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Innovating Consent for Pediatric HCT patients

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Informed consent is fundamental to ethical clinical practice and research. In the context of hematopoietic cell transplantation (HCT), informed consent struggles to meet its ideals of beneficence, justice, and respect for persons(1) given the severity of the disease and complexity of the treatment. As argued by D'Souza and colleagues in *Bone Marrow Transplantation*, (2) and as shown in other studies, including our own in the setting of pediatric HCT, (3) patient and caregiver expectations of consent are often left unmet in both adult and pediatric contexts. For example, participants enroll in studies with limited knowledge about what they are undertaking and find themselves involved in a rote, passive process that fails to inform and gets bogged down by legalistic language. (4) Consent is often requested under conditions characterized by duress. The medical urgency of HCT or associated treatments that are experimental often blurs the line between treatment and research, even from the clinicians' perspective. Furthermore, miscommunication or misunderstanding is almost inevitable because the paper forms are overwhelmingly lengthy and complex. (5)

Greater simplicity in terms of readability and length is a major goal of recent and forthcoming policy regarding informed consent. For example, the NCI's Office of Human Research Protection and FDA developed a joint consensus in the "Development of Informed Consent Documents for Cancer Clinical Trials" for less complicated informed consent documents, (6) and the BMT CTN recently published new recommended guidelines for consent forms. (7) The Notice of Proposed Rule Making (NPRM) that would update the Common Rule calls for greater standardization, simplicity, and readability of forms. (8)

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

However, improving patients' comprehension of what they are consenting to will not be achieved without equal attention to the process of obtaining consent. Universal consent forms will always fall short of meeting the goals of being patient-centered, complete, and fulfilling institutional and regulatory requirements because of the diversity of individual patient needs.(9) Pediatric HCT provides an excellent case example of the need for a more personalized, two-way approach that promotes patient and caregiver activation and utilizes principles of shared decision-making.

The Case for Two-way Communication in Pediatric Hematopoietic Cell Transplantation

HCT is a high-risk, but potentially curative therapy for a number of life-threatening hematological malignancies and non-malignancies affecting children and adolescents. Care decisions can be challenging for patients, particularly in the case of caregivers who consent on behalf of the minor child. Caregivers must distinguish standard treatment from research participation, simultaneously confronting life-and-death circumstances, emotional trauma, urgency to treat, and burden of responsibility. In addition to standard of care, patients enroll in as many as 10 research studies. Each requires its own consent form, as long as 18 pages, which can amount to an overwhelming number of pages to review. Processes and tools that support getting the most relevant information to the right person at the right time, according to an individual's immediate needs would help patients and caregivers navigate the wealth of information they receive at a vulnerable time.

Caregivers of pediatric patients undergoing HCT face significant physical, psychological, and social burden.(10) It is not surprising that the information and communication needs are particularly challenging due to the high-stakes circumstances. Significant distress for children and caregivers occurs across the acute phase of HCT and the HCT procedure itself impacts caregivers' lives for many years. A sense of participation and shared decision-making is a useful coping strategy.(11) Accordingly, it is critical that caregivers (parents) are informed and involved in the delivery of care for medically fragile children. Informed consent discussions are some of the earliest opportunities to actively involve caregivers as they opt for the high-risk HCT procedure and decide whether to participate in a range of clinical trials.

Pediatric patients are frequently brought into the research process early in their care and treatment and upwards of 70% of pediatric cancer patients are enrolled in research, compared with 1-4% of adult cancer patients.(12) Many pediatric oncologists are researchers who switch back and forth between the dual roles of providing patient care and conducting research. Nonetheless, pediatric patients exhibit a high level of sophistication in evaluating complex and serious diagnoses and procedures, contributing to ongoing debates about the role of children's assent as a component of the informed consent process (e.g., if a child's assent is to be included, what age or maturity level is appropriate?).(13)

Activated patients and caregivers (on behalf of the patient) report good two-way communication with their providers and are more likely to be satisfied with their care, share pertinent information regarding symptoms, follow treatment recommendations, and adhere

to prescribed treatments and protocols.(14) Activated caregivers support their children's self-management and communication with providers and are better able to engage in shared-decision making. Shared decision-making in all aspects of health care, including the informed consent process, has been shown to improve clinical outcomes.(15)

In the context of pediatric oncology, parents report a high level of support for research and a strong inclination to share their children's data for future research even with low levels of comprehension about data sharing. However, they also frequently express a strong desire to be a part of decision-making processes suggesting room for improvement.

The Need for a more Personalized, Two-way Approach

Commonly suggested methods for improving the informed consent process aim to balance the goals of informed consent, regulatory and policy requirements, and efficiency. Specific methods include simplifying the forms(16), providing decision aids(17), using interactive computer-based tools(17, 18), having structured discussions(19), or teaching the "repeat back" method(20) and other approaches to enhancing communication skills among those who participate in the consent process(21). However, these proposed interventions still adopt largely top-down, one-size-fits-all approaches that assume a single new approach will meet the diverse needs of many.

Instead, informed consent may better be conceived of as a two-way exchange or feedback loop to be measured and evaluated by its ability to improve shared decision-making, increase patient and caregiver comprehension, motivate activation, and enhance patient/caregiver satisfaction (Table 1). Taking stock of these metrics can ensure a given consent process is effective in meeting its ideals. Informed consent processes should also be evaluated within the context of the current workflow and regulatory structure to better understand their practicability.

As a first step, existing and emerging innovations might be readily extended to the pediatric context. For example, BMT CTN is currently conducting a multi-center study (Protocol 1205) to evaluate the Easy-to-Read Informed Consent for HCT Clinical Trials. The inclusion criteria include adult patients 18 years of age and is currently being conducted as an ancillary study to three existing therapeutic trials (Protocols 1101, 1203, and 1301). It is being evaluated as a mechanism to improve not only comprehension, but also patient satisfaction.(7)

Additionally, existing IRB-approved consent forms might be supplemented, rather than replaced, by a one-page summary sheet. This approach would satisfy the existing legal and institutional requirements while still supporting improvements to the process. For example, a list-display of all of the information provided in the consent form much like a table of contents, executive summary, or Frequently Asked Questions (FAQ) document, with clear references to the long (standard) form, could provide patients and caregivers quick access to the information they care most about (Figure 1). By leaving the content of the consent form untouched, but offering instead a 'menu' of topics for patients and caregivers to quickly identify and focus on the information they care most about, both the legal demands of

consent as well as the ethical demand for a more personalized approach would be satisfied. Such an instrument could engage both pediatric patients and caregivers as partners, leading to change based on “*what matters most*” to them and thereby not letting an overly complex and alienating consent process contribute to the anxiety adult and pediatric HCT patients and their caregivers already face.(3)

Finally, bringing the informed consent process into the digital age affords opportunities to enhance the quality of the process for patients, caregivers, clinicians and researchers. The NPRM would require informed consent documents to be posted online in electronic format. While this would make the documents more accessible, simply posting a PDF document to a website is not likely to improve the process on its own. Instead, leveraging the development of the electronic health infrastructure to support informed consent as a process of shared decision-making may improve transparency, engagement, comprehension, activation, and satisfaction.

In sum, extending innovations to the pediatric context, using supplementary forms that can personalize the process and be used in parallel to existing systems, and leveraging the capacity of electronic health infrastructure should be pursued. Implementing these changes will involve systematic evaluation of these approaches that measure the extent to which they achieve the goals of personalization and two-way decision-making using new or existing validated instruments, such as the CollaboRATE tool (22). Changing current informed consent practices will also entail engaging key stakeholders – patients and caregivers, clinicians and researchers, IRB members – to manage feasibility and assure quality.

Obtaining informed consent should be seen as an opportunity for pediatric HCT patient and caregiver activation, which plays an important role in fostering effective clinician-participant partnerships. While the example provided here focuses on pediatric HCT, testing personalized informed consent processes for all pediatric malignant therapies/cancer clinical trials holds promise. Given the correlation of comprehension, activation, and satisfaction with adherence to treatment, focusing efforts on improving the quality of informed consent as a process of two-way, shared decision making has potentially positive and significant downstream impacts on health care delivery and clinical outcomes.

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		Additional information	Patient (initials)	HCP (initials)
Project summary	We want to be able to learn about how to improve treatments (transplants) for patients like you. In order to do this, we would like to collect information about you, as well as samples of your blood and urine.	Section 2.1, p. 2 Study Purpose Section 4.1, pp. 2-4 Description of what "participation" means Section 1.2, p. 1 About researchers		
Am I eligible?	You are very likely to be eligible for this study because your physician gave you a copy of this. <i>Note that your participation in research is voluntary and is not related to your medical treatment</i>	Section 3, p. 2		
What am I being asked to give permission for?	Use, storage and future use of information about you, blood and urine samples for research	See p. 4		
What do you need from me?	Your permission to be a part of the study. Blood, urine, and information about you will be collected during the normal course of treatment, so participating in this study will not require any additional time or clinic visits.	Section 4.2, pp. 4-5		
Can I participate in other studies?	Yes	Section 5.3, p. 6		
Risks?	Risks of participating in this study are low (minor and extremely rare). <i>If you experience problems or side effects, contact your doctor.</i>	Section 5.1, p. 5		
Benefits?	Probably not for you personally. But, future patients are likely to receive better treatments and health care because of your participation.	Section 5.4, p. 6		
Is my information safe?	We do our best to protect your privacy throughout this process. Some of the ways we do this include secure systems, restricted access, locked offices.	Section 9, pp. 8-9		
What if I change my mind?	You can opt-out of the research at any time. You will continue to receive the normal course of treatment even if you change your mind.	Section 7.2, p. 7		
What can I expect going forward?	You will be notified if anything about the study changes that might lead you to want to not be in it anymore. You will <i>not</i> be paid to participate in the study. Researchers may end your participation in the study, though this is extremely rare.	Section 5.5, p. 6		

Figure 1. Sample form supplementary to informed consent
Supplementary Personalized Consent Short Form (S-PCSF)

Long-Term Evaluation of the Biology and Outcomes of Hematopoietic Stem Cell Transplantation

Do you have any questions about this study for your doctor or for the researchers?

What are your expectations and/or hopes about participating in this research project?

Do you have any concerns?

The purpose of this form is to facilitate communication between patients/research participants and providers/researchers. It is meant to complement, not replace, the traditional consent form, which should be consulted for complete information about the study, participants' rights and responsibilities, and researcher and IRB contact information. (HUM #)

Table 1

Evaluating informed consent as a process: Principles and evaluation

Ethical principle of informed consent	Definition (From Belmont Report)	Current application in informed consent	Personalized, two-way approach	Evaluation metric
Beneficence	<ul style="list-style-type: none"> ■ Do not harm / ■ Maximize possible benefits ■ Minimize possible harms 	<ul style="list-style-type: none"> ■ List of risks and benefits ■ Description of the scope of risks and benefits (e.g., low risk, high risk) 	Ask participants what they perceive as: <ul style="list-style-type: none"> ■ risks ■ benefits ■ scope of possible risks and benefits (low/high) 	<ul style="list-style-type: none"> ■ Comprehension ■ Satisfaction
Justice	<ul style="list-style-type: none"> ■ Fairness 	<ul style="list-style-type: none"> ■ Fair/ equitable selection of research participants 	<ul style="list-style-type: none"> ■ Open reporting 	<ul style="list-style-type: none"> ■ Satisfaction
Respect for persons	<ul style="list-style-type: none"> ■ Autonomy of individuals prioritized ■ Vulnerable populations with diminished autonomy are entitled to protection. 	<ul style="list-style-type: none"> ■ Voluntariness of research; ■ Disclosure/ information 	<ul style="list-style-type: none"> ■ Provide simplified consent forms ■ Provide ongoing communication to assure voluntariness 	<ul style="list-style-type: none"> ■ Comprehension ■ Patient Activation ■ Shared Decisionmaking