Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Repatriation of paediatric haematopoietic stem cell transplant services to Ireland:

Protocol for a Health Technology Assessment

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Contents

1. Introduction

1.1. Background

Allogeneic haematopoietic stem cell transplant (HSCT), sometimes known as a bone marrow transplant (BMT), is the internationally recognised standard of care for paediatric patients with particular inborn errors of metabolism, inborn errors of immunity and certain haemoglobinopathies (depending on the form and severity of disease).

Haematopoietic stem cells are immature cells, which are found in the peripheral blood and in the bone marrow and which can develop into different types of blood cells.[1] Allogeneic HSCT is a process by which donor haematopoietic stem cells are transplanted to the patient by infusion.[2] The goal of treatment is the acceptance of donor stem cells by the patient (engraftment), and the sustained long-term production and release to the peripheral blood of healthy red blood cells, white bloods cells, and platelets (haematopoiesis).[3] As these donor cells are free of the underlying genetic mutations giving rise to the disease, HSCT, if successful, prevents disease progression and may in some conditions be curative.[3]

There is a single paediatric HSCT centre in Ireland, located in Children's Health Ireland at Crumlin, Dublin. This transplant unit is accredited by the Joint Accreditation Committee - International Society of Cellular Therapy and European Bone Marrow Transplantation (JACIE), demonstrating adherence to international standards of HSCT.[4, 5] Clinical care of children undergoing HSCT at the centre is delivered under the supervision of the haematology and or oncology consultants.[6]

While HSCT is available in Ireland to paediatric patients with bone marrow failure syndromes or haematological malignancies, paediatric patients with other conditions requiring HSCT must travel abroad to avail of this treatment.[7-10] Funding for these procedures is provided through the Treatment Abroad Scheme operated by the HSE.[10] However, the requirement for travel can place a significant financial and logistical burden on patients and their families.[8, 9] The long duration of treatment, ranging from three to six months, means that families of patients undergoing HSCT may be separated for extended periods of time. For others, the logistical challenges associated with travelling to receive HSCT represent a prohibitive barrier to accessing this care; as such, some patients are not able to access HSCT treatment.[9] Furthermore, HSCT performed outside Ireland is subject to capacity in the host country, representing a risk to access.

In light of the issues described above, a request was received by HIQA from the National Paediatric Public Health Lead in the Health Service Executive (HSE), with support from specialist clinicians in Children's Health Ireland, to carry out a health technology assessment (HTA) of the repatriation of paediatric HSCT services for these non-malignant indications. This request was prioritised for inclusion in the HIQA HTA work plan. In establishing which domains should be examined within the HTA in order to inform the HSE's decision-making process, it was considered that HSCT is already recognised as the standard of care for the patient cohort under consideration. However, as noted, there are social and ethical issues arising from the location in which HSCTs are provided for these patients. Furthermore, it is anticipated that there may be significant organisational and resource implications associated with the repatriation of the HSCT service. This protocol presents the proposed methodology for estimating the burden of disease for which HSCT is indicated, and for assessing the organisational changes, budget impact, and social, ethical and legal aspects associated with the repatriation of these procedures to Ireland.

1.2. Aims and objectives

The overarching aim of this HTA is to describe the current and proposed HSCT treatment pathways and to identify the implications of the choice of treatment location for both patients and the Irish healthcare system. This HTA will advise on the potential impact of providing HSCT in Ireland for these patients. Regarding this patient cohort, the objectives of this assessment are to:

- describe the epidemiology of these conditions in Ireland and the associated burden of disease
- provide a high-level description of HSCT and the outcomes associated with its use
- describe the current standard of care and treatment pathway and the proposed pathway if HSCT treatment for all paediatric conditions were to be repatriated to Ireland
- assess the governance and organisational implications for the HSE of repatriating HSCT services as well as the implications for the resilience of the service
- assess the budget impact of providing HSCT in Ireland

- consider the social, ethical and legal implications that the provision of HSCT in Ireland may have for patients, their families, the general public and the healthcare system in Ireland

- based on the evidence in this assessment, advise on the impact of the alternative approaches to the provision of HSCT.

1.3. Establishment of the Expert Advisory Group

An appropriately represented Expert Advisory Group (EAG) will be convened as a source of expertise to inform the interpretation of the evidence and development of the advice to the HSE.

This group will comprise nominees from a range of stakeholder organisations, including patient representation, healthcare providers, and clinical and public health experts.

2. Epidemiology and burden of disease

Inborn errors of immunity, inborn errors of metabolism, and haemoglobinopathies encompass broad groups of heterogeneous genetic conditions.[11-14] While HSCT is the standard of care for many patients with these conditions, it is not a treatment option for every patient. Its viability as a treatment option depends on the form and severity of the disease, individual patient characteristics, donor availability and the degree of matching between donor and recipient. [11-14] The British Society of Blood and Marrow Transplantation has listed indications for HSCT in children, as recommended by the UK Paediatric BMT Group;[15] depending on the condition, HSCT may be:

- standard of care
- indicated subject to clinical opinion (requiring careful assessment of risks and benefits)
- developmental, that is, further trials are needed to inform practice
- generally not recommended.

A brief description of these groups of diseases (inborn errors of immunity, inborn errors of metabolism, and haemoglobinopathies), and their management, will be provided. Given the large number of conditions within each disease group, it is beyond the scope of this assessment to provide a comprehensive description of the

epidemiology and burden of disease of each condition. Therefore, this section will focus on the individual conditions for which HSCT is most commonly indicated in Ireland. These include severe combined immunodeficiency (SCID) (an inborn error of immunity), Hurler syndrome (an inborn error of metabolism) and sickle cell disease (a haemoglobinopathy).[7-9]

Where available, national data will be presented from Children's Health Ireland and the HSE's Treatment Abroad Scheme. Data specific to Ireland are important as the presence of certain mutations in the Irish population means that disease prevalence differs from other countries in Europe and internationally. For example, both SCID and Hurler syndrome are more prevalent in individuals of Irish Traveller ethnicity than in the general population. Differences in immigration patterns across countries are also relevant. For example, sickle cell disease is more common in those of African and Caribbean ethnicity.[16] Irish data will be supplemented with data from the international peer-reviewed literature, where appropriate.

Data from the Treatment Abroad Scheme will be used to provide detailed information on the uptake of HSCT for paediatric patients at centres outside Ireland. Clinical opinion will inform the latent demand for patients with haemoglobinopathies who have been unable to access treatment due to services not being available in Ireland. Factors that may lead to changes in demand over time, such as increased safety of HSCT (which may increase demand for HSCT), or the potential future availability of alternative therapies such as gene therapy (which may reduce demand) will be described.

3. Mapping of treatment pathways

The HSCT treatment pathway is the technology under assessment in this HTA. Repatriation of the paediatric HSCT service for non-malignant conditions to Ireland will be considered as an alternative to the current treatment pathway where patients are offered treatment abroad under the Treatment Abroad Scheme. Patients with inborn errors of immunity generally travel to Great North Children's Hospital in Newcastle.[7] Patients with inborn errors of metabolism receive treatment in the Royal Manchester Children's Hospital.[8] In the past, patients with haemoglobinopathies have not been able to access treatment routinely.[9] However, a new service level agreement with St Mary's Hospital, London, was signed in 2022 and is expected to enable these patients to access HSCT at this site.[9] At the time of writing (June 2022), no patient had yet received HSCT treatment under the St Mary's Hospital pathway. Therefore, both the new arrangements (St Mary's Hospital, London, under the TAS), and the previous arrangements (very limited access to HSCT treatment) will be described.

A review of the main international standards and guidelines for HSCT will be presented. JACIE is the primary accreditation body in Europe for HSCT.[4] As Children's Health Ireland at Crumlin is already JACIE-accredited and providing transplants for children with bone marrow failure syndromes or haematological malignancies,[5] this review will focus on recommendations which are of increased relevance for the identified non-malignant indications and for transplant volumes. Special focus will be given to national standards in England, given this is the location of the current treatment providers.

Interviews with clinicians, managers, other healthcare professionals and patients will be conducted to understand the steps in the current treatment pathway. Based on this information and the advice of the EAG, the current and proposed patient pathways will be described.

4. Organisational considerations

The assessment of necessary organisational changes associated with repatriation will be carried out in accordance with the EUnetHTA Core Model.[17]

The available bed capacity at Children's Health Ireland at Crumlin and the new Children's Hospital at the shared St James's Hospital campus will be examined. The impact of the provision of HSCT in Ireland on various other types of resources (such as equipment and laboratory resources) and any additional associated healthcare interventions (for example, extracorporeal photophoresis) will be considered. The ability to recruit or train the required staff to deliver the service will also be considered given the highly specialised nature of the service.

Additional considerations relating to capacity will also be described. These include the potential impact that the expansion of HSCT service provision may have for patients who currently receive HSCT treatment in Ireland, including the prioritisation of procedures. The impact of HSCT repatriation on the resilience, governance, and continuity of care of the service will also be explored. The COVID-19 pandemic has demonstrated the vulnerability that exists with the reliance on travel; changes in capacity levels for HSCT abroad may impact the availability of HSCT for Irish patients, as naturally countries can be expected to provide for their own patients first.

5. Budget impact analysis

A budget impact analysis of the direct healthcare costs associated with the repatriation of paediatric HSCT will be carried out from the perspective of the Health Service Executive (HSE). This will be conducted over a five-year time horizon in line

with national guidelines.[18] Transport costs incurred by the HSE associated with the transport of the patient and their parent(s) via air ambulance or commercial transport will be included.

In the baseline scenario, the comparator for the analysis will be routine care in Ireland. This means the comparator is HSCT provided abroad, as funded under the HSE's Treatment Abroad Scheme.

Patients with haemoglobinopathies have not routinely been able to access HSCT. While a new pathway has been agreed, as yet, no patient from Ireland with a haemoglobinopathy has undergone HSCT through the St Mary's Hospital pathway. Therefore, the comparator of usual care, which consists of medications and blood transfusions, will be considered in a scenario analysis.

The cost of treatment under the Treatment Abroad Scheme will be estimated using data provided by the HSE. The administration costs associated with sending patients abroad across the healthcare system will also be considered. Comparable resource use for the repatriation of these transplants to Ireland will be informed by the current treatment pathways and the process map (Section 3 above) and by using other data sources, including the Hospital Inpatient Enquiry (HIPE) reporting system of the HSE, results of surveys of clinicians and other health care workers, and the international literature. Additional resources associated with establishing the new treatment pathway, such as staff training, will also be accounted for. Applicable cost data will be obtained from Children's Health Ireland, the Department of Health consolidated pay scales for the health sector,[19] NHS cost data,[20] the HSE Activity-Based Funding price list, and the published literature.[21] Costs will be adjusted in line with national guidelines.[18]

In addition to the costs incurred by the HSE, the costs falling outside the public healthcare system will also be collated. In particular, the costs associated with accommodation and subsistence while abroad are substantial and fall on other parts of society including patient and their families as well as on the Department of Social Protection. These costs will be estimated through interviews with patient representatives, medical social workers, clinical nurse specialists and clinicians.

6. Patient–related and social considerations

HSCT is an intensive treatment which places a known burden on patients, their families and their stem cell donors.[22] This section will focus on the additional burden associated with the requirement to travel abroad for HSCT compared with treatment in Ireland.

Methods outlined in the EUnetHTA Core Model will be used to guide the analysis.[17] Patient groups and healthcare workers supporting them will be consulted for their perspectives on their experience of navigating the current pathway and their expectations of treatment under repatriation of these services. A search of the international literature will be conducted to evaluate the patient burden associated with stem cell transplants and travelling abroad for care.

As noted in Section 5 above (Budget impact analysis), the financial burden on families associated with accommodation and sustenance while abroad can be substantial. As such, the HTA will aim to describe the impact of these costs on patients, the availability of social welfare supports to address the financial burden, and the effect of long-term presence abroad on usual social protection entitlements. The logistical burden associated with arranging travel abroad, and the social burden associated with being separated from family and support networks while abroad, will also be documented.

Beyond the general population, specific patient groups likely to be particularly affected by this assessment include first-generation Irish of African descent and members of the Irish Traveller community.[16, 23] These represent vulnerable social groups which require special consideration of the burden that the current treatment pathway places on them.

7. Ethical considerations

The ethical analysis will consider key social and moral norms and values relevant to the choice of treatment pathway and patient access. Key ethical issues outlined in the EUnetHTA Core Model will be used to guide the ethical analysis.[17]

Potential ethical issues may include issues related to:

- ability to access HSCT treatment
- inequities in relation to treatment location, dependent on indication for HSCT
- care and treatment of vulnerable groups
- differences in the availability of supportive treatments, such as extracorporeal photophoresis, between the UK and Ireland
- differences in the availability of procedures which may preserve future fertility
- requirements of patients and families to spend extended time abroad in order to avail of treatment
- requirement of the stem cell donor to travel abroad
- criteria for patient prioritisation and the impact on access to care.

8. Legal considerations

An understanding of the underlying legal framework supporting the patient pathway is an important element of this assessment. Rather than presenting legal issues as a distinct section in the report, the implications to patient care of both existing and impending legislation will be presented within the corresponding HTA domain. For example, the chapter on organisational issues will consider the legal framework underpinning the HSE's Treatment Abroad Scheme and changes arising from the UK's withdrawal from the EU,[10, 24] as well as expected changes to the regulation of fertility-preserving treatments under the proposed Health (Assisted Reproduction) Bill 2022.[25] The chapter on social and ethical considerations will consider social welfare supports to families incurring significant costs while abroad and the effect of their long-term presence abroad on their usual social protection entitlements.

9. Conclusion

This HTA is intended to inform a decision by the HSE on whether or not to repatriate these transplants to Ireland. The repatriation of paediatric HSCT may represent a feasible and affordable alternative to the current treatment pathway and may reduce the burden of travel on patients and their families. It may also reduce inequity in the current provision of paediatric HSCT and increase the resilience of the HSCT service in Ireland for all indications. Considering the current treatment pathway already provides HSCT treatment to these patients, an HTA comprising an analysis of the organisational considerations, social, ethical and legal considerations, and a budget impact analysis will be conducted to inform a decision by the HSE to repatriate treatment and provide HSCT for paediatric non-malignant HSCT indications to Ireland.

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