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# Concordance with comprehensive iron assessment, hepatitis A vaccination, and hepatitis B vaccination recommendations among patients with sickle cell disease and thalassaemia receiving chronic transfusions: an analysis from the Centers for Disease Control haemoglobinopathy blood safety project

**Sherif M. Badawy**[1,2], **Amanda B. Payne**[3], **Mary M. Hulihan**[3], **Thomas D. Coates**[4], **Suvankar Majumdar**[5], **Dominic Smith**[6], **Alexis A. Thompson**[1,2]

[1]Division of Hematology, Oncology and Stem Cell Transplant, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

[2]Department of Pediatrics, Northwestern University Feinberg School Medicine

[3]Division of Blood Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA

[4]Cancer and Blood Disease Institute, Children's Hospital of Los Angeles, Los Angeles, CA

[5]Children's National, Washington, DC

[6]Michigan Department of Health and Human Services, Lansing, MI, USA.

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Non-concordance with preventive recommendations is common among patients with chronic conditions, including sickle cell disease (SCD) and transfusion-dependent thalassaemia (TDT).[1,2] Iron overload is common among chronically transfused patients with SCD and TDT leading to increased morbidity, mortality and cost of care, especially as they live longer.[3-5]

sbadawy@luriechildrens.org .

Authors' contribution

Sherif M. Badawy, Mary M. Hulihan and Alexis A. Thompson designed the research study. Amanda B. Payne analysed the data. Sherif M. Badawy and Amanda B. Payne interpreted the data. Sherif M. Badawy and Amanda B. Payne drafted the paper. Mary M. Hulihan, Thomas D. Coates, Suvankar Majumdar, Dominic Smith and Alexis A. Thompson critically revised the paper and all authors approved the submitted final version of the paper.

Conflict of interest

The authors have no conflict of interest to disclose.

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Supporting Information

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

The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recommendations support completion of hepatitis A (HepA) and hepatitis B (HepB) vaccinations, including SCD and TDT.[6,7] Cardiac iron overload is the leading cause of mortality in TDT,[8] while it is rare in SCD.[9] Guidelines recommend liver iron overload assessment every 1–2 years for patients with SCD receiving chronic transfusions.[10,11] The recommendation for TDT is annual assessment of liver and cardiac iron concentration.[3,8] However, there are limited data on concordance with these recommendations. In the present study, our objective was to evaluate concordance with these preventive recommendations among chronically transfused patients with SCD and TDT. We hypothesised that concordance is suboptimal.

The Blood Safety Surveillance among People with Blood Disorders project was funded by the CDC and was conducted at four large academic medical centres with comprehensive haemoglobinopathy programmes for SCD and TDT in the United States (January 2013 to December 2014). Demographics, medical and vaccination history were obtained. Patients with SCD (HbSS/HbS$\beta^0$) or TDT were included if they received eight or more transfusions annually. Concordance definitions for comprehensive iron assessment and HepA/B vaccination recommendations are summarised in Data S1.

Our present study cohort included 267 patients, 209 with SCD and 58 with TDT (Table I). Among 126 chronically transfused children/adolescents with SCD, 32% (40/126) had a documented complete iron assessment during the study period. Concordance with vaccine recommendations was higher than concordance with iron assessment recommendations; 65% (64/99) of patients with vaccination information had documentation of completion of the HepA series and 86% (108/126) had documentation of completion of the HepB series or vaccine-type serological testing response (Fig 1A). Overall, 9% (nine of 99) with information available for all three preventive services were concordant with all three preventive service recommendations (Fig 1B). Similarly, among 83 chronically transfused adults with SCD, less than half (41%; 34/83) had a documented complete iron assessment during the study period. Concordance with vaccine recommendations was lower among adult patients compared with children/adolescents; 27% (15/56) had documentation of completion of the HepA series and 70% (57/82) had documentation of completion of the HepB series or documentation of vaccine-type serological testing response (Fig 1A). In all, 11% (five of 56) of adult patients were concordant with all three preventive service recommendations (Fig 1B).

Among 25 children/adolescents with TDT, the majority had a documented iron assessment (76%; 19/25) and had documentation of completion of the HepB series or demonstrated vaccine-type serological testing response (86%; 19/22). Only 38% (three of eight) had documentation of completion of the HepA series. Child/adolescent patients with TDT who were concordant with HepA vaccination recommendations were concordant with the other two preventive service recommendations (Fig 1B). All children/adolescents with TDT with complete information were concordant with at least one preventive service recommendation (Fig 1B). Similarly, among 33 adult patients with TDT, the majority had a documented iron assessment (88; 29/33) and had documented completion of the HepB series or demonstrated vaccine-type serological testing response (85%; 28/33) (Fig 1A). All adult patients were

concordant with at least two preventive service recommendations (Fig 1B). A higher proportion of adults with TDT had documentation of completion of HepA series (seven of 11, 64%) than children/adolescents with TDT, although the number of patients with complete information is small in both groups (Fig 1A).

The present retrospective analysis represents the largest study to date of concordance with preventive treatment recommendations in chronically transfused children and adults with SCD or TDT. We found that concordance with recommendations for comprehensive iron assessments and completion of HepA and HepB vaccine series was suboptimal and varied by haemoglobinopathy type and age group.

Concordance with recommendations for comprehensive iron assessments was higher among children/adolescents and adults with TDT compared to those with SCD. Of note, our criteria for iron assessment in SCD were developed in 2014,[11] which was soon after data collection period (2013–2014). There are no prior studies of concordance with this recommendation in SCD. Reports from the Thalassaemia Longitudinal Cohort indicate an increasing in the proportion of patients having comprehensive iron assessment to nearly 90%.[12]

A HepA vaccine was recommended by the CDC-ACIP in 1996 for persons at increased risk of disease, such as travellers and persons with chronic liver disease, clotting-factor disorder, or living in communities with high rates of HepA.[7] This recommendation was expanded in 2006 to include all children aged 12–23 months in the United States.[13] The ACIP has also recommended routine HepB vaccine for all previously unvaccinated children aged <19 years and for adults at risk of HepB infection.[6]

Concordance with preventive service recommendations is multifactorial.[14] The World Health Organization outlined strategies to increase concordance with recommendations, including the patient's need to be supported and not blamed, the need for health systems to evolve to meet new challenges and a multidisciplinary approach.[14] Reported barriers in SCD and TDT included physicians not offering the therapy, health insurance issues and patient beliefs.[1-3] Furthermore, structural and interpersonal racism has been identified as a barrier to quality care among in SCD.[15] Efforts to increase concordance with recommendations in these patient populations should involve a multilevel approach addressing systemic barriers and patient education.

Our present study has limitations. First, this is a cross-sectional study and a number of patients had missing data. Second, limited data collection precluded the ability to examine reasons underlying non-concordance. Third, we may have missed some vaccination records if patients received immunisations elsewhere. Finally, the present study was conducted at large academic medical centres, which may not be generalisable.

In conclusion, chronically transfused patients with SCD and TDT had suboptimal concordance with recommendations for three key preventive measures, annual comprehensive iron assessments and HepA and HepB vaccination. Our present findings highlight the need for a systematic, multidisciplinary process, including haematologists and transfusion medicine specialists, to ensure that all chronically transfused patients with SCD

and TDT receive recommended preventive measures and services, and provide baseline estimates that can be used to monitor improvement over time.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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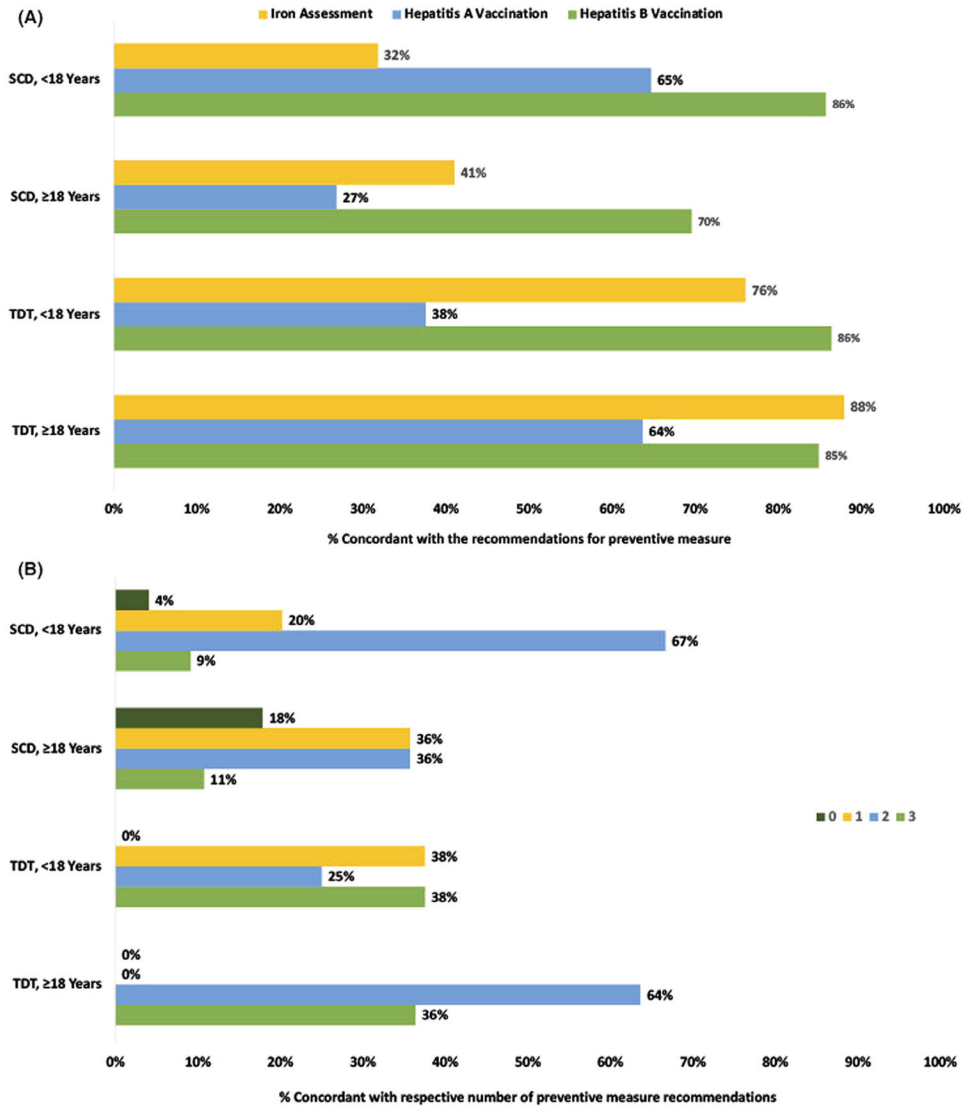


**Fig 1.**

(A) Concordance with the recommendations for preventive measures by haemoglobinopathy type and age group. (B) Distribution of patients by the number of preventive measures they were in concordance with and by haemoglobinopathy type and age group (0, concordance to none of the recommendations; 1, concordance to one of the recommendations; 2, concordance to two of the recommendations; and 3, concordance to all three recommendations). SCD, sickle cell disease, TDT, transfusion-dependent thalassaemia.

**Table I.**

Characteristics of patients with sickle cell disease or transfusion-dependent thalassaemia with an average of eight or more transfusions per year.

| **Sickle cell disease (SCD) cohort**[^] | **Paediatric (<18 years), *N* = 126** | **Adult (≥18 years), *N* = 83** |
|---|---|---|
| Age, years, median (IQR) | 10·7 (7·0–14·4) | 22·9 (19·8–31·4) |
| Male sex, *n* (%) | 55 (44) | 38 (46) |
| Race, *n* (%) | | |
| Black or African American | 115 (92) | 73 (89) |
| Other | 10 (8) | 9 (11) |
| Iron chelation, *n* (%) | 105 (88) | 62 (78) |
| **Transfusion-dependent thalassaemia (TDT) cohort**[#] | **Paediatric (<18 years), *N* = 25** | **Adult (≥18 years), *N* = 33** |
| Age, years, median (IQR) | 8·8 (6·8–12·0) | 25·7 (21·2–32·9) |
| Male sex, *n* (%) | 13 (52) | 13 (39) |
| Race, *n* (%) | | |
| Asian, Native Hawaiian, or Other Pacific Islander | 13 (52) | 19 (57) |
| Other | 12 (48) | 14 (42) |
| Birthplace, *n* (%) | | |
| United States | 19 (79) | 25 (76) |
| Outside of the United States | 5 (21) | 8 (24) |
| Iron chelation, *n* (%) | 24 (100) | 33 (100) |

IQR, interquartile range.

[^]Proportions calculated based on exclusion of records with missing data for characteristic: *n* = 8 missing ethnicity; *n* = 2 missing race; *n* = 19 missing iron chelation information.

[#]Proportions calculated based on exclusion of records with missing data for characteristic: *n* = 1 missing birthplace; *n* = 7 missing iron chelation information.