What Outcomes of Hematopoietic Cell Transplant Matter Most to Patients?

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Financial Disclosures

- None

Learning Objectives

- Discuss the results of the Patient-Centered Outcomes Research Institute-(PCORI-) funded project, Engaging Patients in Developing a Patient-Centered Hematopoietic Cell Transplant Research, led by NMDP/Be The Match.

- List the six major areas aside from survival that were identified by transplant recipients and caregivers as being most important to them.

- Identify transplant recipient- and caregiver-reported challenges with regard to HCT treatment and coordination of care, and the approaches that health care professionals can take to respond to these challenges.

Why Focus on the Patient’s Perspective?

- Historically, the HCT community has focused most on research to improve the potential for *survival*
- We have much work to do in better understanding patients’ perspectives of what other outcomes of transplant are important areas of research to them

> *“Patients think about survival first and quality of life comes later - you don’t really think about what your quality of life is until* ***after it changes”***

Patient-Centered Outcomes Research Institute (PCORI)

http://www.pcori.org/

- Independent, nonprofit organization
- Authorized by Congress in 2010
- Mission:

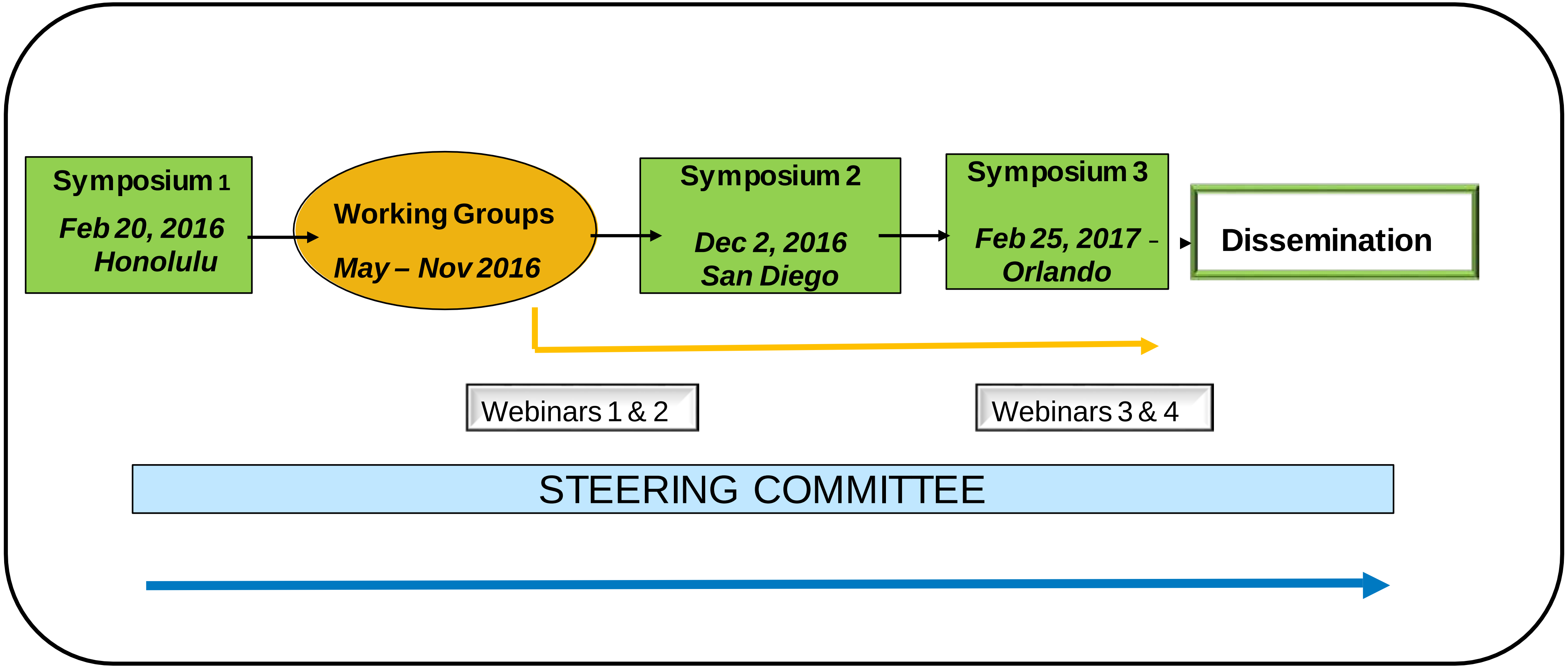
  Fund research that provides patients, their caregivers, and clinicians with evidence-based information needed to make better-informed healthcare decisions.

Engaging Patients in Developing a Patient-Centered Hematopoietic Cell Transplant (HCT) Research Agenda

- **Three aims:**
  1. Recruit and engage a broad community of interested patients and other key stakeholders
  2. Identify and prioritize HCT-related patient-centered outcomes to inform the development of a research agenda
  3. Communicate and promote the agenda to all stakeholders
- **Long term goals**: build research capacity in patient-centered outcomes; leverage partnership to improve outcomes that matter to patients

Burns LJ et al. Biol Blood Marrow Transplant. 2018; 24:1111-1118

Two-Year Work Plan



Symposium 1
Feb 20, 2016
Honolulu

Working Groups
May – Nov 2016

Symposium 2
Dec 2, 2016
San Diego

Symposium 3
Feb 25, 2017 -
Orlando

Dissemination

Webinars 1 & 2

Webinars 3 & 4

STEERING COMMITTEE

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NMDP's PCORI Engagement Award

- **Three specific aims for the next 2 years:**
  1. Recruit and engage a broad community of patients and other key stakeholders interested in PCOR in HCT
  2. Identify and prioritize HCT-related patient-centered outcomes that will inform the development of an HCT PCOR agenda
  3. Communicate and promote the HCT PCOR agenda to all stakeholders
- **Long term**: build HCT PCOR capacity; leverage partnership to advance research agenda

Working Groups: Composition and Tasks

- Populated with representatives from all stakeholders, including patients and caregivers; NMDP staff support

- Tasks:
  - Identify gaps in knowledge through literature review
  - Consider research questions to fill those gaps
  - Prioritize questions by whether they are amenable to testing to see if an intervention improves patient outcomes

Six Working Groups

- Patient, caregiver and family HCT education and support
- Sexual health and relationships
- Physical health and fatigue
- Emotional, cognitive and social health
- Financial burden
- Models of survivorship care delivery

Patient, Caregiver and Family HCT Education and Support Working Group

“It’s important to include the caregiver in patient education”

“Stress to patients that transplant outcomes are different for each patient, and make sure that they know they may feel worse after the transplant.”

Knowledge Gaps

- Patient and caregiver education preferences on:
  - format (electronic, video, print)
  - timing (before transplant, what time points post-transplant)
  - delivery of education (physician, social worker, coordinator, multidisclipinary team meeting)

- What factors predict preferences?

What are the Goals of Education?

Goals of patient, caregiver and family education include:

-Health knowledge
-Distress
-Sense of control / self-efficacy

- Provider goals:

- Patient & caregiver goals:

Priority Goals of Education

Goals of patient, caregiver and family education

-Health knowledge
-Distress
-Sense of control / self-efficacy

- Provider goals:
  - Increase health knowledge
- Patient & caregiver goals:
  - Decrease distress, increase sense of control & self-efficacy

Priority Research Questions

- Which method of education is better at improving self-efficacy and relieving distress of **patients and caregivers:** provider-directed education OR provider-directed education with self-directed education?

- What are the individual (demographics, socioeconomics) patient and caregiver factors that predict self-efficacy and distress with following education?

Sexual Health and Relationships Working Group

“When do I tell my boyfriend that I’m infertile?”

“It was hard to revert back to the husband/wife relationship after being the caregiver for many years.”

Considerations Across Special Populations

- What are the *unique needs* regarding sexual health and relationships for:
  - Adolescent and young adult (AYA)
  - Culturally and linguistically diverse populations
  - LGBTQI population
  - Older (65+) transplant recipients
  - Pediatric survivors
  - Single individuals

Five Focus Areas for Research

1. Sexual Activity
2. Sexual Health
3. Communication
4. Body Image
5. Fertility

Sexual Activity

- Priority question:
  - What can you do and when can you do it?

- Research efforts:
  - Evidence-based guidelines do not currently exist for HCT survivors
  - Recommend guidelines be developed first to inform development of possible interventions

Sexual Health

- Sexual health is not routinely assessed
- Patients and their partners don't know what to expect regarding sexual function
- Small studies have shown effectiveness in the treatment of erectile dysfunction, menopausal symptoms, and female sexual arousal disorder

Sexual Health

- Research efforts should:
  - Identify risk factors for sexual dysfunction post-HCT
  - Include longitudinal studies (pre- and post-HCT)
  - Include prospective, interventional studies for treating sexual dysfunction

Communication

- Focus research questions on the emotional impact of:
  - Disclosing medical history in new relationships: when, what and how
  - Re-establishing intimacy in existing relationships
  - Role changes on patients and their partners

Communication

- Research recommendations:
  - Conduct small pilot projects on possible interventions (couple counseling, individual therapy, role playing)
  - Longitudinal studies to understand role changes before, during, and after transplant

Body Image

- Body image changes are distressing and not routinely discussed
- Recommendations:
  - Explore literature from other populations for guidance (such as burn or trauma, breast and gynecologic cancer patient populations)
  - Conduct small pilot projects of possible interventions

Fertility

- Infertility is associated with complex emotional responses that may result in high risk sexual behavior, and compromise the development of intimate relationships
- Fertility preservation options are not initiated early enough in the cancer therapy trajectory
- Preservation options for pre-pubertal males and females are limited

Fertility

- Recommendations for research:
  - Understand barriers to fertility preservation
    - Access to reproductive specialists
    - Financial / insurance barriers
    - Pre-pubertal population
  - Explore emotional response to infertility with longitudinal studies
  - Understand the impact of infertility on new and established relationships
  - Is there a role for reproductive consultations pre- and post- transplant? Who should be referred?

Physical Health and Fatigue Working Group

“I couldn’t go jogging or swimming anymore, and these were things that validated me…”

“I felt very tired at times, and still do 6 years out.”

Need to Implement Consistent Methodology in Trials

- Instruments:
  - There are many reliable and valid instruments to assess fatigue
  - Inconsistency in use limits understanding in HCT survivors
  - Ideal instrument minimizes patient, clinician, and researcher burden *while maximizing ability to compare outcomes across studies*

- Recommended Instruments and Time Points:
  - Measures: *PROMIS Fatigue* and *Physical Function*
  - Time points: Pre-HCT, D+100, 1 year, 2 years, 5 years+

Need to Develop a Correlative Science Infrastructure

- Patient-reported outcomes (e.g. symptoms), performance measures, and biomarkers may inform ***mechanistic*** understanding

- Few studies have correlated phenotype (self-reported) with biologic measures to elucidate causative pathways
  - e.g. inflammatory markers, cells, cytokines, hormones

- **Proposed next steps**: Convene *patients*, experts in *symptom research*, *objective measures*, and *laboratory investigators* to develop a correlative **biobank;** conduct prospective trials with correlatives

Emotional, Psychological, Social Health and Cognitive Function Working Group

“Depression is very common after transplant and we were not aware of that..”

“I couldn’t make my brain catch up with what I knew it ought to do”

Adult Emotional, Psychological & Social Health:
Current Knowledge

- Acute decline in quality of life (QOL), increase in depression during HCT, gradual improvement 3 months - one year post-HCT
- Clinically meaningful emotional distress is common
- Long-term psychological issues including depression, post-traumatic stress syndrome (PTSD), and general emotional distress persist in 20-30%
- Social functioning and return to work are also big issues: 60-85% of HCT survivors return to work within 6 years
- Risk factors: graft-versus-host disease (GVHD), older age, & fewer social supports

Adult Emotional, Psychological & Social Health:
Limitations = Gaps in Knowledge

- Methodological: small sample sizes, attrition and selection bias, heterogeneous instruments, cross-sectional/retrospective studies
- Heterogeneous populations
- Less long-term follow-up over time
- Lack of cultural, linguistic, and ethnic diversity
- Limited intervention studies
- Limited focus on caregivers

Adult Emotional, Psychological & Social Health: **Recommendations**

- Multicenter studies incorporating better methodology/diversity
- Study autologous and allogeneic HCT survivors separately
- Leverage technology for intervention studies, both acute HCT period and long-term to improve follow-up
- Studies on positive emotional change: resilience
- More dyadic studies of patient-caregivers

Pediatric Emotional, Psychological & Social Health: **Knowledge**

- Impact on *patient:*
  - Younger children have higher QOL than older children
  - More pain, worse general health and lower self-esteem than general population
  - Risk factors: maternal anxiety and depression, ALL, GVHD
- Impact on *family*:
  - Parental stress highest during pre- and acute HCT period
  - Those with highest stress during acute phase are at risk for ongoing high stress.
  - Family conflict associated with behavioral problems

Pediatric Emotional, Psychological & Social Health: **Limitations = Gaps**

- Numerous methodological issues, similar to adult
- What factors (personal vs. external factors) contribute to psychosocial outcomes and adjustment are unknown
- Lack of age-appropriate measures or instruments
- Too often parental assessment is relied upon, yet not always valid
- Reliable comparisons to population norms lacking
- Lack of knowledge about impact on all family members

Pediatric Emotional, Psychological & Social Health: **Recommendations**

- Mixed method approach to research (questionnaires, self- and parent-report, combined with direct interviews with children)
- Longitudinal studies with larger sample size and diversity
- Assess developmental impact on psychological health
- Understand different trajectories in coping and QOL between patients needing an acute transplant vs. those living with chronic conditions

Cognitive Function: **Knowledge**

- Some cognitive dysfunction early post-transplant, but limited data on trajectory over time
- Domains measured:
  - Attention
  - Executive function
  - Information processing
  - Motor speed
  - Verbal ability and memory
  - Visual memory and visuospatial ability

Cognitive Function: **Limitations**

- Studies mostly small, heterogeneous populations without well-matched controls
- Inconsistent findings
- Lack of data on cognitive outcomes in pediatric and older adults
- Lack of longitudinal studies with pre-induction time points and long-term follow-up
- Poor understanding of the mechanism of cognitive problems
- Relationship between emotional distress/depression and cognitive function is unknown

Cognitive Function: **Recommendations**

- Critical need for longitudinal studies with sound methodological design, long-term follow-up, homogeneous patient populations, appropriate pre-transplant assessments
- Incorporate valid measures that are meaningful to patients and families in how deficits affect daily living and functioning, return to work
- Assess the mechanism of cognitive problems during HCT, incorporating fMRI, cognitive neuroscience, event-related potentials (ERPs).

Financial Burden Working Group

"I expected insurance would pay and I would be financially ok coming out of transplant. The hospital helped decipher insurance angles and grants, so I expected to be financially secure, or close to it, but wasn't."

Goal of Research Questions

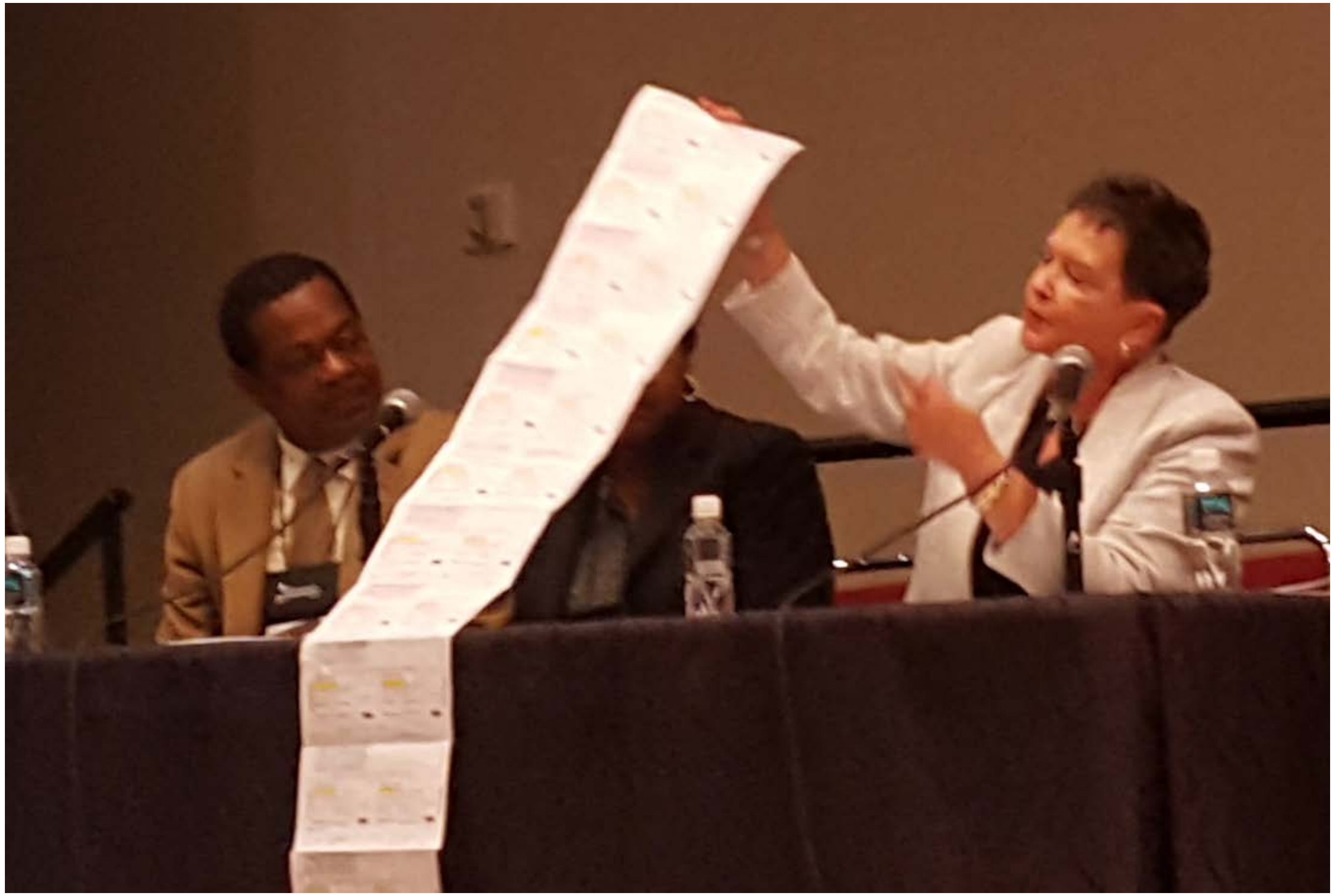
- Better characterize and inform patients of the costs associated with transplant
- Identify and assess current and new approaches to reducing both patient and caregiver patient financial burden
- Assess the role of timing in financial preparation for transplant
- Identify long-term financial burden across various patient and caregiver populations

Research Questions

- What is the best time frame to discuss/address financial information with patients?
- Does financial burden impact quality of life over the long-term?
- Does patient knowledge and use of insurance resources impact financial and health outcomes?
- What is the difference in financial burden across transplant centers with varied resources and interventions?
- How does physician involvement in financial discussions impact outcomes?

Models of Survivorship Care Delivery

“The hospital emergency room that I went to didn’t do transplants, ***nor did any of the doctors know about transplants****,* ***nor did they even believe me*** *when I tried to explain they couldn’t do this, and they couldn’t do that.“*



Access to Survivorship Medical Services: **Knowledge Gaps**

- What is the best way to create a network of providers knowledgeable in post-HCT survivorship care that includes excellent communication between all providers and the patient?

- How do we assess the quality of care provided and patient satisfaction?

Access to Survivorship Services: **Possible Interventions To Test in Trials**

- Telemedicine across transplant center-established network of providers that span specialty, health network, and geographic service area
- Survivorship care plan in which specific providers “sign up” and accept specific responsibilities in the care plan
- Patient-controlled communication tools to providers vs. transplant center-controlled process (survivorship care navigator)
- Centralized electronic medical record with online access to all treating providers vs. conventional approaches

Take Home Points

- Patients and caregivers
  - Provide insights into research topics that are most important to them
  - Their insights may differ from providers
  - Are enthusiastic and invaluable partners
- Six major areas that patients believe research is needed to improve HCT outcomes
- There’s so much work to be done!

Patient and Caregiver Perspective

“Being in the working group gave us a voice”

Important for the transplant community to understand what a long road transplant can be

We thought we’d go through the transplant process and get back to our life; it’s been everything but that

If we weren’t participating, the transplant community wouldn’t be aware of the issues that patients experience

Hope that future patients will have a better experience

Exposed us to information and opportunities that we didn’t know existed

Thanks to our Patients and Caregivers!