RESEARCH PAPER

First Ready, First to Go: Ethical Priority-Setting of Allogeneic Stem Cell Transplant at a Major Cancer Centre

Premier prêt, premier parti : établissement des priorités en matière d'éthique dans le cas de greffe de cellules souches allogéniques dans un grand centre d'oncologie

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Abstract

Medical advancements have now made it possible to provide allogeneic stem cell transplantation (allo-SCTs) to older patients and use stem cells from less well-matched donors. This has resulted in access to a life-saving modality for a greater number of patients with imminent life-threatening illnesses. However, resources have not always kept pace with innovation and expanded volumes. During the summer of 2015 in the province of Ontario, Canada, inadequate resources contributed to a capacity crisis, resulting in extended wait-lists for allo-SCT across the province. This situation presented unique ethical challenges, including the need for ongoing negotiations with health system partners and nimble process management to ensure timely delivery of care. This article reports on the process one organization used to determine how to equitably allocate scarce allo-SCT resources. With the ever-expanding landscape of new and emerging medical technologies, our experience has implications for the ethics of translating other increasingly expensive health technologies to clinical care.

Résumé

Les avancées médicales permettent aujourd'hui d'effectuer des greffes de cellules souches (allogreffe-CS) chez les patients plus âgés et d'utiliser moins de greffons de la part de donneurs qui, eux, peuvent être moins compatibles. Cela permet de sauver la vie d'un plus grand nombre de patients aux prises avec des maladies menaçant leur pronostic vital. Toutefois, les ressources ne suivent pas toujours le rythme des innovations ou l'expansion du nombre de cas. Au cours de l'été 2015, en Ontario, au Canada, des ressources inadéquates ont mené à une crise des capacités qui a donné lieu à une longue liste d'attente pour les allogreffes-CS dans la province. La situation présentait des défis d'ordre éthique particuliers, notamment le besoin de négociations continues entre les partenaires du système de santé et une gestion adroite des processus afin d'assurer une prestation de soins en temps opportun. Cet article fait état du processus mis en place dans une organisation afin de déterminer comment distribuer équitablement les rares ressources pour les allogreffes-SC. Avec l'abondance des nouvelles technologies émergentes, notre expérience a des répercussions sur l'éthique d'apporter, dans les soins cliniques, de nouvelles technologies de soins de santé toujours plus onéreuses.

Introduction

Among hematopoietic malignancies, patients with acute myeloid leukemia (AML) represent approximately half of the potential candidates for allogeneic stem cell transplantation (allo-SCT), in which the diseased bone marrow is replaced with the bone marrow from a healthy sibling or matched donor (Gratwohl et al. 2015). Recent medical and technological advancements in this area have allowed older populations to become candidates for allo-SCT and for the accommodation of less well-matched donors. This has led to an expanded volume of eligible patients. In Ontario, Canada, however, government funding for hospital

programs responsible for allo-SCT has not kept pace with these innovations and the increasing demand. This resource shortcoming contributed to a capacity crisis and resulted in a wait-list that made timely disease management difficult. The result was that patients on the wait-list became at risk of missing the opportunity for a potentially curative transplantation for their disease because of relapse or other medical co-morbidities thus exposing them to further medical complications, including death. While the province was developing a plan for the injection of resources, there arose the opportunity to send patients out of the country to receive allo-SCT. Each Ontario centre was confronted with the ethical challenge of managing wait-lists appropriately and deciding what criteria should be used to assign priority for transplantation at their centre.

Background

AML is a common form of leukemia among adults in Western countries. The median age of diagnosis is 65 years (Deschler and Lubbert 2006) and continues to increase (El Rassi and Arellano 2013). AML is a medically complex disease with multifaceted risk factors. Treatments for AML are labour- and resource-intensive, whether low-dose chemotherapy, best supportive care/symptom management or transplantation. Most patients require chemotherapy to reduce disease bulk, and they then typically undergo further treatments to encourage remission. Based on risk factors, allo-SCT may be offered as a post-remission strategy to obtain the best possible medical outcome. For patients with disease that has not responded to chemotherapy, transplantation remains the only curative option (Döhner et al. 2017). Hence, allo-SCT is an important, and sometimes the only viable, medical option for some patients with AML.

International standards indicate that the target time frame to receive allo-SCT is within 6 weeks of the patient being medically ready for transplantation and a donor being identified (Cancer Care Ontario 2017). The disease can be stabilized with inductions, but the longer a patient waits, the greater their risk of developing significant medical complications due to a compromised immune system and the greater their risk of death from uncontrolled disease or co-morbidities.

Allo-SCT includes the need to locate and secure an appropriate donor, a standardized process implemented at allo-SCT centres overseen by the Canadian Blood Services Stem Cell Registry. This process has also undergone recent technological innovation, necessitating further local facility resources and infrastructure. Donors and patients need to be human leukocyte antigen (HLA) compatible for donated stem cells or bone marrow to have the greatest chance of restoring a patient's immune system and eradicating AML (Hamilton and Copelan 2012). DNA-based testing for antibodies is enabling more precise donor typing to facilitate the determination of an HLA match. This requires the adoption and maintenance of costly new technology and the expansion of laboratory and pathology capacity, including

highly specialized staff. Also, matching donors to patients requires significant human resources and coordination to oversee the locating, typing and management of donor products. Finally, significant coordination at the local site is required to support the clinical needs of these highly complex patients from diagnosis to pre-transplantation and from transplantation to follow-up.

Resources available for allo-SCT in Ontario, however, have not kept pace with transplantation innovations and, therefore, the increased demand. Data compiled by the Worldwide Network for Blood and Marrow Transplantation indicate that the currently accepted target meant to apply across health systems is to perform 250 to 350 allo-SCTs per 10 million people (Gratwohl et al. 2015; Passweg et al. 2016), with transplantations performed within a target time frame of 6 to 8 weeks after disease remission. Available resources in Ontario, however, made possible 250 to 280 transplantations per 10 million people, within a 3- to 6-month post-remission time frame (Cancer Care Ontario 2017). This shortfall in resources led to a situation in which patients with very medically severe conditions were waiting for allo-SCT and potentially missing their window of opportunity for this treatment modality. An investigative report published in spring 2016 identified 255 AML patients as needing allo-SCT across three Ontario hospitals for the year ending on March 31, 2016. This number was contrasted with the 160 allo-SCTs performed across the three hospitals in 2010, prior to the expanded clinical indications for transplantation (Zlomislic 2016).

To ease clinical burden and promote timely care, the Ontario Ministry of Health and Long-Term Care (MOHLTC) developed a temporary process to refer patients to the US to receive allo-SCT and promised an increase in allo-SCT funding to Ontario hospitals over several years. The MOHLTC process required individual physicians to complete an application on behalf of their patient for government-insured medical services to be provided out of the country. It is the responsibility of each Ontario allo-SCT centre to notify patients of this option and forward individual applications, manage wait-lists appropriately and determine what criteria should be used to assign priorities for transplantation within their centre. Eligible patients were then presented with the choice of either staying in the province with the risk of expanded wait times or going out of the country, which involved weighing other benefits and downsides such as loss of wages for support persons (required to accompany patients out of the country) and out-of-pocket costs for travel, accommodation and meals for up to 100 days. Unlike an absolute scarcity of organs for transplantation, allo-SCT involves scarcity of capacity due to limited physical space, human and financial resources and timely donor access. Whereas organ transplantation is primarily about the availability and ethical allocation of a finite product, the former requires nimble and efficient process management of a volatile, dynamic and multidisciplinary system to ensure timely and quality care.

Hospital-based priority-setting decisions about fair allocation of limited treatment or therapies prioritize patients' medical need, expected health benefit or a cluster of

decision-making criteria (Martin et al. 2001; Mielke et al. 2003). At the Princess Margaret Cancer Centre in Toronto (hereafter the "Centre"), a hospital with the largest and most comprehensive malignant hematology program in Canada, priority-setting decisions were initially based on the principle of first-come, first-served, as physicians agreed that the majority of patients are very ill, so medical acuity could not be used as an indicator. However, senior leaders and physicians determined that an ethical framework to ensure fairness and transparency of the SCT decision-making process, as well as an overhaul of the process leading up to allo-SCT, was required. This article reports on the ethical priority-setting and systems improvement process that the Centre undertook to manage allo-SCT.

Developing Substantive Priority-Setting Criteria

In spring 2015, Centre leaders assembled an Allo-SCT Working Group (the "Working Group") comprising physicians, administrators and those involved in patient relations, bioethics and public affairs that met weekly. The purpose of the Working Group was to address the operational and clinical aspects of expanded indications for allo-SCT within limited capacity and resources. During these meetings, the need for an ethical decision-making process was identified by Working Group members out of concern for ensuring fair allocation of allo-SCTs.

The Working Group's ethics process built upon a preliminary ethical framework established by a group of Ontario bioethicists for allo-SCT priority-setting decisions (Wright et al. 2015), which was intended to be adapted to each local Ontario hospital where allo-SCT is performed. The framework was informed by accountability for reasonableness (A4R) and program budgeting and marginal analysis principles (Gibson et al. 2006) and included an iterative process for applying A4R principles (Table 1), as well as additional principles and an initial set of criteria to guide discussion (Table 2). A4R is an established ethical priority-setting process, which incorporates the principles of distributive and procedural justice, and includes five conditions to ensure a fair priority-setting outcome: relevance, publicity, revision, empowerment and enforcement (Table 2). Application of these principles and conditions throughout the priority-setting process helps to ensure that the resulting criteria are perceived as fair and reasonable.

Through six consensus-building meetings from September to December 2015, the Working Group applied the ethical framework and determined substantive priority-setting criteria for fair allo-SCT allocation (Table 1). This included identifying substantive criteria; ranking the relevance of each criterion from 0 to 5, 5 being the most relevant; and reaching consensus on the most relevant criterion to guide allo-SCT allocation decisions.

TABLE 1. Applying the accountability for reasonableness framework to allogeneic stem cell transplantation

Step	Elaboration
Step 1 – Determine the aim and scope of the priority-setting project	• Determine the reach/focus of the priority-setting project • Determine the scope of the priority-setting decision (local hospital, province, resources available, out of country)
Step 2 – Identify the priority-setting committee	• To support and participate in the development/implementation of the process • Identify stakeholders and chairs to lead the initiative
Step 3 – Clarify existing resource mix	• Determine the resources/funds allocated and the number of allo-SCTs available • Identify how many patients are being prioritized at one time
Step 4 – Develop decision criteria with stakeholder input	• Unanimously decide, define and objectively measure criteria to use for prioritization
Step 5 – Define the decision-making process	• Decide who makes the decisions and how these will be made • Consider how often the decision-making body will meet to review the wait-list and identify the data needed to make decisions
Step 6 – Communicate the decision and rationale	• Identify the means by which decisions and alternative treatments (if identified as not priority) and their rationale will be communicated to the patient's clinician
Step 7 – Provide a formal decision review process	• Determine if there will be an appeals process • Define the basis for and who can bring an appeal forward
Step 8 – Evaluate and improve the process	• Determine the means to evaluate the process, its impact on patient outcomes/experiences and clinician experience

TABLE 2. Accountability criteria and principles that guided stakeholder discussion

Principle/Criteria	Elaboration	
Distributive justice	A principle of justice that guarantees equality of opportunity and determines how to set fair limits to healthcare (Daniels 1981).	
Procedural justice	Deliberative democratic procedures that address issues of legitimacy (Daniels and Sabin 1997). This is used if there is a persistent disagreement about rationing.	
Accountability for reasonableness (A4R)	A priority-setting model known as A4R that guides decision makers toward unanimous criteria, relevant to the principles of distributive and procedural justice. This model describes a process by which limited resources can be allocated fairly and reasonably. Five conditions must be met:	
	Publicity condition	Priority-setting decisions and their rationales must be transparent and available to the public.
	Relevance condition	An objective condition that a fair-minded person can agree with even if their preferences and needs are contrary to the criterion. This condition aims to explain why more importance is placed on certain criteria than on others.
	Appeals condition	An opportunity to revise, amend and question priority-setting decisions when presented with further evidence and arguments.
	Empowerment condition	Power differences should be minimized to ensure effective stakeholder participation.
	Enforcement condition	There should be oversight to ensure that publicity, relevance, appeals and empowerment conditions are met.

Results

Aim and scope of priority-setting decisions

Applying the A4R framework (Table 1), the Working Group decided to focus on ethical decision-making about allo-SCT (instead of leukemia or malignant hematology, more broadly) and confined the scope to the Centre with the intent to collaborate with other Ontario hospitals and provincial partners throughout the process or in the near future. The Working Group also identified that the ethical issue was how to ensure fair allocation of limited transplantations due to a shortage of allo-SCT resources and capacity (staff, laboratory and beds), rather than a lack of donor stem cells.

Stakeholders

The Working Group emphasized the need for physician involvement in the ethical decision-making process to provide important medical input and foster collaboration with other physicians and program staff and to operationalize the process outcomes in a consistent fashion. A subgroup comprising allogeneic transplant and leukemia physicians, the medical director, senior leaders and the hospital bioethicist was formed to develop an initial set of substantive criteria to guide priority-setting decisions (Tables 1 and 3).

Developing substantive criteria

The Working Group subgroup identified nine priority-setting criteria as relevant for allo-SCT allocation within the Centre: time on wait-list, medical acuity, donor eligibility, type of transplantation, likelihood of benefit, efficiency, impact on other resources, patient willingness to go out of the country and donor availability (Table 3). The subgroup returned these criteria to the larger Working Group for a broader discussion.

Guided by the principles of distributive justice, in which resources are distributed fairly, and procedural justice, emphasizing a fair and democratic process, the Working Group considered the relevance of the identified criteria before ranking their importance in guiding allo-SCT decisions. Relevance relates to whether fair-minded individuals would consider a criterion's attributes important for guiding priority-setting decisions (Daniels 1981). Table 3 identifies the criterion, the decision as to whether the criterion is relevant to SCT allocation based on consensus from the Working Group and justification for its inclusion/exclusion in the Centre's allo-SCT priority setting. For further information on excluded criteria, please see Appendix 1 (available online at longwoods.com/content/26127).

TABLE 3. Substantive criteria for ethical decision-making about allogeneic stem cell transplantation

Criterion	Decision	Rationale
Time on wait-list	Primary criterion	This is considered the most ethically defensible criterion. Patients will be placed on the wait-list at the time of the transplant consult. Interpreted as "first come, first served," this criterion means that those at the top of the wait-list will be offered the next available transplant slot.
Medical acuity	Not relevant	All patients who require allogeneic stem cell transplant (allo-SCT) are urgent or acute, and it is difficult to determine who is more urgent. Applying this criterion may therefore depend on individual physician judgment and thus risks being applied inconsistently.
Donor eligibility	Not relevant	This is an eligibility criterion, not a priority-setting criterion. To be eligible to receive allo-SCT, patients must have consult eligibility, pre-transplant work-up availability, donor availability and informed consent. Those patients who meet eligibility requirements will be considered in order of time on the wait-list for allo-SCT.
Type of transplant	Not relevant	Some types of allo-SCTs are not currently offered (e.g., haploidentical). However, this is changing, and there will be more kinds of transplants performed in the long term, so allo-SCT will not be limited by this criterion.
Likelihood of benefit	Not relevant	No consensus was reached on how to determine "benefit." Physicians will differ in their reasoning and judgment, making this criterion subjective and therefore likely to be unfair.
Efficiency	Not relevant	The availability of related donors limits the current system. This raised "donor eligibility" as a possible criterion for decision-making; however, efficiency is a goal of the overall program, not a priority-setting criterion.
Impact on other resources	Not relevant	This criterion refers to the consequences of patients receiving or not receiving allo-SCT on the medical system (e.g., requiring further chemotherapy). By addressing the wait-list in a procedural fashion, the impact on other resources will be minimized.
Patient willingness to go out of the country	Not relevant	All patients who meet the international standards for transplant will be offered the opportunity to go out of the country.
Donor availability	Not a priority-setting criterion but is an eligibility consideration when working down the list	This criterion does not affect the patient's place on the allo-SCT wait-list. There is a possibility of cryopreserving unrelated or sibling donor products so they are available when the patient is ready for transplant. This criterion is a factor when assigning the transplant date.

Time on Wait-List as the Most Ethically Defensible Priority-Setting Criterion

The Working Group agreed that *time on wait-list* should be the only criterion to guide allo-SCT priority-setting decisions. This means a "first come, first served" system whereby patients are placed on the wait-list according to when they receive the initial allo-SCT physician consult. Time on wait-list was considered as the most ethically defensible criterion because it could be consistently and objectively applied. Patients at the top of the wait-list would be offered allo-SCT first. This criterion emphasized to the Working Group the need to streamline referral processes so that the timing of allogeneic consult does not unfairly disadvantage or advantage patients. Thus, as the priority-setting process evolved the perception

of what was at stake from an ethical standpoint also evolved. It became clear through multiple discussions with stakeholders that health systems improvement was also ethically salient because it impacted the availability and timeliness of transplantations.

Streamlining organizational processes to promote fairness and equity

The Working Group discussed operational ways to consistently identify who had "first come" so that they would be "first served." It was agreed that once patients were seen by the allo-SCT physician, and transplantation was medically recommended, their names would be added to a single wait-list dated with the time of their initial consult. An allo-SCT date would then be assigned by providing a date to the first eligible person on the list. To be eligible, the patient should have completed the pre-allo-SCT work up, have a donor available and have any co-morbidities under control. For patients to be fairly placed on the wait-list, workflow and organizational processes needed to be streamlined to ensure consult dates were fairly and efficiently allocated, and all consulting physicians consistently added their patients to the wait-list without delay.

Ethical values of equity and fairness also supported a change in the donor work-up to ensure timeliness of donor identification. Donor work-up went from being initiated *after* patients completed chemotherapy to being done *during* chemotherapy, before patients being medically ready for transplantation. At their initial clinical assessment, all AML patients had blood drawn for HLA typing and antibody testing and were asked for information regarding close relatives, so that transplantation search coordinators could begin to identify potential related donors and initiate a search for a matched unrelated donor.

A final consideration involved patients who experience co-morbidities while on the transplantation wait-list. The Working Group decided that these patients would receive the required treatment (e.g., antibiotics) without relinquishing their priority on the list. Patients who received allo-SCT but then later experienced a relapse would begin the wait-list process anew by participating in an initial transplantation consult.

Consideration and Rejection of Medical Acuity and Medical Benefit as Relevant Criteria

In contrast to the traditional principle of triage, our Working Group did not consider medical acuity as a relevant priority-setting criterion. To define medical acuity as a criterion, stakeholders aimed to develop an operational definition for sickness in which "sickness" included being at the highest risk of death, including co-morbidities. According to this criterion, the sickest patients would receive treatment first. However, the Working Group believed that these patients would be less likely to benefit medically from a transplantation. Furthermore, in the context of AML, the criterion of medical acuity would result in patients with the highest likelihood of leukemia remission/eradication never receiving prompt allo-SCT because their transplantation would be delayed continually in favour of someone else

who is sicker. The Working Group felt that this rationale was indefensible because as wait times were extended for patients with less medical acuity, they too would inevitably become sicker.

When discussing who would benefit medically the most from allo-SCT, the Working Group had difficulty reaching agreement. Some physicians argued that science was not yet advanced enough to make these predictions and to determine the best timing for a transplantation between two sick patients. Thus, determinations based on level of sickness or medical benefit would require very specific definitions and eligibility criteria that were subjective, were difficult to define and lacked a robust evidence base and standardized system to rank patients. Applying medical acuity or medical benefit would therefore require individual physician judgment and would carry the risk of being applied inconsistently, which would go against the ethical principle of fair and transparent decision-making upon which reasonable people would agree.

Finally, the Working Group distinguished eligibility criteria from priority-setting criteria and believed that medical acuity or medical benefit is related to the former but not the latter. Patients would first need to be eligible for a transplantation before priority-setting criteria could be applied. Medical acuity or medical benefit as well as other decision-making factors were perceived to inform whether a patient is eligible to receive a transplantation. The Working Group felt that a robust transplantation system would need to take into account disease differences, patient factors (e.g., medical co-morbidities) and the timely availability of a donor. Singling out medical acuity or medical benefit as a priority-setting criterion to determine which patient receives the next transplantation upsets the multifactorial parameters of clinical decision-making and the determination of transplantation eligibility.

Systems management and process improvement

The ultimate ethical goal as agreed upon by the Working Group was utilitarian: to get as many patients in need of transplantation access to transplantation as quickly as possible (i.e., greatest good for the greatest number). Therefore, the Working Group recognized that in addition to priority-setting criteria, a broader, systems-level approach to reducing impediments and enhancing efficiencies within the patient pathway to allo-SCT was ethically required, thus improving eligibility determination and the time frame to receive allo-SCT for patients.

A process to evaluate the system and improve workflow began at the Centre with a formal lean initiative in the fall of 2015 (Scoville and Little 2014). A range of mitigating circumstances were identified that should be taken into account to manage the wait-list, including co-morbidities, timely donor availability and bed capacity. As a result of the initiative, clinical managers and leaders completed current state process mapping, identified opportunities for improvement and delineated the characteristics of an ideal patient journey. The clinical team also identified and reported core metrics daily in huddles to ensure goals

were met. They created action plans, revised existing tools and streamlined the flow of information between coordinators and care teams. In addition, a weekly wait-list meeting was refined so that patient and donor status were reviewed consistently and systematically.

Appeals/revisions

A4R is an iterative process with a mechanism for appeals and revisions as needed, as situations change or at designated time intervals as agreed upon by stakeholders. Although the Working Group initially decided that the most ethical criterion to guide allo-SCT priority setting was "first-come, first-served," after implementing the criterion into Centre procedures, those involved in the allogeneic transplantation program found that this criterion alone did not provide appropriate flexibility because the first person on the wait-list may not be ready for allo-SCT. To allow greater transparency and flexibility within the wait-list so as to use all available allo-SCT slots and not disadvantage those patients who are ready for allo-SCT, the previously agreed-upon "first come, first served" criterion was refined to "first ready, first to go." Patients continued to be placed on the wait-list at their initial allo-SCT consult, but flexibility was permitted within the wait-list structure to allow for individuals' unique disease situation and mitigating circumstances (e.g., donor availability).

As discussions continued and the wait-list became more efficiently managed, it became apparent that wait-list patients could be grouped into four categories: patients ready for transplantation, patients who required some medical work-up, patients who required significant medical work-up and patients who required significant medical work-up and a donor had not yet been identified. Patients within these categories were reviewed at the weekly wait-list meetings to ensure consistency and timeliness of care.

Discussion

Since 2015, wait-lists at this Centre and other allo-SCT centres across Ontario have been significantly reduced as efficiencies, capacity-building efforts and coordination between transplantation centres in Ontario were realized (Cancer Care Ontario 2017). As the time frame to receive allo-SCT within Ontario decreased, there was less rationale for patients to accept going out of the country; however, each centre continued to offer this option, as it was, in part, the result of these patients going out of the country that allowed for a reduction in wait-lists in Ontario.

In 2017, there were 281 patients across Ontario who received an allogeneic transplantation (Cancer Care Ontario 2017). This was a 12% increase in all patients (not just AML) receiving SCT within Ontario from 2015/16 and a 70% increase in volume from 2009/10 (Cancer Care Ontario 2017). However, the number of patients eligible for SCT continues to grow and has not yet reached the expected volumes seen internationally. Therefore, conversation must continue among healthcare partners about the level of investment in health human resources and capital planning that is required to continue to meet current and future need.

Finally, although this article reports on an ethical priority-setting process with utilitarian goals, the individual patient experience should not be forgotten. Unlike other resource allocation systems in which there are limits to individual autonomy in favour of top-down decision-making to benefit public health (Devereaux et al. 2008), our Centre's process recognized patient choice as morally salient. Patients with life-threatening disease are faced with difficult care decisions. Although advances have been made and this is an evolving field, allo-SCT may be associated with significant morbidity and mortality and may not be consistent with a patient's values and preferences. Therefore, it is important that patients are well supported in their decision-making process to make informed decisions about their care, including the decision to not accept transplantation. This requires clinical teams communicating relevant information to support patient understanding but also addressing socio-economic barriers that might prevent some patients from selecting the out-of-country option. For example, by working together with healthcare partners in expanding financial coverage of associated costs for out-of-country transplantation.

Conclusion

By applying an ethical framework to allo-SCT resource allocation, stakeholders were able to set priorities within one Centre upon which it was believed fair and reasonable people would agree. Ethical priority-setting has been implemented in other healthcare contexts to determine the principles, criteria and processes that ought to support decision-making in resource and capacity scarcity (Christian et al. 2006; Frolic et al. 2009; Gibson et al. 2011; Silva et al. 2010). In all of these settings, it is crucial to focus on establishing a process to make timely and fair decisions about the allocation of limited goods and services.

Lessons learned from our experience include setting expectations early with key stakeholders regarding the time and human resource investment required to engage in comprehensive deliberative discussions. Referring back to shared goals when stakeholders grow weary or impatient helps to underscore the purpose and value of the process. A potential limitation of our process is that we did not involve patients directly in our priority-setting discussions. However, patients and families were engaged at the provincial level and provided important advocacy for system developments (including the out of the country program). We recognize that patients are perhaps the most important stakeholders because decisions directly impact their care. There is opportunity as part of the A4R framework for our Working Group to involve patients in revisiting and revising the process in the future.

Cancer care is seeing an increase in the number of those surviving or living with the disease due to major advances in the past decade in prevention, screening and high-quality treatment (Heymach et al. 2018). Adoptive cell immunotherapy (chimeric antigen receptor T-cell therapy) and precision medicine are major clinical cancer advances that use genetics and the body's own immune system to inform targeted treatment. These treatments have shown promising results for otherwise incurable malignancies (Hyman et al. 2017).

However, targeted therapies are increasingly expensive and raise complex access and equity issues related to the availability of potentially life-saving drugs. In this new era of precision medicine, policy makers are increasingly confronted with challenging ethical decisions that include deciding which drugs to fund and how to prioritize individuals for clinical trials of breakthrough therapies (Jecker et al. 2017). By sharing one Centre's process of hospital-based priority-setting, we hope to assist others in ethical priority-setting and policy making in our rapidly evolving and complex healthcare environments.

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