

Impact of maternal immunization on influenza hospitalizations in infants

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In the United States, influenza vaccination is universally recommended for all children 6 months-18 years of age due to the large burden of influenza hospitalizations and outpatient visits in this age group.¹ Infants <6 months of age have the highest rates of pediatric influenza hospitalizations,²⁻⁶ but none of the influenza vaccines are licensed for this age group.⁷⁻⁹ Hence, influenza vaccine is recommended for all close contacts of infants to reduce the likelihood of transmission.¹⁰ It is also recommended for pregnant women since they have an increased risk of influenza-related complications and hospitalizations, with the highest risk during the third trimester.¹¹⁻¹⁶ National data indicate that the proportion of pregnant women who received influenza vaccine has increased from a low of 9% in 2002 through 2003 to a high of 51% in 2009 through 2010 during the H1N1 influenza pandemic.^{1,17,18}

Influenza vaccination during pregnancy is primarily recommended to pro-

We sought to determine whether maternal vaccination during pregnancy was associated with a reduced risk of laboratory-confirmed influenza hospitalizations in infants <6 months old. Active population-based, laboratory-confirmed influenza surveillance was conducted in children hospitalized with fever and/or respiratory symptoms in 3 US counties from November through April during the 2002 through 2009 influenza seasons. The exposure, influenza vaccination during pregnancy, and the outcome, positive/negative influenza testing among their hospitalized infants, were compared using logistic regression analyses. Among 1510 hospitalized infants <6 months old, 151 (10%) had laboratory-confirmed influenza and 294 (19%) mothers reported receiving influenza vaccine during pregnancy. Eighteen (12%) mothers of influenza-positive infants and 276 (20%) mothers of influenza-negative infants were vaccinated (unadjusted odds ratio, 0.53; 95% confidence interval, 0.32–0.88 and adjusted odds ratio, 0.52; 95% confidence interval, 0.30–0.91). Infants of vaccinated mothers were 45-48% less likely to have influenza hospitalizations than infants of unvaccinated mothers. Our results support the current influenza vaccination recommendation for pregnant women.

Key words: infants, influenza hospitalization, influenza vaccine, maternal vaccination, vaccine effectiveness

tect pregnant women themselves. However, a recent randomized controlled trial from Bangladesh and an observational study among Native American

populations reported benefits of influenza vaccine both for mothers and their young infants.^{19,20} Influenza antibodies are efficiently transferred across the pla-

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Presented, in part, at the 2005 Pediatric Academic Societies Meeting in Washington, DC, May 16, 2005.

Received Dec. 16, 2010; revised Feb. 4, 2011; accepted Feb. 14, 2011.

Reprints not available from the authors.

Conflict of Interest: This project was supported by Cooperative Agreement nos. U01/IP000017, U01/IP000022, and U01/IP000147 from the Centers for Disease Control and Prevention. Dr Poehling received support from National Institute of Allergy and Infectious Diseases (K23 AI065805) and Wachovia Research Fund. Dr Staat had funding from Medimmune for respiratory syncytial virus studies; Dr Griffin received grant funding from Medimmune; Dr Edwards received grant funding from Wyeth, Novartis, Sanofi-Pasteur, and CSL with only the CSL funding being related to influenza studies. Dr Staat was on the Medimmune Advisory Board, and Dr Edwards was a consultant to NexBio. Drs Szilagyi, Snively, Payne, Bridges, Chu, Finelli, and Ms Light and Ms Prill have no conflicts to report.

Contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

Publication of this article was supported by the Centers for Disease Control and Prevention and the Association of Maternal and Child Health Programs.

0002-9378/\$36.00 • © 2011 Mosby, Inc. All rights reserved. • doi: 10.1016/j.ajog.2011.02.042

centa and have been observed to provide indirect protection to infants for the first 2-3 months of life, when infants are too young to receive influenza vaccine.^{20,21} We sought to determine whether maternal vaccination during pregnancy was associated with a reduced risk of laboratory-confirmed influenza hospitalizations in infants <6 months of age living in 3 geographically diverse US counties over 7 consecutive influenza seasons. We focused on influenza hospitalizations because they are associated with the highest costs and because most childhood deaths occur among hospitalized patients.^{22,23}

Materials and methods

The New Vaccine Surveillance Network, funded by the Centers for Disease Control and Prevention, conducted active, population-based, laboratory-confirmed influenza surveillance among children hospitalized with influenza in 3 US counties: Davidson County, Tennessee (Nashville); Hamilton County, Ohio (Cincinnati); and Monroe County, New York (Rochester).² Children were eligible for enrollment if they were hospitalized with fever and/or acute respiratory symptoms during the winter from November through April and resided within these 3 counties. Seven consecutive influenza seasons were included: 2002-2003 through 2008-2009 in Nashville, TN, and Rochester, NY, and 2003-2004 through 2008-2009 in Cincinnati, OH. In 2008 through 2009, the seasonal influenza season ended in April 2009, which was prior to the detection of H1N1 in this network.

All enrolled children had nasal and throat swabs obtained for viral culture and/or reverse transcription polymerase chain reaction for influenza A or B as previously described.²⁴ Parents of enrolled children had a standardized questionnaire administered to ascertain presenting symptoms and their duration, birth and medical history, history of maternal influenza vaccination during pregnancy with the enrolled child, and social history. The medical record was reviewed after discharge.

The study population comprised inpatients <6 months of age enrolled

through hospital surveillance with fever and/or acute respiratory symptoms during 1 of the 7 consecutive influenza seasons. Most infants were enrolled as inpatients although some were enrolled as outpatients and subsequently hospitalized. For infants with multiple hospitalizations during an influenza season, only the first hospitalization during the study period was included. Each influenza season was defined as the period spanning the first to last influenza-positive nasal/throat swab among all study infants. Since the opportunity for the mother to receive the influenza vaccine varied by birth month, we divided each influenza season into early, middle, and late season tertiles, based on the day of enrollment of influenza-positive infants. A control group of hospitalized infants without laboratory-confirmed influenza were assigned to early, middle, and late tertiles by comparing their dates of enrollment with the influenza-positive cases.

The primary exposure variable was maternal influenza vaccination status during pregnancy, and the primary outcome variable was the presence or absence of laboratory-confirmed influenza among their hospitalized infants. Categorical variables that can influence hospitalizations in general and thus could potentially influence influenza-related hospitalizations in infants were compared by χ^2 analysis. For adjusted analyses, we created 3 multivariate logistic regression model analyses a priori based on demographic, medical, and social risk factors previously shown to be associated with increased risk of influenza or respiratory hospitalizations.^{2,3,5,25-29} The core demographic model included the following covariates: age, sex, race/ethnicity, site, study year, and tertile of the influenza season. The second model evaluated the core demographic model and 2 medical covariates: prematurity and presence of any high-risk medical conditions in the infant for which influenza vaccine was recommended in persons ≥ 6 months of age.¹⁶ The third model included the core demographic model and 5 additional variables: smoke exposure at home, number of siblings (0 to ≥ 3), day care attendance, insurance status (public/private/none), and whether the in-

fant was ever breast-fed. All model covariates were treated as categorical variables. Confidence intervals (CI) were calculated at the 95% level; P values $\leq .05$ were considered statistically significant. All analyses were computed using STATA software 10.0 (StataCorp, College Station, TX).

From 2005-2006 through 2008-2009, we asked mothers of young infants if they had an influenza-like illness during pregnancy because an influenza illness during pregnancy could lead to the development of protective antibodies for that influenza serotype in the infant. Hence, we performed a subanalysis of the unadjusted and the 3 adjusted models described above to determine the protective effect of either maternal vaccination for all years or influenza-like illness during pregnancy from the last 4 years of the study period.

Human and nonhuman experimentation

The study was approved with informed consent from the parent or guardian by the institutional review boards at each site and the Centers for Disease Control and Prevention.

Results

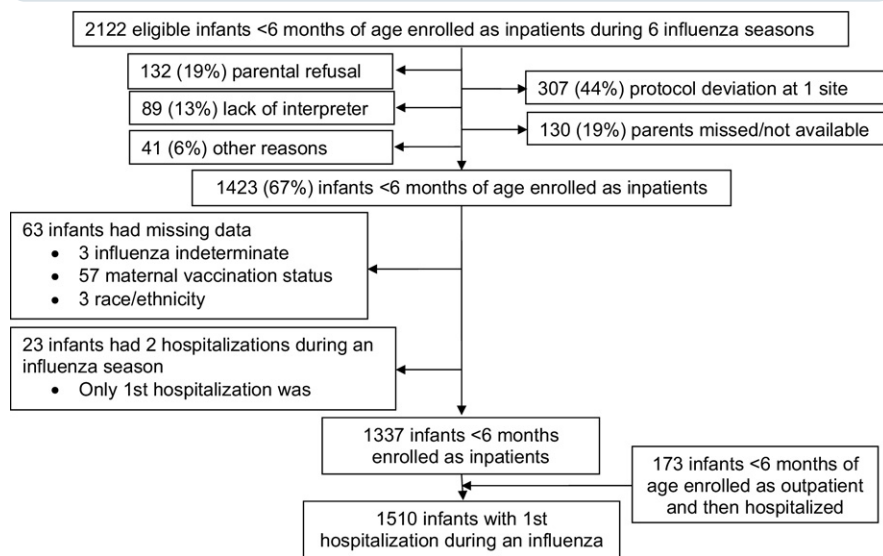
Over 7 influenza seasons, 2122 hospitalized infants were eligible for enrollment in the 3 New Vaccine Surveillance Network sites and 1423 (67%) of the eligible infants were included from the inpatient setting (Figure 1). Reasons for exclusion were 307 (44%) protocol deviations at Cincinnati, OH, 132 (19%) parental refusal, 130 (19%) parents missed or not available, 89 (13%) lack of language translator, 38 (5%) discharged prior to being approached, and 3 (<1%) physician refusal. Of these 1423 hospitalized and enrolled infants, 57 (4%) had unknown or missing maternal influenza vaccination status, 3 (0.2%) had indeterminate influenza status (ie, negative RNA control), 3 (0.2%) had unknown race/ethnicity, and 23 (2%) represented a second study hospitalization during the influenza season and were excluded from analysis. The overall study population comprised these 1337 eligible infants enrolled solely from the inpatient setting and an additional 173 eligible in-

infants who were hospitalized following enrollment in the emergency department and fulfilled all inpatient enrollment criteria. Among these 1510 infants hospitalized with fever and/or respiratory symptoms during the influenza season (Table 1), 151 (10%) had laboratory-confirmed influenza—with 136 (90%) influenza A and 15 (10%) influenza B. Among all hospitalized infants, a higher proportion of infants <2 months than those 2 to <6 months of age were influenza positive. The proportion of infants who were influenza positive varied significantly across study years, ranging from 3% in 2006 through 2007 to 15% in 2003 through 2004.

A total of 294 (19%) mothers reported that they had received the influenza vaccine during that pregnancy (Table 2). This proportion varied by influenza season, ranging from 10% in 2003 through 2004 to 38% in 2008 through 2009, and by age of the infant at the time of enrollment during the influenza season, ranging from 24% for neonates <1 month of age to 9% for infants 4–5 months of age. The proportion of infants whose mothers were vaccinated varied from only 13–15% at the Cincinnati, OH, and Nashville, TN, sites up to 33% at the Rochester, NY, site. The proportion of infants whose mothers were vaccinated was 15% for blacks, 21% for whites, and 22% for Hispanics. Infants with private insurance were more likely to have a vaccinated mother than those with public or no insurance. Breast-fed infants were more likely to have mothers who reported being vaccinated than infants of mothers who never breast-fed. Non-smoking households had a higher proportion of infants whose mothers were vaccinated than households with a smoker.

Among influenza-positive infants during all study years, 12% of their mothers reported influenza vaccination during pregnancy, while among influenza-negative infants, 20% of their mothers reported influenza vaccination, yielding an unadjusted odds ratio (OR) of 0.53 (95% confidence interval [CI], 0.32–0.88). Similar results were obtained in the 3 multivariate models shown in Figure 2. Since a significant proportion of data from Cincinnati,

FIGURE 1
Study population



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OH, was excluded for protocol violations, a sensitivity analysis that included only Rochester, NY, and Nashville, TN, data was performed and yielded similar results to the combined data. In the core demographic model, adjusting for age, sex, race/ethnicity, site, study year, and early, middle, or late influenza season, the OR for having an influenza-positive, hospitalized infant among vaccinated mothers was 0.55 (95% CI, 0.32–0.95). Model 2 included the core demographic model plus prematurity and high-risk conditions and had an OR of 0.55 (95% CI, 0.32–0.94). These medical covariates did not impact the estimate and were not included in the third model. Model 3 included the core demographic model, exposure to smoke, siblings, day care, insurance, and presence of breastfeeding and had an OR of 0.52 (95% CI, 0.30–0.91). As shown, adjustments for covariates did not affect the results substantially. Overall, results of the multivariate modeling suggest that maternal vaccination reduced the risk of influenza by 45–48%.

A total of 110 mothers from 2005–2006 through 2008–2009 reported a history of influenza-like illness during pregnancy, of which 81 (74%) had not received the influenza vaccine during that pregnancy. In a subanalysis combining both maternal influenza vaccination for all 7 years and a his-

tory of an influenza-like illness during pregnancy for 4 years, we found that the unadjusted and adjusted estimates were similar with a 45–49% reduced risk of influenza in the infant.

Comment

Our results indicate that hospitalized infants whose mothers received influenza vaccine during pregnancy were 45–48% less likely to have laboratory-confirmed influenza during their first influenza season compared with infants of unvaccinated mothers. Adding history of influenza-like illness during pregnancy to the analyses had little impact on the OR for having an influenza-positive, hospitalized infant. Given that infants <6 months of age have the highest hospitalization rate among all children^{2–6} and that the vaccine is not licensed for that age group,¹⁶ these data support that infants born to vaccinated mothers benefit from the transfer of maternally derived antibodies.

Four previously published studies support our conclusions. First, a prospective, observational study among Native Americans from 2002 through 2005 found that infants of vaccinated mothers had a 41% reduction of the risk of laboratory-confirmed influenza infection in the inpatient and outpatient settings as

TABLE 1
Characteristics of infants <6 months of age hospitalized with and without laboratory confirmed influenza

Characteristic	Total n = 1510	(row %)		P value
		Influenza + n = 151	Influenza - n = 1359	
Maternal influenza vaccine				
No	1216	133 (11%)	1083 (89%)	.01
Yes	294	18 (6%)	276 (94%)	
Influenza season				
Early	572	51 (9%)	521 (91%)	.51
Middle	485	50 (10%)	435 (89%)	
Late	453	50 (11%)	403 (89%)	
Age group, mo				
0	399	49 (12%)	350 (87%)	< .001
1	507	66 (13%)	441 (87%)	
2-3	411	24 (6%)	387 (94%)	
4-5	193	12 (6%)	181 (94%)	
Sex				
Female	664	68 (10%)	596 (90%)	.78
Male	846	83 (10%)	763 (90%)	
Study site				
Nashville, TN	554	60 (11%)	494 (89%)	.53
Rochester, NY	425	44 (10%)	381 (90%)	
Cincinnati, OH	531	47 (9%)	484 (91%)	
Study year				
2002-2003	99	9 (9%)	90 (91%)	< .001
2003-2004	251	38 (15%)	213 (84%)	
2004-2005	322	40 (12%)	282 (88%)	
2005-2006	176	16 (9%)	160 (91%)	
2006-2007	230	8 (3%)	222 (97%)	
2007-2008	232	29 (13%)	203 (88%)	
2008-2009	200	11 (6%)	189 (95%)	
Race/ethnicity				
White	706	59 (8%)	647 (92%)	.11
Black	439	53 (12%)	386 (88%)	
Hispanic	365	39 (11%)	326 (89%)	
Medical covariates				
Premature				
Yes	178	13 (7%)	165 (93%)	.20
No	1325	138 (10%)	1187 (90%)	
High-risk condition				
Yes	119	7 (6%)	112 (94%)	.12
No	1391	144 (10%)	1247 (90%)	

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determined by viral culture or antibody titers (relative risk, 0.59; 95% CI, 0.37–0.93).²⁰ A second study, a randomized controlled trial of maternal influenza vaccination during pregnancy, was conducted in Bangladesh in 2004 through 2005. In this tropical country with year-round influenza circulation, investigators reported fewer rapid test–confirmed influenza cases among infants of mothers who received influenza vaccine compared with infants of unvaccinated mothers (6 vs 16 infants, respectively) for a vaccine effectiveness estimate of 63% (95% CI, 5–85%). Among 110 infants in the influenza vaccine group and 153 infants in the control group, vaccine effectiveness against unspecified respiratory illness with fever was 29% (95% CI, 7–46%).¹⁹ Third, a matched case-control study compared hospitalized infants with physician-ordered direct fluorescent antibody for seasonal influenza from 2000 through 2009. Cases with a positive influenza test result and controls with a negative test result were matched by date of birth and date of hospitalization. Maternal vaccinations were included only if they were confirmed and given at least 14 days prior to delivery. Effectiveness of maternal vaccination among infants <6 months of age was reported to be 91.5% (95% CI, 62–98%).³⁰ Fourth, a Northern California Kaiser Permanente database study over 5 influenza seasons (1997 through 2002), found that maternal vaccination was associated with a decreased risk of pneumonia or influenza hospitalization in their infants with an adjusted hazard ratio of 0.63 (95% CI, 0.30–1.29), translating into 37% protection.³¹ Our 95% CIs for protection of maternal vaccination from influenza hospitalizations among infants <6 months of age overlap those from each of these studies.

Our study differs from the previously published studies in several ways. First, we included 7 consecutive influenza seasons and used prospective, population-based and laboratory-confirmed surveillance to identify eligible infants. By systematically testing all eligible infants using culture and molecular methods to define influenza infections, we utilized sensitive and specific methods and

avoided the biases associated with physician-ordered testing; the study utilizing physician-ordered testing to identify eligible infants had a much higher proportion of infants with high-risk conditions than our study population. Second, we focused on hospitalizations whereas 2 previous studies included more outpatient visits than hospitalizations. Third, we included 3 diverse geographic regions of the United States whereas all previous studies reported data from 1 geographic region.

Our study has several limitations. Although we enrolled a large proportion of eligible infants, a number of them had to be excluded because of protocol violations, and infants who were and were not included in the study population could have systematically differed. Neither confirmed influenza vaccination status nor documented influenza disease status was available from mothers, and serologic assays were not performed on either infants or mothers. Since the study focused on hospitalized infants and not those seen only in the outpatient clinic or emergency departments, the generalizability of these results to outpatient settings is unknown. However, admission criteria for infants with fever and respiratory symptoms change over the first few weeks of life, so limiting the study population to solely inpatients allowed us to focus on severe outcomes.

Our estimates of maternal vaccination are consistent with national estimates¹⁷ and lower than estimates from one health care system that implemented interventions to increase their maternal vaccination rates.³² We have previously reported higher influenza vaccine coverage among children 6-59 months of age in Rochester, NY, than in Nashville, TN, or Cincinnati, OH.³³ Because of this consistent pattern, these differences seem to reflect geographical differences in influenza vaccination patterns. We found higher rates of maternal vaccination when the infant had private insurance compared with public or no insurance. This differs from the seasonal influenza vaccine coverage reported by the Rhode Island Pregnancy Risk Assessment Monitoring System, which found similar coverage between women with

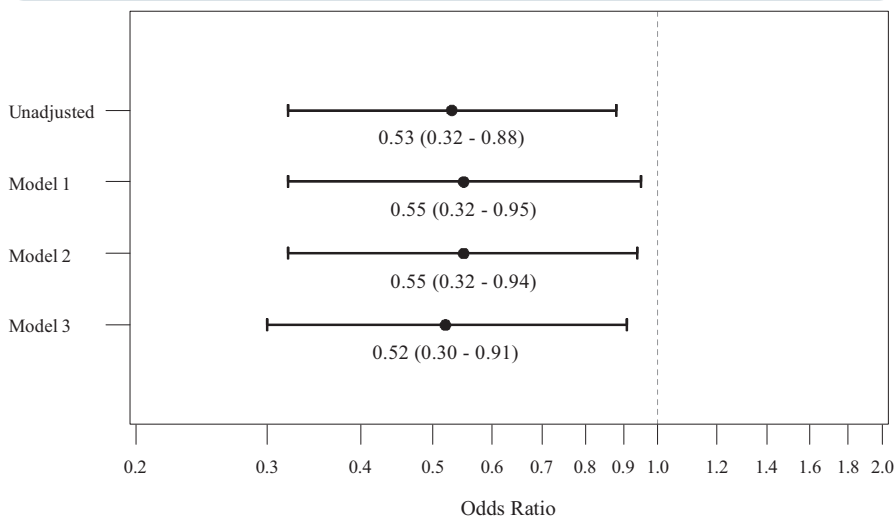
TABLE 1
Characteristics of infants <6 months of age hospitalized with and without laboratory confirmed influenza (continued)

Characteristic	Total n = 1510	(row %)		P value
		Influenza + n = 151	Influenza - n = 1359	
Social covariates				
Exposed to smoke				
Yes	613	62 (10%)	551 (90%)	.85
No	896	88 (10%)	808 (90%)	
No. of siblings				
0	341	33 (10%)	308 (90%)	.10
1	539	42 (8%)	497 (92%)	
2	341	43 (13%)	298 (87%)	
≥3	289	33 (11%)	256 (89%)	
Day care				
Yes	152	7 (5%)	145 (95%)	.02
No	1356	144 (11%)	1212 (89%)	
Insurance				
Public	891	94 (11%)	797 (89%)	.67
Private	507	46 (9%)	461 (91%)	
None	105	10 (10%)	95 (90%)	
Ever breast-fed				
Yes	916	97 (11%)	819 (89%)	.34
No	594	54 (9%)	540 (91%)	

Percentages may not sum to 100% due to rounding.

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FIGURE 2
Infant protection from maternal vaccination



Odds ratio and 95% confidence interval for protection provided by influenza vaccination during pregnancy on laboratory-confirmed influenza hospitalizations among infants for unadjusted and adjusted models.

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TABLE 2
Characteristics of hospitalized infants <6 months of age by maternal influenza vaccination status

Characteristic	Total n = 1510	(row %)		P value
		Vaccinated n = 294	Not vaccinated n = 1216	
Influenza-positive				
No	1359	276 (20%)	1083 (80%)	.01
Yes	151	18 (12%)	133 (88%)	
Influenza season				
Early	572	98 (17%)	474 (83%)	.06
Middle	485	92 (19%)	393 (81%)	
Late	453	104 (23%)	349 (77%)	
Age group, mo				
0	399	96 (24%)	303 (76%)	< .001
1	507	92 (18%)	415 (82%)	
2-3	411	88 (21%)	323 (79%)	
4-5	193	18 (9%)	175 (91%)	
Sex				
Female	664	123 (19%)	541 (81%)	.41
Male	846	171 (20%)	675 (80%)	
Study site				
Nashville, TN	554	84 (15%)	470 (85%)	< .001
Rochester, NY	425	142 (33%)	283 (67%)	
Cincinnati, OH	531	68 (13%)	463 (87%)	
Study year				
2002-2003	99	18 (18%)	81 (82%)	< .001
2003-2004	251	25 (10%)	226 (90%)	
2004-2005	322	43 (13%)	279 (87%)	
2005-2006	176	31 (18%)	145 (82%)	
2006-2007	230	45 (20%)	185 (80%)	
2007-2008	232	57 (25%)	175 (75%)	
2008-2009	200	75 (38%)	125 (63%)	
Race/ethnicity				
White	698	147 (21%)	551 (79%)	.005
Black	430	63 (15%)	367 (85%)	
Hispanic	363	80 (22%)	283 (78%)	
Medical covariates				
Premature				
Yes	178	33 (19%)	145 (81%)	.73
No	1325	260 (20%)	1065 (80%)	
High-risk condition				
Yes	119	22 (18%)	97 (82%)	.78
No	1391	272 (20%)	1119 (80%)	

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public and private insurance. Given that obstetrician-gynecologists have consistently identified financial costs as a major barrier to influenza vaccination of pregnant women,³⁴⁻³⁶ it is possible that differences in vaccine coverage between public and private insurance vary geographically.

Maternal vaccination during pregnancy is recommended since pregnant women have an increased risk of influenza-associated morbidity and mortality.¹¹⁻¹⁵ However, despite this recommendation, pregnant women have traditionally had the lowest influenza vaccine coverage of any group for whom influenza vaccine is specifically recommended.¹⁷ Although most (84.5%) obstetricians support influenza vaccination of all pregnant women,³⁴ few mothers (20%) report being offered influenza vaccination during pregnancy.³⁷ Obstetricians play a critical role in the influenza vaccination coverage of pregnant women. For first pregnancies, obstetricians are often the only medical professional seeing the pregnant women; for subsequent pregnancies, pregnant women may see the pediatrician, however, pediatricians do not tend to vaccinate pregnant women since they are not their patients. Half of all pregnant women who received the monovalent H1N1 vaccine in 2009 through 2010 reported receiving it in the obstetrician-gynecologist office and none reported receiving it in a pediatric office.¹⁸

Because numerous studies have demonstrated comparable or increased influenza antibody titers in the cord blood when compared with maternal levels,^{3,38-43} maternal vaccination should afford some protection of newborn infants against influenza and is supported by our study. Similar to other studies, we found between 45% and 48% protection against laboratory-confirmed influenza hospitalizations among infants whose mothers reported receiving influenza vaccine during pregnancy. Using data from our earlier studies of 4.5 influenza-attributable hospitalizations among 1000 infants <6 months of age² and census data of 4,251,095 live-births in the United States in 2008,⁴⁴ we project that there are an average of 19,130 influenza-attributable hospitalizations among infants <6 months of age per year. A 45-48% reduction in this burden would yield an estimated 8600-9200

TABLE 2
Characteristics of hospitalized infants <6 months of age by maternal influenza vaccination status (continued)

Characteristic	Total n = 1510	(row %)		P value
		Vaccinated n = 294	Not vaccinated n = 1216	
Social covariates				
Exposed to smoke				
Yes	613	83 (14%)	530 (86%)	< .001
No	896	211 (24%)	685 (76%)	
No. of siblings				
0	341	75 (22%)	266 (78%)	.32
1	539	108 (20%)	431 (80%)	
2	341	64 (19%)	277 (81%)	
≥3	289	47 (16%)	242 (84%)	
Day care				
Yes	152	29 (19%)	123 (81%)	.89
No	1356	265 (20%)	1091 (80%)	
Insurance				
Public	891	146 (16%)	745 (84%)	< .001
Private	507	137 (27%)	370 (73%)	
None	105	8 (8%)	97 (92%)	
Ever breast-fed				
Yes	916	207 (22%)	709 (77%)	< .001
No	594	87 (15%)	507 (85%)	

Percentages may not sum to 100% due to rounding.

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fewer influenza-attributable hospitalizations among young infants each year. Thus, our findings suggest that influenza vaccination of pregnant women may reduce the risk of influenza-attributable hospitalization among infants in the first 5 months of life, further supporting the current influenza vaccination recommendations for pregnant women. ■

ACKNOWLEDGMENTS

We are grateful to all the infants and their families who participated and made this study possible. We also appreciate the efforts of many others who provided invaluable support and contributions. They include Monica McNeal, PhD, David Witte, PhD, Vanessa Florian, Diana Henderson, MPH, MSW, Michol Holloway, MPH, Linda Jamison, RN, BSN, CIC, at Cincinnati Children's Hospital Medical Center in Cincinnati, OH; Carol Ann Clay, RN, Erin Keckley, RN, Diane Kent, RN, Mariah Daly, RN, Nayleen Whitehead, Yuwei Zhu, MD, MS, at Vanderbilt University Medical Center in Nashville, TN; and Christina Albertin, MPH, Geraldine Lofthus,

PhD, Kenneth Schnabel, MBA, at University of Rochester School of Medicine and Dentistry at Rochester, NY; and those who provided support for surveillance activities at the Centers for Disease Control and Prevention, including Rane Seither, MPH, Frances Walker, MSPH, Marika Iwane, PhD, and Minnie Wang, MD.

REFERENCES

1. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Morb Mortal Wkly Rep* 2010;59:1-62.
2. Poehling KA, Edwards KM, Weinberg GA, et al. The underrecognized burden of influenza in young children. *N Engl J Med* 2006;355:31-40.
3. Glezen WP, Taber LH, Frank AL, Gruber WC, Piedra PA. Influenza virus infections in infants. *Pediatr Infect Dis J* 1997;16:1065-8.
4. Neuzil KM, Zhu Y, Griffin MR, et al. Burden of inter pandemic influenza in children younger than 5 years: a 25-year prospective study. *J Infect Dis* 2002;185:147-52.
5. Neuzil KM, Mellen BG, Wright PF, Mitchel EF Jr, Griffin MR. The effect of influenza on hospital-

izations, outpatient visits, and courses of antibiotics in children. *N Engl J Med* 2000;342:225-31.

6. Kim HW, Brandt CD, Arrobio JO, Murphy B, Chanock RM, Parrott RH. Influenza A and B virus infection in infants and young children during the years 1957-1976. *Am J Epidemiol* 1979;109:464-79.

7. Groothuis JR, Levin MJ, Rabalais GP, Meiklejohn G, Lauer BA. Immunization of high-risk infants younger than 18 months of age with split-product influenza vaccine. *Pediatrics* 1991;87:823-8.

8. Gruber WC, Darden PM, Still JG, Lohr J, Reed G, Wright PF. Evaluation of bivalent live attenuated influenza A vaccines in children 2 months to 3 years of age: safety, immunogenicity and dose-response. *Vaccine* 1997;15:1379-84.

9. Karron RA, Steinhoff MC, Subbarao EK, et al. Safety and immunogenicity of a cold-adapted influenza A (H1N1) reassortant virus vaccine administered to infants less than six months of age. *Pediatr Infect Dis J* 1995;14:10-6.

10. Poehling KA, Szilagyi PG. Not just for kids: new paradigms for vaccine delivery in pediatrics. *Acad Pediatr* 2009;9:293-4.

11. Mullooly JP, Barker WH, Nolan TF Jr. Risk of acute respiratory disease among pregnant women during influenza A epidemics. *Public Health Rep* 1986;101:205-11.

12. Hartert TV, Neuzil KM, Shintani AK, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. *Am J Obstet Gynecol* 2003;189:1705-12.

13. Dodds L, McNeil SA, Fell DB, et al. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *CMAJ* 2007;176:463-8.

14. Cox S, Posner SF, McPheeters M, Jamieson DJ, Kourtis AP, Meikle S. Hospitalizations with respiratory illness among pregnant women during influenza season. *Obstet Gynecol* 2006;107:1315-22.

15. ACOG Committee on Obstetric Practice. ACOG committee opinion number 305, November 2004: influenza vaccination and treatment during pregnancy. *Obstet Gynecol* 2004;104:1125-6.

16. Fiore AE, Shay DK, Broder K, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR Recomm Rep* 2009;58:1-52.

17. Lu P, Bridges CB, Euler GL, Singleton JA. Influenza vaccination of recommended adult populations, US, 1989-2005. *Vaccine* 2008;26:1786-93.

18. Centers for Disease Control and Prevention. Seasonal influenza and 2009 H1N1 influenza vaccination coverage among pregnant women—10 states, 2009-10 influenza season. *MMWR Morb Mortal Wkly Rep* 2010;59:1541-5.

19. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 2008;359:1555-64.

- 20.** Eick AA, Uyeki TM, Klimov A, et al. Maternal influenza vaccination and effect on influenza virus infection in young infants. *Arch Pediatr Adolesc Med* 2011;165:104-11.
- 21.** Healy CM, Baker CJ. Prospects for prevention of childhood infections by maternal immunization. *Curr Opin Infect Dis* 2006;19:271-6.
- 22.** Fairbrother G, Cassidy A, Ortega-Sanchez IR, et al. High costs of influenza: direct medical costs of influenza disease in young children. *Vaccine* 2010;28:4913-9.
- 23.** Finelli L, Fiore A, Dhara R, et al. Influenza-associated pediatric mortality in the United States: increase of *Staphylococcus aureus* coinfection. *Pediatrics* 2008;122:805-11.
- 24.** Weinberg GA, Erdman DD, Edwards KM, et al. Superiority of reverse-transcription polymerase chain reaction to conventional viral culture in the diagnosis of acute respiratory tract infections in children. *J Infect Dis* 2004;189:706-10.
- 25.** Glezen WP, Greenberg SB, Atmar RL, Piedra PA, Couch RB. Impact of respiratory virus infections on persons with chronic underlying conditions. *JAMA* 2000;283:499-505.
- 26.** Izurieta HS, Thompson WW, Kramarz P, et al. Influenza and the rates of hospitalization for respiratory disease among infants and young children. *N Engl J Med* 2000;342:232-9.
- 27.** Mullooly JP, Barker WH. Impact of type A influenza on children: a retrospective study. *Am J Public Health* 1982;72:1008-16.
- 28.** Wright AL, Holberg CJ, Martinez FD, Morgan WJ, Taussig LM. Breast feeding and lower respiratory tract illness in the first year of life; Group Health Medical Associates. *BMJ* 1989;299:946-9.
- 29.** Sinha A, Madden J, Ross-Degnan D, Soumerai S, Platt R. Reduced risk of neonatal respiratory infections among breastfed girls but not boys. *Pediatrics* 2003;112:e303.
- 30.** Benowitz I, Esposito DB, Gracey KD, Shapiro ED, Vazquez M. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. *Clin Infect Dis* 2010;51:1355-61.
- 31.** Black SB, Shinefield HR, France EK, Fireman BH, Platt ST, Shay D. Effectiveness of influenza vaccine during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants. *Am J Perinatol* 2004;21:333-9.
- 32.** Mouzoon ME, Munoz FM, Greisinger AJ, et al. Improving influenza immunization in pregnant women and healthcare workers. *Am J Manag Care* 2010;16:209-16.
- 33.** Eisenberg KW, Szilagyi PG, Fairbrother G, et al. Vaccine effectiveness against laboratory-confirmed influenza in children 6 to 59 months of age during the 2003-2004 and 2004-2005 influenza seasons. *Pediatrics* 2008;122:911-9.
- 34.** Power ML, Leddy MA, Anderson BL, Gall SA, Gonik B, Schulkin J. Obstetrician-gynecologists' practices and perceived knowledge regarding immunization. *Am J Prev Med* 2009;37:231-4.
- 35.** Schrag SJ, Fiore AE, Gonik B, et al. Vaccination and perinatal infection prevention practices among obstetrician-gynecologists. *Obstet Gynecol* 2003;101:704-10.
- 36.** Gonik B, Jones T, Contreras D, Fasano N, Roberts C. The obstetrician-gynecologist's role in vaccine-preventable diseases and immunization. *Obstet Gynecol* 2000;96:81-4.
- 37.** Yudin MH, Salaripour M, Sgro MD. Pregnant women's knowledge of influenza and the use and safety of the influenza vaccine during pregnancy. *J Obstet Gynaecol Can* 2009;31:120-5.
- 38.** Reuman PD, Ayoub EM, Small PA. Effect of passive maternal antibody on influenza illness in children: a prospective study of influenza A in mother-infant pairs. *Pediatr Infect Dis J* 1987;6:398-403.
- 39.** Puck JM, Glezen WP, Frank AL, Six HR. Protection of infants from infection with influenza A virus by transplacentally acquired antibody. *J Infect Dis* 1980;142:844-9.
- 40.** Englund JA, Mbawuike IN, Hammill H, Holleman MC, Baxter BD, Glezen WP. Maternal immunization with influenza or tetanus toxoid vaccine for passive antibody protection in young infants. *J Infect Dis* 1993;168:647-56.
- 41.** Sumaya CV, Gibbs RS. Immunization of pregnant women with influenza A/New Jersey/76 virus vaccine: reactogenicity and immunogenicity in mother and infant. *J Infect Dis* 1979;140:141-6.
- 42.** Irving WL, James DK, Stephenson T, et al. Influenza virus infection in the second and third trimesters of pregnancy: a clinical and seroepidemiological study. *BJOG* 2000;107:1282-9.
- 43.** Wutzler P, Schmidt-Ott R, Hoyer H, Sauerbrei A. Prevalence of influenza A and B antibodies in pregnant women and their offspring. *J Clin Virol* 2009;46:161-4.
- 44.** Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2008. Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_16. Accessed March 18, 2011.