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Autologous Hematopoietic Stem Cell Transplantation for the Treatment of Multiple Sclerosis

Guidance Statement

CADTH

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Table of Contents

Abbreviations

AHSCT	autologous hematopoietic stem cell transplantation
DMT	disease-modifying therapy
HTERP	CADTH Health Technology Expert Review Panel
MS	multiple sclerosis
RCT	randomized controlled trial
RRMS	relapse-remitting multiple sclerosis

Summary

What Is HTERP's Guidance to Help Health Systems Prepare for Uptake of Autologous Hematopoietic Stem Cell Transplantation for the Treatment of Multiple Sclerosis?

The CADTH Health Technology Expert Review Panel (HTERP) offers the following guidance to help health systems prepare for potential uptake of autologous hematopoietic stem cell transplantation (AHSCT) for the treatment of multiple sclerosis (MS) should emerging evidence continue to signal clinical benefit and an appropriate safety profile:

1. Develop and implement systematic strategies for offering monitoring and follow-up care closer to home for individuals currently offered AHSCT for the treatment of MS and those who may be offered AHSCT for the treatment of MS in the future.
2. Build interprovincial/territorial agreements and other mechanisms that include consideration of financial and logistical support when travel and short-term relocation are required to access AHSCT for MS.
3. Develop clear and transparent guidelines and protocols, including related training, that are acceptable for potential AHSCT candidates, their caregivers, and their clinicians.
4. Ensure transplant centre capacity, budget, and other required resources.
5. Support novel relationships and collaboration among MS and AHSCT health care professionals who would be involved in delivering care.
6. Ensure equity in access and equitable approaches to care delivery are guiding principles in providing AHSCT for treating MS.

Why Did HTERP Develop This Guidance?

HTERP acknowledges that AHSCT is currently offered as a standard option to treat MS for eligible recipients at 2 transplant centres in Canada, with some interprovincial agreements in place. HTERP also acknowledges that published research studies have signalled the potential comparative clinical effectiveness and safety of AHSCT for the treatment of MS in people living with aggressive disease and for whom disease-modifying therapies have typically failed. HTERP acknowledges methodological limitations of the existing literature, which contribute to clinical equipoise. In this context, HTERP developed guidance to help health systems prepare for the uptake of AHSCT for the treatment of MS should emerging evidence continue to signal clinical benefit and an appropriate safety profile.

What Is MS?

MS is a chronic inflammatory autoimmune disorder that affects the central nervous system. In people with MS, inflammation destroys the myelin sheath surrounding nerve fibres which disrupts the ability of the nervous system to transmit signals throughout the body. This process is also accompanied by neurodegeneration. Early symptoms may include fatigue, visual blurring, and difficulties in walking. In advanced stages, people with MS may develop paralysis, pain, tremor, and loss of mobility, which can severely affect their day-to-day life. There are different clinical courses of MS, which are characterized by disease activity and disability progression. The most common course, relapse-remitting multiple sclerosis (RRMS), affects approximately 85% of people with MS and is marked by periods of distinct symptom

flare-up (relapse) followed by periods of remission when symptoms may completely recover, although some symptoms may persist permanently. The other courses of MS are progressive forms, in which symptoms continue to worsen over time either from the onset of the disease or after a period of having RRMS. Approximately 90,000 people in Canada, or about 1 in 400, live with MS.

What Is AHSCT?

AHSCT is a well-established therapy for many blood cancers and is an emerging therapy for treating people with MS and other autoimmune disorders. The conditioning regimen for AHSCT aims to partially or completely destroy autoreactive immune cells that cause damage to the central nervous system, allowing reconstitution of the immune system with stem cells from the same person. Existing evidence suggests that AHSCT could potentially be a therapeutic option for select people with aggressive or highly active RRMS who experience limited disease control with disease-modifying therapies. Because the therapy is intended to be a one-time procedure, AHSCT may alleviate the need for ongoing treatment (as is the case with disease-modifying therapies), sparing patients the adverse events and recurring costs associated with disease-modifying therapies. If the safety and effectiveness of AHSCT becomes well-established, it has the potential to improve quality of life, reduce treatment-related side effects, allow individuals the opportunity to engage in employment and other social activities, and remove the financial costs associated with disease-modifying therapies over a longer time horizon.

The AHSCT procedure introduces an extensive disruption to the lives of transplant recipients and their caregivers. Eligible people and their caregivers who do not already live close to a transplant centre must travel away from their homes and stay at, or remain close to, the transplant centre for at least several months. Recipients and their caregivers are responsible for relocation and short-term accommodation costs as well as other travel expenses associated with the procedure. They must also cover out-of-pocket expenses for rehabilitation and/or take time away from work. The need to travel and relocate near a transplant centre for a period of time and the associated financial costs introduces potential inequities in access to care due to geography and social and/or financial position.

Background

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disorder that affects the central nervous system. In people with MS, inflammation destroys the myelin sheath surrounding nerve fibres which disrupts the ability of the nervous system to transmit signals throughout the body. This process is also accompanied by neurodegeneration.[1] Early symptoms may include fatigue, visual blurring, and difficulties in walking.[1,2] In advanced stages, people with MS may develop paralysis, pain, tremor, and loss of mobility, which severely affect their day-to-day life.

In 2020, the MS Society of Canada estimated that 90,000 people in Canada, or about 1 in 400, live with MS.[3] Risk factors for MS are both environmental and genetic, with a combination of factors contributing to patterns of incidence and prevalence in different populations. For example, females are more than 2.5 times more likely to have MS then males.[4] In Canada, the US, and some European countries, the prevalence of MS is more than 2 times higher

than in other parts of the world.[5,6] Within Canada, there is regional variation in MS prevalence, with higher prevalence observed in the Prairie and Atlantic provinces.[7] There is also a higher prevalence of MS in non–First Nations populations in Canada compared with First Nations populations,[8,9] although the prevalence of MS in First Nations populations in Canada remains higher than in other Indigenous populations outside of Canada. The prevalence of MS in First Nations populations in Canada also seems to be increasing over time,[8] as it is in other populations historically considered at lower risk of MS, including Black[10] and Asian populations.[11] Because some minority ethnic groups, such as First Nations[12] and Black populations,[12] have been reported to experience a more rapid progression of disability from MS, it is possible that some people within these groups may be at increased risk of poorer MS outcomes.

There are different clinical courses or phenotypes of MS, which are characterized by disease activity and disability progression. The most common course, relapse-remitting multiple sclerosis (RRMS), affects approximately 85% of people with MS and is marked by periods of distinct symptom flare-up (relapse) followed by periods of remission when symptoms may completely recover, although some symptoms may persist permanently.[13,14] The other courses of MS are progressive forms, in which symptoms continue to worsen over time either from the onset of the disease (primary progressive) or after a period of having RRMS (secondary progressive).[13,14]

More than a dozen disease-modifying therapies (DMTs) are available to people with MS in Canada.[15] DMTs aim to reduce the frequency and intensity of relapses, reduce the accumulation of lesions in the brain, and delay the onset of disease progression.[15] Primarily for people with RRMS, DMTs can be highly effective in improving clinical outcomes over the short term (≤ 3 years).[16] However, despite effective DMTs, up to 90% people with RRMS are likely to develop progressive forms of MS, with half of them expected to progress within 20 years of disease onset.[17,18] Moreover, first- and second-line DMTs may fail to improve outcomes for some people, or may have limited effects on disease control, although people will still experience the adverse effects associated with DMTs.[19-22]

Autologous hematopoietic stem cell transplantation (AHSCT) is a well-established therapy for many blood cancers. It is also an emerging therapy for treating people with MS and other autoimmune disorders.[23,24] Existing comparative evidence, including 2 randomized controlled trials (RCTs) and 4 retrospective cohort studies, suggests that treatment with AHSCT is associated with significant improvement in clinical outcomes in people living with highly active RRMS disease for whom DMTs have typically failed. These improvements include reduced 1-, 3-, and 5-year disease progression; reduced clinical relapse rate; reduced number and size of lesions on MRI scans; increased function; and improvement in quality of life.[25-28] The same body of evidence also suggests that AHSCT is associated with some expected short-term adverse events (e.g., febrile neutropenia, organ infections, sepsis, and viral reactivations), long-term adverse events (e.g., the development of new autoimmune diseases, mainly thyroid disease), and rare treatment-related deaths or life-threatening complications.[28-30] Longer term data to assess later effects, such as cancer diagnoses and cardiovascular complications up to 20 years post transplant, are not yet available because of the relative nascency of the use of AHSCT to treat MS. However, the evidence is challenging to interpret because of methodological limitations in study designs, including the inability to blind study participants, low overall number of potentially eligible people, heterogeneity among study participants, heterogeneity in conditioning regimens, and use of older DMTs as comparators.

Existing evidence suggests that AHSCT could potentially be a therapeutic option for select people with aggressive or highly active RRMS who experience limited disease control with DMTs. Since the therapy is intended to be a one-time procedure, AHSCT may alleviate the need for ongoing treatment (as is the case with DMTs), sparing patients the adverse events and recurring costs associated with DMTs.[23] In particular, because MS onset tends to occur in one's thirties, if the safety and effectiveness of AHSCT becomes well-established, it has the potential to improve quality of life, reduce treatment-related side effects, allow individuals the opportunity to engage in employment and other social activities, and remove the financial cost associated with DMTs over a longer time horizon.[30]

AHSCT for the treatment of MS is not offered consistently in Canada as part of routine care, and optimal protocols for the procedure are still being refined in clinical trials. Within Canada, centres have led prospective trials examining the role of AHSCT to prevent relapse; there has been limited use outside of research settings with the exception of 2 transplant centres in Canada that offer AHSCT as a standard option to treat MS for eligible recipients. Other Canadian centres have also offered the procedure, including in Quebec and New Brunswick, although not as a standard option. At least 3 phase III RCTs are under way and are expected to be completed before 2026. Although evidence about the type and dosing of conditioning regimens and eligibility criteria for AHSCT is emerging, guidelines from Canada, the US, and Europe recommend that AHSCT may be offered as a treatment option for a subset of people with MS based on age and clinical presentation.[24,31-33]

The conditioning regimen for AHSCT aims to partially or completely destroy autoreactive immune cells that cause damage to the central nervous system, allowing reconstitution of the immune system with stem cells from the same person.[24] The procedure produces an "immune system reset" that limits disability progression and disease activity, and may help a person recover lost function.[34] The AHSCT procedure involves multiple steps, including pre-transplant DMT "wash out," stem cell mobilization, and peripheral blood stem cell collection, immune system conditioning, transplantation, and post-transplant rehabilitation. The entire procedure is delivered over 2 to 6 months, including a hospital stay of typically 3 to 4 weeks, in addition to ongoing monitoring occurring in an outpatient setting for 3 years or more.[35]

The AHSCT procedure introduces an extensive disruption to the lives of transplant recipients and their caregivers. Eligible people who do not already live close to a transplant centre that offers AHSCT for the treatment of MS must travel away from their homes and stay at, or remain close to, the transplant centre for at least several months. Travelling away from their homes, families, and support networks may not be feasible in all circumstances. Caregivers play an important role by providing support during the treatment and rehabilitation processes and also during recovery, helping transplant recipients resume daily activities and adhere to typical medical regimens, and monitor symptoms. Not all eligible candidates may have that critical caregiver support; however, for those that do, their caregivers are also required to travel away from their homes for a period of time. Moreover, recipients and their caregivers are responsible for relocation and short-term accommodation costs as well as other travel expenses associated with the procedure. They must also cover out-of-pocket expenses for rehabilitation and/or take time away from work, which creates an additional barrier for some people who may be eligible for AHSCT. Together, the need to travel and relocate near a transplant centre for a period of time, which includes caregiver support and associated financial costs, introduces potential inequities in access to care due to geography and/or social or financial position.

Objective

This guidance aims to help health systems prepare for the uptake of AHSCT for the treatment of MS should emerging evidence from phase III RCTs continue to signal clinical benefit and an appropriate safety profile as demonstrated through published RCT and non-RCT data.

The target population for this guidance is people living with highly active MS for whom DMTs have typically failed. The target users of this guidance are Canadian health care decision-makers, including those in provincial and territorial ministries responsible for making decisions about health system design and health policy for MS treatments and individuals who are actively researching appropriate management and care for people with MS.

Methods

The CADTH Health Technology Expert Review Panel (HTERP) developed guidance on health system preparedness for AHSCT for the treatment of MS based a CADTH Horizon Scan,[36] an accompanying Rapid Response,[37] insights provided by clinical experts and a patient expert, and published international guidelines, recommendations, and position statements.[24,31-33] Based on the evidence, information, and perspectives presented through these sources, HTERP members developed this guidance through discussion, deliberation, and consensus. Draft guidance was peer reviewed by 2 clinical experts, and final guidance reflects input received through a stakeholder feedback process. Additional information on the HTERP process is found on the Health Technology Expert Review Panel page of the CADTH website.

Guidance and Rationale

HTERP acknowledges that AHSCT is currently offered as a standard option to treat MS for eligible recipients at 2 transplant centres in Canada (Ottawa and Calgary), with some interprovincial agreements in place. In this context, although phase III RCT data are emerging, HTERP advises the following.

1. Develop and implement systematic strategies to monitor and offer follow-up care closer to home for individuals who are currently offered AHSCT for the treatment of MS and those who may be offered AHSCT for the treatment of MS in the future.

   AHSCT for the treatment of MS, and its follow-up, brings extensive disruption to people's lives at a time when they are already dealing with disruptions caused by living with highly active MS. People who receive AHSCT require caregiver support for pre-procedure assessments and follow-up appointments, during ongoing tests, and while performing daily activities during their recovery, including helping treatment recipients adhere to typical medical regimens and assisting with ongoing monitoring. Developing and implementing systematic strategies to provide monitoring and follow-up care closer to home would alleviate some disruption to the lives of those who need to travel away from their homes, families, and support networks for at least several months, thus improving the experiences and quality of life of people receiving this treatment and their caregivers. Some such strategies are in place to support transplant recipients at the 2 Canadian

centres in Ottawa and Calgary; a systematic approach that includes all eligible recipients would help enhance equity in access by alleviating some of the barriers of travel-related challenges, lengthy time away from home, and potential loss of employment income. Such strategies could leverage the use of virtual technologies and/or telemedicine to support patient monitoring and follow-up visits, and support communication between local professionals and specialists from a distance. Providing monitoring and follow-up care closer to home would require local facilities to have appropriately trained health professionals encompassing neurology, stem cell transplant, and supportive care, in addition to required equipment and record keeping strategies, which may include electronic health records.

HTERP acknowledges that published research studies, including 2 RCTs[25,26] and 4 retrospective cohort studies,[27-29,38] have signalled the potential clinical effectiveness and safety of AHSCT for the treatment of MS in people living with highly active disease for whom DMTs have typically failed HTERP also acknowledges the methodological limitations of the existing literature, including the use of older DMTs as comparators when more recent DMTs are comparatively more effective and safer. These limitations contribute to equipoise in the clinical literature, some aspects of which may be resolved through ongoing phase III RCTs, which will be important to monitor. In this context, should emerging evidence continue to signal comparative clinical benefit over standard care and an appropriate safety profile as demonstrated through published RCT and non-RCT data, HTERP advises the following guidance:

2. Build interprovincial/territorial agreements and other mechanisms that include consideration of financial and logistical support when travel and short-term relocation are required to access AHSCT for MS.

   Few stem cell treatment centres across Canadian jurisdictions may offer, or have the capability to offer, the AHSCT procedure. Models of care that rely on a few specialized centres to guide the delivery of AHSCT for MS are likely to result in geographic inequities if mechanisms that support out-of-province (or region) treatment are not consistently implemented. Further, many expenses associated with AHSCT for MS are out-of-pocket expenses for those who access the treatment and are likely to result in economic inequities if mechanisms to provide financial support are not implemented. These expenses may include the cost of rehabilitation, additional treatments for adverse effects, and/or taking time away from work in addition to costs related to travel, relocation, short-term accommodation, and other related expenses. In scenarios where regional centres do not offer AHSCT for the treatment of MS, interprovincial/ territorial agreements that include consideration of financial and logistical support may help ensure equitable access to treatment regardless of the jurisdiction a person resides in. There is an opportunity to build from existing interprovincial agreements for other conditions that require out-of-jurisdiction travel, for example for CAR T-cell therapies or other transplant procedures. Additional strategies to help transplant recipients and their caregivers prepare for and cover additional out-of-pocket costs may further help ensure equitable access to treatment regardless of financial position. These strategies could include public funding, support through not-for-profit organizations, or other approaches. Although supporting additional and typical out-of-pocket costs would have an additional impact on public health care budgets in the short term, it is likely that over a longer time horizon AHSCT to treat MS would provide overall cost savings because it would preclude the need for long-term use of DMTs; however, this hypothesis would need to be tested through formal model-based economic analyses.[39]

3. Develop clear and transparent guidelines and protocols, including related training, that are acceptable for potential AHSCT candidates, their caregivers, and their clinicians.

   Consensus-based guidelines and protocols would be required for eligibility criteria, referral criteria (including indicators for timely assessment and referral before further disease progression that may preclude eligibility), pre-transplant investigations, conditioning regimen design, AHSCT delivery, follow-up care, supportive care, transfer of care between jurisdictions when needed, as well as decision support tools and information for eligible candidates and their caregivers. Guidelines and protocols would ideally be transparent, available, and developed through a funded and coordinated pan-Canadian approach, with reference to published Canadian and international guidelines and recommendations, to help ensure consistent application of the procedure and equitable access for eligible candidates. Additionally, guidelines should be developed through collaboration among clinical and non-clinical teams that would be involved in people's care, including those directly at a transplant centre and those who would refer to a transplant centre and provide follow-up care. Guidelines should be accompanied by a standardized package of information for transplant recipients and their caregivers that could be contextualized for each centre. The development of related training programs for all health professionals involved would be required, (e.g., transplant physicians, neurologists, nurses and supportive care teams) and they may include strategies to support ongoing learning and communication of issues specific to use of AHSCT for MS. Comprehensive training would help reduce potential inequities in access due to differential information among health professionals and, therefore, differential opportunity for discussion of eligibility with potential transplant candidates.

   The specifics of guidelines and protocols were outside the scope of this guidance and would require ongoing review of the emerging evidence base for their development.

4. Ensure transplant centre capacity, budget, and other required resources.

   There is an opportunity to learn about specific resource requirements from models of care for stem cell transplantation for other conditions, specifically those that include satellite programs to manage monitoring and follow-up care post transplant. Ensuring capacity and resources for the provision of AHSCT to treat MS may require reallocation and coordination of existing resources and systems within current transplant programs, and/or cancer programs, and/or other care models through which AHSCT and MS are currently, and often distinctly, funded and delivered in many jurisdictions. AHSCT for the treatment of MS would also have unique requirements for space, technical components, training for health care professionals and/or consideration for additional health professionals (e.g., physiotherapists, mental health professionals), follow-up care, and funds to ensure the procedure can be offered to eligible candidates. There is also an opportunity to explore a value-based framework, connecting funding of AHSCT to outcomes observed, and learn from Canadian initiatives as examples.[40] Conducting a cost-effectiveness analysis and budget impact analysis to better understand the short- and long-term costs and benefits to offer AHSCT in a given jurisdiction may be beneficial.

5. Support novel relationships and collaboration among MS and AHSCT health care professionals who would be involved in delivering care.

   Working relationships between MS neurologists, transplant specialists, and other clinical and non-clinical health professionals who would be involved in delivering AHSCT for treating MS are required to ensure high-quality, person-centred, and seamless coordination of care that reflects the specifics of AHSCT for treating MS as unique from

transplants for other indications. Such relationships may not exist within centres that do not currently offer the procedure. As such, it would be necessary to develop processes for sharing communication and documentation that would help relevant health care professionals collaborate with one another, while also considering the processes that local health professionals would need to be able to communicate and collaborate with specialists from a distance about monitoring and follow-up care. A formalized professional network could be considered.

6. Ensure equity in access and equitable approaches to care delivery are guiding principles in providing AHSCT for treating MS.

   MS affects people across different geographies and ethnicities and across the socio-economic spectrum. There is a risk that efforts to enhance uptake of AHSCT for treating MS could introduce new inequities or exacerbate existing inequities. To help prevent this, equity in access to treatment should be embedded as a guiding principle, with consideration of the distribution of the disease and disease progression across different populations. Several strategies are recommended, as specified in guidance statements 1 to 3 in this report. Keeping equity as a guiding principle in service design and delivery would also require a commitment to engage with affected transplant recipients, caregivers, and health care providers to measure and analyze access and outcomes and to understand which aspects of service delivery and design (e.g., care closer to home, use of virtual technologies, geographical distribution of treatment centres) advance equity.

Considerations

HTERP discussed the following considerations that may help inform jurisdictions and centres planning or considering offering the procedure in the coming years.

Anticipated Volume

- At any given time, a conservative estimate is that 200 people living in Canada have RRMS and may be potentially eligible for AHSCT. The number who would actually be eligible following clinical assessment would be lower. Between 2001 and 2021, 72 people with MS, including 62 with RRMS, received AHSCT at the Ottawa Hospital,[41] with approximately 7 transplants conducted per year. According to the Center for International Blood and Marrow Transplant Research (CIBMTR), 15 transplants for MS, including for neuromyelitis optica, have been reported in Canada since 2020, although this number is likely not representative of the number of eligible recipients. It is possible the number of transplants has been lower during the COVID-19 pandemic.
- Data on AHSCT are available in registries, including 1 maintained by Cell Therapy Transplant Canada (CTTC), which prospectively collects the number of patients who receive AHSCT for a variety of indications. Internationally, the European Bone Marrow Transplant (EBMT) Autoimmune Diseases Working Party does the same; it documented 1,634 transplants from 1994 to 2020. These registries can be monitored to help anticipate interest and demand.
- Health care decision-makers should not expect demand to overwhelm jurisdictions or centres with unmanageable volume when planning for increased uptake of AHSCT for treating MS in the current context and while clinical equipoise remains. Volume is

anticipated to remain manageable at least until phase III RCT data emerge, which will be between 2024 and 2026. These data could potentially resolve some aspects of clinical equipoise because the studies importantly use contemporary DMTs as comparators; however, it is possible that newer DMTs with different safety and effectiveness profiles will be available by the time RCT data are available.

Current and Future State of Evidence

- Evidence from 2 RCTs and 4 retrospective cohort studies with some methodological limitations suggests that treatment with AHSCT is associated with significant improvement in clinical outcomes, including disease progression, clinical relapse, MRI outcomes, the composite outcome "no evidence of disease activity," and quality of life compared with historical DMTs. However, AHSCT was also shown to be associated with expected short-term adverse events, including febrile neutropenia, organ infections, sepsis, and viral reactivations; long-term adverse events, including the development of new autoimmune diseases, mainly thyroid disease; and rare treatment-related mortality or life-threatening complications.[37]
- Recommendations and guidelines related to AHSCT for treating MS have been published by Alberta Health Services,[42] the Canadian MS Working Group,[31] the National Multiple Sclerosis Society (US),[32] the American Society for Transplantation and Cellular Therapy (formerly known as the American Society for Blood and Marrow Transplantation),[33] and EBMT.[24] These recommendations and guidelines are based on evidence from a range of comparative and non-comparative study designs, and provide a foundation for understanding certain clinical aspects of the procedure and the current state of evidence.
- At least 3 phase III RCTs are under way to investigate the safety and efficacy of AHSCT compared with more recently developed DMTs. These studies began in 2018 and 2019 and are expected to complete recruitment and follow-up data collection between 2024 and 2026 (refer to the Horizon Scan for a summary of active trials).
- There is some variation in practice between Canadian centres that offer AHSCT for treating MS and the published recommendations and guidelines, such as eligibility criteria and conditioning regimen design. The results of the ongoing phase III RCTs may help clarify some aspects of clinical equipoise and provide an opportunity to align practice and guidelines. In the presence of clinical equipoise and variation in practice, it is possible that some people living with MS may rely on non–evidence-based information and may choose to access AHSCT outside of Canada at their own expense and without support or follow-up from a local transplant or MS team. A Health Technology Assessment that incorporates the results of the ongoing phase III RCTs and model-based economic analyses may help assess the overall value of offering AHSCT for treating MS.
- Assessing the efficacy, effectiveness, and cost-effectiveness of AHSCT for treating MS is challenging — in particular, assessing the impact on disability progression over an appropriate time period, which would ideally be 5 to 10 years. Challenges are, in part, because blinding participants to study treatments is not possible and recruitment to ensure sufficient study power can take several years because of the low overall number of potentially eligible people. Study recruitment also occurs at the same time as new DMTs with different safety and effectiveness profiles are emerging. As such, comparators used in trials may not necessarily represent the standard of care at the time of study completion. Costs are challenging to estimate because they vary based on numerous factors, including conditioning regimen used, patient selection criteria, and regional variation in practice.[39]

Models of Care and Funding

- Decisions about models of care — including the need for and nature of interprovincial/territorial agreements — may need to be revisited Once the results of ongoing phase III RCTs are published that could potentially resolve some aspects of clinical equipoise. For example, a decision could be made to centralize transplants among designated specialist centres and further develop specific experience and expertise among these centres while implementing strategies to facilitate access to those centres or to rely more fully on existing transplant capacity. Guiding principles include maintaining equity in access and approach to care delivery with a data collection and analysis plan to monitor access and outcomes to identify persistent inequities. This would provide an opportunity to revisit models of care based on principles of universal access for eligible recipients. There is an opportunity to learn from models of care at the 2 transplant centres in Canada that offer AHSCT for treating MS, in addition to models of care for people with other conditions, specifically those that require transplantation and include satellite programs to manage monitoring and follow-up care post transplant. There may also be opportunities to learn about financial and logistical support options when travel and short-term relocation are required to help improve the experiences of people receiving this treatment and their caregivers and to enhance equitable access to the procedure.
- Opportunities should be considered to prepare transplant recipients and their caregivers for out-of-pocket expenses (e.g., through patient education materials, development of clinical-financial pathways) and to reduce out-of-pocket expenses, including systems to support time away from work (e.g., expanded hours of service, bundled appointments, work conducive care facilities, and subsidizing parking and childcare.). There is also an opportunity to plan to use public funding or the support of not-for-profit organizations to help provide financial and logistical support for travel and short-term relocation.

Existing Canadian Interest and Networks

- Offering AHSCT for the treatment of MS will require interest, motivation, and knowledge among MS health care professionals, including transplant physicians, neurologists, and MS specialists. Currently, there is inconsistent interest and knowledge across Canada. To support health system planning, there is an opportunity to engage MS health care professionals to understand the reasons among them for inconsistent interest and knowledge, and the related barriers and opportunities to address them. In April and May 2022, the Canadian Network of MS Clinics conducted a survey to explore potential interest and capability to develop an ACST treatment program for MS. Twenty-six physician members of the network clinics across Canada responded, with positive responses received from physicians in some of Canada's larger cities about interest in having ACST available at their site and comfort discussing the potential with local transplant teams. Some physicians working in smaller centres also indicated having interest, but not the local capacity, to conduct AHSCT. However, these individuals indicated the availability of a transplant team who could monitor people who might receive the treatment elsewhere if there were appropriate training.
- The Foundation for the Accreditation of Cellular Therapy (FACT) accredits centres for both autologous and allogenic transplants. Most transplant centres that could offer AHSCT for treating MS are currently accredited by FACT and can provide a network to share resources and protocols. Similarly, Cell Therapy Transplant Canada (CTTC) has members from all Canadian provinces and could provide a platform for AHSCT research, guidelines, and education to support decision-makers.

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Appendix 1: CADTH Health Technology Expert Review Panel

HTERP is an advisory body to CADTH, which is convened to develop guidance or recommendations on non-drug health technologies to inform a range of stakeholders within the Canadian health care system. HTERP consists of up to 7 core members appointed to serve for all topics under consideration during their term of office, and up to 5 expert members appointed to provide their expertise for a specific topic. The core members include health care practitioners and other individuals with expertise and experience in evidence-based medicine, critical appraisal, health technology assessment, bioethics, and health economics. One patient member is also appointed to the core panel to represent broad patient perspectives and experiences in the health system. For this project, the appointed expert members were 1 transplant physician with expertise in cellular therapies for various immunological disorders including MS, 1 neurologist with expertise in offering AHSCT for treating MS, and 1 patient partner treated for early aggressive MS with AHSCT. For more information, refer to the Health Technology Expert Review Panel page on the CADTH website.

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Conflicts of Interest

HTERP core members' declarations are posted on the CADTH website.

None of the HTERP expert members have associated conflicts of interest to declare.