Immunization Adherence in Children With Sickle Cell Disease: A Single-Institution Experience

Lisa M. Infanti, PharmD; Joshua J. Elder, PharmD; Kyle Franco, PharmD; Stephanie Simms, PharmD; Victoria A. Statler, MD, MSc; and Ashok Raj, MD

OBJECTIVES The Advisory Committee on Immunization Practices (ACIP) recommends additional immunizations for people with asplenia or functional asplenia, such as children with sickle cell disease. Adherence rate to the recommended immunization schedule for functional asplenia remains low for children with sickle cell disease. The purpose of this study was to assess the immunization adherence for this population at a single institution in Kentucky and to evaluate the use of the Kentucky Immunization Registry (KYIR) by providers.

METHODS A single-center retrospective chart review was conducted for 107 children with sickle cell disease ages 2 through 18 years. Immunization histories were obtained from the hospital EMRs, the sickle cell clinic EMR, the KYIR, and by requesting records from primary care physicians. Each patient was documented as either missing or having complete records in the KYIR.

RESULTS The complete adherence rate to the ACIP-recommended immunization schedule for children with functional asplenia was 6% (6 of 107). Nearly all children were compliant with the *Haemophilus influenzae* type B vaccination, whereas the adherence rate for the meningococcal and pneumococcal vaccines ranged from 25% to 77%. The lowest immunization rate was observed in children eligible for the meningococcal B vaccine (25%). Only 3 patients had a complete immunization history documented in the KYIR.

CONCLUSIONS Adherence to the ACIP-recommended immunization schedule for functionally asplenic patients is poor among children with sickle cell disease included in this study. Quality improvement measures should focus on increasing immunization adherence and improving documentation of immunization records in the KYIR for this patient population.

ABBREVIATIONS ACIP, Advisory Committee on Immunization Practices; EMR, Electronic Medical Record; Hib, *Haemophilus influenzae* type B; KYIR, Kentucky Immunization Registry; MenACWY, meningococcal serogroups A, C, W, Y vaccine; MenB, meningococcal serogroup B vaccine; PCV, pneumococcal conjugate vaccine; PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine

KEYWORDS adherence; immunizations; sickle cell disease

J Pediatr Pharmacol Ther 2020;25(1):39–46

DOI: 10.5863/1551-6776-25.1.39

Introduction

Patients with sickle cell disease are inherently more prone to infection due to progressive vaso-occlusive damage to the spleen, leading to a state of functional asplenia and immune system dysfunction. The exact mechanisms of this decrease in immunologic capacity are thought to be multifactorial, including functional asplenia, defects in the complement system, micronutrient deficiencies, and mechanical factors due to vaso-occlusive crisis.^{1,2} Functional asplenia increases the risk of systemic infections caused by encapsulated bacterial organisms, such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*. Additionally, infection with the influenza virus may lead to compromising of respiratory tract mucosal immunity,

acute chest syndrome, and fever, which commonly results in hospital admission to rule out bacterial sepsis.³ To prevent such infections, children with sickle cell disease should receive appropriate prophylactic interventions, including oral penicillin until age 5 years and strict adherence to the Advisory Committee on Immunization Practices (ACIP) recommended immunization schedule for asplenic patients (Figures 1–4).⁴

Background

The specific schedule of immunizations recommended by the ACIP for patients with sickle cell disease includes the *Haemophilus influenzae* type b (Hib) vaccine, pneumococcal vaccines (PCV7, PCV13, PPSV23), and the meningococcal vaccines for serogroups A, C,

Figure 1. Recommended immunization schedule for Hib in patients with sickle cell disease and those relevant for the purpose of this study.⁵

W, and Y (MenACWY), and serogroup B (MenB).⁵ This augmented immunization schedule is supported by a study in which immunization with the pneumococcal conjugate vaccine (PCV) was found to reduce invasive pneumococcal infections in patients younger than 10 years by up to 68%.⁶ The administration of PCV7 and Hib vaccines to children with sickle cell disease was also observed to decrease mortality due to bacterial sepsis.⁷ These immunizations decreased mortality from 0.59 deaths per 100 patient years to 0.52 deaths per 100 patient years for patients with HbSS and HbSβ⁰. In addition, patients with HbSC and HbSβ⁺ had a decrease in mortality from 0.24 deaths per 100 patient years to 0.1 deaths per 100 patient years.^{7,8} Despite the evidence that supports the importance of these vaccines for patients with sickle cell disease, adherence to the recommended immunization schedule is still a concern.⁹

To assess the adherence rate to the influenza vaccine, the pneumococcal vaccines, and oral penicillin for patients with sickle cell disease, a retrospective

cohort study of a Medicaid sample was conducted in 2014.¹⁰ The study found that patients with sickle cell disease had an adherence rate of 21.6% for the influenza vaccine, 43.4% for the PPSV23 vaccine, 18.8% for penicillin prophylaxis, and 77.3% for the PCV7 vaccine. It also concluded that children tended to adhere to the immunization schedule more than adults; however, rates were still low. Other studies have also looked to compare pneumococcal immunization rates in patients with sickle cell disease to non-sickle cell disease control groups.^{11,12} Results from the studies conducted by both Nero et al¹¹ and Wagner et al¹² indicate that patients with sickle cell disease are more adherent to the immunization schedule versus the control groups, but they still have lower immunization rates than other state and national immunization surveys. In addition to studies that observe a lack of compliance among this patient population, adherence concerns are recognized throughout many hematologic clinics in the United States.

Figure 2. Recommended immunization schedule for MenB in patients ≥ 10 years of age with sickle cell disease and those relevant for the purpose of this study.⁵

* Bexsero OR Trumenba, not both

Figure 3. Recommended immunization schedule for Meningococcal acwy (MenACWY) in patients ≥ 2 years of age with sickle cell disease and those relevant for the purpose of this study.⁵

NOTE: wait until at least 4 weeks after completed PCV series to administer

The compelling evidence that prophylactic interventions decrease the risk of infection and mortality among patients with sickle cell disease validates the importance of adhering to the recommended immunization schedule.^{6–8} Despite the evidence available, adherence rates to these interventions remain low, and potential barriers must be identified and resolved in order to prevent poor outcomes among these patients. The primary objective of this study is to assess immunization adherence for children with sickle cell disease at our institution. The secondary objective is to determine the use of the Kentucky Immunization Registry (KYIR) by providers.

Materials and Methods

A retrospective chart review was conducted in December 2017 to assess adherence to immunizations at a single institution. Children with a confirmed sickle

cell disease diagnosis ages 2 through 18 years who are patients at the University of Louisville Physicians Pediatric Cancer & Blood Disorders clinic were included for analysis. Patients who refused vaccines because of personal beliefs or who had a history of anaphylactic reactions to vaccines were excluded from the study.

Immunization records were obtained by reviewing the electronic medical records from the blood disorders clinic, the hospital system, the KYIR, and requesting records from each patient's primary care physician. Each patient's primary care office was contacted by both fax and phone to request records. Patient's name, date of birth, sex, phenotype of sickle cell disease, and the administration dates of Hib, PCV7, and/or PCV13, PPSV23, MenACWY, MenB, and influenza vaccinations were recorded. Once vaccination records were obtained from these various sources, the patient's record was considered to be the most complete compilation of immunization history. Each patient's immunization history

Figure 4. Recommended immunization schedule for pneumococcal vaccines in patients with sickle cell disease and those relevant for the purpose of this study.⁵

2-5 years of age

6-18 years of age

was then evaluated and categorized as “caught-up” or “in need of” additional immunizations. Additionally, immunizations and/or patients who reside in the state of Kentucky and were not found in the KYIR were added to complete their immunization history in the registry.

Descriptive statistics were used to determine the percentage of patients who were compliant with all immunizations compared with those who were not. The adherence to each individual vaccine was also calculated by determining the administration rate within the study population. Lastly, the use of the KYIR by providers was determined by the number of patients who had complete immunization records documented in the registry.

This study was approved by The University of Louisville Institutional Review Board through the Expedited Review Procedure and through 45 CFR 46.116 (D), which grants waiver of informed consent.

Results

Of the 157 patients who met inclusion criteria for the study, 107 had records available for review from all sources and were included for analysis. The most common sickle cell disease phenotype was SS, and the average age was 9.9 years (Table 1). Patients were only evaluated for the vaccines they were eligible for based on their age and previous immunization history, which is why denominators are smaller for some immunizations compared with others (Table 2). All patients were eligible to receive PPSV23 because all patients at the time of chart review were age ≥ 2 years. Only 32 patients were at least 5 years past their first PPSV23 dose to be eligible for the second PPSV23 dose. Of the 32 eligible patients, only 17 had received their second PPSV23 dose. All patients were also eligible to receive the first dose of the MenACWY vaccine; however, only 81 patients were eligible for the second dose of the vaccine series because they had received the first dose at least 8 weeks prior. Lastly, only 56 patients were eligible for the MenB vaccine, because it is not indicated until at least 10 years of age. Of the 14 patients who received the first MenB dose and were at least 8 weeks past the administration date of the first dose, only 4 had received the second MenB dose.

The complete immunization adherence rate, including the influenza vaccine, was 6% (6 of 107). Among all immunizations, the lowest adherence rate occurred with MenB, followed by the second dose of MenACWY and pneumococcal vaccines. The highest adherence rate observed was with the Hib vaccine (Table 2). The adherence rate to dose 2 of any series was less than the adherence rate of dose 1, as suggested by the adherence rates to PPSV23 and MenACWY. Additionally, only 52% of patients had documented influenza vaccines from the 2017–2018 season. As for the use of the KYIR by providers, only 3 patients had a complete immunization history documented in the registry.

Table 1. Baseline Demographics

Patient Demographics	Value (N = 107)
Sex, n (%)	
Male	52 (49)
Female	55 (51)
Age, yr, mean (range)	9.9 (2–18)
Phenotype of SCD, n (%)	
HbSS	64 (60)
HbSC	30 (28)
HbS β^+	8 (7)
HbS β^0	5 (5)

SCD, sickle cell disease

Immunization records from primary care physicians were successfully obtained after one attempt for 19 patients (19/157; 12%), two attempts for 36 patients (36/157; 23%), and three attempts for 52 patients (52/157; 33%). Of the 157 patients initially evaluated, 50 records (32%) were never obtained despite multiple attempts. All attempts were made on different days and documented for reference. The first attempt was made via fax, whereas the second and third attempts were primarily phone calls to the office. The most common reason that records were unable to be obtained was that patients could not be found in the documented primary provider's system or had never actually been seen. Additional reasons for lack of success in obtaining records were unreturned voicemails and refusal of primary provider to send records due to lack of informed consent from the patient or caregiver, despite sending documentation of The University of Louisville Institutional Review Board approved waiver of informed consent.

Discussion

This study shows that most children with sickle cell disease ages 2 to 18 years who attend the Pediatric Cancer & Blood Disorders clinic are missing at least 1 immunization according to the ACIP recommendations for patients with functional asplenia. The lowest immunization adherence rate occurred with MenB, which is also the newest vaccine available. Additionally, the MenB vaccine may not be stocked in clinics because it is a category B recommendation for healthy children, whereas it is a category A recommendation for those patients with sickle cell disease.¹³ Category A recommendations apply to all persons in an age- or risk-based group, in this case the at-risk group being those children with sickle cell disease.¹³ For the otherwise healthy individual, however, immunization with this vaccine holds a category B recommendation, requiring individual clinical decision-making by the practitioner and family to determine if it is appropriate for that patient.¹³ The misinterpretation or lack of awareness of the strength of the recommendation for at-risk patients may also affect the provider's understanding

Table 2. Vaccination Adherence by Vaccine Type

Vaccination	Adherence, % (n)*
Hib	99 (106/107)
PCV13	60 (64/107)
PPSV23 (first dose)	60 (64/107)
PPSV23 (second dose)	53 (17/32)
MenACWY (first dose)	77 (82/107)
MenACWY (second dose)	49 (40/81)
MenB (first dose)	25 (14/56)
MenB (second dose)	29 (4/14)
Influenza	52 (56/107)

Hib, *Haemophilus influenzae* type B vaccine; MenACWY, meningococcal serogroups A, C, W, and Y vaccine; MenB, meningococcal serogroup B vaccine; PCV, pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine

* Denominators differ by vaccine eligibility.

of its importance, and thus decrease adherence rates to this particular vaccination.

The low adherence rate to pneumococcal vaccines may be due to the recent availability of the PCV13 vaccine and recommendations provided by the ACIP in 2010 that patients with sickle cell disease who have only received PCV7 prior should receive 1 supplemental dose of PCV13.¹⁴ This update in recommendations has resulted in the lack of pneumococcal vaccination adherence in many adolescent patients. A recent study assessing the immunization status in children with sickle cell disease who were born in Michigan also observed that 29.1% of patients who received a full PCV7 series had not yet received a PCV13, which was slightly lower than what was observed in this study (40%).¹² However, this 40% does not exclude those patients who never received the PCV7 vaccination and are only missing the fourth PCV13 dose of the series. Similar to the MenB vaccine, administration of the PPSV23 vaccine is not a category A recommendation in otherwise healthy children, which may limit its availability in clinics as well as the provider's understanding of its importance for these patients.

The poor adherence rate to the influenza vaccine (52%) may be falsely low, considering the chart review was conducted in the middle of the season and patients may have received it at another location. In other words, patients who received the influenza vaccine at the end of the season would not have been captured. Additionally, the records of influenza vaccines administered at outpatient pharmacies and other hospitals or emergency departments could not be obtained because of a lack of integration into the medical record. According to the Centers for Disease Control, however, the adherence rate obtained from this study closely reflects adherence rates for both the state of Kentucky as well

as the United States for children ages >6 months to 17 years (55.3% vs 57.9%, respectively).^{15,16} This indicates that perhaps the adherence rate observed was reasonably accurate and that influenza vaccination rates are overall low across the country.

Aside from vaccine-specific barriers, the results observed in this study suggest other global barriers to maintaining up-to-date status in children with sickle cell disease. One potential barrier may be the lack of education that primary care providers and families receive regarding the specific immunizations recommended for this patient population. Bundy and colleagues observed an increased compliance rate for the influenza vaccine in those children with sickle cell disease who attended 2 or more hematologist visits per year, compared with those without a hematologist visit.³ This demonstrates the need for increased availability of providers with knowledge and expertise in sickle cell disease to appropriately manage these patients.¹⁷ Additionally, there may be inconsistencies or incomplete immunization records shared among mutual providers, adding to confusion about which vaccines the patient may need. Therefore, documentation of immunization history may vary from one practice to another unless seamless communication or a shared electronic medical record is involved.

The lack of patient and caregiver knowledge regarding the specific immunization recommendations is one barrier that should be addressed to improve adherence. In a national survey of 1600 parents conducted by the National Network for Immunization Information, many parents reported that they would like to receive more information about how immunizations work, associated side effects, and what the guidelines recommend.¹⁸ In order to provide families with this knowledge, a supplemental handout could be provided at an initial visit along with a discussion about the recommended immunization schedule. Families should also maintain a checklist to keep track of what immunizations were given and which immunizations are needed. An example of this checklist is displayed in the Supplemental Figure.

There may also be a difference between specialist and general physician knowledge of immunization recommendations for patients with sickle cell disease, especially in rural communities where specialty services are lacking.^{3,19} Considering that most immunizations are provided at primary care visits, initiatives should be made to increase awareness and education of the vaccines recommended for this specific patient population. These may include using a free vaccine e-Learn offered by the ACIP, including "You Call the Shots," an interactive web-based immunization training course, or Project ECHO (Extension for Community Healthcare Outcomes). Project ECHO is an internationally recognized telementoring innovation that builds clinician knowledge in diagnosing and treating complex disorders. It allows local clinicians to connect with experts from sickle cell disease centers to learn the necessary

skills to deliver high-quality sickle cell disease care using this proven telementoring model. One of the plans we have in place to educate sickle cell disease providers at our institution and within our geographic area is through the “hub” and “spokes” model of Project ECHO, which is a movement to demonopolize knowledge and amplify the capacity to provide best practice care for underserved people by linking the specialists with the primary care clinicians.

Additionally, authors of the present study have personally spoken at multiple state nursing and physician conferences to help provide education to providers both in and out of Louisville. Providing this education at both a state and a national level along with using a web-based immunization training course are two ways in which we can help primary care providers increase knowledge regarding the immunization schedule for functional asplenia, thus increasing adherence rates in this patient population.

Limited availability of vaccines at specialty clinics due to cost, personnel, and space restrictions represents another potential barrier. The logistics of providing an immunization service at the clinic is challenging, requiring the availability of refrigerators and/or freezers maintained within a specific temperature range, nurses or pharmacists to administer the vaccines, and availability of vaccine information sheets. Therefore, many sickle cell patients are referred from their specialty clinic to their primary care office to obtain the recommended immunizations. The disadvantage of this process, however, is that there may also be inconsistent follow-up to assess if immunization recommendations are being implemented at these primary care visits. In order to begin addressing this barrier, a pilot project was initiated to provide the PPSV23 vaccine to patients seen in the Infectious Diseases clinic, located in the same facility as the Pediatric Cancer & Blood Disorders clinic where patients with sickle cell disease attend. If successful for this specific patient population, administration of this vaccine in the clinic may expand to other services and help to decrease missed opportunities.

At all clinical encounters, including sick and injury visits, patients should be assessed for the need for additional immunizations in order to minimize missed opportunities.²⁰ As part of a quality improvement initiative at our institution, the addition of a dedicated nurse to act as a “vaccine superhero” and advocate within the clinic has been requested, and this has historically proved to be beneficial for our heart transplant population. This nurse would be responsible for administering vaccines, maintaining immunization histories, and ensuring up-to-date immunization status for patients with sickle cell disease, because this type of service has shown to increase compliance among immunocompromised patients.²¹ This intervention may also allow patients to receive vaccines while at their specialty clinic appointments rather than being referred to their primary care

physician. To ensure that the patients included in this study receive the immunizations they are currently missing, recommendations as to what vaccine each individual needs were sent to the Pediatric Cancer & Blood Disorders clinic to have on file to address at upcoming appointments. The providers will then be able to quickly recommend what each of these patients needs in order to be considered caught up. Having the ability to provide patients with immunizations at the specialty clinic will decrease the number of missed opportunities and increase adherence rates.

The documented attempts that were made to contact and obtain records from each primary physician illustrates the inconvenience of trying to obtain patient records, and it supports how a lack of shared documentation may be an additional barrier to immunization adherence. The closest developments to a national immunization registry are community-based and state registries, which serve as a shared database between practices in order to locate and assess immunization history. The KYIR, created in 2015, serves as the state of Kentucky’s shared database among providers. This registry provides key information regarding immunization history, such as reporting of doses administered and the date they were administered. This information is then compiled into a single record for each patient.²² However, in order to maximize the benefit of the registry, all providers must be diligent about updating information so it can be reviewed by other providers. The use of immunization registries has also been shown to increase provider interventions and the percentage of patients up to date, in addition to overall cost savings.^{23,24}

Immunization information systems have estimated that an annual cost of a nationwide network would be \$78 million for children ages 0 to 5 years, but the annual cost offset would be \$280 million.²⁴ These savings would come from the decrease in immunization-assessment activities for children entering kindergarten, duplicated vaccine administration, and the money spent for the Health Plan Employer Data and Information Set reports and the National Immunization Survey. Although immunization registries have been shown to increase immunization rates and interventions, and potentially decrease costs, there still remains a lack of consistent use by providers in the state of Kentucky, as demonstrated by the lack of complete documentation in this study.

To address this barrier and encourage the use of the KYIR, all of the immunization histories obtained for the children living in Kentucky were entered into the registry. This at least increases the documentation of immunization history for those patients included in our study and from the state of Kentucky to 100%. It is also important to recognize that our hospital-based EMR system does integrate with both the KYIR and the CHIRP (Children and Hoosier Immunization Registry

Program); however, this is not the case among all institutions, so further implementation of this integration should be encouraged. Additionally, university-based vaccine experts, including one of the authors of the present paper, speak locally and regionally to bring awareness to the registry in addition to providing education to providers. This will hopefully help to further sustain high rates of documentation into the registry so immunization records may be viewed and assessed among providers.

Conclusion

Children with sickle cell disease are at increased risk of infection and mortality due to encapsulated organisms. Therefore, it is essential that this particular population of patients adhere to the ACIP-recommended immunization schedule for functional asplenia. Because of several existing barriers, such as the lack of knowledge regarding immunization schedule, logistic limitations of maintaining all vaccines in clinics, difficulty in obtaining records from the primary care physician's office, and the lack of consistent documentation into the immunization registry, adherence rates remain low, increasing the risk for infection in this study population. To address this national issue, institutions should identify existing barriers so quality improvement measures can be developed and implemented to improve immunization adherence and overall outcomes for patients with sickle cell disease.

ARTICLE INFORMATION

Affiliations Department of Pharmacy (LMI, JJE, KF, SS), Norton Children's Hospital, Louisville, KY, Division of Pediatric Infectious Diseases (VAS), University of Louisville, Louisville, KY, Division of Pediatric Cancer and Blood Disorders (AR), University of Louisville, Louisville, KY

Correspondence Lisa Infanti, PharmD; lisa.infanti@norton-healthcare.org; mail to: lminfan@gmail.com

Disclosure The author(s) declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data and take responsibility for the integrity and accuracy of the data analysis.

Acknowledgments This work was presented previously at the 12th Annual Sickle Cell Disease Research and Educational Symposium; June 15–17, 2018; Washington, DC.

Accepted June 7, 2019

Copyright Published by the Pediatric Pharmacy Association. All rights reserved.
For permissions, email: mhelms@pediatricpharmacy.org

Supplemental Material

DOI: 10.5863/1551-6776-25.1.39.S

REFERENCES

1. Rees DC, Williams TN, Glawin MT. Sickle cell disease. *Lancet*. 2010;376(9757):2018–2031.
2. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA*. 2014;312(10):1033–1048.
3. Bundy DG, Muschelli J, Clemens GD, et al. Preventive care delivery to young children with sickle cell disease. *J Pediatr Hematol Oncol*. 2016;38(4):294–300.
4. Gaston MH, Verter JI, Woods G, et al. Prophylaxis with oral penicillin in children with sickle cell anemia. *N Engl J Med*. 1986;314(25):1593–1599.
5. Recommended immunization schedule for adolescents aged 18 years or younger. <https://www.cdc.gov/vaccines/schedules/downloads/past/2017-child.pdf>. Accessed September 9, 2019.
6. Adamkiewicz TV, Silk BJ, Howgate J, et al. Effectiveness of the 7-valent pneumococcal conjugate vaccine in children with sickle cell disease in the first decade of life. *Pediatrics*. 2008;121(3):562–569.
7. Quinn CT, Rogers ZR, McCavit TL, et al. Improved survival of children and adolescents with sickle cell disease. *Blood*. 2010;115(17):3447–3452.
8. Quinn CT, Rogers ZR, Buchanan GR. Survival of children with sickle cell disease. *Blood*. 2004;103(11):4023–4027.
9. Walsh KE, Cutrona SL, Kavanagh PL, et al. Medication adherence among pediatric patients with sickle cell disease: a systematic review. *Pediatrics*. 2014;134(6):1175–1183.
10. Beverung LM, Brousseau D, Hoffman RG, et al. Ambulatory quality indicators to prevent infection in sickle cell disease. *Am J Hematol*. 2014;89(3):256–260.
11. Nero AC, Akuete K, Reeves SL, et al. Pneumococcal vaccination rates in children with sickle cell disease. *J Public Health Manag Pract*. 2014;20(6):587–590.
12. Wagner AL, Shrivastwa N, Potter RC, et al. Pneumococcal and meningococcal vaccination among Michigan children with sickle cell disease. *J Pediatr*. 2018;196:223–229.
13. Marshall GS, Tan L. Understanding the Category B recommendation for serogroup B meningococcal vaccine. *Pediatrics*. 2017;139(5):1–3.
14. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children—Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Morb Mortal Wkly Rep*. 2010;59(9):258–261.
15. 2017-18 influenza season vaccination coverage dashboard. <https://www.cdc.gov/flu/fluview/reportshtml/report1718/reportii/index.html>. Accessed September 9, 2019.
16. Estimates of flu vaccination coverage among children – United States, 2017-18 flu season. <https://www.cdc.gov/flu/fluview/coverage-1718estimates-children.htm>. Accessed September 9, 2019.
17. Yusuf HR, Lloyd-Puryear MA, Grant AM, et al. Sickle cell disease, the need for a public health agenda. *Am J Prev Med*. 2011;41(6S4):S376–S383.
18. Sharts-Hopko NC. Issues in pediatric immunization. *MCN Am J Matern Child Nurs*. 2009;34(2):80–88.

19. Harrold LR, Field TS, Gurwitz JH. Knowledge, patterns of care, and outcomes of care for generalists and specialists. *J Gen Intern Med*. 1999;14(8):499–511.
20. Ventola CL. Immunization in the United States: recommendations, barriers, and measures to improve compliance. *P T*. 2016;41(7):426–436.
21. Malone K, Clark S, Palmer JA, et al. A quality improvement initiative to increase pneumococcal vaccination coverage among children after kidney transplant. *Pediatr Transplant*. 2016;20(6):783–789.
22. Kentucky Immunization Registry. <https://chfs.ky.gov/agencies/dph/dehp/ldb/Pages/kyir.aspx>. September 9, 2019.
23. Groom H, Hopkins D, Pabst L, et al. Immunization information systems to increase vaccination rates: a community guide systematic review. *J Public Health Manag Pract*. 2015;21(3):227–248.
24. Committee on Practice and Ambulatory Medicine. Immunization information systems. *Pediatrics*. 2006;118(3):1293–1295.