NHS
Blood and Transplant

A ten year vision for stem cell transplantation and cellular therapies

Innovative Transformational Sustainable

UK Stem Cell Strategic Forum

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1. Foreword

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Stem cell transplantation continues to evolve as a vital, curative therapy for children and adults with blood cancer and blood disorders. Building on the scientific principles underpinning stem cell transplantation, breakthrough cellular therapies - such as CAR-T cells - which promise to further improve patient outcomes have been developed in the last decade. UK clinicians and scientists have played a pioneering role in the development of stem cell transplantation as a break-through therapy from its inception and continue to play a global leadership role in the development and delivery of novel transplant and cellular therapies.

In 2010 HM Government launched the UK Stem Cell Strategic Forum with the explicit aim of improving the outcomes of stem cell transplant patients. Since its establishment, the Forum has served as a highly effective crucible of thought and innovation for key UK stem cell transplantation stakeholders - all united with the common aim of extending the curative benefit of stem cell transplant, and more recently, cellular therapies. The Forum has championed advances such as the creation of a UK aligned registry and high-quality donated cord blood bank, the successful development of the IMPACT clinical trials network - one of only two in the world - and more recently transformative innovations in CAR-T cell therapy which together have led to thousands more UK patients having access to potentially life-saving therapies.

It is fitting then, that this latest report of the Forum - which has been developed at the request of the Department of Health and Social Care - builds on this track record of innovation by providing a long-term blueprint for a thriving stem cell transplant and cellular therapy ecosystem in the UK. We have much to be proud of – a highly skilled transplant clinical community, world class donor registries and an internationally competitive trials infrastructure nested within a world class Life Sciences landscape. But there is still much to be done if we are to ensure all patients, regardless of ethnicity or socio-economic background, have access to consistently effective stem cell transplant and cellular therapies with acceptable short- and long-term toxicities.

The Forum has set out a vision to address the challenges on the horizon by capitalising on the combined strengths of the NHS and the UK academic and scientific community to deliver a resilient, evidence-based and compassionate therapeutic ecosystem for the next decade. It is a vision produced and endorsed by the community of patients, clinicians, scientists, and researchers at the heart of driving progress to date. At its core is the ambition to learn from the lessons of the COVID-19 pandemic to drive improvements in stem cell transplant and cellular therapy outcomes, through the delivery of practice-informing clinical trials, maximising the patient impact of real-world data, future-proofing supply chains and infrastructure, and in the process, contributing to the economic growth of the UK's world-class Life Sciences sector.

We do not underestimate the scale of the ambition laid out in our recommendations. But there is also a very real opportunity to deliver a more robust and responsive system that is well equipped to transform survival and improve the quality of life of thousands of patients.

It has been a privilege to have participated in the discussions between key players in the UK stem cell transplantation and cell therapy community as they coalesce around the ambitious vision set out in this report. By continuing in the spirit of collaboration, we are confident that the community can, with the support of HM Government, embrace the opportunity to deliver a thriving cell therapy system to the benefit of NHS patients and the broader UK Life Sciences ecosystem

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2. Executive summary

Blood cancers represent the fifth most common cancer in the UK, and the third biggest cause of cancer-related deaths. Haematopoietic stem cell transplantation (HSCT) and advanced therapy medicinal products (ATMPs), often referred to as cellular therapies, are highly effective curative therapies used predominantly for patients with blood cancer whose outcome with standard chemotherapy can be predicted to be poor, but also increasingly for patients with non-malignant disorders and autoimmune diseases.

Notwithstanding its remarkable curative potential, it remains the case that up to 50% of patients die of treatment toxicity or recurrent disease using current HSCT and ATMP regimens. Further, access to optimal transplant treatment is limited by patient ethnicity and socioeconomic background. There is therefore an urgent requirement both to ensure increased and equal access to HSCT and ATMP therapy, and to generate robust evidence capable of driving improved patient outcomes. This report of the UK Stem Cell Strategic Forum (UKSCSF) – 'the Forum' - provides a comprehensive vision for achieving that aim, by harnessing the potential of prospective clinical trials and transformative datasets, improving patient access, and building world-class treatment infrastructure.

Since its creation in 2010, the Forum has provided the impetus for significant improvements in the quality of HSCT care, and substantially increased patient access to these curative therapies. Representing a unique platform for interaction and collaboration between key partners within all the UK's devolved health administrations, the Forum has proved a highly effective vehicle, permitting the development of new and effective strategies aimed both at optimising patient outcomes, and maximising the contribution that this clinical and scientific community makes to the UK's Life Sciences proposition.

This latest report of the Forum provides a blueprint for the next decade of progress. Developed for, and by, the haematopoietic stem cell transplantation and cellular therapy (HSCT-CT) community, its recommendations provide a roadmap for the delivery of world-class outcomes in cell and gene therapies including for the first time, ATMPs, at the request of the Minister.

The NHS's track record of delivering complex medical interventions to one of the largest agglomerated populations in the world, coupled with its strategic prioritisation of genomics, data and clinical trials, create multiple opportunities for innovation in HSCT and ATMP delivery which will in turn deliver long-term cost savings to the NHS. The HSCT-CT clinical and scientific community in the UK is at the vanguard of medical innovation and research and has the potential to make a substantial contribution to HM Government's vision for the Life Sciences as a driver of economic growth and job creation by making the UK the "go-to" destination for investment by the global biopharmaceutical sector.

The 24 recommendations in this ambitious strategy set out the initiatives that are needed to realise significant improvements in patient outcomes, experience and quality of life after HSCT and ATMP treatment in the coming decade. Success will be dependent on a strong collaborative effort between the clinical and scientific community, HM Government and devolved health administrations, philanthropy, and patient organisations.

This report also recognises the significant pressures within the healthcare system. It has been developed in the context of identifying both where potential for delivering cost savings may lie, and where possible, how new commercial models might be leveraged to generate new private sector and philanthropic funding streams to deliver the Forum's recommendations.

The Forum's recommendations have been divided into short-, and medium-to-long-term time frames. They cover five key themes around which this report has been structured and which are outlined in this executive summary:

1. Sustainability and resilience in the UK stem cell donor supply chain;
2. Equity in patient access, experience and outcomes;
3. A new vision for HSCT and ATMP data;
4. Global leadership in HSCT and ATMP research; and
5. A strong and sustainable world-class clinical infrastructure.

2.1. Sustainability and resilience in the UK stem cell donor supply chain

The UK aligned stem cell registry now provides a substantial searchable pool of over two million adult stem cell donors and cord blood stem cell units. The registry also has the capability to search overseas registries to provide cells to UK patients.

Despite this, there remains a substantial degree of unmet patient need for optimal 10/10 HLA-matched donors, and a reliance on overseas donors to provide cells for UK patients. This not only compromises equity of access to potentially curative therapy, but also has implications for the sustainability and resilience of the supply chain which have been thrown into sharp relief by the COVID-19 pandemic.

The UK aligned registry is a national asset that should be strengthened and enhanced with targeted support to create:

- Improved resilience in the domestic stem cell supply chain, by increasing the provision of UK stem cells to 45% of total cell provisions to UK patients, and by maintaining a cord blood inventory of 30,000 clinical-grade units;
- Greater equity of access to HSCT, particularly for patients from a minority ethnic background, by further diversifying donor registries and promoting clinical innovation to increase the availability and efficacy of alternative cell sources; and
- Increased provision of stem cell materials to academia and industry for use in research and development.

2.2. Equity in patient access, experience and outcomes

It is increasingly recognised that patient ethnicity and socio-economic status can determine access to and outcomes after complex medical intervention, such as HSCT and treatment with ATMPs. Every effort must therefore be made to ensure equity of access to these potentially life-saving therapies. Of equal importance is ensuring equity in outcomes and quality of life for all patients receiving HSCT and ATMP therapies. Enabling true equity of access to treatment and supportive care is critical to achieving this. Patients should feel empowered throughout their treatment journey, and clinical teams enabled to tailor and personalise care to an individual's holistic needs.

In order to deliver these centrally important aims the HSCT-CT community will require:

- Improved understanding of the impact of ethnicity, socio-economic and geographic factors on access, experience and outcomes of HSCT and ATMP patients, to facilitate strategies to level up services across the patient population; and
- The optimisation of care and support throughout the transplant journey through the provision of comprehensive pre-habilitation and post-transplant rehabilitation services to improve patient quality of life and outcomes.

2.3. A new vision for HSCT and ATMP data

Interrogation of high-quality datasets is increasingly used to improve patient outcomes across the NHS. Building on the strength and breadth of current HSCT and ATMP datasets, there is now a significant opportunity to augment their ability to improve transplant outcomes and innovate practice, aligning with the wider NHS' ambitions to deliver high-quality and readily available data for the benefit of patients.

While resourcing challenges remain, this strategy identifies how the HSCT-CT community can evolve from the use of data to benchmark and provide quality control, to a data ecosystem that enables:

- The real-time identification of improvements and adaptations to clinical practice that support improved patient outcomes, experiences and quality of life;
- The application of machine-learning to transform clinical decision-making by helping to ensure treatment decisions are personalised and provide the optimal chance of survival and return to a good quality of life; and
- UK HSCT-CT data to become a secure national asset that attracts investment into HSCT and ATMP research and innovation from the global Life Sciences sector.

The key to achieving this new vision is the creation of a secure, integrated and sustainable data model for HSCT and ATMPs, that provides a holistic view of the patient experience and clinical outcomes and is a driver for radical positive change. HSCT-CT data must become readily accessible to patients, clinicians, and researchers, putting data and information at the fingertips of those who most benefit from its collection and use.

2.4. Global leadership in HSCT and ATMP research

Outcomes after HSCT and ATMP therapies continue to improve but for many patients, treatment related mortality and morbidity remains unacceptably high. Despite the urgent requirement to improve clinical outcomes, fewer than 10% of HSCT-CT patients enter prospective clinical trials - universally accepted as the bedrock of therapeutic innovation in clinical medicine - specifically designed to improve treatment outcomes. Not only does this limit access to, and delay adoption of, innovative therapeutic strategies with the potential to improve patient outcomes, it also compromises the development of evidence-based NHS commissioning policy.

The UK possesses unrivalled strengths in clinical trial delivery - including the integrated structure and scale of the NHS, the globally respected facilitative research infrastructure provided by the NIHR and NCRI and excellence in genomics and translational science. The IMPACT HSCT trials pilot, established on the recommendation of the Forum in 2014, created one of only two HSCT trials networks in the world. Its success in recruiting more than 1,000 patients to clinical trials during its first four years not only demonstrated the appetite of both patients and clinicians to recruit to prospective transplant trials, but also the ability of such an initiative to serve as a magnet for inward investment by the global biopharmaceutical sector. To build on this foundation, and make a sustainable world-class UK HSCT-CT research offer, there needs to be:

- Increased capacity for the delivery of HSCT and ATMP trials, including expanding the Accelerating Clinical Trials (ACT) initiative – an innovative not-for-profit trials delivery vehicle - to include all UK HSCT-CT allograft centres;
- The development of a national paediatric transplant and cellular therapy trial network; and
- Greater and more equitable participation in clinical trials through national targets for HSCT and ATMP trial recruitment.

2.5. A strong and sustainable world-class clinical infrastructure

The NHS is already delivering on its laudable ambition to deliver high standards of care in, and rapid access to, emerging novel therapies such as ATMPs, while also securing the UK's status as a global leader in facilitating future research and innovation in these therapies.

The anticipated rapid growth in new cellular therapies in a range of different diseases and the attendant substantial implications for NHS infrastructure will create major challenges to sustainable HSCT and ATMP delivery in the future. Urgent and radical transformation is now therefore necessary to scale up both the physical capacity and the workforce required to meet the anticipated future demand created by the advent of new therapies and the changing demographics of the UK. Measures to address this significant challenge should include:

- Creating capacity to meet increased demand, including rapid progress in the adoption of ambulatory care models for delivering HSCT and ATMPs, and strengthening the supporting supply chain in relation to apheresis and cell processing laboratories; and
- Building a workforce fit for the future through understanding current capacity limits and bolstering the clinical and non-clinical specialist workforce.

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3. Summary of recommendations

The time frame for delivery of recommendations identified as short-term is 2022 to 2024. The time frame for delivery of recommendations identified as medium- to long-term is 2025 to 2032.

1. Sustainability and resilience of the stem cell donor supply chain	Time frame
1. The UK aligned registry partners should undertake donor recruitment activity aimed at increasing the availability of UK young male donors, typed to the highest HLA resolution and with CMV status made available. This activity should recruit a minimum of 150,000 young male donors in the period from 2022-2025 with the aim of increasing UK donor provision to 45% of cell supply to UK patients.	Short-term
2. NHS Blood and Transplant (NHSBT) and Anthony Nolan should maintain and replenish a cord inventory of 30,000 clinical grade cord blood units available for provision to UK and overseas HSCT patients.	Short-term
3. In 2022/23, the UK aligned registry should aim for 20% of new donors added to the aligned registry to be from a minority ethnic background. The aligned registry should then publish annual minority ethnic donor recruitment targets each year, with supporting contextual information on unmet need, recruitment strategies, and progress against targets.	Short-term
4. The UK aligned registry partners should continue to expand their community partnership-based approaches to recruiting informed and committed minority ethnic stem cell donors, to grow the diversity of HLA types within the domestic stem cell donor pool.	Short-term
5. Anthony Nolan, NHSBT and the clinical community should expand cord blood education and research, to support greater equity of access to HSCT and improved outcomes from the use of cord blood stem cells.	Medium- to long-term
6. NHSBT and Anthony Nolan should expand the supply of high-quality donor materials that are surplus to clinical requirements to academic and commercial partnerships, to enable innovation in the development of ATMPs in the UK.	Medium- to long-term
2. Securing improvement and equity in access, experience and outcomes for patients	**Time frame**
7. The UK HSCT-CT community should establish a pilot research project to better understand the impact of ethnicity and socioeconomic factors on patient access to HSCT and ATMP treatment and patient outcomes.	Short-term
8. NHS England and devolved administrations should support the HSCT-CT community to pilot a comprehensive pre-habilitation service in three geographically disparate and ethnically and socio-economically diverse regions of the UK.	Short-term
9. NHS England and devolved bodies should conduct a full review of the HSCT and ATMP patient pathways to define the resource needed to deliver personalised care and support. This should examine provider reimbursement levels, and whether extension of the 100-day cut-off in specialised commissioning for allograft recipients should be extended in order to facilitate delivery of comprehensive long term follow-up care by HSCT centres.	Medium- to long-term

3. A new vision for HSCT and ATMP data	Time frame
10. The BSBMTCT should make up-to-date outcomes data for each HSCT-CT centre publicly available on an annual basis, to achieve greater transparency for patients and empower them to make informed decisions about their care.	**Short-term**
11. The Department of Health and Social Care and NHS England, and their devolved counterparts, should ascertain the resource required to collect high-quality HSCT and ATMP patient data, and a mechanism should be established which ensures HSCT-CT centres receive allocated funding to enhance their data management capacity.	**Short-term**
12. A new digital Quality of Life data tool should be developed by the HSCT-CT community to collect self-reported experience and quality of life data for HSCT and ATMP patients.	**Medium- to long-term**
13. An HSCT-CT Data Change Commission should be created, as a collaboration between the BSBMTCT, UK aligned registry partners, NHS England and devolved counterparts, patients, academia and industry, to create an enhanced, accessible and sustainable data model for UK HSCT-CT data by 2025.	**Short-term**
14. The UK HSCT-CT data community should explore ethical approaches to licensing datasets, to develop a sustainable investment model for data infrastructure and further strengthen the national HSCT-CT dataset into an asset that supports improving patient outcomes and the development of new therapies.	**Medium- to long-term**
15. A new outcome-predictive clinical decision-making tool should be developed, applying machine-learning technologies to HSCT-CT data to drive greater personalisation of care in order to empower patients receiving HSCT and ATMP therapies.	**Medium- to long-term**
4. Global leadership in HSCT and ATMP research	**Time frame**
16. The resource and bandwidth of the ACT trials network should be expanded to facilitate trial recruitment by every UK allogeneic HSCT-CT centre in order to drive improvements in treatment outcomes, inform commissioning policy and make the UK a "go to" destination for the delivery of transplant and ATMP trials by the global pharmaceutical sector.	**Medium- to long-term**
17. The ACT initiative should be expanded to develop a UK paediatric HSCT and ATMP trial network to support delivery of practice-informing HSCT-CT trials, including Paediatric Investigation Plans (PIPs).	**Medium- to long-term**
18. UK HSCT-CT clinical trials should be designed with the aim of optimising trial recruitment from all demographic groups, with a target participation rate of 50% of eligible patients in prospective clinical trials.	**Medium- to long-term**
19. The HSCT-CT community should work with NHS commissioners to prioritise and facilitate recruitment to practice informing trials and create a mechanism by which savings generated by clinical trial delivery are re-invested into service delivery and clinical trial infrastructure.	**Medium- to long-term**

5. A strong and sustainable world class infrastructure for HSCT and ATMPs	Time frame
20. NHS commissioners should work with NHS providers to urgently expand the provision of an ambulatory model of HSCT and ATMP treatment in order to provide additional capacity for the anticipated rapid growth in the number of ATMP patients.	**Short term**
21. NHS England and devolved health administrations should undertake an urgent review of the capacity of apheresis services and cell processing laboratories to support HSCT and ATMP delivery. The findings of this review should be used to inform a comprehensive national implementation plan for expanding capacity.	**Short term**
22. NHSBT should create a national network of HTA-licenced apheresis services and cell processing laboratories, with enabling technological innovation that allows HSCT-CT centres to identify where apheresis and cell processing capacity is available in real-time.	**Medium- to long-term**
23. The BSBMTCT should carry out a benchmarking exercise to quantify current levels of staff capacity and physical infrastructure in HSCT-CT centres, and potential for growth, to support capacity planning for the impending increase in ATMP patient numbers and complexity of treatment.	**Short term**
24. NHSBT should lead a collaborative approach aimed at developing a national multi-disciplinary education programme for staff within the UK HSCT-CT workforce to ensure it is capable of delivering world-class care.	**Medium- to long-term**

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4. Introduction

Autologous and allogeneic hematopoietic stem-cell transplantation (HSCT) are potentially curative therapies for blood cancers and blood disorders and, increasingly, other conditions. Advanced therapy medicinal products (ATMPs), also referred to as advanced cell and gene therapies and including chimeric antigen receptor T-cell (CAR-T) therapies, are medical products based on genes, cells and tissues, which can also provide lifesaving or life extending treatment options for patients. A significant number of new ATMPs are expected to become available for an increasing range of cancers and other conditions in the coming years.[1]

In the UK in 2020:[2]

- 1,463 patients were treated with allogeneic HSCT, with 978 of those patients receiving unrelated donor stem cells;
- 1,997 patients received autologous HSCT;
- 12 UK HSCT-CT centres provided innovative CAR-T therapies to children and young people with B-cell acute lymphoblastic leukaemia and adults with diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma.

The UK Stem Cell Strategic Forum (UKSCSF) - the 'Forum' - is a collaborative, voluntary body whose membership is drawn from across the HSCT and ATMP community - including patient representatives, clinicians, donor registries, scientists and researchers, NHS commissioners and the pharmaceutical industry. The Forum is commissioned by the Department for Health and Social Care (DHSC) and is sponsored by NHS Blood and Transplant (NHSBT). Forum membership is set out in Appendix 1.

The Forum was first established in 2010 at the request of the DHSC. Its first two reports, published in 2010 and 2014, and subsequent oversight of implementation, led to the creation of the UK aligned stem cell registry and the UK cord blood bank. The Forum now has an expanded remit to include ATMPs, and its membership includes representatives from the pharmaceutical industry accordingly. Given the synergies in the patient care and experience, research and infrastructure needed to deliver these therapies, it is natural that the considerable expertise retained within the Forum membership can provide expert insight into the action that must be taken to ensure the UK is equipped to deliver these innovative new treatments.

This third report of the Forum provides recommendations to build on the Forum's significant achievements to date, to deliver innovative, sustainable, and world-class services for the full spectrum of cell and gene therapies over the next decade.

4.1 Context

The Forum's recommendations have been developed in the context of significant landscape changes in the health and care setting.

[1] ATMP horizon scanning – profiles & pathways: A forward look to ATMPs due in the NHS 2021 – 2023, NHS England and NHS Improvement, February 2022.

[2] BSBMTCT Data, 2020.

4.1.1 Rapid innovation in treatment

The UK is recognised as a global leader in the development, manufacture and provision of ATMPs, which have the potential to cure or significantly extend survival in many disease areas. The first CAR-T therapies were made available to NHS patients within weeks of European Medicine Agency (EMA) approval and patients in the UK were the first in Europe to have access to them.[3] In 2020, the UK hosted over 12% of global ATMP clinical trials. Over a third of these trials are in oncology (35%) and more than one in ten in haematology (12%), and a growing number of trials are sponsored by commercial organisations.[4] NHS horizon-scanning indicates that significantly more advanced therapy treatments will be launched imminently.[5]

4.1.2 An ambitious vision for the UK Life Sciences sector

In July 2021, the HM Government published its Life Sciences Vision,[6] outlining the ambition to make the UK's Life Science sector one of the great drivers of economic growth in the 21st century. HM Government's approach to realise its vision for a Life Sciences "superpower" is underpinned by:

- Streamlined, efficient and innovative research;
- Clinical research embedded in the NHS;
- Patient-centred research;
- Research enabled by data and digital tools; and
- A sustainable and supported research workforce.

4.1.3 COVID-19

The NHS continues to experience significant pressure as a result of the COVID-19 pandemic, the full impact of which is still unfolding in 2022.

Key aspects of the challenge posed by COVID-19 include:

- Continued pressure on the NHS and treatment backlogs;
- Increased delivery of remote and community care;
- Ongoing pressure on the workforce;
- Fewer opportunities to recruit new potential stem cell donors; and
- A reduction in clinical research activity.

The COVID-19 pandemic has also prompted positive changes. Mutual aid networks for HSCT have been established and transplant centres are increasingly sharing capacity and knowledge across regions and nationally. Infection prevention and control across the NHS is vastly improved compared to before the COVID-19 pandemic, which is particularly important to protect HSCT and ATMP patients outside of transplant units. Stem cell donor registries also employed new strategies to bolster resilience. For example, registries have developed innovative new ways of recruiting potential new donors via digital platforms and have expanded capacity and the evidence base

[3] Cell and Gene Therapy Catapult, ATMP Clinical Trials Report, 2020. 2021.
[4] Cell and Gene Therapy Catapult, ATMP Clinical Trials Report, 2020. 2021.
[5] ATMP horizon scanning – profiles & pathways A forward look to ATMPs due in the NHS 2021 – 2023, NHS England and NHS Improvement, February 2022.
[6] HM Government Life Sciences Vision: Build Back Better: Our Plan for Growth, 2021.

around cryopreservation in stem cell transplantation. At the same time, capacity has been created by the adoption of remote consultations for post-transplant patients.

4.1.4 NHS reform in England

The Health and Care Act 2022 sets out measures to promote and enable collaboration in health and care in England. At the heart of the reforms is the formalisation of Integrated Care Systems (ICSs) as the primary commissioning bodies, including for many specialised services currently centrally commissioned by NHS England. There is also potential for challenges to emerge in implementing reforms across the NHS in England, given remaining COVID-19 pressures on the healthcare system.

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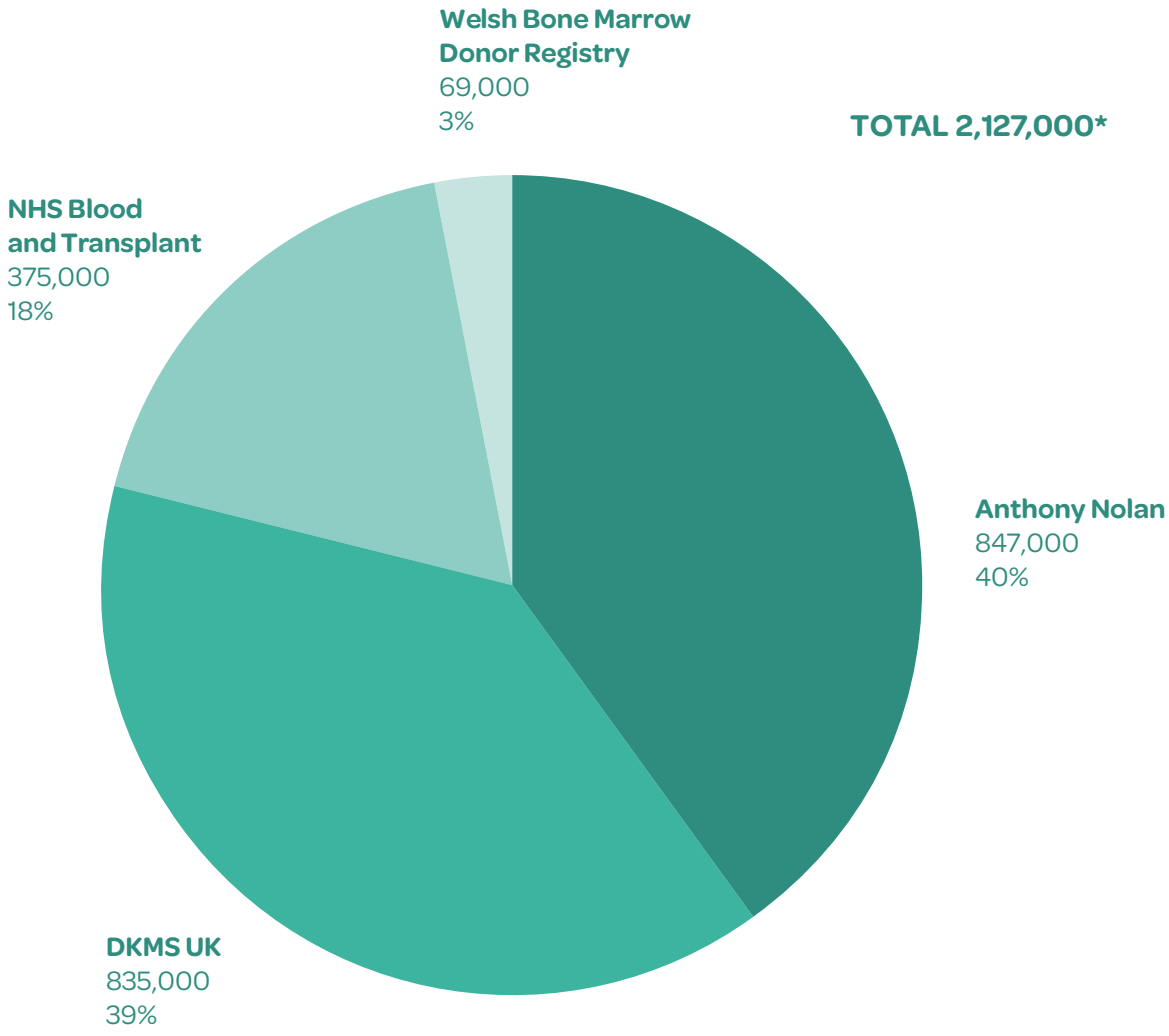
5. Sustainability and resilience of the stem cell donor supply chain

The COVID-19 pandemic raised serious questions about the resilience of UK and global stem cell supply. Widescale border closures and transport disruption highlighted the risks associated with over-reliance on non-domestic stem cell sources for UK patients. While the HSCT community across the world responded swiftly to ensure patients were not significantly adversely affected by issues within the stem cell supply chain, the pandemic made evident that safeguarding and strengthening the aligned registry and cord blood banks in the UK would bring significant benefits.

Figure 1: The UK aligned registry by register



* The total aligned registry for 2020/21 is 2,127,000 – rounded to the nearest thousand. However, the rounding of data presented in this graph will cause a small deviation in the calculated total.

In 2012, upon the recommendation of the Forum, the Anthony Nolan and NHS Stem Cell Registry ("the UK aligned registry") was formed. The UK aligned registry is now a national registry of voluntary stem cell donors in the UK, collaboratively managed by Anthony Nolan, NHS Blood and Transplant (NHSBT), the Welsh Bone Marrow Donor Registry (WBMDR) and DKMS UK. The UK aligned registry partners now provide a pool of over two million registered UK adult stem cell donors,[7] which is searchable for all UK patients requiring a matching adult unrelated donor stem cell source for HSCT. Adult unrelated donors are the main source of stem cells for allogeneic HSCT in the UK, accounting for 59% of allogeneic HSCT in 2020.[8]

Supplementing the adult donor pool is the UK's cord blood stem cell inventory, which currently stands at circa 28,000 clinical-grade units available for use in HSCT. Cord blood is an important source of stem cells for patients who may not have a suitable adult donor, and for ATMP research and development.

The UK aligned registry is a vital public health resource, ensuring patients with a range of life-threatening haematological malignancies and disorders can find a suitable stem cell match from unrelated adult donors or cord blood.

The efforts in the UK to provide a resilient and sustainable source of stem cells for transplantation have also been taken in many other countries. Globally, there are now 39 million voluntary donors and 800,000 cord blood units,[9] including the UK inventory. This global pool of donors is searchable for all UK patients in need.

5.1. Increasing the sustainability and resilience of the UK's stem cell registries

5.1.1. Reducing reliance on overseas donors

The UK aligned registry is available to be searched, via Anthony Nolan, for all UK patients in need of an HLA-matched source of donated stem cells, whether from an adult unrelated donor, or cord blood unit. Anthony Nolan simultaneously searches the global pool of available adult donors and cord blood units in case an overseas donor might be the most clinically appropriate option. Donors are chosen with the aim of securing the best patient outcome, and the degree of HLA match is always the most important factor in donor selection.

The UK is increasingly reliant on overseas donors. In 2017/18, 58% of donated stem cell units provided to UK HSCT-CT were imported from overseas. In 2020/21 that figure was 68%.[10] Further work needs to be undertaken to fully understand factors influencing the increasing reliance on imported stem cells.

Increasing the domestic supply of high-quality stem cell donors is fundamental to reduce reliance on imported cells. Greater use of domestic donors provides clear cost savings and can help to retain and re-invest NHS financial resource in strengthening the domestic supply chain. The Forum supports a target to increase UK-to-UK donor provision to 45% of total supply, achieved through increasing the recruitment of young male donors, as set out in section 5.1.2 of this chapter.

The Forum recommends this target based on the domestic donor supply rate in the USA of circa 50%,[11] given its comparable ethnic minority population demographics to the UK, and on analysis of pre-pandemic domestic supply rates which have reached over 40%.[12] However, the Forum recognises that much more detailed modelling is

[7] UK Aligned Registry, State of the Registry Report, 2020-2021. 2022.
[8] BSBMTCT data, 2021.
[9] WMDA data, 2022.
[10] UK Aligned Registry, State of the Registry, 2020-2021. 2021.
[11] WMDA Global Trends Report, 2021.
[12] Data from Anthony Nolan, 2022.

required to fully understand the potential for increasing domestic supply in the UK and to inform future strategies for donor recruitment to re-dress the balance. Therefore, the target of 45% should be regularly reviewed and informed by the latest modelling and trends. Modelling should include estimates of investment in donor recruitment necessary to achieve domestic supply targets, and analysis of cost savings to the NHS stemming from greater levels of domestic supply.

5.1.2. Prioritising recruitment of young male donors

In 2021, 75% of domestic and imported adult unrelated donors selected for HSCT patients by their clinical teams were aged 30 and under. The same proportion (75%) of adult unrelated donors selected for use were male.[13] The preference for younger male donors within HSCT-CT centres is driven by:

- The use of stem cell units from 10/10 HLA-matched younger donors is associated with better clinical outcomes for patients, including increased survival, and lower rates of side-effects, such as graft vs host disease (GvHD);[14] Male donors often produce higher stem cell yields for clinical use; and
- Using female donors for male patients can lead to an increased risk of GvHD due to genetic factors, whereas male donors do not have an impact on risk of GvHD regardless of a patient's biological sex.[15]

Other factors that are important to clinical teams when selecting donors include:

- Whether donors are HLA-typed to a high resolution; and
- Whether donor cytomegalovirus (CMV) status is available.[16]

Male donors aged under 30 are 13 times more likely to be selected for donation than other people on the UK aligned registry. For this reason NHSBT's British Bone Marrow Registry (BBMR), Anthony Nolan and the WBMDR have donor recruitment criteria specifically targeted at growing the UK "fit panel", a domestic pool of male donors aged under 30 typed to the highest possible HLA resolution.

Increasing the number of young male donors on the UK aligned registry has the potential to significantly increase UK-to-UK supply. Table 1 (overleaf) highlights that all UK registers currently have disproportionately lower numbers of male donors.

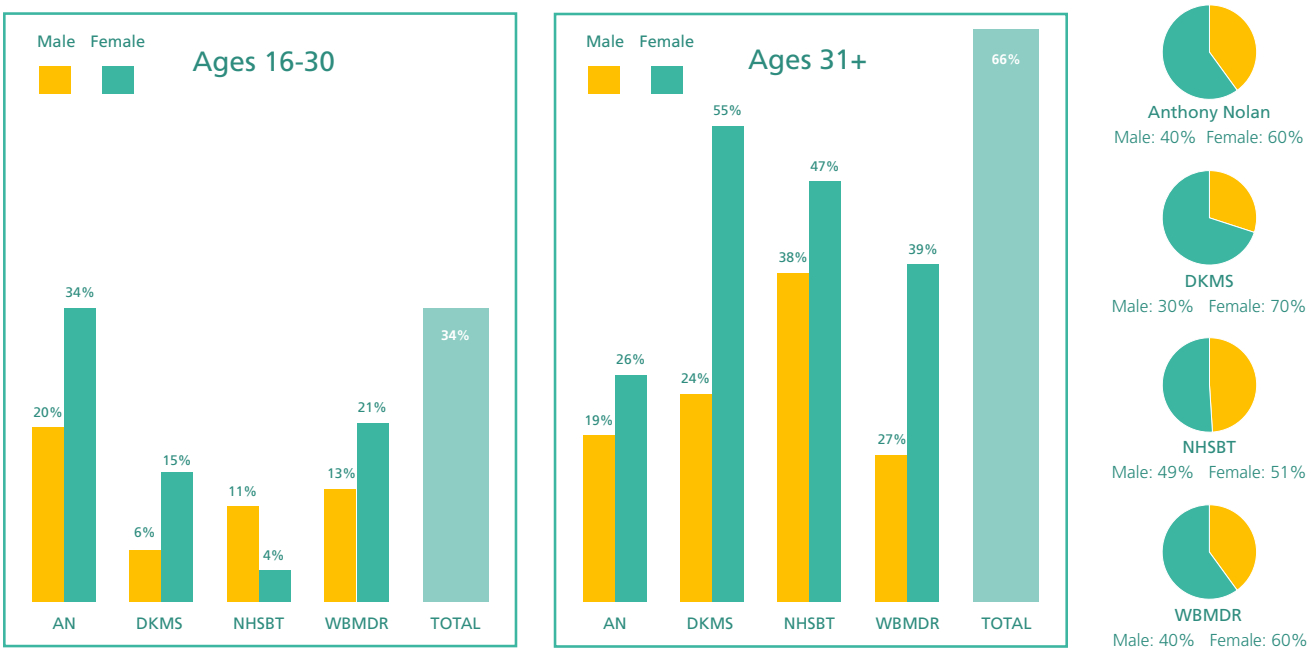
[13] Data from Anthony Nolan, 2021.

[14] Shaw, B. et al. Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most. Biol Blood Marrow Transplant. 2018;24 (5):1049–1056. doi: 10.1016/j.bbmt.2018.02.006.

[15] Kim, H.T. et al. Donor and recipient sex in allogeneic stem cell transplantation: what really matters. Haematologica. 2016;101(10): 1260-1266. doi: 10.3324/haematol.2016.147645.

[16] Mayor, N. et al. Recipients Receiving Better HLA-Matched Hematopoietic Cell Transplantation Grafts, Uncovered by a Novel HLA Typing Method, Have Superior Survival: A Retrospective Study. Biol Blood Marrow Transplant. 2019;25(3):443-450. doi: 10.1016/j.bbmt.2018.12.768.

Table 1: UK aligned registry male/female donor ratios by age



Analysis[17] indicates that building a more resilient and sustainable UK donor registry by recruiting 150,000 more young male donors to the UK registry has the potential to save the NHS £1.1 million per year, by increasing UK donor usage without detracting from patient outcomes (see Appendix 3). Reducing reliance on imported stem cell units will also help mitigate against future supply chain risks.

Recommendation 1: The UK aligned registry partners should undertake donor recruitment activity aimed at increasing the availability of UK young male donors, typed to the highest HLA resolution and with CMV status made available. This activity should recruit a minimum of 150,000 young male donors in the period from 2022-2025 with the aim of increasing UK donor provision to 45% of cell supply to UK patients.

5.1.3. Investment in alternative stem cell sources and treatment modalities

Haplo-identical transplant with post-transplant cyclophosphamide

There is emerging evidence that the use of post-transplant cyclophosphamide (PTCy) treatment for patients receiving donated cells that are not a full 10/10 HLA match improves their outcomes and may even deliver equivalent outcomes to a full 10/10 match.[18] Further clinical research is needed to understand whether the adoption of this practice is appropriate for UK patients. PTCy could transform the utility of the existing UK donor pool and reduce reliance on overseas donors. This would be of particular significance for adult patients from a minority ethnic background, who are significantly less likely to find a 10/10 HLA-matched donor.

[17] Analysis by Anthony Nolan.

[18] Gagelmann, N. et al. Haploidentical Stem Cell Transplantation With Posttransplant Cyclophosphamide Therapy vs Other Donor Transplantations in Adults With Hematologic Cancers: A Systematic Review and Meta-analysis. JAMA Oncol. 2019;5(12):1739–1748. doi:10.1001/jamaoncol.2019.3541.

Umbilical cord blood

Donated cord blood units are an important source of stem cells for use in paediatric HSCT, and for patients, particularly from ethnic minority backgrounds[19], for whom a 10/10 HLA-matched adult unrelated donor cannot be found. Cord transplants can successfully be performed with a greater degree of HLA mismatch.[20]

Cord blood stem cells are vital to the resilience of the UK stem cell supply for treatment in the event of global crises. During the COVID-19 pandemic, the UK aligned registry reported a 30% increase in the utilisation of UK cord blood units in allogeneic transplantation. Future emergency planning should reflect the importance of cord blood units in the event not only of pandemics, but also other disruptive scenarios including nuclear events, where rapid access to off-the-shelf stem cell products suitable for HSCT without close HLA matching may be required. To safely achieve this, there is a need to harmonise standards in stem cell cryopreservation across the UK.

The UK has an inventory of nearly 30,000 clinically viable cord blood units. Since 2015, 30% of demand for cord blood units for patients undergoing HSCT has been met by domestic supply.[21] Sustaining this inventory will support domestic cord blood unit utilisation rates in the UK.

Recommendation 2: NHS Blood and Transplant and Anthony Nolan should maintain and replenish a cord inventory of 30,000 clinical grade cord blood units available for provision to UK and overseas HSCT patients.

5.2. Stem cell provision and access to HSCT

The inequity of access to a best possible 10/10 HLA-matched adult unrelated donor on the basis of ethnicity is well known and addressing this challenge has been a longstanding priority of the Forum.

Analysis by Anthony Nolan has shown that patients of all ethnicities have a roughly equal chance (around 95%) of accessing at least one type of donor cell source for HSCT when taking in to account all possible sources, including cord blood. However, patients from a minority ethnic background have only a 37% chance of finding the optimal 10/10 HLA-matched adult unrelated donor. This compares to a 72% chance for patients from a British, Irish, or Northern European (BINE) ethnic background.

Patients are more likely to find genetically well-matched stem cells from unrelated donors who share their racial group. Large, established stem cell donor registries are disproportionately located in countries with majority BINE populations, such as the UK. People from ethnic minorities can also have more HLA complexity and diversity within their individual ethnicity groups.[22] This means that even if the UK donor pools for each ethnicity were the same size, the chances of finding good matches for patients of different ethnicities would remain lower than for BINE patients.

The UK population is relatively diverse with well-established minority ethnic groups. The chance of finding a well-matched donor varies significantly among the different minority ethnic groups, with mixed ethnicities being the hardest to match. With increasing population diversity in the UK in the future, there will be further growth in the complexity of HLA types in the general population.[23]

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[19] Wynn, L.A. et al. Ethnic diversity and cord blood banking: satisfying the unmet need. Cytotherapy. 2022;(22): S1465-3249. doi: 10.1016/j.jcyt.2022.03.012.

[20] Gluckman, E. History of cord blood transplantation. Bone Marrow Transplant. 2009;(44): 621–626. doi:10.1080/14653240510027136.

[21] Data from Anthony Nolan, 2022.

[22] Yu, N. et al. Larger Genetic Differences Within Africans Than Between Africans and Eurasians. Genetics. 2002;(161)1:269-74. doi: 10.1093/genetics/161.1.269.

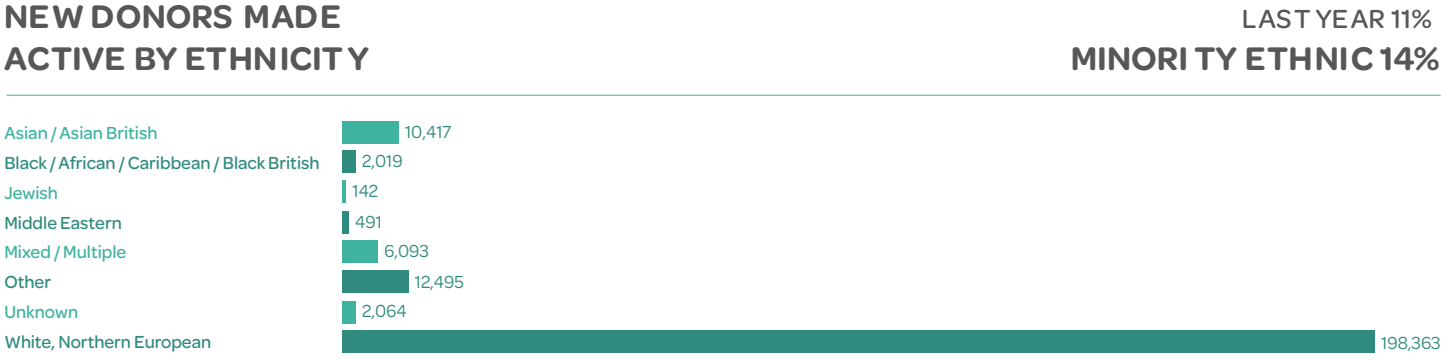
[23] Population Groups by Ethnic Background, England and Wales, Office for National Statistics, 2019.

For these reasons, significantly increasing the number of minority ethnic donors on the UK aligned registry alone will not have a proportionate impact on the chances of patients from a minority ethnic background in finding a 10/10 match to ensure parity with BINE patients. A multi-faceted and global approach is therefore necessary to achieve greater equity for patients from a minority ethnic background, in terms of securing the best chance of a good HSCT outcome. While this includes recruiting more ethnic minority donors in the UK, it also requires focus on supporting overseas donor registries to recruit a more diverse pool of donors that can also be drawn upon to meet UK patient need.

5.2.1. Minority ethnic donor recruitment

As of 31 March 2021, 15% of people on the UK aligned registry are from minority ethnic backgrounds, compared to around 15% of the UK population identifying as having non-White ethnicity.[24,25] While achieving proportionate representation on the UK aligned registry is a step in the right direction, a refreshed approach to minority ethnic donor recruitment remains necessary to improve donor availability for HSCT patients in the UK and overseas.

Figure 2: New donors made active in the UK aligned registry in 2020/21 by ethnicity



There is a pressing need to employ more data-driven decision making to inform resourcing and prioritisation of minority ethnic donor recruitment. This includes modelling and analysis to understand what the annual target for minority ethnic donor recruitment by the aligned registry partners should be.

In 2021, Anthony Nolan initiated a data and insight-driven "register optimisation" project. Using bioinformatics data, the project aims to deliver insights on the optimum size and shape of the UK aligned registry and how and where recruitment, enrichment and retention efforts should be focused. This will enable predictive tools to model UK patient need and how it can be met, which will be particularly useful in informing minority ethnic donor recruitment activity.

NHSBT has developed a sophisticated machine learning model to create prediction scores for donors indicating their likelihood to donate, if identified as a potential match. Work is now being done to help use these predictions to better understand the donor base and apply that learning to donor recruitment strategies.

It is important that HSCT patients from a minority ethnic background and their families understand the approaches to donor recruitment of the UK aligned registry partners and feel empowered to share their views openly. Transparency on the impact of this activity, via open reporting, is also important for patients and families.

For 2022/23 aligned registry partners Anthony Nolan, NHSBT and DKMS have all adopted an ambitious target of recruiting 20% of donors from a minority ethnic background, with associated strategies for reaching these targets.

[24] Population Groups by Ethnic Background, England and Wales, Office for National Statistics, 2019.

[25] UK Aligned Registry, State of the Registry 2020-2021. 2022.

Recommendation 3: In 2022/23, the UK aligned registry should aim for 20% of new donors added to the aligned registry to be from a minority ethnic background. The aligned registry should then publish annual minority ethnic donor recruitment targets each year, with supporting contextual information on unmet need, recruitment strategies, and progress against targets.

5.2.2. A community partnership-based approach to minority ethnic donor recruitment

There is a need for greater collaboration on recruitment activity amongst individual aligned registry partners and community partner organisations who hold valuable expertise in engaging potential new minority ethnic stem cell donors. Organisations who have lived experience and understanding of the cultural or religious barriers and influences to joining the register are far more successful at recruiting donors from minority ethnic backgrounds than UK aligned registry partners alone. Anthony Nolan analysis of donor recruitment activity in 2021/22 shows that on average, 47% of potential new donors who signed up to the UK aligned registry at recruitment events held in collaboration with community-based organisations were from a minority ethnic background, compared to 12% on average across all events.[26]

The last decade has seen the UK aligned registry adopt a more community partnership-based approach to minority ethnic donor recruitment, as recommended by the Forum in its previous reports. Examples of projects initiated under this community-based approach include:

- The expansion of NHSBT and Anthony Nolan's Community Investment Scheme, which funds stem cell donor recruitment roles within community partners such as the African Caribbean Leukaemia Trust (ACLT);
- Engagement of the WBMDR with the Wales Race Forum co-ordinated by Welsh Government; and
- DKMS partnerships with faith organisations to help remove some of the barriers to donation.

Donor attrition (when those on the register identified as a potential match do not donate their stem cells), is significantly higher among donors from an ethnic minority background. Estimates suggest that there is a 56% attrition rate in non-White British donors compared to 35% in White British donors at the verification typing stage.[27] Recruiting informed and committed stem cell donors is key to mitigating against attrition. By working with partners within minority ethnic communities, UK aligned registry partners can achieve a higher level of trust, commitment and understanding in the stem cell donation process among new minority ethnic donors.

Recommendation 4: The UK aligned registry partners should continue to expand their community partnership-based approaches to recruiting informed and committed minority ethnic stem cell donors, to grow the diversity of HLA types within the domestic stem cell donor pool.

5.2.3. Supporting overseas registries

The UK aligned registry and HSCT community must take a global view of how to meet minority ethnic patient need. There is a clear opportunity to increase HLA diversity within the globally available donor pool by supporting the establishment, and growth in capacity and capability, of registries in non-majority BINE populations. Again, with increasing global mixed ethnicity populations, this does not present the comprehensive solution to the lack of availability of 10/10 HLA-matched donors for minority ethnic patients, however it could help to sustain improved ability to meet their needs.

The UK aligned registry partners participate in the World Marrow Donor Association and work individually to support existing and emerging stem cell registries across the world, with DKMS playing a notable role in international registries.

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[26] Analysis by Anthony Nolan, 2022.

[27] Anthias, C. et al. Role of Race/Ethnicity in Donor Decisions about Unrelated Hematopoietic Progenitor Cell Donation: Exploring Reasons for Higher Attrition among Racial/Ethnic Minorities. Biol Blood Marrow Transplant. 2020;26(3):593-599. doi: 10.1016/j.bbmt.2019.10.012.

5.2.4. The role of cord blood in meeting minority ethnic patient need

Cord blood stem cell units represent an important alternative stem cell source for patients from a minority ethnic background.[28] Together, Anthony Nolan and NHSBT have 25 years of expertise in the processing, storage, selection and thawing of cord blood stem cells. However, there is variable experience in the delivery of cord blood transplants within the clinical community across the UK.

To innovate and promote the use of cord blood units, the cord blood HSCT community is undertaking a broad educational initiative, aimed at supporting HSCT-CT centres who offer cord blood transplantation, as well as those who wish to build their cord transplant services. This education programme will include:

- A training and mentorship programme for HSCT-CT centres wishing to build their capacity for use of cord blood stem cells;
- An online 'cord academy' resource for cord blood transplant clinicians; and
- Review and improvement of cord blood transplantation guidance and protocols.

Recommendation 5: Anthony Nolan, NHSBT and the clinical community should expand cord blood education and research, to support greater equity of access to HSCT and improved outcomes from the use of cord blood stem cells.

5.3. Supporting UK innovation

A strong and resilient stem cell supply infrastructure is crucial to meet HM Government's ambitions to expand the scale of research and development undertaken in the UK.

Consent rates suggest that stem cell donors are overwhelmingly supportive of providing material for research and development of new treatments.

NHSBT and Anthony Nolan play a pivotal role in accelerating and facilitating the development of new treatments. Both organisations have the expertise to supply high quality donor materials to clinics, pharmaceutical and biotech companies, and academia, for ethical clinical research and the development of new ATMPs for UK patients. NHSBT and Anthony Nolan also hold expertise in cell processing, cryopreservation, delivery of high value, controlled products, good manufacturing practice, and regulation.

NHSBT works with academic and commercial organisations across the UK, and beyond, to promote, develop, manufacture and distribute new bio-therapies as part of clinical trials, and supports the provision of licensed products such as innovative CAR-T therapies to hospitals. NHSBT is a key partner in the Northern Alliance Advanced Therapy Treatment Centre (ATTC) and the Midlands and Wales ATTC, providing an umbrella under which NHSBT and other NHS organisations work with industry partners to provide systems and solutions to accelerate adoption of advanced therapies.

Anthony Nolan is partnered with the Medical Technology Innovation Facility (MTIF) to provide access to a suite of advanced cell processing routinely used in ATMP manufacturing. Additional partnerships including through the Cell and Gene Therapy Catapult-led consortium enable the delivery of ATMPs for patients.

Recommendation 6: NHSBT and Anthony Nolan should expand the supply of high-quality donor materials that are surplus to clinical requirements to academic and commercial partnerships, to enable innovation in the development of ATMPs in the UK.

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[28] Wynn, L.A. et al. Ethnic diversity and cord blood banking: satisfying the unmet need. Cytotherapy. 2022;(22): S1465-3249. doi: 10.1016/j.jcyt.2022.03.012.

6. Securing improvement and equity in access, experience and outcomes for patients

The ambition of the Forum is to make recommendations that will not only improve access to HSCT and ATMPs, but also optimise outcomes and quality of life for all patients. All patients should have a strong voice in commissioning and service design, and the NHS and wider HSCT-CT community must be empowered to act on patient feedback. This must include achieving greater personalisation of care and addressing unmet physical and emotional needs across the whole treatment pathway. This is of particular importance to HSCT and ATMP patients, as the side- and late-effects of their treatment, both physical and psychological, can last for many years.[29]

6.1. Addressing the impact of health inequalities in HSCT and ATMPs

While there are a number of innate biological factors that can affect survival, such as disease and age, there is also disparity in patient access to, and experience of, HSCT and ATMPs as a result of their background, geographic or socioeconomic circumstances. There is extensive high-quality evidence from outside of HSCT and ATMPs illustrating that there are significant inequalities in outcomes from healthcare on the basis of socio-economic status, geography, ethnicity and other factors. While there is much less evidence from the UK on inequalities in access to and outcomes from HSCT and ATMPs, it is reasonable to expect that health inequalities also apply in this setting, and there is substantial anecdotal and qualitative evidence from UK patients and clinicians to support this view.[30]

These inequalities can and should be addressed through changes in practice.

6.1.1. Factors affecting equity of access to HSCT and ATMPs

Late and under-referral

Late referral into HSCT and CAR-T therapy has been identified by clinical experts as a contributing factor to poor outcomes. In addition, there is consensus in the clinical community that some patients with blood cancers and blood disorders in the UK, for whom HSCT may prove beneficial, are not being referred to HSCT services at all. However, there is very little formal evidence available to help understand the extent and impact of late and under-referral.

A range of challenges exist which limit understanding of the scale of late and under-referral of UK HSCT and CAR-T patients. These include:

- Patient outcomes data held in the BSBMTCT registry is not linked with wider datasets on blood cancer diagnoses in England and the devolved nations. This means it is not possible to interrogate patient registry data to understand the impact of time of referral on HSCT patient outcomes. Further, BSBMTCT data is also only held on patients who receive a HSCT and so cannot be used to examine under-referral;
- There has been limited research with HSCT-CT centres to define and characterise referral patterns with specific reference to late and under-referral of eligible patients; and
- There is no standard definition of late referral, due to the lack of data on referral time to HSCT and CAR-T services from diagnosis and the complexity of disease types referred for transplant/CAR-T.

[29] Armenian, S.H. et al. Longterm health-related outcomes in survivors of childhood cancer treated with HSCT versus conventional therapy: a report from the Bone Marrow Transplant Survivor Study (BMTSS) and Childhood Cancer Survivor Study (CCSS). Blood. 2011;118(5): 1413-1420. doi: 10.1182/blood-2011-01-331835.

[30] APPG on Stem Cell Transplantation and Advanced Cellular Therapies, No Patient Left Behind: The barriers stem cell transplant patients face when accessing treatment and care. 2021.

It is important not only to understand the prevalence and consequences of late or under referral, but also to have the ability to analyse their underlying drivers. Potential patient factors could include:

- Patient demographics, including age; ethnicity and gender;
- Disease;
- Time and location at which a donor search is conducted (in HSCT);
- Complications due to comorbidities; and
- Socioeconomic factors.

There are examples in the UK of improving practice in relation to patient access to these therapies:

- In Wales, 80% of blood cancer patients are managed by the South Wales Blood and Marrow Transplant Programme multidisciplinary team (MDT), resulting in potential HSCT candidates being identified early. Consideration should be given as to how this model could be applied nationally, to create effective regional MDTs which facilitate close communication between district general hospitals and specialist HSCT-CT centres. Moreover, unlike the English datasets, Wales has the Cancer Network Information System Cymru (CaNISC), which allows for patients to be tracked throughout their treatment and follow-up care, leading to improvement in understanding of late referral and its impact; and
- The Cell and Gene Therapy Catapult (CGTC) in collaboration with the ATTC network is soon to launch an initiative that will examine issues relating to referral to CAR-T therapy. Ireland's National Cancer Control Programme has also been making progress in this area under its MDT programme. The insights from these activities could also provide an indication of issues within HSCT.

Ethnicity

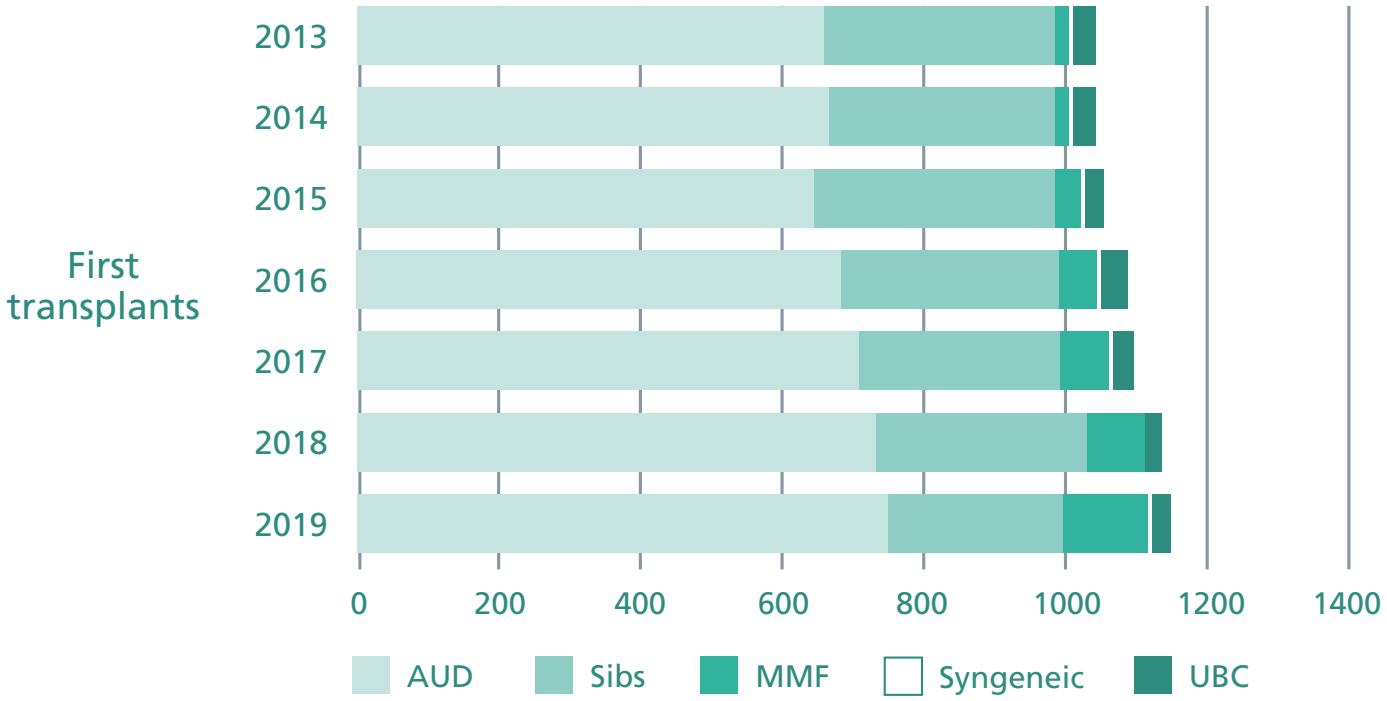
The influence of patient ethnicity on access to an optimal 10/10 HLA-matched adult unrelated donor for allogeneic HSCT is considered in section 5.2 of this report, alongside recommendations that will help to address inequalities in access on the basis of ethnicity.

For patients who don't have an optimal 10/10 HLA matched adult unrelated donor, allogeneic HSCT using either donated umbilical cord stem cells, or donated haplo-identical stem cells, are important alternatives. Patients receiving cord blood HSCTs can often tolerate a higher degree of HLA mismatch than with mismatched adult unrelated donor cells without significantly affecting patient outcomes.[31] Haploidentical HSCT requires only half-matched donor cells, usually donated from a related family member of the patient.

Minority ethnic patients for whom a 10/10 adult unrelated donor is not available should have access to HSCT using these alternative sources of donor cells, regardless of the HSCT-CT centre in which they are being treated. This is critical to securing equitable access to HSCT regardless of patient ethnicity.

[31] Little, A-M. et al. BSHI guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation. International Journal of Immunogenetics. 2021;48(2):75-109. doi: 10.1111/iji.12282.

Figure 3: Number of first HSCT procedures performed 2013-19, by cell source



Key:
AUD = adult unrelated donor
Sibs = sibling
MMF = haploidentical or mismatched family donor
UBC = umbilical cord

Socioeconomic background

It is well established that socioeconomic status has a substantial impact on health outcomes.[32] Important factors such as health literacy, income and the lifestyle that someone can afford, the quality of housing and nutrition available to individuals are all known to be linked to health outcomes.[33] People living in lower income households are more likely to experience poorer health, which could increase co-morbidities in HSCT and ATMP patients and negatively affect transplant-related outcomes and quality of life.[34]

6.1.2. Addressing the impact of ethnicity and socioeconomic-based inequalities

For patients from ethnic minority backgrounds, and those affected by socioeconomic challenges, accessing treatment and navigating their treatment journey is likely to be manifestly more difficult, and their outcomes from treatment are likely to be worse. However, no substantive research has been undertaken to understand the extent to which ethnicity and socioeconomic factors influence patient outcomes from HSCT, and there is a lack of high-quality outcomes data on the basis of patients' ethnicity and socioeconomic status. This makes the creation of strategies to mitigate the impact of inequalities all the more difficult.

Recommendation 7: The UK HSCT-CT community should establish a pilot research project to better understand the impact of ethnicity and socioeconomic factors on patient access to HSCT and ATMP treatment and patient outcomes.

[32] Foster, H. et al. Understanding the influence of socioeconomic status on the association between combinations of lifestyle factors and adverse health outcomes: a systematic review protocol. BMJ Open. 2021;11(5):e042212. doi: 10.1136/bmjopen-2020-042212.

[33] Commission on Social Determinants of Health. CSDH Final Report: Closing the Gap in a Generation: Health Equity Through Action on the Social Determinant of Health. Geneva, Switzerland: World Health Organization; 2008.

[34] The Kings Fund, What are Health Inequalities? 2020.

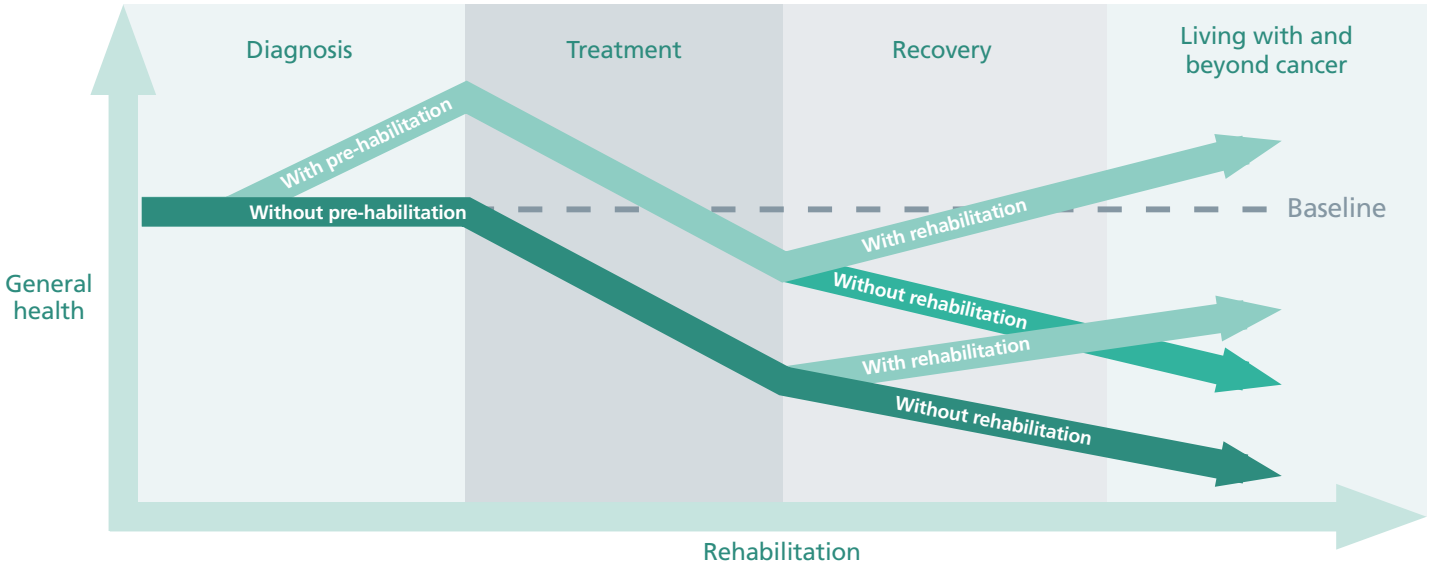
6.2. Transforming HSCT and ATMP care and support to enhance patient quality of life

The 2019 NHS Long Term Plan made a commitment to have in place a Personalised Care Plan (PCP) for every cancer patient by 2021, which includes a needs assessment, care plan and health and well-being information and support.[35] HSCT and ATMP patients would benefit from a personalised approach to the management of their physical, emotional and holistic care and information needs to aid them in achieving a better quality of life post-treatment. This is as true of adult patients as of paediatric patients, and the provision of personalised care must be age appropriate and reflect the different and unique challenges patients face at different stages of their lives. There are currently resource and service planning challenges that inhibit HSCT-CT centres from being able to provide, or confidently signpost to, a comprehensive range of personalised care services to meet all of their patients' identified needs.

6.2.1. Pre-habilitation

Macmillan Cancer Support describes pre-habilitation as "enabling people with cancer to prepare for treatment through promoting healthy behaviours and through needs-based prescribing of exercise, nutrition and psychological interventions. Pre-habilitation is part of a continuum to rehabilitation."[36]

Figure 4: The principle of pre-habilitation:[36]



In HSCT and ATMPs, pre-habilitation is in its infancy. Despite this, evidence is emerging that offering pre-habilitation services may have a significant impact on improving outcomes and patient quality of life post-treatment. Research conducted by clinicians at the University Hospital of Wales and The Royal Marsden has established that the benefits to this patient group could be significant.[37] Side effects such as GvHD and cardio-pulmonary events that can occur after HSCT can be mitigated by improved pre-transplant health.

There is wide variation in the routes HSCT and ATMP patients take before referral into specialist settings, and establishing pre-habilitation services in referral haematology centres (i.e. prior to the first consultation with the

[35] NHS Long Term Plan, 2019.

[36] MacMillan, The National Institute of Health Research, and the Royal College of Anaesthetists. Principles and Guidance for Prehabilitation within Management and Support of People with Cancer. 2020.

[37] Gilmore, H. and Baker, J. Is there a role for prehabilitation in the HSCT patient pathway, The Royal Marsden School. 2020.

HSCT-CT team) will be essential in order to realise the full potential of a pre-habilitation programme. However, evidence suggests that starting pre-habilitation even two weeks before treatment can have a positive impact on outcomes,[38] so co-ordination of these services by HSCT-CT centres would represent a readily implementable service improvement. In a 2021 survey of UK HSCT-CT centres, 78% reported that they did not offer a structured and holistic pre-habilitation service to patients,[39] although examples of excellent practice exist:

- The HSCT-CT centre at Cardiff is currently offering a pre-habilitation service to HSCT and CAR-T therapy patients. The service includes occupational therapy, physiotherapy, pharmacy, psychological support, dietitians, and an advanced nurse practitioner. An evaluation of this service, including data on patient demographics, is expected to report in 2023. Analysis will explore the impact of the service on length of stay in hospital, readmissions, quality of life and patient outcomes; and
- Kings College Hospital's Cancer Rehab team provides a dietetic and physiotherapy service to the haemato-oncological population at King's College Hospital. The pre-habilitation element of this service provides dietetic and physiotherapy screening and intervention to patients who have been consented for a stem cell transplant. 79% of patients referred to dietetic pre-habilitation required specialist nutrition support in order to optimise their nutritional status to better prepare them for HSCT.

The early evidence base indicates that there are potentially significant benefits to patients and the NHS from the wider introduction of pre-habilitation in stem cell transplantation and ATMP delivery, including cost benefits to the NHS associated with reduced re-admission and duration of inpatient spells. There remains, however, a requirement to generate additional high-quality evidence on the patient benefit, feasibility and cost-effectiveness of these services. This evidence should reflect the diverse patient demographics, and system arrangements in the NHS, in order to support evidence-based expansion of these services across NHS settings.

Recommendation 8: NHS England and devolved administrations should support the HSCT-CT community to pilot a comprehensive pre-habilitation service in three geographically disparate and ethnically and socio-economically diverse regions of the UK.

6.2.2. Post-treatment care services

HSCT and ATMPs are invasive and complex treatments that require a significant period of rehabilitation and post-treatment specialist care.

It is estimated there were over 44,000 people living post-transplant in 2021 - over 16,000 living post-allogeneic HSCT and over 27,000 living post-autologous HSCT.[40] Advances in HSCT have resulted in significant increases in the proportion of patients surviving long-term. Across the UK, five-year survival rates for adult allogeneic HSCT have risen from 49% to 51% and, for children, the increase is 73% to 75% (2008-2013 vs. 2014-2019).[41] Five-year survival for adult autologous HSCT has risen from 63% to 68%, and in children, from 51% to 65%, over the same time period. However, HSCT survivors can experience a range of physical and psychological late effects during their recovery. In the first five years after HSCT, it has been reported that 79% of patients experience at least one late-effect, with 26% experiencing three or more late-effects.[42,43,44]

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[38] Faithful, S. et al. Prehabilitation for adults diagnosed with cancer: A systematic review of long-term physical function, nutrition and patient- reported outcomes. European Journal of Cancer Care. 2019;28(4): e13023. doi: 10.1111/ecc.13023.

[39] Miller, L. Interim results of survey conducted by BSBMTCT, 2021.

[40] BSBMTCT correspondence 2022.

[41] BSBMTCT correspondence 2022.

[42] Brewsters, D. et al. High burden of late effects after haematopoietic stem cell transplantation in childhood: a single-centre study. Bone Marrow Transplantation. 2010;45(1): 79-85. doi: 10.1038/bmt.2009.92.

[43] Armenian, S. et al. Longterm health-related outcomes in survivors of childhood cancer treated with HSCT versus conventional therapy: a report from the Bone Marrow Transplant Survivor Study (BMTSS) and Childhood Cancer Survivor Study (CCSS). Blood. 2011;118(5): 1413-1420.

[44] Sun, C. et al. Adverse psychological outcomes in long-term survivors of hematopoietic cell transplantation: a report from the Bone Marrow Transplant Survivor Study (BMTSS). Blood. 2011;118(17): 4723-4731.

In 2019, Anthony Nolan worked with patients, families and clinicians to create a recommended post-transplant care pathway, outlining all services that should be available post-treatment. Not every patient will require every service, but unless HSCT-CT centres are equipped to provide them to all patients in need, the NHS's ambition for every patient to receive the personalised care and support they need is unlikely to be realised. Given the synergies between HSCT and emerging ATMPs such as CAR-T therapies, the pathway is relevant to both treatment types.

Services that patients should be able to access throughout their post-treatment recovery period, however long that may be, are detailed in the pathway, and include:

- Infection and late effects prevention advice;
- Psychological support services;
- Regular post-transplant clinical evaluation;
- Post-HSCT or CAR-T re-vaccination and cancer screening; and
- A holistic needs assessment, supported by access to social care if necessary.

Patient access to the comprehensive range of services outlined in the post-transplant care pathway is patchy across the UK. Of particular concern is lack of access to:

- **Psychological support:** The psychological effects of HSCT can include significant adjustment difficulties and mental health conditions, such as depression and post-traumatic stress disorder.[45] Many patients have reported that the COVID-19 pandemic has increased the anxiety and stress they experience before, during and after their HSCT treatment, and it is expected that these elevated levels of anxiety will remain for some time.[46]

  A 2020 survey of HSCT-CT centres identified that only 33% of centres currently have dedicated psychological support resources embedded within the clinical team. The remaining 67% rely on external psychological care services.[47] In addition, HSCT patients with a non-cancer diagnosis, and families and carers, have significantly limited access to psychological care in comparison to patients with a cancer diagnosis. HSCT-CT centres should be resourced to offer a dedicated and integrated psychologist within their services to all patients who would benefit.

- **Secondary cancer screening:** Allogeneic HSCT recipients appear to have around double the risk of developing secondary solid cancers as the general population, although this varies by type of cancer.[48] Of those patients who survive five years or longer after allogeneic HSCT, secondary cancer is the main cause of death.[49]

  There is no UK guideline on secondary cancer screening in place for HSCT or CAR-T therapy patients. In practice, each UK HSCT-CT centre has its own processes in place for referring patients for screening. Most centres follow the US guidelines, however as these are not tailored to the UK context, interpretation and implementation varies widely. A 2019 survey of HSCT-CT centres found that although most are able to obtain breast and cervical cancer screening for their patients via the national screening programmes, difficulties remain in achieving access to early breast screening for patients who had received total body irradiation.[50]

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[45] Rueda-Lara, M. and Lopez-Patton, M. Psychiatric and psychosocial challenges in patients undergoing haematopoietic stem cell transplants. International Review of Psychiatry. 2014;26(1): 74-86. doi:10.3109/09540261.2013.866075.

[46] Findings from Anthony Nolan patient surveys, 2021.

[47] Survey conducted by BSBMTCT and Anthony Nolan, 2020.

[48] Martelin, E. et al. Incidence and risk factors of secondary cancers after allogeneic stem cell transplantation: analysis of a single centre cohort with a long follow-up. Bone Marrow Transplant. 2019; 54: 334–337. doi: 10.1038/s41409-018-0290-6.

[49] Tichelli, A. et al. Evaluation of Second Solid Cancers After Hematopoietic Stem Cell Transplantation in European Patients. JAMA Oncol. 2019;5(2):229–235. doi:10.1001/jamaoncol.2018.4934.

[50] Dignan, F.L. et al. British Society of Blood and Marrow Transplantation and Cellular Therapy. Survivorship care for allogeneic transplant patients in the UK NHS: changes centre practice, impact of health service policy and JACIE accreditation over 5 years. Bone Marrow Transplant. 2021;56(3):673-678. doi: 10.1038/s41409-020-01067-y.

- **Social work support:** Social workers can identify patients who may need additional support early in their care pathway and provide or signpost to support with financial problems or additional health needs including addiction history or emotional needs. Only a minority of HSCT-CT services currently offer access to a specialist social worker, despite those that do reporting a positive impact of this service.

6.2.3. Commissioning of post-HSCT services

Patients should have equitable access to the full range of care and support services they need to aid their recovery, regardless of where they are treated in the UK. This is not presently the case, and clinical opinion has indicated that this is primarily an issue of resource and funding of services. HSCT-CT centres must either be resourced to offer the full range of services that patients may need during their recovery or have absolute confidence that, when signposting them to services in a primary, secondary or community setting, those services are adequately resourced and have sufficient expertise to meet these patients' specific and complex needs. The resource should follow the patient across their pathway, rather than their pathway and care options being dictated by the source of the available funding, as is currently the case. This is reliant on NHS providers being confident of being reimbursed for services provided.

It is the view of the Forum that the complexity of HSCT and ATMP care dictate that it must remain a nationally-commissioned specialised service, with one responsible commissioner nationally. However, the current arbitrary cut-off for specialised commissioning at 100 days post-HSCT is an ongoing barrier to the delivery of joined-up, person-centred care.[51] After the 100-day point, specialist HSCT-CT centres in England must seek reimbursement for services it offers to patients from the local commissioning body, without the security of certainty that funding is available. Similarly, in Scotland local Health Boards are responsible for planning and delivering care from 100 days after transplant.

A study conducted by Ernst and Young identified that patient need for specialist care services remains significant for a year after allogeneic HSCT, and accounts for significant resource from providers that is not reimbursed. Analysis of hospital activity in England associated with patients transplanted in 2015/16 found that between 100 days and 365 days after discharge, on average, patients experienced 2 elective or non-elective inpatient spells (19 bed days, including 1.2 critical care bed days), 9 day cases or regular day attendances, and 20.2 outpatient appointments. The costs incurred between 100 days and 365 days after discharge were £70 million nationally and an average of £68,033 per patient.[52] Extending the period during which services are commissioned centrally would give HSCT-CT centres more security in providing optimal care for their patients.

Recommendation 9: NHS England and devolved bodies should conduct a full review of the HSCT and ATMP patient pathways to define the resource needed to deliver personalised care and support. This should examine provider reimbursement levels, and whether extension of the 100-day cut-off in specialised commissioning for allograft recipients should be extended in order to facilitate delivery of comprehensive long term follow-up care by HSCT centres.

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[51] Anthony Nolan, A Pathway for Post-transplant Care, 2019.

[52] Ernst and Young, Analysis of hospital activity and costs following allogeneic stem cell transplantation in England, 2021.

7. A new vision for HSCT and ATMP data

The COVID-19 pandemic has demonstrated the power of data to depict NHS healthcare provision in real time, to understand where inequalities exist, and to provide a baseline for rapid research and development and service transformation to address unmet patient need. Improving data is the key to unlocking the potential to transform the delivery of HSCT and ATMPs in the NHS.

The breadth of HSCT and ATMP data encompasses clinical outcomes, patient and donor demographics, genomics, patient experience and quality of life, manufacturing and processing, registry and donor insight, and clinical trials data.

Transforming how the HSCT-CT community provides and uses data has the potential to drive improvements in patient outcomes and quality of life, as well as attracting inward investment from Life Sciences to the UK. This aligns with NHS England's ambition that by 2025, it will 'have a world leading NHS-wide health data research infrastructure that enhances patient care, sustains the NHS and supports innovation'.[53]

Meeting this ambition is particularly important within HSCT in the UK, where there are many unanswered questions concerning optimal treatment strategies, long-term outcomes and patient access to potentially curative therapy especially for ethnic minority groups, as has been detailed throughout this report. Access to high-quality data is central to understanding how best to optimise patient access and outcomes, particularly in the context of aiding identification of health inequalities. With improvements in the collection, analysis and accessibility of HSCT and ATMP data, clinicians could - in the near future - harness data in real time to inform immediate changes to treatment algorithms and, crucially, underpin the design of clinical trials that are more responsive to patient need. There is much that can be achieved in the short, medium and long-term, that will have a transformative impact on patient care.

7.1. Raising the standard of current HSCT-CT data provision

Currently, the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT) has a clear remit and accountability in relation to the collection, analysis and dissemination of patient outcomes data, and the BSBMTCT registry - working closely with NHS bodies - serves as the repository and gateway for information on the outcomes of HSCT, including for commissioning, research and quality improvement purposes.

The BSBMTCT, in partnership with the HSCT-CT clinical community, has created and driven a programme of quality improvement over recent years, and this has succeeded in improving the quality of data reported to the registry. The BSBMTCT also provides annual benchmarking to HSCT-CT centres and NHS commissioners, which has proved an important tool in improving HSCT-CT centre performance consistent with models adopted in other areas of complex clinical care. Data collected from HSCT-CT centres is now more complete and also includes data from patients undergoing CAR-T therapies as well as HSCT. All of this provides a firm foundation for continuing work to further strengthen the data management landscape for HSCT and ATMPs.

BSBMTCT data and reports are shared with HSCT-CT centres and NHS commissioners. While data requests can be made, registry data is not publicly available for patients or other HSCT-CT community stakeholders to access.

The combination of FACT-JACIE accreditation and adherence to BSBMTCT guidelines is intended to ensure that there is consistency in the baseline standards of therapeutic services that UK patients receive during HSCT or CAR-T therapy. However, there is consensus that unwarranted variation remains in patient outcomes.

[53] NHS England, Blog: Collaboration across the system to increase the privacy-protection and speed of life-saving research, 2022.

The BSBMTCT has made significant progress by developing and applying risk-adjustments to HSCT outcomes data to ensure an appropriate comparison of outcomes between centres. However, while this data is available to individual HSCT-CT centres and NHS commissioners, it is not publicly available to patients, donor registries or research organisations.

To better support patients and help them understand HSCT and ATMPs, risk-adjusted outcomes data per HSCT-CT centre for all HSCT-CT and ATMP patients should be regularly published. Patient access to treatment centre-specific outcomes data is standard practice in many areas of care within the NHS, for example, breast cancer, maternity services and solid organ transplantation.

Not only will publishing this data empower patients to be more involved in decision-making about their care, but it will also allow for benchmarking of centres to inform future work in understanding the drivers of variation in patient outcomes, support work to address unwarranted variation and monitor the impact of this work. It is also imperative that the process of accessing this data is simple for patients.

Recommendation 10: The BSBMTCT should make up-to-date outcomes data for each HSCT-CT centre publicly available on an annual basis, to achieve greater transparency for patients and empower them to make informed decisions about their care.

7.2. Addressing data resourcing issues within the NHS

Despite the progress made in recent years, challenges remain in ensuring data collection and reporting by individual HSCT-CT centres is of sufficiently high quality and comprehensive, and consistent:

- There are inconsistencies in how ethnicity is recorded at the wider health system-level both in the UK and internationally, as there is no standard NHS or international categorisation format for recording ethnicity data, creating a barrier to understanding health inequalities;
- There is also an increasing requirement for greater volume and complexity of data collection by HSCT-CT centres, particularly with the advent of new ATMPs; and
- There is limited resourcing of, and training and support for, data managers in some HSCT-CT centres which compromises data collection consistency, dataset granularity and long-term follow-up. Currently funding for data management resource is included in the HSCT tariff in England but clinical leaders have reported that this funding is often top sliced by NHS Trusts and is not available to fund data managers. There are similar data management resourcing challenges in Scotland, Wales and Northern Ireland.

HSCT-CT patients deserve to be able to access comprehensive and integrated data to aid them in making informed decisions about their care, and although data quality has been much improved by BSBMTCT in recent years, NHS commissioners must have confidence that data can support decision-making in service provision requirement. Importantly, clinicians will only be able to improve outcomes with patients through transformational research, benchmarking and clinical practice improvement if data is available and public. The foundation of good data is to ensure that data collection is adequately resourced.

Recommendation 11: The Department of Health and Social Care and NHS England, and their devolved counterparts, should ascertain the resource required to collect high-quality HSCT and ATMP patient data, and a mechanism should be established which ensures HSCT-CT centres receive allocated funding to enhance their data management capacity.

7.3. Improving the quality of HSCT-CT data

Digital transformation is a core ambition of NHS England, and within its transformation agenda, it recognises that "a digitised, connected health and care system will enable services to be delivered more effectively and productively, with citizens at the centre".[54]

7.3.1. Patient-reported data

To fully understand patient outcomes from HSCT and ATMPs, the NHS and the HSCT-CT community must be able to harness and understand patients' own insights into their experiences of treatment and care. This can be achieved through better capture of self-reported outcomes. Patient-reported Outcomes Measures (PrOMs) and Patient-report Experience Measures (PrEMs) provide a clearer picture of how patients themselves view their experience, and how they measure the 'success' of their treatment. Moreover, this data can also be used to understand the factors outside of treatment itself, including ethnicity and socioeconomic factors, that may be impacting patient outcomes and leading to health inequalities.

At present, with the notable exception of Wales, PrOMs and PrEMs are not routinely or comprehensively collected from patients who have HSCT or ATMPs. The Forum understands that early access arrangements for CAR-T therapies did include collection of some quality-of-life outcomes data, but this has not been published. A means of collecting, and publishing, patients' self-reported quality of life outcomes data, in a consistent and thorough way, is urgently needed.

Recommendation 12: A new digital Quality of Life data tool should be developed by the HSCT-CT community to collect self-reported experience and quality of life data for HSCT and ATMP patients.

7.3.2. A transformational data model

The Forum recognises that excellence in relation to data collection and provision exists within other disease and treatment areas in the NHS. For example, the UK Cystic Fibrosis Registry (UKCFR) is an exemplary model. It is the repository for all relevant data within cystic fibrosis, including patient data, PrOMs and PrEMs, staffing level data, and clinical trials data, enabling a fully holistic and comprehensive understanding of cystic fibrosis outcomes, experience and care provision. The UKCFR publishes an accessible annual report on this data, and also makes data available by public or commercial request to patients, NHS commissioners, clinicians, academic researchers, and pharmaceutical partners. The registry is also linked to other relevant data registries, including organ transplantation registries, to ensure a comprehensive picture of the cystic fibrosis patient journey. This registry is sustainable, with a charging model for commercial data requests, and co-ownership of all data procured in partnership with commercial interests.

A similar holistic and sustainable data model can be achieved for HSCT and ATMPs and could:

- Integrate data sets to provide a comprehensive view of the full HSCT or ATMP patient pathway;
- Make data publicly available to help patients and their families understand HSCT and ATMPs, and make informed decisions;
- Give clinical teams the evidence they need to improve the quality of care;
- Improve the ability to monitor the safety and effectiveness of new ATMP treatments or HSCT protocols;
- Provide data for research and development to improve treatment and develop new treatment options; and
- Help NHS commissioners provide appropriate funding to HSCT-CT centres.

[54] NHS Transformation Directorate, 2022.

The new data model should be equipped to provide real time data to inform where immediate change in patient care protocols could improve outcomes and experience. NHSBT has achieved this capability within solid organ transplantation, informing changes that benefit kidney transplantation waiting times, and changing practice to account for the implications of COVID-19 on transplant patients. It is not acceptable that HSCT-CT patients do not currently have equitable access to data relevant to their care in comparison to solid organ transplant patients.

A high-quality HSCT and ATMP data model will also inform the design of future clinical trials. A review of the potential of NHS data published in April 2022[55] advised that NHS England's programme of Trusted Research Environments (TREs) are adopted as a standard platform and used by both researchers and the public in order to build trust in data quality and integrity. TREs are secure platforms where researchers can access and use data in a single secure environment but further details concerning their implementation is awaited. It is advisable however that the HSCT-CT community should ensure the new model for data provision is compliant with the standards NHS England expects from TREs, with a view to ensuring the HSCT-CT registry model will be eligible for TRE status, or be able to be immediately integrated into the relevant TRE.

NHS England has also set out its ambition to make appropriate data sharing the norm and not the exception across health, adult social care and public health.[56] HSCT-CT data is currently fragmented, with donor-related data held by UK aligned registry partners and patient-related data held by BSBMTCT, with no supporting link to wider disease-specific data registries. The consequence of this is an inability to readily access a complete picture of the patient journey, from diagnosis to recovery, preventing analysis on health inequalities, unmet need, and non-HSCT-CT centre interventions in the patient's recovery pathway. In line with the current vision for data held by FACT-JACIE and EBMT, the Forum recommends that a new data model must facilitate greater linking of data sets.

It will be important that the change programme required to create a more accessible and sustainable data model for HSCT and ATMPs is undertaken as a collaborative effort between all HSCT-CT data stakeholders. This includes the BSBMTCT, UK aligned registry partners, patients, NHS representatives and academic and commercial research partners. The Forum supports the initiation of work that can move the HSCT-CT data community towards the creation of a new model, via the establishment of a HSCT-CT Data Change Commission. This must include representatives from all relevant HSCT-CT data stakeholders and should be established with the ambition of a new data model being in effect by 2025.

Recommendation 13: An HSCT-CT Data Change Commission should be created, as a collaboration between the BSBMTCT, UK aligned registry partners, NHS England and devolved counterparts, patients, academia and industry, to create an enhanced, accessible and sustainable data model for UK HSCT-CT data by 2025.

[55] Goldacre, B. Department for Health and Social Care Independent Report: Better, Broader, Safer: Using Health Data for Research and Analysis. 2022.

[56] Department for Health and Social Care: Data Saves Lives: Reshaping Health and Social Care with Data, June 2022.

7.4. Achieving sustainability in a new HSCT-CT data model

HSCT-CT data has the potential to become a significant national Life Sciences asset. An ethical and transparent licensing model for data requests from the diverse components of the UK and global Life Sciences sector will contribute to financial sustainability and generate income that can be re-invested into future data improvement activities. Moreover, as this asset develops, the model can become a trusted steward of HSCT-CT data, providing ethical advice and expertise to data users that can also generate income.

At present, data generated by clinical trials in ATMPs is almost exclusively held by the pharmaceutical company. It is rarely made available to inform future research, despite the NHS infrastructure facilitating these trials. Therefore, in addition to the transactional income generated by data provision, there are also opportunities for collaboration with clinical trial partners in the biopharmaceutical sector to use the new HSCT-CT model and create co-ownership of newly generated data, which can then be used in future research.

The creation of this data asset, in combination with the establishment of ACT, a financially sustainable infrastructure for transplant and ATMP trials, will also support HM Government's ambition to grow the UK Life Sciences sector. The Forum recognises NHS England's work on ensuring the commercialisation of data is ethical, and all work that would monetise HSCT-CT data should be compliant with the General Data Protection Regulation (GDPR) and good ethical practice. The ability to rapidly access robust data will attract the pharmaceutical industry to base more trials in the UK, particularly for new ATMPs, delivering inward both inward economic investment and job creation, and also cost savings associated with trials to the NHS.

Recommendation 14: The UK HSCT-CT data community should explore ethical approaches to licensing datasets, to develop a sustainable investment model for data infrastructure and further strengthen the national HSCT-CT dataset into an asset that supports improving patient outcomes and the development of new therapies.

7.5. Realising the full potential of data to improve patient outcomes

Emerging machine-learning approaches can support the HSCT-CT community to move beyond benchmarking, reporting and understanding activity in real time, and towards using data to better predict patient experience and outcomes, and inform clinical decision-making on that basis. The HSCT-CT community's exploration of how machine-learning can be deployed should include work to develop an algorithm that can inform a transformational clinical decision-making tool. This tool could empower clinical teams and patients to make informed decisions about their care.

The Forum recognises the advancements made in this area by international organisations. The European Society for Blood and Marrow Transplantation (EBMT) has used its large HSCT patient data registry to support big data and machine learning approaches to clinical decision making in HSCT.[57] In addition, the Center for International Blood and Marrow Transplant Research (CIBMTR), the HSCT-CT data registry in the USA, has developed algorithms to both predict availability of potential stem cell donors, and survival-based outcomes. NHSBT has also used machine learning to develop an algorithm that supports clinical decision-making in solid organ transplantation.

[57] Shouval, R. et al. Machine learning and artificial intelligence in haematology. Br J Haematol. 2021; 192(2), 239-250. doi: 10.1111/bjh.16915.

The ambition of the Forum is that data is used to develop a clinical decision-making tool that can put the following information at the fingertips of HSCT-CT clinicians:

- Percentage chance of finding a 10/10 matched AUD or cord blood unit;
- Implications of patient variables such as disease type, HLA and CMV match status of donor, age and co-morbidities on treatment survival and likely post-treatment complications; and
- Alternative treatment options and available clinical trials.

This will have the following benefits:

- Personalised clinical decision making for patients with serious, high-risk indications in relation to HSCT and non-HSCT approaches, including ATMPs, which are all continually evolving across many indications;[58]
- Greater personalisation of supportive care, including suitability for cost-saving ambulatory care; and
- Stronger analysis of health economic aspects related to delivery of HSCT and ATMPs within the finite resources of the NHS.

Recommendation 15: A new outcome-predictive clinical decision-making tool should be developed, applying machine-learning technologies to HSCT-CT data to drive greater personalisation of care in order to empower patients receiving HSCT and ATMP therapies.

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[58] Snowden, et al. Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2022. Bone Marrow Transplant. 2022; 19:1-23. doi: 10.1038/s41409-022-01691-w. Epub ahead of print. PMID: 35589997; PMCID: PMC9119216.

8. Global leadership in HSCT and ATMP research

Increased donor availability, coupled with advances in HSCT technology, have resulted in incremental improvement in patient outcomes over the last decade but it remains the case that many HSCT recipients still die of either transplant toxicity or recurrent disease.[59] Similarly, although CAR-T therapy provides an additional potentially curative treatment option for patients with relapsed leukaemia or lymphoma, the majority of patients die of recurrent disease after CAR-T cell therapy.

Despite the pressing need for novel strategies to improve outcomes for both HSCT and CAR-T recipients, historically less than 5% of patients have entered clinical trials designed to improve outcome after transplant or ATMP therapy. A similar deficit exists in the design and recruitment of trials designed to increase access to transplant therapies. Coupled with the current rapid development of new HSCT and ATMP therapies with the potential to transform clinical outcomes there is now an urgent requirement for a concomitant expansion in the capacity for delivery of practice informing prospective trials in HSCT and ATMP therapies for UK patients.

Consistent with HM Government's Life Sciences vision[60] of building on the strategic assets of the NHS to make the UK a "go to' destination for the delivery of trials, the further expansion and development of IMPACT, the established national transplant trials network, is essential in order to drive further improvements in patient outcomes and create early and more equitable access to innovative therapies. The growth of a HSCT and ATMP trials infrastructure within the UK will also increase the potential to attract inward investment by the global biopharmaceutical sector and drive economic growth and job creation.

8.1. Optimising the delivery of HSCT and ATMP trials

The creation of a national HSCT clinical trial network to improve patient outcomes was a key recommendation of the 2014 Forum Report. Supported by the BSBMTCT, NIHR and the Office for Life Sciences, the IMPACT transplant trials network was launched in 2017 and utilised the successful "Hub and Network" model pioneered by the UK Trials Acceleration Programme. Funded by a £3.4 million grant from Anthony Nolan, NHSBT and Leuka, the IMPACT pilot consisted of a trial delivery hub based in the Cancer Research UK Clinical Trials Unit in Birmingham University and a network of 23 IMPACT-affiliated HSCT-CT centres. Through a peer review process, initial research nurse funding was provided for ten of the affiliated centres, on the basis that if the four-year pilot was successful, a means of sustainably expanding the network of funded centres would be identified in the future.

Representing one of only two HSCT trial networks in the world, IMPACT has recruited more than 1,050 patients to seven practice-informing prospective HSCT trials in its first four years of operation - more than double its recruitment target despite the operational challenges presented by the COVID-19 pandemic. Notable amongst the IMPACT trials have been the completion of Pro-DLI, the first randomised trial of prophylactic donor lymphocyte infusion in acute myeloid leukaemia and the rapid recruitment to AMADEUS, the largest randomised trial of maintenance oral azacitidine therapy. This trial attracted in excess of £6 million funding from the biopharmaceutical sector and has been delivered as a registration enabling trial with enhanced pharmacovigilance and monitoring.

The IMPACT pilot has already resulted in a doubling in the number of patients transplanted for acute leukaemia who are entered into prospective clinical trials and increased access to novel therapies for UK patients. Its establishment as an internationally significant and highly effective trials infrastructure has served as a magnet for inward investment into the UK Life Sciences ecosystem by the global pharmaceutical sector.

[59] BSBMTCT Executive Summary of Transplant & Cellular Therapy outcomes in UK/ROIA report for Commissioners, 12th edition, 2021.

[60] HM Government, Taskforce on Innovation, Growth and Regulatory Reform independent report, 2021.

8.1.1. Creating more capacity in the HSCT trials infrastructure

The initial IMPACT pilot was primarily funded from philanthropic and charitable income. Despite its success, the impact of the COVID-19 pandemic on these income streams required the identification of an alternative, and more resilient funding model.

A new financial model was identified and developed after extensive consultation with the clinical haemato-oncology and HSCT community, blood cancer charities, donor registries, the National Institute for Health Research (NIHR) and the National Cancer Research Institute (NCRI). Predicated on the delivery of a mixed portfolio of clinically-prioritised, industry-sponsored, and academic investigator-initiated trials, a not-for-profit and commercially nimble trial delivery vehicle, Accelerating Clinical Trials Ltd (ACT), was established in 2021. ACT has received strong support from the pharmaceutical sector as an innovative trials delivery model which leverages the strengths of the UK haemato-oncology and transplant community to deliver practice informing prospective trials of novel drug and cellular therapies. It is noted that similar innovative trial delivery vehicles such as Protas are being developed in other disease areas within the UK, Europe and the USA.

ACT will fund both the Trials Acceleration Programme and IMPACT research nurse networks and have the capacity to deliver both registration enabling industry-sponsored and investigator-initiated trials. Funded by a £5 million pump-priming grant it is anticipated that ACT will become financially sustainable in its fourth year. The linked DIDACT Foundation will support ACT to ensure the trials it delivers are prioritised by the clinical academic community, and consistent with NCRI and NIHR priorities. DIDACT will also fund a training programme for current and future clinical triallists and research nurses, provide sponsorship capacity for investigator-initiated trials and advise on re-investment of anticipated future financial surpluses generated by ACT to patient benefit.

The ACT model will:

- Establish a more financially sustainable model for delivery of HSCT and blood cancer trials, with the networks able to host pharmaceutical company sponsored trials;
- Provide UK investigators with a competitive proposition for leadership of academic and commercial trials;
- Increase access to novel therapies for UK patients;
- Support the delivery of embedded genomic and translational studies in conjunction with basic biology laboratories; and
- Create new income streams which will be re-invested to the benefit of UK transplant and blood cancer patients.

The Forum supports ACT's central ambition to provide a financially sustainable model of transplant trial delivery and extend provision of core research nurse funding to all UK allogeneic transplant centres. The Forum also supports the expansion of ACT's scope to support trials in emerging novel cell and gene therapies thereby providing an infrastructure to attract greater pharmaceutical sector investment in the UK providing accelerated patient access to potentially transformative cellular therapies through a world class cellular therapy trial network.

Recommendation 16: The resource and bandwidth of the ACT trials network should be expanded to facilitate trial recruitment by every UK allogeneic HSCT-CT centre in order to drive improvements in treatment outcomes, inform commissioning policy and make the UK a "go to" destination for the delivery of transplant and ATMP trials by the global pharmaceutical sector.

8.1.2. Increasing support for paediatric clinical trials

At present ACT's focus is on increasing capacity for HSCT-CT trials in adults. However, there is equal need for more research to improve outcomes of paediatric HSCT and ATMP treatments, and the Forum supports ACT's ambition to develop a UK HSCT-CT trial network for children. HSCT and ATMPs are pivotally important curative strategies in the treatment of leukaemia and other blood cancers in children and are of increasing importance in the management of non-malignant diseases such as haemoglobinopathies and metabolic diseases. Treatment regimens used in paediatric HSCT are associated with adverse effects on growth and fertility, secondary malignancies, and significant psychological consequences. Prospective trials aimed at improving survival and minimising late-effects in children have been identified as a priority by the clinical HSCT community.

A recent survey of paediatric HSCT-CT centres in the UK revealed that only 11% of paediatric patients were entered into such studies. UK HSCT-CT centres have reported that common barriers to establishing paediatric clinical trials include lack of research nurse resource, lack of principal investigator time, and lack of support for trial management.

Consultation with the paediatric HSCT-CT community and patient groups has identified strong support for the funding of a paediatric HSCT-CT trial by ACT. Such a network would provide core research nurse and data manger funding for up to 12 paediatric transplant centres in order to increase capacity and minimise delays at centres as well as working to build synergies with the adult IMPACT network.

Furthermore, increasing access for paediatric patients to therapies licensed in adults through paediatric investigation plans (PIPs) is a priority and could be facilitated by ACT's structure.

Recommendation 17: The ACT initiative should be expanded to develop a UK paediatric HSCT and ATMP trial network to support delivery of practice-informing HSCT-CT trials, including Paediatric Investigation Plans (PIPs).

8.2. Achieving greater and equitable participation in clinical trials

8.2.1. Improving trial recruitment

Improving patient outcomes through robust clinical trials is dependent on increasing patient participation in trial development and delivery. Participation in research and clinical trials should form a core component of NHS culture and be embedded in patient pathways. Pharmaceutical companies often cite low patient recruitment as a barrier to establishing trials. In 2015, 19% of UK clinical trials closed due to failure to recruit sufficient patient participants, and 86% did not recruit sufficient numbers in the allotted time frames.[61]

Participation in clinical trials in HSCT and ATMPs is being improved via the work of IMPACT, and now ACT. If ACT can be expanded, it will have the benefit of securing more equitable geographic representation of patients within UK trials. The Forum therefore recommends all HSCT-CT clinical trials adopt ambitious targets for recruitment among eligible patients, to enable monitoring of performance in this area.

Underrepresentation of people from minority ethnic groups in UK cancer research clinical trials has been recognised for many years.[62] Ensuring ethnic diversity in clinical trials is vital to enhance the validity and generalisability of clinical trials. The NIHR has a target of 30% of minority ethnic patient recruitment to clinical trials. The Forum's ambition extends beyond this, to a target of 50% of all eligible patient recruitment to

[61] Huang, G.D. et al. Clinical trials recruitment planning: A proposed framework from the Clinical Trials Transformation Initiative, Contemp Clin Trials. 2018; 66:74-79. doi: 10.1016/j.cct.2018.01.003.

[62] GGodden, S., Ambler, G. and Pollock, A.M. Recruitment of Minority Ethnic Groups into Clinical Cancer Research Trials to Assess Adherence to the Principles of the Department of Health Research Governance Framework: National Sources of Data and General Issues Arising from a Study in One Hospital Trust in England. J Med Ethics. 2010; 36(6):358–362. doi: 10.1136/jme.2009.033845.

trials, regardless of ethnicity. The Forum recognises the importance of NIHR's INCLUDE guidance, outlining a pathway to increasing participation from patients in all under-served groups, including patients from ethnic minority backgrounds. The intention of the pathway is to increase equitable access to trials, and better patient representation. All clinical trials in HSCT and ATMPs should work towards adopting this pathway in patient recruitment.

Recommendation 18: UK HSCT-CT clinical trials should be designed with the aim of optimising trial recruitment from all demographic groups, with a target participation rate of 50% of eligible patients in prospective clinical trials.

8.3. Creating and supporting a 'trials-ready' HSCT-CT culture within the NHS

The principle of embedding clinical trials and research within the NHS is explicitly acknowledged and prioritised by HM Government and the NIHR.[63] The imminent increase in the number of HSCT and ATMP treatments for blood cancer will require significant growth in, and retention of key trials personnel including research nurses, data managers and pharmacists. Investment in dedicated nurses, pharmacy resource and support staff for clinical trials will be critical to secure greater and more equitable patient recruitment. The investment required to fund a skilled workforce can be identified from the financial envelope created by both the financial savings and economic benefit delivered to the NHS by efficient clinical trial delivery.

Recent research demonstrated that trial recruitment to a portfolio of blood cancer trials permitted 1,727 patients to access drugs regimens worth more than £250 million at no cost to the NHS.[64] Moreover, within HSCT-CT, practice-informing trials such as the recently delivered FIGARO trial of conditioning regimens in AML can result in changes to treatment protocols that deliver cost-savings within the NHS.[65]

The substantial financial savings to the NHS which accrue from efficient clinical trial delivery, coupled with the broader benefits to the UK Life Sciences sector, should be more explicitly acknowledged in the identification of new funding streams to support trials development. More accurate identification of the cost-savings delivered by efficient clinical trial delivery would permit re-investment into HSCT and ATMP innovation and service delivery.

Recommendation 19: The HSCT-CT community should work with NHS commissioners to prioritise and facilitate recruitment to practice informing trials and create a mechanism by which savings generated by clinical trial delivery are re-invested into service delivery and clinical trial infrastructure.

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[63] HM Government Policy Paper, The Future of UK Clinical Research Delivery, June 2021.

[64] Fox, T. et al. Trial re-investment to build better research for better impact. The Lancet. 2019; 394(10199):635-636. doi: 10.1016/S0140-6736(19)31363-7.

[65] Craddock, C. et al. Augmented reduced intensity regimen does not improve post allogeneic transplant outcomes in Acute Myeloid Leukaemia. J Clin Oncol. 2021; 39(7):768-778. doi: 10.1200/JCO.20.02308.

9. A strong and sustainable world class infrastructure

Advanced cellular therapies such as HSCT and ATMPs are an important therapeutic strategy in many malignant and non-malignant diseases due to their curative potential. They represent novel treatment options that will prove lifesaving or life-extending for patients who would otherwise have limited or no treatment options. The regenerative medicine market, of which HSCT and ATMPs are a subset, raised around £15 billion of investment globally in 2020, a 50% increase on 2019.[66]

The UK plays a globally significant leadership role in the design, delivery and adoption of novel cellular therapies.

NHS England horizon scanning has identified 30 new ATMPs that are likely to go through NICE appraisal by the end of 2023 alone.[67] 14 ATMPs for non-haematological disease indications are likely to be submitted to NICE by 2023, representing a major expansion in the eligible patient population for these therapies.[68]

Simultaneously, indications for both autologous and allogeneic HSCT continue to expand. In recent years autologous HSCT in multiple sclerosis has become an option, and potentially curative allogeneic HSCT is now available to more patients with sickle cell disease.

It is likely the number of patients receiving HSCT and ATMPs will continue to grow over the coming decade. If the UK health system can modernise and transform to meet the challenge inherent in delivering this significant uplift in volume promptly, safely and while maintaining standards, the benefits to patients and to the economy will be significant.

9.1. Creating capacity to meet future demand

The COVID-19 pandemic brought to light the significant stress in the system not only within HSCT-CT centres, but within the apheresis and laboratory support services that are critical to delivering HSCT and ATMP therapies. There are critical capacity challenges in delivering services to meet even current levels of demand. Without significant transformation the UK will not be able to deliver these services at an adequate level to sustain the UK as a global leader in cell therapy treatment development and delivery. Added to this is a lack of comprehensive analysis and modelling to understand the level of expansion that will be needed over the coming decade to meet future demand associated with the radical increase in newly available ATMP therapies.

Ten of the 48 HSCT-CT centres in the UK are currently delivering CAR-T therapies for adults, and 12 deliver to children and/or young adult patients.[69] NHS England has set out an ambition for the majority of HSCT-CT centres in the UK to deliver ATMPs to patients. The Welsh and Scottish Governments are similarly ambitious for the delivery of ATMPs for patients.[70] However, HSCT-CT infrastructure in the UK will not have capacity to meet the impending increase in demand, even if all current centres are able to offer these treatments.

The fundamental and urgent infrastructure challenge will require collaborative working between NHS bodies, HM Government and devolved administrations, academia and the HSCT-CT clinical community to resolve. Without transformational planning and investment, the physical infrastructure for HSCT and ATMP delivery will comprehensively fail to meet increasing patient demand created by the expansion of ATMPs in the near future.

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[66] Cell and Gene Therapy Catapult data, 2020.

[67] ATMP horizon scanning – profiles & pathways A forward look to ATMPs due in the NHS 2021 – 2023, NHS England and NHS Improvement, February 2022.

[68] ATMP horizon scanning – profiles & pathways A forward look to ATMPs due in the NHS 2021 – 2023, NHS England and NHS Improvement, February 2022.

[69] NHS England data on CAR-T Therapy, 2022.

[70] Welsh Government, Advanced Therapies Statement of Intent, 2019.

9.1.1. Transforming care settings

HSCT and ATMPs are currently almost exclusively delivered via an inpatient model which has changed very little in the past 20 years, despite the emergence of innovative new delivery models, globally and in pockets of the UK, that could promote equally safe but more cost-effective care.

Ambulatory care capacity must be urgently increased to realise the clear and evidenced potential it has to support the sustainable delivery of autologous and allogeneic HSCT and ATMPs. It is entirely feasible that a significant proportion of HSCT and ATMP patients could be treated in an ambulatory setting and would not need admitting to an inpatient bed during their entire treatment episode. This would allow HSCT-CT centres to do more within a smaller infrastructure footprint.

Most importantly, this approach is nearly universally popular with patients. Those UK centres that have been able to offer some ambulatory care provision report that the ability to be in a home-from-home environment and retain independence is of central importance to patients. Ambulatory care helps retain patient autonomy, promotes baseline physical activity levels and can provide psychological benefits compared to inpatient admissions.

There are other benefits of ambulatory care.[71,72,73,74,75,76] These include:

- No significant additional risks to patient safety;
- Lower staff requirement, particularly out-of-hours;
- Associated cost-savings with reduced staff requirement and reduced inpatient bed requirement;
- Nurses reported a positive experience working in ambulatory care;
- Treatment start dates could be planned in advance as lower reliance on bed availability; and
- Potential reduction in infection.

Well-managed and well-resourced ambulatory pathways and facilities are needed to monitor patients and intervene where necessary, to keep patients safe and maintain a high quality of care. Technologies such as remote monitoring devices are likely to play a pivotal role in achieving this. Upfront investment will be required to ensure more HSCT-CT centres can establish ambulatory care services. However, this short-term upfront investment will reduce the need for the more significant and long-term capital investment that would be required to simply increase inpatient capacity to accommodate growth in patient demand.

Moreover, once established, there are cost savings associated with ambulatory care. Retrospective analysis of University College London Hospital data conducted in 2012 indicated that nursing costs associated with an ambulatory care model were two-thirds lower than in the inpatient setting[77], and data analysis undertaken in

[71] Sive, J. et al. Hotel-based ambulatory care for complex cancer patients: A review of the University College London Hospital experience. Leuk Lymphoma. 2012; 53(12):2397-404. doi: 10.3109/10428194.2012.694430.

[72] Comerford, D. and Shah, R. Ambulatory approach to cancer care. Part 1: the patient experience. Br J Nurs. 2018; 27(17):S4-S12. doi: 10.12968/bjon.2018.27.17.S4.

[73] Comerford, D. and Shah, R. Ambulatory approach to cancer care. Part 2: the role of nurses and the multidisciplinary team and safety. Br J Nurs. 2019; 28(4):S20-S26. doi: 10.12968/bjon.2019.28.4.S20.

[74] Comerford, D. and Shah, R. Ambulatory approach to cancer care. Part 3: starting and maintaining the service and its challenges and benefits. Br J Nurs. 2019; 28(17):S4-S8. doi: 10.12968/bjon.2019.28.17.S4.

[75] Holbro, H. et al. Safety and cost-effectiveness of outpatient ASCT in patients with multiple myeloma. Biol Blood Marrow Transplant. 2013; 19(4):547-51 doi: 10.1016/j.bbmt.2012.12.006.

[76] Reid, et al. Outpatient administration of BEAM conditioning prior to autologous stem cell transplantation for lymphoma is safe, feasible, and cost-effective, Cancer Med. 2016 Nov; 5(11): 3059–3067.

[77] Sive, J. et al. Hotel-based ambulatory care for complex cancer patients: A review of the University College London Hospital experience. Leuk Lymphoma. 2012; 53(12):2397-404. doi: 10.3109/10428194.2012.694430.

Canada in the same year suggested a whole treatment cost differential of CAN$42,737 and CAN$62,259 when comparing HSCT via ambulatory care to inpatient HSCT respectively.[78]

The need to increase capacity to meet growing patient demand is urgent. Feasibility studies and implementation planning should be started immediately to enable every UK HSCT-CT centre to offer ambulatory care to appropriate patients.

Recommendation 20: NHS commissioners should work with NHS providers to urgently expand the provision of an ambulatory model of HSCT and ATMP treatment, in order to provide additional capacity for the anticipated rapid growth in the number of ATMP patients.

9.1.2. Strengthening the supply chain

The delivery of HSCT and ATMPs requires a resilient and flexible supply chain of supporting services, separate to the cells themselves. The most significant of these are apheresis services for cell harvest, and laboratory services for cell processing. The increasing number of ATMP procedures has created intense pressure on these supporting services. Current capacity is not sufficient to meet even today's level of demand. This is not only relevant to patients, causing delay to treatment, but is also impacting domestic stem cell donor provision, where instances of lack of apheresis capacity for cell harvest has led to the selection of alternative overseas donors in the past year, at higher cost to the NHS.[79]

The Forum welcomes NHS England's intention to undertake a review of apheresis capacity and believes this should be replicated in devolved health administrations. Without significant expansion, apheresis capacity will not be sufficient to either meet demand to support patient treatment, nor to support research and development in HSCT and ATMPs, curtailing growth in the UK medical innovation sector. The pharmaceutical industry will be more likely to establish new ATMP trials, store and process products in the UK if these support services are available, reliable and operating to a high standard. There are also very significant capacity issues associated with the cell processing laboratories in the UK, which are vital to support HSCT and in producing ATMP starter materials. The cell processing laboratory infrastructure also supports research and development in this field, and issues with capacity are similar to those associated with the apheresis network. As such, the Forum urges NHS bodies to undertake a similar review of laboratory capacity with urgency, to inform a corresponding implementation plan for increasing capacity to meet the future demand.

Recommendation 21: NHS England and devolved health administrations should undertake an urgent review of the capacity of apheresis services and cell processing laboratories to support HSCT and ATMP delivery. The findings of this review should be used to inform a comprehensive national implementation plan for expanding capacity.

At present, there is no national system for clinical teams to identify which services have good capacity at any given time. HSCT-CT centres should be able to identify which services have the capacity to provide services with the fastest turnaround times and be free to use the service that will expedite time to treatment for their patients. The Forum would therefore support the creation of a national network of Human Tissue Authority (HTA)-licenced apheresis and cell processing laboratories, supported by technological innovation to allow clinical teams to identify where capacity lies in real time.

Recommendation 22: NHSBT should create a national network of HTA-licenced apheresis services and cell processing laboratories, with enabling technological innovation that allows HSCT-CT centres to identify where apheresis and cell processing capacity is available in real time.

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[78] Holbro, H. et al. Safety and cost-effectiveness of outpatient ASCT in patients with multiple myeloma. Biol Blood Marrow Transplant. 2013; 19(4):547-51 doi: 10.1016/j.bbmt.2012.12.006.

[79] Insight from Anthony Nolan, 2022.

9.2. Building a workforce fit for the future

Investment in the NHS workforce is just as important as in physical infrastructure to increase resilience and sustainability in the delivery of HSCT and ATMPs. Clinical leaders report that the HSCT-CT workforce is already strained, and completely insufficient to safely support the expected growth in demand. Delivering ATMPs safely at significantly higher volume will require widescale additional training and growth both within, and potentially outside, the haematology specialism.

The British Society of Haematology's (BSH) 2019 workforce report identified several very significant challenges within the existing general haematology workforce which are reflected within the specialist HSCT-CT workforce. Shortfalls in the haematology workforce are leading to delays in access to diagnostics and novel treatments.[80] Factors contributing to the shortfall include an ageing workforce, reduced numbers of trainees, and increased incidence of stress and sickness. It is important to note that these challenges are not just within clinical haematology teams, but among the laboratory workforce too.

Expertise in ATMP delivery, and managing treatment complications, is concentrated within HSCT-CT services. The potential rapid growth in patient numbers means not only are there likely to be critical shortages of specialist haematology staff, but also a lack of skills within that workforce to see patients treated with new ATMPs safely and effectively. There is also a need to focus on addressing staff and skills shortages in relation to clinical nurse specialists (CNSs), clinical psychologists, nutritionists, physiotherapists, pharmacists, HSCT-CT technicians and palliative care support staff.

9.2.1. Understanding the workforce gaps

As a basic measure, the current workforce capacity, including levels of training and skill, must be better understood to inform future planning. This must be informed by understanding of the adequate staff to patient ratio to safely deliver HSCT and ATMPs, such as CAR-T therapies, to aid analysis of the extent to which the workforce must be scaled up to meet future demand.

Recommendation 23: The BSBMTCT should carry out a benchmarking exercise to quantify current levels of staff capacity and physical infrastructure in HSCT-CT centres, and potential for growth, to support capacity planning for the impending increase in ATMP patient numbers and complexity of treatment.

9.2.2. Upskilling the specialist workforce

The advent of new ATMPs has brought with it the need for further education and training of the full clinical and non-clinical HSCT-CT workforce to ensure they are delivered safely and effectively to patients. The Forum recognises the exemplary work that is being undertaken by the Advanced Therapy Treatment Centre (ATTC) network, London Advanced Therapies (LAT) and the Cell and Gene Therapy Catapult (CGTC), in partnership with Health Education England (HEE) eLearning for healthcare, in developing a new eLearning programme targeted at healthcare and academic professionals.

There must be support for the universal availability of these training programmes to support clinical and administrative teams. As patient numbers grow, there will be a requirement for a greater proportion of the workforce to feel confident in delivering these therapies, and this will only be achieved if they are able to fully access the necessary training. In addition, it is only by ensuring the highest standards of training are available on

[80] British Society for Haematology Workforce Report 2019.

an equitable basis to the whole national workforce that patients will receive an equitable high standard of care regardless of the centre in which they are treated.

Recommendation 24: NHSBT should lead a collaborative approach aimed at developing a national multi-disciplinary education programme for staff within the UK HSCT-CT workforce to ensure it is capable of delivering world-class care.

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10. Glossary

ACT: Accelerating Clinical Trials Ltd
ATMP: Advanced Therapy Medicinal Products/Advanced Cell and Gene Therapies
BMT CRG: Blood and Marrow Transplantation Clinical Reference Group
BSBMTCT: British Society of Blood and Marrow Transplantation and Cellular Therapies
BSH: British Society for Haematology
CAR-T: Chimeric Antigen Receptor Cell Therapies
CGCT: Cell and Gene Therapy Catapult
CMV: Cytomegalovirus
EBMT: European Society for Blood and Marrow Transplantation
HEE: Health Education England
HLA: Human Leukocyte Antigen
HSCT: Haematopoietic Stem Cell Transplantation
HSCT-CT: Haematopoietic Stem Cell Transplantation and Cellular Therapies
HTA: Human Tissue Authority
HTA Agencies: Health Technology Appraisal Agencies
MDT: Multi-disciplinary Team
MHRA: Medicines and Healthcare Products Regulatory Agency
NHS: National Health Service
NHSBT: NHS Blood and Transplant
NICE: National Institute for Health and Care Excellence
NIHR: National Institute for Health Research
PTCy: Post-transplant Cyclophosphamide
UKSCSF: UK Stem Cell Strategic Forum
WHO: World Health Organisation
WBMDR: Welsh Blood and Marrow Donor Registry
WMDA: World Marrow Donor Association

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11. Appendices

11.1. Appendix 1: Membership of the UKSCSF

Gillian Adams
Patient representative; Member of the European Society for Blood & Marrow Transplantation Clinical Outcomes Working Group; Non-Executive Director, Academy for Healthcare Science (AHCS) and Member of NHS England National Programme of Care Board, Blood and Infection

Nic Alderson
Chief Operating Officer, Anthony Nolan

Hugh Allen
Chief Strategy Officer, Anthony Nolan

Professor Persis Amrolia
Consultant in Bone Marrow Transplant, Great Ormond Street Hospital for Children NHS Foundation Trust; Professor of Transplantation Immunology, Institute of Child Health and Research Professor at National Institute for Health Research

Dr Jacqueline Barry
Chief Clinical Officer, Cell and Gene Therapy Catapult

Henny Braund MBE
Chief Executive Officer, Anthony Nolan

Professor Ronjon Chakraverty
Consultant Haematologist, University College London Hospital NHS Foundation Trust; Professor of Haematology and Cellular Immunotherapy, University College London and Medical Director for IMPACT Clinical Trials Network

Emma Cook
Head of Welsh Bone Marrow Donor Registry, Welsh Blood Service

Professor Charles Craddock CBE
Forum Chair; Academic Director of the Centre for Clinical Haematology, University Hospitals Birmingham NHS Foundation Trust and Professor of Haemato-oncology, University of Birmingham

Dr Robert Danby
Consultant Haematologist, Oxford University Hospitals NHS Foundation Trust; Medical Director, Anthony Nolan and Chair of the UK Cord Blood Initiative

Dr Fiona Dignan
Consultant Haematologist and Clinical Director for Haematology, Manchester University NHS Foundation Trust; Chair, Bone Marrow Transplantation Clinical Reference Group and Secretary of the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT)

Jonathan Graves
Advanced Therapies Lead, Department of Health and Social Care

Dr James Griffin
Consultant Haematologist, University Hospitals Bristol NHS Trust and Medical Director, Cell, Apheresis and Gene Therapies, NHS Blood and Transplant

Sharon Hodgson
National Programme of Care Manager, Blood and Infection, NHS England

Daniel Hollyman
Director, Cell, Apheresis and Gene Therapies, NHS Blood and Transplant

Ed Jenkins
Business Franchise Head of Cell and Gene Therapy, Novartis

Julia Lee
Head of the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSCMTCT) Data Registry

Orin Lewis OBE
Chief Executive Officer, African Caribbean Leukaemia Trust and Chair of the National Black, Asian and Minority Ethnic Transplant Alliance

Professor David Marks
Director of Bone Marrow Transplant Unit, University Hospitals Bristol NHS Foundation Trust and Professor of Haematology, University of Bristol

Dr Gail Miflin
Chief Medical Officer & Clinical Services Director, NHS Blood and Transplant

Dr Kim Orchard
Senior Lecturer and Consultant Haematologist, University Hospital Southampton NHS Foundation Trust; Director, Wessex Blood and Marrow Transplant Programme and Past President British Society of Blood and Marrow Transplantation & Cellular Therapy (BSBMTCT)

Professor Antonio Pagliuca
Professor of Stem Cell Transplantation, King's College London and King's College Hospital NHS Foundation Trust and Chief Medical and Scientific Advisor, Anthony Nolan

Guy Parkes
Head of Stem Cell Donation and Transplant, NHS Blood and Transplant

Dr Victoria Potter
Consultant Haematologist and Director of Stem Cell Transplantation, King's College Hospital NHS Foundation Trust and Secretary, British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT) Clinical Trials Committee

Anita Ralli
Associate Director, Government Affairs, Gilead Sciences

Dr Tracey Rees
Head of the Welsh Transplantation and Immunogenetics Laboratories, Welsh Bone Marrow Donor Registry

Dr Deborah Richardson
Consultant and Honorary Clinical Senior Lecturer in Haematology, Bone Marrow Transplantation and Cellular Therapies, University Hospital Southampton NHS Foundation Trust; Medical Director, Wessex Blood and Marrow Transplant Cell Collection Unit and Treasurer of the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT)

Anke Roexe
Senior Programme Manager, National Specialist and Screening Services Directorate, NHS Scotland

Professor John Snowden
Director of Blood and Marrow Transplantation Programme, Sheffield Teaching Hospitals NHS Foundation Trust and President of the British Society of Blood and Marrow Transplantation and Cellular Therapy (BSBMTCT)

Professor Marc Turner
Director, Scottish National Blood Transfusion Service and Professor of Cellular Therapy, University of Edinburgh

Professor Paul Veys
Director of the Bone Marrow Transplant Unit, Great Ormond Street Hospital

Dr Keith Wilson
Director, South Wales Blood and Marrow Transplant Programme; Clinical Senior Lecturer in Haematology, Cardiff University School of Medicine and Honorary Consultant Haematologist, Cardiff and Vale University Health Board

Professor Robert Wynn
Consultant Paediatric Haematologist and Director of Paediatric Bone Marrow Transplant Programme, Manchester University NHS Foundation Trust and Honorary Clinical Professor in Paediatric Haematology, University of Manchester

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11.2. Appendix 2: Progress against 2014 UKSCSF Objectives

Recommendation	Detail

1. **The Anthony Nolan and NHS Stem Cell Registry should continue to expand the UK's 'fit panel' to 150,000 donors. There should be a continued emphasis on recruiting young, male, ethnically-diverse donors predominantly aged between 16 and 30. Donors should be typed at high or allelic-level resolution.**	• As of 2020/21 the aligned registry includes over 2.1 million stem cell donors.
	• Over 234,000 new donors were added to the registry in 2020/21. This is fewer than 2019/20 reflecting the cancellation of face-to-face recruitment activity due to the COVID-19 pandemic.
	  • In 2020/21, 69% of those added to the aligned registry were female
	  • 45% of those added to the registry were aged under 30
	  • 14% of those added to the registry were from a minority ethnic background
	  • Over 35,000 men aged under 30 were added to the registry in 2020/21
	  • In 2017/18, UK donors were selected for 42% of UK patients, the highest share since 2010/11. In 2020/21, this dropped to 32%.
	• Partnerships with DKMS UK, NHSBT and organisations such as the Rik Basra Leukaemia Campaign, Team Margot, and ACLT (African Caribbean Leukaemia Trust) have expanded reach to Black, Asian and minority ethnic communities.
	• NHSBT's Community Investment Scheme is providing £440,000 to community-based projects to raise awareness of stem cell donation amongst Black, Asian and minority ethnic communities in partnership with Anthony Nolan
	• Anthony Nolan has only recruited potential new donors aged between 16-30 since 2012. The Anthony Nolan Phenotype Project builds on the work of the 'fit panel'. As of 1 July 2021, 10,637 young male Anthony Nolan donors have been typed to allelic-level and their ABO and CMV status has been added to the register.
	• NHSBT altered its recruitment criteria to exclusively recruit blood donors who are either Caucasian male or Black, Asian and minority ethnic, male or female, aged 17-40. This ensures that all recruitment and typing resource is directed at 'fit panel' growth.
	• WBMDR recruits only donors aged 17-30 who are all typed at ultra-high resolution with ABO, CMV status and CCR5 and currently has a fit panel of 7,185 high resolution/ultra-high resolution typed 17-30 male donors with ABO and CMV available.

Recommendation	Detail
2. **The Anthony Nolan and NHS Stem Cell Registry should continue to develop evidence-based strategies to further improve donor availability when approached for donation. Stem cell supply organisations should undertake or commission research to better understand donor behaviours in relation to stem cell donation.**	• The impact of the pandemic in 2020/21 led to an increase in unavailability of donors worldwide. Attrition at the stage of verification typing from Anthony Nolan donors has increased in 2020/21 to 40%, up from 34% in 2019/20. • Anthony Nolan is working with the WMDA to better understand and communicate the availability of donors to assist in efficient donor selection. • In the case of donors from the Phenotype Project, attrition drops dramatically (12% in 2017) – showing the benefit of up-to-date contact information and ongoing engagement. Anthony Nolan has an established programme of mass and targeted retention communication, including a "first year on the register" journey to increase awareness and understanding, targeted asks to increase engagement and commitments, and regular education communication at key points throughout the year. • NHSBT has deployed a machine-learning model with 75% reliability to help identify donors who are most likely to go through with donation based on their blood donation record. Donors are assigned a reliability score that helps identify best donor choice.
3. **Anthony Nolan and NHS Cord Blood Bank should establish an inventory of 30,000 cord blood donations by 2018. Beyond 2018, inventory growth to 50,000 donations should be funded via income generated through donation provision. Inventory utilisation should be maximised by banking only those donations likely to contain a clinically useful dose of stem cells, equivalent to 14x10^8 total nucleated cells before processing. 30% – 50% of donations should include Black, Asian and minority ethnic parentage.**	• Collection of umbilical cord blood units was paused during the COVID-19 pandemic which slowed progress, however the total cord bank is close to 28,000 units. • The target for collections with Black, Asian and minority ethnic parentage is consistently met with over 26% of the cord blood bank from minority ethnic donors. • Cord blood banks apply a 14x10^8 TNC threshold to their clinical processing and are constantly seeking process improvements that increase the number meeting this threshold. • Since 2015, a total of 192 cord blood units from the Anthony Nolan and NHS cord blood banks have been used for lifesaving transplants for UK patients. • Cord blood utilisation in the UK during 2020/21 increased to the second highest in-year amount since cord blood has been available as a transplant option.

Recommendation	Detail
4. **Anthony Nolan and NHSBT should work with midwives and community groups with direct access to families, especially those from ethnic minorities, to raise awareness of the medical benefits of unrelated donor stem cell transplantation.**	• Anthony Nolan has co-created, with the NHS maternity units in which it is based, a delayed cord clamping leaflet which aims to give balanced information to the donor and to reduce the impact of delayed cord clamping on the volume of cord blood collections. • Anthony Nolan has successfully piloted a translation service to increase accessibility for families from minority ethnic backgrounds. It plans to roll this out in 15 languages across all cord blood collection sites alongside local involvement from ethnic minority community groups.
5. **UK stem cell supply organisations should continue to implement next-generation DNA sequencing platforms for unambiguous HLA typing of selected adult donors and cord blood donations. The combined strengths of UK partners in the genomics of histocompatibility with particular reference to transplantation should be exploited to advance the UK Government's Life Sciences strategy.**	• Both Anthony Nolan and NHSBT have moved on to next generation DNA sequencing platforms. • NHSBT and WBS have extended this HLA typing level to patient typing. • WBMDR donors are also HLA typed using next generation DNA sequencing and the WBMDR panel has more than 50,000 donors HLA typed to high/ultra-high resolution. • 63% of donors are now typed to the highest possible resolution.
6. **Anthony Nolan, NHSBT, WBMDR, BSBMT and BSHI should collaborate to improve the selection and provision of adult donor and cord blood stem cells by gathering and sharing performance data, providing expert guidance, and supporting education**	• Anthony Nolan and NHSBT continue to run extra services for UK Transplant Centres within the Cord Support Programme aiming to boost Transplant Centre confidence in using cord blood as a source of graft and to subsequently increase overall cord usage in the UK. • The WBS/WBMDR donor selection for the University Hospital of Wales is undertaken by Clinical Scientists in H&I ensuring expert led selection and guidance to the transplant clinicians at MDT meetings. This collaboration supports two-way education and training. • Annual Graft Selection Strategy Workshops (GSSW) are run online by the Aligned Registry to ensure continued sharing of data and expertise both with and between transplant clinicians. In November 2020, GSSW had a record number of attendees (115) with 70% of them from UK Transplant Centres and 30% from Aligned Registry partners.

Recommendation	Detail
7. Funding should be identified to support and improve the collection and analysis of patient outcome data. A more complete outcomes database should be established and interrogated by consolidating the patient and donor-related data held by BSBMT and organisations of the Anthony Nolan and NHS Stem Cell Registry.	• The BSBMTCT conducted a survey of Transplant Centres to better understand how resources are deployed on data management and where there are opportunities for improvement. • Anthony Nolan and the BSBMTCT work in partnership to host regular training days for data managers, aimed at highlighting the crucial role of accurate and timely outcome data to the commissioning of services and patient-focused research. • Anthony Nolan and the BSBMTCT are developing a strategic partnership which will further improve the collection, analysis and use of outcomes data. • Anthony Nolan is funding a rotating data manager post to provide three Transplant Centres with additional resource and provide proof-of-principle for long-term NHS investment in data management resource.
8. Anthony Nolan and NHS Stem Cell Registry should continue to develop and implement IT platforms to facilitate the rapid import and export of stem cell donations.	• NHSBT led the initiative to implement the European Marrow Donor Information System (EMDIS) – Cord which automates the transfer of cord blood information to NMDP, France and Italy increasing visibility of UK cords in searches. • The work done in collaboration with the NMDP to ensure Anthony Nolan and NHSBT unrelated donors and cords are available in the up-front search in the US has resulted in both organisations seeing a 100% increase in exports to the US. • In 2013 the WBMDR became a donor centre for the NMDP ensuring that WBMDR donors are also listed in up-front searches in the US. • In partnership with the World Marrow Donor Association (WMDA), WMDA, ZKRD (The German National Bone Marrow Donor Registry) and the National Marrow Donor Programme (NMDP), Anthony Nolan provided project management, design, business analysis and governance support to WMDA to re-engineer Bone Marrow Donors Worldwide (BMDW) – WMDA's global donor search platform, now the Search & Match algorithm.
9. A national stem cell transplantation trials network should be established to facilitate and promote high-quality prospective, randomised and controlled early phase clinical trials of new molecular and cellular therapies for patients with haematological malignancies.	• IMPACT – the UK's stem cell transplant clinical trial partnership – was launched in 2017 as a four-year pilot. Funded by Anthony Nolan, Leuka and NHSBT, the initiative includes a dedicated 'hub' hosted by the University of Birmingham and a network of 23 participating Transplant Centres. This has accelerated trial design and patient recruitment. • Seven clinical trials have been worked up and approved. Two trials have completed recruitment (Pro-DLI and COVID-19 BMT). Four trials have opened (ALL-RIC, AMADEUS, COSI & MOTD) and a further trial is in set-up (RATING).

Recommendation	Detail
10. Basic science laboratories should be encouraged to participate in relevant clinical trials to derive novel information on predictive biomarkers, in this way developing a stratified and personalised approach to stem cell transplantation.	• Several retrospective studies investigating the role of different predictive biomarkers in the outcome of haematopoietic cell transplantation have been published by scientists within the Anthony Nolan Research Institute since 2014. • Particular focus has been given to the role of the highly polymorphic HLA and Killer-cell Immunoglobulin-like Receptor (KIR) genes. Many studies have been conducted as international collaborations with groups overseas, particularly the USA. • Donor selection practice has changed as a result of some of this work, which should lead to improved patient outcomes. • Measurable Residual Disease (MRD) is a prognostic biomarker in acute myeloid leukaemia and was evaluated prospectively as a prognostic biomarker in the UK FIGARO trial. It is also being investigated as surrogate marker for novel therapies in the COSI and AMADEUS trials by the Clinical Immunology Service, University of Birmingham and the Molecular Oncology Diagnostics Unit, Guy's Hospital, London
11. Commissioning processes should encourage the development of regional centres of excellence for recipients of alternative donor transplants which reflect geographic constraints and are consistent with broader national policies including the delivery of early phase trials in regenerative medicine. There should be a consistent national approach for commissioning patient care after 100 days post-transplant.	• The Blood and Marrow Transplant Clinical Commissioning Group (BMT CRG) has finalised a quality review process, which describes how it reviews BSBMTCT provider-level quality data on behalf of NHSE/I. This has been invaluable in developing a better understanding of trends across the country and areas for improvement. • Looking ahead, the BMT CRG is in the process of reviewing the adult and paediatric indications tables, and associated policies. This will identify areas where further work is required to ensure equity of access. The BMT CRG are working closely with BSBMTCT on this work. • The BMT CRG also plans to undertake work aimed at improving value and reducing variation (such as capturing innovations and learning from COVID-19 working) and supporting the continued introduction of ATMPs. • A new post-transplant care pathway was published in May 2019 clearly setting out the services and support packages that are central to patients' recovery. It was developed by Anthony Nolan in collaboration with an Expert Steering Group consisting of leading healthcare professionals, local NHS representatives and patients.

Recommendation	Detail
12. **The well-established human and capital infrastructure currently supporting regenerative cell therapies for patients with bone marrow disorders should be fully exploited in delivering innovative regenerative cell therapies for other disorders.**	• The 2021 Forum has considered advanced therapies as well as stem cell transplantation.

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11.3. Appendix 3: Anthony Nolan analysis of cost benefit of recruiting more young male donors to the UK stem cell registries

Using analysis of the donation rates of donors on the Anthony Nolan register the below model outlines the impact of recruiting 150,000 young male donors and typing them to the highest resolution as well as making their CMV status available.

Anthony Nolan estimates the potential for the UK to provide a further 135 donations per annum for UK patients, increasing the market share from 32% in FY 20-21 to 45% over five years. This improved capacity for the UK to supply the UK demand will enable potential cost savings for the NHS of around £1.1 million per annum after the three years of recruitment.

Table 3: An estimation of additional UK donors selected for UK patients through expansion of the UK register

	Additional Donors made available (by end of year)	Additional donations by UK donors per annum	Additional Market share	Total Market share	Annual cost saving (£)	Cost per product (based on donations 1050)
FY 20-21	-	-	-	32%	-	£20,372
Year 0	50000	16	1.5%	34%	133k	£20,245
Year 1	50000	68	4.9%	38%	566k	£19,883
Year 2	50000	115	4.5%	43%	960k	£19,457
Year 3	0	134	1.9%	45%	1,125k	£19,301
Year 4	0	135	0.0%	45%	1,126k	£19,300

This growth would further support the resilience of the registry by increasing the number of UK donors selected for patients across the globe.

Methodology

The results of modelling are based on a longitudinal study of donors available on the Anthony Nolan donor register, for at least one day, since April 2015. Anthony Nolan compared the efficiency of Phenotype Project donors, availability of CMV status, HLA commonality in the UK (based on the predicted phenotype frequencies on the AN register), gender and ethnic background.

The rates of donation per 10,000 donor years available were calculated for each of these donor groups to account for donors registered or deleted during the study period. These rates were calculated both for donations to UK patients and international patients in order to more accurately model UK donations, these results are shown in Table 2.

The model used the following assumptions:

- The volume of recruitment is based on 150,000 donors over a 3-year period (50,000 per year).
- The donor years available is based on the days available which is a cumulative sum of the following each month:
  - Donors recruited in any given month will contribute ½ the number of days within the given month, accounting for recruitment throughout the month.
  - Donors recruited prior to current month will contribute a full month of days.
- The types of donors recruited will be male, CMV enriched, British, Irish or Northern European (BINE) and typed to the same level of a donor from the Phenotype Project.
- 18% of the donors recruited will be from the top 2,500 phenotype rank based on analysis of the current phenotype frequencies of the Anthony Nolan register. The remaining 82% will reflect the donation rate of a donor from > 2,500 phenotype rank.
- The volume of transplants will remain stable throughout and based our assumption on the volume of unrelated donor transplants facilitated for UK patients in 2019-20 prior to the COVID-19 pandemic.
- The average cost of a stem cell product from the UK, EU and outside the EU are £14,680, £20,000 and £32,205 respectively. The increased UK market share is then used to calculate the proposed saving to the NHS. Therefore, the assumptions do not account for fluctuations in the cost of stem cell products. A summary of the weighted cost per product can be seen in Table 1.
- The types of donors recruited will reflect the phenotype frequencies on the Anthony Nolan register as of April 2021.
- Non-UK supply will remain at a 75:25 split EU:non-EU for the remaining demand each year.

Risks/caveats/potential improvements for the model

Below are some factors that might improve the model further as well as some caveats and risks to the model:

- The model is based on unrelated adult donor donations only, therefore assumes usage of cord/haploidentical transplant and other methods of transplant remains the same;
- The model does not consider the impact of worldwide recruitment on UK selection, it has to be noted that Germany have 5.5 million donors typed at high resolution as of January 2020 adding 831,000 donors to their register within 2019. This ensures they can meet the needs of 70% of German patients receiving a transplant from an unrelated adult donor;
- The analysis is based on predicted phenotype frequencies of the current Anthony Nolan register, some of which have a low relative probability. It is not possible to recruit based on HLA type and therefore, this could impact actual donation rates experienced;
- The model uses an estimation of the potential impact of improved typing based on the phenotype of donors and makes assumptions on the diminishing returns.

Table 4: Donation rates per 10k donor years available by donor group

Enrichment level	Phenotype rank	Gender	Ethnicity	Donation rate per 10k donor years	Donation rate per 10k donor years (UK)	Donation rate per 10k donor years (INT)
Phenotyped	<= 2,500	Male	BINE	78.5	57.9	20.6
			MEB*	117.0	95.0	21.9
CMV enriched	<= 2,500	Male	BINE	20.3	16.3	4.0
			MEB	63.3	23.7	39.6
		Female	BINE	1.5	1.1	0.4
			MEB	0.0	0.0	0.0
	> 2,500	Male	BINE	13.7	4.1	9.7
			MEB	10.1	1.7	8.4
		Female	BINE	5.6	1.7	3.8
			MEB	6.3	0.9	5.5
Not CMV enriched	<= 2,500	Male	BINE	10.8	8.1	2.7
			MEB	11.0	9.2	1.8
		Female	BINE	0.8	0.5	0.3
			MEB	3.1	3.1	0.0
	> 2,500	Male	BINE	10.1	3.0	7.1
			MEB	3.9	1.1	2.8
		Female	BINE	3.6	1.1	2.6
			MEB	2.6	0.5	2.1

*Only a small proportion of MEB donors would be included in the top 2,500 phenotype rank

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