7. MULTIDISCIPLINARY CARE AND REFERENCE CENTRES FOR 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 for blood transfusion and iron chelation, even if and when they are provided appropriately and in accordance to international standards, become gradually inadequate to sustain life, maintain well-being, and achieve social integration. For this reason, specialists in several medical disciplines, such as cardiologists, hepatologists and endocrinologists, and others, are called upon to contribute by monitoring and offering proactive management of 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), separate from the main haematology or paediatric wards where they were normally admitted initially, arose first in places where patients with these disorders were treated in sufficient numbers. This prompted policymakers and health care professionals to recognise and respect that the needs of these patients are quite different from those of patients with malignant haematological conditions. Therefore, through the years, different arrangements (Table 1 below) were promoted with regards to providing more targeted, specialised service to patients with haemoglobin disorders.

Table 1. Provision of a specialised service 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 remained well into their adolescence and in many cases into their 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 on outpatient principle 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 patient NGOs in collaboration with pharmacists/Red Cross/ health care professionals

The necessity of providing specialised care that is extended beyond the basic care of transfusion and iron chelation began to be recognised in those centres where:

1. was high disease(s) prevalence amongst the population, whether indigenous (Cyprus, Greece, Italy) or the well-established and integrated migrant population (e.g., UK, France);
2. The scientific community and the national health competent authorities recognised the important medical, public health, social and economic repercussions related to the disorders in the absence of any 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 programmes were developed under national coordination and support to allow 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 to offer specialised, disease-specific training/education to the different medical specialties and to tackle many organisational challenges to ensure appropriate coordination. Where such steps were taken led to successful, meaningful integration of services, including active research activity, and reference or expert centres began to spring up.

Such centres developed first in the 1980s in Mediterranean countries of Cyprus, Greece and Italy, and in the UK, as well as in France which were developed more in the context of national strategies on rare diseases (RDs). However, they all initially developed without any structured guidance or being based on any specific criteria. Both the knowledge and experience of what 'optimal' care was for these disorders, as well as the research activity to better understand their pathophysiology and patients' 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, ageing patients and the services, the patient care pathways and the quality standards these role that any reference/expert centre for haemoglobin disorders should be fulfilling. Gradually, as

these first centres gained their reputation, they were officially assigned by the country's national competent authorities as reference or expert centres and their quality standards would undergo regular and professional reviews. Patients with haemoglobin disorders within and gradually from outside these countries began to be referred to these centres by their treating physicians for consultation, second opinion or for receiving specialised services that did not exist in their own area, region or country.

National competent authorities and health care specialists across the world began to acknowledge the value of effectively addressing these disorders and to gather knowledge and experience at their national levels. In so doing, they started to set up, particularly in the 1990s, clinics/centres with variable levels of expertise and offering different ranges of services of variable quality standards. Most of these, however, provided mainly basic care, including blood transfusion and iron chelation, while multidisciplinary care (MCD), which is essential for growing patients and the major component of a reference/expert centre, was and still is largely lacking.

Most countries where more than 80% of the patients with these disorders live have poor/weak medical and public health infrastructures and very importantly they do not offer universal health and social care coverage because of their weak economies. As their focus is on other health priorities such as communicable and common non-communicable diseases (NCSs), they often do not provide more advanced haematology therapies.

In a few of these countries, even non-government organisations (NGOs) such as the Red Crescent or Cross and patient/parent oriented ones, were encouraged by competent national authorities to contribute to the management of haemoglobin disorders. These have developed through the years and, in collaboration with medical and other health care professionals, important services for patients have been confined only to transfusion and iron chelation therapies. Certainly in such settings, provision of any extended specialised treatment is not possible. Patients, therefore, need to be referred to hospital settings in an uncoordinated manner where most medical specialists do not have specialised knowledge of the treatment of haemoglobin disorders.

TIF's work for more than 35 years in more than 60 countries, across all WHO regions, has exposed the naked truth: the development and integration of MDC services into the management of patients with these disorders and the promotion and establishment of reference/expert centres are components of care that are far from being adopted or implemented. Such advances can only happen if and when the basic, essential medical care in a centre or across a country has reached those quality levels that allow patients to grow satisfactorily, integrate socially and have a reasonably acceptable, decent quality of life. This prerequisite can only be achieved when the medical and public health infrastructures and quality standards are adequately strengthened in the context of universal health coverage. To date,

such improvements have yet happened in most of the countries, particularly in the developing ones, where the majority of patients with these disorders live and the youngest of whom do not live beyond the second decade of their lives, confirms the fact that those patients 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 is reflected in the improvement of clinical and social outcomes [2], which have already happened in some countries, while at the same time, and very importantly, it is related to the healthcare system and the consideration of the cost-effectiveness in terms of public health [3].

Basic to the success of the 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 ones must be well organised, well-coordinated, and interested in becoming involved and in acquiring experience in these conditions. Very importantly, they need to be supported and facilitated by the healthcare system of the country. 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 specialty.

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 includes the availability of proactive, quality and specialised interventions, and in this context different medical specialists should be involved well before the appearance of complications (i.e., regular involvement early in a patient's life). In a multi-organ disease like thalassaemia, there is no doubt as to 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 have medical attachments to the same hospital. This is because regular meetings of the members of the MDC group must occur regularly and also when an emergency decision for the health/condition of a patient needs to be taken. It is understood, however, that this may not be possible, but technology through teleconferences and telemedicine tools have given us valuable solutions for such challenges.

THE ROLE OF THE COORDINATOR/LEADERSHIP

In order for the interdisciplinary team to function effectively, which could be reflected in the desired outcomes of early detection and reversal or minimisation of organ damage, the principles of teamwork 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 best 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 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 [4], ensuring its effectiveness is important and this can be achieved in a number of ways such as through:

- Holding joint clinics
- Having regular team meetings
- Attending 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.

Also, involving patients in the discussions and decisions which concern their lives is critical, and every effort should be made by all of the MDC team to establish a well-structured and regular programme of active and meaningful patient engagement.

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

An example of the structure of interdisciplinary team for the care of haemoglobin disorders, as extracted from some well-established European Reference Centres with successful patient outcomes, is presented in the table below *(Table 2)* [5]:

Table 2. Interdisciplinary team for the care of haemoglobin disorders

SPECIALTY	DESCRIPTION
HAEMATOLOGIST/ PAEDIATRICIAN/ INTERNIST	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
SPECIALISED NURSES	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
CARDIOLOGIST	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
ENDOCRINOLOGIST	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
HEPATOLOGIST	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
PSYCHOLOGIST/SOCIAL WORKER	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 of 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 health care team may also be necessary.
OBSTETRICIANS	A member of the collaborative team in intended and ongoing pregnancies. Pre-pregnancy counselling along with mainly the haematologist, endocrinologist and cardiologist is essential but teamwork during gestation is also necessary for good outcomes.
DENTAL CARE	All patients should be routinely monitored for dental and maxillary complications at least yearly.

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, was explored in Jordan [6]. In this qualitative study, nurses indicated their belief in holistic care as the patients faced various challenges associated with 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 is recognised. Studies such as this give a clear indication of the experiences of the nursing staff but also of the

need for a team of professionals to offer psychosocial support to their haemoglobinopathy patients.

The mental health needs of haemoglobiniopathy patients have been recognised as being frequent and playing a significant role in the quality of life, which should be a major focus 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 [7].

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 [8].

Likewise bone disease, as measured by bone mineral density (BMD), is a frequent and painful addition to patient experience. In a study of 135 Palestinian patients, with various haemoglobin disorders, most below the age of 30 years, 77% of TM subjects, had low BMD levels. Those with low BMD had lower haemoglobin mean values and higher serum ferritin levels, confirming the need to maintain hemoglobin levels above 9.3 g/dL and ferritin below 2300 ng/ml [9]. 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) [10].

In conditions which affect quality of life to such an extent, like bone pain, all means to investigate and diagnose early bone disease so that treatment and relief measures can be taken early. In this respect, a group from Bulgaria investigated serum Sclerostin (a glycoprotein secreted mainly by mature osteocytes controlling bone remodelling) and found that adult patients with TDT who express abnormally high serum levels of sclerostin are negatively associated with bone mineral density. Therefore serum Sclerostin has the potential to serve as one of the markers associated with severe osteoporosis in beta thalassaemia patients. However, this claim needs futher validation [11].

Many other important heath care specialists are needed particularly when the centres are treating sickle cell disease (SCD) patients as well, 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-co-ordinated access in this case are included in Table 3 below (which is by no means exhaustive):

Table 3. Indicative list of key specialist services

- Erythrocytapheresis
- Pulmonary hypertension team
- Fertility, contraception and sexual health services
- Consultant neurologist
- Consultant ophthalmologist
- Consultant nephrologist
- Consultant urologist with expertise in managing priapism and erectile dysfunction
- Orthopaedic service
- Specialist imaging including:
  - MRI tissue iron quantification of the heart and liver with regularly standardise software to ensure accuracy and reliability of iron measurement
  - Trans-cranial Doppler ultrasonography (children)
- Polysomnography and ENT surgery
- Bone marrow transplantation services

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 continued concordance to prescribed treatment. 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 important to better understand their needs and thus to better plan and appropriately reform related policies. The aim for every government and treating physician is certainly to achieve their patients' good health and quality of life, associated with a high level of social integration. Indeed, this can only happen if and when the patient remains at the centre of decisions.

REFERENCE OR EXPERT CENTRES FOR HAEMOGLOBIN DISORDERS

Considerable work on this topic has been conducted mainly by the European Commission of the EU 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 characterising haemoglobin disorders, which are also considered RDs. The difference, however, is that, contrary to the many thousands of other RDs, there is currently ample and reliable knowledge and experience on haemoglobin disorders with regards to early and accurate diagnosis, specialised monitoring, appropriate management and effective prevention.

The European Commission 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 both across Europe and more importantly across 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, and they are importantly directed towards developing national plans in every EU member country to address more effectively the needs of RDs. Within this work, the European Commission established the EUCERD (European Union Committee of Experts on Rare Diseases) to focus on developing quality criteria for centres of expertise for RDs in member states (2011) and recommendations on establishing RD European Networks (ERNs) (2013) [12]. In this context the idea of ERNs was integrated into an EU Directive 2011/24/EU, which is related to the application of EU patients' rights in cross-border healthcare, acknowledging that this is a major step towards more effectively promoting 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 [13].

Within 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. Considerable work is being undertaken by this network to pool together knowledge and expertise from across the EU on these disorders [14].

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), more relevant to haemoglobin disorders and other rare anaemias and in which TIF was a major partner. Through this activity, TIF and 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 [15]. This book reflects the extensive work that the EU has undertaken for over two decades for the benefit of rare anaemias including haemoglobin disorders and it represents a major contribution, indeed, towards the creation of a much needed European infrastructure of expertise around rare anaemias. The authors of this chapter of the fourth 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.

The EU directive on cross-border healthcare includes benefits, outlined below in Table 4, that facilitate and safeguard the rights of patients with RDs, including rare anaemias and haemoglobin disorders, to obtain cross-border health care, underscoring the importance of developing and pooling together specialised knowledge and experience as well as of networking between centres of expertise. These ideas and policies, if and when tailored to the needs and prevailing situation across any country or World Health Organisation region of the world, could significantly benefit patients with haemoglobin disorders, the health care specialists and the health care systems at large 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 [16]. It has thus focused particular attention and considerable work on its educational programme since its establishment in 1986, and in this context, TIF initiated in 2017 a new project titled "TIF's Certification Programme", which is focused on empowering national competent authorities, healthcare professionals and patient communities to dedicate work on promoting the MDC component and the establishment of reference/expert centres into their management strategy [17].

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) including the range and quality standards of the services provided by each of them [18]. The aim of TIF is (i) to identify those centres already qualified to perform the role of a reference centre today; (ii) to provide, through its scientific advisors, support to those treatment centres that have the potential to upgrade their services; and (iii) to support other treatment centres to reach at least acceptable levels of basic quality care for their patients; and (iv) very importantly to support the networking between them at the national level and of the reference/expert centres at the regional and international levels.

The programme focuses on applying specific quality standards to 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 recognizing any centre as a reference/ expert centre is certainly the quality of services, and its patient-centred care and not just availability of various technical components necessary for thalassaemia (and other haemoglobin disorders) care. It includes following national or international evidence-based guidelines that 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 significant contributions to research as evidenced by peer reviewed publications.*
9. *Establish networking with secondary treatment centres, as well as other expert centres nationally, to provide education and share knowledge and expertise as well as to provide expert opinions on challenging 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. *Provides evidence through specific tools, including patient-reported outcomes, that patient's survival, clinical outcomes and quality of life have improved, as well as patients' satisfaction.*

In addition, (i) there must be evidence of government and more specifically health system support; (ii) patients should have free access to treatment modalities; (iii) the centres' administrative structure, working hours and clinical space availability must also be taken into consideration, with the patient experience in mind; (iv) deficiencies and gaps must be promptly identified and corrected; (v) regular assessments must be made of the experience and knowledge of professional staff; 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 CONCERNS**
• 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 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 cohabitator.
• 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, nationally or internationally 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 noted all strengths and weaknesses, the survey team will present a report and also make suggestions for quality improvement where necessary.
• Quality improvement is a systematic approach to changes aiming to upgrade services and correct any deficiencies in the governance, structure and functions of the service. 'Quality improvement includes better patient experience and outcomes, by changing provider behaviour' (Dr John Ovretveit: "Does improving quality save money?")

• 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 a 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 two years before the evaluation team is called back to the centre to ensure that quality of care has been maintained.

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, and this can only be achieved if and when its value to the patients, the health care professionals and the healthcare system itself are well recognised by the competent authorities. 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 audit and peer review, 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 methodologies where and when possible.

TIF, through this basic programme outlined above, mainly aims to initiate an effort towards raising awareness on the value of MDC and reference centres in improving patient survival and quality of life, as a few countries have documented (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.

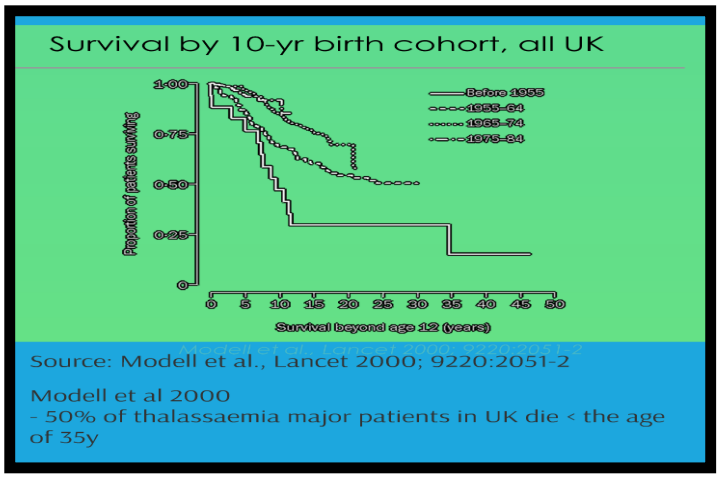
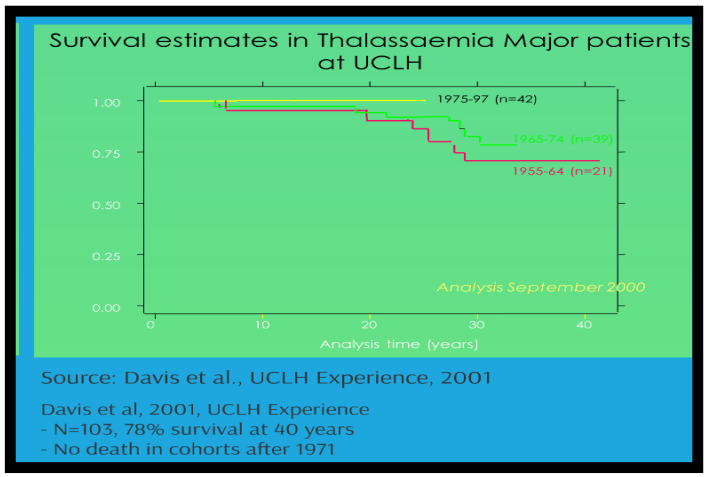


Figure 1. Survival by 10-year birth cohort, all UK [19]

Figure 2. Survival estimates of thalassaemia major patients at UCLH [20]



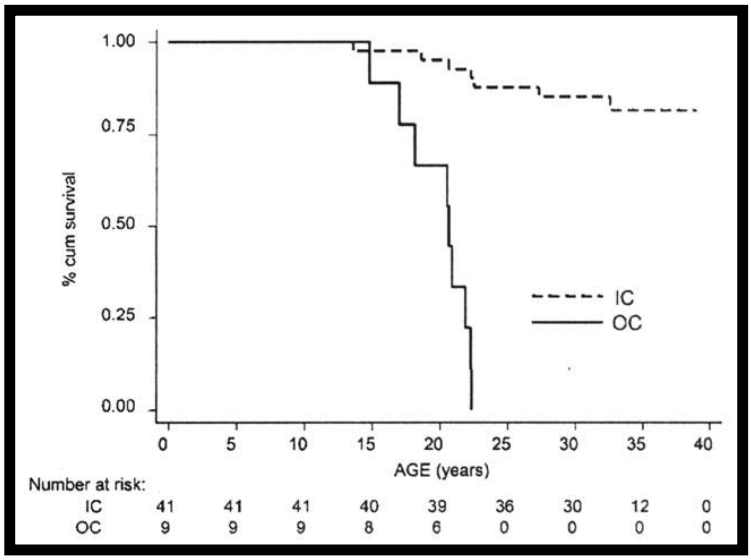


Figure 3. Kaplan-Meier overall survival curves of patients referred to specialised centres (IC) versus patients referred to nonspecialised centres (OC). Log-rank P-value <0.0001; hazard ratio of OC versus IC adjusted for sex (Cox model): 18.1, 95% confidence interval = 4.7-69.0; P<0.001.* [21]. *IC, specialised centre; OC, non-specialised centre.

HOW UK HAEMOGLOBINOPATHY SERVICES WORK:

NATIONAL HAEMOGLOBINOPATHY PANEL (NHP)

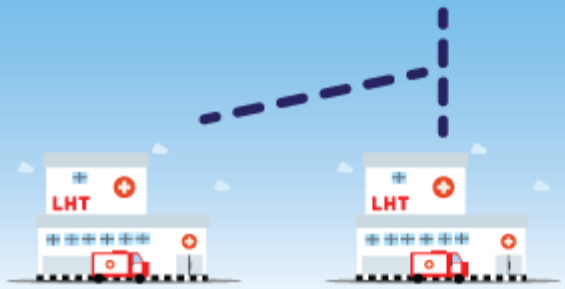
- Ensure the provision of a nationally consistent approach to care as envisaged by the Clinical Reference Group and approved by commissioners
- Coordinate the actions taken at SHTs and HCCs levels to deliver access to specialist oversight and to reduce unwarranted variation
- Provide SHT and HCC access to national expert clinical opinion with regard to the treatment of complex patients
- Support 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
- Monthly video Clinical Multi-Discipilinary Team (MDT) for complex cases
- Email MDT for emergency cases requiring additional specialist input
- Recommendation of high cost therapies
- Ensure equity of service of provision

HAEMOGLOBINOPATHY COORDINATING CENTRES (HCC)

- Designated by the NHS to provide specialist care for haemoglobinopathies, including SCD, thalassaemia and other rare anaemias
- Offer paediatric and/or adult care
- May be predominantly for Thalassaemia or SCD

SPECIALIST HOSPITAL TREATMENT CENTRES (SHT)

- Designated by the NHS to provide specialist care in local hospitals that do not have specialist designation but are linked to a specialist centre
- Patients based in these centres must have a comprehensive annual review at the SHTs



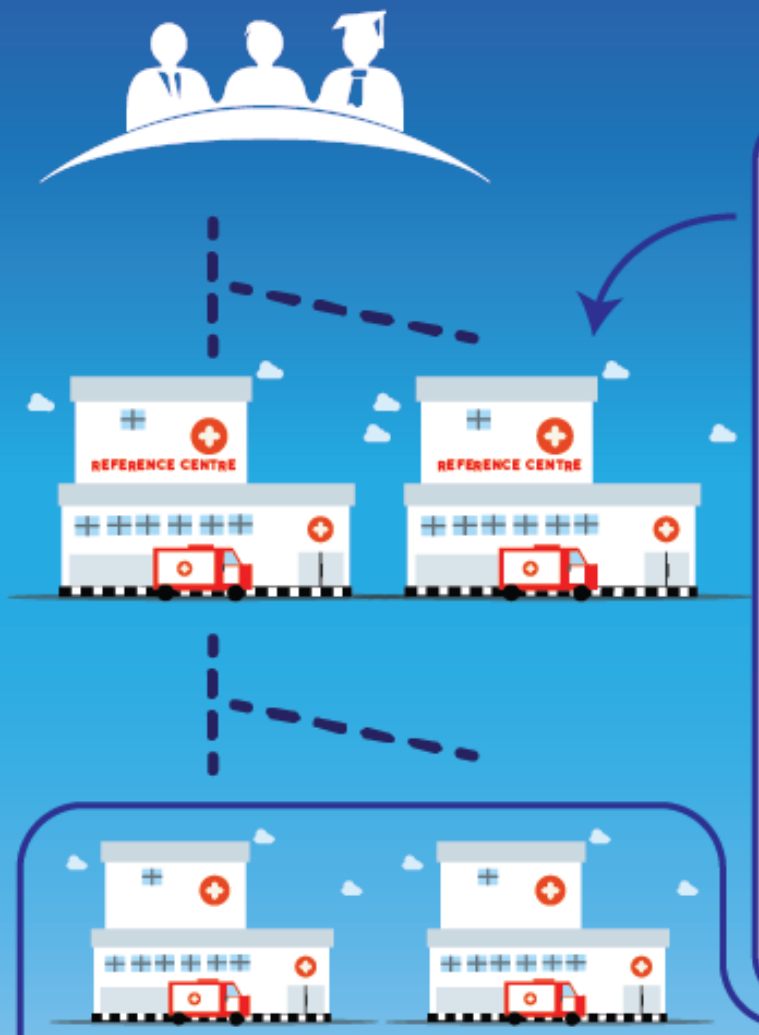
LOCAL HOSPITAL TREATMENT CENTRES (LHT)

- No specialist designation
- Linked to a specialist centre

HOW ITALIAN HAEMOGLOBINOPATHY SERVICES WORK:

NATIONAL COORDINATION COMMITTEE

- To act as a link between the Ministry, the Regions and the Health Centers
- To verify the homogeneous distribution of Care Centers throughout the country, reporting any deficiencies
- To review and update the process and efficiency indicators
- To verify the compliance of the Health Authorities and the Hospitals of the treatment centers
- To coordinate training and information initiatives
- To start the procedures for the accreditation of centers, according to European criteria (ERNs) and with models already implemented in other countries
- To propose agreements between regions with the aim of standardizing patient management at national level through the creation of supra-regional services: e.g. provision of remote expertise



REGIONAL OR INTERREGIONAL REFERENCE CENTRES

- Regional Reference Centers are designated by the Regions based on their level of care and scientific excellence, competence and experience
- The Regional Reference Centers are tasked with the provision of second and third level services, the coordination of regional network activities, the development of relationships between Network authorities for the dissemination and integration of diagnostic and therapeutic protocols
- It is the exclusive duty of the center 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 Centers 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 Centers with the aim of saving resources, better quality of services and prevention actions

THALASSAEMIA AND OTHER HAEMOGLOBINOPATHIES CENTRES

- Thalassemia and Haemoglobinopathy Centers are designated by the Regions based on their level of competence and experience and where the epidemiological distribution of the diseases dictates the need for their operation.
- The Centers have a duty to provide quality assistance to patients and to cooperate with the Regional or Interregional Center 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 center to inform the patient at the end of the procedure of the results of the diagnosis, for purposes of consulting, management and epidemiological management.

SITE

Discussion and Conclusions

Patients globally are indeed faced with huge unmet needs in basic medical care and to an even larger extent with regards to accessing MDC and experts with accumulated expertise reviewing their clinical status in reference centres. Both of these latter elements are unfortunately largely missing, and according to TIF's records of over 35 years' work at country level, 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 as both humans and patients.

It is hoped that the work of every country around the world will contribute towards achieving significant progress in the prevention and management of these disorders. To achieve this every country must promote the UN Sustainable Development Goals 2030 [22] and the disease-specific decisions, resolutions and programmes of the WHO (e.g., WHO EB118.R1 on Thalassaemia & other Hemoglobinopathies [23], and Resolution WHA59.20 on sickle cell anaemia [24]), as well as those on blood and patient safety, just to name a few key ones related to these disorders. Such support will 'allow' these institutions to further improve and introduce more specialised care, as described in this chapter.

Health and 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 also containing costs. Unfortunately, existing evidence of the cost-effectiveness of integrated care is limited particularly with regards to haemoglobin disorders. Future economic evaluation should target methodological issues to aid policy decisions with more robust evidence based on reliable, nationwide data [25] (Aguilar Martinez et al., 2014). TIF has made an effort in the context of this Global Review to include a cost of disease generic model (see relevant chapter) to support decision makers in making a country specific estimateion of the cost of care of 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 the work of TIF over 35 years of its existence, greatly supported by the WHO, and through its collaboration with the UN, the United Nations Economic and Social Council (ECOSOC), the EC/EU, a large group of medical and scientific bodies and experts, and very importantly by the patients and families themselves, at national and international level, 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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