Trivalent Inactivated Influenza Vaccine Is Not Associated With Sickle Cell Crises in Children

WHAT'S KNOWN ON THIS SUBJECT: Children with sickle cell disease are at high risk of complications from influenza infection and have been recommended to receive annual influenza vaccine since the 1970s. Few safety studies, however, have examined the safety of influenza vaccine in this population.

WHAT THIS STUDY ADDS: This large cohort study did not find an association between influenza vaccination and hospitalization for sickle cell crises in children with sickle cell anemia.

abstract

FREE

BACKGROUND AND OBJECTIVES: Children with sickle cell disease are considered at high risk for complications from influenza infection and are recommended to receive annual influenza vaccination. However, data on the safety of influenza vaccination in children with sickle cell anemia are sparse.

METHODS: Using a retrospective cohort of children aged 6 months to 17 years in 8 managed care organizations that comprise the Vaccine Safety Datalink and who had a diagnosis of sickle cell anemia from 1999 to 2006, we conducted matched case-control and self-controlled case series studies to examine the association of trivalent inactivated influenza vaccination with hospitalization for sickle cell crisis in the 2 weeks after vaccination.

RESULTS: From an original pool of 1085 pediatric subjects with a diagnosis of sickle cell anemia, we identified 179 children with at least 1 sickle cell crisis during any influenza season (October 1–March 31). In the matched case-control study (matching on age category, gender, Vaccine Safety Datalink site, and season), the odds ratio of hospitalization for a crisis in vaccinated compared with unvaccinated children was not significant: 1.3 (95% confidence interval 0.8–2.2). In the self-controlled case series study of hospitalized cases, the incident rate ratio for hospitalization with sickle cell crisis in the 2 weeks after trivalent inactivated influenza vaccination was also not significant: 1.2 (95% confidence interval 0.75–1.95).

CONCLUSION: This large cohort study did not find an association of influenza vaccination and hospitalization for sickle cell crises in children with sickle cell anemia. *Pediatrics* 2012;129:e54–e59

AUTHORS: Simon J. Hambidge, MD, PhD,[a,b,c,d] Colleen Ross,[a] Jason Glanz, PhD,[a,d] David McClure, PhD,[a] Matthew F. Daley, MD,[a,c] Stan Xu, PhD,[a] Jo Ann Shoup, MA, MSW, MS,[a] Komal Narwaney, MD, MPH,[a] James Baggs, PhD,[e] Eric Weintraub, MPH[e] and the Vaccine Safety Datalink Team

[a]Institute for Health Research, Kaiser Permanente Colorado, Denver, Colorado; [b]Department of Community Health Services, Denver Health, Denver, Colorado; [c]Department of Pediatrics, University of Colorado School of Medicine, Aurora, Colorado; [d]Department of Epidemiology, University of Colorado School of Public Health, Aurora, Colorado; and [e]Immunization Safety Office, Division of Healthcare Quality and Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

KEY WORDS

children and adolescents, childhood immunization, influenza vaccine, sickle cell disease, vaccines

ABBREVIATIONS

CI—confidence interval
ICD-9-CM—*International Classification of Diseases, Ninth Revision, Clinical Modification*
MCC—matched case control
MCO—managed care organization
TIV—trivalent inactivated influenza vaccine
SCCS—self-control case series
VSD—Vaccine Safety Datalink

The findings and conclusions in this report are those of the authors and do not necessarily represent the views or policies of the Centers for Disease Control and Prevention or America's Health Insurance Plans.

Dr Hambidge, who is the principal investigator, made substantial contributions to conception and design of the study, acquisition of data, and analysis and interpretation of data; drafted the article and revised it critically for important intellectual content; and had final approval of the version to be published. Ms. Ross, who is the lead analyst, made substantial contributions to acquisition of data and to analysis and interpretation of data; drafted the article; revised it critically for important intellectual content; and had final approval of the version to be published. Drs Glanz McClure, Daley, and Xu, Ms Shoup, and Dr Narwaney made substantial contributions to the design of the study, analysis and interpretation of data, and critical revision of the article for important intellectual content; they had final approval of the version to be published. Dr Baggs and Mr Weintraub made substantial contributions to the design of the study and revised the article critically for important intellectual content; they had final approval of the version to be published. The Vaccine Safety Datalink working group made substantial contributions to the design of the study, revised the article critically for important intellectual content, and had final approval of the version to be published.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-1294

doi:10.1542/peds.2011-1294

Accepted for publication Sep 19, 2011

(Continued on last page)

There are an estimated 31 000 children with sickle cell disease in the United States.[1] These children are at increased risk of complications from influenza infection[2] and since the 1970s have been recommended to receive annual influenza vaccination.[3] However, there are sparse data on the safety of influenza vaccine in this population. In a large population-based study of the safety of more than 69 000 influenza vaccines administered to more than 45 000 children aged 6 to 23 months, a small number of children had sickle cell disease. In these children, there was an elevated but nonsignificant association of influenza vaccination with hospitalization for a sickle cell crisis in the 14 days after vaccination.[4] On the basis of these results, we undertook a large case-control study of all children with sickle cell disease in the Vaccine Safety Datalink (VSD) over a period 7 years (1999–2006). We asked whether influenza vaccination is temporally associated with hospitalization for sickle cell crises in this population.

METHODS

Study Setting and Population

The setting for this study was the 8 managed care organizations (MCOs) sites across the United States that comprise the VSD, a Centers for Disease Control and Prevention–funded project that links large databases and additional administrative and medical information from MCOs.[5,6] The institutional review boards at each of the MCOs approved this study. The study population included all children in the VSD cohort from 1999 to 2006 with a diagnosis of sickle cell anemia in any medical setting (outpatient, emergency department, or inpatient).

A potential case was any child in the automated data of the MCOs aged 6 months through 17 years who was hospitalized with a primary diagnosis of sickle cell anemia and who was continuously enrolled in the MCO during the influenza season of hospitalization. We used the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code of sickle cell anemia (ICD-9 282.6×) to identify children with sickle cell disease during the time of year when most influenza vaccine is administered (October 1–March 31 of each year). If a child was hospitalized more than once during a given influenza season, only the first hospitalization was used in the analysis. Hospitalizations over multiple influenza seasons for the same child were treated as independent events.

Medical Record Review

The medical records of potential cases were reviewed to confirm hospitalization for sickle cell crises, including pain crisis, acute chest syndrome,[7] and splenic sequestration crisis. At 1 VSD site, only a subset of electronically identified potential cases with ICD-9-CM code 282.62 (sickle cell crisis) was reviewed to confirm case status (100 of 179, or 56%). Four hundred thirty-nine charts were reviewed by 2 abstractors who were blinded to vaccination status. Abstractors used a standard chart review tool to confirm a sickle cell crisis and entered the data into a Microsoft Access database. Both reviewers' data were compared using SAS version 9.1 (SAS Institute, Cary, NC), and all discrepancies were resolved by a board-certified pediatrician. We did not review charts of control children to confirm either the diagnosis of sickle cell disease or vaccination status.

Study Design

Our primary study design was a matched case-control (MCC) with the date of hospitalization for sickle cell crisis set as the index date. Children with chart-confirmed hospitalization for sickle cell crises (the "cases") were matched with 4 control subjects who also had sickle cell anemia but were not hospitalized with a sickle cell crisis from 14 days before to 14 days after the case's hospitalization index date. Cases were matched with 4 controls using index date of hospitalization, VSD site, gender, and age category (6–23 months, 24–59 months, 60 months–17 years). For 21 cases, only 1 to 3 controls were available for matching across all 4 categories. Because each control was matched by VSD site and the date of hospitalization of the index case, this design implicitly controls for seasonal fluctuations of sickle cell crises. Vaccination status was assessed retrospectively after assignment of case or control status; a case or control child who received influenza vaccine within 14 days before the index date was classified as "exposed." Two cases could not be matched to any controls and were excluded from the analysis.

To avoid bias by indication (children more likely to be hospitalized with sickle cell crises may also be more likely to receive influenza vaccine), we used a case-only design (the self-controlled case series, or SCCS design)[8] in which each case acts as its own control; only vaccinated cases were analyzed. The SCCS method controls for both measured and unmeasured confounding and has been shown to be as powerful as a full cohort study when exposure (ie, vaccine coverage) rates are high and the risk periods after vaccination are brief.[9]

Exposure

The exposure of interest was trivalent inactivated influenza vaccine (TIV). For young children who received 2 influenza vaccines in their first season of vaccination, as recommended,[10] both vaccines were included in the analysis. For all cases and controls, we examined exposure to TIV in a 14-day risk window before the index date of hospitalization

for the case. We used a 14-day risk window as the usual complications from an inactivated vaccine, such as fever, are seen within a relatively short time window after vaccination.[4,11]

Analysis

Because the number of TIV doses declines sharply in the latter part of the influenza season (data not shown), there is little chance of finding an exposed case after January. Therefore, we limited the analysis to periods when most TIV was administered, between October 1 and January 31 of each influenza season.[12] This resulted in the removal of 3 TIV-exposed children who were vaccinated in the months of February or March. For the matched case-control study, we used conditional logistic regression to calculate matched odds ratios and 95% confidence intervals (CIs). For the SCCS design, we used conditional Poisson regression to estimate the incidence rate ratios and 95% CIs for hospitalization with sickle cell crisis in the 14 days after TIV compared with a 14-day control period either before vaccination or after the 14-day risk window. For all SCCS analyses, we adjusted for within-season calendar time by including month of the year as a categorical variable in the models. In addition to the main SCCS analysis, we also analyzed outcomes stratified by age and gender.

RESULTS

There were, on average, 2.2 million children per year aged under 18 years in the VSD cohort from 1999 to 2006, of which 1085 children had a diagnosis of sickle cell anemia during influenza season (October 1 to March 31). In electronic administrative data, there were 439 potential hospitalizations for sickle cell pain crises, for which 404 charts were available for review and 241 were unique for individual children in separate influenza seasons (Fig 1).

Table 1 depicts selected characteristics of the children in the SCCS design and the cases and controls in the MCC design. Of the 269 chart-confirmed hospitalizations, 48 (18%) occurred in children aged younger than 5 years. There was a trend toward higher hospitalization rates for sickle cell crisis earlier in the study; the rate of hospitalization for sickle cell crises in all children with sickle cell disease dropped from 6 to 7 per 100 children in the first 5 years to 4 to 5 per 100 children in the last 2 years of the study. Figure 2 depicts seasonal variation in receipt of influenza vaccine and hospitalization for sickle cell crisis, by week. Over all 7 years of the study, influenza vaccination peaked between the week of October 15 and November 12, whereas hospitalization for sickle cell crises remained relatively high from October 1 through December 17, before declining in later December and January.

In the MCC study, after matching cases to controls on age category, gender, VSD site, and influenza season, the risk of hospitalization for sickle cell crisis in the 2 weeks after influenza vaccination was 1.3 (odds ratio 1.2, 95% CI 0.8–2.2) in vaccinated children (Table 2). In the SCCS study, the incident rate ratio for hospitalization for pain crisis or fever in the 2 weeks after influenza vaccination was 1.2 (incidence rate ratios 1.2, 95% CI 0.75–1.95) compared with control time periods unrelated to vaccination (Table 3). There was no significant association of influenza vaccination with hospitalization by gender or age group. No children aged 24 to 59 months were hospitalized for sickle cell crisis in the 2 weeks after influenza vaccination.

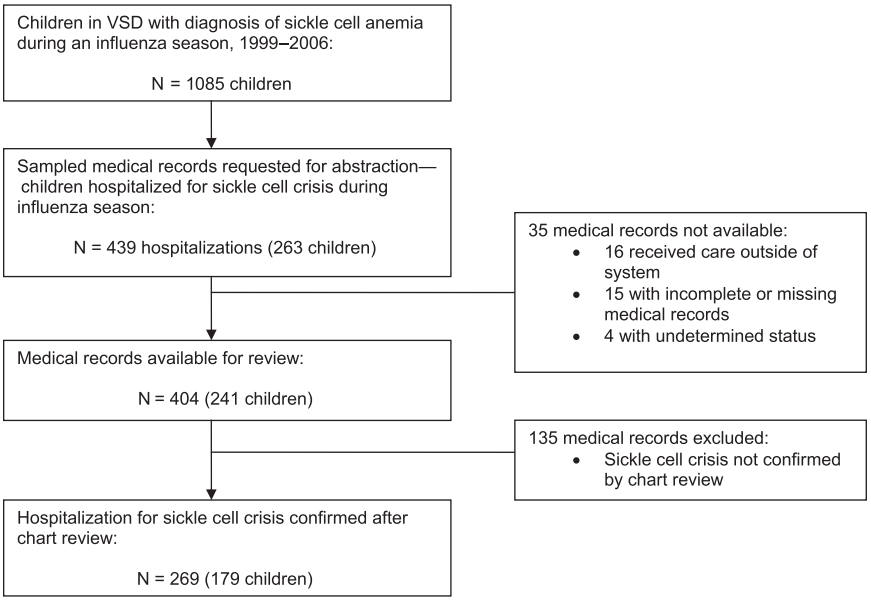

FIGURE 1
Identification of children with sickle cell crisis in the VSD cohort.

DISCUSSION

Our study adds to the sparse literature on the safety of TIV,[13] or other types of influenza vaccine,[14,15] in children with sickle cell disease. The study design allowed us to identify sickle cell crisis events with individual-level electronic data and validate exposure and outcomes through detailed medical record review, a strength of the VSD.

We studied a cohort of 269 children aged 6 months through 17 years with sickle cell disease and hospitalized during an influenza season, to identify any associated risk of sickle cell crises

TABLE 1 Characteristics of Children in Different Study Populations

	Children in SCCS Design[a]	Cases in MCC Design[b]	Controls in MCC Design[c]
Vaccination season			
October 1, 1999—March 31, 2000	22	41	154
October 1, 2000—March 31, 2001	20	46	184
October 1, 2001—March 31, 2002	22	44	164
October 1, 2002—March 31, 2003	24	48	179
October 1, 2003—March 31, 2004	24	40	151
October 1, 2004—March 31, 2005	16	25	96
October 1, 2005—March 31, 2006	19	25	97
Vaccination month			
September	2		1
October	59		215
November	60		261
December	22		99
January	1		26
February	2		
March	1		
Gender			
Male	66	126	482
Female	81	143	543
Age			
6–23 mo	12	20	71
24–59 mo	18	28	99
60 mo–17 y	117	221	855
Total	147	269	1025

Hospitalizations of the same child in different influenza seasons are reported as independent events. In all, 179 children were hospitalized 269 times.

[a] Children vaccinated with TIV during the same influenza season when they were hospitalized for a sickle cell crisis.

[b] Children hospitalized with sickle cell crisis during an influenza season; not all are vaccinated.

[c] Children not hospitalized with sickle cell crisis during the 28 days surrounding the hospitalization of the matched case.

TABLE 2 Results of MCC Study Design

Case Control Ratio	Cases, *n*	Matched Controls, *n*[a]
	8	1
	6	2
	7	3
	246	4
Influenza Vaccination History	Controls	Cases
Not vaccinated in risk window[b]	962	248
Vaccinated in risk window	63	21
Vaccinated, %	6.2	7.8
	Odds Ratio	95% CI
	1.3	0.8–2.2

[a] Matched on index date of hospitalization (and therefore influenza season), age category (6–23 mo, 24–59 mo, 60 mo–17 y), VSD site, and gender. Two cases could not be matched to any controls and were excluded from the analysis.

[b] Risk Window = 2 weeks prior to sickle cell crisis hospitalization date (cases) or matched index date (controls).

with influenza vaccine. The study screened more than 2 million children from 8 MCOs across 7 influenza seasons. Most of the hospitalizations (82%) occurred in children aged 5 to 17 years. Of note, we found the rate of hospitalization for sickle cell crisis was greater in earlier years of the study, possibly suggesting improvements in outpatient management of sickle cell disease. In addition, the percent of children immunized against influenza increased from 43% in 2000–2001 to 76% in 2005–2006, likely reflecting secular trends in pediatric influenza vaccination practices.

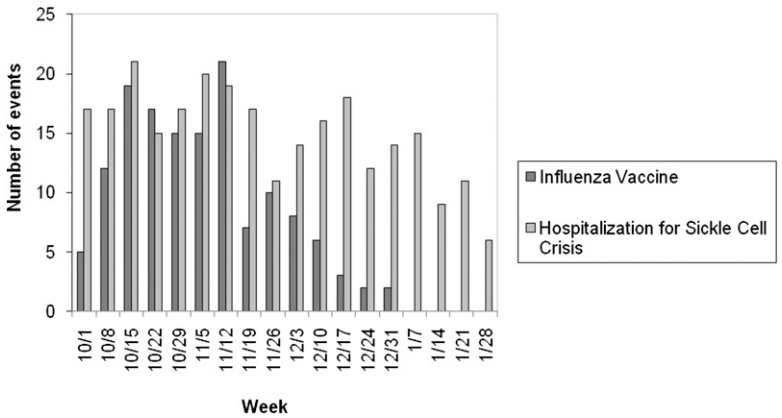

FIGURE 2
Number of influenza vaccinations and hospitalizations for sickle cell crises by week, 1999–2006. In addition to these influenza vaccinations, 2 children received influenza vaccine in September over the 7 years of this study. These vaccines are included in the analysis but not depicted in the graph.

Across all analyses (MCC and SCCS), we found no statistically significant risk of hospitalization for sickle cell crisis within the 2 weeks after TIV in children aged 6 months through 17 years. These results offer reassurance to patients, families, and caregivers to children with sickle cell disease that influenza vaccine can be safely used to prevent the sequelae of influenza virus in this population.

There are several potential limitations to our study. Children who received influenza vaccine outside of their MCO could bias the results by inappropriately being classified as unexposed. If these children present for care at their MCO, their outside vaccination records should be entered into the MCO's immunization registry, but the rate of outside vaccine capture varies by MCO.[16] Also, the influenza season is associated with a decrease in weather temperature, which is a known trigger for pain crisis and possibly introduces temporal bias in the analysis. There may have been bias by indication: children with more severe disease may be more likely to be vaccinated and to be hospitalized. Such

TABLE 3 Results of Self-Controlled Case Series Design

Model	IRR	95% CI	*p* Value	*n*	TIV Exposure[a]	No TIV Exposure
All children	1.21	0.75–1.95	.43	144[b]	21	123
Boys	1.07	0.50–2.28	.86	63	8	55
Girls	1.33	0.72–2.44	.36	81	13	68
Age						
6–23 mo	1.23	0.25–6.04	.80	11	2	9
24–59 mo	NA			17	0	17
60 mo–17 y	1.38	0.83–2.29	.22	116	19	97

IRR, incidence rate ratio; NA, not applicable; cannot calculate IRR because there were no case children with exposure to TIV. All analyses adjusted for month of year.

[a] In 2 weeks before hospitalization for sickle cell crisis.

[b] Three children excluded (compared with Table 1) because they received influenza vaccine late in influenza season, when it is highly unlikely they could be an exposed case (see Analysis section of Methods).

a bias has been shown in children with asthma[17] but would lead to a falsely elevated association between vaccination and hospitalization and is not suggested in our results because the point estimates of both the MCC and the SCCS studies are the same. If there were bias by indication, the point estimates of the MCC design should be elevated compared with the SCCS. We did not review the charts of all potential cases because of sampling at 1 site; however, we did review 404 of 518 potential charts (78%); 79 were not sampled, and 35 medical records were not available. Finally, we did not review the charts of control children to confirm the diagnosis of sickle cell disease nor vaccination status. However, if this lack of chart review had introduced bias into the analysis, the results of the MCC design (which uses controls) and the SCCS design (which does not) would differ, but the point estimates of the 2 designs were identical.

These findings will help to inform ongoing policy recommendations for influenza vaccine for children with sickle cell anemia, considered a high-risk population by the Advisory Committee on Immunization Practices recommendations since the 1970s.[18] Because the risk of hospitalization due to influenza complications in children with sickle cell disease is 56-fold compared with children without sickle cell disease,[2] our study findings will provide valuable information to clinicians seeking to reassure parents of children with sickle cell disease about the safety of annual influenza vaccination.

ACKNOWLEDGMENTS

Financial support for this study was provided in full [if applicable; in part] by the Centers for Disease Control and Prevention (contract number 200-2002-00732), through America's Health Insurance Plans.

We thank the following individuals for their medical records review: Kaiser Permanente Colorado: Kate Burniece; Harvard Pilgrim Health Care: Grace Lee; Southern California Kaiser: Sarah Fisher, Zendi Solano, Nancy Canul, and Ana Espinosa Rydman; Kaiser Foundation Hospital Center for Health Research: Kristina Booker; Northern California Kaiser Permanente: Pat Ross, Sandy Bauska, and Barry Nichols.

We thank the following individuals for project management support: Patti Benson (Group Health Cooperative), Lina Sy (Kaiser Permanente Southern California), Paula Ray (Northern California Kaiser Permanente), Jill Mesa (Kaiser Foundation Hospital Center for Health Research), and Leslie Kuckler (Health Partners).

We also acknowledge the following VSD team sites for their contribution of data: Department of Population Medicine, Harvard Pilgrim Health Care Institute and Harvard Medical School, Harvard Vanguard Medical Associates, Northern California Kaiser Permanente Division of Research, Southern California Kaiser Permanente, Group Health Cooperative, Marshfield Clinic Research Foundation, Kaiser Permanente Northwest, and Health Partners Research Foundation.

Simon Hambidge, MD, PhD, who is the principal investigator, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Members of the Vaccine Safety Datalink Team (in addition to the authors): Charlene Gay, Harvard Pilgrim Health Care; James D. Nordin, MD, MPH, HealthPartners Research Foundation; Roger Baxter, MD, Kaiser Permanente of Northern California; Steven J. Jacobsen, MD, PhD, Kaiser Permanente of Southern California; Stephanie Irving, MHS, Marshfield Clinic Research Foundation; Allison Naleway, PhD, Northwest Kaiser Permanente; Lisa A. Jackson, MD, MPH, Group Health Research Institute.

REFERENCES

1. Amendah DD, Mvundura M, Kavanagh PL, Sprinz PG, Grosse SD. Sickle cell disease-related pediatric medical expenditures in the U.S. *Am J Prev Med*. 2010;38(suppl 4):S550–S556
2. Bundy DG, Strouse JJ, Casella JF, Miller MR. Burden of influenza-related hospitalizations among children with sickle cell disease. *Pediatrics*. 2010;125(2):234–243
3. Fiore AE, Shay DK, Broder K, et al; Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR Recomm Rep*. 2009;58(RR-8):1–52
4. Hambidge SJ, Glanz JM, France EK, et al; Vaccine Safety Datalink Team. Safety of trivalent inactivated influenza vaccine in children 6 to 23 months old. *JAMA*. 2006;296(16):1990–1997

5. Chen RT, Glasser JW, Rhodes PH, et al; The Vaccine Safety Datalink Team. Vaccine Safety Datalink project: a new tool for improving vaccine safety monitoring in the United States. *Pediatrics*. 1997;99(6):765–773
6. DeStefano F; Vaccine Safety Datalink Research Group. The Vaccine Safety Datalink project. *Pharmacoepidemiol Drug Saf*. 2001; 10(5):403–406
7. Platt OS. The acute chest syndrome of sickle cell disease. *N Engl J Med*. 2000;342 (25):1904–1907
8. Farrington CP, Nash J, Miller E. Case series analysis of adverse reactions to vaccines: a comparative evaluation. *Am J Epidemiol*. 1996;143(11):1165–1173
9. Glanz JM, McClure DL, Xu S, et al. Four different study designs to evaluate vaccine safety were equally validated with contrasting limitations. *J Clin Epidemiol*. 2006; 59(8):808–818
10. Centers for Disease Control and Prevention. Recommended immunization schedules for persons aged 0 through 18 years—United States 2010. *MMWR Recomm Rep*. 2010;58 (51&52):1–4
11. France EK, Glanz JM, Xu S, et al. Safety of the trivalent inactivated influenza vaccine among children: a population-based study. *Arch Pediatr Adolesc Med*. 2004;158(11): 1031–1036
12. 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):954–963
13. Glezen WP, Glezen LS, Alcorn R. Trivalent, inactivated influenza virus vaccine in children with sickle cell disease. *Am J Dis Child*. 1983;137(11):1095–1097
14. Steinberg E, Overturf GD, Portnoy B, Powars DR, Boyer KM, Cherry JD. Serologic and clinical response of children with sickle cell disease to bivalent influenza A split virus vaccine. *J Pediatr*. 1978;92 (5):823–825
15. Souza AR, Braga JAP, de Paiva TM, Loggetto SR, Azevedo RS, Weckx LY. Immunogenicity and tolerability of a virosome influenza vaccine compared to split influenza vaccine in patients with sickle cell anemia. *Vaccine*. 2010;28(4):1117–1120
16. Greene SK, Shi P, Dutta-Linn MM, et al. Accuracy of data on influenza vaccination status at four Vaccine Safety Datalink sites. *Am J Prev Med*. 2009;37(6):552–555
17. Kramarz P, Destefano F, Gargiullo PM, et al; Vaccine Safety Datalink team. Does influenza vaccination prevent asthma exacerbations in children? *J Pediatr*. 2001;138 (3):306–310
18. Centers for Disease Control and Prevention. Recommendation of the Public Health Service Advisory Committee on Immunization Practices: Influenza vaccine. *MMWR Morb Mortal Wkly Rep*. 1978;27(32): 285–292

(Continued from first page)

Address correspondence to Simon Hambidge, MD, PhD, Mail Code 1914, 660 Bannock St, Denver, CO 80207. E-mail simon.hambidge@dhha.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *Dr Baxter reports receiving grants from Sanofi Pasteur, GSK, Novartis, MedImmune, Protein Sciences, and Merck. Dr Jackson reports consulting work for Sanofi Pasteur, GSK, and Novartis; receipt of grant funding from Sanofi Pasteur, GSK, Novartis, and Wyeth/Pfizer; and additional support from Pfizer and Novartis. The other authors have indicated they have no financial relationships relevant to this article to disclose.*

Trivalent Inactivated Influenza Vaccine Is Not Associated With Sickle Cell Crises in Children

Simon J. Hambidge, Colleen Ross, Jason Glanz, David McClure, Matthew F. Daley, Stan Xu, Jo Ann Shoup, Komal Narwaney, James Baggs, Eric Weintraub and the Vaccine Safety Datalink Team

Pediatrics 2012;129;e54
DOI: 10.1542/peds.2011-1294 originally published online December 12, 2011;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Trivalent Inactivated Influenza Vaccine Is Not Associated With Sickle Cell Crises in Children

Simon J. Hambidge, Colleen Ross, Jason Glanz, David McClure, Matthew F. Daley, Stan Xu, Jo Ann Shoup, Komal Narwaney, James Baggs, Eric Weintraub and the Vaccine Safety Datalink Team

Pediatrics 2012;129;e54
DOI: 10.1542/peds.2011-1294 originally published online December 12, 2011;