Influenza-Related Hospitalization and ED Visits in Children Less Than 5 Years: 2000–2011

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abstract

BACKGROUND AND OBJECTIVES: In the United States, recommendations for annual influenza vaccination gradually expanded from 2004 to 2008, to include all children aged ≥6 months. The effects of these policies on vaccine uptake and influenza-associated health care encounters are unclear. The objectives of the study were to examine the annual incidence of influenza-related health care encounters and vaccine uptake among children age 6 to 59 months from 2000–2001 through 2010–2011 in Davidson County, TN.

METHODS: We estimated the proportion of laboratory-confirmed influenza-related hospitalizations and emergency department (ED) visits by enrolling and testing children with acute respiratory illness or fever. We estimated influenza-related health care encounters by multiplying these proportions by the number of acute respiratory illness/fever hospitalizations and ED visits for county residents. We assessed temporal trends in vaccination coverage, and influenza-associated hospitalizations and ED visit rates.

RESULTS: The proportion of fully vaccinated children increased from 6% in 2000–2001 to 38% in 2010–2011 ($P < .05$). Influenza-related hospitalizations ranged from 1.9 to 16.0 per 10 000 children (median 4.5) per year. Influenza-related ED visits ranged from 89 to 620 per 10 000 children (median 143) per year. Significant decreases in hospitalizations ($P < .05$) and increases in ED visits ($P < .05$) over time were not clearly related to vaccination trends. Influenza-related encounters were greater when influenza A(H3N2) circulated than during other years with median rates of 8.2 vs 3.2 hospitalizations and 307 vs 143 ED visits per 10 000 children, respectively.

CONCLUSIONS: Influenza vaccination increased over time; however, the proportion of fully vaccinated children remained <50%. Influenza was associated with a substantial illness burden particularly when influenza A(H3N2) predominated.

WHAT'S KNOWN ON THIS SUBJECT: Influenza represents a leading cause of morbidity and a rare cause of death in children. Annual influenza vaccination was gradually expanded to include all children ≥6 months in 2008. The impact of these recommendations on disease burden is unclear.

WHAT THIS STUDY ADDS: We assessed the burden of influenza-related health care encounters in children aged 6 to 59 months from 2000 to 2011. In this ecologic exploration, influenza vaccination and influenza-related emergency department visits increased over time, whereas hospitalizations decreased. Influenza-related health care encounters were greater when A(H3N2) circulated.

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Before 2004, annual influenza vaccination was recommended only for persons age ≥6 months at high risk for influenza complications.[1] However, few children with high-risk conditions, including those with asthma, the most common pediatric high-risk condition, were vaccinated.[2,3] Several modeling studies demonstrated the substantial burden of influenza in young children without high-risk conditions.[4–6] Thompson et al[6] estimated average annual influenza-related hospitalizations in US children <5 years to be 10.8 per 10 000 person-years from 1979 through 2001. The Centers for Disease Control and Prevention (CDC)-funded New Vaccine Surveillance Network (NVSN) used sensitive molecular techniques to detect influenza virus in hospitalized children, yielding similar estimates of 9 hospitalizations per 10 000 children age <5 years.[7,8] Based in part on these findings, the Advisory Committee on Immunization Practices recommended annual influenza vaccine for all US children age 6 to 23 months in 2004,[9] all children ≥59 months in 2006,[10] and all older children in August 2008.[11] As of 2010, annual influenza vaccine was recommended for all persons age ≥6 months.[12]

Annual variability in influenza activity, strain virulence, and population immunity to circulating strains makes assessing the impact of these vaccination policy changes challenging.[13,14] However, with increasing uptake of influenza vaccines, influenza-related health care visits should decrease over time. We assessed changes in the age- and season-specific incidence of influenza-related hospitalizations and emergency department (ED) visits in children 6 to 59 months living in Davidson County, TN, during 11 consecutive influenza seasons from 2000–2001 through 2010–2011.

METHODS

Population and Setting

Residents of Davidson County, TN, age 6 to 59 months during influenza seasons from 2000–2001 through 2010–2011 were included.[15]

Sources of Data

From 2000 through 2008, the CDC-sponsored NVSN enrolled Davidson County children age 0 to 59 months hospitalized with acute respiratory illness (ARI) or fever whose parents or legal guardians consented to participate in the study. Enrollment in the pediatric ED occurred from 2003–2004 through 2010–2011, except for 2004–2005. From 2009 through 2011 the CDC-sponsored Influenza Vaccine Effectiveness Surveillance Network used a similar enrollment methodology.[8,16–19] In this report, children age <6 months were excluded because influenza vaccine is not approved for this age group.

Enrollment occurred at 2 academic hospitals (1 small hospital closed during the study years), 1 community hospital, and 1 ED in Davidson County. Demographic and clinical characteristics for enrolled children were recorded through a standardized questionnaire, and nasal and throat swabs were collected for influenza testing. Both viral culture and real-time reverse transcription polymerase chain reaction (rRT-PCR) were initially performed on all samples to detect influenza virus[16,17,20] until May 2009 when cultures, which yielded almost no additional detections, were abandoned. CDC personnel performed rRT-PCR during the first study year; thereafter, the Williams Research Laboratory at Vanderbilt performed the testing by using identical methods.[21] Laboratory confirmation was established by a positive rRT-PCR or viral culture for influenza.

Enrollment sites accounted for ~95% of all ARI/fever admissions and ~50% of all ARI/fever ED visits of Davidson County children <5 years, based on data from the Tennessee Hospital Discharge Data System (HDDS) (http://health.state.tn.us/statistics/specialprojects.htm#hdds). The HDDS includes hospitalization and ED visit data for all Tennessee residents for all nonfederal Tennessee hospitals, including patient date of birth, dates of admission and discharge, and discharge diagnoses (http://health.state.tn.us/statistics/specialprojects.htm#hdds).

Ethical Considerations

NVSN and Influenza Vaccine Effectiveness Surveillance Network protocols were approved by the institutional review boards of Vanderbilt, other surveillance hospitals, and CDC.

Estimates of Influenza-related Visits

For these calculations, we applied previously described surveillance-sampling methods, and used data from HDDS and CDC-sponsored surveillance studies.[8,18,19,22] We defined an ARI/fever visit as any hospitalization or ED visit with the following *International Classification of Diseases, Ninth Revision, Clinical Modification* discharge diagnosis codes: pneumonia and influenza (480–487), bronchitis (490), asthma (493), acute respiratory infections including bronchiolitis (460–466), dyspnea and respiratory abnormalities (786), fever (780.6), and otitis media (381–382).[6,23] Previous medical record review indicated that these discharge codes were assigned to most study participants presenting with ARI/fever, including 98% of influenza-positive and 80% of influenza-negative enrollees.[18] We calculated the proportion of study hospitalizations and ED visits that were due to influenza. We multiplied these proportions by the number of ARI/fever hospitalizations and ED visits by age-eligible county residents identified from the HDDS to estimate the total number

of influenza-related hospitalizations in county residents aged 6 to 59 months each influenza season.

Definition of Influenza Season

Influenza surveillance began the first week of November or the first week when influenza virus was detected in 2 or more hospitalized patients at one of the surveillance hospitals, whichever came first,[17] except for the unusual year 2009–2010 during the H1N1 pandemic, in which surveillance began on May 3, 2009, and ended on December 5, 2009. The influenza season encompassed all consecutive weeks when influenza viruses were circulating in Davidson County as determined by influenza virus strains detected in the Vanderbilt Hospital Clinical Laboratory.

Similarity Between Circulating and Vaccine Viruses

We determined the degree of similarity between circulating strains and vaccine strains using antigenic characterization data from local viruses and CDC data.[24–26] The degree of similarity was calculated as the product of 2 proportions: the proportional distribution of influenza A(H1N1), A(H3N2), and B viruses circulating and the proportion of each virus strain that was antigenically related to the strains included in the commercially available vaccine for each season (see Supplemental Figures) based on CDC criteria (http://www.cdc.gov/flu/weekly/weeklyarchives2004-2005/04-05summary.htm).

Vaccination Coverage

To estimate population vaccination coverage, we determined vaccination status of study children who tested negative for influenza, based on both parental report and confirmation through provider record review. Study children were considered vaccinated if they received 2 doses of influenza vaccine in the current season or 1 dose if the child was vaccinated in the previous season except for 2009–2010 when 2 doses of the monovalent pandemic vaccine were required.[12]

Statistical Analysis

Each influenza season was divided into 8-week periods, with the last period <8 weeks when the total weeks encompassing the season was not a multiple of 8. The proportions of influenza-related hospitalizations and ED visits for each period were reported and their 95% confidence intervals (CIs) were computed using the Wilson method for the binomial distribution.[27] HDDS data were assumed to provide complete enumeration of ARI/fever-related hospitalizations and ED visits. To estimate the number of influenza-related hospitalizations and ED visits with their 95% CIs, we multiplied our proportions and the upper and lower bounds of their CIs by the number of ARI/fever-related hospitalizations and ED visits from the HDDS in each period.[18,19] The estimated total number of influenza-related encounters for each season was calculated by summing estimated numbers from the seasonal periods. We computed the rate by dividing these numerators by the population of Davidson County children age 6 to 59 months for each year by using July Census estimates (http://factfinder2.census.gov/faces/nav/jsf/pages/community_facts.xhtml). Poisson regression models were used to assess trends in rates of hospitalization and ED visits throughout all 11 study seasons. Seasons were represented by using a restricted cubic spline function with 3 knots to increase the flexibility of the model.[28] Poisson regression also was used to assess trends in vaccine uptake. We included in the basic model, the seasonal periods, the estimates of influenza-related hospitalizations and ED visits, and the population estimates for each year. To explore the sensitivity of our estimates for selected seasons that were outliers, separate analyses were conducted excluding the 2009–2010 pandemic season, for which vaccine was unavailable for most of the season, and the 2003–2004 season, which was atypical in timing and severity. We also compared the median estimates of influenza-related hospitalization and ED visits for the seasons in which influenza A(H3N2) predominated to the remaining seasons by using binomial approximations.[29,30] We compared baseline characteristics of enrolled participants by using Pearson χ^2 tests. We considered $P < .05$ as statistically significant. All analyses were conducted by using Stata version 10 (Stata Corp, College Station, TX).

RESULTS

Study Population

The Davidson County population increased from 570 000 to 628 000 over the study years, with the proportion age <5 years ~7% in both years. There was little change in the proportion of white (~65%) or black (~27%) children, but there was an increase in Hispanic children from ~5% to 10%. During the study years, we enrolled a median of 87% of eligible children. Baseline characteristics among enrolled subjects remained relatively stable throughout the study period, with medians of 56% (49–62) girls, 43% (39–49) white, 35% (30–40) black, and 98% (97–99) insured. Paralleling changes in the population, the proportion of Hispanic children enrolled increased from 6% in 2000 to 12% in 2010.

Influenza Hospitalizations and ED Visits

With the exception of the pandemic influenza period in 2009, seasonal influenza activity spanned from 8 to 18 weeks (median 15 weeks) (Table 1). During these 10 seasons, the proportion of ARI/fever visits in which influenza was detected ranged

from 5% to 50% for hospitalizations (median 13%) and 10% to 48% for ED visits (median 15%). During these same periods, we identified 106 to 206 ARI/fever hospitalizations (median 142) and 3100 to 5619 ARI/fever ED visits (median 4422) among Davidson County children aged 6 to 59 months (Fig 1 A and B). From May 3 to December 4, 2009, there was only 1 wave of pandemic influenza in children, encompassing 31 weeks of continuous circulation. The proportion of ARI/fever visits in which influenza was detected was 6% for hospitalizations and 10% for ED visits. However, during peak influenza A(H1N1)pdm09 activity, August 23 through October 17, influenza was detected in 18% and 32% children with hospitalizations and ED visits, respectively.

The estimated number of influenza-related hospitalizations ranged from a high of 60 to a low of 7 annually, yielding respective rates of 16.0 (95% CI 10.9–20.8) in 2003–2004 and 1.9 (0.5–6.0) in 2002–2003 per 10 000 Davidson County children aged 6 to 59 months (Tables 1 and 2). The median hospitalizations per 10 000 children were 4.5 (95% CI 1.9–11.1) for the 10 non pandemic seasons and 5.2 (2.3–12.6) during the pandemic.

TABLE 1 Data Used to Derive the Influenza-related Health Care Encounters in Children 6 to 59 Months in Davidson County, TN, During 11 Consecutive Influenza Seasons

Season (*n* wk)	No. of Acute Respiratory Illness Visits		% Influenza Detected		Estimated No. of Influenza-associated Visits	
	Hospital	ED	Hospital	ED	Hospital	ED
2000–01 (8)	119	NA	10.8	NA	13	NA
2001–02 (14)	146	NA	17.7	NA	29	NA
2002–03 (11)	126	3005	5.3	11.7	7	351
2003–04 (10)	138	4422	47.2	48.4	60	2324
2004–05 (13)	106	NA	27.1	NA	28	NA
2005–06 (15)	151	3814	15.9	9.8	20	352
2006–07 (18)	206	4983	5.7	11.8	10	575
2007–08 (17)	187	4678	13.8	27.5	35	1258
2008–09 (15)	136	4174	7.4	14.9	11	584
2009–10 (46)	476	12 447	4.3	7.6	22	1238
2010–11 (16)	192	5619	8.3	24.2	16	1418

NA, not applicable, no ED surveillance done in 3 study years.

The estimated number of influenza-related ED visits ranged from a high of 2324 to a low of 352 visits annually, yielding respective rates of 620 (95% CI 489–757) in 2003–2004 and 89 (32–244) in 2005–2006 per 10 000 Davidson County children aged 6 to 59 months (Tables 1 and 2). The median ED visits per 10 000 children were 143 (95% CI 58–320) for the 10 non pandemic seasons and 290 (137–540) during the pandemic.

Influenza-related hospitalizations tended to decrease over time in

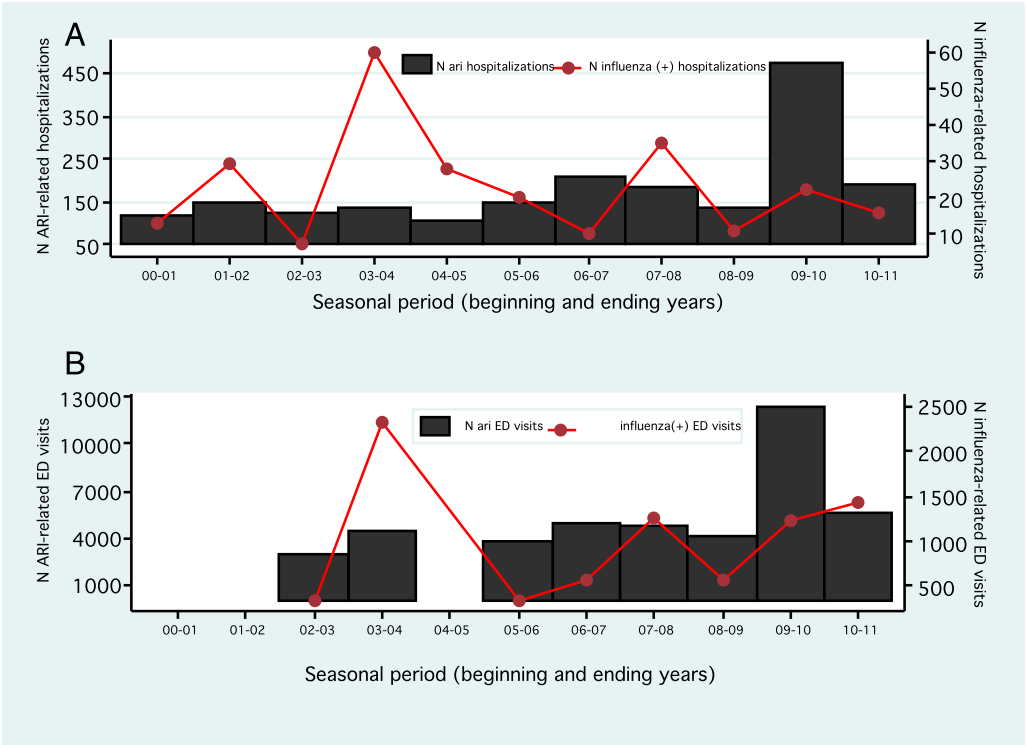

FIGURE 1
Total number of ARI/fever visits (bar) for Davidson County children 6 to 59 months from the Tennessee HDDS, and total estimated influenza-associated ARI/fever visits (connected line) for (A) hospitalizations and (B) ED visits over 11 consecutive influenza seasons from 2000–2001 through 2010–2011.

TABLE 2 Estimates of Vaccine Uptake and Influenza-related Health Care Encounters per 10 000 Children 6 to 59 Months in Davidson County, TN, During 11 Consecutive Influenza Seasons

Season (*n* wk)	Predominant Influenza Strain	% Circulating and Vaccine Strains Similar[a]	% Vaccinated (95% CI)	Influenza Hospitalizations Per 10 000 (95% CI)	Influenza ED Visits Per 10 000 (95% CI)
2000–01 (8)	A(H1N1)	56	5.9 (2.7–12.2)	3.8 (1.5–8.5)	NA
2001–02 (14)	A(H3N2)	90	1.9 (0.8–4.9)	8.2 (5.3–18.0)	NA
2002–03 (11)	A(H1N1)	97	1.5 (0.3–8.2)	1.9 (0.5–6.0)	96 (46–205)
2003–04 (10)	A(H3N2)	11	5.1 (3.0–8.5)	16.0 (10.9–20.8)	620 (489–757)
2004–05 (13)	A(H3N2)	32	18.5 (15.5–21.9)	7.2 (4.1–12.1)	NA
2005–06 (15)	A(H3N2)	63	16.9 (13.1–21.4)	5.0 (2.5–11.3)	89 (32–244)
2006–07 (18)	Influenza B	60	14.2 (10.6–18.7)	2.5 (1.0–7.7)	143 (58–320)
2007–08 (17)	A(H3N2)	25	22.9 (18.9–27.5)	8.5 (4.1–13.2)	307 (204–444)
2008–09 (15)	Influenza B	84	27.7 (23.7–32.0)	2.6 (0.9–6.2)	139 (72–268)
2009–10 (46)#	A(H1N1)pdm09	95	8.0 (5.0–10.0)	5.2 (2.3–12.6)	290 (137–540)
2010–11 (16)	Influenza B	98	38.0 (25.0–46.0)	4.0 (1.2–10.9)	353 (229–513)

[a] Percentage of circulating strains present in the vaccine for the seasonal period based on local data except in 2006–2007 in which we used CDC data because local data were inconclusive. Pandemic vaccine became available late in the epidemic. NA, not available.

models that both included and excluded the pandemic year 2009–2010 ($P < .05$) (Fig 2). When we excluded the 2003–2004 season, the year with the highest hospitalization rate, this reduction was no longer statistically significant ($P = .442$) (Table 3). Influenza-related ED visits increased over time both including and excluding the pandemic year 2009–2010 or the 2003–2004 season ($P < .05$) (Supplemental Figures).

Overall, influenza A(H3N2) predominated during 5 seasons, including 3 consecutive seasons from 2003–2004 through 2005–2006 (Table 2). Influenza B predominated during 3 seasons including 2006–2007, 2008–2009, and 2010–2011. Influenza A(H1N1) predominated in only 2000–2001 and 2002–2003. Influenza A(H1N1)pdm09 emerged and predominated in 2009–2010. During the years when influenza A (H3N2) predominated, influenza-related hospitalization rates were greater (range 5.0–16.0, median 8.2) than in the other 6 years (range 1.9–5.2, median 3.2, $P < .05$). Influenza-associated ED visit rates were also greater when influenza A(H3N2) circulated (range 89–620, median 307) than in the other 5 years (range 100–353, median 143, $P < .05$).

Similarity Between Circulating and Vaccine Viruses

The degree of similarity between circulating influenza strains and vaccine components ranged from 11% in 2003–2004 to 99% in 2002–2003 and 2009–2010. Influenza-related hospitalizations and ED visits were highest in 2003–2004 followed by 2007–2008, when there was an especially poor match between the A (H3N2) virus circulating and the vaccine strain (Table 2) (Supplemental Figures).

Changes in Estimated Vaccination Coverage

The proportion of children completely vaccinated remained <6% from 2000 through 2004, before influenza vaccine was routinely recommended for all children, However, vaccine uptake increased progressively and was highest in 2010–2011 when 38% of the enrolled children were completely vaccinated. An exception was the low uptake during the pandemic of 2009–2010, when pandemic-strain influenza vaccine was not available until late in that season (Table 2). Overall, full vaccination coverage increased over time but remained <50%, whether the pandemic year 2009–2010 was included ($P < .001$, Fig 2 and Table 3).

DISCUSSION

During 11 consecutive influenza seasons, influenza-associated illnesses accounted for a median of 11% of all ARI/fever hospitalizations and 14% of all ARI/fever ED visits among children <5 years during a median of 15 weeks when influenza was in circulation. During the pandemic year, 2009–2010, we observed low proportions of both ARI/fever hospitalizations and ED visits in which influenza was detected; however, overall rates of influenza-associated encounters were similar to those during nonpandemic years due to a high proportion of influenza during the pandemic peak coupled with the long season. Overall influenza-related hospitalizations tended to decrease over time, whereas influenza-related ED visits increased over time in models that both included and excluded the pandemic year 2009–2010. However, the decline in hospitalizations was sensitive to exclusion of 2003–2004, and neither of these trends was clearly related to the increasing trend in vaccination coverage.

Influenza vaccination coverage increased gradually from 2004–2005 when universal vaccine was recommended for all children 6 to 23 months, peaking at 38% in 2010–2011. It also increased over time in models that both included and excluded the pandemic year 2009–2010. However, our estimates of vaccine coverage confirmed by medical record review were lower than those of the National Health Interview Survey that was based on a different assessment method

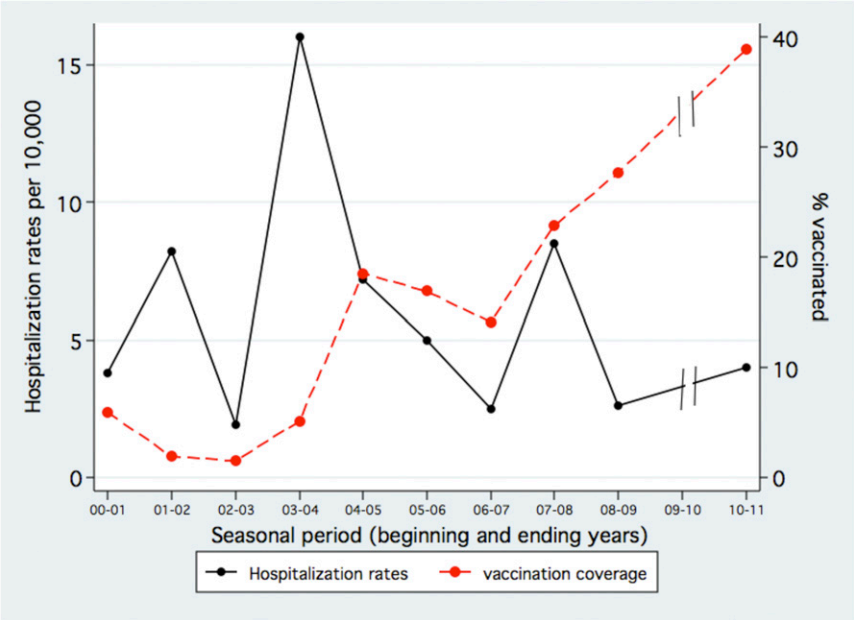

FIGURE 2
Influenza-related hospitalizations per 10 000 children age 6 to 59 months living in Davidson County, TN, and influenza vaccine coverage for 11 consecutive influenza seasons from 2000–2001 through 2010–2011.

(http://www.cdc.gov/nchs/data/nhis/earlyrelease/201012_04.pdf).

Our estimates of influenza-related hospitalization rates were consistent with those of Poehling et al,[17] who estimated influenza-related hospitalizations in 3 US communities, including Nashville, Davidson County, TN, from 2004 to 2009 by using a weighted method to account for days of surveillance and the proportion of children enrolled. That study found 4 to 10 influenza-related hospitalizations per 10 000 children aged 0 to 59 months with the highest rates noted in 2007–2008 and the lowest in 2008–2009. However, our ED visit rates are higher likely related to differences in age groups and location.[7,8]

Influenza-related hospitalizations tended to decrease modestly over the period with progressive increase in the vaccination coverage. However, this reduction was no longer statistically significant in a sensitivity analysis that excluded 2003–2004, which had low vaccination coverage and poor similarity between circulating and vaccine strain. This is in contrast to the findings of Kwong et al,[31] who evaluated the impact of universal influenza vaccine on health care visits in Ontario and reported a reduction in hospitalizations, ED visits, and outpatient visits in children <5 years. ED visits in Davidson County in this report remained elevated and actually increased despite the increase in vaccination coverage whether we included 2003–2004 or the pandemic year 2009–2010 in the models. Changes in insurance or availability of nonemergency outpatient care, or institution of ED observation units might have affected trends in both ED visit and hospitalization rates.[32,33] In addition, other factors, such as circulating influenza strain and increased awareness about influenza, could have increased use of the ED.

Overall influenza vaccination coverage remained low (<50%) in children <5 years, and it is likely that substantially greater vaccination coverage levels and/or new vaccination strategies will be required before broad population-level decreases in rates of influenza-associated medical visits can be documented. Earlier reported influenza vaccine effectiveness studies in this population combined with 2 other sites reported vaccine effectiveness estimates of 44%, 57%, 48%, 65%, and 56% for 5 consecutive influenza seasons 2003–2004 through 2007–2008.[14,34] In June 2014, the Advisory Committee on Immunization Practices recommended the preferential use of live attenuated influenza vaccine over inactivated vaccine in children aged 2 to 8 years, based on studies showing higher effectiveness of live vaccine in young children.

Our estimates of influenza-related hospitalization rates were consistent with previous studies demonstrating a higher likelihood of influenza A (H3N2) causing severe disease in comparison with other strains of influenza.[35–37] It may be that influenza vaccine is also less effective for these strains. Interestingly, Black et al[38] evaluated immunogenicity and efficacy of 1 influenza A(H3N2) vaccine in 4707 children 6 to 71

TABLE 3 Regression Coefficient and *P* Value Obtained for Trend in Vaccine Coverage, Influenza-related Hospitalization Rates, and Influenza-related ED Visits Over Time in Children 6 to 59 Months in Davidson County, TN, During 11 Consecutive Influenza Seasons

Models Assessing Trends	Regression Coefficient	*P* Value
Vaccine coverage, all years	9.87	<.001
Vaccine coverage, excluding 2009–2010	13.5	<.001
Influenza-related hospitalization rates, all years	−1.98	.048
Influenza-related hospitalization rates, excluding 2009–2010	−2.20	.028
Influenza-related hospitalization rates, excluding 2003–2004	−0.77	.442
Influenza-related ED visit rates, all years	18.44	<.001
Influenza-related ED visit rates, excluding 2009–2010	17.84	<.001
Influenza-related ED visit rates, excluding 2003–2004	5.37	<.001

months of age, in the presence and absence of adjuvant, and suggested that young children needed higher antibody titers for protection than the conventionally cited hemagglutination inhibition titer of 1:40.

Of note, all 6 seasons (including 2003–2004) with higher hospitalization rates than the median had either low vaccination coverage or poor similarity between circulating and vaccine strains. However, the 2003–2004 season was unusual for several reasons, including the circulation of a drifted influenza A(H3N2) virus and the poor similarity with the available vaccine components.[24] The emergence of influenza A(H1N1)pdm09 makes the 2009–2010 season unique, and difficult to compare with seasonal periods. Furthermore, the pandemic vaccine was not widely available until the latter weeks of peak virus circulation.[39]

This study estimated the incidence of laboratory-confirmed influenza-related hospitalization or ED visits over 11 consecutive years, including the 2009–2010 pandemic. Estimating the incidence of influenza-related medical encounters during this relatively long period by using the same methods to identify children hospitalized or receiving care in the ED provided an opportunity to examine the variability in disease burden and the possible effects of changes in vaccine recommendations on vaccination coverage. Although there was a significant reduction of influenza-related hospitalizations over time, this finding was sensitive to exclusion of the 2003–2004 season, which suggests that the reduction is likely driven in part by that season. Also, our study period did not provide enough years of data to assess the seasonal trend, predominant strain, and degree of similarity between circulating strain and seasonal vaccine in a single model. Continuing evaluation will be needed to assess the impact of influenza vaccine recommendations. Finally, the generalizability of results from 1 geographic region over 11 seasons is limited.

CONCLUSIONS

Influenza vaccination of children increased over time, particularly since 2004–2005 when influenza vaccination was recommended for children ages 6 to 23 months; however, vaccination remained <50%. Influenza still causes substantial burden in young children. Optimal vaccine uptake with good match between circulating and vaccine strains has the potential for reducing disease burden in young children. More data are needed to assess long-term trends in influenza-associated medical care use in children.

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