Global haematology

Incorporating national disease burden in GBD estimates of haemoglobinopathies in Italy

The Global Burden of Disease (GBD) study represents an incredible source of information to quantify and understand the magnitude and impact of all conditions, including common and rare diseases, on patients' quality of life, mortality, and morbidity. Emerging evidence suggests that detailed national studies are needed to inform, calibrate, and validate GBD estimates. This need is also supported by action on local GBD network, such as the Italian GBD network, cross-talking with the global GBD network.

Thalassaemia and sickle cell disease are haemoglobin disorders distributed worldwide and represent an increasing public health burden. These inherited disorders tend to be highly prevalent in malaria-endemic regions across sub-Saharan Africa, the Middle East, and Southeast Asia, which tend to be data poor, and classified as rare diseases in Europe and North America, which are usually data rich. The change of classification terminology in transfusion-dependent thalassaemia and non-transfusion dependant thalassaemia represent a challenge when collecting epidemiological data required to correctly estimate the burden of such conditions. For example, Brousse and colleagues previously highlighted that the GBD 2021 study of sickle cell disease likely underestimated the number of patients with sickle cell disease in France and in the UK and overestimated the number of deaths for patients with sickle cell disease younger than 5 years. Although Brousse and colleagues do not get into detailed analyses of France and UK data, we believe it is important to go deeper using detailed national data especially in countries where haemoglobinopathies are endemic such as Italy. Thus, we collected detailed national data on haemoglobin disorders across Italy by 131 comprehensive specialist centres connected through the Società Italiana Talassemie ed Emoglobinopatie (SITE). Here, we use SITE data to estimate the burden of thalassemia and sickle cell disease in Italy and provide a detailed comparison of our estimates with those of the GBD 2021. Using 2019 data, our comparative indicators were: number of patients, number of deaths, the years of life lost (YLLs), the years lived with disability (YLDs), and disability-adjusted life years (DALYs) for thalassaemia and sickle cell disease in Italy. Data on the number of patients were collected across the 131 SITE centres. Data on mortality and morbidity were available from eight of the largest comprehensive centres, covering about 30% of the Italian patients with haemoglobin disorders. Consistency between SITE and GBD 2021 estimates was defined as some overlap between the 95% confidence intervals of the two estimates (further details are in the appendix p 1).

SITE data on the number of patients were collected using specific age groups and binary sex (appendix p 1), and disease severity was based on clinical records (appendix p 1). Data from the survey of the eight centres were used to count the number of deaths in 2019 in these centres. Due to small numbers, we used data from the 5 years preceding 2019, to calculate age-specific mortality to extrapolate the number of deaths across the whole country, using patient counts from the 131 centres and data from the general population. The age of death attributed to each extrapolated death was the mean of the age category considered (appendix p 2). The age-specific and overall number of patients and deaths in Italy were directly compared with the ones reported in the GBD 2021. The GBD 2021 uses standard 5-year age groups. Data were therefore reprocessed to align the age groups between the two data sources. YLLs, YLDs, and DALYs were calculated using the standard WHO methodology, which is consistent with the GBD approach. The YLLs were calculated by multiplying the number of deaths in each age-groups by the standard loss function specifying years of life considering the deaths in that age-group (appendix pp 2, 5). In the case of YLDs, the calculation was performed considering the patient's population divided according to the severity of the disease (appendix pp 2, 6). A mean value of disability weight was used for each category. The disability weights were obtained by the table reported in the GBD 2021 study and grouping by pathology and health state name and description. A simulation was conducted with different set of weights to identify the most likely set of parameter values equivalent to those used in the GBD 2021 estimations of YLDs. Overall DALYs were calculated by summing YLDs and YLLs.

Using the SITE data, we estimated 7169 thalassaemia patients in 2019, which overlapped with the GBD 2021 estimate of 6497 (95% CI 5432–7602). Despite the agreement in the overall number of patients, the age-specific distribution of the SITE data revealed that the Italian thalassaemic population was significantly older than estimated by GBD 2021 (figure A; estimated mean age 38·1 years [37·7–38·5] for SITE population, estimated mean age 20·7 years [20·2–21·1] for GBD 2021). The SITE estimated national annual number of deaths (figure B) for thalassaemia was 35 (27–56), corresponding to 1370 YLLs (1064–2656); while GBD 2021 estimated 30 deaths (25–33) and 1247 YLLs (1090–1378) (appendix p 7). Using real-world national data on thalassaemia severity from our previous analysis, we estimated

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SITE data can be requested to the corresponding author. GBD data used in this study are available through open access publication and the GBD data vizualization portal (https://vizhub.healthdata.org/gbd-compare/).

FBP reports being on an advisory board on sickle cell disease for the Fondation Fabre; on an advisory board for the development of St Jude's Global Hematology Registry; and a subject matter expert on anaemia and haemoglobinopathies for the IHME's Global Burden of Disease (GBD). All other authors declare no competing interests.

For **GBD studies in haematology** see **Articles** *Lancet Haematol* 2023; **10:** e585–99 and *EClinicalMedicine* 2024; **72:** 102619

For the **Italian GBD network** see https://www.italian-gbd-initiative.it/

For more on the **letter from Brousse and colleagues** see **Correspondence** *Lancet Haematol* 2023; **10:** e792

For the **analysis on haemoglobin disorders across Italy** see *Haematologica* 2025; **110:** 1211–16

For more on the **WHO methodology** see https://cdn.who.int/media/docs/default-source/gho-documents/global-health-estimates/ghe2019_daly-methods.pdf?sfvrsn=31b25009_7

See **Online** for appendix

For more on **GBD 2021 disability weights** see https://ghdx.healthdata.org/record/ihme-data/gbd-2021-disability-weights

For **GBD data for other chronic disorders** see https://vizhub.healthdata.org/gbd-results/

For the **new G6PD classification** see *Bull World Health Organ* 2024; **102:** 615–17

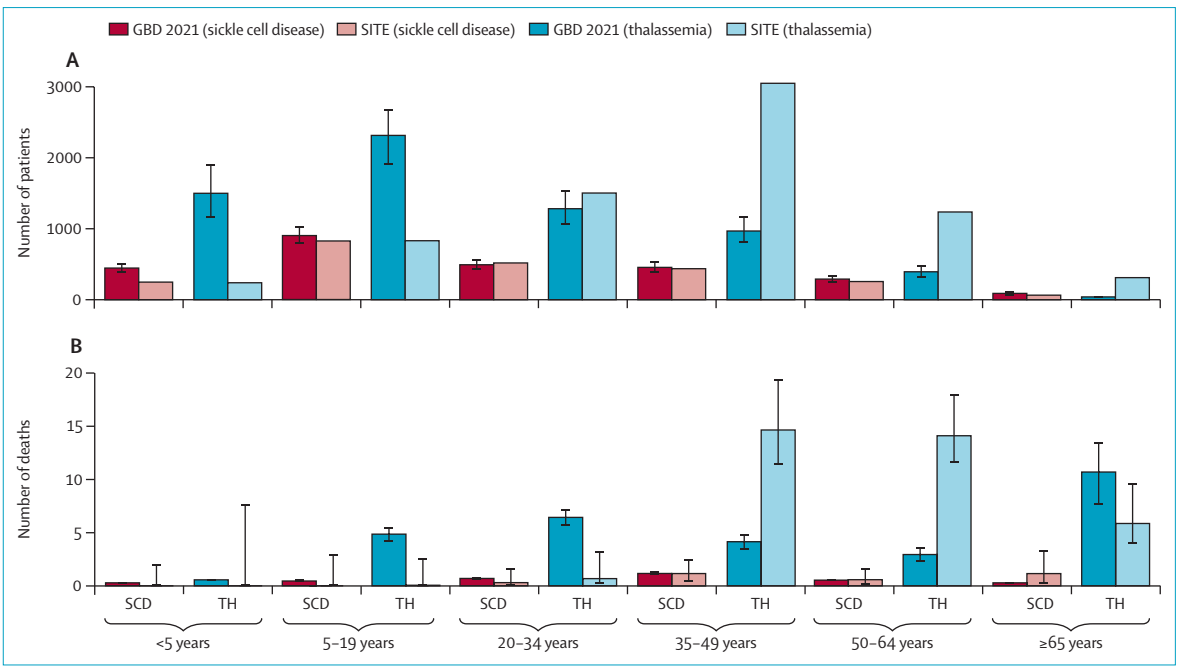

***Figure*: Comparison between GBD 2021 and national specific disease SITE 2019 data**
(A) Distribution according to age for patients with thalassaemia or SCD. (B) Distribution of deaths according to age for patients with thalassaemia or SCD. Error bars represent 95% CIs. GBD=Global Burden of Disease study. SCD=sickle cell disease. SITE=*Società Italiana Talassemie ed Emoglobinopatie*. TH=thalassaemia.

867 YLDs (371–1952), which is 5·8-times greater than in GBD 2021 (149 YLDs [93–224]). This result is likely due to the difference in the age distribution of the patients in the two datasets. Overall, the estimate of the DALYs for thalassaemia in 2019 added up to 2237 (1435–4608), which overlaps with the GBD 2021 estimates (1396 [1227–1559]). When we accounted for the severity of thalassaemia, we estimated 5205 individuals with transfusion-dependent thalassaemia and 1964 with non-transfusion dependant thalassaemia. The SITE estimates of YLLs, YLDs, and DALYs for transfusion-dependent thalassaemia were 1062 YLLs [95% CI 821–1528], 790 YLDs [95% CI 369–1750]), and 1852 DALYs (95% CI 1190–3277), respectively. For non-transfusion dependent thalassaemia, these estimates were 309 YLLs (243–1129), 76 YLDs (3–202), and 385 DALYs (245–1331). No estimates for TDT and NTDT are currently included in the GBD.

Data from the SITE survey estimated that 2348 individuals had sickle cell disease, which was similar to GBD 2021 estimate (2675 [95% CI 2354–3015]). The age distribution was comparable for all categories except in sickle cell disease patients younger than five years for which our estimate was substantially lower than in GBD 2021 (figure A). The estimated number of deaths for sickle cell disease was 2·9 (0·7–13·7; figure B), corresponding to 111 YLLs (30–762); whereas the GBD 2021 estimated 3·4 (3·1–3·8) deaths and 182 YLLs (161–204; appendix p 7). GBD 2021 estimated 164 YLDs (120–217) for sickle cell disease. We calculated 477 YLDs (142–1021) based on real-world disease severity proportions. In the GBD 2021 study, the percentage of patients with sickle cell disease who had a severe phenotype could not exceed 12–19%. This result means that the most likely distribution from GBD 2021 was 30% of patients with no-symptoms, 55% with mild-moderate, and 15% severe. The estimate of the DALYs for sickle cell disease in Italy in 2019 was 588 (172–1783).

When extrapolated globally, our estimates of YLDs due to haemoglobinopathies (YLDs $2{\cdot}0 \times 10^6$) are substantially higher than those due to other chronic disorders such as chronic kidney disease due to diabetes type 1 ($0{\cdot}28 \times 10^6$), chronic kidney disease due to hypertension ($1{\cdot}36 \times 10^6$), and myelodysplastic, myeloproliferative, and other haematopoietic neoplasms ($0{\cdot}25 \times 10^6$). In addition, diseases classified in GBD as "other haemoglobinopathies and haemolytic anaemias" or "G6PD deficiency" might be underestimated in GBD studies, similarly to our observation on thalassaemia and sickle cell disease. Indeed, "haemolytic anaemias" group different disorders such as membranopathies (eg, hereditary spherocytosis, stomatocytosis, elliptocytosis, and xerocytosis), which have a heterogeneous global distribution. Furthermore, the recent revision of G6PD classification needs to be taken into consideration when assessing data on YLDs in patients with G6PD deficiency with or without chronic haemolysis.

In conclusion, our study shows that the GBD 2021 produced reliable estimates for some indicators, but lacked

precision in relation to the age distribution of patients and deaths, and specificity in relation to the severity of thalassaemia and sickle cell disease that underlines the YLD and DALY estimates. The classification of thalassaemia into transfusion-dependent thalassaemia and non-transfusion dependent thalassaemia better reflects the severity of these disorders in patients, is widely used for the management of patients and the development of new treatments, and should be incorporated into future GBD work. Although these findings are based on haemoglobin disorders in Italy alone, we believe that they demonstrate the ongoing need for high quality national epidemiological data in general. Furthermore, they provide valuable insights for the interpretation of the GBD estimates in other countries and for other conditions, particularly when used to guide national policies.

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Digital haematology

Perspectives of potential haematopoietic stem-cell donors on education TikToks

TikTok is a rapidly growing social media platform on which users develop, interact with, or share short vertical videos (TikToks). Although TikToks have immense potential to be harnessed to affect health knowledge, attitudes, and behaviours, little research guides TikToks' potential public health applications. Since 2020, we have led the development and use of a large TikTok library to engage diverse young adults to haematopoietic stem-cell donation. This library, including hundreds of TikToks starring diverse performers, has generated hundreds of thousands of views and engagements across social media platforms. These TikToks have also been used in national donor recruitment campaigns, educating about donation and supporting potential donors to register to donate. Drawing from this expertise, we set out to generate lessons to guide development and use of TikToks for public health applications by conducting a qualitative analysis to explore perspectives of potential haematopoietic stem-cell donors on donation education TikToks.

From June 1, to July 30, 2021, we recruited young-adults aged 17–35 from diverse populations who were potential stem-cell donors for semi-structured focus groups to share their perspectives on 30 donation-education TikToks (for more details see appendix pp 2–8, 11–12, 29–31). These TikToks were selected from the Canadian donor recruitment organisation Stem Cell Club's TikTok library, to showcase performers from diverse ancestral backgrounds, key educational topics in donation, and multiple engagement strategies (for definitions see appendix pp 9–10). Participants were recruited through posts on social media groups. Participants (n=46) reported a median of 5 h per week viewing TikToks. Although the majority were regular TikTok users, 28% (13/46) viewed TikToks primarily through other apps (ie, Facebook or Instagram) or were shown them through friends or family (for more details and participant quotations see appendix pp 5–28).

Perspectives overall

Participants' reception was enthusiastically positive, and respondents said that they learned a lot and described the TikToks as engaging, attractive, cool, fun, or "up-to-the-mark", with one participant sharing "some of those TikToks really hit different, and I'm just like, wow." The strong positive reception was consistent even among individuals who disliked TikTok in general or did not use the app.

TikToks as educational resources

Participants emphasised how easily or how much they learned. They felt the TikToks enhanced their awareness, were a "launching pad" to learn more, and allowed them to feel connected to the subject. Participants valued TikToks covering a broad range of educational topics. They were inspired by TikToks outlining the need for diverse participants to address disparities in access to stem-cell transplantation, with such content felt to notably standout. Participants reflected positively on TikToks providing attitudinal guidance. They described TikToks outlining the social value of participation (ie, that it's cool, fun, or attractive to romantic partners) as appealing. Participants similarly valued TikToks outlining the moral value of participation, reporting feeling empathy and appreciating that everyone has to make a contribution. Participants emphasised the importance of learning that the process was quick, easy, and simple. Participants valued learning who benefits from donation and about registration eligibility criteria; the registration and donation process; associated safety, privacy, and confidentiality issues; and stories of people personally affected.

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For the **TikTok library to engage diverse populations to haematopoietic stem-cell donation** see *Bone Marrow Transplant* 2024; **59:** 1184–89

For the **donation-education TikToks** see https://youtube.com/playlist?list=PL9prrDkqE0rS4UJeJMVr7GlitrpV605uu