


Pneumococcal vaccination coverage among children with sickle cell anemia, sickle cell trait, and normal hemoglobin

Sarah L. Reeves¹  | Hannah K. Jary¹ | Jennifer P. Gondhi¹ | Mary Kleyn² | Abram L. Wagner³ | Kevin J. Dombkowski¹

¹Child Health Evaluation and Research Center, University of Michigan, Ann Arbor, Michigan

²Michigan Department of Health and Human Services, Lansing, Michigan

³Department of Epidemiology, University of Michigan, Ann Arbor, Michigan

Correspondence

Sarah Leasure Reeves, 300 North Ingalls, Rm 6D19 Ann Arbor, MI 48109-5456.

Email: sleasure@umich.edu

Abstract

Background: Children with sickle cell anemia and sickle cell trait are at an increased risk of invasive pneumococcal disease compared to children with normal hemoglobin. We assessed and compared pneumococcal vaccination status among these three groups.

Procedure: Children with sickle cell anemia and sickle cell trait were identified using Michigan newborn screening records (1997–2014); each child was matched to four children with normal hemoglobin based on age, Medicaid enrollment (at least 1 year from 2012–2014), race, and census tract. Vaccination records were obtained from the state's immunization system. Pneumococcal vaccine coverage (PCV7 or PCV13 depending on date of administration) was assessed at milestone ages of 3, 5, 7, and 16 months. The proportion of children with vaccine coverage at each milestone was calculated overall and compared among children with sickle cell anemia, sickle cell trait, and normal hemoglobin using chi-square tests.

Results: The study population consisted of 355 children with sickle cell anemia, 17,319 with sickle cell trait, and 70,757 with normal hemoglobin. The proportion of children with age-appropriate pneumococcal vaccination coverage was low at each milestone and generally decreased over time. Children with sickle cell anemia were more likely to be covered compared to children with sickle cell trait or normal hemoglobin.

Conclusions: Despite higher pneumococcal vaccination coverage among children with sickle cell anemia, opportunities for improvement exist among all children. Targeted interventions will benefit from mechanisms to identify children with increased risks such as sickle cell anemia or trait to improve pneumococcal vaccination coverage among these groups.

KEYWORDS

invasive pneumococcal disease, Medicaid administrative claims, pneumococcal conjugate vaccine, pneumococcal polysaccharide vaccine, sickle cell anemia, sickle cell trait

1 | INTRODUCTION

Invasive pneumococcal disease (IPD), an infection caused by *Streptococcus pneumoniae*, is a significant source of pediatric morbidity and mortality in the United States.¹ To protect against IPD, the Advisory Committee on Immunization Practices (ACIP) established a recommendation beginning in 2000 that all children receive four doses of the

pneumococcal conjugate vaccine (PCV) at 2, 4, 6, and 12–15 months of age.² As of October 6, 2000, children were recommended to receive the 7-valent PCV formation (PCV7); after March 12, 2010, the recommendation was updated to the 13-valent PCV formation (PCV13). Since these recommendations, approximately 84% of children have received these four PCV doses by 35 months of age.³ Given the effectiveness of the vaccine, the incidence of IPD has also dropped substantially among children less than 5 years old.^{1,4,5} However, an estimated 3,700 deaths in the United States still resulted from pneumococcal meningitis and bacteremia in 2013.⁶

Children with chronic conditions are particularly vulnerable to the threat of IPD, such as those with cancer, cardiovascular disease,

Abbreviation: ACIP, Advisory Committee on Immunization Practices; IPD, invasive pneumococcal disease; MCIR, Michigan Care Improvement Registry; NBS, newborn screening; NHLBI, National Heart, Lung, and Blood Institute; PCV7, 7-valent pneumococcal conjugate; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; US, United States

diabetes, or organ transplantations.^{7,8} Sickle cell anemia, a subtype of sickle cell disease, is another chronic condition associated with a higher risk of IPD due to the asplenia experienced by many with the disease.⁹ Without intervention, children with sickle cell anemia are over 100 times more likely to have IPD than children with normal hemoglobin.¹⁰ The ACIP recommends that children with specific chronic conditions, including sickle cell anemia, should receive the routine four doses of PCV as well as one to the two additional doses of pneumococcal polysaccharide (PPSV) between the ages of 2 to 18 years to protect against *S. pneumoniae*;^{1,4,8,11} this is supported by the National Heart, Lung, and Blood Institute (NHLBI) recommendations.¹²

Although children with sickle cell anemia are identified as high risk for IPD, this does not extend to sickle cell trait, the carrier status of the disease. Historically, sickle cell trait has been considered benign,^{13,14} yet recent reports demonstrate that it may be less asymptomatic than previously thought.^{13,15,16} For example, children with sickle cell trait are at an increased risk of IPD as compared to children with normal hemoglobin.¹⁷ Yet, nothing is known regarding the pneumococcal vaccination coverage among children with sickle cell trait. This may be attributable to difficulty identifying those living with sickle cell trait in the United States, as it is estimated that only 20% of adults are aware of their carrier status.^{18–20} However, all children with sickle cell trait are identified at birth through newborn screening (NBS) records. Therefore, the goal of this study is to use NBS records and an immunization registry to assess and compare pneumococcal vaccination status among children with sickle cell anemia, sickle cell trait, and normal hemoglobin.

2 | METHODS

This was a cohort study of age-appropriate pneumococcal vaccination coverage among children with sickle cell anemia, sickle cell trait, and normal hemoglobin enrolled in Michigan Medicaid. This study was deemed exempt by the University of Michigan (HUM00096573) and Michigan Department of Health and Human Services (MDHHS; IRB#201502-07-NR-(R1)) IRBs.

2.1 | Study population

Children enrolled in the Michigan Medicaid program for at least 1 year during the period 2012–2014 were eligible for inclusion in our study. Children with sickle cell anemia and sickle cell trait were identified using Michigan NBS records for all births statewide during the period 1997–2014. In this study, children with hemoglobin (Hb) SS and Hb S β^0 -thalassemia were considered to have sickle cell anemia. These children, as well as those with sickle cell trait, were linked to Michigan Medicaid records through a common electronic birth certificate identifier using a previously validated method.²¹ Since all children in Michigan are screened at birth for a wide range of conditions, NBS data served as our gold standard for sickle cell anemia and trait case identification. Among children identified as sickle cell anemia or trait, those with at least 1 year of continuous enrollment in Michigan Medicaid (2012–2014) were eligible for inclusion in this study. Consistent

with the Healthcare Effectiveness Data and Information Set (HEDIS) recommendation, children enrolled for at least 11 months during any calendar year were considered continuously enrolled.²² Children with any other forms of health insurance during their Medicaid enrollment period were excluded to maximize the capture of claims among children with Medicaid coverage.

We created a matched comparison group using Michigan Medicaid records and NBS data. For each sickle cell anemia and sickle cell trait case, 10 children enrolled in Michigan Medicaid were matched to each case based upon year of birth, year(s) of enrollment in Michigan Medicaid, child's race, and the census tract of residence during Medicaid enrollment. These matched children were linked to NBS records using name, date of birth, and Medicaid ID. Only children with confirmed normal hemoglobin were eligible for the matched control group; those with abnormal or missing NBS records were excluded. Among the remaining eligible children with confirmed normal hemoglobin, four comparison children were randomly chosen for each child with sickle cell anemia or trait in the study population. Each comparison child with confirmed normal hemoglobin was matched to only one sickle cell anemia or trait case across the entire study period. Given the birth cohort of eligible children began in 1997, all children were under 18 years of age for all potential years of Medicaid enrollment.

As our final step, we linked all children eligible to be in the study population (sickle cell anemia, sickle cell trait, and normal hemoglobin) to their corresponding information in the state immunization registry, the Michigan Care Improvement Registry (MCIR), based on Medicaid ID, name, and date of birth. Since its inception in 1996, Michigan law has required that all vaccination doses administered to persons less than 20 years of age be reported to MCIR within 72 hr. The registry is automatically populated by electronic birth records; children born in Michigan are loaded into MCIR shortly after birth, regardless of their vaccination status. While parents may opt out of the automatic inclusion to MCIR, this is an uncommon occurrence and affects fewer than 0.1% of children aged 0–10 years. MCIR coverage rates show close alignment with the National Immunization Survey (NIS) and Michigan continues to serve as a CDC-funded Sentinel State for the use of registries for immunization surveillance.^{23,24} Any children who were not matched by exact Medicaid ID and/or first and last name, as well as a date of birth within 1 day were excluded from further analysis. Consequently, our final study population consisted of children with sickle cell anemia, sickle cell trait, and normal hemoglobin with valid vaccination records in the state of Michigan.

2.2 | Measures

Using the MCIR IDs obtained from the matching process, pneumococcal vaccination records (vaccine type and date administered) were obtained from MCIR for all children in the study population. Valid pneumococcal doses obtained met the following conditions: submitted or subsequently approved by a provider, not deleted, not duplicated, and a valid dose, per ACIP guidance for minimum age and dose intervals. These doses were used to assess age-appropriate pneumococcal vaccine coverage for each child at milestone ages of 3, 5, 7, and 16 months; these milestone ages allow for a 1 month grace period

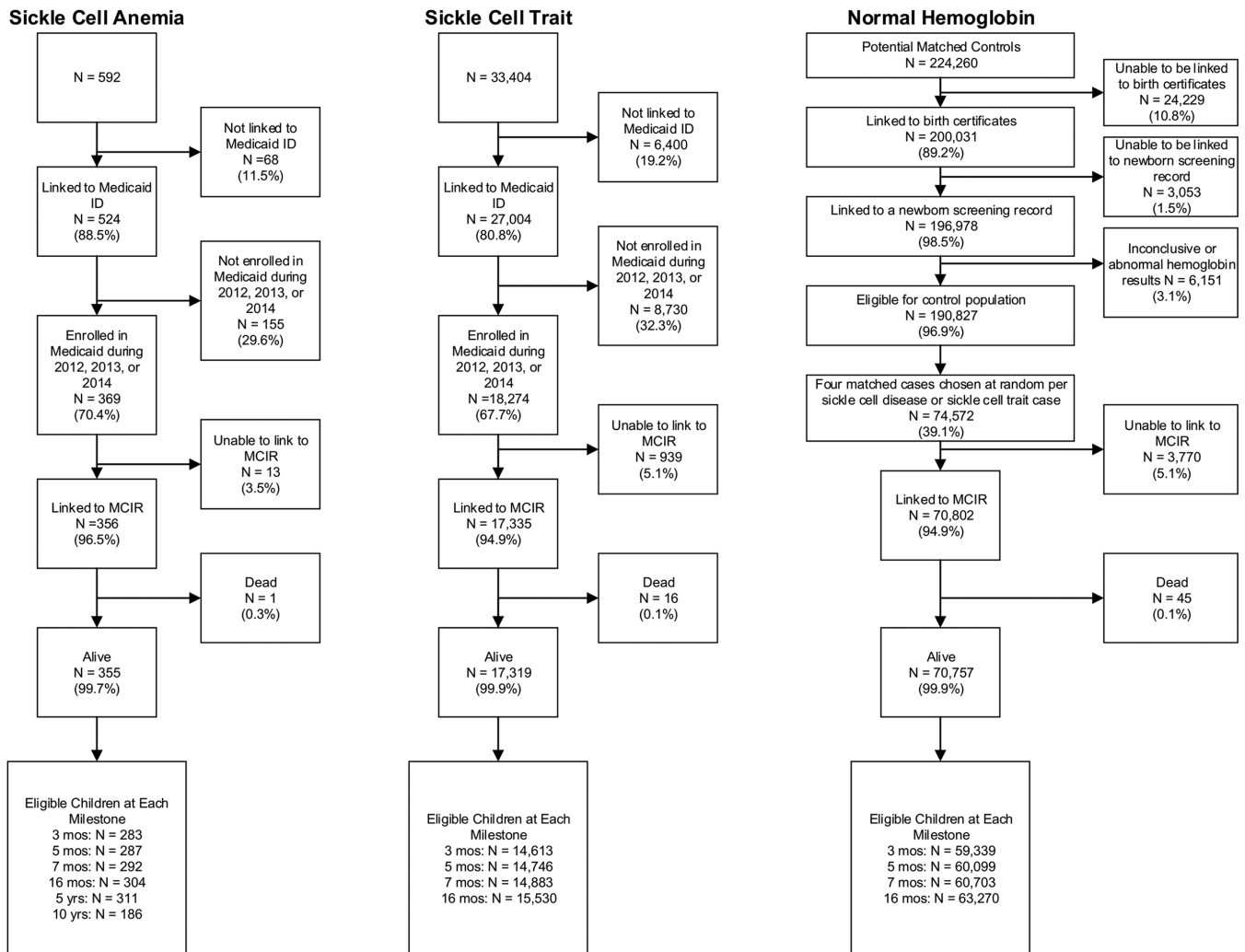


FIGURE 1 Study population, Michigan births 1997–2014

following the ACIP recommended ages for dose administration. From October 6, 2000 to March 12, 2010, the recommended dose of PCV was a seven strain (PCV7); after that date, children were recommended to receive PCV13, the 13-strain formulation. Therefore, doses of PCV7 were considered valid between the above dates; doses of PCV13 were considered valid after March 12, 2010, with a 1 year overlap period in which either formulation was considered valid. Due to differences in each birth cohort's age over time and PCV recommendation changes, the number of children eligible (i.e., in the denominator) for each age milestone differ, and are specified in Figure 1.

Age-appropriate vaccination coverage (yes/no) was based on whether the child had received the recommended number of valid pneumococcal vaccines at each age milestone, irrespective of disease status (Table 1).⁸ Appropriate coverage was assessed at each child's milestone age, independent of their status at the previous milestone age; however, it was necessary for a child to have received all recommended doses by each milestone (Table 1). For example, a 5-month-old child would be considered appropriately covered if they had received two valid doses of PCV by that age, irrespective of their coverage at 3 months. In addition, the ACIP and NHLBI recommend

two doses of PPSV for children with sickle cell anemia.^{8,12} Therefore, among the children in the study population with sickle cell anemia, age-appropriate PPSV coverage was conservatively determined at milestones of 5 years plus 1 month, and 10 years plus 1 month; to be appropriately covered, the child must have also received all four PCV doses by these milestone ages (Table 1).

2.3 | Statistical analysis

Frequencies and percentages were calculated for demographic characteristics of children in the study population. The proportion of children with age-appropriate vaccine coverage (yes/no) at each milestone was calculated overall, and among each group within the study population (sickle cell anemia, sickle cell trait, and normal hemoglobin). The proportion of children with age-appropriate vaccination coverage was compared across groups using Pearson's chi-square tests; *P*-values < 0.05 were used to determine significant differences. When significant differences across groups were present at milestones, two-proportion z-tests were performed to identify which study population groups were significantly different in the proportion of coverage. All analyses were performed using SAS 9.4.

TABLE 1 Outcome variables

ACIP recommended age ^b	Milestone age assessed	Doses required for appropriate coverage ^a	Study populations assessed
2 months	3 months	1 PCV	All (sickle cell anemia, sickle cell trait, normal hemoglobin)
4 months	5 months	2 PCV	All
6 months	7 months	3 PCV	All
12–15 months	16 months	4 PCV	All
2–5 years	61 months (5 years + 1 month)	4 PCV + 1 PPSV	Sickle cell anemia only
5 years after previous dose	121 months (10 years + 1 month)	4 PCV + 2 PPSV	Sickle cell anemia only

^aFrom October 6, 2000 to March 12, 2010, the recommended dose of PCV was seven-valent (PCV7); after that date, children were recommended to receive PCV13, the 13-valent formulation. Therefore, doses of PCV7 were considered valid between the above dates; doses of PCV13 were considered valid after March 12, 2010, with a 1 year overlap period in which either formulation was considered valid.

3 | RESULTS

From 1997–2014, a total of 592 children with sickle cell anemia and 33,404 children with sickle cell trait were born in the state of Michigan. Among these children, 369 (62.3%) with sickle cell anemia and 18,274 (54.7%) with sickle cell trait were continuously enrolled in Michigan Medicaid (with no gaps in coverage) for at least 1 year from 2012–2014. A total of 196,978 children with potentially normal hemoglobin were identified using Michigan Medicaid records linked to their corresponding NBS record; among these children, 6,151 (3.1%) were excluded due to missing or abnormal hemoglobin status in NBS records. Among the 190,827 (96.9%) remaining children, a sample of 4 children with normal hemoglobin ($n = 74,572$) were chosen for each sickle cell anemia and sickle cell trait case, resulting in a total of 93,215 children eligible for matching to MCIR records. A total of 88,493 children (95%) were successfully matched to their MCIR records. After excluding the 62 children flagged as deceased in Medicaid, the final study groups were 355 with sickle cell anemia, 17,319 with sickle cell trait, and 70,757 with normal hemoglobin (Figure 1).

Among all children in the study population, most were black (77.8% of sickle cell anemia, 81.3% of sickle cell trait, and 81.1% of normal hemoglobin; Table 2). There was a slightly higher proportion of females to males in the sickle cell anemia group (51.8% female) compared to the sickle cell trait (48.9%) and normal hemoglobin (49.3%) groups (Table 2). Overall, there were more young children (born 2009–2014) than older adolescents (born 1997–2002).

A total of 279,241 pneumococcal vaccination doses were obtained from MCIR for these children, which were administered between January 1, 1997 and May 15, 2017 by a provider, and not deleted or duplicated.

Overall, the proportion of children with age-appropriate PCV vaccination coverage generally decreased with each successive age milestone, with 69.4% ($n = 51,680$) at 3 months, 49.5% ($n = 37,222$) at 5 months, 34.8% ($n = 26,393$) at 7 months, and a small increase to 38.3% ($n = 30,260$) at 16 months. Assessment of age-appropriate PCV vaccination coverage by hemoglobin status revealed significant differences in coverage at each age milestone (Figure 2). PCV vacci-

nation coverage was significantly higher among those with sickle cell anemia at each milestone, both when compared with sickle cell trait and with normal hemoglobin groups individually. When comparing the sickle cell trait and normal hemoglobin groups, vaccination coverage was significantly higher in the normal hemoglobin group at 7 and 16 months; however, these differences are not clinically meaningful (difference in rates <1%).

Among children with sickle cell anemia, age-appropriate pneumococcal vaccination coverage at 5 and 10 years, which included both PCV and PPSV doses, was 64.3% at 5 years and then decreased to 52.7% at 10 years. For comparison, PPSV coverage with this same vaccination schedule for children with sickle cell trait and normal hemoglobin (for whom PPSV is not routinely recommended) were predictably low, at less than 1% each, and not significantly different from one another.

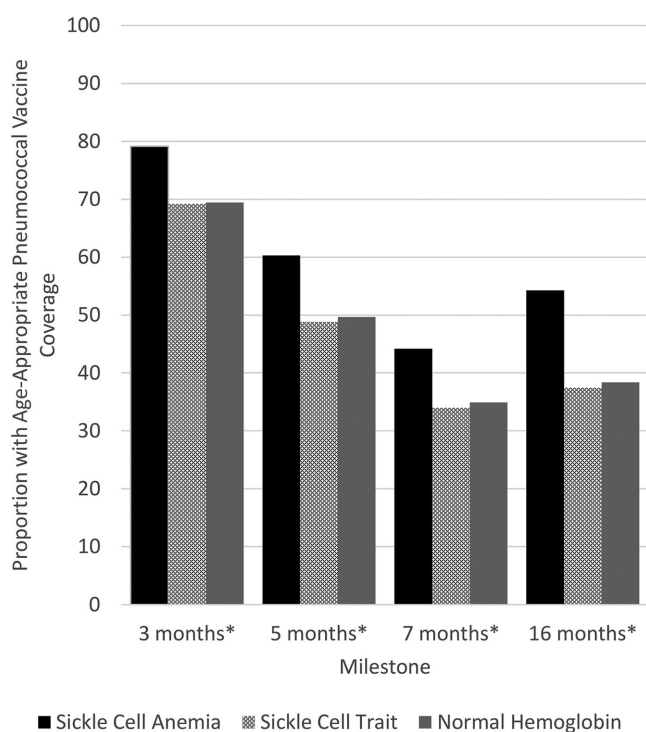
4 | DISCUSSION

We assessed and compared age-appropriate pneumococcal vaccination coverage among children with sickle cell anemia, sickle cell trait, and normal hemoglobin enrolled in Michigan Medicaid. Although pneumococcal vaccination coverage was higher among children with sickle cell anemia, opportunities for improvement existed among all children. Therefore, continued emphasis on programs which increase vaccination coverage is necessary to reach 90% coverage as specified by Healthy People 2020.²⁵ Emphasis should be placed on specific strategies targeting children with sickle cell anemia and sickle cell trait, two vulnerable subgroups who are at an increased risk of infection as compared to children with normal hemoglobin.^{10,17}

The proportion of children in our study population with age-appropriate coverage at the end of the four-dose PCV series was substantially lower than other reports of PCV completion rates of 66–84%.^{3,26} This may be due to the allowance of additional months to complete the series in other studies, as well as the characteristics of our study population. Specifically, racial disparities exist in PCV vaccination, with black children less likely to receive the four-dose PCV

TABLE 2 Demographic characteristics of study population by hemoglobin status (n = 88,431)

		Sickle cell anemia n = 355	Sickle cell trait n = 17,319	Normal hemoglobin n = 70,757
Race, n (%)	White	9 (3%)	1,449 (8%)	5,855 (8%)
	Black	276 (78%)	14,086 (81%)	57,390 (81%)
	Native American, Other	0 (0%)	51 (0%)	207 (0%)
	Unknown	69 (19%)	1,301 (8%)	5,570 (8%)
Ethnicity, n (%)	Asian	0 (0%)	4 (0%)	16 (0%)
	Hispanic	1 (0%)	428 (2%)	1,719 (2%)
Sex, n (%)	Female	184 (52%)	8,465 (49%)	34,866 (49%)
	Male	171 (48%)	8,854 (51%)	35,891 (51%)
Birth year, n (%)	1997–2002	101 (28%)	4,937 (29%)	20,199 (29%)
	2003–2008	125 (35%)	6,088 (35%)	24,832 (35%)
	2009–2014	129 (36%)	6,294 (36%)	25,726 (36%)

**FIGURE 2** Age-appropriate pneumococcal vaccine coverage of children enrolled in Michigan Medicaid.*Chi-square P -value <0.01

vaccination series as compared to white children.^{25,27} In addition, children with sickle cell anemia tend to live in less affluent census tracts as compared to children without sickle cell anemia.²⁸ As our study population consisted of children with normal hemoglobin that were matched to children with sickle cell anemia and sickle cell trait on race, census tract, and Medicaid enrollment, our study population was reflective of a lower socioeconomic status as compared to other studies, as well as the population of children in the United States as a whole. Therefore, these rates, although substantially below other reports, are reflective of vaccination coverage among a vulnerable group of children.

Compounding the concern of low vaccination coverage in our study population, black children and children of lower socioeconomic status are at an increased risk of IPD as compared to more white and affluent children.^{27,29–31} Therefore, particular emphasis on programs to increase vaccination coverage overall in this population are needed. The Task Force on Community Preventive Services recommends a variety of strategies to improve immunization coverage, including reminder/recall, childcare/school vaccination requirements, and provider assessment/feedback.³² In addition, the Task Force strongly recommends multicomponent interventions that include education.³² Specific adjustments to these methods may result in increased vaccination coverage among vulnerable populations. For example, education, assessment, and provision of vaccinations in the context of Women, Infants, and Children (WIC) and home visiting programs has been effective in increasing receipt of vaccinations among populations of lower socioeconomic status.³² In a study of parent perceptions regarding reminder/recall approaches, parents with lower education and public health insurance for their child were more likely to prefer that reminder/recall notifications come from the health department rather than the child's doctor.³³ Centralized reminder/recall from health departments has also been proven to be more effective in increasing vaccination coverage as well more cost-effective than practice-based reminder/recall.^{34–36}

Although children with sickle cell anemia had higher vaccination coverage, up to 45% were still not adequately vaccinated against IPD by 16 months of age. This is slightly lower than previously reported; however, our assessment of PPSV coverage, as well as the indication that children with sickle cell anemia were covered at a higher rate than children without sickle cell disease, are reflective of other findings.^{37,38} Given the significant room for improvement among this particularly vulnerable population, strategies that specifically target this subgroup of the population to increase vaccination coverage are necessary. As children with sickle cell anemia have at least eight times the healthcare encounters per year as compared to children without sickle cell anemia, strategies that utilize healthcare visits may be most effective to increase vaccination coverage.^{39–42} For example, increasing sickle

cell-specific education of providers about the increased risk of IPD among this population, electronic health record prompts to providers, and in-office education of parents, may be effective strategies among this high-utilization population.

This study is unique in the ability to assess pneumococcal vaccination coverage in children with sickle cell trait. Our results show that these children did not have a meaningfully different rate of vaccination coverage as compared to children with normal hemoglobin. This is not surprising, as sickle cell trait is not a high-risk condition in which pneumococcal vaccination is emphasized; therefore, these children fall under the same recommendations as a child with normal hemoglobin. Similarly, children with sickle cell trait are not specifically recommended to receive PPSV. However, a comparison of IPD rates among black children with sickle cell trait, hemoglobin C trait, or normal hemoglobin enrolled in Medicaid found that black children with sickle cell trait have a 77% increased risk of laboratory-confirmed IPD as compared to children with normal hemoglobin, even after adjusting for age, gender, time (pre-PCV7, transition year, or post-PCV7), and high-risk conditions.¹⁷ Given the potential increased risk of infection among these children, it may be appropriate to emphasize pneumococcal vaccination among this population. However, a barrier to outreach to these children is that the majority of children or parents, as well as health providers, are unaware of the child's sickle cell trait status.^{18–20} This is likely reflective of a lack of follow-up among births diagnosed as sickle cell trait, as well as decreased emphasis on primary care physician notification and counseling as compared to sickle cell anemia.¹⁹ A continued neglect of opportunities for outreach to those diagnosed with sickle cell trait has been identified as a gap in the US healthcare system; development of policies for communication and follow-up of sickle cell trait status should be addressed within the US healthcare agenda.^{16,19} In addition, further research is necessary to understand the potential increased risk of IPD among children with sickle cell trait, as well as their immune response to PPSV vaccination to clarify the role that vaccination could play in reducing the susceptibility of this population to IPD. Given that 8% of all black births in the US are identified as sickle cell carriers,⁴³ any increases in pneumococcal vaccination coverage or reduction of IPD among this population could potentially reduce racial disparities in both pneumococcal vaccinations and IPD rates in the United States.

4.1 | Limitations

This study has limitations. First, we were subject to any missing or incorrect data recorded in MCIR. In addition, our study population was limited to children enrolled in Michigan Medicaid; this may not be generalizable to the population of children as a whole. However, a major strength of this paper lies in the identification of children as cases of sickle cell anemia, sickle cell trait, or normal hemoglobin using NBS records; therefore, the misclassification of children by exposure status was nearly nonexistent. In addition, we did not have data regarding mortality from IPD, which would provide context to the implications of undervaccination among these high-risk populations.

5 | CONCLUSIONS

In conclusion, strategies are necessary to increase pneumococcal vaccination coverage among all children. Specific strategies to increase vaccination coverage among the most vulnerable, such as children with sickle cell anemia, sickle cell trait, and low socioeconomic status, should be emphasized. Without targeting these specific subgroups, racial disparities in both pneumococcal vaccination coverage, as well as incidence of IPD, will continue to exist.

ACKNOWLEDGMENTS

This work was funded by the Blue Cross Blue Shield of Michigan Foundation (#2149.ii). This study was deemed exempt by the University of Michigan (HUM00096573) and Michigan Department of Health and Human Services (MDHHS; IRB#201502-07-NR-(R1)) IRBs. The study was designed by Sarah L. Reeves and Kevin J. Dombkowski. Data were collected and the manuscript drafted by Sarah L. Reeves, Hannah K. Jary, and Jennifer P. Gondhi and Newborn Screening Program results were provided by Mary Kleyn. Statistical analyses were conducted by Sarah L. Reeves, Hannah K. Jary, Jennifer P. Gondhi, and Abram L. Wagner. All authors contributed to interpreting results and approved the final manuscript. No financial disclosures were reported by the authors of this paper.

CONFLICT OF INTEREST

The authors have no conflicts of interest. No financial disclosures were reported by the authors of this paper.

ORCID

Sarah L. Reeves  <http://orcid.org/0000-0002-9145-0183>

REFERENCES

- Centers for Disease Control and Prevention. Pneumococcal disease: surveillance and reporting. 2016. Available from: <https://www.cdc.gov/pneumococcal/surveillance.html>. Accessed October 7, 2017.
- Centers for Disease Control and Prevention. Prevention of pneumococcal disease among infants and children – use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2010;59(RR-11):1–19.
- Centers for Disease Control and Prevention. Immunization. 2017. Available from: <https://www.cdc.gov/nchs/fastats/immunize.htm>. Accessed August 30, 2017.
- Centers for Disease Control and Prevention. Vaccines and preventable disease. 2016. Available from: <https://www.cdc.gov/vaccines/vpd/pneumo/index.html>. Accessed October 07, 2017.
- Black SB, Shinefield HR, Hansen J, Elvin L, Laufer D, Malinoski F. Postlicensure evaluation of the effectiveness of seven valent pneumococcal conjugate vaccine. *Pediatr Infect Dis J*. 2001;20:1105–1107.
- Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System (NNDSS): Invasive Pneumococcal Disease (IPD) (*Streptococcus pneumoniae*) 2017 Case Definition. 2017. Available from: <https://www.cdc.gov/nndss/conditions/invasive-pneumococcal-disease/case-definition/2017/>. Accessed October 07, 2017.

7. Yildirim I, Shea KM, Little BA, Silverio AL, Pelton SI. Vaccination, underlying comorbidities, and risk of invasive pneumococcal disease. *Pediatrics*. 2015;135:495–503.
8. Nuorti JP, Whitney CG, Centers for Disease Control and Prevention. Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2010;59(RR-11):1–18.
9. Cober MP, Phelps SJ. Penicillin prophylaxis in children with sickle cell disease. *J Pediatr Pharmacol Ther*. 2010;15:152–159.
10. Martin OO, Moquist KL, Hennessy JM, Nelson SC. Invasive pneumococcal disease in children with sickle cell disease in the pneumococcal conjugate vaccine era. *Pediatr Blood Cancer*. 2018;65.
11. Centers for Disease Control and Prevention. Sickle cell disease (SCD): 5 tips to help prevent infections. 2016. Available from: <https://www.cdc.gov/ncbddd/sicklecell/healthyliving-prevent-infection.html>. Accessed October 3, 2017.
12. National Heart Lung and Blood Institute. Evidence based management of sickle cell disease. 2014. Available from: https://www.nhlbi.nih.gov/sites/default/files/media/docs/sickle-cell-disease-report%20020816_0.pdf. Accessed June 2, 2018.
13. Hampton ML, Anderson J, Lavizzo BS, Bergmen AB. Sickle cell “nondisease.” A potentially serious public health problem. *Am J Dis Child*. 1974;128:58–61.
14. Perrine RP, Brown MJ, Clegg JB, Weatherall DJ, May A. Benign sickle-cell anaemia. *Lancet*. 1972;2:1163–1167.
15. Khan U, Kleess L, Yeh J, Berko C, Kuehl S. Sickle cell trait: not as benign as once thought. *J community Hospital Intern Med Perspect*. 2014;4:25418.
16. Goldsmith JC, Bonham VL, Joiner CH, Kato GJ, Noonan AS, Steinberg MH. Framing the research agenda for sickle cell trait: building on the current understanding of clinical events and their potential implications. *Am J Hematol*. 2012;87:340–346.
17. Poehling KA, Light LS, Rhodes M, et al. Sickle cell trait, hemoglobin C trait, and invasive pneumococcal disease. *Epidemiology*. 2010;21:340–346.
18. Harrison SE, Walcott CM, Warner TD. Knowledge and awareness of sickle cell trait among young African American adults. *West J Nurs Res*. 2017;39:1222–1239.
19. Taylor C, Kavanagh P, Zuckerman B. Sickle cell trait—neglected opportunities in the era of genomic medicine. *JAMA*. 2014;311:1495–1496.
20. Treadwell MJ, McClough L, Vichinsky E. Using qualitative and quantitative strategies to evaluate knowledge and perceptions about sickle cell disease and sickle cell trait. *J Natl Med Assoc*. 2006;98:704–710.
21. Korzeniewski SJ, Grigorescu V, Copeland G, et al. Methodological innovations in data gathering: newborn screening linkage with live births records, Michigan, 1/2007–3/2008. *Matern Child Health J*. 2010;14:360–364.
22. Centers for Medicare and Medicaid Services. Quality rating system measure technical specifications. 2016. Available from: <https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityInitiativesGenInfo/Downloads/2016-QRS-Measure-Technical-Specifications.pdf>. Accessed April 5, 2018.
23. American Immunization Registry Association. Comparing and communicating vaccination coverage estimates from immunization information systems, the National Immunization Survey, and related assessments. 2017. Available from: http://repository.immregistries.org/files/resources/59a031b40e94f/comparing__communicating_vaccination_coverage_estimates_from_iis_nis_and_related_assessments_-_fi.pdf. Accessed April 5, 2018.
24. Q&A About IIS Sentinel Sites. 2016. Available from: <https://www.cdc.gov/vaccines/programs/iis/activities/sentinel-sites.html>. Accessed April 7, 2018.
25. Office of Disease Prevention and Health Promotion. Healthy people 2020 immunization and infectious diseases. Available from: <https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives>. Accessed October 3, 2017.
26. McCarthy NL, Irving S, Donahue JG, et al. Vaccination coverage levels among children enrolled in the Vaccine Safety Datalink. *Vaccine*. 2013;31:5822–5826.
27. McLaughlin JM, Utt EA, Hill NM, Welch VL, Power E, Sylvester GC. A current and historical perspective on disparities in US childhood pneumococcal conjugate vaccine adherence and in rates of invasive pneumococcal disease: considerations for the routinely-recommended, pediatric PCV dosing schedule in the United States. *Hum Vaccin Immunother*. 2016;12:206–212.
28. Reeves SL, Braun TM, Dombkowski KJ, Fullerton HJ, Boulton ML, Lisabeth LD. The role of neighborhoods in the receipt of transcranial Doppler screening among children with sickle cell disease. *J Pediatr Hematol Oncol*. 2015;37:269–273.
29. Flannery B, Schrag S, Bennett NM, et al. Impact of childhood vaccination on racial disparities in invasive *Streptococcus pneumoniae* infections. *JAMA*. 2004;291:2197–2203.
30. Poehling KA, Talbot TR, Griffin MR, et al. Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. *JAMA*. 2006;295:1668–1674.
31. Spicer JO, Thomas S, Holst A, Baughman W, Farley MM. Socioeconomic and racial disparities of pediatric invasive pneumococcal disease after the introduction of the 7-valent pneumococcal conjugate vaccine. *Pediatr Infect Dis J*. 2014;33:158–164.
32. Task Force on Community Preventive Services. Recommendations regarding interventions to improve vaccination coverage in children, adolescents, and adults. Task Force on Community Preventive Services. *Am J Prev Med*. 2000;18(1 Suppl):92–96.
33. Saville AW, Beaty B, Dickinson LM, Lockhart S, Kempe A. Novel immunization reminder/recall approaches: rural and urban differences in parent perceptions. *Acad Pediatr*. 2014;14:249–255.
34. Kempe A, Saville A, Dickinson LM, et al. Population-based versus practice-based recall for childhood immunizations: a randomized controlled comparative effectiveness trial. *Am J public Health*. 2013;103:1116–1123.
35. Kempe A, Saville AW, Dickinson LM, et al. Collaborative centralized reminder/recall notification to increase immunization rates among young children: a comparative effectiveness trial. *JAMA Pediatr*. 2015;169:365–373.
36. Kempe A, Saville AW, Beaty B, et al. Centralized reminder/recall to increase immunization rates in young children: how much bang for the buck. *Acad Pediatr*. 2017;17:330–338.
37. Beverung LM, Brousseau D, Hoffmann RG, Yan K, Panepinto JA. Ambulatory quality indicators to prevent infection in sickle cell disease. *Am J Hematol*. 2014;89:256–260.
38. Nero AC, Akuete K, Leasure Reeves S, Dombkowski KJ. Pneumococcal vaccination rates in children with sickle cell disease. *J Public Health Manag Pract*. 2014;20:587–590.
39. Reeves SL, Madden B, Freed GL, Dombkowski KJ. Transcranial Doppler screening among children and adolescents with sickle cell anemia. *JAMA Pediatr*. 2016;170:550–556.
40. Reeves SL, Fullerton HJ, Cohn LM, et al. Missed opportunities for transcranial Doppler screening among children with sickle cell disease. *Clin Pediatr (Phila)*. 2016;55(12):1093–1099.

41. Raphael JL, Dietrich CL, Whitmire D, Mahoney DH, Mueller BU, Giardino AP. Healthcare utilization and expenditures for low income children with sickle cell disease. *Pediatr Blood Cancer*. 2009;52:263–267.
42. Boulet SL, Yanni EA, Creary MS, Olney RS. Health status and health-care use in a national sample of children with sickle cell disease. *Am J Prev Med*;38:S528–S535.
43. Centers for Disease Control and Prevention. Sickle Cell Disease, Data and Statistics. <https://www.cdc.gov/ncbddd/sicklecell/data.html>. Accessed June 2, 2018.

How to cite this article: Reeves SL, Jary HK, Gondhi JP, Kleyn M, Wagner AL, Dombkowski KJ. Pneumococcal vaccination coverage among children with sickle cell anemia, sickle cell trait, and normal hemoglobin. *Pediatr Blood Cancer*. 2018;65:e27282. <https://doi.org/10.1002/pbc.27282>