



## 8. MULTIDISCIPLINARY CARE AND REFERENCE CENTRES IN ADDRESSING HAEMOGLOBIN DISORDERS

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### INTRODUCTION

The lifelong and multi-organ nature of transfusion-dependent thalassaemia is well reflected in the very content of this book. As patients advance in years, the basic needs in blood transfusion and iron chelation, even if and when they are provided appropriately and in accordance with international standards, become gradually inadequate to sustain life, maintain wellbeing, and achieve social integration. For this reason, specialists in several medical disciplines including, but not confined to, the heart, liver, and endocrine system, are called upon to contribute by monitoring and proactively managing iron toxicity and organ dysfunction in their field of expertise [1]. These considerations and needs lead to significant and multiple challenges in the organisation of integrated services so that the best possible conditions for patient care are achieved.

Historically, and based on TIF's experience through its global work, the need for establishing day transfusion centres for patients with transfusion-dependent thalassaemia (and other haemoglobin disorders) that are separate from the main haematology or paediatric wards, where they were "naturally" admitted initially, arose first in areas and places where patients with these disorders were treated in sufficient numbers. This prompted policymakers and healthcare professionals to recognise and respect that the needs of these patients are quite different from those of patients with malignant haematological conditions. So, through the years, different arrangements (as seen in Table 1 below) were promoted with regards to providing more targeted, specialised service to patients with haemoglobin disorders.

*Table 1. Provision of a specialised services to patients with haemoglobin disorders*

1. Within haematology departments: Development of RBC (non-malignant) clinics separated from malignant haematology services.
2. Dedicated space within paediatric units where patients are treated well into adolescence and in many cases into adulthood.
3. Dedicated space within haematology units (amongst malignant haematology/oncology patients) or transfusion centres of hospitals.
4. Development of "independent" thalassaemia units/centres based as outpatient day care services, attached to/associated with tertiary level hospitals.
5. Within general paediatric or paediatric/oncology or general haematology wards/clinics without any arrangement for a dedicated space or development of specialised services.
6. Development of centres run by NGOs in collaboration with pharmacists/Red Cross/ and other health care professionals.

Provision of specialised care that extends beyond the basic care of transfusion and iron chelation began to be recognised as an absolute necessity in those centres where:

1. There was high disease prevalence amongst the population, whether in the indigenous population (Cyprus, Greece, Italy) or in the well-established and integrated migrant population [2] (e.g., UK, France).
2. The scientific community and the national health competent authorities recognised these as important disorders with medical, public health, social, and economic repercussions, which need effective national policies for their prevention and appropriate management.
3. As a result, these disorders were prioritised on the country's national health agenda and disease specific policies and nationally coordinated and supported programmes were developed allowing patients to grow, age, and have a good quality of life.

The integration of specialised multidisciplinary care services into the management of patients with these disorders brought about the need for specialised, disease-specific training/education of the different medical specialties and many and multiple organisational challenges to ensure appropriate co-ordination. Where such steps were taken and where these led to successful, meaningful integration of services, including active research activity, Reference or Expert Centres began to spring up.

Such centres developed first in the 1980s in Mediterranean countries Cyprus, Greece and Italy, and then in the UK and France, although more in the context of Rare Diseases (RDs) national strategies. The knowledge and experience of what "optimal" care entailed for these disorders, as well as the better understanding of their pathophysiology and medical needs, were in those early days quite limited. The development of Reference/Expert Centres was guided almost solely by the needs of the growing number of patients who survive and require services, the patient care pathways, and the quality standards that these centres developed through the years. Experience and knowledge of the desired outcomes became the core basis for setting the standards and defining the role a Reference/Expert centre for Haemoglobin Disorders. Gradually these first centres were officially recognised not only for their reputation but also for their results, and so they were assigned by the country's national competent authorities as Reference or Expert Centres. Patients with haemoglobin disorders began to be referred to these centres by their treating physicians for consultation, second opinion, or for receiving the specialised services that did not exist in their own area, region, or country.

As national competent authorities and healthcare specialists across the world began to acknowledge the value of effectively addressing these disorders and to gather knowledge and experience at the national level, clinics/centres of variable levels of expertise, offering different ranges of services of variable quality standards, began to spring up, particularly in the 1990s, in different countries across the world. Most of these, however, provided mainly basic care, including blood transfusion and iron chelation, while multidisciplinary care (MCD), which is essential for the growing patients and a major component of a Reference/Expert centre, was and still is largely lacking.

In most countries, where more than 80% of the patients with these disorders live, there is limited medical and public health infrastructure, including hamatology and blood transfusion services. They, very importantly, lack universal health and social care coverage. Deficits are related mainly to weak economies and their focus on other health priorities, including communicable and common non-communicable diseases (NCSs), and these factors have not allowed the quality advances for haemoglobin disorders to take place

In a few of these countries, non-government organisations (NGOs) were created to promote unmet needs and some were even encouraged by competent national authorities to contribute to the management of haemoglobin disorders, giving them either financial and social support or actually developing clinical services. These have developed through the years, in collaboration with medical and other healthcare professionals. However, important services for patients are confined to transfusion and iron chelation therapies. Certainly, in such settings, provision of any extended specialised treatment is not possible. Patients, therefore, need to be and are referred to see medical specialists in hospital settings in an uncoordinated manner. However, these specialists may not have specialised knowledge in the treatment of haemoglobin disorders.

TIF, for more than 35 years in more than 60 countries across all regions of the world, has worked to bring awareness that the development and integration of MDC services for the management of patients with these disorders. However, the promotion and establishment of Reference/Expert Centres is far from being adopted or implemented for the majority of the global patient population. Such advances can only happen if and when the basic, essential medical care across a country has achieved those quality standards that allow patients to grow satisfactorily, assume social integration, and have a decent quality of life, avoiding premature death. This prerequisite can only be achieved when the medical and public health infrastructures and quality standards are adequately strengthened in the context, as previously mentioned, of a universal healthcare system. To date, such improvements are still to happen in most of the countries, particularly in the developing world where the majority of patients with these disorders live. The majority of patients are young and do not reach beyond the second decade of their lives; this alone confirms the fact that they are still receiving suboptimal basic care.

Bringing fragmented services together in an organised, collaborative manner and adopting international guidelines and standards of care are indeed very challenging, but it has been demonstrated beyond any doubt that such an effort maximises the patients' benefits and facilitates their very cumbersome treatment pathways with timely interventions. Such an approach of Integrated Care Pathways is reflected in the improvement of clinical and social outcomes [3], which has already happened in some countries. Achievements that have been experienced are related to healthcare planning of each country's healthcare system in which public health officials consider cost-effectiveness [3, 4] of optimal care.

Basic to the success of multidisciplinary or interdisciplinary, integrated management of thalassaemia patients is the quality of the relationship between the haematology (or paediatric) team and the various supporting physicians across medical disciplines. The latter must be well organised and coordinated, and interested in becoming involved and acquiring experience in these conditions, and very importantly they need to be supported and facilitated by the country's healthcare system. Random consultations do not contribute to efficiency and effectiveness because accumulation of sufficient experience and knowledge requires a dedicated group of medical experts in the MDC, who will indeed be willing to receive education and better understanding of the management of haemoglobin disorders for those aspects that fall within their medical speciality.

In many centres the multidisciplinary approach to thalassaemia is even misunderstood as having a specialist to refer to once a complication has arisen. The whole concept of MDC and of a Reference Centre lies in the availability of proactive, quality, and specialised interventions. In this context, different medical specialists should be involved well before the appearance of complications, i.e., early in the patients' life. In a multi-organ disease like thalassaemia, there is no doubt of the necessity and benefits of this approach, and TIF has focused considerable attention on promoting this concept and on creating those tools and advisory groups that could support it.

Furthermore, it is more functional if all members of the MDC team belong/have medical attachments to the same hospital. This is because meetings of the members of the MDC group must occur regularly and also when

an emergency decision needs to be taken for a patient's health/condition. It is understood, however, that this may not be possible, but teleconferencing technology and telemedicine tools have given us valuable solutions for such challenges [5].

## THE ROLE OF THE COORDINATOR/LEADERSHIP

In order to achieve effective functioning of the interdisciplinary team, which could be reflected in the desired outcomes of early detection and reversal or minimisation of organ damage, the principles of teamworking and good communication must include first of all a competent team coordinator who is an expert physician in the clinical management of haemoglobin disorders. This should be the lead physician (haematologist, paediatrician etc.) who is responsible for the routine, everyday care and who sees each patient most often. Mature leadership will ensure that scheduled visits to each specialist are implemented and that in turn different specialists communicate timely and comprehensively report their results to allow the treating specialist to reach a decision on any treatment adjustments.

As the issue of communication is central to the functioning of the MDC team, ensuring its effectiveness is important, and this can be achieved in a number of ways, for example:

- Joint clinics
- Regular team meetings
- Case conferences
- Sharing of results, along with interpretation and discussion for joint decisions
- Using electronic disease-specific medical records with full access to all members of the team
- **Involving patients in the discussions and decisions which concern their lives is critical and every effort should be made by all to establish a well-structured and regular programme of active and meaningful patient engagement.**

Some of the key barriers that may prevent the the MDC to work effectively include: (i) a lack of appropriate and structured coordination and efficient communication; (ii) a lack of or poor involvement of dedicated physicians across medical disciplines; (iii) inadequate implementation of common shared decisions; (iv) a lack of sufficient time given by the involved physicians to interact productively and discuss the cases comprehensively; and (v) inadequate access to, or lack of, well-informed patient records.

Table 2 presents an example of the structure of an interdisciplinary team for the care of haemoglobin disorders was extracted from some well-established European Reference Centres [7, 8] with successful patient outcomes.

*Table 2. Interdisciplinary team for the care of haemoglobin disorders*

Specialty	Description
<b>Haematologist/ Paediatrician/ Internist</b>	Usually, the physician in charge of the routine care, including monitoring of iron load. Usually coordinates the multidisciplinary team. Is supported by other more junior physicians according to the number of patients.
<b>Specialised Nurses</b>	Specially trained and experienced haemoglobinopathy nurses who, apart from routine duties like supervising blood transfusions and triage of patients, because of their closer contact with patients, have a significant role in counselling and psychosocial support.
<b>Cardiologist</b>	A special interest and experience in the cardiac complications of thalassaemia. Monitors all patients from childhood, collaborates with the lead physician on any management modifications and takes charge when complications like arrhythmias arise.
<b>Endocrinologist</b>	Monitors all patients usually from early adolescence for these very common complications of thalassaemia. Apart from liaison with the multidisciplinary team, there is collaboration with gynaecologists in the case of infertility and pregnancy. Also, part of the team managing bone disease.
<b>Hepatologist</b>	Liver disease is increasing in the ageing thalassaemia population. Liver function is monitored from an early age by the clinic team but persisting disturbance of liver function, iron overload, and viral hepatitis require a consultation with a liver specialist
<b>Psychologist/ Social Worker</b>	These are essential supportive services and should be part of team at all times. Many issues may not be recognised by other physicians or nurses, and periodic visits to the psychologist could bring matters to the surface for all patients. They are not just for referral when acute emotional problems arise. Especially where universal health coverage is not available, financial hardship and social isolation can contribute to negative patient outcomes. Support for the healthcare team may also be necessary.
<b>Obstetricians</b>	A member of the collaborative team in intended and ongoing pregnancies. Pre-pregnancy counselling, along with care mainly from a haematologist, endocrinologist, and cardiologist, is essential, but teamwork during gestation is also necessary for good outcomes.
<b>Dental Care</b>	All patients should be routinely monitored for dental and maxillary complications at least yearly.

## Specialised Nurses

The role of nurses cannot be overemphasised since they are the professional staff most in contact with patients as they supervise blood transfusions as well as other clinical procedures; they are also usually present during the patient's interview with the treating physician. The psychosocial care needs of children and their families, from the perspectives of nurses, were explored in Jordan. In this qualitative study, nurses indicated their belief in holistic care as the patients face various challenges associated the condition and its treatment, as well as social burdens, and therefore they need social support from the community. The nurses recognised the need for special knowledge and skills focusing exclusively on thalassaemia and its treatment, including communication skills as an effective way to interact with children and their families and build a therapeutic relationship with them. Although nurses believe in the importance of providing psychosocial support, the need for specialised individuals was recognised [9]. Studies such as this give a clear indication of the experiences of the nursing staff, but also for the need of psychosocial support offered by a team of professionals within a service for haemoglobinopathy patients.

The mental health needs of haemoglobinopathy patients have been recognised as being frequent and to play a significant role in the quality of life, which should be a major goal of holistic care. A recent report from Saudi Arabia demonstrated depression in 45.4% of sickle cell patients, while the rate of anxiety was 22.7%. This is a considerable burden, which the multidisciplinary service must address [10]. The role of nurses in controlling blood transfusions, including safety, and medications is also of primary importance.

The role of community nurses in raising awareness concerning thalassaemia, which can benefit both the blood donation programme and the prevention programme, is recognised and utilised in few locations [11].

## Endocrinologists

Endocrine disorders are also found in most multitransfused patients in whom iron overload is almost unavoidable. In 89 patients with thalassaemia major from the Eastern Province of Saudi Arabia, despite their young age (2 to 30 years, mean age 15.5 years), primary hypothyroidism was found in 17% (subclinical hypothyroidism in 37.7%) and diabetes in 13.6%. The rates were lower in those compliant to chelation therapy [12]. However, several factors affect the endocrine glands in thalassaemia, and so many patients develop more than one endocrinopathy [13]. This is a collection of co-morbidities affecting the ageing patient, which require specialised attention and add to the burden of disease and the requirement for care to achieve the desired outcomes.

Likewise, bone disease, as measured by bone mineral density (BMD), is a frequent and painful addition to patient experience. In Indonesia the percentage of adult thalassaemia major and intermedia patients with low bone mass density was 68% at a median age 25 years (range 18-68 years) [14].

In conditions which affect quality of life to such an extent, like bone pain, all means must be taken to investigate and diagnose early bone disease so that patients can receive treatment and relief measures.

## Cardiologists and Hepatologists

Cardiologists and hepatologists are basic members of the MDC team since heart and liver complications are not only frequent but are also major causes of amenable mortality, along with serious infections [15, 16, 17].

Many other important healthcare specialists are needed particularly when the centres are also treating sickle cell disease (SCD) patients, which is the usual case in most centres across countries. Some of the key specialist services to which treating physicians and patients should have timely and well-coordinated access in this case are included in Table 3 below (which is by no means exhaustive):

*Table 3. Indicative list of key specialist services*

<ul style="list-style-type: none"> <li>• Erythrocytapheresis</li> </ul>	<ul style="list-style-type: none"> <li>• Orthopaedic service</li> </ul>
<ul style="list-style-type: none"> <li>• Pulmonary hypertension team</li> </ul>	<ul style="list-style-type: none"> <li>• Specialist imaging including:                             <ul style="list-style-type: none"> <li>○ MRI tissue iron quantification of the heart and liver with regularly standardise software to ensure accuracy and reliability of iron measurement</li> <li>○ Trans-cranial Doppler ultrasonography (children)</li> <li>○ Polysomnography and ENT surgery</li> <li>○ Bone marrow transplantation services</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• Fertility, contraception and sexual health services</li> </ul>	
<ul style="list-style-type: none"> <li>• Consultant neurologist</li> </ul>	
<ul style="list-style-type: none"> <li>• Consultant ophthalmologist</li> </ul>	
<ul style="list-style-type: none"> <li>• Consultant nephrologist</li> </ul>	
<ul style="list-style-type: none"> <li>• Consultant urologist with expertise in managing priapism and erectile dysfunction</li> </ul>	

## THE PLACE AND ROLE OF THE PATIENT IN THE MDC OF HIS/HER CONDITION

In the multidisciplinary team, one essential member, constituting the central component, is most frequently forgotten or his or her importance is under-recognised. This is the patient (or parent in the case of children). The patient's involvement is important for the carer-patient relationship and in particular with regards to the need to support his/her self-management and for the continued patient concordance to prescribed treatment. There is need to listen to and understand patient concerns [18]. The patient, however, requires education, continued provision of reliable and up to date information, along with strong encouragement and empowerment to take charge of his/her life under specialist guidance. Treatment planning should take into consideration as far as possible patient preferences, choices, and lifestyle so that every effort to reach concordance is made. The active and meaningful engagement of patients is substantial in the better understanding of the patient's needs and, thus, in the better planning and more appropriate reforming of related policies. The aim for every government and treating physician is certainly for their patients to achieve good health and quality of life, associated with a high level of social integration. And indeed, this can only happen if and when the patient remains at the centre of decisions. Patient involvement aims to improve patient experience and achieve greater quality of care that is comprehensive and considers physical, socioeconomic, mental, and emotional well-being [19].

## REFERENCE OR EXPERT CENTRES FOR HAEMOGLOBIN DISORDERS

Considerable work on this topic has been conducted mainly by the European Commission and particularly since the 1990s in the context of its work on promoting quality services for RDs across the EU. The many and complex challenges faced by patients/families and treating physicians in the early and accurate diagnosis, management, and monitoring of RDs are similar to those for haemoglobin disorders, which in many settings are classified as RDs. Haemoglobin disorders are different in that, contrary to the many other RDs, ample and reliable knowledge and experience exist with regards to early and accurate diagnosis, specialised monitoring, appropriate management, and effective prevention, resulting in improved outcomes [15, 16, 17].

The European Commission has recognised RDs as a priority action area since the mid-1990s, and since then, the different EU initiatives addressing RDs have been predominantly focusing on bringing together scattered resources and expertise across Member States. This is an effort that is certainly needed in the case of haemoglobin disorders in Europe and in countries with developing economies where the majority of patients with these disorders live. In addition, such EU initiatives and policies aimed at strengthening and empowering research activities directed at providing more innovative drugs and therapies for RDs. Importantly, the EU policies directed every Member State towards developing national plans to address more effectively the needs of RDs. Within this work, the European Commission established a special committee of experts, the EUCERD (European Union Committee of Experts on Rare Diseases), which focused work on developing quality criteria for centres of expertise for RDs in member states (2011) [20] and recommended establishing RD European Networks (ERNs) (2013) [EUCERD, 2011]. In this context the idea of ERNs was integrated into EU Directive 2011/24/EU to apply EU patients' rights in cross-border healthcare, acknowledging that this is a major step towards promoting more effectively the sharing of knowledge/expertise and best practices and the creation of clearer structures and networks in the area of RDs, by bringing together highly specialised providers across the EU (European Parliament, 2011) [21].

Of the 24 ERNs established to cover 24 different RDs or families of RDs, aiming to share best practices for their care and cure, the European Blood Network (EuroBloodNet) is the one focused on blood disorders including haemoglobin disorders [22]. Considerable work is being undertaken by this network to pool together knowledge and expertise from across the EU on these disorders (EuroBloodNet, 2021).

In the context of the above work of the EU, a number of relevant projects were launched, including the European Network for Rare and Congenital Anaemias (ENERCA), covering haemoglobin disorders and other rare anaemias, with which TIF was a major partner. Through this activity, TIF, along with other European and international medical and scientific experts in rare anaemias, contributed to the completion, amongst other important deliverables, of a book titled *The Recommendations for Centres of Expertise in Rare Anemias: A White Book* [7]. This document reflects the extensive work that the EU has undertaken for over two decades for the benefit of rare anaemias including haemoglobin disorders, and the book is a major contribution towards the creation of a much-needed European infrastructure of expertise around rare anaemias. The authors of this chapter of the 4th edition of the *Guidelines for the Management of Transfusion Dependent Thalassaemia* felt that the above description was essential, as the experience gained through the years by EU member countries in this field can be extended to constitute a sound basis for countries outside and well beyond Europe to build on.

Some of the benefits outlined below in Table 4 are in the context of the EU directive (2011/24/EU) (mentioned above) on facilitating and safeguarding the rights of patients with RDs, including rare anaemias and haemoglobin disorders, to obtain cross-border healthcare. They underscore the importance of developing and pooling together specialised knowledge and experience, as well as of networking between centres of expertise. From these ideas and policies, tailored to the needs and prevailing situation across any country or region of the world, patients with haemoglobin disorders, the healthcare specialists, and the healthcare systems in general could benefit significantly, as has been the case with the RDs across the EU.

*Table 4. Benefits of cross-border healthcare in the EU for patients with rare diseases*

- Providing patients and health professionals access to experts and expertise throughout all European member states, regardless of the country of origin or practice, thereby reducing inequalities and maximising the cost-effective use of resources.
- Implementing epidemiological surveillance throughout the EU that gathers comparable data on patients affected by RAs and launching preventive programmes for tackling RAs.
- Fostering best practices for prevention, diagnosis, and clinical management.
- Promoting the dissemination of knowledge, the sharing of expertise, supporting research, and increasing awareness of RAs.
- Facilitating the transposition of the Directive 2011/24/EU of 9 March 2011 on the application of patients' rights in cross-border healthcare. The European Reference Networks (ERN) between healthcare providers and Centres of Expertise is a main point of interest of the directive, especially for rare diseases. The networks will be a tool to "improve the access to diagnosis and the provision of high-quality healthcare to all patients who have conditions requiring a particular concentration of resources or expertise and could also be focal points for medical training and research, information dissemination and evaluation, especially for rare diseases".

TIF, as a patient-driven umbrella organisation, has a constitutional mandate to continually identify ways and tools to promote the quality of care provided to patients with haemoglobin disorders [5]. TIF has thus focused

particular attention and considerable work on its educational programme since its establishment in 1986, and in this context, TIF has initiated a new project titled “TIF’s Certification Programme”, focused on the empowerment of national competent authorities, healthcare professionals, and patient communities to include in their management strategies the promotion of the MDC component and the establishment of Reference/Expert Centres. In this new programme international thalassaemia experts have been recruited, standards for centres have been discussed, and in 2025, a programme of visits to centres that have volunteered to become Reference Centres began.

TIF’s vision through this project is to first identify and develop an extended list of centres/clinics within a country that treat patients with haemoglobin disorders, followed by an effort, supported by TIF’s International experts, to classify them based on set criteria (see below) of the range and quality standards of the services each centre provides [5]. The aim of TIF is to (i) identify those centres already qualified to perform the role of a Reference Centre today; (ii) to provide, through its scientific advisors, support to those in treating centres that have the potential to upgrade their services; (iii) to support other treating centres to reach at least acceptable levels of quality basic care for their patients; and (iv) very importantly to support the networking between them at the national level. The Reference/Expert Centres at regional and international levels will be promoted as practical teaching centres for healthcare professionals of all needed disciplines for multidisciplinary care.

The programme focuses on the application of specific quality standards for Reference Centres involved with the care of patients with thalassaemia and other haemoglobin disorders. The TIF Quality Standards are based on the general principles already developed by the relevant organisations, as outlined in Table 5 below.

*Table 5. General principles used for the development of TIF Quality Standards*

- ✓ The Joint Commission International (JCI): *Survey process Guide for Ambulatory Care* (3rd edition, 2015); European Union Committee of Experts on Rare Diseases (EUCERD): *Quality Criteria for Centres of Expertise for Rare Diseases in Member States* (2011); and EUCERD *Recommendations on Rare Disease European Networks* (2013)
- ✓ Guidelines for Good Clinical Practice
- ✓ US Institute of Medicine: *Quality Improvement*
- ✓ US Department of Health and Human Services, Health Resources and Service Administration: *Quality Improvement*
- ✓ UK NHS, Peer review of health services for people with haemoglobin disorders: (2015 Review)
- ✓ TIF *Guidelines for the management of transfusion dependent thalassaemia* (3rd edition, 2014)
- ✓ TIF *Guidelines for the management of non-transfusion dependent thalassaemia* (2013)
- ✓ Specific standards, such as the “International Collaboration for Transfusion Medicine (ICTMG): Red blood cell specifications for patients with haemoglobinopathies: a systematic review and guideline” (2017)
- ✓ ENERCA White Book
- ✓ European Guidelines for the certification of Haemophilia Centres EUHANET 2013.
- ✓ Current literature reviews

*The criterion for recognising any centre as a Reference/ Expert Centre is certainly the quality of services, with emphasis on patient-centred care and not just availability of various technical components necessary for the care of thalassaemia (and other haemoglobin disorders). It includes following national or international evidence-based*

*guidelines, which allow for good patient outcomes. The services that should be provided by a Reference/Expert Centre may include (but are not confined to):*

1. *The capacity to provide expert diagnosis of the disease, as well as its long-term complications.*
2. *The capacity to provide expert case management, based on best practice guidelines, including a multidisciplinary approach and psychosocial support. These requirements imply experienced healthcare personnel in adequate numbers to ensure continuity of care.*
3. *Healthcare workers should be in a structured environment with clearly defined roles and hierarchy.*
4. *Maintain a patient registry with ability to report patient outcomes and other epidemiological information. Electronic information systems must be regarded as essential tools for the provision of quality services.*
5. *Have auditing of clinical and laboratory guidelines.*
6. *Serve a sufficient number of patients to maintain staff experience. What is a sufficient number of patients is not clear, but a consensus should be reached – initial proposal is for at least 50 transfusion-dependent patients.*
7. *Provide patients with sufficient knowledge and information to promote partnership models and self-management support.*
8. *Make a significant contribution to research as evidenced by peer-reviewed publications.*
9. *Establish networking with secondary treatment centres to provide education and share knowledge and expertise, as well as to provide expert opinion on challenging cases, and also with other centres of expertise cases.*
10. *Establish networks/collaborations with other Reference Centres outside the country – regional and international – to share best practices.*
11. *Maintain close links with patient organisations and other community resources at national, regional and international level.*
12. *Make a major contribution to educational activities.*
13. *Provide evidence of the improvement of survival outcomes, clinical outcomes, and patients' quality of life and satisfaction through specific tools including patient-reported outcomes.*

In addition, (i) there must be evidence of government and more specifically health system support, (ii) free access of patients to treatment modalities, (iii) the centres' administrative structure, working hours, and clinical space availability must also take into consideration the patient experience, (iv) deficiencies and gaps must be promptly identified and corrected, (v) the experience and knowledge of professional staff must be regularly assessed, and (vi) the patient perceptions of the quality of the services and the relationship with the staff should be monitored regularly through professional tools and taken into account in quality assessment.

TIF Standards, as described in TIF's project for assessing the quality of the services provided to patients with haemoglobin disorders in the different domains comprising a Reference Centre, are outlined in Tables 6–12 below.

*Table 6. TIF Quality Standards for Reference Centres – Governance criteria*

## 1. Governance

- The existence of a hierarchical structure, ordained by law and policy. This should include a chief executive/ managing director and a professional team, which is coordinated and includes multidisciplinary services, recognising the complex pathology of haemoglobin disorders.
- A clear definition of the centre's mission and the existence of policies and programmes to fulfil the mission.
- Ensuring staff qualifications, experience, and continual education.
- Monitoring and evaluating the functions of the centre by the management, including staff performance and patient safety.
- The existence of plans for quality improvement and advocacy to health authorities.
- Connection with patient support associations and patient representation on advisory bodies, taking into account all stakeholders' views regarding matters of priority and focus on any quality improvement activity.
- All decisions are based on data obtained through patient records and outcomes, as well as any new developments that have been noted through publications and trials.
- A culture promoting ethical practices in all aspects of administration and clinical care, considering internationally accepted patients' rights.

*Table 7. TIF Quality Standards for Reference Centres – Safety criteria*

## 2. Safety

- Staff education on safety is programmed.
- Patient identification is clear in individual records (electronic or paper based) of blood transfusions and laboratory results.
- There is effective patient communication and explanation of all interventions.
- Haemovigilance and pharmacovigilance are practised, including drug safety alerts.
- There are evidence-based hand hygiene guidelines.
- There are measures to reduce accidents, such as falls, in the centre. A secure environment is planned and regularly inspected. Hazardous material handling and disposal (such as of needles) are part of the centre's daily procedures.
- There are treatment rooms and resuscitation equipment.
- The country's fire services have certified the centre for fire safety. This includes regular testing of any devices required for fire control.
- Cigarette and other smoking is forbidden on the premises.
- Emergency procedures are in place in the event of power and water cuts or contamination. Monitoring water quality is performed regularly.

*Table 8. TIF Quality Standards for Reference Centres – Access to care criteria*

**3. Access to Care**

- The centre clearly serves benign haematology patients and does include malignancies, as they constitute a dangerous and vulnerable cohabitor.
- Patient flow: there must be adequate numbers of patients of each diagnostic group: at least 50 thalassaemia patients and/or 50 SCD patients for the centre to be regarded as experienced.
- Continuity of care is safeguarded by low staff turnover and the presence of experienced and qualified caregivers.
- Clinical records with lifetime data are kept.
- Multidisciplinary care is provided with a referral system where necessary, and there is collaboration with in-patient services.
- Networking with secondary centres, as well as with other centres of excellence, national or international, is an added value. A twinning programme with an academic centre is also an additional advantage.
- Any existing electronic health record must fulfil all the requirements of patient safety, including patient consent, confidentiality, and anonymisation in data storage and sharing of data for research.
- Barriers to patient access, including distance, language, cultural or religious barriers, are considered and dealt with.
- Respect for patient rights and time is a must in all cases.
- Informed consent for all procedures is obtained.

*Table 9. TIF Quality Standards for Reference Centres – Doctor: Patient Partnership criteria*

**4. Partnership Model**

- Adequate information about the disease and any treatment decisions, including possible side effects, is always provided to patients and their families.
- Patients are given choices about their treatment.
- Self-management is encouraged.
- Special attention to patient adherence is given and the patients supported appropriately.
- Workshops for patients/families are held regularly, at least once a year.

*Table 10. TIF Quality Standards for Reference Centres – Existence/Implementation of Guidelines criteria*

## 5. Guidelines and Standards for Clinical Care

- Evidence-based national guidelines, put together by experts in the field, or international guidelines (e.g., TIF's) are used in the centre and adhered to.
- Pain screening is performed, and a pain management system is in place.
- Assessing the quality of laboratory and other technologies used to monitor patients is the responsibility of the clinical team, which must alert the providers of any divergent or inaccurate results.
- Infection control procedures are part of the clinical standards of the centre.
- Availability of food during day care is necessary and the quality and nutritional value must be monitored.
- Blood transfusion procedures and standards according to international directives are kept.
- Any medical treatment, such as IV fluids and exchange transfusions, are provided according to standards that ensure patient safety.
- Continual medical and other professional education are part of the centres long term programme.
- Staff qualifications, skills, knowledge, and experience are defined and described, along with the job description of each.
- Staff/patient ratio is defined approximately as 1 doctor per 100 patients and 1 nurse per 50 patients.

*Table 11. TIF Quality Standards for Reference Centres – Actions for quality improvement criteria*

## 6. Quality Improvement

- Having surveyed all aspects of the service, and having noted all strengths and weaknesses, the survey team will present a report and make suggestions for quality improvement where necessary.
- Quality improvement is a systematic approach to upgrading services and correcting any deficiencies in the governance, structure, and functions of the service. "Quality improvement includes better patient experience and outcomes, by changing provider behaviour" [9] (Dr John Øvretveit: "Does improving quality save money?" [10])
- The way in which change is introduced and implemented is a matter of concern and may require expert advice. In this process the following are considered:
  - External influences, such as governmental policies or interest, budgetary support, professional requirements.
  - Understanding the issues involved at all levels, including why a problem exists.
  - Setting goals and monitoring progress.
  - Choosing the tools to bring about change. These could be skills development, computerisation, updating guidelines etc.
- Full staff engagement is necessary. There often needs to be a multidisciplinary approach to change-making.
- The patient's voice must be involved at all stages of quality improvement. Patients/families can also effectively monitor the effects and benefits of change since they experience the whole 'patient pathway'.
- Studying other centres' experience in change-making: Have the changes been successful elsewhere?

*Table 12. TIF Quality Standards for Reference Centres – Information Management criteria.***7. Information Management**

- Patient records (paper or electronic) are kept with due consideration to confidentiality, security, and accuracy of data.
- The retention time of records in a haemoglobinopathy setting is lifelong, since the current clinical condition may be influenced by past events and disease control (such as iron levels).
- Standard diagnosis codes are kept (e.g., ICD10).
- E-health systems are assessed and tested prior to implementation, for quality and patient safety.
- Protection against loss, unauthorised access. or use is ensured.
- Policies and procedures concerning record keeping are clearly directed to all the staff, through documents and training.
- The patient should be clearly identified on each record.
- Those authorised to have access to clinical records are clearly defined.

Through this Certification Programme, TIF may provide:

- On-site audit of the centre's performance by external reviewers with regards to the quality of the processes, outcomes, and structures involved in the care it provides to haemoglobinopathy patients.
- Technical support and recommendations for improvement to reach desired outcomes.
- Networking opportunities with other regional and international centres for the exchange of knowledge and expertise.

Successful centres are granted the Certificate of TIF Collaborating Reference Centre for Haemoglobinopathies and provided with needs-based technical support and personalised recommendations for continuous improvement in order to reach the desired outcomes.

The Certificate is valid for a period of 2 years before the evaluation team is called back to the centre to ensure that quality of care is maintained.

*Table 13. The key goals of this programme***THE KEY GOALS OF THIS PROGRAMME ARE TO:**

- ✓ Provide authoritative scientific opinions and advice on key topics in clinical management, including accurate diagnostic techniques, blood safety, correct iron monitoring, and dealing with complications through a multidisciplinary approach in order to achieve continuous improvement within the healthcare delivery system for haemoglobinopathies worldwide;
- ✓ Provide a mechanism for internal and external peer evaluation towards excellence, and ensure each centre's accountability for the service they provide to thalassaemia patients;
- ✓ Establish an international network of reference centres for the worldwide delivery of quality healthcare services for haemoglobinopathies;
- ✓ Improve patient and programme safety in all activities and initiatives;
- ✓ Facilitate all patients' access to expert management and contribute to the reduction of inequalities in the care that patients receive;
- ✓ Provide educational and training outlets for the centre's staff to stimulate the organisation's quality improvement efforts. Secondary centres will have the opportunity to send staff for training and continuing medical education at certified centres;
- ✓ Provide networking opportunities with other regional and international treating centres and benefit from staff training and tele-consultation to enable stakeholders to promote quality services from central level (government);
- ✓ Enhance community confidence in thalassaemia care in all affected countries.

Certainly, such upgrading of a centre's services and quality standards requires considerable national collaboration, support and funding. This can only be achieved if and when its value to the patients, the healthcare professionals, and the healthcare system itself is well recognised by the competent authorities. And it must be emphasised that TIF's close and official collaboration with the national authorities is a prerequisite for any activity related to this project.

This initial work of TIF cannot and is not meant to replace the value of quality assessing tools, including simple but valuable ones such as audits and peer reviews, already practiced in many countries mainly of the Western world. And certainly, it is not meant to replace those special accrediting organisations which offer their work at a cost to assess and establish quality standards in the services provided by health institutions – hospitals, clinics or centres, public or private.

Indeed, TIF strongly encourages competent authorities to adopt such a methodology where and when possible, especially since the quality of services and care is directly related to survival and quality of life [30].

TIF, mainly through this basic programme outlined above, aims to initiate an effort towards raising awareness on the value of MDC and Reference Centres in improving survival and quality of life of patients with these disorders, as has been documented in a few countries (Figures 1–3). It aims to offer a simpler methodology as a first step to support the upgrading of services provided by treating centres, particularly, but not only, in developing economies, by introducing the practice of MDC and by better acknowledging the value of the idea of pooling knowledge and experience and sharing best practices through the existence of Reference/Expert Centres.

Figure 1. Survival by 10-year birth cohort, all UK [31]

UK registry (N=736)

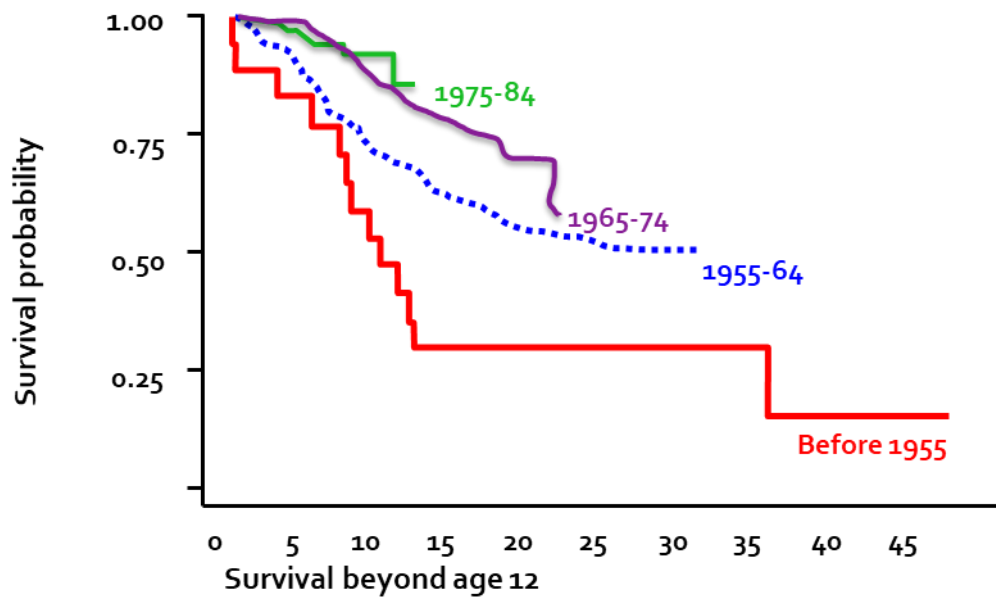


Figure 2. Survival estimates of thalassaemia major patients at UCLH 2 [Porter & Davis et al., 2002]

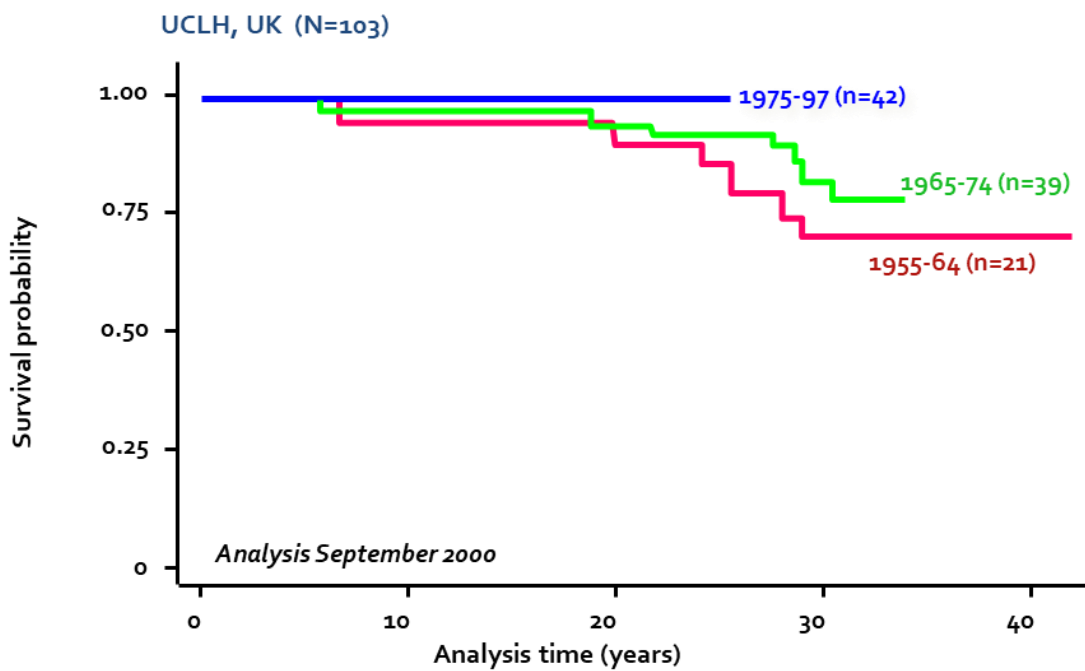
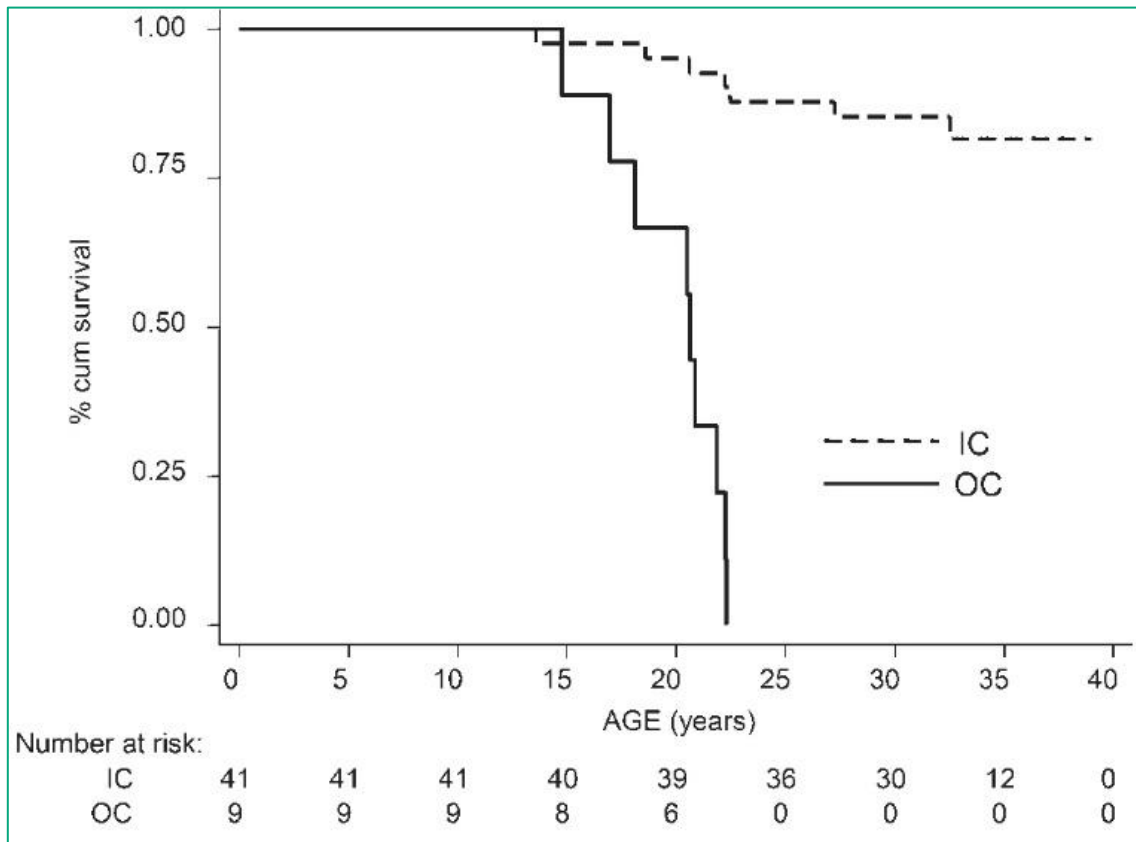


Figure 3. Kaplan-Meier overall survival curves of patients referred to specialised centres (IC) versus patients referred to nonspecialised centres (OC). Log-rank P-value <0.0001; hazard ratio of OC versus IC adjusted for sex (Cox model): 18.1, 95% confidence int



## How the United Kingdom's Haemoglobinopathy Services Work

### National Haemoglobinopathy Panel (NHP)

- Ensures the provision of a nationally consistent approach to care, as envisaged by the Clinical Reference Group and approved by commissioners.
- Coordinates the actions taken as Specialist Hospital Treatment Centres (SHTs) and Haemoglobinopathy Treatment Centres (HCCs) levels to deliver access to specialist oversight and to reduce unwarranted variation.
- Provides SHT and HCC access to national expert clinical opinion regarding the treatment of complex patients.
- Supports the introduction of commissioned innovative therapies by acting as a national panel to consider individual patients most able to benefit and to enable patients to have access to these therapies, irrespective of where they live.
- Has monthly video meetings with Clinical Multi-Disciplinary Team (MDT) for complex cases.
- Emails MDT for emergency cases requiring additional specialist input.
- Makes recommendations for high-cost therapies.
- Ensures equity of service of provision.

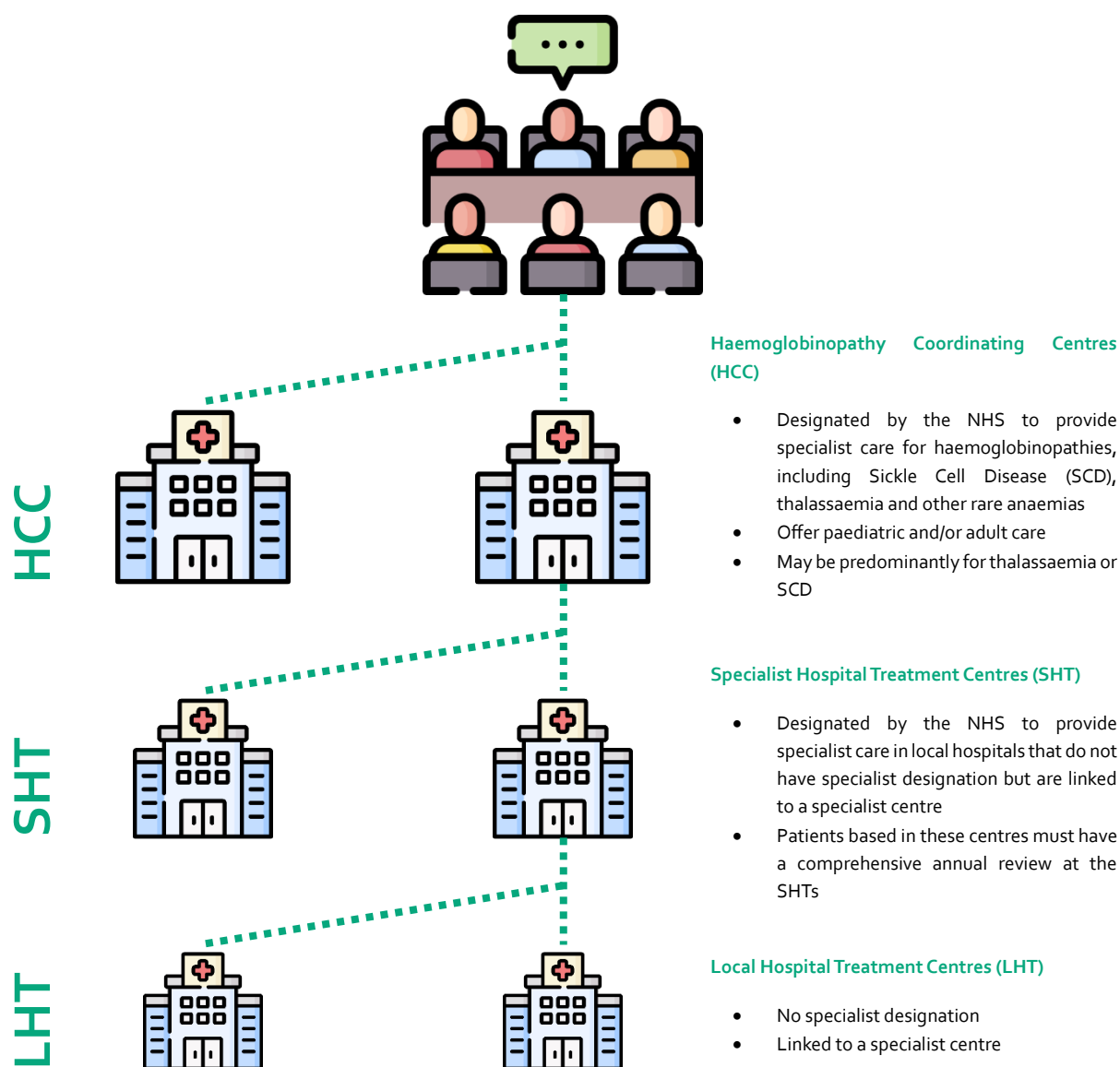
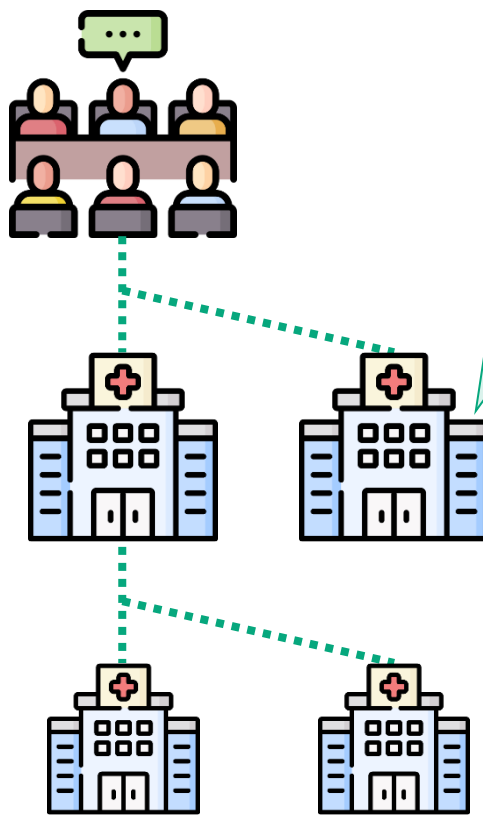


Figure 4. How the United Kingdom's Haemoglobinopathy Services Work

## How Italian Haemoglobinopathy Services Work

### National Coordination Committee

- Acts as a link between the Ministry, the Regions and the Health Centres.
- Verifies the homogeneous distribution of Care Centres throughout the country, reporting any deficiencies.
- Reviews and updates the process and efficiency indicators.
- Verifies the compliance of the Health Authorities and the Hospitals of the treatment centres.
- Coordinates training and information initiatives.
- Starts the procedures for the accreditation of centres, according to European criteria (ERNs) and with models already implemented in other countries.
- Proposes agreements between regions with the aim of standardising patient management at the national level through the creation of supra-regional services: e.g., provision of remote expertise.



### Regional or Interregional Reference Centres

- Regional Reference Centres are designated by the Regions based on their level of care and scientific excellence, competence and experience
- The Regional Reference Centres are tasked to provide second- and third-level services, coordinate regional network activities, develop relationships between Network authorities for the dissemination and integration of diagnostic and therapeutic protocols
- It is the exclusive duty of the centre to inform the patient, at the end of the procedure, about the results of the diagnosis for the purpose of sectoral consultation, management and epidemiological management.
- Interregional Centres can be established at the proposal of the National Coordination Committee and at the initiative of two and/or more Regions, through special agreements for the assignment of supraregional tasks to one or more Regional Reference Centres with the aim of saving resources, better quality of services and prevention actions.

### Thalassaemia and other Haemoglobinopathies Centres

- Thalassaemia and Haemoglobinopathy Centres are designated by the Regions based on their level of competence and experience and where the epidemiological distribution of the diseases dictates the need of their operation.
- The Centres have a duty to provide quality assistance to patients and to cooperate with the Regional or Interregional Centre and with the National Network in all activities of epidemiological, therapeutic and research importance as well as in those of education and information.
- It is the sole duty of the centre to inform the patient at the end of the procedure of the results of the diagnosis, for purposes of consulting, management and epidemiological management.

Figure 5. How Italy's Haemoglobinopathy Services Work

## DISCUSSION AND CONCLUSIONS

Patients globally are indeed faced with huge unmet needs both in basic medical care and, especially, in regards to accessing MDC and expert review of their clinical status in Reference Centres with accumulated expertise. Both of these latter elements are unfortunately largely missing. According to TIF's records of over 35 years' work in over 60 countries across the world, such components are provided to less than 2% of the patients globally, constituting a severe violation of their rights both as humans and as patients.

It is hoped that the work of every country around the world towards promoting the UN Sustainable Development Goals 2030 [33], the work of the WHO (e.g., WHO EB118.R1 on Thalassaemia & other Hemoglobinopathies) [34] and Resolution WHA59.20 on sickle cell anaemia [35]), and blood and patient safety, to name a few key aspects of these disorders, will contribute towards achieving significant progress in the prevention and management of these disorders and will help to further improve and introduce more specialised care, as described in this chapter.

Healthcare and other care services are becoming increasingly strained, and healthcare authorities worldwide need to invest in integrated care particularly in the case of chronic, complex diseases such as the haemoglobin disorders, to first and above all deliver higher quality services for the patients while at the same time containing costs. Unfortunately, existing evidence of the cost-effectiveness of integrated care of people with haemoglobin disorders is limited. Future economic evaluation should target methodological issues to aid policy decisions with more robust evidence based on reliable, nationwide data [2]. TIF has made an effort in the context of this Global Review to include a generic, cost of disease model (see Chapter 11 Estimating the Cost of Thalassaemia Care) to support decision-makers in estimating country-specific costs of care for patients with TDT.

**It is also hoped that the 4th edition of TIF's Guidelines for the Management of Transfusion Dependent Thalassaemia, slated for publication, and TIF's over-35 years of work, greatly supported by the WHO, and in collaboration with the United Nations Economic and Social Council (ECOSOC), the EC/EU, a large group of medical and scientific bodies and experts, and very importantly with the patients and families themselves, at national and international levels, will all contribute to the efforts of every country in providing a better future and ensuring more equality for patients with thalassaemia and other haemoglobin disorders.**

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