5. BLOOD – THE GLOBAL SCENE TIF'S PERSPECTIVE

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INTRODUCTION

About Haemoglobin Disorders

Blood transfusion therapy is the cornerstone of management of many patients with chronic anaemias, from hereditary to acquired conditions. Indeed, regular transfusions are the standard of care for the treatment of β-thalassaemia major (TM). For sickle cell disease (SCD), transfusions provide effective treatment and prevention of many complications, including a decreased risk of stroke; for myelodysplastic syndromes (MDS) transfusions are an integral part of supportive care.

Although β-thalassaemia major disorders can be grouped together as "transfusion-dependent", it is important to note that the clinical onset of anaemia, the degree of haemoglobin reduction and related severity, and transfusion requirements remain widely variable across patients. There are several management practice guidelines (mainly coming from the Thalassaemia International Federation (TIF) available for these disorders which include recommendations on transfusion treatment regimens. However, current real-world practice approaches within these populations of patients may not reflect the ideal treatment circumstances that can occur in leading Western medical centres. Moreover, such information has not been widely compared across geographical regions. In addition, it was reported in studies that transfusion-dependent patients with thalassaemia intermedia (TI) or non-transfusion-dependent thalassaemia had received transfusions for a considerable proportion of their lifetimes and had a relatively heavy transfusion burden. Many patients with milder β-thalassaemia genotypes (such as HbE/β-thalassaemia) may start life independent of transfusion but later, and based on their clinical progression, may become transfusion dependent, as described in TIF's *Guidelines for the Clinical Management of NTDT* (2017), more recently updated and upgraded into two publications ((A.) *Guidelines for the Management of NTDT β-thalassaemia*, 2023; (B) *Guidelines for the Management of NTDT α-thalassaemia*, 2023), respectively. The percentage of patients classified as NTDT is at present largely unknown, albeit this is expected to be considerably higher particularly in populations where such genotypes are higher in prevalence (e.g., West Pacific and Southeast Asian regions). However, one can appreciate the huge need to focus on improving blood supplies, and the safety and quality of blood transfusion (BT) services across the world, acknowledging the fact that consequent to significant improvements occurring globally and in the absence of effective national prevention programmes, the number of patients with these disorders in need of BT is exponentially increasing.

Spectrum of Thalassaemia Syndromes

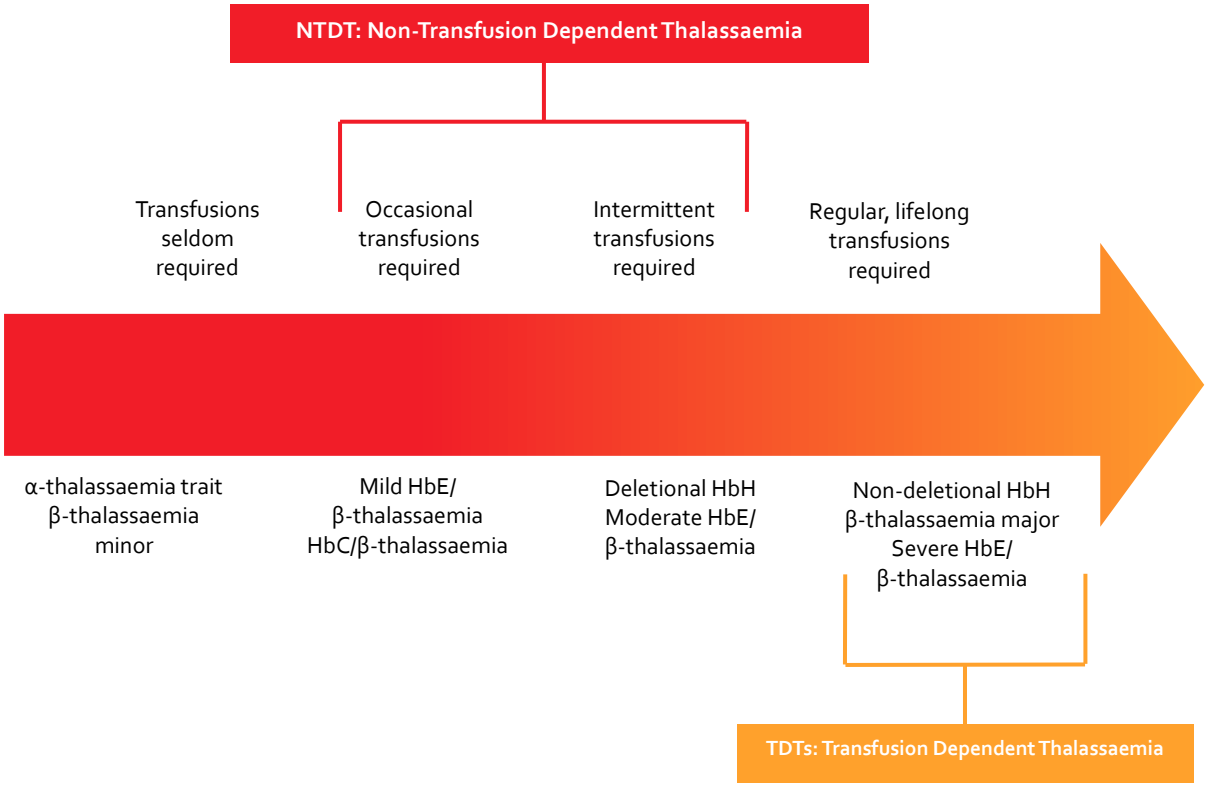

Figure 1. Phenotypic classification of thalassaemia syndromes based on clinical severity and transfusion requirement. Source: Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT), 3rd edition, 2014.

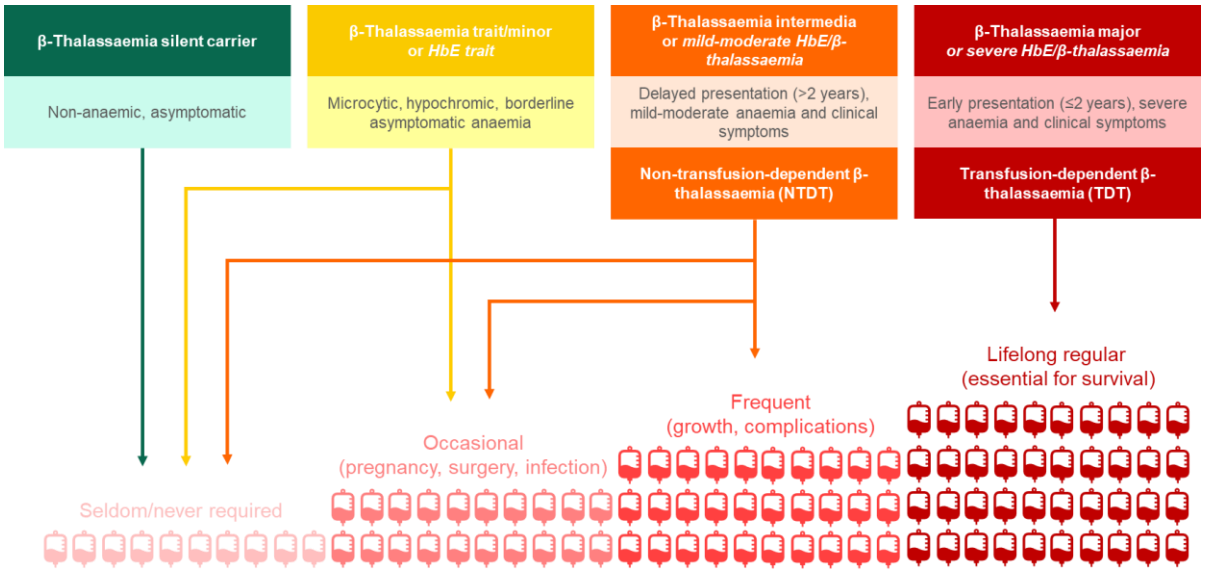

Figure 2. Transfusion requirement in various β-thalassaemia phenotypes [1, 2]. Hb, haemoglobin

According to the WHO, about 118.54 million blood donations are collected worldwide (https://www.who.int/news-room/fact-sheets/detail/blood-safety-and-availability). Even if there are roughly 600000 thalassaemia patients needing regular blood transfusions then a rough estimate is that they will need 13 million units per year (just over 11% of the global donations. , It is expected that in the absence of national disease-specific prevention programmes and registries such numbers will remain inaccurate and are to be considered grossly underestimated with particular regard to the needs for blood. Indeed, efforts towards developing well designed and disease-specific national registries and prevention programmes are of immense importance, and TIF for many years has remained focused on promoting such disease specific activities.

For more comprehensive information on the wide variability and heterogenous needs for blood by patients with transfusion-dependent β-thalassaemia (A), non-transfusion-dependent β-thalassaemia (B), and α thalassaemia (C), some related extracts from TIF's Guidelines are included in this chapter for facilitating the reader to better understand the great needs for blood transfusion therapy and to improve policies on both the safety and availability of blood.

Below is an extract from the Blood Transfusion chapter in TIF's Guidelines (A). Please refer to the respective guideline found in TIF's Guidelines for more comprehensive information if needed. Important considerations related to transfusion therapy in patients with transfusion dependent thalassaemia include:

- Aims of blood transfusion
- Haemovigilance
- Blood donations
- Blood component specification
- Compatibility testing and alloimmunisation
- Criteria for initiating transfusion therapy
- Transfusion thresholds and frequency
- Volume to be transfused
- Transfusion and the spleen
- Adverse reactions

An effective transfusion regimen will result in:

- Good growth and development,
- Good energy levels,
- **Sufficient suppression of intra and extramedullary haematopoiesis.**

A safe transfusion regimen will:

- Use a product that is collected, tested, selected, issued, and administered adherent to established quality and safety regulations and guidance,
- Be administered by staff trained in blood transfusion,
- Involve informed patient consent,

- Be performed in a system with a good haemovigilance structure.

It is recommended that:

- Before embarking on transfusion therapy, patients should have extended red cell antigen typing that includes at least A, B, O, C, c, D, E, e, and Kell, (though preferably a full red cell phenotype/genotype panel).
- If the patient is already transfused, antigen typing can be performed using molecular rather than serological testing.
- All patients with thalassaemia should be transfused with ABO and Rh (C, c, D, E, e) and Kell compatible blood to avoid alloimmunisation against these antigens.
- There should be a valid group and antibody screen available prior to transfusion being administered.

Criteria for initiating transfusion therapy

For deciding whom to transfuse, the following should be included in the investigations:

- Confirmed diagnosis of thalassaemia
- Laboratory criteria:
- Haemoglobin level (Hb) <70 g/l on 2 occasions, > 2 weeks apart (excluding all other contributory causes such as infections) Clinical criteria irrespective of haemoglobin level:
    - Significant symptoms of anaemia
    - Poor growth / failure to thrive
    - Complications from excessive intramedullary haematopoiesis such as pathological fractures and facial changes
    - Clinically significant extramedullary haematopoiesis

Below are extracts from Guidelines (B) referring to β-thalassaemia intermedia:

A variety of β-thalassaemia phenotypes can result from heterozygous, compound heterozygous, or homozygous inheritance of β-globin gene mutations, or their co-inheritance with structural haemoglobin variants such as haemoglobin E or other secondary genetic modifiers. Transfusion-dependence has recently become an essential factor in classifying the various phenotypes of β-thalassaemia. Patients requiring lifelong regular transfusion therapy for survival are considered as having transfusion-dependent β-thalassaemia (TDT), such as patients with β-thalassaemia major or severe haemoglobin E/β-thalassaemia. On the other hand, non-transfusion-dependent β-thalassaemia (NTDT) – the focus of Guidelines (B) – is the term used for patients who do not require lifelong regular transfusions for survival, such as patients with β-thalassaemia intermedia or mild-moderate haemoglobin E/β-thalassaemia; although they may require occasional or even frequent transfusions in certain clinical settings and for defined periods of time. See the flowchart below on how diagnosis is worked out.

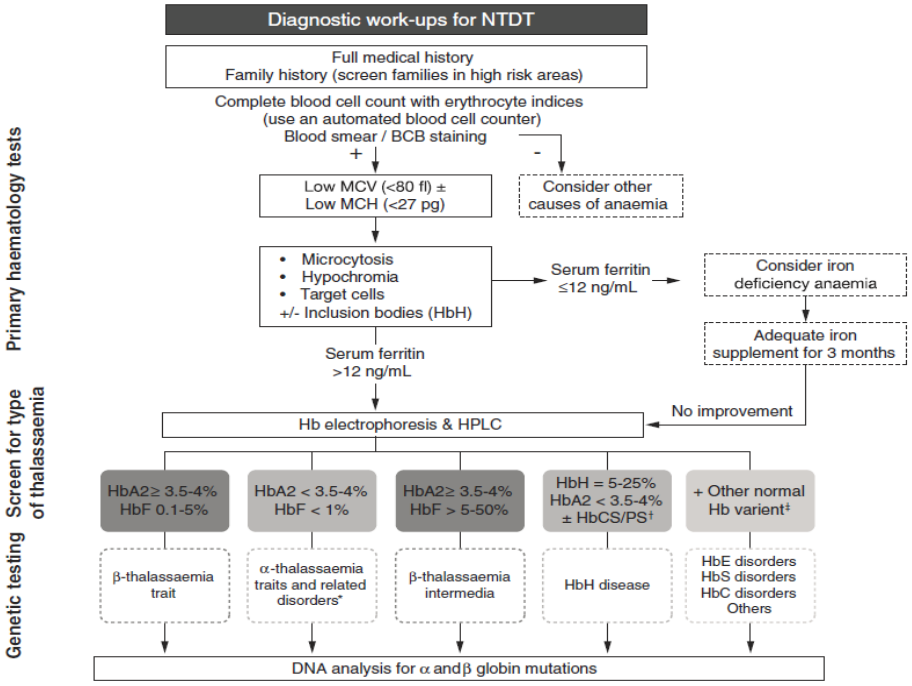

*Figure 3. Laboratory work-up to facilitate diagnosis of non-transfusion-dependent ß-thalassaemia (NTDT). *α-thalassaemia traits and related disorders include αo and α+-thalassaemia by deletions and non-deletional α-thalassaemia mutations. †There are two main types of HbH disease: 1) deletional HbH due to deletions (- -/-α); and 2) non-deletional HbH disease caused by αo-thalassaemia and non-deletional mutation (--/αTα). ‡The common disorders associated with Hb structural variants include homozygous HbE, HbE/ß-thalassaemia and HbE with other variants such as HbE/HbS or HbE/HbC or HbE/HbD, HbS (sickle), HbS/ß-thalassaemia, homozygous HbC and HbC/ß-thalassaemia. These diagnoses can be confirmed using appropriate globin genotyping. Reproduced with permission. Hb, haemoglobin; HbF, foetal haemoglobin; HbCS, haemoglobin Constant Spring; HbPS, haemoglobin Pakse; BCB, brilliant cresyl blue; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; HPLC, high-performance liquid chromatography. Source: Guidelines for the Management of Non-Transfusion Dependent ß-Thalassaemia (TDT), 3rd edition, 2023*

MANAGEMENT OF INEFFECTIVE ERYTHROPOIESIS AND ANAEMIA

General principles

Despite transfusion-independence being an inherent characteristic of NTDT, it is now evident that associated anaemia needs to be regularly monitored with management indicated in various acute and chronic clinical settings. Irrespectively, management of chronic anaemia in patients with NTDT needs to be individualised with careful assessment of benefits and risks of intervention. As mentioned earlier, it is now established that patients with a haemoglobin level ≤10 g/dL are at highest risk of morbidity and mortality from chronic anaemia and underlying ineffective erythropoiesis (see Figure 4, below) and thus may be most ideal candidates for long-term intervention to raise haemoglobin level and prevent future serious and often irreversible clinical complications. Patients with any degree of anaemia combined with ineffective erythropoiesis/anaemia-related symptoms or complications may also be considered for short/limited-term intervention to raise haemoglobin levels and alleviate their symptoms, especially in instances where evidence of benefit is established.

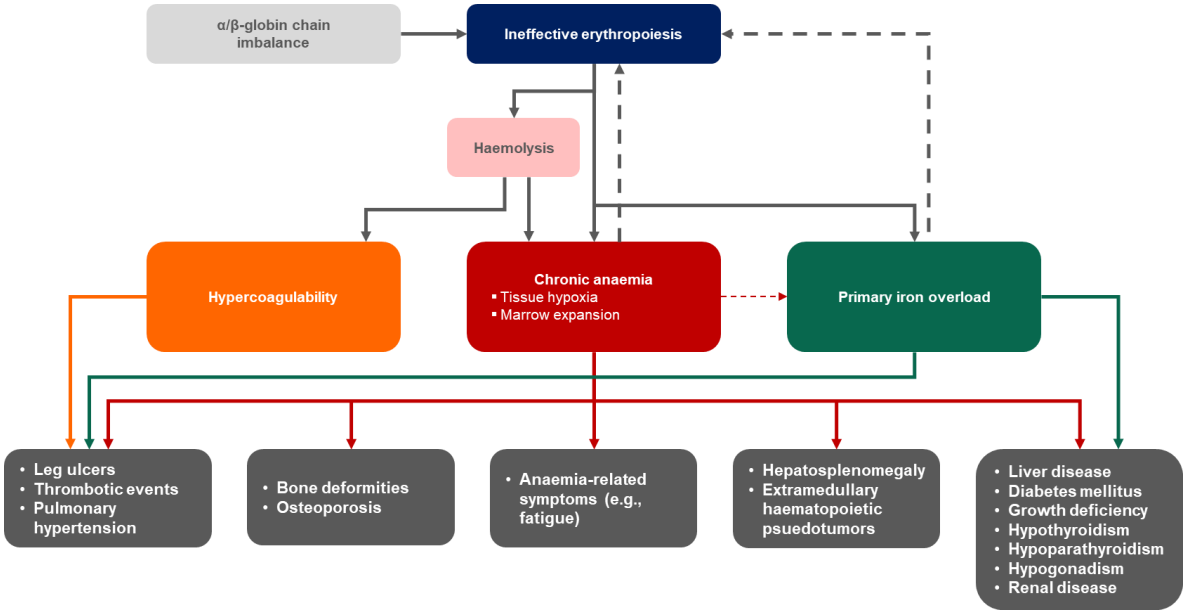

Figure 4. Ineffective erythropoiesis and anaemia at the core of pathophysiology and clinical complications in non-transfusion-dependent β-thalassemia (NTDT). Source: Guidelines for the Management of Non-Transfusion Dependent β-Thalassaemia (NTDT), 3rd edition, 2023

It should be stressed, however, that transfusion receipt is not always a measure of underlying disease severity as it can also be attributed to access blood products or reflect a physician or patient choice, with varying practices worldwide, especially in patients with moderate phenotypes. In recent clinical trials, the use of the NTDT/TDT classification has commonly been associated with the patient's transfusion profile in the past six months (e.g., <6 red blood cell units denoting NTDT). This may be practical when taking immediate management decisions, especially as related to anaemia and iron overload. However, the natural course of a patient's disease course should always be taken into consideration since many patients with NTDT go on to become TDT following permanent morbidity development, while also some patients with TDT can become NTDT following interventions that decrease transfusion requirement. Disease severity and prognostic scoring systems have been recently developed for β-thalassaemia, but further validation and data from real-world feasibility may be needed before wide utilisation.

Transfusion therapy

Transfusions remain the ideal intervention in acute clinical settings that require immediate improvement of haemoglobin level or sustaining it in view of anticipated blood loss or physiologic changes, such as during acute infection, pregnancy, and surgery.

Transfusion therapy is effective in supplying normal erythrocytes and suppressing ineffective erythropoiesis. Upon transfusion therapy, erythroid activity decreases to 1-2 times normal levels with pretransfusion haemoglobin values between 10 and 11 g/dL, 1-4 times normal levels with values between 9 and 10 g/dL, and 2-6 times normal levels for values between 8.6 and 9 g/dL. There is a direct correlation between linear growth and development and the magnitude of transfusion therapy NTDT patients receive during childhood. Although clinical trials evaluating the role of transfusion therapy in NTDT patients are lacking, cross-sectional studies have consistently showed that patients who were receiving regular transfusions had lower rates of leg ulcers, thrombotic events, pulmonary hypertension, silent brain infarcts, and extramedullary haematopoietic

pseudotumours. A recent analysis from Italy showed that NTDT patients who started transfusion therapy in adulthood had a slowed down progression of disease. Another recent survival analysis of a global cohort of 2,033 patients with NTDT identified a subset of 254 patients (12.5%) who were eventually placed on regular transfusion programmes, starting at a median age of 10 years. The remaining 1,779 patients received only sporadic or no transfusions at all. Survival was significantly worse in non-regularly transfused patients compared to regularly transfused patients for all-cause and cardiovascular disease-related mortality. Such cardioprotective effects of regular transfusions in NTDT has also been reported from Oman.

Rather than enforcing a long-term transfusion regimen, regular blood transfusion, if initiated in patients with NTDT, should ideally be for a short/limited term and be tailored or withdrawn when the desired outcomes are achieved. Patients having long-term regular transfusions should be managed as per the TIF guidelines for transfusion-dependent β-thalassemia (TDT) patients. The concern with long-term regular transfusion therapy in NTDT patients is the risk of secondary iron overload and end-organ failure. Transition to transfusion-dependence may also have an impact on patient's mental well-being and quality of life, as it may implicate disease progression and require complete lifestyle modification. The magnitude of transfusion load is directly linked to healthcare resource utilisation, as well as to clinical and economic burdens. Patients with NTDT who begin transfusions as adults are also at very high risk for developing red cell alloimmunisation and serious haemolytic transfusion reactions. The risk of alloimmunisation is highest in splenectomised patients and during pregnancy.

PRACTICAL RECOMMENDATIONS AND EXPERT INSIGHTS

1. Unless contraindicated, blood transfusions can be considered to manage anticipated haemoglobin drop in acute clinical settings such as during acute infection, pregnancy, blood loss, or surgery.
2. Patients with NTDT should be considered for short, limited or long-term intervention targeting ineffective erythropoiesis and anaemia.
3. When transfusion therapy is considered:
    a. For monitoring and management of iron overload
    b. The risk of alloimmunization should be considered, especially in the following subgroups of patients: pregnant women, splenectomised patients, never or previously minimally transfused patients.
    c. Blood processing and administration characteristics should generally be similar to those applied in TDT:
        i. Blood storage for <2 weeks, conditioning to achieve mean 24-hour post transfusion red blood cell survival ≥75%
        ii. Leucoreduced packed red blood cells (≤1 x 106 leucocytes/unit) with haemoglobin content ≥40 g (pre-storage filtration preferred)
        iii. ABO and Rh(D) matched blood
        iv. h (C, c, E, e) and Kell matching highly recommended
        v. Appropriate infections and viral vaccinations and screening of donor and recipient

Below is information and extracts from the Guidelines (C), referring to α-thalassaemia and mainly HbH disorder.

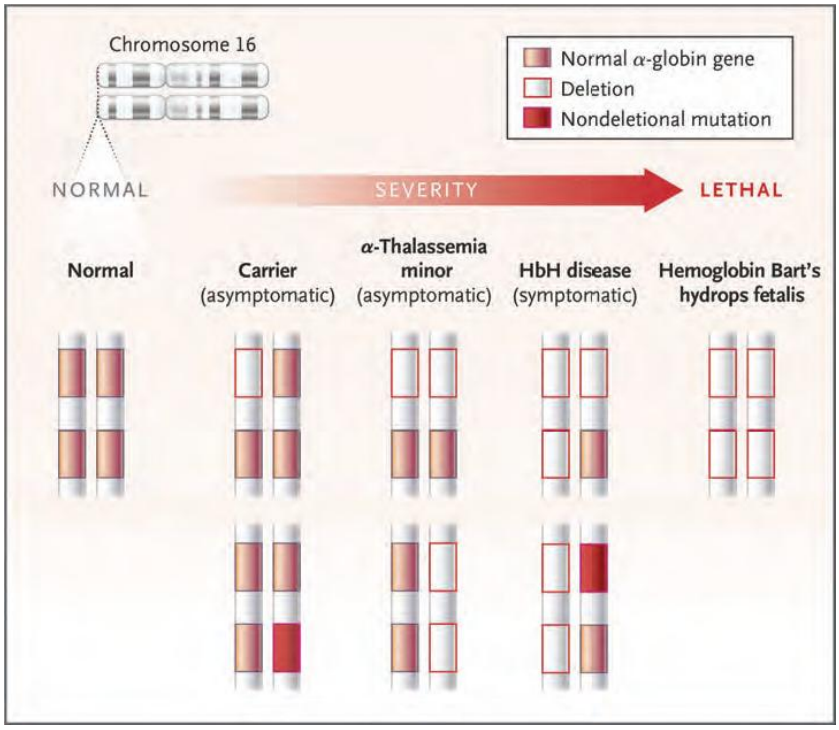

Figure 5. Classification of α-thalassaemia defects (reproduced with permission from Piel FB and Weatherall DJ. N Engl J Med. 2014). Source: Guidelines for the Management of α-Thalassaemia (TDT), 2023

Table 1. Clinical and haematologic manifestation of deletional and non-deletional forms of haemoglobin H Source: Guidelines for the Management of α-Thalassaemia (TDT), 2023

Clinical manifestation	Deletional HbH disease	Non-deletional HbH disease
Haemoglobin (g/L)	85 (range 69–107)	72 (range 38–87)
Mean corpuscular volume (MCV) (fl)	54.0 (range 46.0–76.0)	65.2 (range 48.7–80.7)
Mean corpuscular haemoglobin (MCH) (pg)	16.6 (range 14.3–24.7)	18.6 (range 14.8–24.8)
Reticulocytosis	+	++

CLINICAL PRESENTATION AND MANAGEMENT OF DELETIONAL HAEMOGLOBIN H DISEASE

Patients with HbH disease can present with episodic exacerbation of haemolysis or transient aplastic events during infections. While haemolytic (or aplastic) episodes can occur in individuals with deletional HbH disease, various publications from different regions have uniformly recognised the milder natural history of deletional HbH disease compared with non-deletional HbH disease. However, heterogeneity in clinical manifestations of deletional HbH disease is observed due to unexplained reasons. When compared with non-deletional HbH disease, in the absence of other disease modifiers, clinically severe acute haemolytic episodes requiring transfusions are not characteristic of deletional HbH disease and blood transfusion is seldom necessary. Even during significant infections, the haemoglobin level usually stays over 70 g/L and is unlikely to drop below 60

g/L. It is noteworthy that the risk of requiring blood transfusion in deletional HbH disease varies in different regions. Published case series report that 29% of patients in Thailand, 14% in Italy, and 3% in California were transfused on one or more occasions. It is possible that environmental variables (recurrent infections, malaria, or nutrition) modify the phenotypic expression of HbH disease, and they increase the probability of needing blood transfusion.

Children with deletional HbH have similar incidences of common paediatric febrile illnesses compared with their peers. Patients with fever can be seen in the clinic on the next day unless an urgent visit is warranted by the reported symptoms. Checking haemoglobin level urgently is not necessary as a sudden drop in haemoglobin level is not expected. However, if there is concern based on severity or duration of illness or the development of pallor with or without jaundice, a complete blood count, reticulocyte count, and haemolytic tests should be obtained. While aplastic crisis from parvovirus infection is possible, it has been rarely reported to cause severe anaemia in deletional HbH disease.

Summary and Recommendations

Transfusions

- Regular transfusions are not required.
- Episodic transfusions are not needed during most febrile illnesses, unless the haemoglobin level drops below 60 g/L in young children or 65 g/L in adolescents and adults.
- Transfusion may be needed for surgery or other specific indications.

CLINICAL PRESENTATION AND MANAGEMENT OF NON-DELETIONAL HBH DISEASE

Transfusion management

Patients should receive blood transfusions in cases of acute exacerbation of anaemia, typically occurring after episodes of acute illness. This intervention is recommended when the haemoglobin level drops below 70 g/L or when there is accompanying symptoms of anaemia, with an aim to restore Hb to 80-90 g/L.

The decision to initiate regular transfusions in non-deletional HbH disease should be approached differently in children and adults. Failing to provide adequate transfusion support for children with more severe anaemia or ineffective erythropoiesis can lead to undesirable outcomes, including stunted growth and changes in facial bone structure. In cases of massive splenomegaly, hypersplenism may eventually develop, necessitating splenectomy. Unlike some paediatric patients with NTD β-thalassaemia/HbE, who can remarkably adapt to low Hb levels, for those with non-deletional HbH a similar level of haemoglobin may not be adequate to facilitate optimal growth, pubertal development, and daily activities. This is because total measured haemoglobin in patients with non-deletional HbH disease is not all functional, as the total haemoglobin consists of a variable proportion of Hb Bart's (γ_4) and HbH (β_4), which are unable to deliver oxygen to tissues, and patients with higher proportion of these nonfunctional Hb are likely to encounter more severe clinical symptoms.

Once initiated, blood transfusions should usually be scheduled every 3 to 6 weeks, with pre-transfusion haemoglobin aimed at a slightly lower level (80-90 g/L), in comparison to that aimed for β-TM. This is because there is generally less degree of ineffective erythropoiesis to be suppressed in nondeletional HbH. It is

important to periodically re-assess these patients for tapering off or withdrawing blood transfusions when a sustained clinical benefit is achieved. This is to minimise unnecessary transfusional iron overload. Most often, discontinuation of blood transfusions is considered when secondary sexual characteristics are fully developed or maximum adult height is reached, unless the patients have other indications for continuing regular transfusions into adulthood.

It is important to keep in mind that transfusion requirements of individual patients can be dynamic. Children and adolescents who do not require transfusions initially may later become transfusion dependent. Therefore, regular assessment of clinical symptoms and haemoglobin (Hb) levels at each visit (every 3–6 months, as discussed earlier) is imperative during childhood and early adulthood. By contrast, affected patients who are born with hydrops foetalis or who require frequent transfusions during the first 6 months of life usually remain transfusion-dependent, unless cured through haematopoietic stem cell transplantation.

In certain transfusion-dependent patients with rare genotypes of non-deletional HbH, the proportion of non-functional Hb Bart's and HbH can remain high (>20%), even when following a conventional transfusion regimen. Similar to that identified in survivors of BHFS, these patients exhibit subtle improvements in growth and the persistence of massive hepatosplenomegaly despite standard transfusion treatments. Such cases may necessitate a more aggressive transfusion regimen, akin to that employed in BHFS survivors, which aims to achieve a pre-transfusion functional Hb level of 90-100 g/L. Functional Hb is calculated as total Hb x (1- [HbH % + Hb Bart's %] / 100). In BHFS survivors, maintaining this level of pre-transfusion functional Hb was found to reduce haemolysis and enhance tissue oxygenation, resulting in improved clinical symptoms. However, it is of utmost importance to carefully evaluate whether the benefits of this aggressive transfusion regimen outweigh the increased risk of iron overload for individual patients with severe non-deletional HbH disease.

The majority of adult patients with non-deletional HbH disease have mild to moderate anaemia and do not require blood transfusions. However, episodic (on-demand) transfusions may be necessary in cases of haemolytic crisis to achieve a target Hb level of 80-90 g/L. Leucocyte-depleted red blood cells should be administered at a volume of 10-15 ml/kg (1–2 units for adults) one or more times based on the severity of anaemia. To manage haemolysis effectively, it is crucial to identify and address the underlying causes of inflammation and infection, such as pregnancy, oxidative stress, hypersplenism, and pyrexia. Frequent transfusions may be considered in more severely affected adult patients for prevention of disease-related complications, such as significant bone deformities and, in rare instances, extramedullary haematopoiesis (EMH), and for improvement of their quality of life. Regular blood transfusions should be considered for secondary prevention or treatment of thromboembolic diseases, pulmonary hypertension, and EMH pseudotumours.

Summary and Recommendations for TDT

The recommendations, however, provided by international experts in the *Guidelines* (A) constitute the basis for the requirements of blood transfusion therapy if and when needed for β thalassaemia intermedia, α thalassaemia, and HbH disorders.

- Red blood cell transfusion at a volume of 10-15 ml/kg should be considered one or more times to manage acute haemolytic episodes in patients of all ages when Hb <70 g/L with an aim to restore Hb to 80-90 g/L. It is recommended that "effective" haemoglobin be measured at a steady state. Effective haemoglobin can be calculated as total Hb x (1- [HbH % + Hb Bart's %] / 100).

- Regular blood transfusions are considered for prevention of significant growth failure, facial bone changes, failure of secondary sexual development, and massive splenomegaly in paediatric patients. They should also be considered for patients with the following: (i) Hb at a steady-state of <70 g/L; (ii) Hb at a steady-state of 70-80 g/L with the presentation of symptoms before 2 years of age and/or spleen size ≥3 cm below costal margin
- A pre-transfusion haemoglobin target of 80-90 g/L is acceptable in most patients. However, those with a high proportion of circulating HbH and those with ineffective erythropoiesis may require a higher pre-transfusion haemoglobin level.
- Periodic re-assessment of TD paediatric and young adult patients is critical for tapering off or withdrawing blood transfusion when a sustained clinical benefit is achieved.
- Adult patients with non-deletional HbH typically do not require regular blood transfusion due to mild to moderate anaemia.
- Frequent transfusions may be considered in more severely affected adult patients for primary prevention of disease-related complications and for improvement of their quality of life.
- Regular blood transfusion should be considered for managing complications such as thrombotic diseases, cerebrovascular complications, and pulmonary hypertension.
- Monitoring and management of transfusion-dependent (TD) patients should be performed similar to patients with transfusion-dependent β-thalassaemia.

Adequacy and safety of blood transfusion for addressing the needs of TDT include three (3) main pillars.

1. Use of donor erythrocytes with an optimal recovery and half-life in the recipient,
2. Achievement of appropriate haemoglobin level,
3. Avoidance of adverse reactions, including transmission of infectious agents.

According to international recommendations, prior to initiating transfusion therapy, the following are important considerations (See Annex I Class of Recommendation & Level of Evidence):

- Confirmation of diagnosis of thalassaemia with appropriate clinical and laboratory criteria (IIA).
- Careful donor selection and screening, aiming at voluntary, regular, non-remunerated blood donors (IIA).
- Before first transfusion, performance of extended red cell antigen typing of patients at least for C, E and Kell (IIA).
- At each transfusion, give ABO, Rh(D) compatible blood. Matching for C, E and Kell antigen is highly recommended (IIA). For example, in Albania the rate of alloantibody formation dropped from 10.1% to 1.7% after application of a strict Rh and Kell matching policy [3].
- Before each transfusion, perform a full crossmatch and screen for new antibodies, or, in centres that meet regulatory requirements, perform electronic issue (IA).
- Use leucoreduced packed red cells. Pre-storage filtration is strongly recommended, but blood bank pre-transfusion filtration is acceptable. Bedside filtration is only acceptable if there is no capacity for pre-storage filtration or blood bank pre-transfusion filtration (IA).
- Use washed red cells for patients who have had severe allergic reactions (IIA).

- Transfuse red cells stored in citrate-phosphate- dextrose-A (CPD-A) within 1 week of collection and red cells stored in additive solutions within 2 weeks of collection (IA).
- Transfuse every 2-5 weeks, maintaining pre-transfusion haemoglobin above 90-105 g/l or higher levels (110-120 g/l) for patients with cardiac complications (IA).
- Support from international and regional (mainly European Union) policies, programmes, resolutions, regulations, directives and recommendations.
- Keep a record of red cell antibodies, transfusion reactions, and annual transfusion requirements for each patient (IIA).
- Keep the post-transfusion haemoglobin below 140-150 g/l (IIA).

GRADING OF RECOMMENDATIONS

Where relevant, recommendations in these guidelines are accompanied by ratings of the level of evidence and/or class of recommendations based on the following criteria:

Level of Evidence

- **Grade A:** Data derived from multiple randomised clinical trials or meta-analyses.
- **Grade B:** Data derived from single randomised clinical trial or large non-randomised studies.
- **Grade C:** Consensus of the experts and/or small studies, retrospective studies, or registries.

Class of Recommendations

- **Class 1:** There is evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
- **Class 2:** There is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
- **Class 2A:** The weight of evidence is in favour of usefulness/efficacy and therefore should be considered.
- **Class 2B:** The usefulness/efficacy is less well established by evidence/opinion and therefore may be considered.
- **Class 3:** There is evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Global Policy Landscape

The disease-specific Executive Board decision of the World Health Organization (WHO) encourages every Member State to develop adequate BT services, including transfusion therapy guidelines and standards of care for patients with haemoglobin disorders:

WHO EB118.R1 THALASSAEMIA AND OTHER HAEMOGLOBINOPATHIES (2006)

Article 1 (4). The Executive Board, urges Members States "*to develop and strengthen medical services, within existing primary health-care systems, in partnership with parent or patient organizations*"

World Health Organization (WHO)

Blood adequacy, safety and quality, patient safety, and prevention of transfusion-transmitted viral hepatitis have been the focus of the WHO and other relevant official bodies at the regional and international levels for many decades now, as seen in Table 2.

Table 2. WHO resolutions & Executive Board decisions relating to blood

WHO resolutions & Executive Board decisions relating to blood*
WHA28.72. Utilization and supply of human blood and blood products (1975)
EB79.R1. Blood and blood products (1987)
WHA55.18. Quality of care: patient safety: resolution (2002)
EB115.R15. Blood safety: proposal to establish World Blood Donor Day (2005)
WHA58.13. Blood safety: proposal to establish World Blood Donor Day: resolution (2005)
WHA63.12. Availability, safety and quality of blood products: resolution (2010)
WHA63.15. Viral hepatitis: resolution (2010)

In addition, the WHO has more recently focused considerable work on the protection of the blood supply during infectious outbreaks and on the collection of reliable data with regards to the existing situation of BT services across the WHO regions of the world, as evidenced Table 3:

Table 3. WHO reports on blood supply and transfusion services

WHO reports on blood supply and transfusion services*
Protecting the blood supply during infectious disease outbreaks: guidance for national blood services (2019)
WHO Action framework to advance universal access to safe, effective and quality assured blood products 2020–2023 (2020)
Global database on blood safety (GDBS) : Global Status Report on Blood Safety and Availability (2018–2021)

In particular, the WHO's *Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023*, which aligns with the WHO's *Thirteenth General Programme of Work 2019–2023* and *Delivering Quality-Assured Medical Products for All 2019–2023: WHO's five-year plan to help build effective and efficient regulatory systems*, aims to provide strategic direction to global efforts to address present obstacles as regards safety and availability of blood products. It recommends the implementation of a series of national, regional and international resolutions, goals, and strategies to ensure blood safety with focused, well defined strategic objectives. More specifically, in the Action Framework (2020-2023), the WHO reaffirms the importance

of haemovigilance as one of the strategic objectives of global efforts to improve capacity to monitor, investigate, and assess adverse events in blood donors and transfusion recipients.

Global Database on Blood Safety

Table 4. Previous GDBS Reports

Global database on blood safety (GDBS) reports
Global status report on blood safety and availability 2021
Global Database on Blood Safety: summary report 2011
Global Database on Blood Safety: summary report 2009
Global Database on Blood Safety: summary report 2008
Global Database on Blood Safety: report 2001–2002
Global Database on Blood Safety: summary report 1998–1999

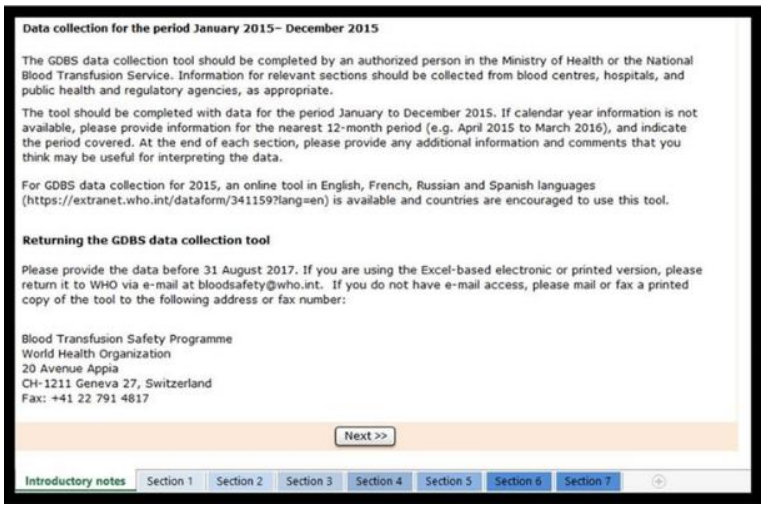

Figure 6. Data collection for the next GDBS Report, as published on WHO website.

Particularly relevant, the WHO published a guidance document on the **protection of blood supply during infectious disease outbreaks** shortly before the Covid-19 pandemic in 2019 and an interim guidance document on the management of blood supply and collection of convalescent plasma in the context of the COVID-19 pandemic in February 2021. In the former document, extensive guidance is provided on a number of important pillars to ensure readiness of blood services to develop national plans to respond to any emerging infectious threads to the sufficiency and/or safety of the blood supply, including global collaboration in monitoring for infectious threats, accurate and reliable information about a threat, good understanding of its/their implication(s), possible actions to respond, and risk assessment of threat amongst others. Very importantly the significance of reliable, updated, and continuous communication to the public, education of staff, donors and healthcare professionals, as well as appropriate adherence to clinical use of blood and haemovigilance programmes in a well-coordinated manner at national level, were included as important pillars in the said document.

In the WHO **Interim Guidance** (February 2021, during the COVID-19 pandemic), key points included the encouragement of member states for their blood transfusion services to take steps to avert potential shortages of blood and components and to promote, amongst other guidance, effective awareness campaigns on the

importance of maintaining an adequate national blood supply using different communication platforms to reach all segments of the population.

In addition, and in support of the vision to use blood components and products in the most appropriate way possible and avoid wastages and clinically unnecessary transfusions, thus contributing to a more sustainable blood supply at national level, WHO have been developing **guidelines on the clinical use of blood/transfusion** since the 1990s and are periodically updated. These have contributed significantly through the years to the blood supply chain and more appropriate investment of blood transfusions, where these were officially integrated into the National Transfusion Services policies and where these have been/are appropriately monitored for their implementation and outcome.

The concept of **patient blood management**, more actively promoted by WHO and others in recent years, focuses on improving health outcomes by clinically indicated treatment of underlying causes of anaemia and may in this way prevent the use for blood transfusion long before transfusion is even considered. The WHO has published a policy brief titled *The Urgent Need to Implement Patient Blood Management*. This work fills another gap in the chain that exists globally in addressing the risks for iron deficiency, anaemia, blood loss, and coagulopathy in a comprehensive and multidisciplinary approach, from which, further to the patients and care givers, health insurance systems and health authorities, including public healthcare systems at large, will be amongst the beneficiaries.

Patient blood management, an evidence-based bundle of care to optimise medical and surgical patient outcomes by clinically managing and preserving a patient's own blood, is a key concept that needs to be further implemented and expanded on a global level through the development and implementation of accredited, standardised programmes that will contribute to the best possible allocation of blood supplies and the minimisation of inappropriate use of blood. This is especially relevant in times of shortages of blood donations, such as during infectious disease outbreaks.

The United Nations (UN) and the WHO have also focused considerable attention on encouraging Member States across the world to transform their healthcare systems to universal coverage-based ones. This constitutes a very important goal of the UN SDG (UN Sustainable Development Goals) for 2030, as seen in Figures 7 and 8.

Universal Health Coverage

Figure 7. UN Resolution: 67/81. Global health and foreign policy (2012)

Figure 8. UN Resolution: 67/81. Global health and foreign policy (2012) - continued

GLOBAL ECOSYSTEM

An ecosystem is defined as "a system, or a group of interconnected elements, formed by the interaction of a community of organisms with their environment". Comprised of different stakeholders, active in different fields relevant to blood safety and adequacy, the global blood ecosystem revolves around five, often interconnecting, pillars: policymaking; the development and promotion of safety standards; the oversight of blood services; the provision of education and training opportunities to patients, doctors, laboratory scientists and blood donors; and advocacy.

Policymaking

The **World Health Organization (WHO)** has been at the forefront of the movement to improve blood and blood product safety and availability, as mandated by successive World Health Assembly resolutions, the earliest dating from 1975. However, significant challenges remain in providing access to sufficient, affordable, and sustainable supplies of blood and blood products, while ensuring the quality and safety of these products in the presence of known and emerging threats to public health.

To address these challenges, the WHO collaborates with member states, collaborating centres and partners in order to recommend policies, share information and knowledge, and coordinate technical support and to maximise the impact of on-the-ground events to increase blood donations and to support blood system strengthening and universal access to blood transfusion. Its contribution and leadership in the field of blood safety and availability have been outlined further above.

At the regional level, the **European Union (EU)** works to address common challenges amongst its Member States, i.e. interruptions in supply, the exposure of citizens to avoidable risks, unequal levels of safety and quality, and barriers to the exchange of blood, tissues and cells across Europe. This is achieved by the EU Member States adopting EU Directives and Regulations. A **new Regulation** on standards of quality and safety for substances of human origin intended for human application was proposed by the European Commission, agreed upon by the European Parliament and the Council, and adopted in 2024. This will introduce novelties in

the EU blood ecosystem, including a strong EU oversight of blood establishments, harmonised standards, and an EU alert system for blood shortages.

Standards

To protect the right of patients to health, the **Council of Europe (CoE)** has issued a number of recommendations, based on the Guidelines and Standards developed by the European Directorate for the Quality of Medicines & HealthCare, in collaboration with the European Committee on Blood Transfusion, which aims to oversee and coordinate the Council of Europe's work in the field of blood transfusion and advise the Committee of Ministers on all questions within its field of competence. Its overall aim is to ensure social rights by elaborating and promoting high ethical, safety, and quality standards in the field of blood transfusion. These recommendations are known as the "Blood Guide", i.e., the Council of Europe's *Guide to the preparation, use and quality assurance of blood components*, which governs blood safety practices across Europe.

The **Association for the Advancement of Blood & Biotherapies (AABB)** sets standards that optimise and advance quality and safety for the blood and biotherapies field in the United States. Since 1957, AABB standards have been the backbone of AABB's mission and are currently applied to AABB-Accredited facilities in more than 50 countries and to other facilities to advance their quality and safety measures. AABB Standards combine internationally accepted quality management system requirements with relevant technical requirements for each discipline, from specification of equipment, materials management, and organisational structure to documents, resource management, and programme assessment.

Oversight of Blood Establishments

The **Centres for Disease Control and Prevention (CDC),** in the United States of America, is one of the federal agencies responsible for promoting the safety of the U.S. blood supply. CDC conducts investigations and oversees surveillance of blood collections and donations.

The **U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER)** is responsible for regulatory oversight of the U.S. blood supply. It promulgates and enforces standards for blood collection and for the manufacturing of blood products, including both transfusible components of whole blood, pharmaceuticals derived from blood cells or plasma, and related medical devices. It also inspects blood establishments and monitors reports of errors, accidents, and adverse clinical events. CBER works closely with other parts of the Public Health Service (PHS) to establish blood standards, and to identify and respond to potential threats to blood safety or supply.

In the European region, the **European Centre for Disease Prevention and Control (ECDC)** works to (i) provide scientific advice; (ii) strengthen Europe-wide disease surveillance; and (iii) support preparedness and responses to disease outbreaks.

Education

Education in the field of blood donation, safety, and adequacy is provided by a great number of stakeholders, either patient groups, healthcare professionals (Transfusion Medicine specialists), or blood donation bodies. The International Society of Blood Transfusion (ISBT), having as a mission to advance knowledge and education by advocating for the welfare of blood donors and patients, is a source of reference for healthcare professionals globally.

Key stakeholders providing educational opportunities at the international, regional, and country levels include:

- International level: International Society of Haematology; International Society for Experimental Hematology (ISEH); International Foundation for Patient Blood Management; International Society for Laboratory Hematology (ISLH); International Haemovigilance Network (IHN); International Federation of Red Cross and Red Crescent Societies (IFRC); and International Federation of Blood Donor Organizations (IFBDO/FIODS).
- Regional level: European Hematology Association (EHA); Pan Arab Hematology Association; Africa Society of Blood Transfusion; and American Society of Hematology (ASH).
- Country level: National Haematology/Transfusion Medicine Societies.

Advocacy

Besides patient associations, such as TIF (PIBA), representing transfusion-dependent communities, the work of the initiative Blood & Beyond Alliance in Europe is also noteworthy, given that this is the first multi-stakeholder group aiming at raising awareness of the impact of blood transfusion on patients, supporting networks, healthcare systems, and society at large and having an overarching goal to help advance policies and practices that improve patient outcomes by optimising blood management and supporting innovation across Europe.

THE GLOBAL SCENE OF BLOOD TRANSFUSION SERVICES TO DATE ACROSS THE SIX WHO REGIONS – TIF'S PERSPECTIVE

The focus of this chapter of the *Global Status Report* is to attempt to identify the challenges that TDT patients face with regards to blood transfusion (BT) therapy. The information extracted from the WHO's GDBS Report of 2021 (with 2018 data) and other work of the WHO, more specifically at the regional level, EMRO-Strategic framework for blood safety and availability, and EM/LAB/389/E and Supply of Blood for Transfusion in Latin American and Caribbean countries 2016 and 2017, is complemented with published information, where available, and information and data from the relevant EU competent bodies, as well as data and information compiled through TIF's work across more than 60 countries in the six regions of the world (as defined why WHO).

About WHO's Global Status Report on Blood Safety and Availability (2021)

The Global Status Report on Blood Safety and Availability (GDBS) requests and analyses data from ministries of health of World Health Organisation (WHO) Member States. The terminologies used in the survey questionnaire were given standardised definitions to promote consistent reporting. Where possible, efforts were made to validate the data reported to WHO with WHO regional and country offices. Countries were contacted for clarification or correction when discrepancies or unusual patterns were observed. Efforts were also made to validate GDBS data by comparing them with data available from other published sources. However, not all the data provided by all countries could be systematically verified. In particular, answers to the

questions on the existence of policies, programmes, or mechanisms could be affected by individual interpretation of the questions asked.

The results should support changes required to achieve safe blood supply through various levers, such as regulation, oversight, citizen and community engagement, and adequate funding. The report also provides an opportunity for WHO and other organisations to suggest appropriate guidance.

This 2021 report continues to recognise that inadequate and unsustainable financing of blood services is a major factor that impedes efforts to improve blood safety in developing countries. Governments should ensure adequate, sustainable financing for national or regional blood programmes. The financing mechanisms for blood services should be integrated within the financial structure of national healthcare systems. Countries with significant support for external donor funding should take proactive measures to mobilise domestic sources and reduce dependence on external funding, to ensure the quality and sustainability of blood transfusion services.

While best attempts have been made to obtain accurate data from countries, the data submitted by national health authorities have not been independently verified. Data accuracy therefore depends on the data collection systems in countries, and this report can only reflect the information provided by WHO Member States. While many countries report comprehensive national data on blood availability and safety, others provide limited information on the activities of a subset of blood centres in the country. Incomplete data and potentially different interpretations of some indicators affected our ability to analyse some of the information received from countries.

The Global Picture as Captured by the Latest WHO GDBS

Across the WHO regions (ranked by percentage), 19 (58%) countries in the Americas, 15 (60%) in the Western Pacific, 30 (71%) in Europe, 14 (78%) in the Eastern Mediterranean, eight (80%) in South-East Asia, and 39 (91%) in Africa reported having a national blood policy. Similarly, 19 (45%) countries in Europe, 12 (48%) in the Western Pacific, 17 (52%) in the Americas, 11 (61%) in the Eastern Mediterranean, 34 (79%) in Africa, and eight (80%) in South-East Asia reported having a multiyear strategic plan for blood safety in 2018 (Figure 9).

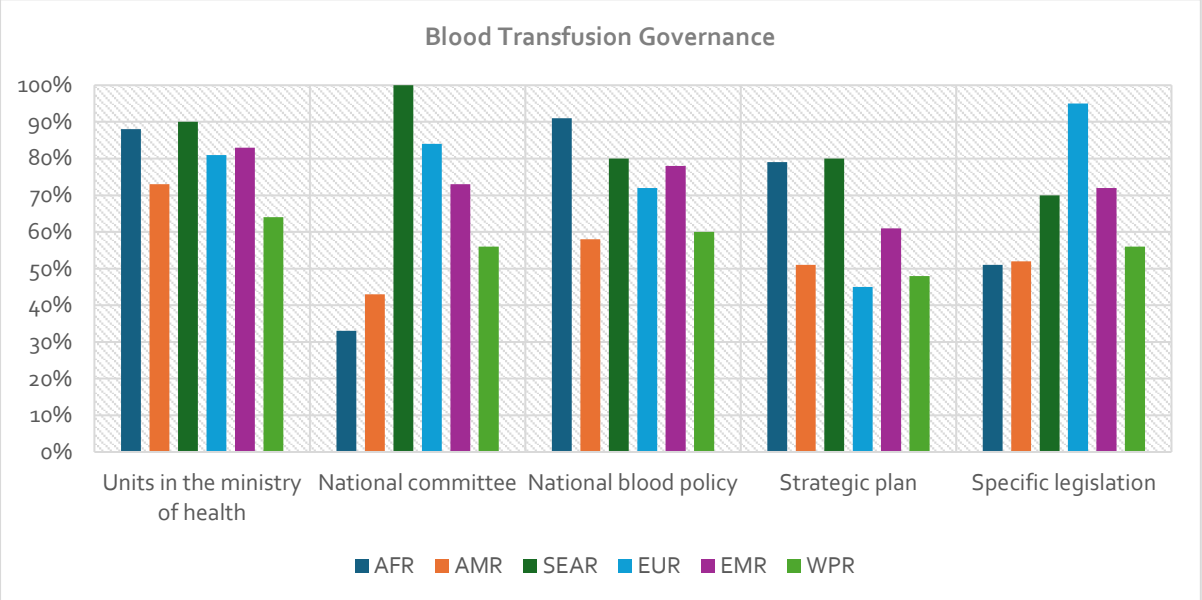

Figure 9. Governance mechanisms for blood transfusion by WHO region, 2018

Table 5. Estimated blood donations by WHO region (2018)

Region	Estimated whole blood donations (millions)	Estimated apheresis donations (millions)	Total (millions)	% of global population
Africa	6.1	0.003	6.1	14%
Americas	21.6	2.5	24.1	13%
Southeast Asia	21.6	0.7	22.3	26%
Europe	24.8	5.9	30.7	12%
Eastern Mediterranean	8.8	0.2	9	9%
Western Pacific	23.2	3.1	26.3	26%
Global (rounded totals)	106.1	12.4	118.5	100%

There were wide variations in blood donation rates among countries, ranging from 0.6 to 53.0 per 1,000 population. The whole blood donation rate (median) was 31.5 donations per 1,000 population per year (range 10.9–53.0) in high income countries, 16.4 (range 4.6–47.6) in upper-middle-income countries, 6.6 (range 1.9–25.0) in lower-middle-income countries, and 5.0 (range 0.6–10.9) in low-income countries. Across WHO regions, the donation rates ranged as follows: 0.6 to 35.3 (median 5.4) in Africa; 2.7 to 36.8 (median 14.6) in the Americas; 1.9 to 25.3 (median 10.6) in South-East Asia; 4.4 to 53.0 (median 32.1) in Europe; 0.6 to 25.3 (median 14.3) in the Eastern Mediterranean; and 3.4 to 47.6 (median 16.1) in the Western Pacific.

Sixty countries reported collecting less than 10 whole blood donations per 1,000 population per year in 2018. Of these, 34 countries are in the WHO African Region, four in the Region of the Americas, five in the South-East Asia Region, four in the European Region, four in the Eastern Mediterranean Region, and nine in the Western Pacific Region (Figure 5). Given that seven countries that reported collecting less than 10 whole blood donations per 1,000 population in 2013 did not respond to GDBS 2018, these figures have changed little since the last report.

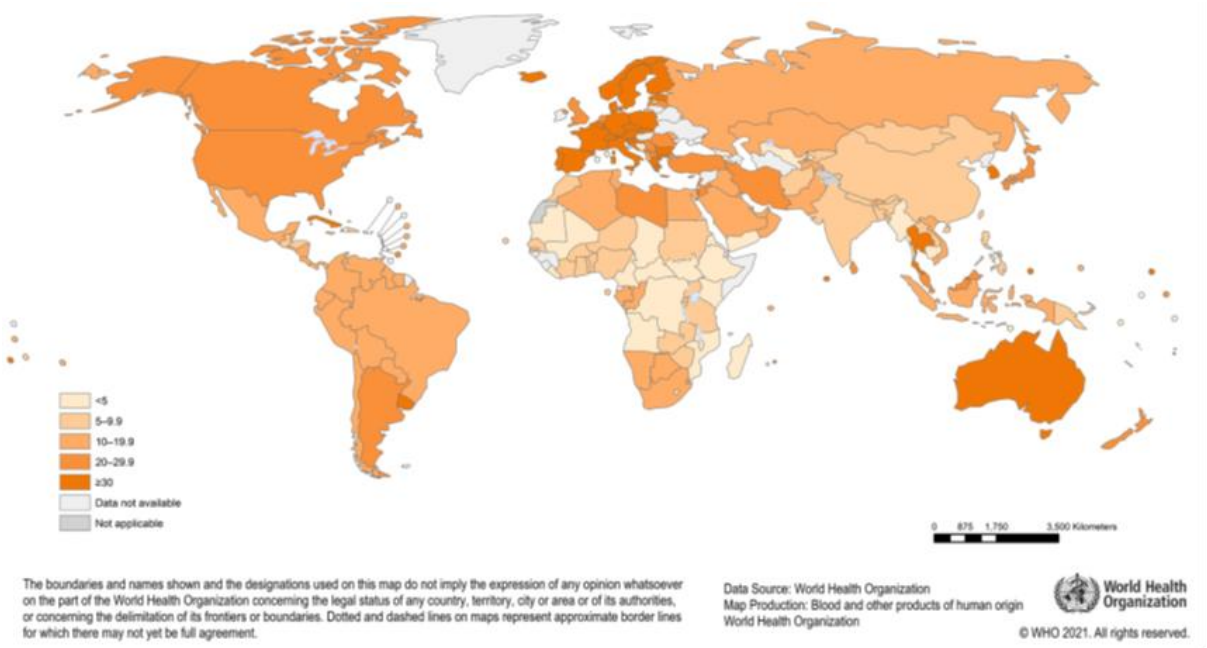

Figure 10. Whole blood donations per 1,000 population, 2018

Repeat voluntary non-remunerated blood donation practices, which constitute a significant pillar of the safety of blood, have as follows:

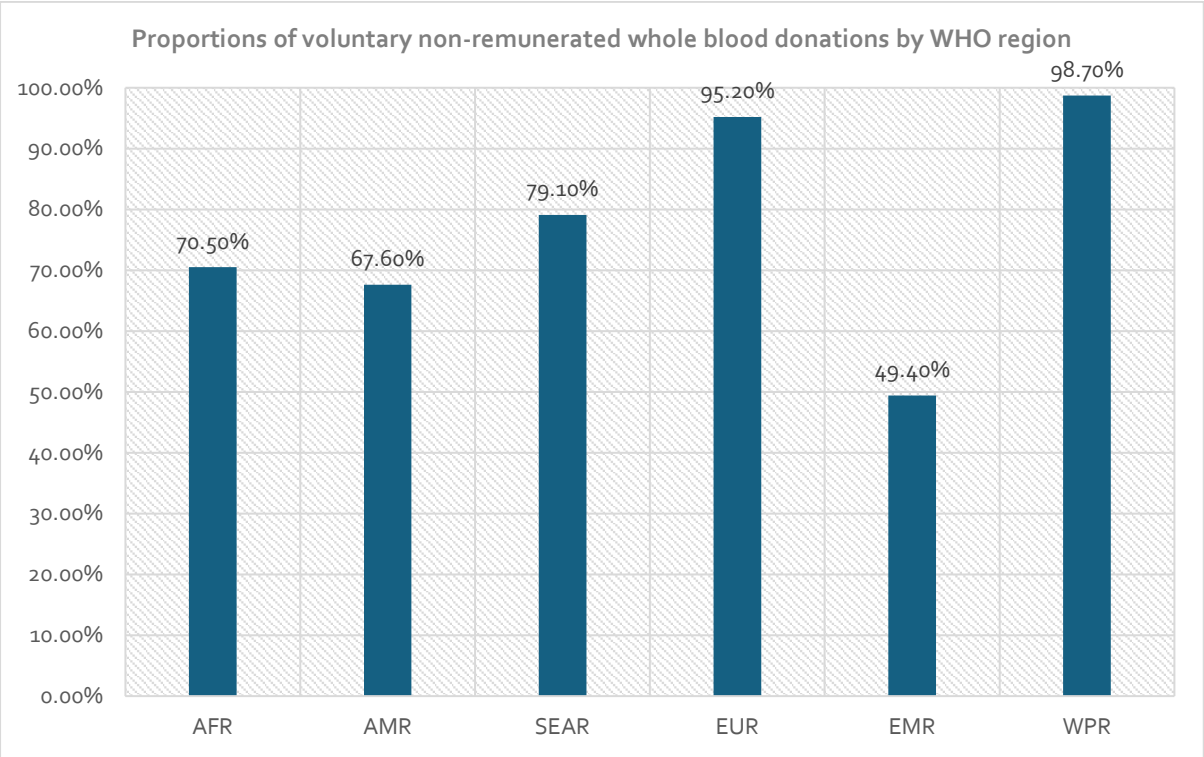

Figure 11. Proportions of voluntary non-remunerated whole blood donations by WHO region (%)

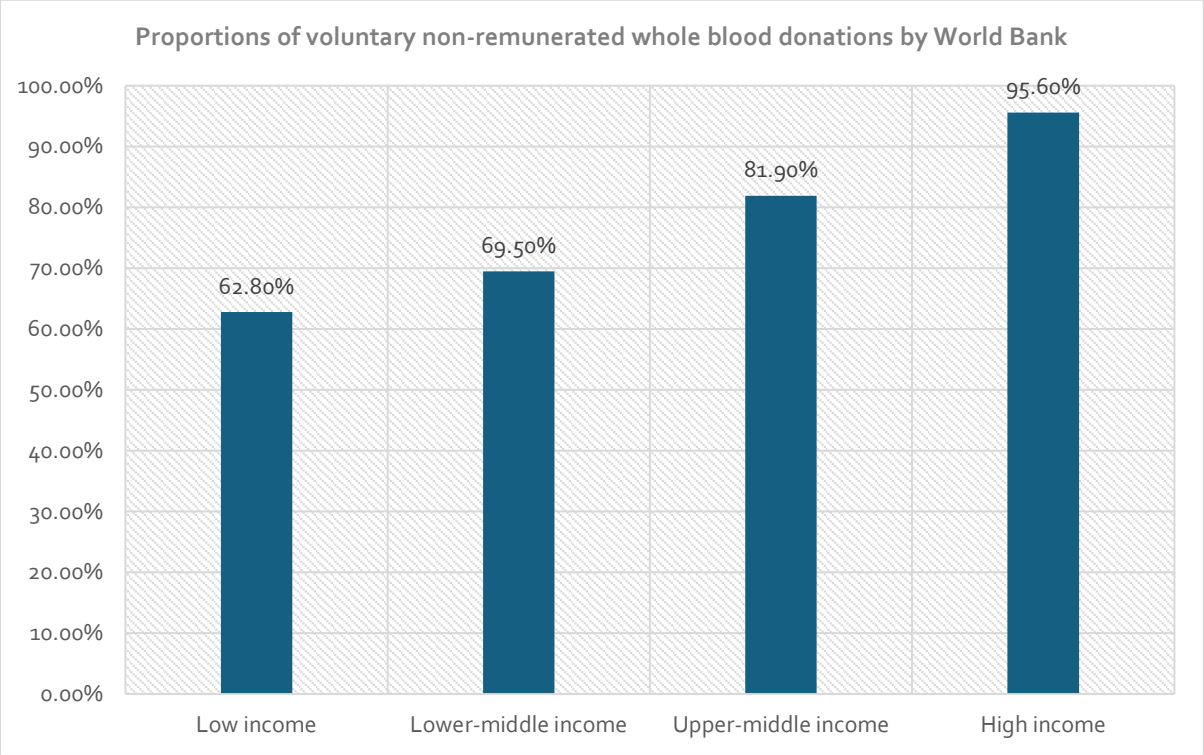

Figure 12. Proportions of voluntary non-remunerated whole blood donations by World Bank (%)

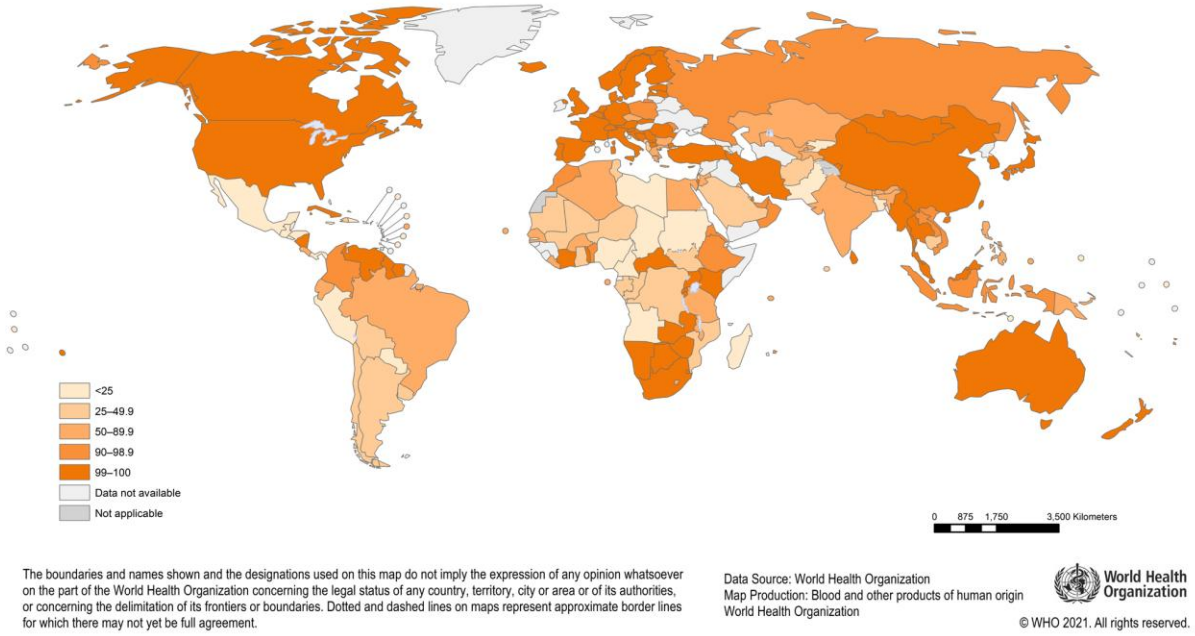

Figure 13. Proportion of voluntary non-remunerated donations (whole blood and apheresis donations combined) by country (2018)

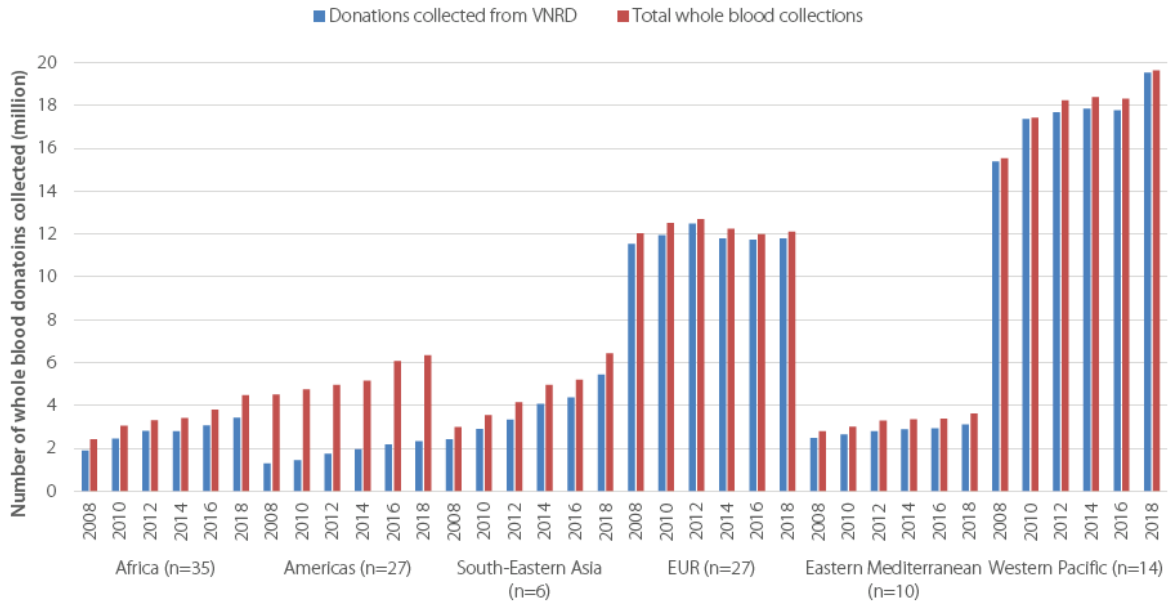

Figure 14. Total whole blood collections and voluntary non-remunerated donations (millions) by WHO region (2008–2018)

Table 6. Donations given by repeat voluntary non-remunerated blood donors by WHO region (median and range, %)

Region	Median	Range	Interquartile range
Africa (n=7)	38	30-76	-
Americas (n=16)	20	0.3-87	16-54
Southeast Asia (n=6)	57	5-86	31-63
Europe (n=35)	90	0.1-100	68-93
Eastern Mediterranean (n=9)	37	1-88	18-45
Western Pacific (n=18)	56	2-96	32-83

The results of the studies on the reason for donor deferral rates, which is an important component contributing to blood shortages leading to insufficiencies to address appropriately the lifelong dependence of patients with thalassaemia in many countries across the world, highlighted low weight in lower income countries, low haemoglobin and travel history in high income countries, and low haemoglobin and high-risk behaviour in upper middle-income countries, as shown in Figure 15.

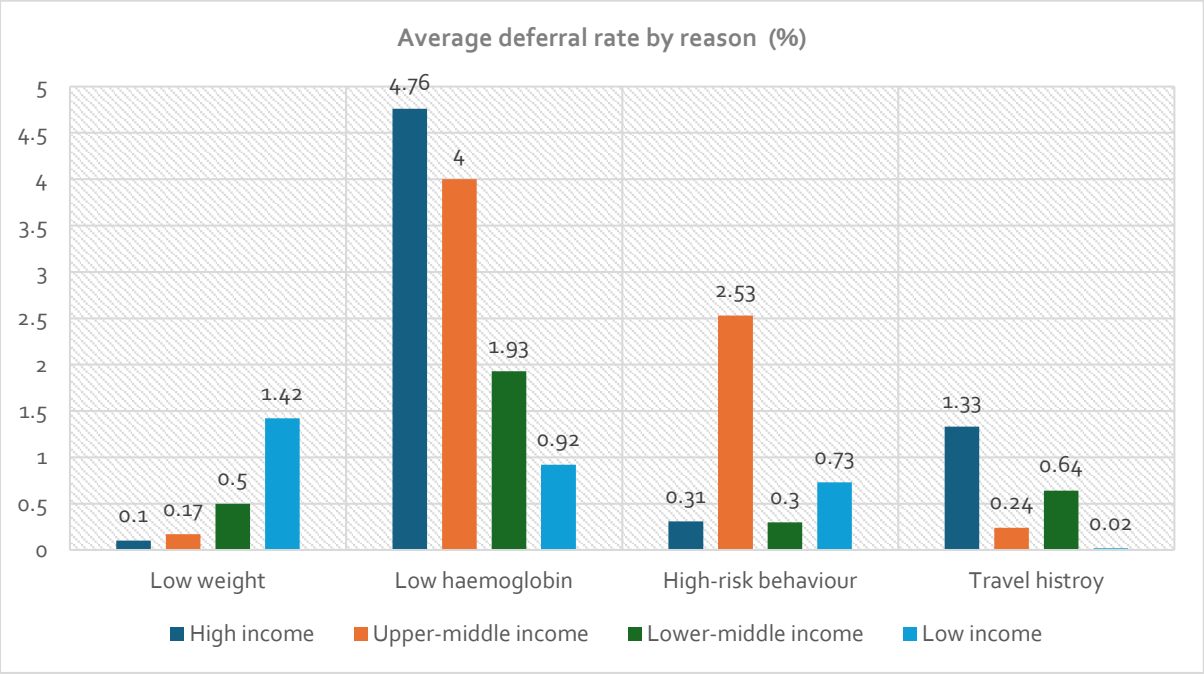

Figure 15. Donor deferral rate (%) by reason in countries in different income groups

Processing of blood into components is another major element contributing to the effectiveness of blood transfusion therapy in patients with haemoglobin disorders, including thalassaemia, and in particular the use of the red blood cell component of blood (the missing one).

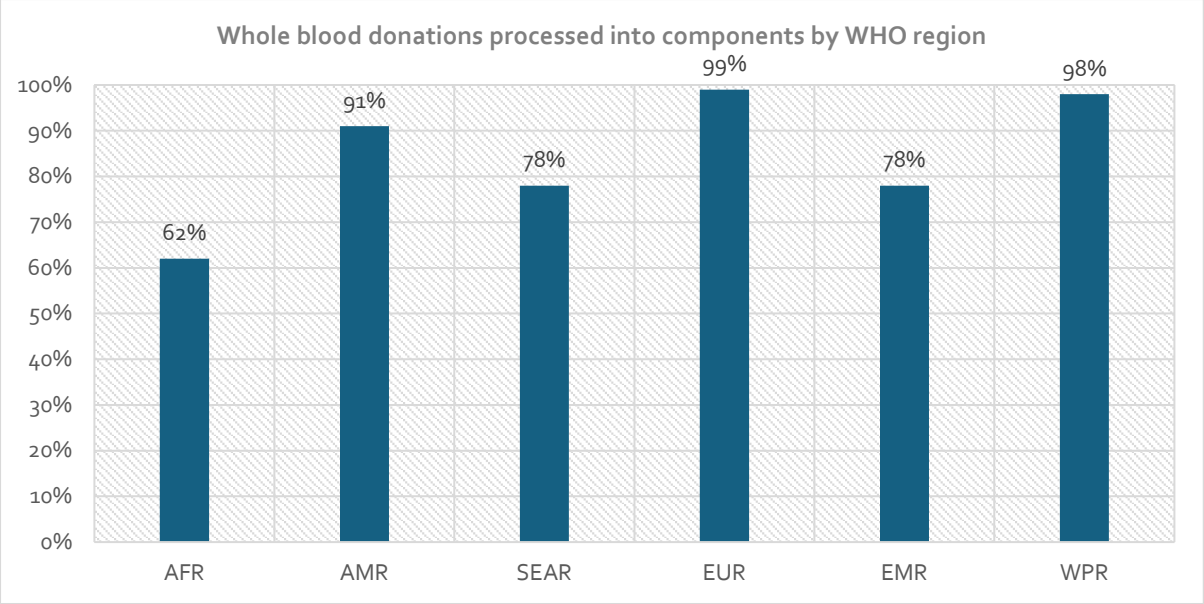

Figure 16. Whole blood donations processed into components by WHO region (%)

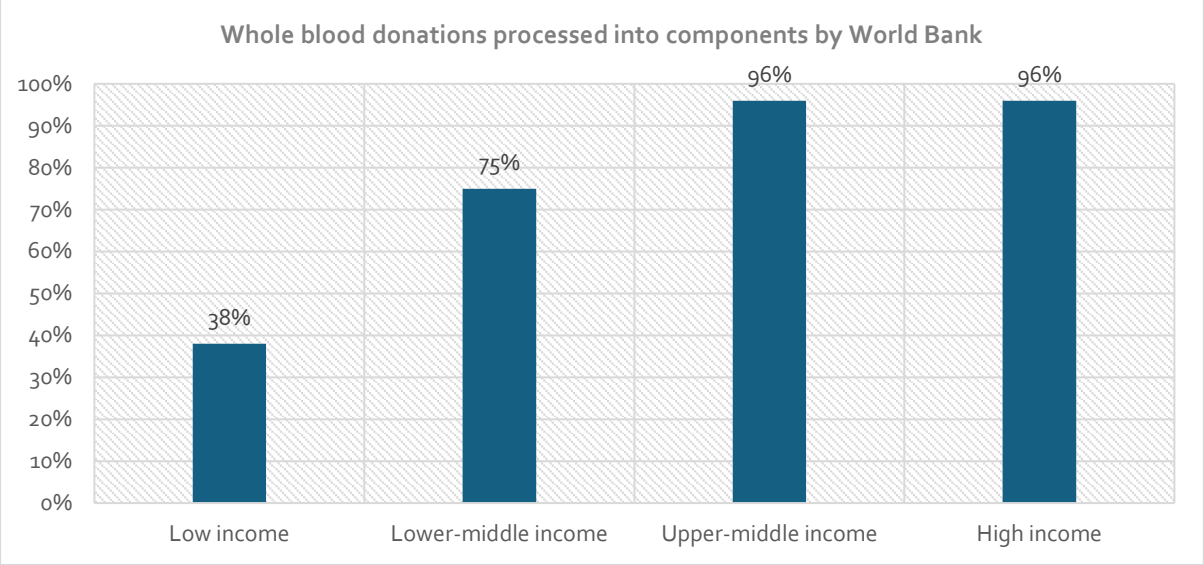

Figure 17. Whole blood donations processed into components by World Bank (%)

Table 7. Proportion of blood donations processed into components: number of countries in each percentage grouping by WHO region, 2018

Region	< 25%	25-<50%	50-<75%	75-<90%	90-100%
Africa (n=43)	15	4	3	3	18
Americas (n=31)	0	2	0	6	22
Southeast Asia (n=10)	0	2	1	2	5
Europe (n=39)	0	0	0	2	37
Eastern Mediterranean (n=14)	0	2	0	4	8
Western Pacific (n=20)	1	2	0	5	12

Component Separation

Blood separation into its components is another major concern since concentrated RBCs constitute the recommended appropriate component of blood needed for effective transfusion therapy of TDT patients. Although component separation is occurring widely across the world, to-date in some, mainly World Bank income groups low-middle income countries (LMIC) and low income countries (LIC), the red cell components transfused per 1,000 population is only 5.38 units and 3.41 units of red cells, respectively. One can understand the importance of this when looking at data demonstrating that only 1% of blood in the upper-middle income countries (UMIC) is transfused as whole blood, whereas 24% and 85% of blood in LMIC and LIC, respectively, was transfused as whole blood.

Unfortunately, data for the implementation of the other processes (apart from component separation) that contribute to the quality, safety, and importantly effectiveness of BT therapy in TDT patients, such as those described earlier in this chapter, in the context of the international recommendations for BT in these patients, are extremely limited in the published literature, and when available they are only derived from small groups of patients in a country and do not reflect the national policies. The only parameters that TIF can use with a certain level of reliability in order to relate the effectiveness of BT therapy are the survival rates and the age distribution information from official nationwide published data. This data, however, for many countries even with high prevalence of haemoglobin disorders is still largely missing.

Table 8. Units of red cell products transfused per 1,000 population by World Bank income group

Income group	Median	Interquartile range (IQR)
Low income (n=19)	4.3	2.6-6.0
Lowe-middle income (n=34)	5.5	3.2-10.3
Upper-middle income (n=39)	12.7	8.7-19.4
High income (n=43)	28.8	21.5-37.2
All (n=135)	12.3	5.6-24.9

Table 9. Units (millions) of red cell products transfused by WHO region, 2013 and 2018

Region	All red cell products transfused			% whole blood transfusion	
	2013	2018	% diff.	2013	2018
Africa (n=30)	3.32	3.85	16	28.0	28.3
Americas (n=16)	3.40	3.55	4	1.2	0.3
Southeast Asia (n=9)	4.50	5.60	24	32.2	27.3
Europe (n=31)	20.92	19.79	5	0.6	0.4
Eastern Mediterranean (n=8)	3.14	4.18	33	22.3	27.9
Western Pacific (n=18)	17.18	18.69	9	2.9	2.1
Total (n=112)	52.90	55.7	5	7.0	7.7

Comment

The most RBC products are donated in Europe (745,173,774 population, 2021) and in the West Pacific (more than 1.9 billion/ 1,900,000,000 population).

A major challenge is the extent of total blood donations discarded for a number of reasons as seen in Tables 10 and 11, and in Figure 18.

Table 10. Percentage (median and interquartile range) of total whole blood donations discarded by World Bank income group

Income group	Median	Interquartile range (%)
Low (n=24)	9.6	4.3-14.8
Lower middle (n=37)	8.0	5.9-11.6
Upper middle (n=36)	6.7	3.1-8.7
High (n=41)	4.1	2.9-7.4

Table 11. Percentage (median and range) of donations discarded due to reactivity for markers of TTIs by World Bank income group

Income group	Median	Interquartile range (%)
Low (n=24)	5.8	2.7-10.9
Lower middle (n=36)	4.4	2.8-6.8
Upper middle (n=33)	1.9	0.9-3.7
High (n=29)	0.5	0.3-1.7

Apart from transfusion transmissible infectious threats (as seen in Table 12), the significant percentage of blood discarded constitutes another major concern particularly in low-middle income countries. The causes include expired blood, as well as another significant 28% for a number of other reasons (Figure 18).

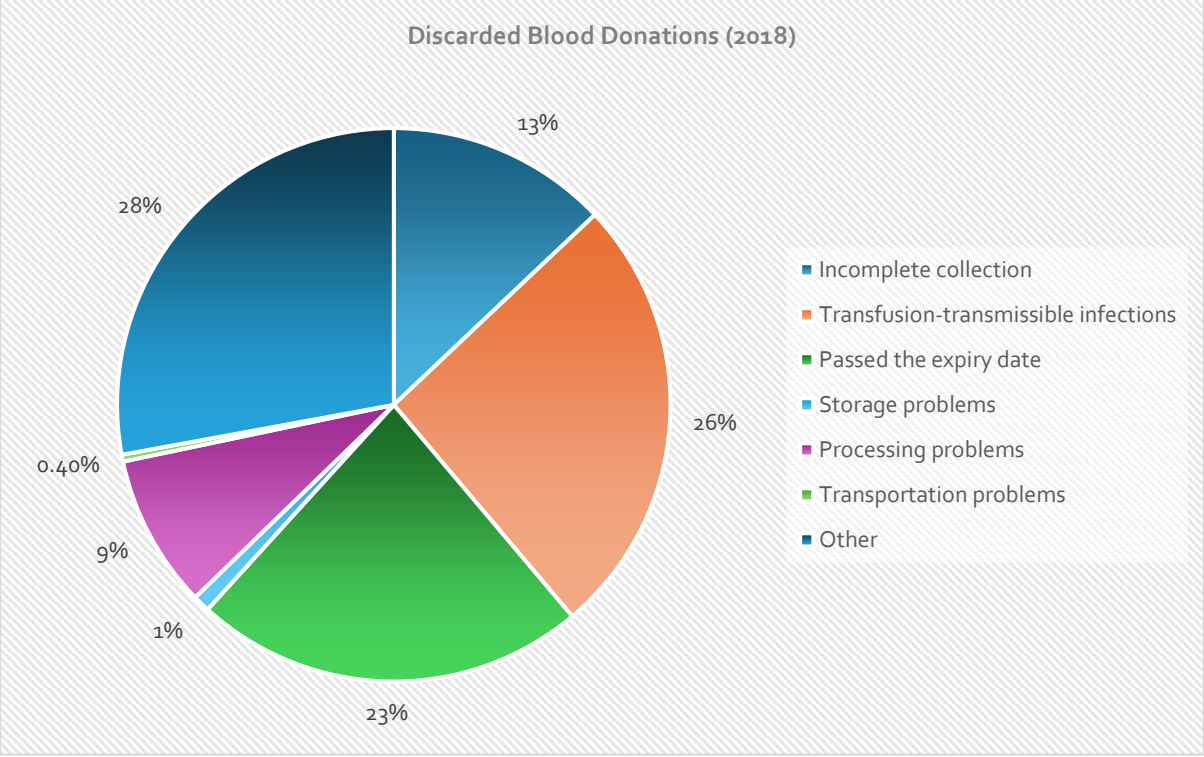

Figure 18. Distribution of discards of blood donations by reason, 2018

Donations that are positive to HIV, HBV, HCV, and syphilis that were discarded are significantly higher in lower income countries and, in the case of HBV and syphilis, in low-middle income countries as well.

Table 12. Proportions of blood donations with positive/reactive results on screening tests by income group

Income group	Proportion of blood donations with positive/reactive results (median and Interquartile range, %)			
	HIV	HBV	HCV	Syphilis
High	0.002 (<0.001-0.01)	0.02 (0.005-0.12)	0.007 (0.002-0.06)	0.02 (0.003-0.12)
Upper middle	0.10 (0.03-0.23)	0.29 (0.13-0.62)	0.19 (0.07-0.36)	0.35 (0.13-1.10)
Lower middle	0.19 (0.04-0.62)	1.70 (0.70-4.74)	0.38 (0.12-0.99)	0.69 (0.19-1.38)
Low	0.70 (0.28-1.60)	2.81 (2.00-6.02)	1.00 (0.50-1.67)	0.90 (0.60-1.81)

Although considerable efforts are still needed to improve or even develop hemovigilance programmes across the globe, available data report the following with regards to serious adverse transfusion reactions (Figure 19).

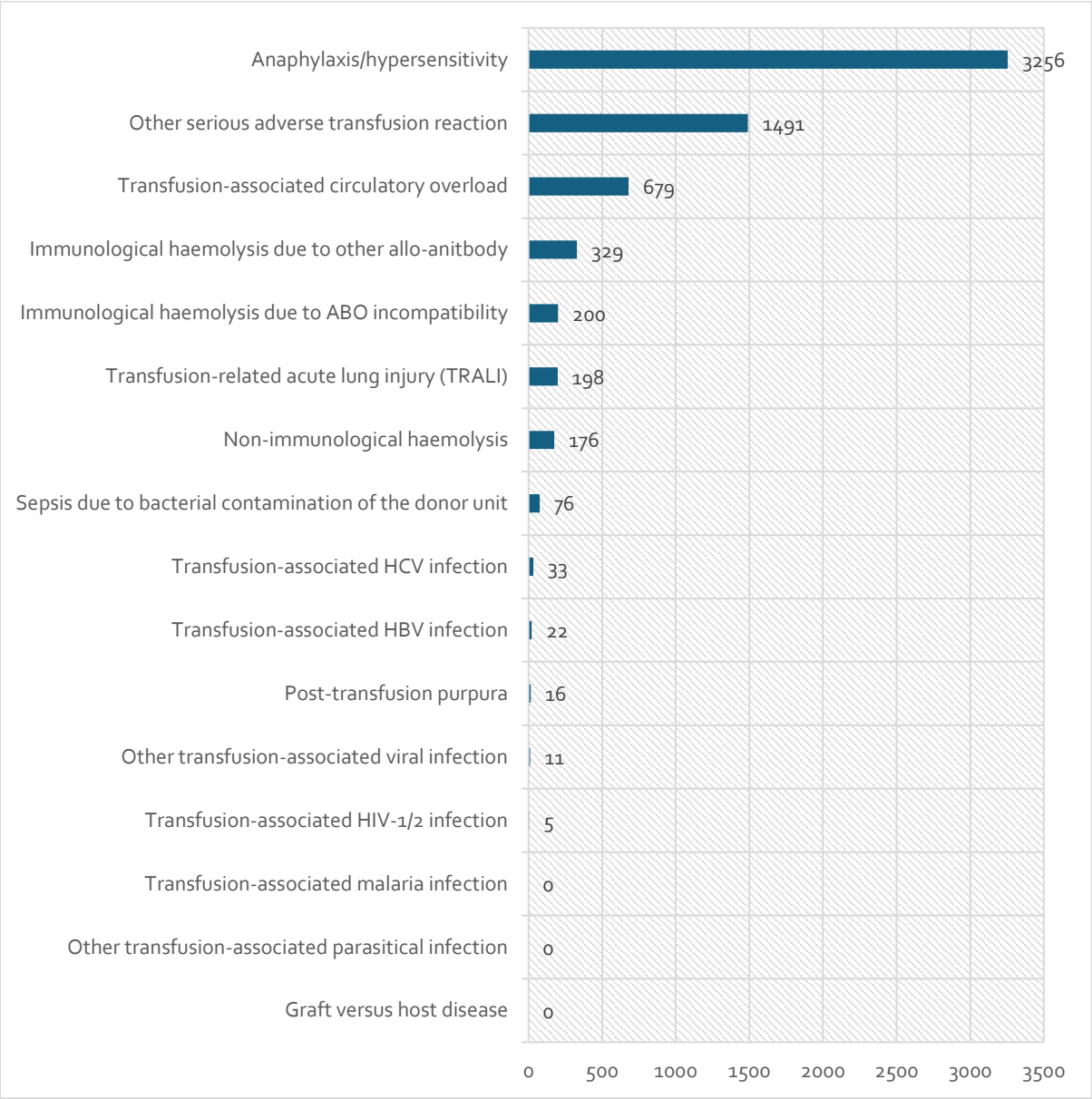

Figure 19. Serious adverse transfusion reactions reported

Higher incidences of serious adverse reactions are reported in the South-East Asian region and the lowest in the Western Pacific region (Table 13).

Table 13. Incidence of serious adverse reaction (per 100 000 units of components transfused) by WHO region

	Serious adverse reaction	Total number of components transfused/issued	Incidence
Africa (n=5)	214	1 457 280	14.7
Americas (n=7)	1 045	5 654 075	18.5
Southeast Asia (n=3)	1 395	2 722 070	51.2
Europe (n=31)	2 634	27 238 559	9.7
Eastern Mediterranean (n=4)	409	4 070 358	10.0
Western Pacific (n=12)	795	11 892 266	6.7
Total (n=62)	6 492	53 034 608	12.2

Countries which implemented further testing than for just HIV, HBV, HCV, and syphilis, either by testing all donations or by selectively testing for malaria, HTLV 1 and 2, and Chagas disease, are mentioned in Tables 14, 15 and 16 below.

Table 14. Malaria testing policy in 51 countries

Region	Testing for all donations (microscopy)	Selective testing (microscopy)	Selective testing (sntibody testing)
Americas	Brazil*		
Southeast Asia	Bangladesh* Bhutan India* Sri Lanka	Mexico	
Europe		Indonesia** Myanmar** Nepal*	Belgium Greece Italy Luxembourg Netherlands Portugal Spain Switzerland United Kingdom
Eastern Mediterranean	Pakistan* Saudi Arabia Yemen**	Finland** Norway** Sweden**	Kuwait Qatar*** United Arab Emirates
Western Pacific	Philippines	Malaysia Viet Nam	Australia Singapore
* Microscopy or antigen testing ** Antigen testing *** Selective testing for antigen and antibody			

More comprehensive testing for some pathogens including malaria, HTLV1+2, and Chagas disease are shown below:

Table 15. Malaria testing policy in several countries

Americas	Europe	Eastern Mediterranean	Western Pacific
Argentina	France	Iran (Islamic Republic of)*	Australia
Brazil	Greece	Kuwait	China*
Canada	Israel	Oman	New Zealand*
Trinidad and Tobago	Luxembourg*	Qatar	Republic of Korea*
USA	Netherlands*	Saudi Arabia	Viet Nam*
	Norway*	United Arab Emirates	
	Portugal*		
	Romania		
	Spain		
	Sweden*		
	United Kingdom*		
* Selective testing			

Table 16. Testing for Chagas disease

Test for all donations	Selective testing		
Argentina	Belgium	Italy	Sweden
Brazil	Canada	Portugal	Switzerland
Mexico	France	Spain	USA
Trinidad and Tobago			

As previously mentioned, more attention is needed to standardise definitions with regards to the hemovigilance programmes. As seen below on the map (Figure 20), there are many challenges identified, even if such programmes are reported to exist in a number of countries.

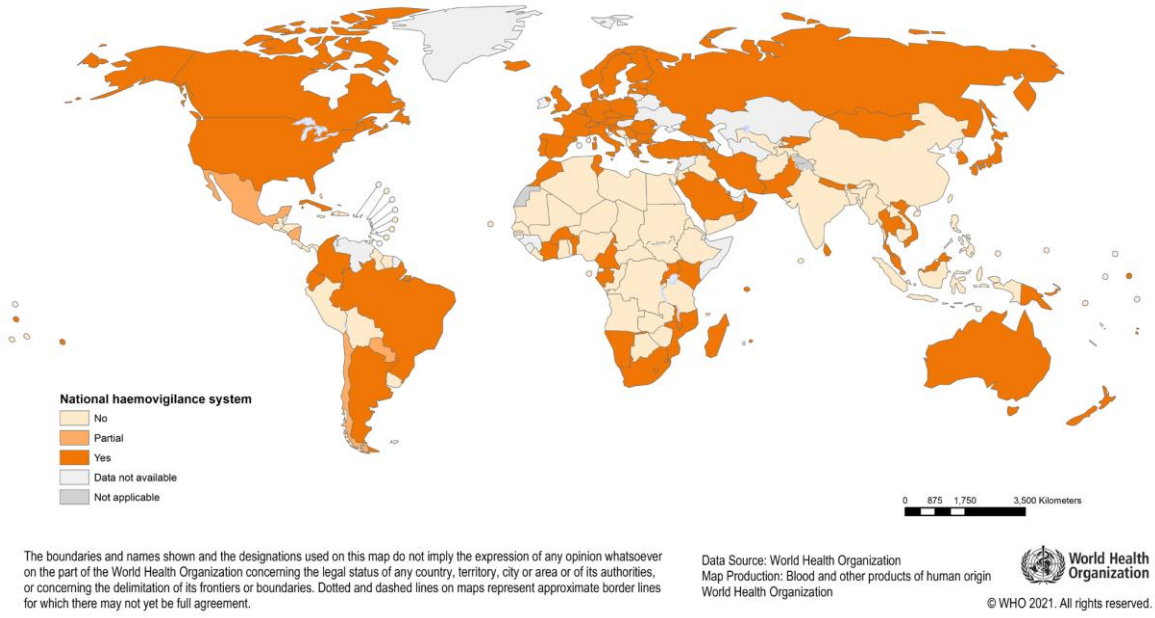

Figure 20. Distribution of countries reporting the existence of national haemovigilance systems, 2018

A study was published in 2023 (*Transfusion* 2023; 63:982-992), which used Vigibase, the WHO global database of individual case safety report (ICSRS) and based on the WHO designation of blood as medicine and hence subject to pharmacovigilance reporting between 1968–2021. Despite limitations, the findings suggested a significant underreporting of adverse reactions and adverse events from blood products: many countries underreport in their national hemovigilance, others use passive report systems, others use different surveillance systems with different legal and mandatory reporting requirements or use different case definitions/criteria to determine adverse reactions, and differences in patient populations, amongst other reasons. Although the study demonstrated the broad range and high number of adverse reactions and adverse events associated with the use of blood products, higher than any other existing hemovigilance data-collection database, further research is required, as stated by the authors of this study, to characterise and confirm the potential risk of using blood products in patients and the rates and incidences of adverse reactions and adverse events. However, considerable effort is required at the local, national and international level to raise awareness amongst users and healthcare professionals of the importance of considering, identifying, and reporting cases of suspected adverse reactions and adverse events associated with the use of blood products of human origin, particularly in countries from regions including South-East Asia and the Eastern Mediterranean, where very few reports were observed.

Certainly, several reports, including a comprehensive review of the literature including a Swiss perspective published in the Journal of Clinical Medicine 2022 (J. Clin. Med. 2022, 11, 2.859) [6], highlighted the importance of detailed documented standardised definitions for adverse events and adverse reactions and the need for sensitisation of medical staff to the importance of hemovigilance programmes.

In a TIF survey (2020–2024) related to BT therapy with nearly 2,000 subjects (N=1,989), TD patients responding from 28 LMICs and LICs, through 32 National Thalassaemia Association members of TIF, the following patient perspectives and challenges were captured:

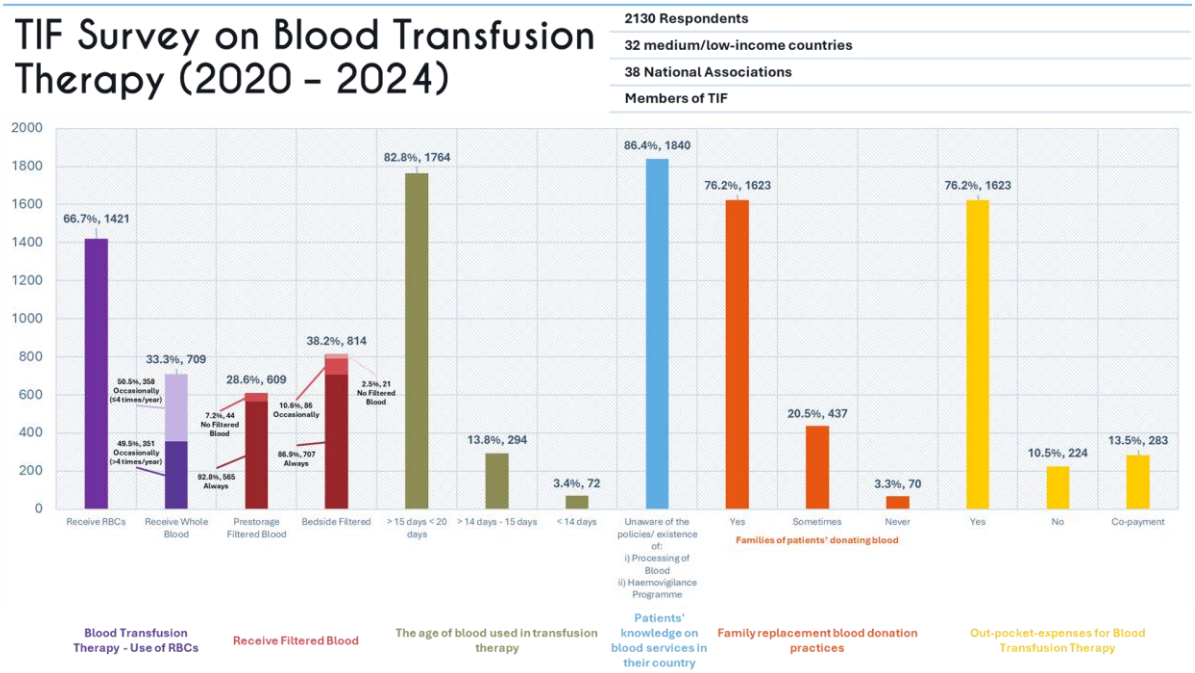

Figure 21. TIF Survey on Blood Transfusion Therapy (2020–2024)

In summary, and despite great achievements made in BT services, including for specific diseases, in many countries with developing economies through the years, some of the key challenges that many still encounter include:

- Lack of, limited, or underdeveloped centralised Blood Transfusion Services.
- Cultural and/or religious beliefs and/or attitudes that can discourage blood donations to a smaller or larger extent.
- The community at large is not sufficiently and/or appropriately educated on the value and need for blood donations and how these contribute to treatment protocols that are often-lifesaving.
- Females in some countries and/or communities are not allowed to or are discouraged from becoming blood donors.
- Component separation is still weak in many countries and patients with TDT are on occasions deprived of red cells, the essential component for their treatment.
- Military, private, social security, Red Cross, and university blood services, mainly donation, often do not cooperate, resulting in an inadequate distribution/provision of blood components to needy people.
- Suboptimal quality control over every aspect of blood transfusion services, leading to transfusion-related reactions/adverse events and co-morbidities in a percentage of TDT patients, the exact extent of which is largely unknown.
- Transportation systems, often in large countries, that are inadequate to address the needs of those in areas far from transfusion centres and/or those in geographical isolation resulting from climate conditions, including seasonal flooding. Delivering blood/components/products in a timely manner and under appropriate conditions can be and is, very challenging.
- Power failures and equipment breakdown resulting mainly, but not only, from restricted or absent equipment maintenance.
- In many, if not most, of these countries, inadequate financial resources are allocated for strengthening blood services and often funds, even when made available, reach provinces/rural areas late and/or are inconsistent with the publicly announced allocation. This leads to challenges in establishing appropriate processing policies for the BT of TDT patients including routine full antibody screening prior to early transfusion, pre-storage or bedside filtering, extended blood groups phenotypes and others including appropriate storage of blood.
- Patients are still receiving, on occasion, whole blood and/or "older" age RBC concentrate than that recommended in International Guidelines for the appropriate functioning of the transfused RBCs.
- Very importantly the knowledge of patients on the blood transfusion services provided in their country and the disease-specific policies (storage, processes, etc.) regarding the processing of blood they receive is extremely confined across the world.

Furthermore, programmes that could contribute significantly to blood supply savings, including importantly the clinical use of blood/ patient management policies, are in place in only a very few countries, indeed particularly of the developing world. This is mainly due to the lack of relevant and continued educational programmes for medical and other healthcare professionals on their value and vast contribution to the saving and sustainability of national blood supplies.

More specifically for the optimal transfusion therapy of TDT, additional challenges lie in the lack of, or very limited, knowledge and expertise of transfusion professionals. Their knowledge on what safe and effective transfusion therapy is for these patients is rather confined; in addition, a lack of adoption and/or adherence to the relevant international guidelines by many, if not most, of them is quite the case. Weak patient/parent engagement and financial challenges in covering many aspects of their access to transfusion centres and services, particularly in those countries devoid of universal health coverage, constitute major additional obstacles in the provision of effective transfusion therapy to these patients.

Most healthcare systems in the developing countries are today in the transition stage of applying universal coverage to health services, a very important component of allowing appropriate and timely access of patients to quality BT and other medical care. However, the COVID-19 pandemic with its huge public health, social and economic repercussions, has indeed greatly delayed this very important change across these countries.

Regional Snapshot

Looking at the situation with regards to BT services in each region separately (except AFR where TIF has an extremely confined number of members) and based on available data, the vast heterogeneity in the quality of these services becomes even more evident. Many and multiple challenges are faced by TDT patients in accessing effective and safe transfusion therapy within and across countries of the different regions of the world. Below is a snapshot of TIF's membership across the six WHO Regions (Figure 22, Table 17).

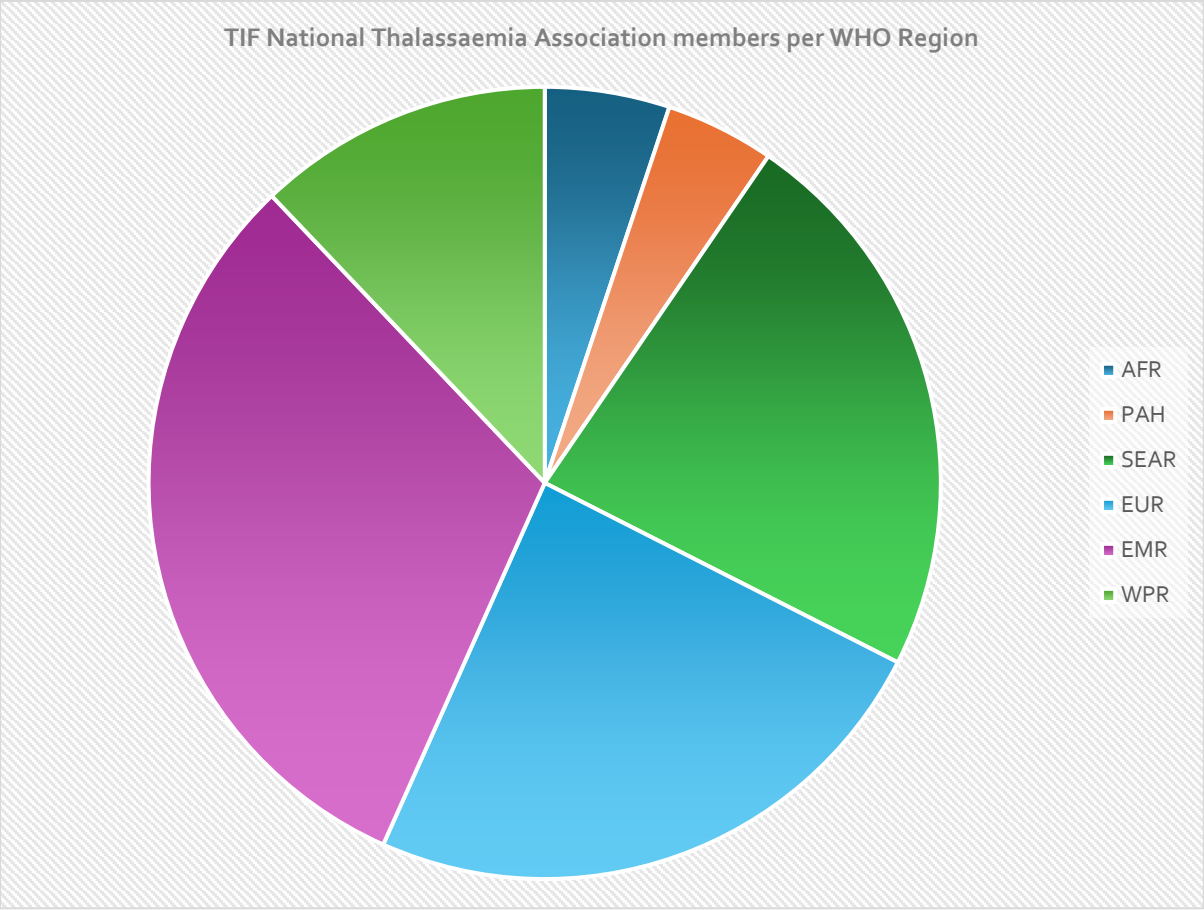

Figure 22. TIF's members: 157 National Thalassaemia Associations in 64 countries

Table 17. Breakdown of TIF's members per region (according to WHO division of regions)

Eastern Mediterranean Region (EMR)			
Country	No. of TIF Members	Country	No. of TIF Members
Afghanistan	3	Morocco	2
Bahrain	1	Pakistan	21
Egypt	2	Saudi Arabia	3
Iran (Islamic Rep. of)	3	Sudan	1
Iraq	5	Tunisia	1
Jordan	1	United Arab Emirates	2
Kuwait	1	West Bank & Gaza Strip	1
Lebanon	1	Yemen	1
Total: 49 members in 16 countries			

South-East Asia Region (SEAR)			
Country	No. of TIF Members	Country	No. of TIF Members
Bangladesh	5	Nepal	1
India	24	Sri Lanka	2
Indonesia	1	Thailand	1
Maldives	2		
Total: 36 members in 7 countries			

Western Pacific Region (WPR)			
Country	No. of TIF Members	Country	No. of TIF Members
Australia	2	New Zealand	1
Cambodia	1	Philippines	2
China*	6	Singapore	1
Indonesia	1	Viet Nam	1
Malaysia	4		
Total: 19 members in 9 countries			

European Region (EUR)			
Country	No. of TIF Members	Country	No. of TIF Members
Albania	1	Italy	6
Azerbaijan	2	Luxembourg	1
Belgium	1	Malta	1
Bulgaria	2	Netherlands	1
Cyprus	1	Portugal	1
France	2	Romania	2
Germany	3	Spain	1
Greece	3	Sweden	1
Ireland	1	Turkey	5
Israel	2	United Kingdom	3
Total: 38 members in 21 countries			

Region for the Americas (PAH)			
Country	No. of TIF Members	Country	No. of TIF Members
Argentina	2	Trinidad & Tobago	1
Brazil	1		
Canada	2	USA	1
Total: 7 members in 5 countries			

African Region (AFR)			
Country	No. of TIF Members	Country	No. of TIF Members
Algeria	2	Nigeria	1
Congo	1		
Ghana	1	South Africa	1
Mauritius	2		
Total: 8 members in 6 countries			

"CAPTURING" THE SITUATION BY REGION

Eastern Mediterranean Region (EMR)

This Region includes 22 countries with a population of 664,336,000 people.

49 National Thalassaemia Associations from 16 countries of the EMR are members of TIF, promoting and advocating for the rights of more than 70% of the EMR thalassaemic population for access to quality health, social, and other care specific for their disease.

The 34th session of WHO Regional Committee that took place in 1987 for the Eastern Mediterranean Region endorsed resolution EM/RC 34/R.9, which focused on the development of national blood transfusion services in the countries of the region. Significant challenges, however, remain to-date despite the great progress made through the years in providing access to sufficient, affordable, and sustainable supplies of blood and blood products. Ensuring the quality and safety of these products in the presence of known and emerging threats to public health has been a major challenge, and in response, a strategic framework for blood safety and availability was endorsed by the 63rd session of the Regional Committee in 2016 in Resolution EM/RC63/R.6 for the years 2016–2025.

Blood Adequacy in the Region

Today only about 6% of the global blood supply is collected in the EMR, which comprises about 10% of the world's population and which includes many countries with high prevalence of haemoglobin disorders that rely on blood transfusion therapy, lifelong and regularly (or periodically). Approximately 30% of the countries in the region, including countries with a high prevalence of haemoglobin disorders, have insufficient or unsustainable national blood supplies.

Blood donation rates range from 2.8 to 24 per 1,000 population per year, with a median of 12.1 per 1,000. A little over 30% of the countries (i.e., 5 out of 16) are collecting less than 10 whole blood donations per 1,000 population. These countries are the United Arab Emirates, Egypt, Afghanistan, Jordan, and Morocco. To underscore the heterogeneity of the situation, one of the countries in this region, Iran, which is in addition a WHO Collaborating Centre in Transfusion Medicine, reports 24 donations per 1,000 population.

The data in the tables below was taken from the *Global Status Report on Blood Safety and Availability 2021*, published by the World Health Organization:

Table 18. Blood centres & data coverage in EMR (2018)

BLOOD CENTRES & DATA COVERAGE (2018)

Country	Number of Blood Centres In the Country			Number of Blood Centres Covered By The Report			Estimated % of Blood Donations
	Stand-alone	Hospital-based	Total	Stand-alone	Hospital-based	Total	
Low Income (LIC)							
Afghanistan	1	288	289	1	101	102	
Syria	/	/	/	/	/	/	/
Lower-Middle Income (LMC)							
Egypt	28	...	...	28	0	28	33
Iran	91	0	91	91	0	91	
Lebanon	/	/	/	/	/	/	/
Morocco	6	11	17	6	11	17	
Pakistan	...	...	...	120	486	606	95
Tunisia	7	25	32	7	25	32	
Upper-Middle Income (UMC)							
Iraq	/	/	/	/	/	/	/
Jordan	4	37	41	1	0	1	...
High Income (HIC)							
Bahrain	0	3	3		1	1	90
Kuwait	1	0	1	1	0	1	
Oman	1	15	16	1	12	13	81.2
Qatar	1	0	1	1	0	1	
Saudi Arabia	/	/	/	/	/	/	/
UAE	5	7	12	4	7	11	93

... : Not reported/not available
/ : No response
Blank (in the last column) : 100%

From the data collected to-date, only the blood banks of Pakistan, Bahrain, and UAE reflect more than 80% of the total blood collected. The rest of the countries give very confined data, and Egypt reported data from 28 blood centres that reflect only 33% of the country's blood donations.

Table 19. Blood donations in EMR (2018)

BLOOD DONATIONS (2018)

Country	No. Whole Blood Donations Collected (excluding autologous donations)										
	VNRD	VNRD from 1st time donors	VNRD from repeat donor	Family/replacement donations	Paid donations	Others	Total	% of VNRD	% of family/ replacement	% of paid donations	Blood donations per 1,000
Low Income (LIC)											
Afghanistan	82 904	...	...	127 723	0	0	210 627	39.40%	60.60%	0.00%	5.7
Syria	/	/	/	/	/	/	/	/	/	/	/
Lower-Middle Income (LMC)											
Egypt	305 718	300 000	5 718	121 142			426 860	71.60%	28.40%		4.0
Iran	2 069 273	245 412	1 823 861	0	0	0	2 069 273	100%	0%	0%	24.0
Lebanon	/	/	/	/	/	/	/	/	/	/	23.2
Morocco	298 842	...	...	22 494	0	0	321 336	93%	7%	0%	9.0
Pakistan	410 599	...	...	1 903 709			2 314 308	17.70%	82.30%		10.2
Tunisia	56 795	...	...	164 009	0	0	220 804	25.70%	74.30%	0.00%	18.8
Upper-Middle Income (UMC)											
Iraq	/	/	/	/	/	/	/	/	/	/	14.6
Jordan	35 652	24 244	11 408	29 171	0	0	64 823	55%	45%	0%	6.2
High Income (HIC)											
Bahrain	19 546	...	...	0	0		19 546	100%	0%	0%	13.0
Kuwait	43 467	14 278	29 189	34 564	0	0	78 031	55.70%	44.30%	0.00%	18.0
Oman	51 615	25 625	25 990	5 792	0		57 407	89.90%	10.10%	0.00%	12.5
Qatar	30 209	12 952	17 257	26	0	0	30 235	99.90%	0.10%	0.00%	11.7
Saudi Arabia	/	/	/	/	/	/	/	/	/	/	16.2
UAE	120 320	73 070	47 250	2 565	4 361	0	127 246	94.60%	2%	3%	2.8

... : Not reported/not available
Blank : Not required/not applicable
/ : No response
VNRD : Voluntary non-remunerated donations

Table 20. Clinical use of blood & blood components in EMR

CLINICAL USE OF BLOOD & BLOOD COMPONENTS

Country	Date Year	No. Hospitals Performing Blood Transfusion	No. Units of Blood Components Issued/Transfused (excluding autologous blood units)							
			Whole blood	Red cells	Whole blood derived platelets	Apheresis platelets	Fresh frozen plasma	Plasma	Cryo-precipitate	
Low Income (LIC)										
Afghanistan	2018	...	179 878	14 340	12 959	0	3 381	0	69	
Syria	2015	/	/	/	/	/	/	/	/	/
Lower-Middle Income (LMC)										
Egypt	2018	...	1 276	411 288	91 907	20 816	311 797	17 129	76 620	Units issued
Iran	2018	929	3 779	1 962 214	906 420	20 958	661 378	11 756	128 337	Units issued
Lebanon	2018	/	/	/	/	/	/	/	/	/
Morocco	2018	633	...	...	...	...	...	...	...	
Pakistan	2018	606	921 204	735 678	304 448	...	...	450 316	49 703	Units issued
Tunisia	2018	...	...	...	...	...	...	...	...	
Upper-Middle Income (UMC)										
Iraq	2018	/	/	/	/	/	/	/	/	/
Jordan	2018	113	61 997	61 997	...	...	...	...	...	Units issued
High Income (HIC)										
Bahrain	2018	17	...	...	...	...	...	...	...	
Kuwait	2018	43	0	91 455	0	...	...	...	101 320	Units issued
Oman	2018	18	...	...	...	...	...	...	...	
Qatar	2018	28	27	25 373	20 012	843	6 120	3 072	3 300	Units transfused
Saudi Arabia	2018	/	/	/	/	/	/	/	/	/
UAE	2018	...	0	108 709	19 625	9 585	32 238	1 000	6 701	Units issued

... : Not reported/not available
Blank : Not required/not applicable
/ : No response
* 1 unit of blood component is defined as the preparation from whole blood donations of 450 ml
** 1 unit of apheresis platelets usually contains 200 - 450 x 10 000 000 000 platelets

Table 21. Policy, governance, quality assurance and monitoring in EMR (2017–2018)

POLICY, GOVERNANCE, QUALITY ASSURANCE AND MONITORING (2017/18)

Country	Unit within MoH with responsibility for governing blood provision & transfusion activities	National Blood Policy	Multiyear national strategic plan for blood safety or equivalent	Specific Legislation Covering the Safety & Quality Of Blood And Blood Products for Transfusion	National Blood Committee (or equivalent)	Specific Government Budgetary Line Item For The NBTS/BTS	System of Cost Recovery for NBTS/BTS	National standards for the collection, testing processing, storage & distributuion of blood and blood components	National Guidelines On The Appropriate Clinical Use Of Blood
Low Income (LIC)									
Afghanistan	Yes	Yes	No	...	Yes	No	No	Yes	No
Syria	/	/	/	/	/	/	/	/	/
Lower-Middle Income (LMC)									
Egypt	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Iran	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Lebanon*	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No
Morocco	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pakistan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tunisia	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	...
Upper-Middle Income (UMC)									
Iraq*	Yes	No	No	No	Yes	No	No	...	No
Jordan	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
High Income (HIC)									
Bahrain	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kuwait	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Oman	Yes	Yes	...	...	Yes	Yes	No	Yes	Yes
Qatar	No	No	No	No	No	Yes	No	Yes	Yes
Saudi Arabia*	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
UAE	Yes	Yes	No	Yes	No	Yes	...	Yes	...

... : Not reported/not available
/ : No response
Blank : Not required/not applicable
* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

TIF's Perspective in the Region

Information compiled by TIF in 2018 (Jan-Dec) from 350 patients of 20 member associations, and in 2024 (Jan-Dec) from 210 patients of 16 member associations, and in the context of a questionnaire/survey distributed to 18 countries, members of TIF in the EMR, identified some key needs of patients in accessing optimal transfusion therapy. Despite the fact that this is a region with significant focus, for some decades now, on prioritising haemoglobin disorders, with both thalassaemia and SCD on their national health agendas, the information below warrants attention and calls for urgent improvements in the area of BT services. Patients are reporting that:

From 48.2% in 2018, in 2024 38.6% are receiving inadequate in amount and/or interrupted or belated transfusion therapy.

- From 52.8% in 2018, in 2024 58.2% have pre-transfusion haemoglobin levels throughout the year of ≤ 90 g/l (80-90 g/l, average 88 g/l), 32.6% of whom are <80 g/l (75-80 g/l, average 78 g/l).
- From 38.6% in 2018, in 2024 26.4% are receiving red cell concentrates on average 4 times a year that were not always pre-stored or bedside filtered.
- From 86.4% in 2018, in 2024, 72.6% were not aware of the way the blood provided to them was processed, stored, or transported.
- From 62.8% in 2018, in 2024, 75.6% received blood more than 14 days old.
- From 62.4% in 2018, in 2024, 70.9% were involved in family/friends' campaigns to donate blood.
- From 18.6% in 2018, in 2024, 12.8% had received at least one whole blood transfusion in the previous year, 6.4% of whom reported receiving whole blood transfusions.
- Foreign patients, mainly migrant workers or refugees or displaced individuals in this Region (of whom there are very large numbers [4]), anticipate many challenges in the timely access of appropriate BT therapy. For example, Jordan with a population of 6.6 million hosts 3 million refugees from Iran, the West Bank, Gaza Strip, and the Syrian Arab Republic, while Lebanon, with a population of 4.5 million, hosts 1.5–2 million refugees from the Syrian Arab Republic.

Southeast Asia Region (SEAR)

SEAR includes 11 countries (Bangladesh, Bhutan, Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste) with a population of 1,947,632,000 people.

27 National Thalassaemia Associations from 7 countries of the Region are members of TIF (Bangladesh, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand).

Together with the Western Pacific Region (WPR), they represent the countries where more than 80% of patients with haemoglobin disorders - thalassaemia syndromes (α and β) and SCD (outside Africa), and combined forms of these, are born and live. This is the part of the world where >90% of α- and β-thalassaemia and HbE (and combined forms of these) patients exist with variable clinical severity and dependence on transfusion therapy. These forms were previously referred to as intermediate forms or thalassaemia intermedia with regard to their milder clinical outcome, and in more recent years they have been grouped under the designation of non-transfusion dependent thalassaemias (NTDT). Some of these, nevertheless, need occasional BT or may at some point convert to totally transfusion-dependent forms.

The availability of blood across the countries of this region varies considerably and even within a country. Red cell units range from 33.15 (in Thailand) to 2.56 (Timor-Leste) per 1,000 population.

Four (4) countries, Thailand, Maldives, Sri Lanka, and Indonesia, have more than 10 red cells units available per 1,000 population annually, and these are countries with high prevalence of thalassaemia syndromes. In other

countries, also with high prevalence of TDT patients, including India, Bangladesh, and Myanmar, significant challenges in blood supplies are anticipated, albeit published data are lacking. In addition, many countries of this region face other types of challenges: Maldives and Nepal, for example, face geographical constraints, whereas India, Thailand, and Indonesia are challenged with large and diverse populations and/or large distances, coupled, in some instances, with frequent climatic disasters. Altogether, these play an important role in making blood difficult to access for these patients at time intervals recommended for their needs, even when, and if, blood is available and appropriately processed. The under-5 mortality rates, to which haemoglobin disorders contribute significantly in these parts of the world, and which reflect to a great extent the quality of healthcare provided in a country, is less than 10% in only three (3) countries (v. Sri Lanka, Thailand, and Maldives), and reaches rates of more than 20% in others (v. Bangladesh, India, Indonesia, Myanmar, and Nepal).

Haemoglobin disorders have been acknowledged as one of the non-communicable disease (NCD) priorities in most countries of both regions in the last 15–20 years. Important research work and disease-specific programmes and policies since then have been promoted in many of these countries, including strengthening the blood supply and accessing safe and effective chelation and other aspects of holistic management, including social care. To-date, however, there is still a lack of national coordination, in some more than in the others, and a lack of adequate funding in most countries in both areas for the control of these disorders, namely prevention and management (including transfusion therapy, which constitute the cornerstone of effective management).

The estimated number of annual births with β-thalassaemia in this region is roughly 20,420, with about 50% (nearly 10,000) being TDT, notwithstanding the fact that, in the absence of national registries and updated epidemiological studies, these numbers are considered inaccurate and a gross underestimation.

Looking at the prevailing situation in some countries individually and mainly those with high prevalence of thalassaemia and other haemoglobin disorders, including SCD, the challenges in effectively addressing BT therapy of these disorders are made truly evident.

The data in Tables 22–27 were taken from the *Global Status Report on Blood Safety and Availability 2021*, published by the World Health Organization:

Table 22. Blood centres & data coverage in SEAR (2018)

BLOOD CENTRES & DATA COVERAGE (2018)

Country	Number of Blood Centres In the Country			Number of Blood Centres Covered By The Report			Estimated % of Blood Donations
	Stand-alone	Hospital-based	Total	Stand-alone	Hospital-based	Total	
Lower-Middle Income (LMC)							
Bangladesh	54	288	342	3	87	90	90
India	...	...	...	...	...	...	...
Indonesia	222	198	420	212	159	371	78.2
Myanmar	1	391	392	1	155	156	95
Nepal	70	38	108	70	38	108	
Sri Lanka	2	101	103	2	101	103	
Upper-Middle Income (UMC)							
Maldives	1	21	22	1	20	21	95
Thailand	13	160	173	13	0	13	41.9

... : Not reported/not available
Blank Cell (in the last column) : 100%

Table 23. Blood donations in SEAR (2018)

BLOOD DONATIONS (2018)

Country	No. Whole Blood Donations Collected (excluding autologous donations)										
	VNRD	VNRD from 1st time donors	VNRD from repeat donor	Family/replacement donations	Paid donations	Others	Total	% of VNRD	% of family/ replacement	% of paid donations	Blood donations per 1,000
Lower-Middle Income (LMC)											
Bangladesh	171 000	...	...	590 115	0		761 115	22.50%	77.50%	0.00%	4.7
India	9 424 000	...	...	2 976 000	0		12 400 000	76%	24%	0%	9.0
Indonesia	3 480 051	989 612	2 490 439	327 097	14 567		3 821 715	91%	8.60%	0.40%	14.2
Myanmar	96 018	41 305	54 713	921	0	0	96 939	99.00%	1.00%	0.00%	1.9
Nepal	225 696	67 708	157 988	46 226	0	0	271 922	83%	17%	0%	9.7
Sri Lanka	450 640	...	...	0	0	0	450 640	100%	0%	0%	20.8
Upper-Middle Income (UMC)											
Maldives	2 335	852	1 483	4 131	0		6 466	36.10%	63.90%	0.00%	13.7
Thailand	1 112 497	152 536	959 961	0	0	0	1 112 497	100.00%	0%	0%	15.6

... : Not reported/not available
Blank Cell : Not required/not applicable
VNRD : Voluntary non-remunerated donations

Table 24. Laboratory test requirements for screening donated blood for transfusion-transmissible iInfections in SEAR (2017–2018)

LABORATORY TEST REQUIREMENTS FOR SCREENING DONATED BLOOD FOR TRANSFUSION-TRANSMISSIBLE INFECTIONS (2017/18)

Country	Chagas disease		Malaria			HTLV-1/2	
	Ab	Others	Smear microscopy	Ag	Others	Ab	Others
Lower-Middle Income (LMC)							
Bangladesh				Y			
India*			Y	Y			
Indonesia				S			
Myanmar			S				
Nepal			S				
Sri Lanka			Y				
Upper-Middle Income (UMC)							
Maldives							
Thailand							

Y : Required for all donations
S : Required for selected donations
Blank : Not required/not applicable
* Data of 2017/2018 was not available, data of earlier years were listed in the table

Table 25. Number & proportion of donations tested positive/reactive for TTI markers in SEAR (2018)

NUMBER & PROPORTION OF DONATIONS TESTED POSITIVE/REACTIVE FOR TTI MARKERS (2018)

Country	HIV 1+2		
	Positive/reactive, no.	No. donations tested	%*
Lower-Middle Income (LMC)			
Bangladesh	77	761 115	0.01
India	…	…	0.14
Indonesia	11 791	3 813 871	0.31
Myanmar	879	457 657	0.19
Nepal	113	271 922	0.04
Sri Lanka	29	450 640	0.006
Lower-Middle Income (LMC)			
Maldives	5	6 562	0.08
Thailand	821	1 122 497	0.07

… : Not reported/not available

* Proportion, expressed as positive/reactive per 100 donations tested

Table 26. Clinical use of blood & blood components in SEAR (2018)

CLINICAL USE OF BLOOD & BLOOD COMPONENTS (2018)

Country	No. Hospitals Performing Blood Tranfusion	No. Units of Blood Components Issued/Transfused (excluding autologous blood units)							
		Whole blood	Red cells	Whole blood derived platelets	Apheresis platelets	Fresh frozen plasma	Plasma	Cryo-precipitate	
Lower-Middle Income (LMC)									
Bangladesh	342	761 115	84 465	34 495	20	59 481	10	113	Units issued
India	…	…	…	…	…	…	…	…	
Indonesia	…	521 337	2 741 680	597 706	12 457	113 005	24 681	14 910	Units transfused
Myanmar	391	36 470	56 212	10 098	8	38 506	2 137	2 564	Units issued
Nepal	…	20 500	68 000	42 000	…	20 000	1 000	1 000	Units issued
Sri Lanka	103	0	412 154	134 059	17 682	156 512	…	48 622	Units issued
Upper-Middle Income (UMC)									
Maldives	91	…	6 390	0	0	…	0	0	Units issued
Thailand	1 332	0	1 049 777	428 189	13 448	215 837	562	235 027	Units issued

… : Not reported/not available

Blank : Not required/not applicable

* 1 unit of blood component is defined as the preparation from whole blood donations of 450 ml

** 1 unit of apheresis platelets usually contains 200 - 450 x 10 000 000 000 platelets

Table 27. Policy, governance, quality assurance and monitoring in SEAR (2017–2018)

POLICY, GOVERNANCE, QUALITY ASSURANCE AND MONITORING (2017/18)									
Country	Unit within MoH with responsibility for governing blood provision & transfusion activities	National Blood Policy	Multiyear national strategic plan for blood safety or equivalent	Specific Legislation Covering the Safety & Quality Of Blood And Blood Products for Transfusion	National Blood Committee (or equivalent)	Specific Government Budgetary Line Item For The NBTS/BTS	System of Cost Recovery for NBTS/BTS	National standards for the collection, testing processing, storage & distributuion of blood and blood components	National Guidelines On The Appropriate Clinical Use Of Blood
Lower-Middle Income (LMC)									
Bangladesh	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
India*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Indonesia	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Myanmar	No	No	No	Yes	Yes	Yes	No	Yes	Yes
Nepal	Yes	Yes	...	...	Yes	...	Yes	Yes	Yes
Sri Lanka	Yes	Yes	Yes	...	Yes	Yes	No	Yes	Yes
Upper-Middle Income (UMC)									
Maldives	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
Thailand	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

... : Not reported/not available

* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

In **BANGLADESH** (lower-middle-income country), with an estimated prevalence of thalassaemia patients of 60,000 – 70,000, the annual blood donations (2017) were estimated to be 756,061 (i.e., 4.82 red cell units per 1,000 population). There is no centralised blood collection system. Blood banks belong to a combination of government and private services (80%), the Red Cross Society (11%), voluntary institutions (5%), and private organisations (4%). Blood collection is based on about 70% replacement and on less than 30% voluntary practices. The Safe Blood Transfusion Program (SBTP), a unit of the Ministry of Health supports 203 centres by providing equipment, regular supply of kits, reagents, blood bags, and training. 66.8% (169) of blood transfusion centres belonging to the public sector are integrated within the hospitals and located in seven divisions in the country. A situation assessment was carried out in 2011 by experts in blood transfusion and programme management personnel of the Directorate General of Health Service under the Ministry of Health in collaboration with the World Health Organization (WHO) and the OPEC Fund for International Development (OFID). Findings of this assessment include a significant shortage of trained staff in each centre and inadequate premises, supplies, and equipment [5]. To what extent the situation has improved since that report is uncertain. However, HCV, HBV, and HIV were 13.51%, 3.37%, and 0%, respectively. Moreover, 2% of the patients were found to be co-infected with both HBV and HCV [6].

Blood legislation was put forward in April 2002, and National Guidelines for Thalassaemia have existed since 2019, albeit no data exist with regards to nationwide disease specific survival, morbidity, and mortality rates, and consequently no information is available on the age distribution of patients. Despite immense efforts being made through the years, mainly on behalf of healthcare professionals and patient organisations, clinical management and social care remain largely suboptimal. In addition, a nationally coordinated prevention programme is still not in place, leading to large numbers of annual affected births that add significantly to the burden of transfusion, medical, and other care of the country.

INDIA (lower-middle-income country) is a subcontinent with a population 1,380,004,385 people (17.7% of the total global population). It has an estimated prevalence of patients with TDT of 150,000 with a predicted annual number of affected births of 12,500. It is evident that the challenges to addressing timely and effective BT therapy and the medical and other care of patients with these disorders across this huge, multi-ethnic, densely populated country are many and multiple. The deficiencies are magnified each year, acknowledging the fact that to-date and despite the huge work undertaken by the government, healthcare professionals, and patient organisations in the last three decades, there is no nationally coordinated effective prevention programme in place. Annual blood donations (2017–2018) are 11,100,000, i.e., 7.69 red cell units/1,000.

An estimated 2 million units/year of packed red cells are needed to address the needs of TDT in the country, based on current estimates.

The Ministry of Health and Family Welfare and Blood Cell National Health Mission in 2016 developed Guidelines for the Management and Prevention of Thalassaemia, and significant steps towards improvement have indeed been achieved including in the area of blood transfusion therapy.

From 2,626 functional blood banks across the country, identified in 2016 by the Ministry of Health and Family Welfare, 76% were public and not-for-profit owned and 24% were owned by the private sector. However, 61% of these were situated in eight states, out of which only two (Maharashtra and Gujarat) have a high thalassaemia prevalence.

The blood banks / million population in high thalassaemia prevalence states, including Uttar Pradesh (1.2), West Bengal (1.3), Rajasthan (1.5), Chhattisgarh (2), is less than the national average of 2.2 blood banks / 1,000,000 population. It was estimated in 2017 that the annual collection was 11.1 million units of blood while the demand was 14.6 million units. Moreover, only 12.6% and 11.2% of blood banks have actually enrolled in External Quality Control Systems (EQAS) for immunohematology and TTIs, respectively. The mean assessment score was very low = < 35 (contrary to 62 for most) in Uttar Pradesh (which has 13 blood banks, constituting 5% of all blood banks), followed by Odisha (with 3 blood banks, constituting 4% of all blood banks). Of the annual blood collection from all blood banks in 2015, which was 11,645.79, around 70% (71.9%) units were collected by VNRBD practices.

In the context of voluntary donation practices, the percentage of repeat donors ranges between 0–30% only (as opposed >90% in the EU), a component that undoubtably needs strengthening.

Although the average annual collection of blood units per 100 individuals was reported to be <1% (meeting WHO's requirements), the great challenge, as reported by TIF member National Thalassaemia Associations and treating physicians, lies in the huge disparity in collection and distribution between states, which is an element present in many countries lacking comprehensive and centralised national coordination of blood supplies.

However, in 2014 the National Blood Cell under the National Health Mission (NHM) launched by the government of India, set up a mission to ensure accessibility, adequacy, safety, and quality of blood across the country. The mission was for planning, networking and developing new policies, including (1) establishing 1,599 blood storage units; (2) setting up new blood banks (74 in 89 districts that did not have one); (3) strengthening blood collection and voluntary donation practices; and (4) promoting regular quality assessment tools including the investment in a comprehensive network of Blood Banks and Blood Storage Units, which will facilitate real time blood stock availability. There is no comprehensive published update on the progress of this.

With regards to TDT patients, the National Blood Transfusion Council (NBTC) issued laws for the provision of free blood to all thalassaemia patients since 2014, and furthermore it published national guidelines on the management and prevention of haemoglobin disorders in 2016. Moreover, thalassaemia has been included in the context of its disability legislation – an important contribution to addressing the traveling expenses to transfusion units amongst other benefits. However, many challenges are still seen to-date with regards to the access of TDT patients to free and optimal transfusion therapies and adequate quality blood. Certainly, more accurate and reliable data are needed at a nationwide level to assess more accurately the level of the effectiveness of BT therapy for TD patients across the country both in terms of availability and quality of blood.

Data available today derive from small or large groups of patients in centres/hospitals/clinics, in one or more States, and are consequent to the work and interest of some medical/scientific specialists. As such, the data do not reflect to any extent the nationwide picture. Even so, TIF's data demonstrate huge inequalities across the country, with patients reporting as having timely access to optimal transfusion therapy mainly in larger or capital cities, while rural areas and certain states which have a high prevalence of these disorders are more likely to receive irregular, not appropriately processed, and even whole blood transfusions. Despite truly impressive efforts and newly developed legislation and recommendations by governments and non-governmental organisations (NGOs) in the last 15–20 years, which have been strengthened even more in more recent years,

patients are still struggling to an extent that is not well defined to obtain free transport to treatment centres and free treatment, including every aspect of BT services. There are areas of very high prevalence of haemoglobin disorders for which there is an almost total absence of any reliable data, and this is the first and biggest problem most of the countries are facing: lack of national data due to the absence of disease-specific national registries.

In a recent article, Dr JS Arora (general secretary at National Thalassemia Welfare Society & Federation of Indian Thalassemics), a well-known physician in the field of thalassaemia, pointed out that there have been two recent cases in 2022. The first one was in Nagpur where four children, suffering from thalassemia, became positive for human immunodeficiency virus (HIV) infection, allegedly after a blood transfusion. The other report was from Hyderabad, where a three-year-old thalassaemic patient allegedly contracted HIV after receiving blood. He concludes that such instances call for the immediate attention of government and advocacy groups to work together and ensure better blood screening and testing standards so that every patient gets safe blood and lives a healthy life, advocating for appropriate technologies like NAT testing [7]. The Union Ministry of Health and Family Welfare has recently released the updated edition of the National Standards for Blood Centres and Blood Transfusion Services, incorporating the developments in blood collection, storage, and transfusion technologies. The main issue that plagues blood banking system in the country is fragmented management. The standards vary from state to state, city to city, and even centre to centre in the same city. There is also a shortage of trained healthcare professionals in the field of transfusion medicine.

INDONESIA (upper-middle-Income country) has a population of 273,523,615 people, contributing to 3.51% of the global population. It has an estimated prevalence of thalassaemia of 10,531/100,000 population and annual blood donations (2017) reaching 2,886,233 (i.e., 11.18 red cell units/1,000 population).

Thalassaemia syndromes constitute one of the NCD priorities in the healthcare system of Indonesia and truly exemplary work has been done through the years by the government, healthcare professionals, and the patient community, mainly in the area of BT and clinical care and less on a national prevention programme.

Free healthcare for TDT patients has been included in the burden package of the government health insurance programme for the poor (JAMKESMAS) since 2010 and in the National Health Insurance programme since 2014. National guidelines for the management of TDT have been available since 2012, and adherence to them across the country, despite geographical challenges, has gradually been improving.

The Indonesian Red Cross or government hospitals are responsible for blood centres, and 80% of blood donations are based on VNRBD practices, while the rest rely on replacement and, occasionally, paid donation practices. The major challenges faced by TDT patients include: (i) adequacy of blood supplies, (ii) unequal distribution of blood supplies, and (iii) timely access of patients to BT services, particularly in rural areas.

Although 4.5 million blood units are targeted annually as per estimated needs, only about 50% are actually collected. The collection of the rest has to rely mainly on families and friends, and on occasion on paid donations; the latter usually occurring in the 34 remote areas. For example, under normal circumstances Jakarta has an excess of units. In 2014, it had 60% excess supplies whereas at the same time West Papua had a 96.3% blood shortage. Such a heterogeneous situation culminates, as expected, in great inequalities in terms of access of patients to their appropriate and timely care.

MALDIVES (upper-middle-income country) has a population of 540,544 people (0.01% of the global population). It has an estimated prevalence of patients (2017) of 861/100,000 population (mainly TDT) and annual blood donations (2017) reaching 12,652 (i.e., 2,759 red cell units available per 100,000 population, or 27.59 per 1,000 population.

Maldives is a country with a long history in recognising the need to effectively address the control of thalassaemia, as it is an island with one of the highest carrier rates globally (>17%). There has been strong

government support and patient/parent engagement in promoting disease-specific policies since the early 1990s.

The National Thalassaemia Centre and the National Blood Transfusion Services merged in 2012 to form the Maldives Blood Services. All thalassaemia patients receive free BT services, medical and other care. However, 70–80% of blood supplies come from family replacement donors while only 10–30% of the donors are volunteers; no paid donations are reported to occur. There are only a few other blood banks on the other islands outside Male, but with very poor networking between them.

The major challenges include the blood donation practices that need to undergo transition to regular, voluntary ones and the weak blood bank system that needs national coordination, particularly in terms of strengthening networking amongst the blood banks across the many small islands and the main one in Male. There is sufficient medical expertise in the Maldives and a great focus is given on continuously improving the quality of medical care, including BT therapy, for all patients across the country, albeit no national data exist on survival rates and/or age distribution of its patients.

MYANMAR (lower-middle-income country) has a population of 54,409,800 and contributes 0.70% of the global population. Annual blood donations reached 170,743 in 2017 with red blood cell units available per 100,000 reaching 323, i.e., 3.23/1,000 population. A high under-5 mortality rate was reported in 2018, reaching 47.2 per 1,000 live births. It is a country with a very rough estimation of ~4,000 patients with thalassaemia. HbE/β-thalassaemia accounts for 46–58% of the haemoglobin disorders, β-thalassaemia for 5.4 to 22% and α-thalassaemia for 6–37%. It has a "national blood and blood products law" since 2003 and a nationally coordinated blood transfusion service.

There are 359 hospital blood banks with an annual demand of 200,000 units of blood, which exceeds its collected blood supplies. Voluntary donation practices are reported to have increased to 85%, but blood shortages for thalassaemia patients still constitute an important challenge. **A report in 2019 on World Blood Donation Day mentions that the National Blood Bank was short of about 600 blood transfusions that were needed for patients every day.**

There are no published data on survival and age distribution of patients with haemoglobin disorders in this country, as is the situation in many other countries across all six regions of the world. These disorders do not constitute a priority on its national health agenda to-date; neither has any disease-specific policy nor programme been developed. It is likely that high rates of morbidity and mortality occur in this country amongst patients with haemoglobin disorders, and the challenges, including accessing adequate supplies of appropriately processed blood/red cells, are truly immense.

NEPAL (lower-middle-income country) has a population of 29,136,808 people (0.37% of the global population). Nepal has an estimated 250–300 patients (currently known to be under treatment) with thalassaemia and has annual donations (2017–2018) of nearly 240,000 units, that is, 7.90 red cell units per 1,000 population. It has a high under-5 mortality rate of 32.2 per 1,000 live births (2018), to which thalassaemia potentially contributes significantly. The national blood policy, approved in 1991, was revised in 2006 and 2012, and Nepal's 2017 "National Guideline for Sickle Cell Disease and Thalassemia Management" by the Ministry of Health. More than 80% of blood is collected through VNRBDs, albeit replacement donations are still in practice to a certain extent and according to needs. **Of a total of 113 blood transfusion establishments, only 13 blood banks have component services and many of the 50 of the 77 districts that have blood transfusion centres lack quality standards.** Thus, patients have to travel long distances to access safe blood transfusions, mainly to Kathmandu.

Consequently, in this country timely access to adequate and quality BT services constitutes a major challenge with >75% of the patients (76.8%) in TIF's data (2018 survey) reporting as **struggling to keep their pre-transfusion haemoglobin level >70 g/l, and nearly 15% of the patients who responded (14.8%) reported receiving, at least once a year, whole blood instead of red cells** (TIF's 2018 data). No data however exist in

published reports on survival rates or age distribution to assess the extent of the weaknesses of the country to respond effectively to control and manage this disease, including the huge gaps that exist in the effectiveness of BT services for these patients (the number of whom, in the absence of prevention, is exponentially increasing).

SRI LANKA (lower-middle-ncome country) has a population of 21,413,249 people (0.27% of the global population). It is a country with an estimated 2,000 TD patients (and more irregularly transfused) and with annual blood donations (2018) of nearly 500,000 units, reflecting 19.24 red cell units per 1,000 population. It has a very low under-5 mortality rate (2018). Replacement donation practices constituted the main source of blood, although this is rapidly changing. Nevertheless, no published report gives a reliable update of the progress. Since 1995, four regional centres across the country have started providing free-of-charge blood (based on VNRBD practices) and chelation therapy to TDT patients. However, these do not cover the needs of all patients across the country, and a national programme is needed to effectively include the appropriate care for all patients across the country.

Sri Lanka has one of the best nationally coordinated Blood Transfusion Services in South Asia, established back in 1999 and designated by the WHO as a Collaborating Centre in 2018. There is no stand-alone blood bank in the NGO or private sector. 60–70% of donations are separated into components and the goal is to achieve VNRBD practices for 100% of the donations.

Despite these advances, it was reported by treating experts that over 60% of TDT and a percent of previously NTDT patients but now transfusion dependant do not maintain levels of pre-transfusion haemoglobin of more than 90 g/l (which is the international recommendation) despite being transfused regularly and with apparently adequate amounts. Further research is warranted to identify the causes.

Sri Lankan government, healthcare professionals, and researchers have done considerable work in improving their medical and public health services for addressing this disorder through the years, albeit the patient population in the country, from the very limited published information, is still very young, suggesting that high rates of mortality due to inadequate medical care is occurring.

THAILAND (upper-middle-income country) has a population of 69,799,978 people (0.90% of the global population). It is estimated that nearly 100,000 patients with thalassaemia major live in Thailand, together with a very large number of NTDT patients. Collectively they reach over 400,000 in total, as reported by national treating experts, a proportion of whom at some point in time will become transfusion dependent. The country reports annual blood donations of 2,341,571 (2017), reflecting 33.15 red cell units per 1,000, and has very low under-5 mortality rate (2018), thus reflecting a good quality healthcare and public health infrastructure. The prevalence of α-thalassaemia is between 5.5%–30%, β-thalassaemia between 1–9%, and HbE between 5–50%. At present, there are 12 Regional Blood Centres with branches in 157 provincial hospitals and with blood obtained from almost 100% VNRBD practices. Overall, 2% of the eligible adult population donates blood. However, the challenge, here again, is with regards to remote provinces where they face great difficulties in ensuring adequate and timely blood supplies to the TDT patients. In the capital of Bangkok, for example, there is an excess (that may reach 40%), which is transported throughout the country to address the blood insufficiencies in the remote parts. Efforts are in progress to develop low-cost blood collection units and distribution centres in areas that are either lacking or are too far to be reached in a timely manner to address the needs of TDT patients and other transfusion-dependent diseases.

Lack of *national registries*, a lack of reference/expert centres, and updated epidemiological studies constitute common deficiencies that have not allowed the collection of reliable nationwide data on the quality and/or range of the services the transfusion and treating centres are providing to TD thalassaemia patients.

Furthermore, despite reported existence of transfusion guidelines in most of the countries of the Region, the level of adherence to these is to-date unknown.

Patients still face many challenges in most countries either with regards to timely and uninterrupted access to adequate and effective transfusion or to the appropriateness for these patients of processed, stored blood/red cells (also expressed in the Global Survey, the results of which were described earlier).

VNRBD practices need to be significantly strengthened in many countries, and the number of regular donors need to be increased in almost all of them, acknowledging the huge contribution that such practices have to the safety of blood supplies.

Strong national coordination of transfusion services needs to be established where it does not exist, and it needs to be strengthened where it does. Very importantly, blood transfusion services, as well as all other medical/public health services need to be brought under truly patient centred, universally covered healthcare systems to alleviate patients and families across the region of having to identify family/friend donors and of the financial burden (small or large) that many of them face in accessing some treatment, including transfusion-related services.

It is recognised that there are vast differences in geographic and population sizes and that there is a heterogeneous distribution of patients across the region and within countries, varying strengths and weaknesses in the medical and public health infrastructures, different risk levels for communicable diseases that countries still need to continue to address. Certainly, different strengths and weaknesses in economies exist across countries, and there is a vast heterogeneity in blood donation and collection practices in blood component separation and in processing and distribution, just to mention a few of the important elements needed to be addressed more effectively across this region. It may, thus, be very challenging to establish uniform protocols for addressing the medical needs of these patients, including transfusion needs, across the region. However, there is first a need to improve the basics, including the establishment of nationwide coordination of blood services with uniform standards and quality practices across all blood banks, public and private, equity in blood distribution, and to improve donor education (particularly with regards to regular donation) with a main focus on VNRBD practices.

In addition, the provision of all services, including BT therapy for TDT patients, should be made free of charge by law until universal coverage-based healthcare systems emerge in every country across the world. At the same time, however, the development of disease-specific prevention programmes is of paramount importance in ameliorating the public health burden, including blood transfusion, but also the social and economic burdens at the country level and by extension at the regional and international levels.

Upgrading existing, and conducting new, epidemiological work, including micro-mapping, and developing disease-specific national registries, particularly in large countries, will contribute significantly to the better, more targeted planning and promotion of appropriate disease specific policies, including a more accurate assessment of the needs for blood.

Considerably more data is needed to assess at any level the real status quo, including BT services for haemoglobin disorders in this region, as is sadly the case with other regions of the world as well.

Western Pacific Region (WPR)

The WPR includes 28 countries (Australia, Brunei, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Laos, Malaysia, Marshall Islands, Micronesia, Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Samoa, Singapore, Solomon Islands, South Korea, Taiwan, Tonga, Tuvalu, Vanuatu, and Vietnam) with a population of 1,889,901,000 people.

19 National Thalassaemia Associations from 11 countries of the region (Australia, Cambodia, China, Hong Kong, Indonesia, Malaysia, New Zealand, Philippines, Singapore, Taiwan and Vietnam) are members of TIF.

Together with the Southeast Asia Region (SEAR), they represent the countries where more than 80% of patients with haemoglobin disorders – thalassaemia syndromes (α and β) and SCD (outside Africa), and combined forms of these – are born and live. This is the part of the world where >90% of α- and β-thalassaemia and HbE (and combined forms of these) exist with variable clinical severity and dependence on transfusion therapy. These forms were previously referred to as intermediate forms or thalassaemia intermedia with regard to their milder clinical outcome, and in more recent years they have been grouped under the designation of non-transfusion dependent thalassaemias (NTDT). Some of these, nevertheless, need occasional BT or may at some point convert to totally transfusion-dependent forms.

In conclusion, in this region and despite the considerable efforts made by governments, healthcare professionals and patient organisations across the countries in the last 2–3 decades, there are still great and multiple challenges to effectively address the medical needs of patients with haemoglobin disorders, including BT therapy. Some of the needs are common to the countries across the region and some are specific to each country.

The data in the Tables 28–33 were taken from the *Global Status Report on Blood Safety and Availability 2021* published by the World Health Organization:

Table 28. Blood centres & data coverage in WPR (2018)

BLOOD CENTRES & DATA COVERAGE (2018)

Country	Number of Blood Centres In the Country			Number of Blood Centres Covered By The Report			Estimated % of Blood Donations
	Stand-alone	Hospital-based	Total	Stand-alone	Hospital-based	Total	
Lower-Middle Income (LMC)							
Cambodia	/	/	/	/	/	/	/
Laos	18	0	18	18	0	18	
Papua New Guinea	/	/	/	/	/	/	/
Philippines	/	/	/	/	/	/	/
Vietnam	/	/	/	/	/	/	/
Upper-Middle Income (UMC)							
China	452	0	452	452	0	452	
Malaysia	/	/	/	/	/	/	/
High Income (HIC)							
Australia	/	/	/	/	/	/	/
Brunei	0	5	5	0	4	4	90
Singapore	1	0	1	1	0	1	

/ : No response

Blank (in the last column) : 100%

Table 29. Blood donations in WPR (2018)

BLOOD DONATIONS (2018)

Country	No. Whole Blood Donations Collected (excluding autologous donations)										
	VNRD	VNRD from 1st time donors	VNRD from repeat donor	Family/replacement donations	Paid donations	Others	Total	% of VNRD	% of family/ replacement	% of paid donations	Blood donations per 1,000
Lower-Middle Income (LMC)											
Cambodia	/	/	/	/	/	/	/	/	/	/	3.5
Laos	45 982	19 242	17 471	2 998	0		49 070	93.70%	6.10%	0.00%	6.9
Papua New Guinea	/	/	/	/	/	/	/	/	/	/	/
Philippines	/	/	/	/	/	/	/	/	/	/	8.2
Vietnam	/	/	/	/	/	/	/	/	/	/	10.8
Upper-Middle Income (UMC)											
China	13 661 423	...	...	39 196	0		13 700 619	99.70%	0.30%	0.00%	/
Malaysia	/	/	/	/	/	/	/	/	/	/	22.6
High Income (HIC)											
Australia	690 759						690 759	100%			27.7
Brunei	15 537	2 825	9 864	0	0		15 537	100%	0%	0%	/
Singapore	115 826	24 349	91 477	0	0	0	115 826	100%	0%	0%	21.0

... : Not reported/not available
Blank : Not required/not applicable
/ : No response
VNRD : Voluntary non-remunerated donations

Table 30. Laboratory test requirements for screening donated blood for transfusion-transmissible infection in WPR (2017/18)

LABORATORY TEST REQUIREMENTS FOR SCREENING DONATED BLOOD FOR TRANSFUSION-TRANSMISSIBLE INFECTIONS (2017/18)

Country	Chagas disease		Malaria			HTLV-1/2	
	Ab	Others	Smear microscopy	Ag	Others	Ab	Others
Lower-Middle Income (LMC)							
Cambodia							
Laos							
Papua New Guinea							
Philippines*			Y				
Vietnam*			S				
Upper-Middle Income (UMC)							
China						S	
Malaysia			S				
High Income (HIC)							
Australia*					S	Y	
Brunei							
Singapore					S		

Y : Required for all donations
S : Required for selected donations
Blank : Not required/not applicable
* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

Table 31. Number & proportion of donations tested positive/reactive for TTI markers IN WPR (2018)

NUMBER & PROPORTION OF DONATIONS TESTED POSITIVE/REACTIVE FOR TTI MARKERS (2018)

Country	HIV 1+2		
	Positive/reactive, no.	No. donations tested	%*
Lower-Middle Income (LMC)			
Cambodia	/	/	/
Laos	129	49 070	0.26
Papua New Guinea	/	/	/
Philippines	/	/	/
Vietnam	/	/	/
Upper-Middle Income (UMC)			
China	...	...	...
Malaysia	/	/	/
High Income (HIC)			
Australia	7	1 329 849	<0.001
Brunei	7	15 988	0.04
Singapore	6	124 229	0.004

... : Not reported/not available

/ : No response

* Proportion, expressed as positive/reactive per 100 donations tested

Table 32. Clinical use of blood & blood components in WPR (2018)

CLINICAL USE OF BLOOD & BLOOD COMPONENTS (2018)

Country	No. Hospitals Performing Blood Tranfusion	No. Units of Blood Components Issued/Transfused (excluding autologous blood units)							
		Whole blood	Red cells	Whole blood derived platelets	Apheresis platelets	Fresh frozen plasma	Plasma	Cryo-precipitate	
Lower-Middle Income (LMC)									
Cambodia	/	/	/	/	/	/	/	/	/
Laos	57	17 731	31 522	751	0	2 174	0	559	Units issued
Papua New Guinea	/	/	/	/	/	/	/	/	/
Philippines	/	/	/	/	/	/	/	/	/
Vietnam	/	/	/	/	/	/	/	/	/
Upper-Middle Income (UMC)									
China	...	41 745	22 607 300	523 970	1 778 523	...	...	...	Units issued
Malaysia	/	/	/	/	/	/	/	/	/
High Income (HIC)									
Australia	/	/	/	/	/	/	/	/	/
Brunei	4	0	15 995	2 080	563	2 555	0	86	Units transfused
Singapore	21	0	111 070	58 240	9 614	23 908	42	18 986	Units transfused

... : Not reported/not available

Blank : Not required/not applicable

/ : No response

Table 33. Policy, governance, quality assurance and monitoring in WPR (2017–2018)

POLICY, GOVERNANCE, QUALITY ASSURANCE AND MONITORING (2017/18)

Country	Unit within MoH with responsibility for governing blood provision & transfusion activities	National Blood Policy	Multiyear national strategic plan for blood safety or equivalent	Specific Legislation Covering the Safety & Quality Of Blood And Blood Products for Transfusion	National Blood Committee (or equivalent)	Specific Government Budgetary Line Item For The NBTS/BTS	System of Cost Recovery for NBTS/BTS	National standards for the collection, testing processing, storage & distributuion of blood and blood components	National Guidelines On The Appropriate Clinical Use Of Blood
Lower-Middle Income (LMC)									
Cambodia*	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Laos	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Papua New Guinea	Yes	Yes		Yes	Yes	No	No	Yes	No
Philippines*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Vietnam*	No	No	No	Yes	Yes	No	Yes	Yes	No
Upper-Middle Income (UMC)									
China	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Malaysia*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
High Income (HIC)									
Australia*	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Brunei	No	No	No	No	No	Yes	No	Yes	No
Singapore	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes

Blank : Not required/not applicable

* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

Below, three countries with significant disease prevalence are briefly described with regards to their BT services.

CHINA (upper-middle-income country) has a population of 1,439,323,776 people (18.47% of the global population). It is officially divided into 23 provinces, 5 autonomous regions, 4 direct-controlled municipalities (Beijing, Tianjin, Shanghai and Chongqing), and the special administrative regions (SAR) of Hong Kong and Macau.

All southern provinces of China have a high prevalence of haemoglobin disorders, both α- and β-thalassaemia, that are located in one of the regions of the world with the highest α-thalassaemia carrier rates. Despite great improvements made through the years in establishing prevention programmes that have been shown to be quite effective in some of these provinces, the management of patients remains to-date a huge challenge and an immense unmet need. Carrier rates for β-thalassaemia vary from 1.1% in Guizhou to 6.78% in Guangxi, and for α-thalassaemia from 5% in Hong Kong SAR to 14.95% in Guangxi and 12.96% in Guangdong and Haiwan. Despite the Blood Donation Law that came into effect in 1998, the huge progress achieved in the increase of blood supplies and in the implementation of safety policies (including NAT on all donations), patients report many challenges with regards to the receipt of timely, uninterrupted, and adequate BT therapy, which is indeed a major concern. This is despite the promotion of a more coordinated and consolidated infrastructure of BT services in current years. Three important challenges remain: (i) sustainability of VNRBD; (ii) blood service cost assessment; and (iii) recovery, systematic, and objective evaluation of blood service safety. There is no data to-date to confirm the achievement of a goal that had been set to reach 1.5% of donors/population rate by 2020, which would have been translated as a 50% increase over 5 years (2016–2020). The amount of blood donated annually, unfortunately, does not keep up with the increased demand. This is partially in consequence to the government launching 2,000 national health insurance reforms that seek to provide health insurance coverage to all citizens.

The WHO recommends a minimum of 20–25 donors per 1,000 population. However, with 11.2 million donors and a population of 1.33 billion, China has a rate of only 8.4 donors per 1,000 population, with over 60% being first time donors [8, 9]. Statistics from 2015 revealed that approximately 22 million whole blood donations with VNRBD were collected, reaching 99%. The unmet need for blood is severe not only in the remote rural areas, which is expected to some extent in very large countries with huge populations, but also in the more economically developed large cities, where the number of patients is increasing (either due to patients relocating residence or patients travelling to receive advanced treatment), while at the same time blood collection and thus blood supplies are not proportionally increased. In Beijing, for example, transfusion needs increased from 53.6 million units in 1998 to 140 million units in 2008, a transfusion rate of 57 units per 1,000

population; higher than that of Canada (32/1,000), the EU (40/1,000) and the USA (49/1,000). In Nanjing, where the prevalence of TDT is known to be very high, the transfusion collection was 20 million units in 2011, accounting for only 75% of its clinical demand for blood, and in a 2014 published study [8], family replacement donation represented 6.6% of all blood collected and as high as 9.9% during seasonal shortage.

Considerable work needs to be done in donor recruitment, management, and retention and on revisiting transfusion costs, defining VNRBD and implementing a universal programme of haemovigilance. Taiwan (China) and Hong Kong SAR have demonstrated high quality work in the transfusion and other medical treatment of patients with TDT and have acquired, for decades now, excellent levels of disease-specific knowledge and expertise. Establishment of an effective well-structured networking system with the Southern Provinces, some of which also have great medical expertise, will be extremely valuable. This will allow sharing of best practices and allow the central and provincial governments to recognise the cost effectiveness of providing optimal nationally coordinated BT and other medical care to TDT patients.

CAMBODIA (lower-middle-income country) [10], [11] has a population of 16,718,965 people (0.21% of the global population). It has an annual whole blood collection of 76,511, most of which (79%) is separated into components; only 26.5% of the blood supplies, however, come from VNRBD practices. An infectious disease rate of 5.9% has been reported amongst blood donors. Cambodia established its first blood policy in 2003 and its first National Strategic Plan for Blood in 2008, while in 2013 it developed its Blood Reference Centres. It has 21 provincial Blood Transfusion Centres across the country and four of these are Key Regional Centres. In terms of blood service delivery, the blood supply to rural areas is often very challenging due to geographical isolation and, as a result of seasonal flooding, which brings outbreaks of malaria and dengue fever. Moreover, 20% of government spending occurs at the provincial and local levels, which is consistently delayed and often differs from initial budget amounts, imposing a heavy burden on individuals to finance their own healthcare.

TIF supported healthcare professionals in Cambodia in 2006 to develop National Guidelines for the Management of Thalassaemia, but the level of adherence to them is largely questionable. This is because thalassaemia has not been included as a priority disease on the national health agenda and no disease-specific policy has been developed since then. TIF's information indicates that many challenges are faced by patients, particularly outside the capital, and morbidity and mortality rates of TDT patients are anticipated to be high.

VIET NAM [12] (lower-middle-income country) has a population of 97,338,579 people (1.25% of the global population). Thalassaemia is common in this country, with carrier rates of α-thalassaemia, β-thalassaemia and HbE, and combined forms of these, varying amongst the different ethnic groups. For more information see Chapter on Epidemiology.

The number of patients, in the absence of a national registry, is largely unknown, and it is reported that the largest treating centres are: (i) at the National Institute of Haematology and Blood Transfusion; and (ii) several outpatient clinics at the National Hospital of Paediatrics, Children No. 1 Hospital, and Blood Transfusion and Haematology Hospital Ho Chi Minh City, and Central Hue Hospital. Provincial hospitals provide BT therapy for patients, but with widely variable quality.

Viet Nam has an annual quantity of blood/million of 0.45 and blood units/100 people of 0.55, one of the lowest globally. Thus, given the range of clinical severity of patients, BT therapy for TDT patients is anticipated to be largely suboptimal, in terms of both availability and quality, reflected by the very young population of patients throughout the country, as reported to TIF in a 2015 survey (>70% of known patients registered in the big hospitals are <15 years of age).

Region of the Americas (PAHO)

The Region of the Americas (PAHO) includes 42 countries with a population of 992,155,000 people.

National Thalassaemia Associations from four countries of the region are members of TIF.

Since 1999 several resolutions on blood safety have been adopted by the PAHO: CD41.R15(1999); CD46 R5(2005); CE 142.R5(2008); CD48.R7(2008).

In 2014, the countries of the Pan American Region approved a Plan of Action for Universal Access to Safe Blood for 2014–2019 (Document CD5316), together with an associated Resolution CD53R6.

Latin America and Caribbean countries, as assessed in 2017, are in need of 10 million units, per year. The blood donor rate stands at 17.7 units/1,000 population and only 46% of their collected blood comes from VNRBD practices [13]. Four out of 42 countries of Latin America and the Caribbean collect 75% of all blood units reported in PAHO in 2011, namely Brazil, Mexico, Argentina, and Columbia. Only 10 out of the 42 countries have achieved 100% VNRBD; two of these in Latin America and eight in the Caribbean.

In the analysis below, focus is given only to Brazil, Argentina, and Trinidad & Tobago, where most of the patients with haemoglobin disorders in the PAHO live, while the USA and Canada will be addressed separately.

The data in Tables 34–39 were taken from WHO's *Global Status Report on Blood Safety and Availability 2021*.

Table 34. Blood donations in PAHO

BLOOD DONATIONS

Country	Date Year	No. Whole Blood Donations Collected (excluding autologous donations)										
		VNRD	VNRD from 1st time donors	VNRD from repeat donor	Family/replacement donations	Paid donations	Others	Total	% of VNRD	% of family/ replacement	% of paid donations	Blood donations per 1,000
Upper-Middle Income (UMC)												
Argentina	2017	495 000	297 000	198 000	609 532	0		1 104 532	44.80%	55.20%	0.00%	24.9
Brazil	2017	2 395 417	1 447 387	948 030	1 465 433	0		3 860 850	62%	38%	0%	18.9
High-Income (HIC)												
Canada	2018	/	/	/	/	/	/	/	/	/	0	21.7
Trinidad & Tobago	2017	4 737	1 180	3 557	16 746	0		21 483	22.10%	77.90%	0.00%	15.8
USA	2018	5 934 137	1 235 853	4 468 618	1 113	0	0	5 935 250	99.90%	0.10%	0.00%	18.2

Blank : Not required/not applicable
/ : No response
VNRD : Voluntary non-remunerated donations

Table 35. Blood centres & data coverage in PAHO

BLOOD CENTRES & DATA COVERAGE

Country	Date Year	Number of Blood Centres In the Country			Number of Blood Centres Covered By The Report			Estimated % of Blood Donations
		Stand-alone	Hospital-based	Total	Stand-alone	Hospital-based	Total	
Upper-Middle Income (UMC)								
Argentina	2017	38	149	187	34	129	163	95
Brazil	2017	...	...	3 071	...	...	...	
High-Income (HIC)								
Canada	2018	/	/	/	/	/	/	/
Trinidad & Tobago	2017	0	7	7	0	7	7	
USA	2018	65	0	65	5	0	5	62

... : Not reported/not available
/ : No response
Blank (in the last column) : 100%

Table 36. Laboratory test requirements for screening donated blood for transfusion-transmissible infections in PAHO (2017–2018)

LABORATORY TEST REQUIREMENTS FOR SCREENING DONATED BLOOD FOR TRANSFUSION-TRANSMISSIBLE INFECTIONS (2017/18)

Country	Chagas disease		Malaria			HTLV-1/2	
	Ab	Others	Smear microscopy	Ag	Others	Ab	Others
Upper-Middle Income (UMC)							
Argentina	Y					Y	
Brazil	Y		Y			Y	
High-Income (HIC)							
Canada	S					Y	
Trinidad & Tobago	Y					Y	
USA	S					Y	

Y : Required for all donations

S : Required for selected donations

Blank : Not required/not applicable

Table 37. Number & proportion of donations tested positive/reactive for TTI markers in PAHO

NUMBER & PROPORTION OF DONATIONS TESTED POSITIVE/REACTIVE FOR TTI MARKERS

Country	Date Year	HIV 1+2		
		Positive/reactive, no.	No. donations tested	%*
Upper-Middle Income (UMC)				
Argentina	2017	1 654	1 102 875	0.15
Brazil	2017	8 636	3 143 417	0.28
High-Income (HIC)				
Canada	2018	/	/	/
Trinidad & Tobago	2017	49	21 645	0.23
USA	2018	855	6 951 668	0.01

/ : No response

* Proportion, expressed as positive/reactive per 100 donations tested

Table 38. Clinical use of blood & blood components in PAHO

CLINICAL USE OF BLOOD & BLOOD COMPONENTS

Country	Date Year	No. Hospitals Performing Blood Tranfusion	No. Units of Blood Components Issued/Transfused (excluding autologous blood units)						
			Whole blood	Red cells	Whole blood derived platelets	Apheresis platelets	Fresh frozen plasma	Plasma	Cryo-precipitate
Upper-Middle Income (UMC)									
Argentina	2017	1 135	7 335	1 016 808	491 700	59 197	291 240	12 281	23 000
Brazil	2017	...	937	1 329 853	491 640		291 710	9 899	63 391
High-Income (HIC)									
Canada	2018	/	/	/	/	/	/	/	/
Trinidad & Tobago	2017	...	...	...	...	...	...	...	...
USA	2018	...	...	...	...	...	...	...	...

... : Not reported/not available
Blank : Not required/not applicable
/ : No response
* 1 unit of blood component is defined as the preparation from whole blood donations of 450 ml
** 1 unit of apheresis platelets usually contains 200 - 450 x 10 000 000 000 platelets

Table 39. Policy, governance, quality assurance and monitoring in PAHO (2017–2018)

POLICY, GOVERNANCE, QUALITY ASSURANCE AND MONITORING (2017/18)

Country	Unit within MoH with responsibility for governing blood provision & transfusion activities	National Blood Policy	Multiyear national strategic plan for blood safety or equivalent	Specific Legislation Covering the Safety & Quality Of Blood And Blood Products for Transfusion	National Blood Committee (or equivalent)	Specific Government Budgetary Line Item For The NBTS/BTS	System of Cost Recovery for NBTS/BTS	National standards for the collection, testing processing, storage & distributuion of blood and blood components	National Guidelines On The Appropriate Clinical Use Of Blood
Upper-Middle Income (UMC)									
Argentina	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Brazil	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
High-Income (HIC)									
Canada	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Trinidad & Tobago	Yes	Yes	No	No	No	Yes	No	Yes	Yes
USA	Yes	...	...	Yes	Yes	...	Yes	Yes	Yes

... : Not reported/not available

ARGENTINA (upper-middle-income country) has a specific law, specific budget and national policy, but no national transfusion committee. Argentina collected 1,026,846 units of blood (2015) with a blood donation rate of 20.55/1,000 population, with only 45.66% from VNRBD practices, 54.34% from replacement, and 85% of its units separated into packed RBCs. TIF's archives record around 350 patients with TDT in this country. Treating physicians reported (in 2015) that the major challenge was, and still is, the empowerment of society to donate blood voluntarily and regularly, since patients and families are still struggling to identify family members and friends as donors to achieve adequate blood supplies for their needs.

Screening is very well established in 100% of the collected blood for HIV 1+2, HbsAg, HCV, and syphilis. In addition, T. cruzi, HTLV.1 +3, and anti-HBC are routinely screened for. Medical expertise for addressing haemoglobin disorders is available in the country, and although no published national data is available on survival and/or age distribution, it is likely that appropriate quality of care is provided. However specific data, such as survival rates and age distribution of the patients, are needed to allow a better understanding of the effectiveness of the transfusion therapy and other care provided to patients with TDT.

BRAZIL (upper-middle-income country) also has a specific law, specific budget, and a national policy. Brazil, with 3 million (3,335,035) units of blood collected in 2015 (blood donation rate per 1,000 people of 16.51), reported that 61.25% of its blood supply is derived from VNRBD practices, while a similar percentage to that of

Argentina (i.e., 86.33% of its supply) is separated in blood components. Screening is performed on 100% of its collected blood for HIV, HbsAg, HCV, and syphilis, as well as for T. cruzi, HTLV 1 and 3, and anti-HBC.

With 662 TDT patients recorded in TIF's archives and an estimated 30,000–50,000 SCD patients, ensuring the safety and adequacy of blood for their transfusion needs is of utmost importance. There is sufficient medical expertise in this country, which indicates that, together with the above information and the complementary information from TIF's National Thalassaemia Association members, it is likely that the majority of patients across this country are obtaining adequate medical care, albeit with limited published data on national survival and age distribution.

TRINIDAD & TOBAGO (high income country) has a population of 1.3 million people. The blood units collected annually total 21,121, with only 18.41% from VNRBD practices. There are close to 100 TDT patients, with a larger number of SCD patients, since the sickle cell trait is prevalent in approximately 1 in 10 persons in this country. Based on TIF's data, appropriate clinical practices and sufficient medical expertise are available. It is thus expected that further to the heavy burden of identifying donors, the survival and quality of life of patients will be at satisfactory levels, albeit once again more specific data is needed to confirm and/or identity gaps and weaknesses.

For North America, **CANADA** AND **USA** (both high income countries), with a total population of 37.59 million and 328.2 million people, respectively, also have blood shortages. Both countries have very robust public health infrastructure, including nationally coordinated and high-quality standards of transfusion services, with nearly 100% of the blood is collected following VNRBD practices. In addition, the medical community has considerable knowledge and expertise in the management of haemoglobin disorders, and scientists have been conducting considerable research activity on these disorders for many decades.

In particular, the Centers for Disease Control and Prevention (CDC) in the USA contribute, through many different research projects, to significant improvements in BT therapy for these disorders. Patients with TDT and other haemoglobin disorders are anticipated to receive adequate, safe, and appropriately processed/stored blood as recommended in international guidelines. Updated published information on survival rates, age distribution, and morbidity/mortality rates of each state and nationwide is not available or is only partially available.

However, an important difference between Canada and the USA concerns the principle of universal healthcare coverage, which Canada enjoys, contrary to the USA where the healthcare system is based on private insurance and one's income. Strong efforts are exerted by the central government, patient-oriented NGOs, and the community of healthcare professionals in the USA to identify solutions and measures to cover the cost of every aspect of care, including BT therapy, and monitoring of every patient in any of the states. However, it is inevitable that some patients face challenges in accessing timely appropriate care, including transfusion therapy. Patient organisations, such as the Cooley's Anemia Foundation (CAF) in the USA, are making every effort to contribute to filling in gaps and inequities and strengthening research.

Moreover, blood transfusion therapy and identifying appropriate donors proves to be a challenge, because of multiethnic populations in the USA who come from many parts of the world where NTDT syndromes and SCD are more prevalent, and patients may initiate BT at a later point in their lives.

Despite the known high standards of BT services in these two countries, published national data on survival and age distribution are largely missing, mainly as a result of the absence of nationally coordinated disease-specific health registries. Some data are available through the excellent work of patient organisations, including CAF, albeit more nationwide information is needed.

European Region (EURO)

The European Region includes 53 countries with a population of 916,315,000 people.

TIF members in the region include 39 National Thalassaemia Associations from 20 countries.

EURO is a region where only about 8% of the global patient community with haemoglobin disorders live. Most of the countries, at least within the European Union and the United Kingdom, have robust medical, public health, and social care infrastructures, including nationally coordinated BT services, and some of them have established strong haemovigilance programmes. Haemoglobin disorders, consequent to migration through the decades, have been introduced into the populations of many countries in EURO and are to-date included in the wider family of rare diseases. Some of these countries, mainly the United Kingdom and France, have developed national disease-specific programmes (including BT ones) to address the needs of these patients. In most other EU countries, whether in the indigenous population (e.g., Spain, Bulgaria, Romania) or in the migrant groups (e.g., Germany, Netherlands and more recently Central and Northern European countries), patients' needs are addressed in the context of the paediatric or haematology services of their healthcare systems. However, in all of them, disease-specific programmes and services for transfusion therapy have been amongst their public health concerns and priorities. In Southern Europe (mainly Italy, Greece, and Cyprus), these disorders are of high prevalence in the indigenous populations, and numerous national disease-specific policies and programmes have been developed since the 1960s to address the care and management of those patients. BT services have been a key focus of these policies, and blood donor campaigns and advocacy for blood quality and safety have been impressively strong for decades now in these countries. Nevertheless, challenges still exist, particularly in blood adequacy and to a certain extent in securing 100% VNRBD practices. Greece, for example, still reports importing blood and having about 30% of its blood supplies deriving from family donations. Patients in some other countries of the EU and extended Europe, including Bulgaria, Romania, Albania and Turkey, face similar challenges and perhaps to a bigger extent, based on patients' reports. Blood adequacy and safety remain a key focus of the work of all countries in effectively addressing haemoglobin disorders, and, in this context, blood shortages and donor recruitment and retention are still key challenges.

The data in Tables 40–45 were taken from the WHO's *Global Status Report on Blood Safety and Availability 2021.*

Table 40. Blood centres & data coverage in EURO (2018)

BLOOD CENTRES & DATA COVERAGE (2018)

Country	Number of Blood Centres In the Country			Number of Blood Centres Covered By The Report			Estimated % of Blood Donations
	Stand-alone	Hospital-based	Total	Stand-alone	Hospital-based	Total	
Upper-Middle Income (UMC)							
Albania	1	31	32	1	31	32	
Azerbaijan	/	/	/	/	/	/	/
Bulgaria	6	23	29	6	23	29	
North Macedonia			21			21	
Turkey	/	/	/	/	/	/	/
High Income (HIC)							
Cyprus	4	0	4	4	0	4	
Denmark	0	5	5	0	5	5	
France	18	0	18	18	0	18	
Germany	/	/	/	/	/	/	/
Greece	/	/	/	/	/	/	/
Italy	0	278	278	0	278	278	
Malta	/	/	/	/	/	/	/
Netherlands	/	/	/	/	/	/	/
Sweden	0	26	26	0	26	26	
United Kingdom	/	/	/	/	/	/	/

/ : No response

Blank (in the last column) : 100%

Table 41. Blood donations in EURO (2018)

BLOOD DONATIONS (2018)

Country	No. Whole Blood Donations Collected (excluding autologous donations)										
	VNRD	VNRD from 1st time donors	VNRD from repeat donor	Family/replacement donations	Paid donations	Others	Total	% of VNRD	% of family/ replacement	% of paid donations	Blood donations per 1,000
Upper-Middle Income (UMC)											
Albania	9 282	...	...	23 144	650	11	33 087	28.00%	70.00%	2.00%	11.5
Azerbaijan	/	/	/	/	/	/	/	/	/	/	/
Bulgaria	167 424	36 115	45 332	130 551	2 209		300 184	55.80%	43.50%	0.70%	42.7
North Macedonia	53 915	5 451	48 465	271	0	0	54 186	99.50%	0.50%	0.00%	28.7
Turkey	/	/	/	/	/	/	/	/	/	/	29.4
High Income (HIC)											
Cyprus	63 008	0	63 008	0	0		63 008	100%	0%	0%	49.6
Denmark	206 990	16 773	190 217	0	0	0	206 990	100%	0%	0%	35.7
France	2 512 870	387 109	2 125 761	0	0		2 512 870	100%	0%	0%	37.4
Germany	/	/	/	/	/	/	/	/	/	/	51.1
Greece	/	/	/	/	/	/	/	/	/	/	46.6
Italy	2 569 275	371 093	2 198 182	0	0	0	2 569 275	100%	0%	0%	42.5
Malta	/	/	/	/	/	/	/	/	/	/	34.0
Netherlands	/	/	/	/	/	/	/	/	/	/	25.5
Sweden	409 187	29 146	409 187	0	0		409 187	100%	0%	0%	40.2
United Kingdom	/	/	/	/	/	/	/	/	/	/	3.8

... : Not reported/not available

Blank : Not required/not applicable

/ : No response

VNRD : Voluntary non-remunerated donations

Table 42. Laboratory test requirements for screening donated blood for transfusion-transmissible infections in EURO (2017–2018)

LABORATORY TEST REQUIREMENTS FOR SCREENING DONATED BLOOD FOR TRANSFUSION-TRANSMISSIBLE INFECTIONS (2017/18)

Country	Chagas disease		Malaria			HTLV-1/2	
	Ab	Others	Smear microscopy	Ag	Others	Ab	Others
Upper-Middle Income (UMC)							
Albania							
Azerbaijan	/	/	/	/	/	/	/
Bulgaria							
North Macedonia							
Turkey	/	/	/	/	/	/	/
High Income (HIC)							
Cyprus							
Denmark					S		
France	S					S	
Germany*							
Greece					S	Y	
Italy					S		
Malta							
Netherlands*					S	S	
Sweden	S			S		S	
United Kingdom*					S	S	

Y : Required for all donations

S : Required for selected donations

Blank : Not required/not applicable

/ : No response

* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

Table 43. Policy, governance, quality assurance and monitoring in EURO (2017–2018)

POLICY, GOVERNANCE, QUALITY ASSURANCE AND MONITORING (2017/18)

Country	Unit within MoH with responsibility for governing blood provision & transfusion activities	National Blood Policy	Multiyear national strategic plan for blood safety or equivalent	Specific Legislation Covering the Safety & Quality Of Blood And Blood Products for Transfusion	National Blood Committee (or equivalent)	Specific Government Budgetary Line Item For The NBTS/BTS	System of Cost Recovery for NBTS/BTS	National standards for the collection, testing processing, storage & distributuion of blood and blood components	National Guidelines On The Appropriate Clinical Use Of Blood
Upper-Middle Income (UMC)									
Albania	No	No	No	Yes	Yes	Yes	No	Yes	Yes
Azerbaijan	/	/	/	/	/	/	/	/	/
Bulgaria	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
North Macedonia	...	No	No	Yes	No	Yes	Yes	Yes	No
Turkey	Yes	Yes	...	Yes	Yes	Yes	Yes	Yes	Yes
High Income (HIC)									
Cyprus	Yes	Yes	Yes	Yes	...	Yes	Yes	Yes	No
Denmark	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
France	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Germany*	Yes	Yes	...	Yes	Yes	No	Yes	Yes	Yes
Greece*	Yes	Yes	Yes	Yes	Yes	Yes	...	Yes	Yes
Italy	Yes	Yes	Yes	Yes	Yes	Yes	...	Yes	Yes
Malta	Yes	No	No	Yes	Yes	Yes	No	Yes	...
Netherlands*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sweden	Yes	No	No	Yes	Yes	No	Yes	Yes	No
United Kingdom*	...	Yes	Yes	Yes	Yes	...	No	Yes	Yes

... : Not reported/not available

/ : No response

Blank : Not required/not applicable

* Data of 2017/2018 was not available, therefore data of earlier years were listed in the table

Table 44. Number & proportion of donations tested positive/reactive for TTI markers in EURO (2018)

NUMBER & PROPORTION OF DONATIONS TESTED POSITIVE/REACTIVE FOR TTI MARKERS (2018)

Country	HIV 1+2		
	Positive/reactive, no.	No. donations tested	%*
Upper-Middle Income (UMC)			
Albania	5	23 312	0.02
Azerbaijan	/	/	/
Bulgaria	143	169 633	0.08
North Macedonia	0	20 771	0
Turkey	/	/	/
High Income (HIC)			
Cyprus	2	63 008	0.003
Denmark	0	278 975	0
France	25	2 926 942	<0.001
Germany	/	/	/
Greece	/	/	/
Italy	83	2 991 082	0.003
Malta	/	/	/
Netherlands	/	/	/
Sweden	0	491 036	0
United Kingdom	/	/	/

Blank : Not required/not applicable

/ : No response

* Proportion, expressed as positive/reactive per 100 donations tested

Table 45. Clinical use of blood & blood components in EURO

CLINICAL USE OF BLOOD & BLOOD COMPONENTS (2018)

Country	Date Year	No. Hospitals Performing Blood Tranfusion	No. Units of Blood Components Issued/Transfused (excluding autologous blood units)							
			Whole blood	Red cells	Whole blood derived platelets	Apheresis platelets	Fresh frozen plasma	Plasma	Cryo-precipitate	
Upper-Middle Income (UMC)										
Albania	2018	32	391	22 452	4 217	...	14 508	7 643	466	Units issued
Azerbaijan	2017	/	/	/	/	/	/	/	/	/
Bulgaria	2018	172	92	155 525	26 712	2 145	100 310	100		Units issued
North Macedonia	2018	55	...	...	...	...	...	...	...	
Turkey	2018	/	/	/	/	/	/	/	/	/
High Income (HIC)										
Cyprus	2018	65	0	61 574	5 208^	335	12 004		113	Units transfused
Denmark	2018	...	0	195 049	36 128^	1 948	20 438	1 441	956	Units transfused
France	2018	...	0	2 295 441	208 585^	118 859	287 922	0	0	Units transfused
Germany	2018	/	/	/	/	/	/	/	/	/
Greece	2018	/	/	/	/	/	/	/	/	/
Italy	2018	1 544	18	2 443 359	170 867^	55 596	140 395	0	1 786	Units transfused
Malta	2018	/	/	/	/	/	/	/	/	/
Netherlands	2018	/	/	/	/	/	/	/	/	/
Sweden	2018	...	0	390 404	47 608^	16 128	41 569	0	0	Units transfused
United Kingdom	2018	/	/	/	/	/	/	/	/	/

... : Not reported/not available

Blank : Not required/not applicable

/ : No response

^ : In adult therapeutic doses

* 1 unit of blood component is defined as the preparation from whole blood donations of 450 ml

** 1 unit of apheresis platelets usually contains 200 - 450 x 10 000 000 000 platelets

In the EU (including the United Kingdom until the end of 2019), as shown in Figure 23, from 15 million donors, 20 million units of blood were collected, all of which undergo component separation in 1,400 blood establishments.

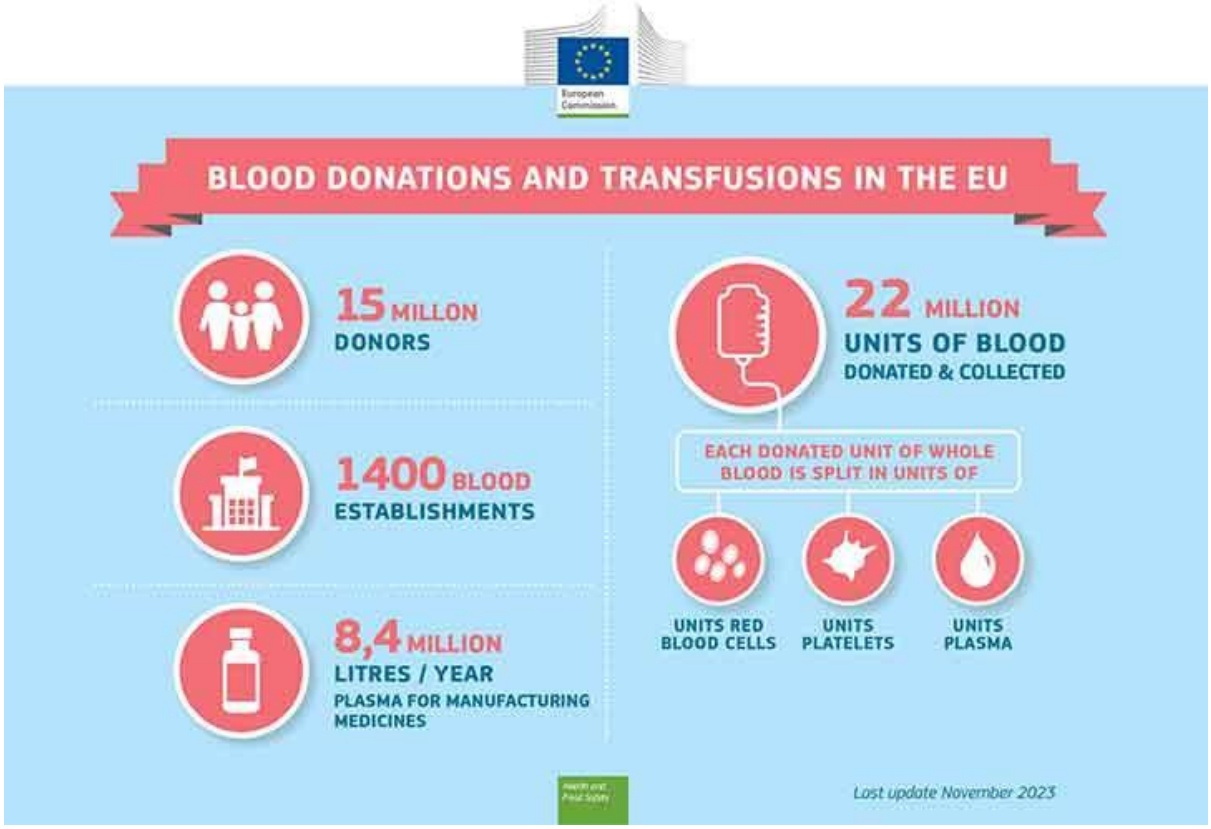

Figure 23. Blood donations and transfusions in the EU. Source: https://ec.europa.eu/health/blood_tissues_organs/blood_en

Figure 24 identifies the periodic variation in blood donor demographics in Europe. It demonstrates that the percentage of blood donors (those who have ever given blood), although steadily increasing between 1994 and 2009, decreased in 2014 in almost all countries, except France, the United Kingdom, and Cyprus. Although a decrease was not reported for Portugal, its general performance over the years with regard to the percentage of those who have ever given blood is rather weak. Countries with a focus on haemoglobin disorders, e.g. France, Greece, and Cyprus, have demonstrated numbers above the EU average, while Germany and the United Kingdom have kept their percentage at just about the EU average. Italy, however, with a very high prevalence of TD haemoglobin disorders, has shown significantly lower rates than the EU average, while Austria, with a much lower prevalence of TD haemoglobin disorders (which have been more recently introduced), exhibits the highest performance as reflected by the high percentage of people who have ever given blood. Certainly, increases in the numbers of blood donors does not necessarily contribute to effectively addressing BT therapy of patients with haemoglobin disorders. The absence or suboptimal functioning of patient management/clinical use of blood programmes and the exponentially increasing needs for blood transfusion in addressing other medical conditions pose significant challenges for blood supplies to meet national needs, including those required by TDT patients throughout their lives.

Moreover, another study [14], as shown in the maps below (Figure 25), showed that perceived blood transfusion safety and personal motivation amongst EU citizens may be stronger determinants of willingness to donate than just receiving certain incentives. EU-wide strategies for donor recruitment and retention should thus take both overall and country-specific patterns into account, including, for example, education on the importance of donating.

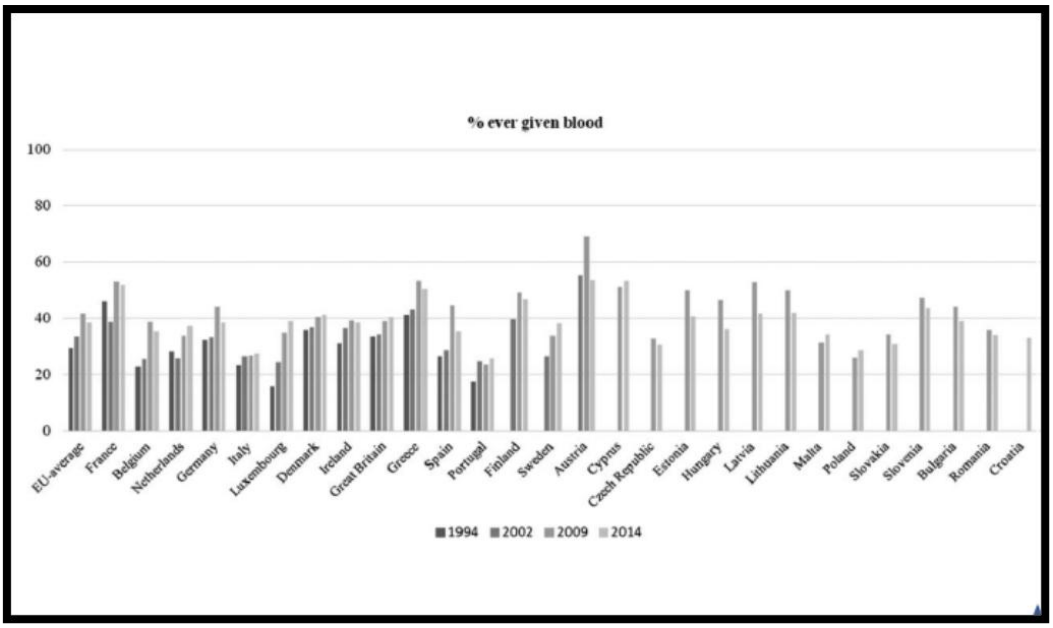

Figure 24. Periodic variation in blood donor demographics. Source [13].

Figure 25. Blood donor motivation perceptions in the EU. Source: Huis In 't Veld EMJ, de Kort WLAM, Merz EM [14].

Overall, from that same study, 37.9% (n=8,471) of all 6,434 respondents included participants across EU Member States who had ever donated blood (Map 1), 76% would be willing to do so again [14]. However, only 56.3% of those with no previous history of blood donations would be willing to donate in the future (Map 2). In Greece, for example, a representative of the Panhellenic Association of Patients NGO reported in the context of a conference in January 2020 that 90% of the individuals who meet the criteria for blood donation do not donate. In conclusion, and although the level of blood donation across the EU is amongst the highest globally, as seen in Figure 26, below, relating GDP/person to whole blood donation per 1,000 population, blood shortages still constitute the major concerns amongst both patients with TD haemoglobin disorders, their treating physicians, and BT services across the EU and beyond. Such concerns were very much demonstrated particularly during the Covid-19 pandemic. Indeed, the pandemic underscored the challenge and the need for

every country in every region of the world to strengthen public health services in the context of centrally and quality coordinated BT services. Even in the EU, where at least blood safety has truly reached very satisfactory levels, blood shortages were reported by all patients, which, if that occurred only temporarily, is a major concern.

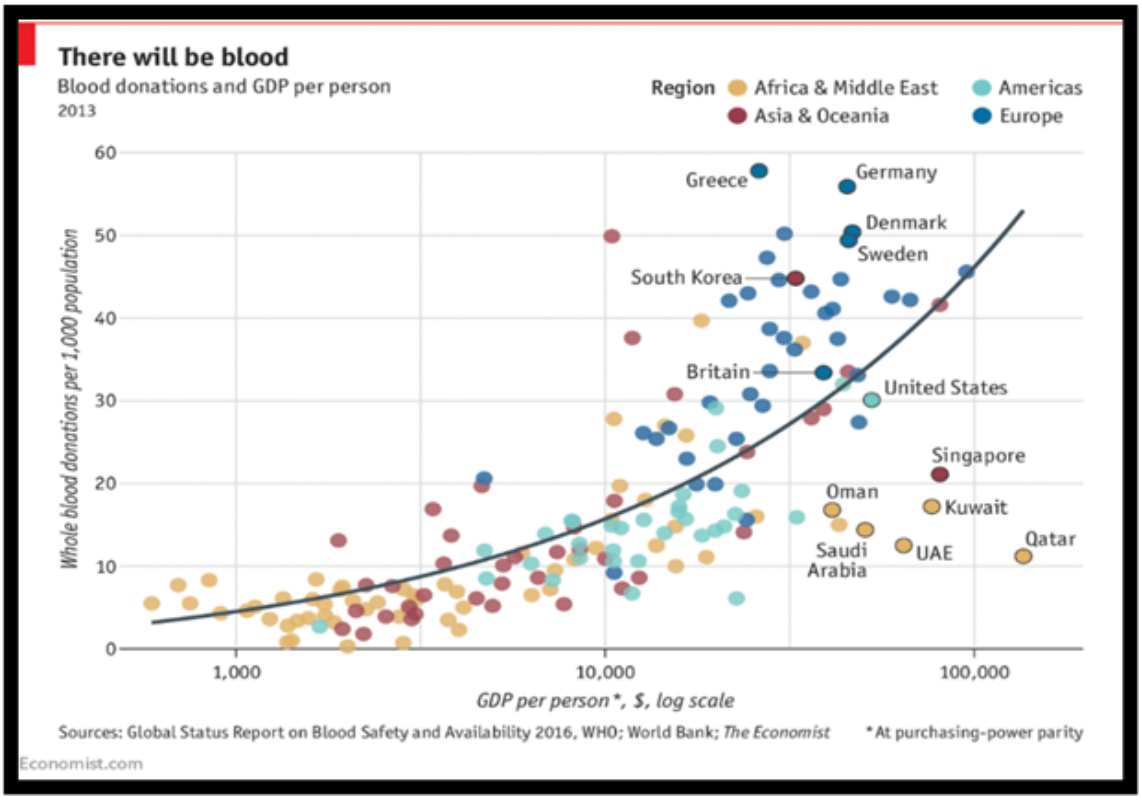

Figure 26. Blood donations and GDP per person (2013)

Overall, in the EU, published evidence on the survival, quality of life, and age distribution of patients with TD haemoglobin disorders indicates that the majority of TD patients are receiving optimal or nearly optimal medical care, including blood transfusion therapy. However, policymakers need to seriously consider the heavy migration influxes in recent years from countries mainly of the Middle East and other parts of the world where the prevalence of haemoglobin disorders is medium to high. Disease-specific policies and programmes need to be developed and/or existing ones need to be improved to address the emerging needs of these populations and allow public health systems to make the necessary adjustments in order to meet the needs of TDT patients in a timely and adequate fashion. Nonetheless, at the same time the quality and safety of the national transfusion services as a whole must not be jeopardised.

Regional Policy Landscape

It is noteworthy to mention that, in the European Region, the tools that EU has promoted for its people with regards to blood, cell, and tissue safety mainly concerns the proposed regulation on substances of human origin that combines the following past directives:

- Commission Directive 2004/33/EC on the technical requirements for blood and blood donation
- Commission Directive 2005/61/EC on the traceability requirements and notification responsibilities in case of serious adverse reactions and events
- Commission Directive 2005/62/EC that sets out Community standards and specifications relating to the quality system for a blood bank

The legal framework defining the quality and safety standards for blood and its components is very strong in the EU and is set out in Directive 2002/98/EC, also referred to as the European Blood Directive. It covers all steps in the transfusion process, including donation, collection, testing, processing, storage, and distribution.

To help implement this main act, the European Commission and the Council of Europe (CoE) have proposed and adopted, in close collaboration with EU national authorities, other additional acts. It is important to note that EU Member States can always choose to apply more stringent rules to the quality and safety of blood and blood products than those outlined above.

In 2020, the European Commission carried out the first formal evaluation of the EU blood and tissues and cells legislation that showcased the need to replace the existing directives with a regulation on the centralised monitoring and coordination of blood establishments and the harmonisation across Member States, facilitating cross-border exchange of substances of human origin (SoHO) and improving patient access to the therapies they need. In July 2022, the European Commission adopted the proposal for a regulation on standards of quality and safety for SoHO intended for human application ("SoHO Regulation"). As of December 2022, the proposed Regulation is under consultation and discussion in the European Parliament and Council.

It is noteworthy also that some EU Member States with high disease prevalence, such as Cyprus, use more than 30% of their blood supplies annually on addressing transfusion needs of patients with TD haemoglobin disorders. Similarly, in Greece 20–25% of the 580,000–600,000 units used annually in the hospitals (i.e., 120,000–130,000) are for TDT patients. Apparently, this is not sufficient for their needs; thus, family replacement practices are still in place for more than 30% of the collected blood, and Greece has imported blood for years to meet the needs of BT therapy. A similar percentage, between 18%–30%, is noted in Italy, with the majority of EU Member States being around 16%–18%. It is evident that regular VNRBD practices and safeguarding blood supply levels through specific policies and programmes at national and European levels are of utmost importance for patients with TDT. This is particularly important as these patients are ageing due to the quality of care. The burden of identifying donors for family replacement practices and/or importing blood are practices that transfusion services, healthcare professionals, and patients aim to abolish.

The CoE regularly reviews and updates technical requirements in its *Guide to the Preparation, Use and Quality Assurance of Blood Components and Good Practice Guidelines for Blood Establishments*. In addition, it prepares ad-hoc guidelines on different topics, in regard to the safety and quality of substances of human origin (SoHO).

The European Centre for Disease Prevention and Control (ECDC) prepares risk assessments and preparedness plans whenever epidemiological outbreaks are of relevance for blood, tissues, cells, and organs. In addition, the European Commission provides funding for actions in the area of SoHO through the EU Health Programme, mainly in the form of projects or joint actions with national authorities.

1. Two guides on Patient Blood Management (PBM). One targeted for health authorities and the other for hospitals
2. The Joint Action VISTART, to promote and facilitate the harmonisation of inspection, authorisation, and vigilance systems for blood, tissues and cells
3. Eurobarometer reports outlining the European public's attitude to the donation, transfusion, and/or application of blood, tissue, and cells
4. An EU-wide mapping exercise of the market for blood, blood components, and plasma derivatives, focusing on their availability for patients
5. Catie - Competent Authority Training of Inspections in Europe. The development of training sessions for inspectors in the field of blood and blood components
6. EUOBU - A guide on EU Optimal Blood Use
7. DOMAINE - A project to create a safe and sufficient donor population in Europe: comparing and recommending good donor management practice
8. EuBIS - The development of pan-European standards and criteria for the inspection of blood establishments
9. The development of a Pan-European standard operating procedure (SOP) for best practice in ensuring the quality and safety of blood

A number of actions aim to support the EU mandate on safety and quality, and they can also serve to promote other policy priorities such as improving the availability of SoHO or the efficiency of the health systems that support donation and supply. Nonetheless, despite all the progress in safety regulations and practices in Europe, the danger to multi-transfused patients is ever present. A recent report from Italy describes an HCV outbreak in a group of transfused thalassaemia major outpatients, which started in May 2016 and ended in July 2017. This outbreak investigation identified seven new HCV infections and four HCV reinfections amongst 128 patients. The investigation concluded that transmission from hospital personnel or patient-to-patient transmission may have occurred, using genome sequencing to support epidemiological data [15].

In the 2017, 2018 and 2019 reports of the European Committee (Partial Agreement) on Blood Transfusion CD-P-TS, titled *The Collection, Testing and Use of Blood and Blood Components in Europe*, the following observations were made (Tables 46–54):

Table 46. Donors, first time donors and inhabitants, 2019

	Donors						% First time donors	
Country	Inhabitants	Total	Per 1,000 inhabitants	Regular & repeat	First time	% First time	Donating	Tested only
AUSTRIA	8859000	307074	0	204130	59863	19	90	18
BULGARIA	7000039	130219	19	92953	37266	29	100	0
CROATIA	4076000	94862	23	94862	11758	12	100	calculated
CYPRUS	888000	43813	49	42132	5484	13	100	0
CZECH REPUBLIC	10669324	277432	26	258388	58688	21	100	not performed
DENMARK	5822763	128851	22	184084	31202	24	53	0
ESTONIA	1324820	30534	23	26151	4383	14	100	0
FINLAND	5561389	116100	21	105390	14408	12	95	5
GERMANY	83166711	2331777	28	2054405	405142	17	88	12
GREECE	10500000	402983	38	287845	57569	14	70	30
HUNGARY	9770000	0	calculated	208131	45153	calculated	100	calculated
IRELAND	4921500	82730	17	69137	13593	16	84	16
ITALY	60359546	1683470	28	1397472	362601	22	66	34
NORTH MACEDONIA	2000000	32790	16	32790	4943	15	100	NA
REPUBLIC OF MOLDOVA	2807801	54545	19	39462	15083	28	100	0
MONTENEGRO	620029	16579	27	11736	4843	29	100	0
NETHERLANDS	17280000	366713	21	366713	36941	10	0	100
NORWAY	5367580	96603	18	96603	18625	19	0	100
POLAND	38382576	614579	16	467838	146741	24	NA	NA
PORTUGAL	10286263	200556	19	175569	24987	12	100	0
SLOVAK REPUBLIC	5457873	130798	24	107264	23534	18	66	0
SLOVENIA	2081000	59996	29	50672	9324	16	100	0
SWEDEN	10327589	207933	20	178134	29799	14	0	152

NA: not applicable; ND: not determined.

Table 47. Collection of whole blood, autologous blood and blood (apheresis) components, 2019

	Whole blood collections				Apheresis collections					
Country	Whole blood units (WBU)	WBU per 1,000 inhabitants	Autologous WBU	% Autologous WBU	Plasma apheresis (L)	Plasma (L) per 1,000 inhabitants	Platelets apheresis (U)	RBC apheresis (U)	Granulocytes apheresis (U)	Multi-component apheresis (U)
AUSTRIA	32409	0.0	NA	NA	500360	0.056480415	30129	64	131	5207
BULGARIA	169006	24.1	59	0.0003491	35.41	0.005058543	2261	0	0	0
CROATIA	190543	46.7	19	9.9715E-05	1352	0.331697743	5792	0	0	0
CYPRUS	62690	70.6	9	0.000143564	ND	ND	199	0	ND	ND
CZECH REPUBLIC	423310	39.7	4350	0.010276157	625700	58.64476512	29900	1196	2	52
DENMARK	204817	35.2	0	0	41817	7.181642117	2379	0	0	0
ESTONIA	50077	37.8	0	0	2062	1.556437856	1918	0	0	591
FINLAND	198339	35.7	0	0	0	0	4391	0	9	0
GERMANY	3754435	45.1	761	0.000202694	2143075.87	25.7684336	303353	2984	450	45148
GREECE	382833	36.5	510	0.001332174	0	to be calculated	17106	0	0	0
HUNGARY	377058	38593.4	2310	0.006126378	0	0	18370	0	218	0
IRELAND	132118	26.8	0	0	0	0	18489	0	0	0
ITALY	2566446	42.5	8220	0.003202873	236499	3.918170624	52784	673	117	59888
NORTH MACEDONIA	53528	26.8	3	5.60454E-05	NA	NA	505	NA	NA	0
REPUBLIC OF MOLDOVA	58249	20.7	45	0.000772545	8898.9	3.16934854	2519	0	0	1285
MONTENEGRO	19216	31.0	0	0	0	0	0	0	0	0
NETHERLANDS	418251	24.2	na	NA	181069	10.47853009	5274	0	0	na
NORWAY	171837	32.0	0	0	7890	1.469936172	6572	1669	0	145
POLAND	1242012	32.4	533	0.000429142	27587	0.718737586	48078	48	94	29049
PORTUGAL	305577	29.7	54	0.000176715	0	0	5229	2	20	1009
SLOVAK REPUBLIC	224836	41.2	333	0.00148108	48.6	0.008904568	11885	47	22	329
SLOVENIA	81941	39.4	100	0.00122039	1365	0.655934647	1754	0	0	0
SWEDEN	406006	39.3	16	3.94083E-05	19872	1.924166425	0	416	NA	NA

NA: not applicable; ND: not determined.

Table 48. Profile of donations, 2019

	whole blood donations			red cell apheresis		plasmapheresis donations	platelet apheresis
Country	% voluntary, non-remunerated	% from replacement donors	% from autologous donors	% voluntary, non-remunerated	% from autologous donors	% voluntary, non-remunerated	% voluntary, non-remunerated
AUSTRIA	100	NA	#VALUE!	100	20.3	100	NA
BULGARIA	22	78	0.0003491	ND	ND	0	0
CROATIA	100	0	0.010	0	ND	100	100
CYPRUS	100	ND	0.014	ND	ND	ND	100
CZECH REPUBLIC	100	0	1.028	100	0	30	42
DENMARK	100	0	0.000	ND	ND	100	100
ESTONIA	100	0	0	ND	ND	100	100
FINLAND	100	0	0	ND	ND	100	100
GERMANY	100	0	0.020	100	0.1	100	100
GREECE	65	35	0.133	0	to be calculated	0	0
HUNGARY	100	0	0.613	ND	ND	ND	100
IRELAND	100	0	0	ND	ND	ND	100
ITALY	100	0	0.320	100	0.0	100	100
NORTH MACEDONIA	95	5	0.006	0	NA	NA	100
REPUBLIC OF MOLDOVA	96	4	0.077	ND	ND	93	100
MONTENEGRO	44	56	0	0	ND	0	ND
NETHERLANDS	100	na	NA	ND	ND	100	100
NORWAY	100	0	0.000	100	0	100	100
POLAND	95.66	4.25	0.043	100	0	97.2	98.4
PORTUGAL	100	0	0.018	100	0	NA	100
SLOVAK REPUBLIC	100	0	0.148	100	0	100	100
SLOVENIA	100	0	0.122	0	ND	100	100
SWEDEN	100	0	0.004	100	1.4	100	100

NA: not applicable; ND: not determined.

Table 49. Use of blood and blood components for transfusion, 2019

Country	Blood and blood components	Whole blood (WBU)	% Total RBC from WBU	RBC concentrates (U)	RBC (U) per 1,000 inhabitants
AUSTRIA	Issued	NA	NA	379,203	0
BULGARIA	0	39	0.02	170,680	24
CROATIA	Distributed	0	0	186,488	46
CYPRUS	Distributed	ND	ND	61,143	69
CZECH REPUBLIC	Issued	220	0.06	394,711	37
DENMARK	Transfused	0	0.00	191,293	33
ESTONIA	Issued	8	0.02	48,818	37
FINLAND	Distributed	0	0	190,437	34
GERMANY	Issued	25	0.00	3,492,955	42
GREECE	0	0	e calculated	397,558	38
HUNGARY	0	0	0.00	362,782	37,132
IRELAND	Issued	1	0.000008	123,645	25
ITALY	Transfused	1,110	0.05	2,449,139	41
NORTH MACEDONIA	Issued	66	0.13	48,875	24
REPUBLIC OF MOLDOVA	Issued	48	0.09	55,166	20
MONTENEGRO	Transfused	17	0.10	16,335	26
NETHERLANDS	Distributed	654	0.16	407,460	24
NORWAY	Transfused	0	e calculated	154,176	29
POLAND	Distributed	37	0.00	1,178,074	31
PORTUGAL	Transfused	22	0.01	293,892	29
SLOVAK REPUBLIC	Issued	60	0.03	198,373	36
SLOVENIA	Issued	0	0	78,473	38
SWEDEN	Transfused	0	0.00	381,862	37

Table 50. Special processing of blood components, 2019

	Red blood cells	
Country	**Leuco depleted %**	**Irradiated %**
AUSTRIA	33	5
BULGARIA	10	0
CROATIA	100	10
CYPRUS	100	10
CZECH REPUBLIC	66	7
DENMARK	100	5
ESTONIA	100	6
FINLAND	100	3
GERMANY	100	6
GREECE	35	25
HUNGARY	20	11
IRELAND	100	12
ITALY	6	16
NORTH MACEDONIA	27	NA
REPUBLIC OF MOLDOVA	100	0
MONTENEGRO	0	0
NETHERLANDS	na	5
NORWAY	100	8
POLAND	28	9
PORTUGAL	100	ND
SLOVAK REPUBLIC	75	NA
SLOVENIA	100	6
SWEDEN	100	5

NA: not applicable; ND: not determined.

Table 51. Donation testing strategy for infectious agents – %, 2019

Country	Anti-HIV 1/2	HIV Ag	HBs Ag	Anti-HBc	anti-HCV	HCV Ag	Anti-HTLV 1/2	Syphilis	Malaria	Anti-HEV	Other
AUSTRIA	100	100	100	ND	100	ND	ND	50	ND	ND	Neopterin (100%); CMV-AK (40%); WNV-NAT (100%)
BULGARIA	100	100	100	ND	100	100	ND	100	ND	ND	
CROATIA	100	100	100	ND	100	ND	ND	100	1	ND	
CYPRUS	100	100	100	0	100	100	0	100	ND	ND	WNV (24%); CMV IgM (7%)
CZECH REPUBLIC	100	100	100	5	100	25	ND	100	ND	ND	
DENMARK	100	100	100	11	100	ND	ND	0	?	ND	
ESTONIA	100	ND	100	ND	100	ND	ND	100	0.1	ND	
FINLAND	99	99	99	0.1	99	ND	ND	99	0.38	ND	
GERMANY	100	ND	100	100	100	ND	ND	100	ND	ND	
GREECE	100	100	100	0	100	0	100	100	0	0	WNV
HUNGARY	0	0	0	0	0	0	0	0	0	0	
IRELAND	100	100	100	0	100	ND	ND	100	ND	ND	
ITALY	100	100	100	ND	100	ND	ND	100	NA	ND	Chagas' dsease (ND); WNV (28%)
NORTH MACEDONIA	100	100	100	ND	100	ND	ND	100	ND	ND	
REPUBLIC OF MOLDOVA	100	100	100	ND	100	ND	ND	100	ND	ND	
MONTENEGRO	100	100	100	ND	100	ND	ND	100	ND	ND	
NETHERLANDS	100	0	100	100	100	0	0	100	0	0	Q fever; Anti-Parvovirus B19 IgG; Anti-CMV IgG
NORWAY	100	100	100	50	100	ND	0.2	50	4	ND	Chagas
POLAND	100	99	100	ND	100	15	ND	100	ND	ND	
PORTUGAL	100	100	100	100	100	100	100	100	ND	ND	Chagas disease - Trypanosoma Cruzi ab (ND)
SLOVAK REPUBLIC	100	100	100	100	100	ND	ND	100	ND	ND	
SLOVENIA	100	100	100	100	100	ND	ND	100	ND	ND	WNV (30%)
SWEDEN	100	100	100	7.3	100	ND	7	100	ND	ND	

ND: not done

Table 52. Donation testing strategy for infectious agents – % (continued), 2019

	Which donations					Individual donation or size of minipool				
Country	**HIV**	**HBV**	**HCV**	**HEV**	**Other NAT**	**HIV**	**HBV**	**HCV**	**HEV**	**Other NAT**
AUSTRIA	All	All	All	All	HAV, PARVO B19, WNV NAT	MP96	MP96	MP96	MP96	AD (MP)
BULGARIA	NA	NA	NA	None		NA	NA	NA	ND	
CROATIA	All	All	All	None	WNV	IT	IT	IT	0	AD (IT)
CYPRUS	All	All	All	None	WNV	IT	IT	IT	ND	AD (IT)
CZECH REPUBLIC	NA	NA	NA	None		MP	0	0	0	
DENMARK	All	All	All	None		IT	IT	IT	ND	
ESTONIA	All	All	All	None		IT	IT	IT	ND	
FINLAND	All	All	All	None		IT	IT	IT	ND	
GERMANY	All	NA	All	All	WNV	MP96	MP96	MP96	MP96	
GREECE	All	All	All	0		0	0	0	0	
HUNGARY	0	0	0	0		00	00	00	0	
IRELAND	All	0	0	0		MP	0	0	0	
ITALY	All	All	All	None	WNV	IT	IT	IT	ND	AD (IT)
NORTH MACEDONIA	None	None	None	None		ND	ND	ND	ND	
REPUBLIC OF MOLDOVA	All	All	All	None		MP6	MP6	MP6	ND	
MONTENEGRO	None	None	None	None		0	0	0	0	
NETHERLANDS	All	All	All	Labile		MP6	MP6	MP6	MP24	
NORWAY	None	None	None	None		0	0	0	0	
POLAND	All	All	All	None		MP4, MP6	MP4, MP6	MP4, MP6	ND	
PORTUGAL	All	All	All	None		IT	IT	IT	ND	
SLOVAK REPUBLIC	All	All	All	None	WNV	IT	IT	IT	ND	AD (IT)
SLOVENIA	All	All	All	NA		IT	IT	IT	NA	
SWEDEN	None	None	None	None		ND	ND	ND	ND	

NA: not applicable; ND: not done
All: all donations; First: first time donations only; Labile: labile blood products
MP: minipool, IT: individual testing
AD: all donations

Table 53. NAT testing, 2019

HBs Ag	**Comments**
FINLAND	We DO NOT test donations discarded at the donation site. In 2019 1.1% of donations.
REPUBLIC OF MOLDOVA	We use the electrochemiluminescence (ECLIA) method

Anti-HBc	**Comments**
CROATIA	50 % of blood establishments do it with other testing strategy.
CZECH REPUBLIC	If ID-NAT IR or RR, than the anti-HBc test is automatically added to donation. Anti-HBc test is also a part of obligatory confirmatory testing for all HBV (sero/molecular) positive donations or control samples.
FINLAND	testing of first-time donors is performed by several BEs
GERMANY	Donors with a history of possible earlier HBV are tested for anti-HBcAb before donation.
NETHERLANDS	Persons, tested positive for anti-HBc, can further donate blood if a sensitive assay for HBV-Genom results negative and if anti-HBs antibody-titer stays above 100 IU/l.
NORWAY	All blood donations were routinely tested for the presence of anti-HBc; donations positive for anti-HBc antibodies were then investigated for anti-HBs; donations showing anti-HBs levels <200 mIU/mL were not released for clinical or manufacturing use.
SWEDEN	Percent donations tested is an estimate. We test new donors and when the previous donation was more than 6 months ago.

anti-HCV	**Comments**
CZECH REPUBLIC	combined test antibody + antigen is done by several BEs
FINLAND	We DO NOT test donations discarded at the donation site. In 2019 1.1% of donations.
REPUBLIC OF MOLDOVA	We use the electrochemiluminescence (ECLIA) method

HCV Ag	**Comments**
AUSTRIA	25% do other testing strategy.
CZECH REPUBLIC	combined test antibody + antigen is done by several Bes

Anti-HTLV 1/2	**Comments**
GERMANY	Not mandatory. Anti-HTLV I/II screening tests are used by some of the blood establishments.
NETHERLANDS	Only first time tested donors (without donation).
NORWAY	Percent donations tested is an estimate. We test new donors that are born, or have lived for more than 6 months during their first 5 years, in certain countries.
PORTUGAL	o First time donations o Donors living in or originating from high prevalence areas o Donors with sexual partners who come from high prevalence areas o In donors whose parents are from high prevalence areas

Syphilis	**Comments**
AUSTRIA	Syphilis testing of plasma donations for producing plasma derivatives is not legally binding.
CYPRUS	Syphilis IgG/Igm
FINLAND	We DO NOT test donations discarded at the donation site. In 2019 1.1% of donations.
GERMANY	Not required for donations of plasma for fractionation.
REPUBLIC OF MOLDOVA	We use the electrochemiluminescence (ECLIA) method
NORWAY	Percent donations tested is an estimate. We test new donors and when the previous donation was more than 6 months ago.

Table 54. NAT testing (continued), 2019

HBV	Comments
CYPRUS	We use individual donation nucleic acid testing (ID-NAT)
CZECH REPUBLIC	NAT is performed by only few BEs in minipools / pools of different size. Circa 25 % of all donations is tested, overall prevalence / incidence data are not available
FINLAND	Such as in serological screening tests; we DO NOT NAT-test donations discarded at the donation site.
GERMANY	No Data. HBV NAT test performed by blood donation service on a voluntary basis for more than 75% of all donations.
IRELAND	seronegative sample is tested by NAT
REPUBLIC OF MOLDOVA	The first step is the electrochemiluminescence (ECLIA) test. All the negative donations in the first step are NAT tested.
NETHERLANDS	A multiplex real-time PCR test was used to simultaneously screen donated blood for HIV-1 RNA, HIV-2 RNA, HCV RNA, and HBV DNA.
NORWAY	Performed by the plasma fractionater on plasma for fractionation.
POLAND	Ad. B98: Type of analysis: Minipool and individual testing, additionally ad.B100: 3 OBI, ad.B101: 8 OBI
SLOVAK REPUBLIC	NAT testing started from May 2019 and is performed only in processing centers of National transfusion Service of the Slovak Republic (71% of all donations in 2019 were performed by National Transfusion Service). NAT testing is not performed by hospital based BEs.

HCV	Comments
CYPRUS	We use individual donation nucleic acid testing (ID-NAT)
CZECH REPUBLIC	NAT is performed by only few BEs in minipools / pools of different size. Circa 25 % of all donations is tested, overall prevalence / incidence data are not available
FINLAND	Such as in serological screening tests; we DO NOT NAT-test donations discarded at the donation site.
IRELAND	seronegative sample is tested by NAT
REPUBLIC OF MOLDOVA	The first step is the electrochemiluminescence (ECLIA) test. All the negative donations in the first step are NAT tested.
NETHERLANDS	A multiplex real-time PCR test was used to simultaneously screen donated blood for HIV-1 RNA, HIV-2 RNA, HCV RNA, and HBV DNA.
NORWAY	Performed by the plasma fractionater on plasma for fractionation.
POLAND	Ad. B104: Type of analysis: Minipool and individual testing
SLOVAK REPUBLIC	NAT testing started from May 2019 and is performed only in processing centers of National transfusion Service of the Slovak Republic (71% of all donations in 2019 were performed by National Transfusion Service). NAT testing is not performed by hospital based BEs.

Other NAT	Comments
AUSTRIA	WNV: 29% of the estabslishments; just in WNV season
CROATIA	WNV: Seasonal NAT testing (15.05. - 30.11.2019.), 105.313 donations were tested.
CYPRUS	WNV: This test was performed in 2019 only for the period from 1st July until 31st October (TMA and NAT), for all donations.
GERMANY	Not mandatory. Testing or deferral for four weeks after residence in an area with ongoing transmission of WNV to humans for more than two consecutive days, starting after leaving this area. Measures must be applied from 1st of June to 30th of November.
ITALY	In 2019, a total of 12 donors were positive to WNV NAT test.
SLOVAK REPUBLIC	RNA WNV testing: during the period of the risk (1.8.-31.11. 2019) all donations collected in affected region. 12 500 donations were tested in Bratislava region, all with negative results. (12500 = 5% of all donations in Slovakia in 2019)

Conclusions

Transfusion practices for TDT patients differ across countries and geographical regions of the world. This may be linked to (1) the availability of blood/packed RBCs and their accessibility to patients; (2) the expertise and attitudes of treating physicians; (3) costs of BT and national economies; (4) competing medical/public health priorities; and (5) the use of different transfusion guidelines or lack of adherence/implementation of guidelines. Very importantly, the differences in the quality of transfusion services may exist as a result of the differing standards related to the volume of RBCs contained in each unit and to differences in logistical factors. As a consequence, physicians, mainly in large countries, may provide more blood per session, thus extending the period between sessions.

TIF's work and other published information have demonstrated that the proportion of patients with TM receiving transfusion therapy for most of their lifetime is consistent across all geographical regions. However, in the case of thalassaemia intermedia, patients receiving transfusion therapy for a large part of their lifetime is documented more in the South-East Asia and Western Pacific Regions than in Europe or other parts of the world. This may be justified as patients with the more severe phenotype HbE/β-thalassaemia are most

prevalent in these parts of the world, and consequently the needs for strengthening their BT services are indeed greater.

The only well-established national survival data and age distribution cohorts are still those deriving from the national registries of Cyprus, Greece, and Italy.

- Cyprus – The median age was demonstrated to be 40.9 years (30/12/18) (Figures 27 & 28) [16], [17], and patient survival rate is steadily increasing as quality of care has improved through the years.
- Greece – The median age was demonstrated to be 36–45 years for TM patients, 46–55 years for TI patients, and 41–50 years for SCD patients (Figure 29) [18], [19].
- Italy – Amongst 3,986 patients in 36 centres (>50% of the total patient population), 68% of TM patients were aged ≥35 years and 11% ≤ 18 years (Figure 30) [20], [21], [22].

Cyprus

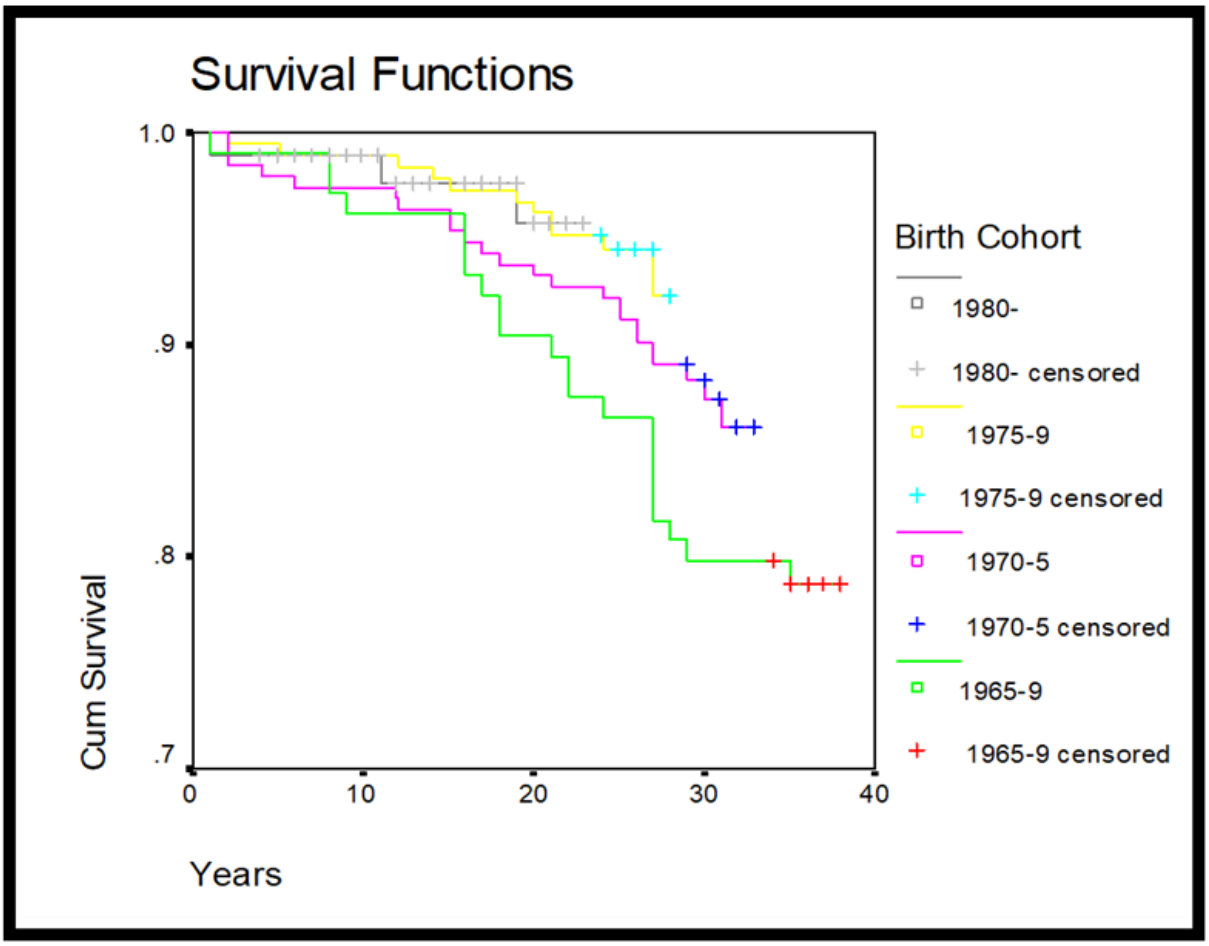

Figure 27. Cyprus Thalassaemia Registry (care of Dr S. Christou 2006)

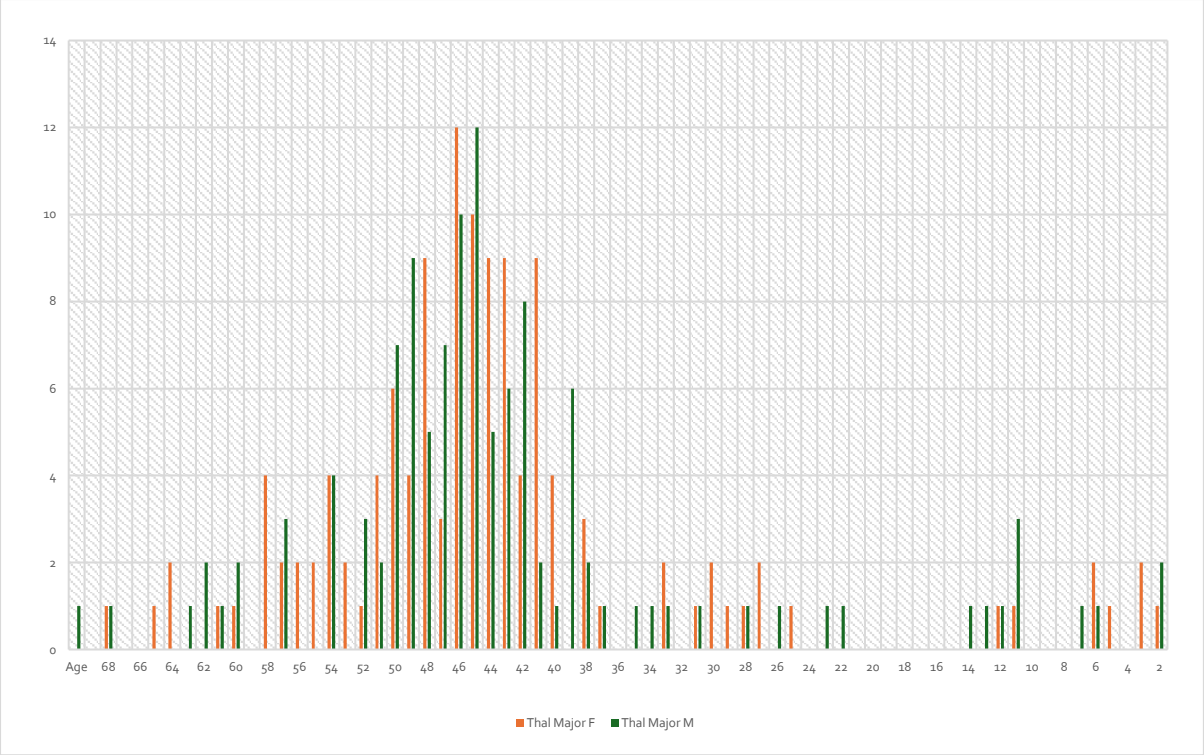

Figure 28. Cyprus Thalassaemia Registry (care of Dr S. Christou 2020)

Greece

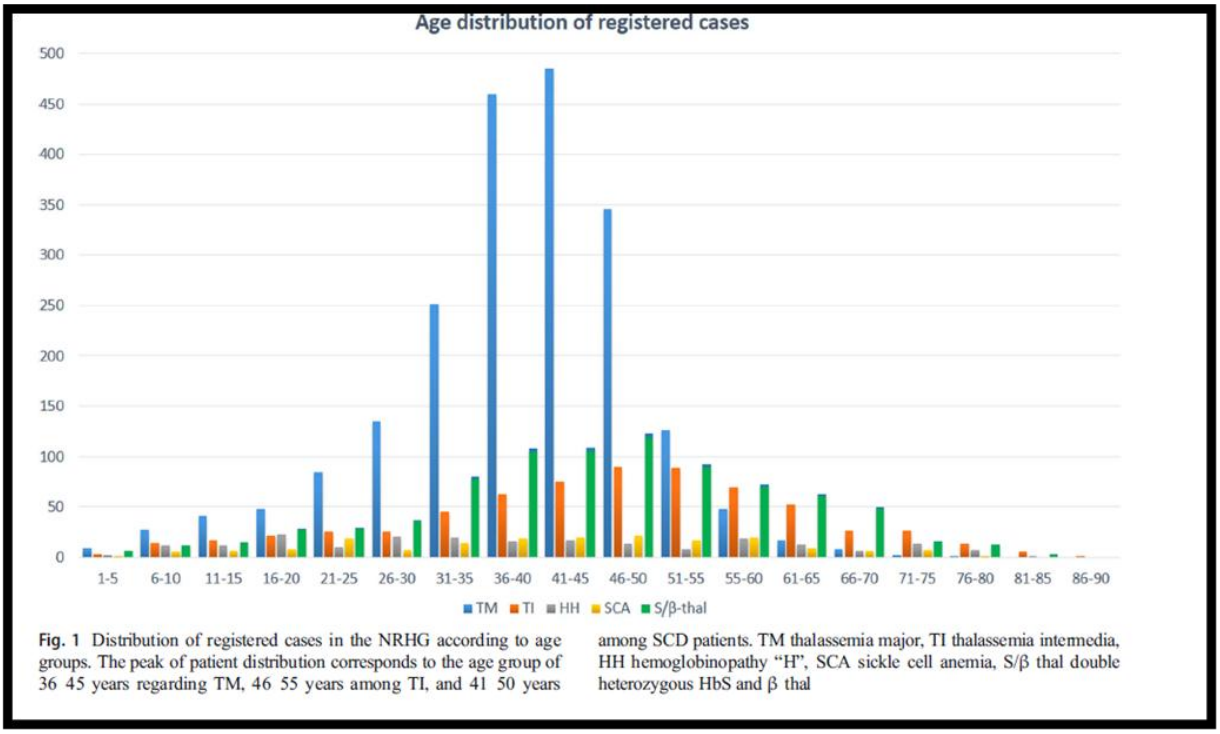

Figure 29. Age distribution of thalassaemia patients in Greece

Italy

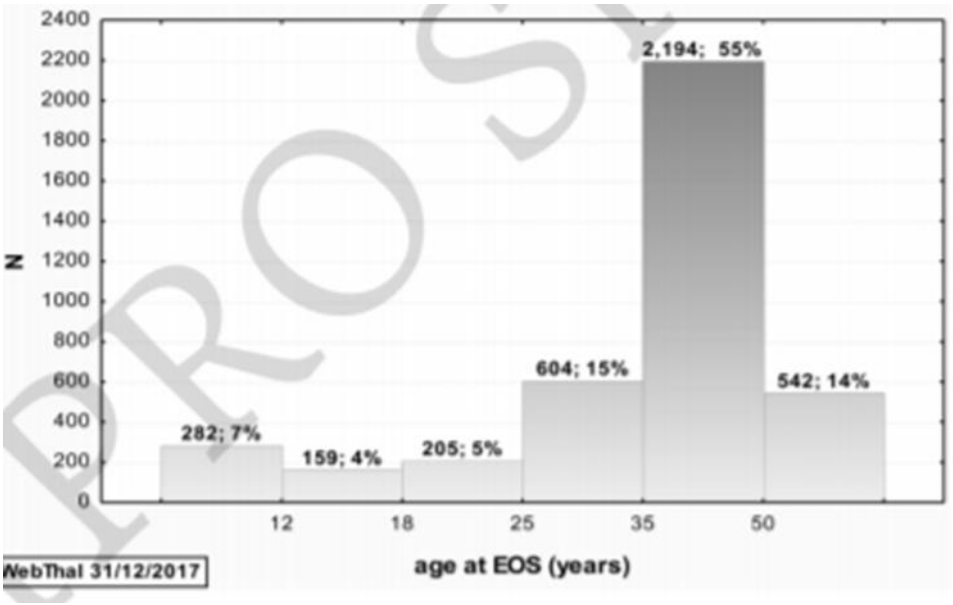

Figure 30. Age distribution of patients with thalassaemia syndromes in Italy (2017)

In the **United Kingdom,** optimal care is available and medical expertise exists in a patient-centred universal coverage healthcare system with very robust BT services. Still, only around 50% of the patients are over 24 years old and a very small percentage are over 50 years [23].

Table 55. Thalassaemia registrations by commissioning hub (United Kingdom). Source: www.nhr.nhs.uk

Region	Registrations	Region	Registrations
London	853	Thames Valley & Wessex	50
West Midlands	261	East of England	40
Northwest	205	Northeast & Cumbria	23
Yorkshire & Humber	196	Southwest	17
East Midlands	99	Southeast	0

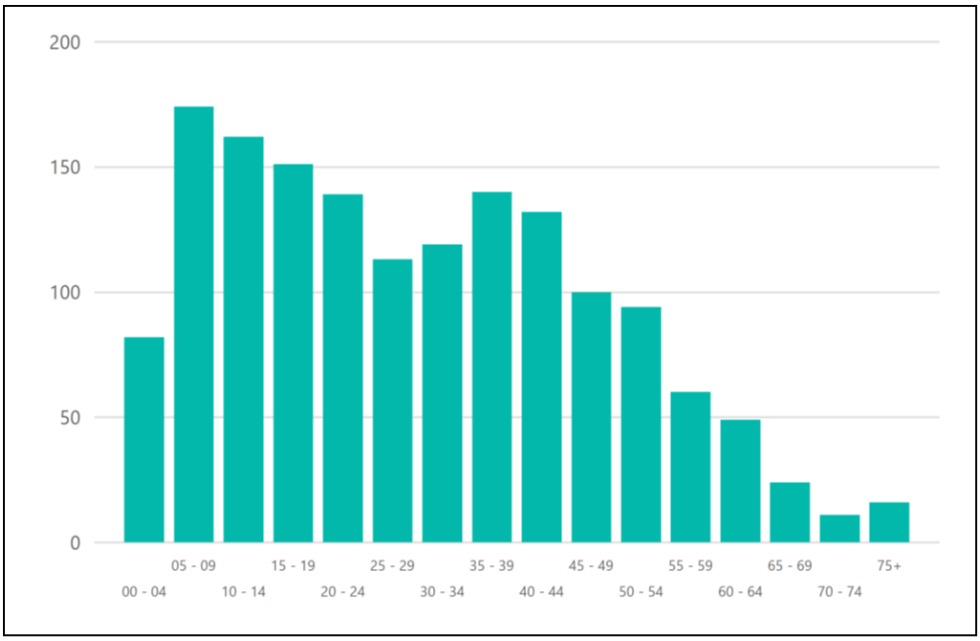

Figure 31. Thalassaemia patients by age group (United Kingdom). Source: www.nhr.nhs.uk

Iran (Islamic Rep. of) also maintains a national registry. In an analysis of 1,831 patients in Northern Iran (about 10% of the total patient population in the country), the mean age of patients was 30 ± 9.7 years, while in a larger study of 5,491 patients across the country, the mean age was only 23.8 ± 11.3 years [24], [25].

In **Taiwan (China)**, amongst 454 patients, the median age was 17.2 years (0.1–48.0 years), 58.1% of the patients being younger than 20 years [26].

Similarly, in **Albania,** according to a report addressed to TIF in 2015 and based on data from patients with haemoglobinopathies, amongst 165 TDT patients of a single centre in the University of Tirana, the age of the patients was between 2 and 14 years (Manika Face-Kraeka, Eleni Nastas, Anina Godo, Bledi Kreka, Elizana Petrela, Anjeza Kalaci; personal communication, 2021).

Even though **France** maintains a national registry for thalassaemia, there has not been an update since 2010. In this report, 267 out of 378 patients with TM had a median age of 20 years. In an EHA abstract from 2019 (patients were included between 01/01/2005–31/01/2019), from a total of 666 patients, 441 with TM, the median age was 23 years [27], [28].

Thalassaemia is a relatively rare condition in **Spain,** but increasing migrations may alter this in the coming years. A national registry of haemoglobinopathies was created in 2014 and the first report was published in 2017. The registry includes data on 715 patients of which the majority (615) have SCD and only 73 are recorded as having β-thalassaemia. The median age was 8.9 years (0.2–33.7) for thalassaemia. This age distribution is of course more in line with poorly developed health systems and developing countries. The rarity of the condition is the main reason, and the need for organised services is evident [29].

In the context of **Malaysia**'s data, based on the most recent report of 2020 on 8,681 patients, the majority, 64.45%, were in age groups between 0 and 24.9 years of age; the largest number of patients were aged between 10.1 and 14.9 years (17.46%). This is across the whole spectrum of severity including HbE/ β-thalassaemia, TM, TI, and HbH disease. Amongst TM, the peak age group is 10.0–14.9 years, while for HbE/ β-thalassaemia it is 15–20 years [30].

Similarly, the great majority of patients in **the Maldives,** which maintains a national registry, is also less than 20 years old (2014 data) (From TIF records).

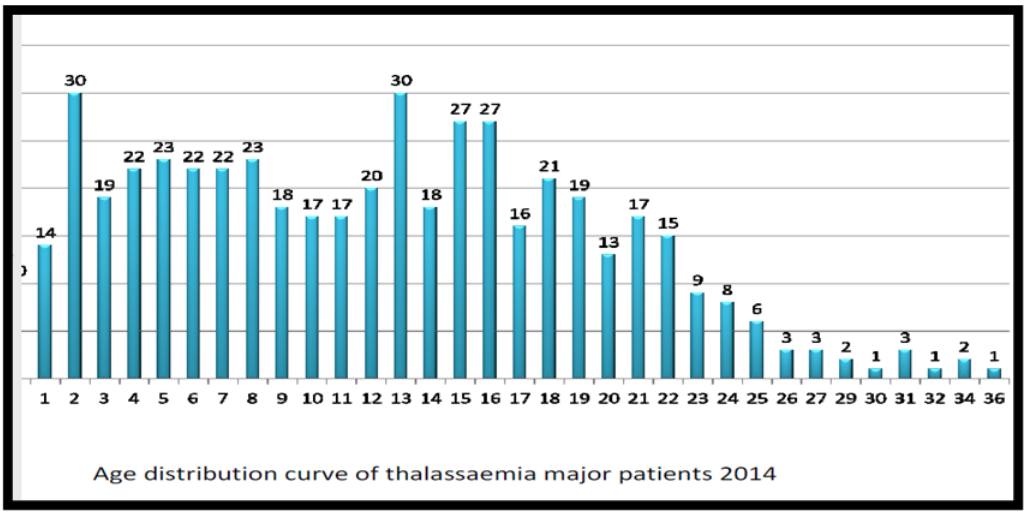

Figure 32. Age distribution curve of thalassaemia major patients in the Maldives (2014)

In **Turkey,** according to the national registry data of 2017, amongst 2,046 patients from 27 thalassaemia centres, 95% of whom are β-thalassaemia major and 11.5% NTDT, the age of 72% of the above patients is below 20 years of age [31].

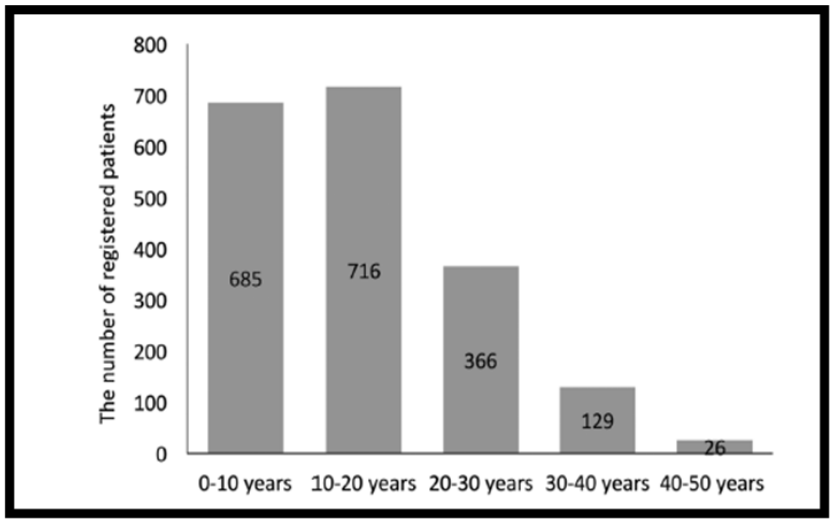

Figure 33. Age distribution of patients in Turkey (2017)

Sri Lanka has no national registry but in a recent report of 1,774 patients from 23 centres, 68.7% with β-thalassaemia major and 20.3% with HbE/β-thalassaemia and 2% with sickle cell/ β-thalassaemia had an age distribution as follows [32]:

- Mean age of β-thalassaemia major: 13.2 years
- Mean age of HbE /β-thalassaemia: 21.5 years

In **Thailand**, with an anticipated 40% of its population being carriers of thalassaemia (α and/or β and/or HbE), a retrospective analysis of the Children's Department at Siriraj Hospital in Bangkok, between 1974 and 2014, regarding morbidity levels extracted the following information through the national database:

- Out of a total of 4,303 patients with thalassaemia, 2,623, 317, 691, and 672 had β-thalassaemia/HbE, β-thalassaemia major, HbH disease, and HbH/Constant Spring, respectively.
- β-thalassaemia major had the highest death rate (7.5 times over population controls) followed by β-thalassaemia/HbE (3.1x), while patients with α-thalassaemia (HbH and HbH/HbCS) had the same mortality as the non-thalassaemic population.
- The majority of β-thalassaemia major patients died from anaemia, suggesting that most patients are receiving inadequate transfusion support (Figure 47) [33].

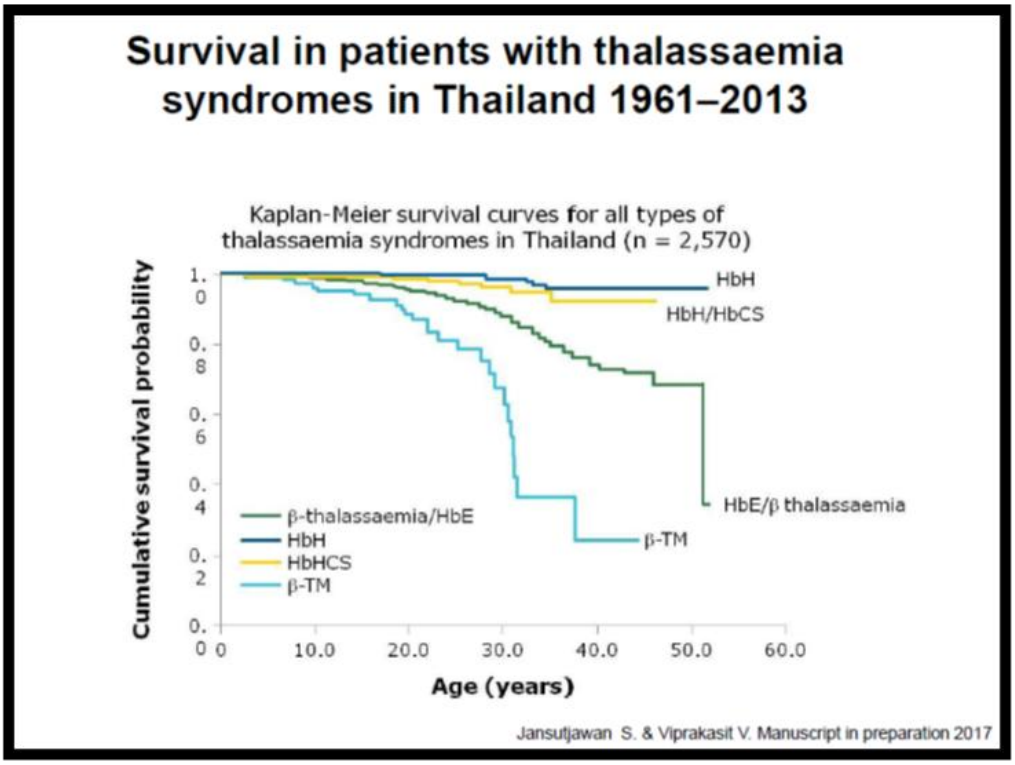

Figure 34. Survival of thalassemia patients in Thailand

These findings suggest that management, including transfusion therapy, which is the cornerstone of management of severe TDT syndromes across the world, and in particular in the developing world, where more than 80% of this patient population lives, remains quite suboptimal and indicates the need for urgent action. This is necessary to improve the standard of care and enhance the long-term survival of this population of patients with a highly prevalent condition. Contrary to many other thousands of rare diseases, for haemoglobin disorders there is ample and reliable knowledge and experience on how to effectively prevent the disease and appropriately treat the patients. The data described in this chapter demonstrate beyond any doubt that the patients' human rights for equal access to quality healthcare, as described within the UN and the WHO resolutions and/or declarations, and ratified by almost every country around the globe, are hugely violated.

Globally, taking into account the carrier rates and the calculated anticipated annual affected births, it appears certain that a significant percentage of TD patients die annually as a result of suboptimal care, including inadequate or inappropriate transfusions [33].

A study reported that approximately 25,000 TD children are born with β-thalassaemia worldwide each year, and only 3,000 (11.7%) actually receive blood transfusions [33]. As a direct consequence, many of these die each year, with the highest mortality rates being in the SEAR and EMR regions, estimated in 2008 by the WHO at 9,021 and 7,443 deaths each year, respectively [33].

Adverse events associated with BT can be acute (e.g., haemolytic, infectious shock, and severe allergic reactions) or delayed (e.g., TTI's alloimmunisation and disease related to iron load, cardiac, hepatic, and endocrine dysfunctions.) Absence of appropriate reporting grossly underestimates the incidence of such transfusion-related adverse reactions and poses challenges in promoting corrective measures.

Many developing countries have shown a substantial increase of VNRBD practices. Nonetheless, there is still a big gap between volume of blood collected and increasing clinical demand for blood. These countries share the common challenge of how to best utilise the limited financial resources to improve blood safety and availability for their populations.

In conclusion, appropriate/clinical use of blood, patient management programmes, quality systems, integrating health economics and evidence-based budgeting, and provision of updated training and education of healthcare professionals constitute all essential tools that are missing or partially absent from all countries, particularly of the developing world (low, lower-middle, and middle-income countries) [34]. These, in addition to inadequate country level data, consequent to the absence of national registries, patient healthcare records, and well-structured haemovigilance programmes, constitute multiple challenges.

TIF's Patients' Voice – A Global Perspective

The patients' perspective, reflected in the responses of 3,200 patients from 48 National Thalassaemia Associations, in 42 countries and five regions of the world, to a TIF questionnaire conducted between January–December 10, 2018, indicated the great challenges faced in the area of BT.

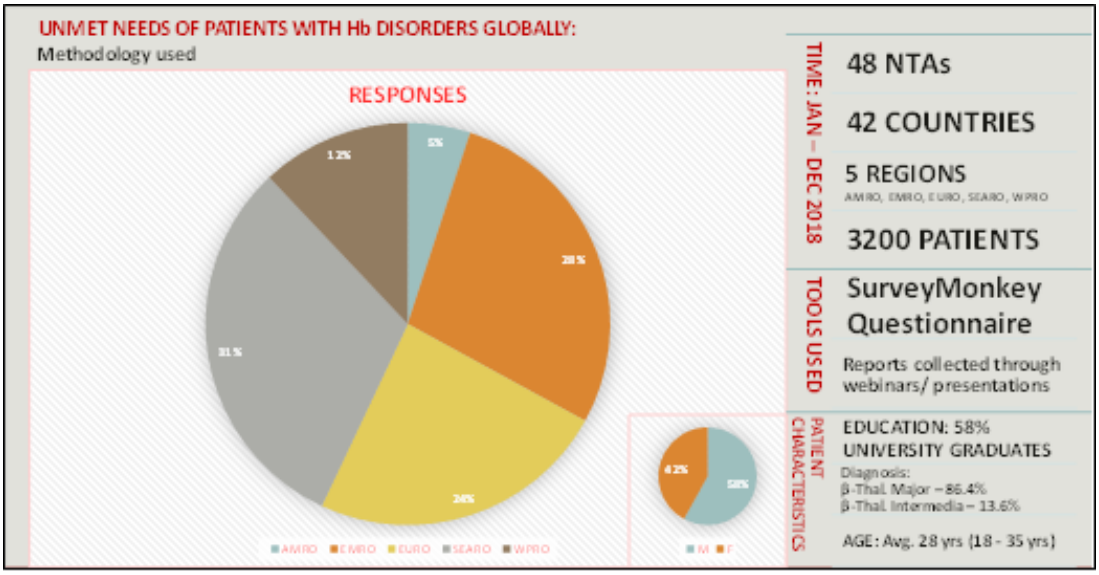

Figure 35. Response demographics to TIF's survey to document unmet needs

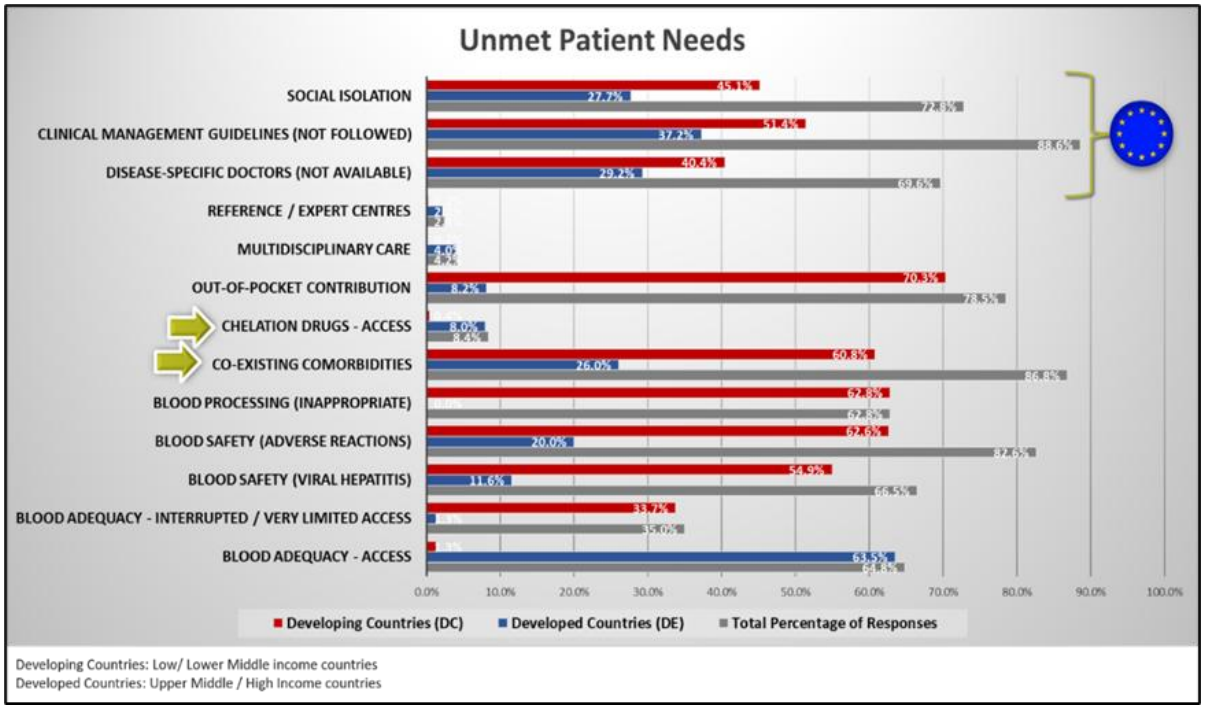

Figure 36. Unmet patient needs as documented by TIF's global survey.

The Patients' Voice – A Global Perspective

The patients' perspective, reflected in the responses of 2,200 patients from 48 National Thalassaemia Associations, in 42 countries and five regions of the world, to a TIF questionnaire conducted between January 2023–10 December 2023, indicated that, despite big or small improvements in a number of parameters studied, many great challenges faced in the area of BT therapy still exist and multiple efforts from a number of relevant stakeholders, including patients organisations, are needed to address them effectively.

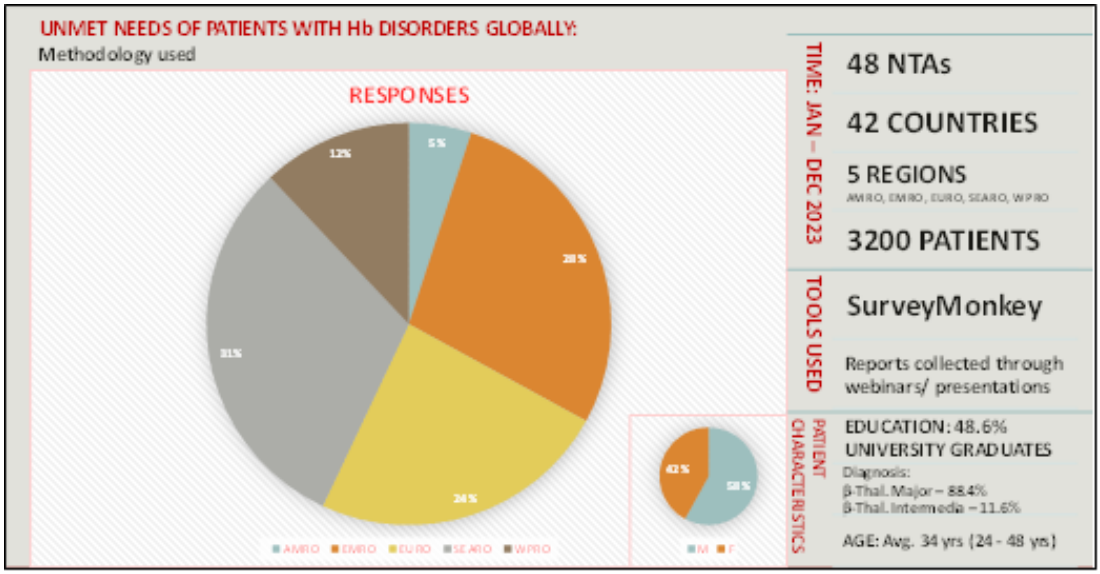

Figure 37. Response demographics to TIF's survey to document unmet needs

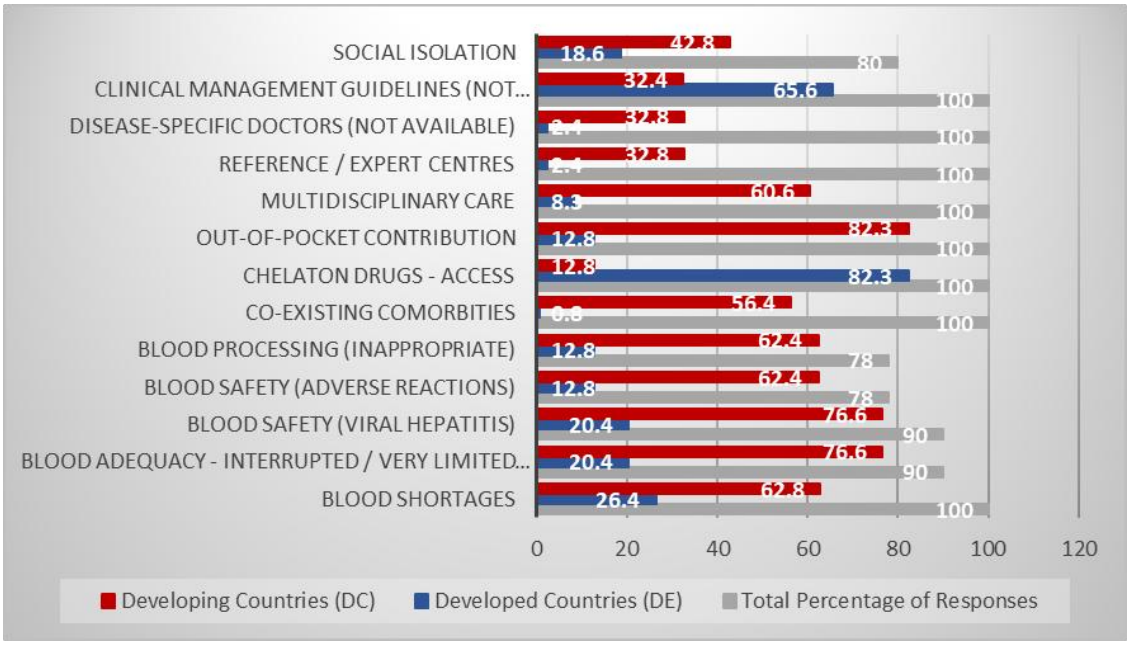

Figure 38. Unmet patient needs as documented by TIF's global survey

Last but not least, the WHO's *Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023* aims to provide a strategic direction to global efforts to address present barriers to the safety and availability of blood products. The WHO *Action framework* aligns with the WHO *13th General Programme of Work 2019–2023* and the WHO's *Delivering Quality-Assured Medical Products for All 2019–2023: five-year plan to help build effective and efficient regulatory systems*, and speaks to the implementation of a series of national, regional, and international resolutions, goals, and strategies to ensure safe blood as an integral component to the achievement of the Sustainable Development Goals. **Reaching the overall goal of universal access to safe, effective, and quality-assured blood products can only be achieved through effective collaboration between WHO, its Member States, and relevant organisations.** The WHO will be drawing on new and existing partners globally in its efforts to coordinate the implementation of this global framework to ensure access to safe blood products worldwide, in accordance with the following strategic objectives [35].

The six strategic objectives are:

1. An appropriately structured, well-coordinated and sustainably resourced national blood system
2. An appropriate national framework of regulatory controls, national standards and quality assessment programmes
3. Functioning and efficiently managed blood services
4. Effective implementation of patient blood management to optimize clinical practice of transfusion
5. Effective surveillance, haemovigilance and pharmacovigilance, supported by comprehensive and accurate data collection systems
6. Partnerships, collaborations, and information exchanges to achieve key priorities and jointly address challenges and emerging threats at global, regional, and national levels

TIF will continue to work with WHO, which is performing a significant role in this area, and with other relevant stakeholders to support the quality of transfusion therapy that patients with these conditions receive in every country of the world and in particular in the lower-middle income countries where more than 80% of this patient population lives.

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ANNEX I

Class of Recommendation

I. There is evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.

II. There is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.

III. The weight of evidence is in favour of usefulness/efficacy and therefore should be considered.

IV. The usefulness/efficacy is less well established by evidence/opinion and therefore may be considered.

V. There is evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Level of Evidence

A. Data derived from multiple randomised clinical trials or meta-analyses.

B. Data derived from a single randomised clinical trial or large non-randomised studies.

C. Consensus of opinion of the experts and/or small studies, retrospective studies, registries.