Received: 5 January 2024 | Revised: 17 June 2024 | Accepted: 25 June 2024

DOI: 10.1002/pbc.31190

Pediatric Blood & Cancer

SIOP INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

aspho The American Society of Pediatric Hematology/Oncology

WILEY

RESEARCH ARTICLE

Limited access to transcranial Doppler screening and stroke prevention for children with sickle cell disease in Europe: Results of a multinational EuroBloodNet survey

Vincenzo Voi[1] | Victoria Gutierrez-Valle[2] | Daniela Cuzzubbo[3] | Corrina McMahon[4] | Maddalena Casale[5] | Maria Del Mar Mañú Pereira[2] | Mirco D'Agnolo[6] | Baba P. D. Inusa[7] | Mariane de Montalembert[8] | Raffaella Colombatti[6]

[1]Centro per le Emoglobinopatie, Dipartimento di Scienze Cliniche e Biologiche, Università di Torino, Ospedale San Luigi Gonzaga, Turin, Italy

[2]Vall d'Hebron Institut de Recerca, VHIR, Barcelona, Spain

[3]Clinica di Onco-Ematologia Pediatrica, Azienda Ospedaliero Universitaria Meyer, Florence, Italy

[4]Children's Health Ireland at Crumlin, Crumlin, Ireland

[5]Università degli studi della Campania Luigi Vanvitelli, Naples, Italy

[6]Pediatric Hematology Oncology, Department of Women's and Children's Health, Azienda Ospedale-University of Padova, Padua, Italy

[7]Paediatric Haematology, Evelina Children's Hospital, Guy's and St Thomas' Hospital, London, UK

[8]Pediatrics, Referral Center for Sickle Cell Disease, Necker Hospital, APHP, Paris, France

Correspondence
Raffaella Colombatti, Department of Women's and Child's Health, University of Padova, Via Giustiniani 3, 35128, Padua, Italy.
Email: raffaella.colombatti@unipd.it

This manuscript was presented as an *oral communication at the American Society of Hematology (ASH) Meeting, December 2021*: Daniela Cuzzubbo, Victoria Gutierrez-Valle, Maddalena Casale, Vincenzo Voi, Corrina McMahon, Maria Del Mar Mañú Pereira, Mariane de Montalembert, Baba P. D. Inusa, Raffaella Colombatti. Limited access to transcranial Doppler screening and stroke prevention for children with sickle cell disease in Europe: Results of a multinational EuroBloodNet survey. *Blood*, Volume 138, Supplement 1, 2021, Page 915, ISSN 0006–4971, https://doi.org/10.1182/blood-2021-147298.

Funding information
European Reference Network on Rare Hematological Diseases, Grant/Award Number: 10108571; ERN-EuroBloodNet; European Union within the framework of the Fourth EU Health Programme

Abstract

Background: Ensuring equitable access to adequate standard of care for patients with rare hematological disease is one of the aims of the European Reference Network (ERN) EuroBloodNet. Stroke is one of the most devastating complications for children with sickle cell disease (SCD). For effective prevention of stroke risk, annual transcranial Doppler (TCD) according to a defined protocol is recommended for patients aged 2–16 years, with red blood cell transfusion therapy for those at risk. There is no information regarding screening for stroke risk and stroke prevention programs in Europe.

Methods: Seven SCD experts of five healthcare providers (HCPs) of ERN EuroBloodNet developed an online survey to assess the access to TCD screening and stroke prevention programs for children with SCD in Europe.

Results: Eighty-one experts in 77 HCPs from 16 European countries responded to 16 online questions. Thirty-two of 77 (51%) HCPs were EuroBloodNet reference centers, and 36% physicians reported not having a dedicated TCD/TCD imaging service for children with SCD. Only 30% of physicians provided estimates that all their patients received annual TCD according to the standard protocol due to lack of trained staff (43%), lack of TCD instruments (11%), refusal of patients due to logistical difficulties (22%), and lack of funds for dedicated staff or equipment (11%).

Abbreviations: ERN, European Reference Network; HCP, healthcare provider; ICA, internal carotid artery; MCA, middle carotid artery; SCA, sickle cell anemia; SCD, sickle cell disease; STOP, Stroke Prevention Trial; TCD, transcranial Doppler; TCDi, imaging transcranial Doppler.

[Correction added on 25 July 2024, after first online publication: The order of the first and surnames for some of the authors has been corrected in this version].

Conclusions: This multinational European survey provides the first comprehensive picture of access to TCD screening and stroke prevention in European countries. Identifying the potential underlying causes of the lack of effective standardized screening, this survey also addresses possible dedicated actions to cover these needs.

KEYWORDS
children, EuroBloodNet, Europe, sickle cell disease, stroke, transcranial Doppler

1 | INTRODUCTION

Children with sickle cell disease (SCD) are at increased risk of cerebrovascular events such as ischemic stroke, silent infarcts, and neurocognitive impairment.[1] Complex pathophysiological mechanisms are implied in the development of large-vessel cerebral vasculopathy and ischemic stroke, including chronic anemia, hemolysis, and vaso-occlusive events, which activate inflammatory and coagulation cascades.[1] However, Adams et al. in the Stroke Prevention Trial in Sickle Cell Anemia (STOP) demonstrated the pivotal role of a single diagnostic tool, transcranial Doppler ultrasound scanning (TCD), to identify children with sickle cell anemia (SCA) at high risk of ischemic stroke based on increased cerebral velocities in the middle cerebral artery (MCA) and the internal carotid artery (ICA).[2] Patients with abnormal TCD velocities have a 40% risk of experiencing an ischemic stroke in the following 3 years, and monthly transfusion has been shown to decrease the risk of stroke in patients with abnormal TCD.[2,3] Hence, Adams et al. in 1998 recommended those with abnormal cerebrovascular flow velocities be offered prophylactic blood transfusion therapy to prevent stroke between ages 2 and 16 years.[2,3] Therefore, TCD screening for stroke prevention is now mandatory in all guidelines for the management of children with SCA utilizing a specific protocol for intracranial vessel evaluation, based on the STOP criteria[3,4–8]: children are categorized according to the STOP criteria of ICA and MCA time-averaged maximum mean velocities (TAMMVs): abnormal for TAMMV ≥200 cm/s, conditional for TAMMV 170–199 cm/s, normal for TAMMV 70–169 cm/s, and low for TAMMV less than 70 cm/s. TCD imaging (TCDi) is used in some settings instead of TCD, with or without adjusted thresholds for categorization.[4,9]

Guideline implementation in the real world is challenging. It requires healthcare service organization and capacity building, as well as knowledge and competency maintenance, which can be particularly difficult for rare diseases.[10,11] In fact, in spite of the increase in SCA as a health issue in Europe in the past decades and the development by scientific societies of national guidelines tailored to the different healthcare settings to standardize management of children and support pediatricians and hematologists in day-to-day care, the information available on the quality of the TCD screening is limited to educational experiences in a few countries.[12,13] No evaluation of stroke prevention programs has been performed so far in Europe. As more disease-modifying therapies become available for children with SCD, it is mandatory to be aware of TCD availability, screening practices, and real-world data on stroke prevention strategies for children with SCD in Europe in order to provide the best tailored personalized care.

EuroBloodNet is the European Reference Network (ERN) on rare hematological disorders, established by the European Union in 2016 to improve the healthcare delivery and overall quality of life of patients with a rare hematological disease in Europe (Figure S1). The EuroBloodNet members recognized as experts centers for red blood cell disorders were first labeled by their National Ministries according to their own procedures, which may differ from one country to another country, and secondly approved by the ERN-EuroBloodNet according to the criteria defined by the network in 2016 (available at www.eurobloodnet.eu). Demonstrating adequate level of expertise and capacity to provide specialized care in SCD, including TCD screening to children with SCD, was a mandatory requirement to become a member reference center or affiliated in the red blood cell defects subnetwork: expert centers had to meet the minimal number of 30 TCD/TCDi procedures per year.[14]

In this study, we wanted to evaluate availability of and access to TCD or TCD TCDi screening and stroke prevention programs for children with SCA in European expert centers, STOP protocol criteria knowledge and application, and identify barriers to their implementation, and plan coordinated actions for improvement.

2 | MATERIALS AND METHODS

2.1 | Survey mode and questionnaire

This was a descriptive study. An online survey was developed by seven SCD experts working in healthcare providers (HCPs) that were members of the ERN-EuroBlodNet, coming from five European countries.

The survey aimed to evaluate the availability of and access to TCD screening and stroke prevention programs, the STOP protocol criteria knowledge, and application by European expert centers; it aimed also to identify any barriers to screening and stroke prevention programs, and plan actions. The survey consisted of 16 online questions, specifically tailored to the European Health Care Organization in the field of rare diseases, and the detailed content is listed in Table S2. The survey questions were grouped in the following topics: availability of TCD service and equipment; knowledge of screening and treatment protocols; and service access.

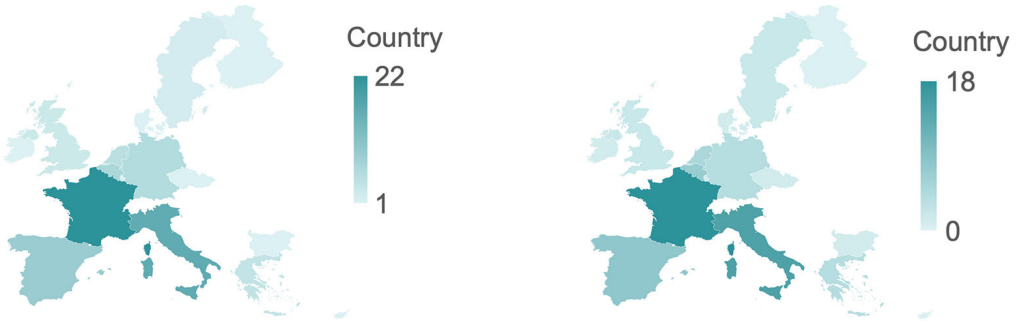

FIGURE 1 Number of centers involved per country (left) and number of centers whose responder is a member of a National Scientific Society (right).

To develop the survey, online research was performed to identify previous publications on this topic. There were no questionnaires identified at the time of the survey preparation neither in Europe or the United States, hence the development of the multiple-choice questions was agreed among the expert group during two meetings. The survey was pilot tested in a small group of five experts from five European countries before launch. The survey was distributed only in English as all the respondents were from expert centers and/or representatives of scientific societies, therefore the common language of communication is English.

The link to complete the survey was sent to all representatives of the HCPs and the Red Cell Disorder representatives in each HCP within the EuroBloodNet network, as well as to national representatives of scientific societies within European countries. If two providers responded from the same HCP, an email was sent to both of them with the request to review the answers and find an agreement. The final common response was then included in the survey data.

2.2 | Statistical methods

The purpose of this report is to provide a comprehensive overview of the research conducted. Descriptive statistics were used to present the results and to describe the characteristics of the samples. The study did not have any predefined hypotheses. Comparison between categorical variables was made by the Fisher exact test for the evaluation of differences in proportions. All the data were analyzed with the software GraphPad Prism Version 8 and expressed as number of events. Statistical significances were assessed with a p-value less than .05 accepted as statistically significant.

3 | RESULTS

3.1 | Respondents' characteristics

Eighty-two physicians from 78 HCPs, with 81 being hematologists and pediatric hematologists from 77 HCPs located in 16 European countries responded to the survey (14/16 in Western Europe). Only European HCPs were included in this analysis. Thirty-two of 77 (51%) HCPs were identified as EuroBloodNet reference centers, while 14/77 (18%) were still in the process of being evaluated to be recognized as expert centers, six were affiliated to a network center and 25 were not members.

The number of HCPs per country and their affiliation with a national scientific society are shown in Figure 1.

Sixty-seven of 77 HCPs staff detailed their field of expertise: 24% were pediatric hematologists, 3% adult hematologists, and 58% provided both pediatric and adult care. A dedicated staff for SCD was not present in four centers.

The total number of patients being managed by the HCPs is shown in Figure 2. Twelve centers had greater than 200 patients in the age range 1–16 years.

3.2 | TCD screening services and practices

Total 36% physicians reported not having a dedicated TCD/TCDi service for children, with examination being performed by cardiologists (10%), general radiologists (28%), needing to be sent to another center for testing (31%), or TCDs not being performed at all (31%). Seventy-four percent reported requesting annual TCD for their patients, but to the question "What percentage of your patients receives annual TCD," only 28% provided estimates that all their patients managed to actually receive annual TCD, due to lack of trained staff (43%), lack of TCD instruments (11%), refusal of patients due to logistical difficulties (22%) (i.e., TCD in another city), lack of funds for dedicated staff or equipment (11%), or other reasons.

Regarding the equipment availability, 9% reported not knowing if their hospital had a TCD or a TCDi device, 32% reported having both, 13% only TCD, 35% only TCDi, and 11% none.

Only 74% of hematologists/pediatric hematologists were aware of the protocol in use at their center by the staff performing TCD/TCDi; the STOP criteria were applied by only 64% of the physicians, mainly due to non-evaluation of the ICA but only of the MCA. The extracranial part of the carotid artery was evaluated only in 30% of the respondents.

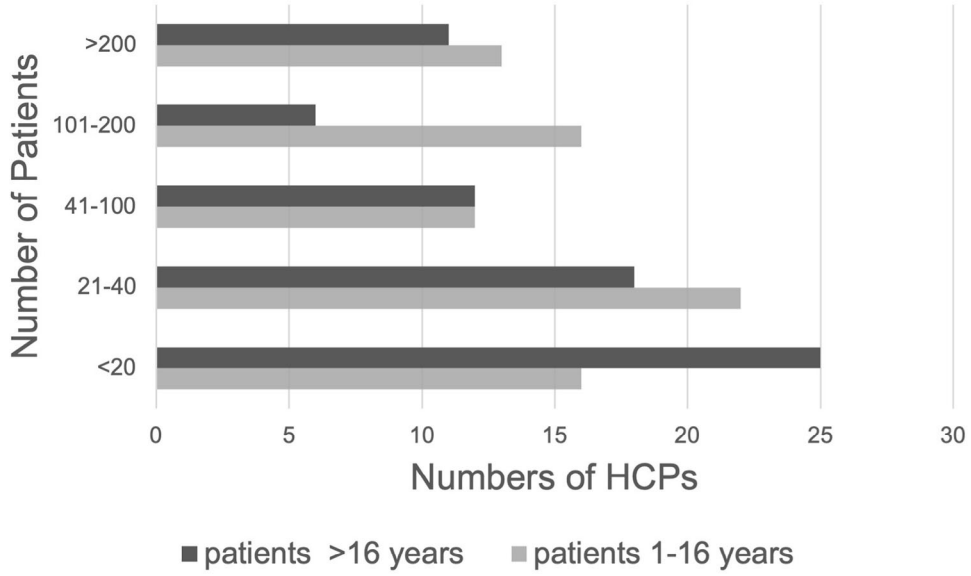

FIGURE 2 Number of patients and age of patients taken in care per healthcare provider (HCP).

3.3 | Stroke prevention protocol in case of abnormal TCD/TCDi

In case of abnormal/conditional TCD results, the approach varied and was not uniform across centers: a transfusion program is prescribed in 84% of centers in case of abnormal TCD, in 16% in case of conditional TCD, and in 9% the choice depends on the parents. The target hemoglobin S thresholds in case a red blood cell transfusion regimen is prescribed, was less than 30% for 83% of the centers, less than 50% for 16% of them; the remaining ones did not consider the hemoglobin S threshold as a therapeutic target, but relied on the normalization of the TCD results.

3.4 | Access to screening and care in reference centers compared to other centers

Responses to the questionnaire's topics differed between reference centers and the other centers only for some answers. Expert centers more frequently had a dedicated TCD Unit in their institution (Figure 3), confirming a higher availability of facilities, as expected. However, even in expert centers having TCD facilities, patients are sent to other hospitals (Figure 4) to perform TCD due to lack of trained staff. Although only around 30% of physicians provided estimates that all their patients received annual TCD follow-up; these data varied among centers with expert centers having the highest percentage (Figure 5). Moreover, expert centers had the highest number of annual TCD/TCDi performed, above the threshold requested to maintain competency, and a higher proportion of pediatricians and hematologists was aware of the protocol to screen children with SCD, although even in expert centers, three physicians reported not knowing the protocols (Figure 6) and five did not know the thresholds used to classify responses.

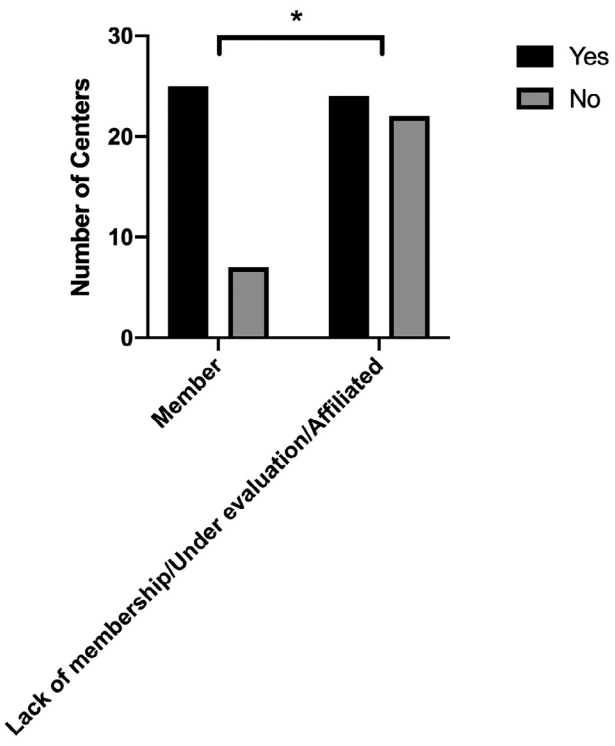

FIGURE 3 Response to Question 3 "Is there a dedicated TCD unit in your center?" according to type of center (EuroBloodNet member compared to others: affiliated, application under evaluation, not member). *p*-Value: $*p < .05$; $**p < .01$; $***p < .001$; ns: not significant).

4 | DISCUSSION

Our survey reports the first comprehensive overview of the availability of and access to TCD screening and stroke prevention programs across European countries. Initiated within the framework of the

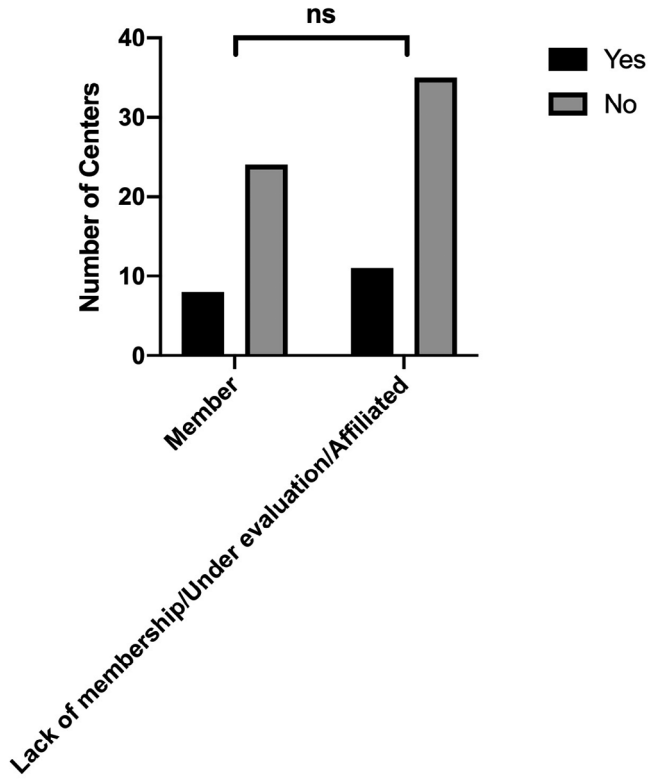

FIGURE 4 Response to Question 6 "Do your patients perform TCD/TCDi in another hospital" according to the type of center (EuroBloodNet member compared to others: affiliated, application under evaluation, not member). *p*-Value: $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$; ns: not significant).

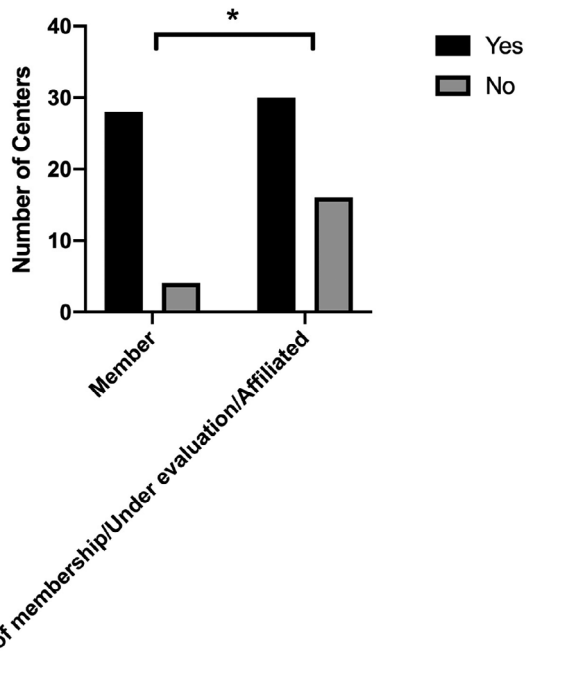

FIGURE 6 Response to Question 10 "Are you aware of the protocol performed at your center?" according to the type of center (EuroBloodNet member, compared to others: affiliated, application under evaluation, not member). *p*-Value: $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$; ns: not significant).

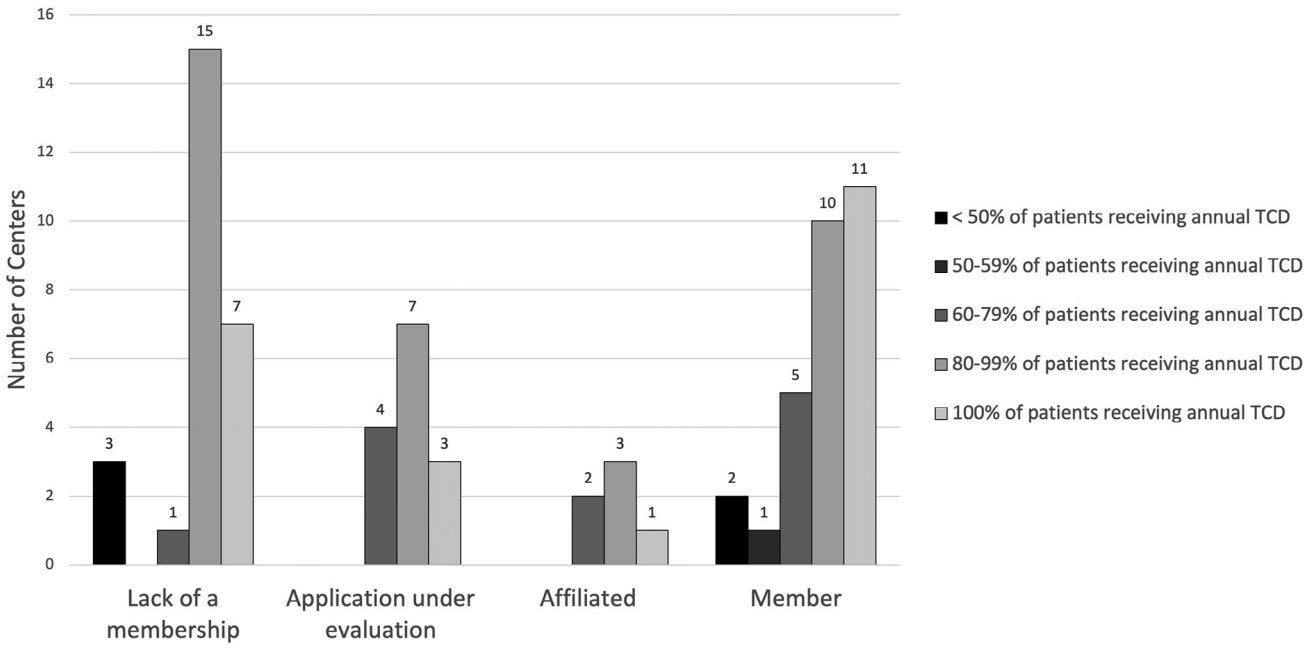

FIGURE 5 Response to Question 8 "What is the percentage of patients who actually have annual TCD in your center?" according to the type of center (EuroBloodNet member, affiliated, application under evaluation, not member).

EuroBloodnet HCPs network, our respondents comprised not only members but also affiliated HCPs, those undergoing evaluation for European body membership, and non-members. The large response from 81 experts in 77 HCPs spanning 16 European countries underscores the recognition of the importance of this issue and the substantial interest among numerous physicians regarding access to care and monitoring protocols for children with SCD.

In fact, previous surveys considering the access to TCD and the application of guidelines in the real-world, outside clinical trials, in the United States, who pioneered the procedure, have been disappointing.[15–17] Moreover, creating specialized services and expertise, as well as maintaining competencies and monitoring indicators requires funding, which has been largely low for SCD compared to other rare diseases,[18] although comprehensive figures from Europe are lacking.

Our survey brings attention to a prevailing insufficiency in accessing a crucial element of prevention and care for children with SCD. This inadequacy poses a risk of exacerbating the burden of disabilities stemming from stroke and cerebral chronic organ damage, including silent infarcts and impaired cognition.[1,19] Therefore, the deficiencies in screening and preventive measures could determine potential economic and social repercussions.[20–22]

We identify an urgent need to address the root cause of inadequate and unsatisfactory access to TCD screening and stroke prevention programs, which were identified in our survey. First, the lack of adequately trained staff to perform TCD requires training programs for neurologists or neurosonologists and technicians, specifically on SCD protocols. These could benefit from collaboration with various scientific societies and continuous training within the ERNs and the health systems. Examples from pilot European experiences and other low-resource settings demonstrate that this is feasible,[13,23,24] but requires adequate funding and should include theoretical sessions, hands-on-session, regular monitoring, and periodical assessment of key indicators. The advances in medical technology, distance learning systems, and competence maintenance through eHealth and artificial intelligence supervision could offer a great opportunity for networks of centers and hub-and-spoke systems to improve, with the limited time available in the already overburdened health systems.[25,26]

Second, the lack of knowledge regarding best practices and TCD/TCDi screening protocols by the hematology community also raises the need for education for hematologists to adequately interpret the results of TCD reports and multidisciplinary team efforts. As a result of this survey, an inaugural international conference was organized in 2023 by experts in the field for members of EuroBloodNet and other representatives of the hematology and neurosonology community.[27]

Third, the lack of equipment is a fundamental issue to address, and in spite of the initial cost of instruments that are needed in specific settings it could be an investment that, acting on prevention, will reduce the number of strokes and complications. Dedicated funding should be allocated through the opportunities that European or national funding schemes offer, as recently recommended by the Lancet Commission.[28]

Moreover, future research should better address the comparison of results between different technologies, such as TCD and imaging TCD.

Our survey presents some limitations. We analyzed the adherence to the STOP protocol that takes into consideration only the evaluation of the MCA and the ICA. We currently know that the other cerebral vessels and the extracranial circulation also contribute to comprehensively determine stroke risk,[29,30] although not yet included in standard-of-care evaluation. The evaluation of the other intracranial vessel and the external circulation should therefore be considered in training courses and in maintenance competencies programs in the future. We also did not evaluate the burden of overt stroke or cerebral vasculopathy in our survey, and such data will be crucial to determine the efficacy of our preventive measures in Europe in the future. Those data are currently being collected through EuroBloodNet's European Rare Blood Disorders Platform (ENROL) and Rare Anaemia Disorders European Epidemiological Platform (RADEEP), and will help measure the overall clinical impact of our screening programs.[14] Lastly, our survey was not validated broadly and there could have been a potential for sampling bias.

5 | CONCLUSIONS

Our data show that less than 30% of physicians estimate that all children with SCD followed in European centers receive annual TCD according to established guidelines. This first multinational European survey allowed the identification of issues related to the lack of access to TCD, lack of trained staff, lack of adequate protocols for implementation of TCD and treatment afterwards, which will need to be addressed through dedicated actions. Optimizing TCD screening and stroke prevention programs is the opportunity to test and reduce inequities in healthcare for children with a rare disorder in Europe.

ACKNOWLEDGMENTS

This project is supported by the European Reference Network on Rare Hematological Diseases (ERN-EuroBloodNet)—Project ID No. 10108571. ERN-EuroBloodNet is partly co-funded by the European Union within the framework of the Fourth EU Health Programme. Full list of participants to the survey is given as Supporting Information S3.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The source data will be available on request to the corresponding author. Due to the rarity of the disease in some centers, for ethical and legal standards, data cannot be publicaly be shared.

REFERENCES

1. Brousse V, Kossorotoff M, de Montalembert M. How I manage cerebral vasculopathy in children with sickle cell disease. *Br J Haematol*. 2015;170:615-625.

2. Adams R, McKie V, Nichols F, et al. The use of transcranial ultrasonography to predict stroke in sickle cell disease. *N Engl J Med*. 1992;326(9):605-610.
3. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *N Engl J Med*. 1998;339(1):5-11.
4. DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. *Blood Adv*. 2020;4(8):1554-1588.
5. Allali S, Taylor M, Brice J, de Montalembert M. Chronic organ injuries in children with sickle cell disease. *Haematologica*. 2021;106(6):1535-1544.
6. Colombatti R, Perrotta S, Samperi P, et al. Organizing national responses for rare blood disorders: the Italian experience with sickle cell disease in childhood. *Orphanet J Rare Dis*. 2013;8:169.
7. de Montalembert M, Ferster A, Colombatti R, Rees DC, Gulbis B, European Network for Rare and Congenital Anaemias. ENERCA clinical recommendations for disease management and prevention of complications of sickle cell disease in children. *Am J Hematol*. 2011;86(1):72-75.
8. Cario HGR, Jarisch A, Kulozik AE, Kunz JB, Lobitz S. AWMF-Leitlinie 025/016 Sichelzellkrankheit. AWFM; 2014. Accessed August 1, 2023. https://www.awmf.org/uploads/tx_szleitlinien/025-016l_S2k_Sichelzellkrankheit_2014-12_verlaengert.pdf
9. Padayachee ST, Thomas N, Arnold AJ, Inusa B. Problems with implementing a standardised transcranial Doppler screening programme: impact of instrumentation variation on STOP classification. *Pediatr Radiol*. 2012;42(4):470-474.
10. Mogayzel PJ, Dunitz J Jr, Marrow LC, Hazle LA. Improving chronic care delivery and outcomes: the impact of the cystic fibrosis Care Center Network. *BMJ Qual Saf*. 2014;23(1):i3-i8.
11. Hulbert ML, Manwani D, Meier ER, et al. Consensus definition of essential, optimal, and suggested components of a pediatric sickle cell disease center. *Pediatr Blood Cancer*. 2023;70(1):e29961.
12. Greenwood S, Deane C, Rees OL, et al. The significance of inadequate transcranial Doppler studies in children with sickle cell disease. *PLoS One*. 2017;12(7):e0181681.
13. Inusa BPD, Sainati L, MacMahon C, et al. An educational study promoting the delivery of transcranial Doppler ultrasound screening in paediatric sickle cell disease: a European multi-centre perspective. *J Clin Med*. 2019;9(1):44.
14. Mañú Pereira MDM, Colombatti R, Alvarez F, et al. Sickle cell disease landscape and challenges in the EU: the ERN-EuroBloodNet perspective. *Lancet Haematol*. 2023;10(8):e687-e694.
15. Schlenz AM, Phillips S, Mueller M, et al. Practice patterns for stroke prevention using transcranial Doppler in sickle cell anemia: DISPLACE consortium. *Pediatr Blood Cancer*. 2020;67(4):e28172.
16. Phillips SM, Schlenz AM, Mueller M, Melvin CL, Adams RJ, Kanter J. Identified barriers and facilitators to stroke risk screening in children with sickle cell anemia: results from the DISPLACE consortium. *Implement Sci Commun*. 2021;2(1):87.
17. Reeves SL, Madden B, Freed GL, Dombkowski KJ. Transcranial Doppler screening among children and adolescents with sickle cell anemia. *JAMA Pediatr*. 2016;170(6):550-556.
18. Farooq F, Mogayzel PJ, Lanzkron S, Haywood C, Strouse JJ. Comparison of US Federal and Foundation funding of research for sickle cell disease and cystic fibrosis and factors associated with research productivity. *JAMA Netw Open*. 2020;3(3):e201737.
19. Montanaro M, Colombatti R, Pugliese M, et al. Intellectual function evaluation of first generation immigrant children with sickle cell disease: the role of language and sociodemographic factors. *Ital J Pediatr*. 2013;39:36.
20. Luengo-Fernandez R, Burns R, Leal J. Economic burden of non-malignant blood disorders across Europe: a population-based cost study. *Lancet Haematol*. 2016;3(8):e371-e378.
21. Lee S, Vania DK, Bhor M, Revicki D, Abogunrin S, Sarri G. Patient-reported outcomes and economic burden of adults with sickle cell disease in the United States: a systematic review. *Int J Gen Med*. 2020;13:361-377.
22. Thielen FW, Houwing ME, Cnossen MH, et al. Cost of health care for paediatric patients with sickle cell disease: an analysis of resource use and costs in a European country. *Pediatr Blood Cancer*. 2020;67(9):e28588.
23. Ghafuri DL, Covert Greene B, Musa B, et al. Capacity building for primary stroke prevention teams in children living with sickle cell anemia in Africa. *Pediatr Neurol*. 2021;125:9-15.
24. Brown LC, Hampton KC, Bloom EM, Lawson D, Cooper SH, Meier ER. No child left behind: building a comprehensive sickle cell disease care oasis in the Lake County, Indiana care desert. *Pediatr Blood Cancer*. 2022;69(8):e29619.
25. Haug CJ, Drazen JM. Artificial intelligence and machine learning in clinical medicine, 2023. *N Engl J Med*. 2023;388(13):1201-1208.
26. Cooper A, Rodman A. AI and medical education—a 21st-century pandora's box. *N Engl J Med*. 2023;389(5):385-387.
27. International neurovascular training course on sickle cell disease. EuroBloodNet; 2023. Accessed December 20, 2023. https://eurobloodnet.eu/media/upload/arxius/Congresses/DEP-International-neurovascolar-padova-mar23.pdf
28. Piel FB, Rees DC, DeBaun MR, et al. Defining global strategies to improve outcomes in sickle cell disease: a Lancet Haematology Commission. *Lancet Haematol*. 2023;10(8):e633-e686.
29. Kwiatkowski JL, Granger S, Brambilla DJ, et al. Elevated blood flow velocity in the anterior cerebral artery and stroke risk in sickle cell disease: extended analysis from the STOP trial. *Br J Haematol*. 2006;134(3):333-339.
30. Bernaudin F, Arnaud C, Kamdem A, et al. Incidence, kinetics, and risk factors for intra- and extracranial cerebral arteriopathies in a newborn sickle cell disease cohort early assessed by transcranial and cervical color Doppler ultrasound. *Front Neurol*. 2022;13:846596.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Voi V, Gutierrez-Valle V, Cuzzubbo D, et al. Limited access to transcranial Doppler screening and stroke prevention for children with sickle cell disease in Europe: Results of a multinational EuroBloodNet survey. *Pediatr Blood Cancer*. 2024;e31190. https://doi.org/10.1002/pbc.31190