Transcranial Doppler Screening Among Children and Adolescents With Sickle Cell Anemia

Sarah L. Reeves, PhD; Brian Madden, MS; Gary L. Freed, MD; Kevin J. Dombkowski, DrPH

IMPORTANCE With transcranial Doppler (TCD) screening, we can identify children and adolescents with sickle cell anemia who are at the highest risk of stroke. An accurate claims-based method for identifying children and adolescents with sickle cell anemia was recently developed and validated that establishes the necessary groundwork to enable large population-based assessments of health services utilization among children and adolescents with sickle cell anemia using administrative claims data.

OBJECTIVE To assess the feasibility of using administrative claims data to identify and describe the receipt of TCD screening among children and adolescents with sickle cell anemia and to characterize opportunities for intervention.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cross-sectional study using Medicaid claims data from 2005 to 2010. Medicaid claims data were obtained from the following states: Florida, Illinois, Louisiana, Michigan, South Carolina, and Texas. Children and adolescents 2 to 16 years of age with sickle cell anemia were identified by the presence of 3 or more Medicaid claims with a diagnosis of sickle cell anemia within a calendar year (2005-2010). A total of 4775 children and adolescents contributed 10,787 person-years throughout the study period. Data were analyzed in 2015. A subset of children and adolescents enrolled for 2 or more consecutive years was identified to examine potential predictors of TCD screening, which included age, sex, previous receipt of TCD screening, state of residence, and health services utilization (well-child visits, outpatient visits, emergency department visits, and inpatient visits).

MAIN OUTCOMES AND MEASURES Receipt of TCD screening was assessed by year and state. Using logistic regression with generalized estimating equations, we included associated predictors in a multivariable model to estimate odds of TCD screening.

RESULTS For a total of 4775 children and adolescents 2 to 16 years of age, TCD screening rates increased over the 6-year study period from 22% to 44% (P < .001); rates varied substantially across states. A subset of 2388 children and adolescents with sickle cell anemia (50%) was enrolled for 2 or more consecutive years. Each year of increasing age was associated with 3% lower odds of TCD screening (odds ratio, 0.97 [95% CI, 0.95-0.98]; P = .002). Previous receipt of TCD screening (odds ratio, 2.44 [95% CI, 2.11-2.81]; P < .001) and well-child visits (odds ratio, 1.10 [95% CI, 1.03-1.18]; P = .007) were associated with higher odds of receiving a TCD screening.

CONCLUSIONS AND RELEVANCE Despite national recommendations, TCD screening rates remain low. Successful strategies to improve TCD screening rates may capitalize on the numerous health care interactions among children and adolescents with sickle cell anemia.
Sickle cell disease (SCD) is a hereditary chronic condition primarily affecting minority children in the United States and associated with substantial morbidity and mortality.\(^1,4\) It exists in multiple subtypes; the subtype conferring the highest risk of morbidity and mortality is sickle cell anemia (hemoglobin SS). Sickle cell anemia is associated with an elevated risk of stroke; without intervention, reports indicate that 10% of children with sickle cell anemia will have a stroke prior to the age of 20 years.\(^5,6\) Elevated cerebral blood velocities are associated with an increased risk of stroke, which can be assessed using transcranial Doppler (TCD) screening.\(^7\) The Stroke Prevention Trial in Sickle Cell Anemia (STOP) demonstrated that, among children with at least 2 high blood flow velocities as detected by TCD screening, receipt of chronic blood transfusions reduced the risk of stroke by 92% compared with the standard care.\(^8\)

Recently, the National Heart, Lung, and Blood Institute released an expert panel report detailing evidence-based guidelines for the treatment of SCD.\(^9,10\) These guidelines strongly recommend that children and adolescents with sickle cell anemia receive annual TCD screenings from 2 to 16 years of age. Although this recommendation is consistent with those published for the prior decade,\(^11\) prior studies indicate that TCD screening rates remain low.\(^12-14\) Most reports of TCD screening rates have been limited to studies from comprehensive sickle cell centers where the identification of the target population is enabled by either a medical record review or registries within a comprehensive sickle cell center, or limited to a state Medicaid program.\(^12-15\)

Achieving a population-based perspective on TCD screening has been hampered by the inherent challenges of identifying children with sickle cell anemia among large populations for which medical record reviews would be cost prohibitive. In population-based studies of other chronic conditions, administrative claims data have been successfully used to conduct asthma surveillance\(^16,17\) and a wide array of studies characterizing health services utilization.\(^18-20\) A claims-based method for identifying children with sickle cell anemia with a high degree of sensitivity and specificity was recently developed and validated.\(^21\) The accuracy of this claims-based method establishes the necessary groundwork to enable large population-based assessments of health services utilization among children and adolescents with sickle cell anemia using administrative claims data. With that in mind, our objective was to assess receipt of TCD screening among a multistate population of children and adolescents with sickle cell anemia and to characterize opportunities for intervention.

**Methods**

We performed a cross-sectional study of TCD screening rates among children and adolescents with sickle cell anemia using a multistate set of Medicaid administrative claims data. The study was approved by the institutional review board at the University of Michigan. Informed consent was not required because the data were deidentified.

**Table 1**

<table>
<thead>
<tr>
<th>Key Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
</tr>
<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td><strong>Meaning</strong></td>
</tr>
</tbody>
</table>

**Data Source and Study Population**

Our target population was drawn from the Medicaid programs for 6 states with an average to high prevalence of SCD: Florida, Illinois, Louisiana, Michigan, South Carolina, and Texas.\(^22\) Administrative data from Medicaid Analytic eXtract (MAX) for the years 2005 to 2010 were acquired from the Centers for Medicare and Medicaid Services, including enrollment history and all claims for inpatient, outpatient, emergency department, laboratory, and outpatient pharmacy health services. At the time of this study, these were the most recent MAX data available. Using a validated method, we identified our study population as children and adolescents with 3 or more claims for hemoglobin SS within a year.\(^21\) In a similar manner, we obtained all administrative claims data for all services provided to these children and adolescents.

Children and adolescents 2 to 16 years of age were eligible to be in the study population, consistent with recommendations for annual TCD screening.\(^10\) Eligible children and adolescents were required to be enrolled in Medicaid for at least 1 calendar year (from January 1 to December 31) from 2005 to 2010. Children and adolescents could contribute multiple years of enrollment during the study period. Because chronic blood transfusions are likely to be indicative of prior stroke or treatment for children and adolescents with a high blood flow velocity as detected by previous TCD screening,\(^2,8\) using procedure codes, we excluded children and adolescents who received more than 6 blood transfusions in a year (Table 1).

**TCD Screening and Health Services Utilization**

Receipt of TCD screening was classified dichotomously (yes/no) within each calendar year using procedure codes. The accuracy of this approach has previously been validated; compared with the gold standard of medical record reviews, Medicaid administrative claims for receipt of TCD screening have a sensitivity of 94% (95% CI, 83%-99%) and a specificity of 100% (95% CI, 91%-100%) among children enrolled in Michigan Medicaid.\(^23\)

**Potential Predictors of TCD Screening**

To assess potential predictors of TCD screening, we identified a subgroup of the study population already specified. This
subset consisted of children enrolled for at least 2 consecutive years in Medicaid; children could contribute multiple intervals. Successive 2-year intervals could include a common year (eg, 2007-2008 and 2008-2009). The requirement of 2 years of enrollment was necessary to ensure that the potential predictors occurred prior to the assessment of receipt of TCD screening. Our primary outcome, receipt of TCD screening, was assessed during the second year of enrollment of each 2-year interval; predictors were measured in the first year of enrollment with the exception of age, which was classified as of January 1 of the second enrollment year. We evaluated potential associations between receipt of TCD screening and the following predictors: age, sex, prior use of health services (SCD-related inpatient, SCD-related outpatient, emergency department, or well-child visits), previous receipt of TCD screening, calendar year, and state of residence. Table 1 describes the procedure and provides the diagnosis codes used to classify these health services.24–26

Statistical Analysis

Frequencies and percentages (or means and standard deviations) were determined for demographic characteristics, overall and by state. Among the study population of children with sickle cell anemia enrolled in Medicaid for at least 1 year, the proportion of children receiving annual TCD screening was calculated by state for each year in the study period (2005-2010). The presence of trends in TCD screening rates were also assessed over time and by state using linear regression and analysis of variance. Potential predictors of TCD screening were assessed only among the subset of the study population enrolled for at least 2 years. Means and standard deviations of the number of annual health services visits were assessed; health services were measured in the first year of enrollment. Logistic regression was used to estimate the bivariate associations between each potential predictor and receipt of TCD screening. Because multiple periods of enrollment were allowed for each child, generalized estimating equation models with robust standard errors were used to account for the correlation among children. Counts of health care services and age were modeled as continuous variables; predictors showing an association (P < .20) with receipt of TCD screening were included in a final multivariable model. Odds ratios (ORs) with 95% CIs were used to assess the final associations. For all models, regression diagnostics were performed to assess normality of error variances.

Results

A total of 4887 children and adolescents with sickle cell anemia between 2 and 16 years of age were identified during the study period, contributing a total of 11,542 person-years of enrollment. Overall, 112 children and adolescents (2%) representing 755 person-years (7%) were excluded owing to receipt of 6 or more blood transfusions during a calendar year. The final study population consisted of a total of 4775 children and adolescents (98%) contributing 10,787 person-years (93%). States varied in the total number of person-years contributed to the study population as follows: Florida with 3186 person-years (30%), Texas with 1948 person-years (18%), Louisiana with 1800 person-years (17%), Illinois with 1722 person-years (16%), Michigan with 1281 person-years (12%), and South Carolina with 850 person-years (8%). In 2005, the mean (SD) age of children in the study population was 8.0 (3.8) years, and 47% were females (Table 2).

Overall, among children and adolescents enrolled in Medicaid for at least 1 year, TCD screening rates increased from 22% (2005) to 44% (2010) during the study period (Figure). Screening rates varied by year and by state, with Texas having the lowest screening rate at any time point (7% in 2005). Overall, these rates increased over time (P < .001) and varied by state (P = .004).

The evaluation of predictors of TCD screening was performed among the subset of the study population enrolled for at least 2 consecutive years, which consisted of 2388 children and adolescents (50%). On average, eligible children and adolescents had 2.1 SCD-related inpatient hospitalizations, 20.0 SCD-related outpatient visits, 3.7 emergency department visits, and 0.7 well-child visits within the first year of their enrollment (Table 3). Bivariate analysis indicated that age; number of well-child, outpatient, emergency department, and inpatient visits; previous receipt of TCD screening; state of residence; and calendar year were independently associated with receipt of TCD screening. The multivariable model predicting receipt of TCD screening confirmed this association for age, number of well-child and inpatient visits, receipt of TCD screening in the first year of the enrollment period, state of residence, and calendar year (Table 4). Each year of increasing age (OR, 0.97 [95% CI, 0.95-0.98]; P = .002) was associated with decreased odds of receiving a TCD screening. Previous re-

Table 1. Claims-Based Definitions of Variables Using Medicaid Analytic eXtract Data (2005-2010)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data Set</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient visit</td>
<td>Inpatient file</td>
<td>Any event within file</td>
</tr>
<tr>
<td>Outpatient visit</td>
<td>Other services</td>
<td>Event labeled physician, other practitioner, outpatient hospital, and clinic (other categories such as dental, laboratory, and home health excluded)</td>
</tr>
<tr>
<td>Transcranial Doppler</td>
<td>Other services</td>
<td>HCPCS codes 93886, 93888, 93890, 93892, and 93893</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Other services</td>
<td>HCPCS codes 09883, 36455, 86999, S3906, S5938, S09882, and 36430</td>
</tr>
<tr>
<td>Well-child visit</td>
<td>Other services</td>
<td>HCPCS codes 99381-5, 99391-5, 99543, and 83655 and ICD-9 codes V202, V700, V701, and V705-9</td>
</tr>
<tr>
<td>Emergency department visit</td>
<td>Other services</td>
<td>Place of service: emergency department; HCPCS codes 99281-5 and G0380-5 and Revenue codes 0450-2 and 0459</td>
</tr>
<tr>
<td>Sickle cell disease-related health care</td>
<td>Inpatient and other services file</td>
<td>ICD-9 codes 28260-4, 28268, 28269, 28241, and 28242</td>
</tr>
<tr>
<td>Sickle cell anemia</td>
<td>Inpatient and other services file</td>
<td>ICD-9 codes 282.61 and 282.62</td>
</tr>
</tbody>
</table>

cept of TCD screening (OR, 2.44 [95% CI, 2.11-2.81]; \( P < .001 \)) and increasing number of well-child visits (OR, 1.10 [95% CI, 1.03-1.18]; \( P = .007 \)) were associated with higher odds of receiving a TCD screening. The odds of receiving a TCD screening were lower for children and adolescents with sickle cell anemia in Florida, Illinois, Michigan, South Carolina, and Texas than for those in Louisiana. The odds of receiving a TCD screening were higher in 2009 (OR, 1.32 [95% CI, 1.09-1.60]) and 2010 (OR, 1.30 [95% CI, 1.10-1.53]) than in 2005 (Table 4).

Discussion

Transcranial Doppler screening is the only method to identify children and adolescents with sickle cell anemia who are at the highest risk of stroke, and its importance has recently been underscored by National Heart, Lung, and Blood Institute guidelines that strongly recommend children with sickle cell anemia receive an annual TCD screening. A consistent assessment of TCD screening rates and the identification of strategies to improve these screening rates are essential to improve the health of these high-risk children and adolescents.\(^\text{10}\) Our findings indicate that although TCD screening rates have increased over time, even the highest rates we report are suboptimal. Substantial opportunity for improvement exists; potentially successful strategies may capitalize on the numerous health care interactions of these children and adolescents within a year, particularly among those who have not previously received a TCD screening. However, numerous challenges also exist to increasing TCD screening rates; addressing these barriers on multiple levels may be the most successful strategy to increase these rates.

Despite increasing over time, TCD screening rates remained suboptimal across each state in our sample, and this was especially evident among older children. Screening rates differed by state at baseline, but the majority of states had increased to similar screening rates in 2010, with the exception of Illinois, which performed suboptimally. Differences in screening rates across states could potentially be attributable to variation in insurance policies and sickle cell clinic-specific factors by state. Few factors affected the receipt of TCD screening because a similar proportion of children and adolescents received a TCD screening irrespective of the presence of an SCD-related inpatient, SCD-related outpatient, or emergency department visit. A decreased likelihood of receipt of TCD screening with increasing age is consistent with other studies\(^\text{12-14}\); however, we reported that increasing outpatient visits were not associated with receipt of TCD screening. This differs from a previous study\(^\text{27}\) at a comprehensive sickle cell center indicating that increased outpatient visits were associated with increased TCD screening rates, although our study also includes care provided at sites other than comprehensive sickle cell centers and may differ for that reason. The increased likelihood of receipt of screening with the presence of a well-child visit may indicate that children receiving well-child visits are more likely to use other preventive care services. Our findings also indicate that the likelihood of receiving a TCD screening increases among those who have previously received a TCD screening, which suggests that a subgroup of children are consistently receiving TCD screenings. As a consequence, interventions focused on initiating TCD screenings among children previously unscreened may be an effective mechanism to increase the likelihood of receiving subsequent TCD screenings.

Because substantial gaps exist between the National Heart, Lung, and Blood Institute recommendations for an annual TCD screening and the proportion of children and adolescents receiv-
Transcranial Doppler Screening for Sickle Cell Anemia

opportunities.30-33 One quality-improvement strategy that has
with health care professionals but experiencing missed
did not increase baseline rates of TCD screening,
effectiveness of reminder letters for TCD screenings showed that
these letters did not increase baseline rates of TCD screening,
which is consistent with patients having adequate contact
(Reprinted)  Copyright 2016 American Medical Association. All rights reserved.

Successful strategies to increase TCD screening rates will also
likely need to target barriers that may be experienced by both
health care professionals and patients’ caregivers. For example,
aschool-based interventions have been successful in
improving asthma self-management skills, and web-based inter-
ventions have been successful in encouraging behavior change
among adolescents with diabetes.40,41

Successful strategies to increase TCD screening rates will also
likely need to target barriers that may be experienced by both
health care professionals and patients’ caregivers. For example,
asurvey of pediatric hematologists, neurologists, and primary
care physicians treating children with SCD indicated that these
health care professionals may be lacking in self-efficacy, outcome
expectancy, and knowledge with respect to specific TCD screening
guidelines. In addition, a need to increase caregivers’ knowledge
about the risk of stroke among children and adolescents with
SCD has been previously identified.38,39 Additional barriers fac-
ing the families of these children and adolescents may include
health literacy, motivation, and competing priorities. It will be
imperative to include mixed methods research, such as patient
surveys and focus groups of key stakeholders, to gain clarity on
the most effective use of resources to improve TCD screening
rates in this high-risk population. Strategies that have proven
successful in increasing the receipt of preventive care in other ped-
iatric chronic conditions should additionally be explored. For

example, school-based interventions have been successful in
improving asthma self-management skills, and web-based inter-
ventions have been successful in encouraging behavior change
among adolescents with diabetes.40,41

Limitations to this study exist. This study relies on the com-
pleteness and accuracy of administrative claims data to deter-
mine receipt of TCD screening. However, a prior study23 dem-
strated that administrative claims data are highly sensitive and
specific with regard to identifying receipt of TCD screening com-
pared with the gold standard of a medical record review. Although
our claims-based method is believed to be accurate, we were un-
able to ascertain the reasons behind the lack of receipt of TCD
screening. For example, we were not able to determine whether
a health care professional chose to initiate transfusions for stroke
prevention irrespective of receipt of TCD screening or whether a
parent refused the TCD screening recommendation. In addition,
we were unable to account for specific practices at comprehen-
sive sickle cell centers that may have influenced receipt of
TCD screening, such as physician-prescribing behaviors and the
availability of facilities in which to perform a TCD screening. Our
study population consists of children and adolescents who have
a history of using sickle cell anemia–related health care. There
may be a subgroup of children with sickle cell anemia whose par-
ents do not access health care reported as being related to this
condition, although we expect this group to be small.34 We also
assume that the subgroup of children without sickle cell anemia-
related health care would also be less likely to receive a TCD
screening; therefore, our rates may be overestimating the true
rate of TCD screening among children with SCD.

Table 3. Annual Health Care Utilization Among 2338 Children and Adolescents With Sickle Cell Anemia Enrolled in Medicaid for at Least 2 Consecutive Years From 2005 to 2010

<table>
<thead>
<tr>
<th>Type of Visit</th>
<th>Visits, Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCD-related inpatient</td>
<td>2.1 (2.2)</td>
</tr>
<tr>
<td>SCD-related outpatient</td>
<td>20.0 (16.6)</td>
</tr>
<tr>
<td>Emergency department</td>
<td>3.7 (3.6)</td>
</tr>
<tr>
<td>Well-child</td>
<td>0.7 (0.9)</td>
</tr>
</tbody>
</table>

Abbreviation: SCD, sickle cell disease.

* Health care measured in first year of enrollment; children and adolescents eligible to contribute multiple 2-year intervals.

Table 4. Multivariable Model Predicting Receipt of TCD Screening for 2338 Children and Adolescents With Sickle Cell Anemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.97 (0.95-0.98)</td>
</tr>
<tr>
<td>Type of visit</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>0.96 (0.93-1.00)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>Emergency department</td>
<td>1.01 (0.99-1.03)</td>
</tr>
<tr>
<td>Well-child</td>
<td>1.10 (1.03-1.18)</td>
</tr>
<tr>
<td>Previous TCD screening</td>
<td>2.44 (2.11-2.81)</td>
</tr>
<tr>
<td>State</td>
<td></td>
</tr>
<tr>
<td>Florida</td>
<td>0.63 (0.52-0.76)</td>
</tr>
<tr>
<td>Illinois</td>
<td>0.42 (0.34-0.53)</td>
</tr>
<tr>
<td>Louisiana</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Michigan</td>
<td>0.44 (0.35-0.56)</td>
</tr>
<tr>
<td>South Carolina</td>
<td>0.76 (0.57-1.05)</td>
</tr>
<tr>
<td>Texas</td>
<td>0.42 (0.33-0.52)</td>
</tr>
</tbody>
</table>

Year

<table>
<thead>
<tr>
<th>Year</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>2006</td>
<td>0.84 (0.72-0.98)</td>
</tr>
<tr>
<td>2007</td>
<td>1.01 (0.86-1.19)</td>
</tr>
<tr>
<td>2008</td>
<td>1.01 (0.85-1.19)</td>
</tr>
<tr>
<td>2009</td>
<td>1.32 (1.09-1.60)</td>
</tr>
<tr>
<td>2010</td>
<td>1.30 (1.10-1.53)</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; TCD, transcranial Doppler.
Conclusions

Despite national recommendations, annual TCD screening rates remain low, particularly among adolescents. Successful strategies to increase screening among children and adolescents with sickle cell anemia may be aimed at more effective prompts to identify patients eligible for a TCD screening during the numerous health care encounters typically experienced by this population. However, the effectiveness of specific mechanisms by which missed opportunities can be remediated requires additional study.