
- Estimated influenza illnesses, medical visits, hospitalizations, and deaths in the United States — 2017–2018 influenza season | CDC. 2019 Mar 26 [accessed 2019 May 13]. <https://www.cdc.gov/flu/about/burden/2017-2018.htm>.
- Louie JK, Schechter R, Honarmand S, Guevara HF, Shoemaker TR, Madrigal NY, Woodfill CJI, Backer HD, Glaser CA. Severe pediatric influenza in California, 2003–2005: implications for immunization recommendations. *Pediatrics.* 2006;117(4):e610–618. doi:10.1542/peds.2005-1373.
- Neuzil KM, Zhu Y, Griffin MR, Edwards KM, Thompson JM, Tollefson SJ, Wright PF. Burden of inter-pandemic influenza in children younger than 5 years: a 25-year prospective study. *J Infect Dis.* 2002;185(2):147–52. doi:10.1086/338363.
- Neuzil KM, Mellen BG, Wright PF, Mitchel EF, Griffin MR. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *N Engl J Med.* 2000;342(4):225–31. doi:10.1056/NEJM200001273420401.
- Jules A, Grijalva CG, Zhu Y, Talbot HK, Williams JV, Poehling KA, Chaves SS, Edwards KM, Schaffner W, Shay DK, et al. Influenza-related hospitalization and ED visits in children less than 5 years: 2000–2011. *Pediatrics.* 2015;135(1):e66–74. doi:10.1542/peds.2014-1168..
- Zhou H, Thompson WW, Viboud CG, Ringholz CM, Cheng P-Y, Steiner C, Abedi GR, Anderson LJ, Brammer L, Shay DK. Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993–2008. *Clin Infect Dis.* 2012;54(10):1427–36. doi:10.1093/cid/cis211.
- Newland JG, Laurich VM, Rosenquist AW, Heydon K, Licht DJ, Keren R, Zaoutis TE, Watson B, Hodinka RL, Coffin SE. Neurologic complications in children hospitalized with influenza: characteristics, incidence, and risk factors. *J Pediatr.* 2007;150(3):306–10.
- Mistry RD, Fischer JB, Prasad PA, Coffin SE, Alpern ER. Severe complications in influenza-like illnesses. *Pediatrics.* 2014;134(3):e684–90.
- CDC. Key facts about seasonal flu vaccine. Centers for Disease Control and Prevention. 2018 Sep 6 [accessed 2019 Jun 21]. <https://www.cdc.gov/flu/prevent/keyfacts.htm>.
- Ferdinandi JM, Olsho LEW, Agan AA, Bhat N, Sullivan RM, Hall M, Mourani PM, Thompson M, Randolph AG. Effectiveness of influenza vaccine against life-threatening RT-PCR-confirmed influenza illness in US children, 2010–2012. *J Infect Dis.* 2014;210(5):674–83. doi:10.1093/infdis/jiu185.
- Flannery B, Reynolds SB, Blanton L, Santibanez TA, O'Halloran A, Lu P-J, Chen J, Foppa IM, Gargiullo P, Bresee J, et al. Influenza vaccine effectiveness against pediatric deaths: 2010–2014. *Pediatrics.* 2017;139(5):e20164244. doi:10.1542/peds.2016-4244.
- Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Bresee JS, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices — United States, 2017–18 influenza season. *MMWR Recomm Rep.* 2017;66(2):1–20. doi:10.15585/mmwr.rr6602a1.
- Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices—United States, 2018–19 influenza season. *MMWR Recomm Rep.* 2018;67(3):1–20. doi:10.15585/mmwr.rr6703a1
- Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines. *MMWR Recomm Rep.* 2016;65(No. RR-5):1–54. doi:10.15585/mmwr.rr6505a1
- Poehling KA, Edwards KM, Griffin MR, Szilagyi PG, Staat MA, Iwane MK, Snively BM, Suerken CK, Hall CB, Weinberg GA et al. The burden of influenza in young children, 2004–2009. *Pediatrics.* 2013;131(2):207–16.
- Neuzil KM, Jackson LA, Nelson J, Klimov A, Cox N, Bridges CB, Dunn J, DeStefano F, Shay D. Immunogenicity and reactogenicity of 1 versus 2 doses of trivalent inactivated influenza vaccine in vaccine-naïve 5–8-year-old children. *J Infect Dis.* 2006;194(8):1032–39. doi:10.1086/jid.2006.194.issue-8.
- Allison MA, Daley MF, Crane LA, Barrow J, Beaty BL, Allred N, Berman S, Kempe A. Influenza vaccine effectiveness in healthy 6- to 21-month-old children during the 2003–2004 season. *J Pediatr.* 2006;149(6):755–762.e1. doi:10.1016/j.jpeds.2006.06.036.
- Hofstetter AM, Natarajan K, Martinez RA, Rabinowitz D, Vawdrey DK, Stockwell MS. Influenza vaccination coverage and timeliness among children requiring two doses, 2004–2009. *Prev Med.* 2013;56(3):165–70. doi:10.1016/j.ypmed.2012.11.018.
- Bhatt P, Block SL, Toback SL, Ambrose CS. A prospective observational study of US in-office pediatric influenza vaccination during the 2007 to 2009 influenza seasons: use and factors associated with increased vaccination rates. *Clin Pediatr (Phila).* 2010;49(10):954. doi:10.1177/0009922810370868.
- Pabst LJ, Chaves SS, Weinbaum C. Trends in compliance with two-dose influenza vaccine recommendations among children aged 6 months through 8 years. *Vaccine.* 2013;31(31):3116–20. doi:10.1016/j.vaccine.2013.04.080.
- Estimates of flu vaccination coverage among children — United States, 2017–18 flu season | fluVaxView | seasonal influenza (Flu) | CDC. 2019 Feb 26 [accessed 2019 May 22]. <https://www.cdc.gov/flu/fluVaxView/coverage-1718estimates-children.htm>.
- Salmon DA, Dudley MZ, Glanz JM, Omer SB. Vaccine hesitancy: causes, consequences, and a call to action. *Am J Prev Med.* 2015;49(6):S391–S398. doi:10.1016/j.amepre.2015.06.009.
- Hofstetter AM, Simon TD, Lepere K, Ranade D, Strelitz B, Englund JA, Opel DJ. Parental vaccine hesitancy and declination of influenza vaccination among hospitalized children. *Hosp Pediatr.* 2018;8(10):628–35. doi:10.1542/hpeds.2018-0025.

27. Quinn SC, Jamison AM, An J, Hancock GR, Freimuth VS. Measuring vaccine hesitancy, confidence, trust and flu vaccine uptake: results of a national survey of White and African American adults. *Vaccine*. 2019;37(9):1168–73. doi:10.1016/j.vaccine.2019.01.033.
28. Gust DA, Kennedy A, Shui I, Smith PJ, Nowak G, Pickering LK. Parent attitudes toward immunizations and healthcare providers the role of information. *Am J Prev Med*. 2005;29(2):105–12. doi:10.1016/j.amepre.2005.04.010.
29. Strelitz B, Gritton J, Klein EJ, Bradford MC, Follmer K, Zerr DM, Englund JA, Opel DJ. Parental vaccine hesitancy and acceptance of seasonal influenza vaccine in the pediatric emergency department. *Vaccine*. 2015;33(15):1802–07. doi:10.1016/j.vaccine.2015.02.034.
30. Smith PJ, Humiston SG, Marcuse EK, Zhao Z, Dorell CG, Howes C, Hibbs B. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the health belief model. *Public Health Rep*. 2011;126(2_suppl):135–46. doi:10.1177/00333549111260S215.
31. Oladejo O, Allen K, Amin A, Frew PM, Bednarczyk RA, Omer SB. Comparative analysis of the Parent Attitudes about Childhood Vaccines (PACV) short scale and the five categories of vaccine acceptance identified by Gust et al. *Vaccine*. 2016;34(41):4964–68. doi:10.1016/j.vaccine.2016.08.046.
32. Scott VP, Opel DJ, Reifler J, Rikin S, Pethe K, Barrett A, Stockwell MS. Office-based educational handout for influenza vaccination: a randomized controlled trial. *Pediatrics*. 2019 Jul 10;144:e20182580. doi:10.1542/peds.2018-2580.
33. Opel DJ, Mangione-Smith R, Taylor JA, Korfiatis C, Wiese C, Catz S, Martin DP. Development of a survey to identify vaccine-hesitant parents. *Hum Vaccin*. 2011;7(4):419–25. doi:10.4161/hv.7.4.14120.
34. Graubard BI, Korn EL. Predictive margins with survey data. *Biometrics*. 1999;55(2):652–59. doi:10.1111/j.0006-341X.1999.00652.x.
35. Moving to a World Beyond “ $p < .05$ ”: The American Statistician: Vol 73, No sup1. [accessed 2019 Jul 31]. doi:10.1080/00031305.2019.1583913.
36. Allan K, Fallon B, Maguire J, Tran D. 2473 How does acquiring a vaccine-preventable disease impact parental and physician responses to vaccine hesitancy? *Open Forum Infect Dis*. 2018;5 (Suppl 1):S741. doi:10.1093/ofid/ofy210.2126.
37. Sadaf A, Richards JL, Glanz J, Salmon DA, Omer SB. A systematic review of interventions for reducing parental vaccine refusal and vaccine hesitancy. *Vaccine*. 2013;31(40):4293–304. doi:10.1016/j.vaccine.2013.07.013.
38. Schmid P, Rauber D, Betsch C, Lidolt G, Denker M-L. Barriers of influenza vaccination intention and behavior – a systematic review of influenza vaccine hesitancy, 2005 – 2016. *PLoS One*. 2017;12(1):e0170550. doi:10.1371/journal.pone.0170550.
39. Bianco A, Mascaro V, Zucco R, Pavia M. Parent perspectives on childhood vaccination: how to deal with vaccine hesitancy and refusal? *Vaccine*. 2019;37(7):984–90. doi:10.1016/j.vaccine.2018.12.062.
40. Williams SE, Morgan A, Opel D, Edwards K, Weinberg S, Rothman R. Screening tool predicts future underimmunization among a pediatric practice in tennessee. *Clin Pediatr (Phila)*. 2016;55(6):537–42. doi:10.1177/0009922815615823.
41. Larson HJ, Jarrett C, Eckersberger E, Smith DMD, Paterson P. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of published literature, 2007–2012. *Vaccine*. 2014;32(19):2150–59. doi:10.1016/j.vaccine.2014.01.081.
42. Danis K, Georgakopoulou T, Stavrou T, Laggas D, Panagiotopoulos T. Socioeconomic factors play a more important role in childhood vaccination coverage than parental perceptions: a cross-sectional study in Greece. *Vaccine*. 2010;28(7):1861–69. doi:10.1016/j.vaccine.2009.11.078.
43. Kepka D, Warner EL, Kinney AY, Spigarelli MG, Mooney K. Low human papillomavirus (HPV) vaccine knowledge among Latino parents in Utah. *J Immigrant Minority Health*. 2015;17(1):125–31. doi:10.1007/s10903-014-0003-1.
44. Peterson P, McNabb P, Ramya Maddali S, Heath J, Santibañez S. Engaging communities to reach immigrant and minority populations: the Minnesota Immunization Networking Initiative (MINI), 2006–2017. *Public Health Rep*. 2019;134:003335491983457. doi:10.1177/0033354919834579.
45. Biasio LR. Vaccine hesitancy and health literacy. *Hum Vaccin Immunother*. 2016;13(3):701–02. doi:10.1080/21645515.2016.1243633.
46. Humiston SG, Lerner EB, Hepworth E, Blythe T, Goepf JG. Parent opinions about universal influenza vaccination for infants and toddlers. *Arch Pediatr Adolesc Med*. 2005;159(2):108–12. doi:10.1001/archpedi.159.2.108.
47. Fitch P, Racine A. Parental beliefs about vaccination among an ethnically diverse inner-city population. *J Natl Med Assoc*. 2004;96:1047–50.
48. Le Saux N. Dispelling myths held by parents about the influenza vaccine. *Paediatr Child Health*. 2009;14(9):618–20. doi:10.1093/pch/14.9.618.
49. Lin CJ, Nowalk MP, Zimmerman RK, Ko F-S, Zoffel L, Hoberman A, Kearney DH. Beliefs and attitudes about influenza immunization among parents of children with chronic medical conditions over a two-year period. *J Urban Health*. 2006;83 (5):874–83. doi:10.1007/s11524-006-9084-z.
50. Chau JPC, Lo SHS, Choi KC, Chau MHK, Tong DWK, Kwong TKY, Thompson DR. Factors determining the uptake of influenza vaccination among children with chronic conditions. *Pediatr Infect Dis J*. 2017;36(7):E197–E202. doi:10.1097/INF.0000000000001550.
51. Keane MT, Walter MV, Patel BI, Moorthy S, Stevens RB, Bradley KM, Buford JF, Anderson EL, Anderson LP, Tibbals K, et al. Confidence in vaccination: a parent model. *Vaccine*. 2005;23 (19):2486–93. doi:10.1016/j.vaccine.2004.10.026.
52. Chen C-H, Chiu P-J, Chih Y-C, Yeh G-L. Determinants of influenza vaccination among young Taiwanese children. *Vaccine*. 2015;33(16):1993–98. doi:10.1016/j.vaccine.2015.01.032.
53. Ewig CLY, Tang KM, Leung TF, You JHS. Influenza vaccine coverage and predictive factors associated with influenza vaccine uptake among pediatric patients. *Am J Infect Control*. 2018;46 (11):1278–83. doi:10.1016/j.ajic.2018.04.219.
54. Jarrett C, Wilson R, O’Leary M, Eckersberger E, Larson HJ. Strategies for addressing vaccine hesitancy – A systematic review. *Vaccine*. 2015;33(34):4180–90. (WHO Recommendations Regarding Vaccine Hesitancy). doi:10.1016/j.vaccine.2015.04.040.
55. Eskola J, Duclos P, Schuster M, MacDonald NE. How to deal with vaccine hesitancy? *Vaccine*. 2015;33(34):4215–17. WHO Recommendations Regarding Vaccine Hesitancy. doi:10.1016/j.vaccine.2015.04.043.
56. Henrikson NB, Opel DJ, Grothaus L, Nelson J, Scrol A, Dunn J, Faubion T, Roberts M, Marcuse EK, Grossman DC. Physician communication training and parental vaccine hesitancy: a randomized trial. *Pediatrics*. 2015;136(1):70–79. doi:10.1542/peds.2014-3199.
57. Shen S (Cindy), Dubey V. Addressing vaccine hesitancy. *Can Family Physician*. 2019;65:175–81.
58. Nyhan B, Reifler J. Does correcting myths about the flu vaccine work? An experimental evaluation of the effects of corrective information. *Vaccine*. 2015;33(3):459–64. doi:10.1016/j.vaccine.2014.11.017.