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Approximately 40 000 children with sickle cell anemia require screening with TCD and treating with hydroxyurea for stroke prevention in three states in northern Nigeria

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To the Editor:

Strokes are a preventable, major cause of permanent neurological morbidity and mortality in children with sickle cell anemia (SCA) living in Nigeria.[1] Globally, over 300 000 children

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CONFLICT OF INTEREST

The authors declare no competing financial interests.

are born with SCA annually,[2] and Nigeria accounts for approximately 50% of all affected births.[3] In high-resource settings, stroke prevalence can be reduced by 10-fold with transcranial Doppler (TCD) screening and monthly blood transfusion therapy when compared to no TCD screening.[4] There has been a dramatic impact in decreasing the stroke rate in children with SCA living in high-resource settings. However, no evidence-based strategy has been introduced in the low-resource settings where the majority of children with SCA live. To decrease life-long morbidity and mortality associated with strokes in children with SCA, our team initiated a primary stroke prevention trial using hydroxyurea therapy for children with SCA, 5 to 12 years of age (NCT02560935) living in Kano Nigeria.[5]

Since 2012, our stroke prevention program in children with SCA has matured to include neighboring states to Kano in northern Nigeria, Katsina and Kaduna. Two initial steps were required to establish a regional stroke prevention program in these low-resource settings; 1) assessment of children with SCA requiring TCD screening; and 2) ensuring sustainability of the stroke prevention program beyond R01 funding (5R01NS094041).

We provide here the first estimates of the total number of children with SCA requiring TCD screening in Kano, Katsina and Kaduna in northern Nigeria, and strategies to ensure sustainability of the stroke prevention program. Our approach can be extrapolated to other regions of sub-Saharan Africa, with large numbers of children with SCA that require screening, and treatment for primary stroke prevention.

Based on the estimated number of children evaluated in the past several years at the seven pediatric clinics in the three states, approximately 40 000 children will require TCD screening annually. Total number of children requiring annual TCD screening are estimates because of no state sponsored newborn screening programs and the absence of electronic health records. Further, 40 000 is a clear conservative estimate of children with SCA in the region because this number reflects only the children seen in the SCD clinics. Among this cohort, we anticipate 10% will have an abnormal TCD measurement. This corresponds to 4 000 children in the three-state region requiring life-long hydroxyurea therapy for primary stroke prevention. As a comparison, in our ongoing randomized controlled trial for stroke prevention (SPRING Trial, NCT02560935) in Kano and Kaduna, a total of 3 120 TCD assessments were done in one year among four sites, corresponding to approximately 60 TCD assessments per week. The current reach of 8% (3 120 of 39 119) for TCD screening is simply too low to have a public health impact on stroke prevention in the region.

As an indication of the immense public health challenge to prevent strokes in children with SCA in the region, approximately 1.5 times more children with SCA are being followed in the three-state region in Nigeria than the entire U.S. (~40 000 vs ~28 000; respectively).[6] Prior to 2012, neither TCD screening nor hydroxyurea therapy were part of standard care in the region. As a direct result of our goal of providing a sustainable solution for primary stroke prevention in this region, we now have seven hospitals providing TCD screening (Table 1).

Several barriers had to be overcome before establishing a sustainable and widespread implementation of TCD screening in northern Nigeria. First is a partnership with the state

governments to provide hydroxyurea to the children with abnormal TCD measurements, because many of the families cannot afford indefinite hydroxyurea therapy at $0.13 (U.S. dollar, July 30, 2019) per day from Bond Chemical, a Nigerian-based pharmaceutical company. Second is the access to a TCD machine with an average cost of approximately $20 000. Third is the need for providers with formal training and certification in TCD assessment.

To the credit of the government leadership of all three states, each has activated a plan to increase screening and treatment for primary stroke prevention. Specifically, in the last 12 months, the government of Kano state has passed a law where a fixed percentage of the state revenue will be allocated to the care of individuals with SCA, with priority placed on purchasing hydroxyurea therapy for primary stroke prevention. Equally impressive, for children with abnormal TCD measurements, the state officials from Katsina have purchased hydroxyurea. Hospital leadership from Kaduna has purchased hydroxyurea for children with abnormal TCDs, while awaiting the start of the state supported program to provide hydroxyurea free of charge for children with abnormal TCD measurements. Recently, to address the deficits of TCD screening, our team secured donations of 10 TCD machines, adding to 9 machines in the region that were acquired through grants and philanthropy. Important to ensure sustainability, for the first time, two nurses in Kano were certified to perform TCD assessments in SCD clinics, a role previously designated to physicians. Leadership of the other hospitals has also agreed to permit task-shifting of TCD screening to nurses.

Lessons learned for increasing reach for TCD screening in northern Nigeria are applicable in the U.S., where children with SCA also have an unacceptable low TCD reach. Over a six-year study period among 4 775 children from six states in the U.S., only 22% to 44% received TCD screening.[7] We believe strategies for improving TCD reach in northern Nigeria can be used to improve TCD reach in the U.S.

In summary, over 100-fold more (150 000 vs 1 300)[3,8] children with SCA are born each year in Nigeria when compared to the U.S. region-specific solutions, including strong partnerships with local governments, are required to reach the maximum number of children with SCA, screened with TCD, and treated with hydroxyurea therapy for primary stroke prevention. Potentially successful strategies in Nigeria to improve TCD screening and treatment may be implemented in the U.S.

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TABLE 1

Standard care primary stroke prevention programs initiated in northern Nigeria (Kano in 2013, Kaduna, 2016, and Katsina, 2019). Prior to our stroke prevention program transcranial Doppler (TCD) was not offered and hydroxyurea therapy was not part of standard care for approximately 40 000 children with sickle cell anemia (SCA) in these three states. All three state governments have agreed to provide hydroxyurea free-of-charge to children with SCA and abnormal TCD measurements. Estimates of the number of children registered and seen should be considered approximates due to the absence of electronic health records and newborn screening program

Study site	Children with SCA (age: 0–12 years) evaluated weekly, N	Total number of children registered with SCA and evaluated in the last 2 years	TCD evaluation as standard of care; combined SCD and clinic days for TCD assessment
KANO			
Aminu Kano Teaching Hospital	80	2010	Yes, Tuesday
Murtala Muhammad Specialist Hospital	160	17 810	Yes, Monday–Friday
HasiyaBayero Pediatric Hospital	108	11 129	Yes, Wednesday
Muhammad Abdullahi Wase Specialist Hospital	42	470	Yes, Tuesday and Thursday
KADUNA			
Baraudikko Teaching Hospital	40	1200	Yes, Wednesday and Thursday
KATSINA			
Federal Medical Center Katsina	20	500	Yes, Monday–Friday
General Hospital Katsina	200	6000	No

Abbreviations: N, number; SCA, sickle cell anemia.