DEVELOPMENT OF A PATIENT-REPORTED OUTCOME MEASURE (PROM) TO FULLY REPORT A PROPOSED CORE OUTCOME SET

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BACKGROUND

In coreHEM, a core outcome set (COS) for hemophilia gene therapy (GT) was identified by multi-stakeholder consensus.[1] When consistently measured, the COS will inform a value-based approach to evaluate the risks and benefits of GT. First steps to determining appropriate measurements for each outcome were previously reported.[2] One outcome, mental health (MH) outlook, was regarded as highly important to capture the potential transformational impact of GT, however no instruments that measured MH when receiving a novel treatment were identified. An instrument with a summary score evaluating concepts that contribute to MH was deemed desirable, along with qualitative data to capture the impact of a potential cure. While coreHEM exhibited broad overlap in mapping to a hemophilia value framework, gaps were identified for the MH outlook outcome and this outcome was prioritized for data collection/publication.[3,4] coreHEM MH is a patient-reported outcome measure (PROM) development project initiated to provide a content-validated instrument that can be used to measure this outcome.

METHODS

A conceptual framework and interview guide for MH outlook in hemophilia were developed from a literature/evidence review. Concept elicitation (CE) interviews were used to refine the framework and identify additional concepts. Participants were asked about how living with and treating their hemophilia impacted their MH outlook, with a focus on attitudes and the range of feelings one experiences. PROM items were developed from priority concepts, with some items mapping directly to a concept and some items covering overlapping concepts. Cognitive debriefing sessions were held in two rounds to test the PROM; items were updated iteratively. Cognitive debriefing for content validation prioritized the understandability of the items and the relevance of the concepts.

RESULTS

Table 1. Participant Demographics

	Concept Elicitation Interviews (n=32)	Cognitive Debriefing Round 1 (n=17)	Cognitive Debriefing Round 2 (n=9)
Age (years) Mean ± SD	37.7 (16.2)	38.8 (14.7)	42.7 (13.9)
Country (%)			
Australia	2 (6.3)	4 (23.5)	--
Canada	8 (25)	6 (35.3)	4 (44.4)
United Kingdom	6 (18.8)	2 (11.8)	2 (22.2)
United States	16 (50)	5 (29.4)	3 (33.3)
Type of hemophilia (%)			
A	27 (84.4)	11 (64.7)	5 (55.6)
B	5 (15.6)	6 (35.3)	4 (44.4)
Severity Level (%)			
Moderate	6 (18.8)	1 (5.9)	--
Severe	26 (81.3)	16 (94.1)	9 (100)

Thirty-two people with hemophilia (PWH) participated in concept elicitation interviews. Twenty-six PWH participated in cognitive debriefing interviews; 5 of these were returning interviewees from the CE interviews that gave feedback on the changes made compared with earlier versions of the PROM. Eligibility criteria was males aged 15 or older with moderate or severe hemophilia A or B.

Figure 2. Sample PROM Items

Section 1. General Mental Health Outlook Items

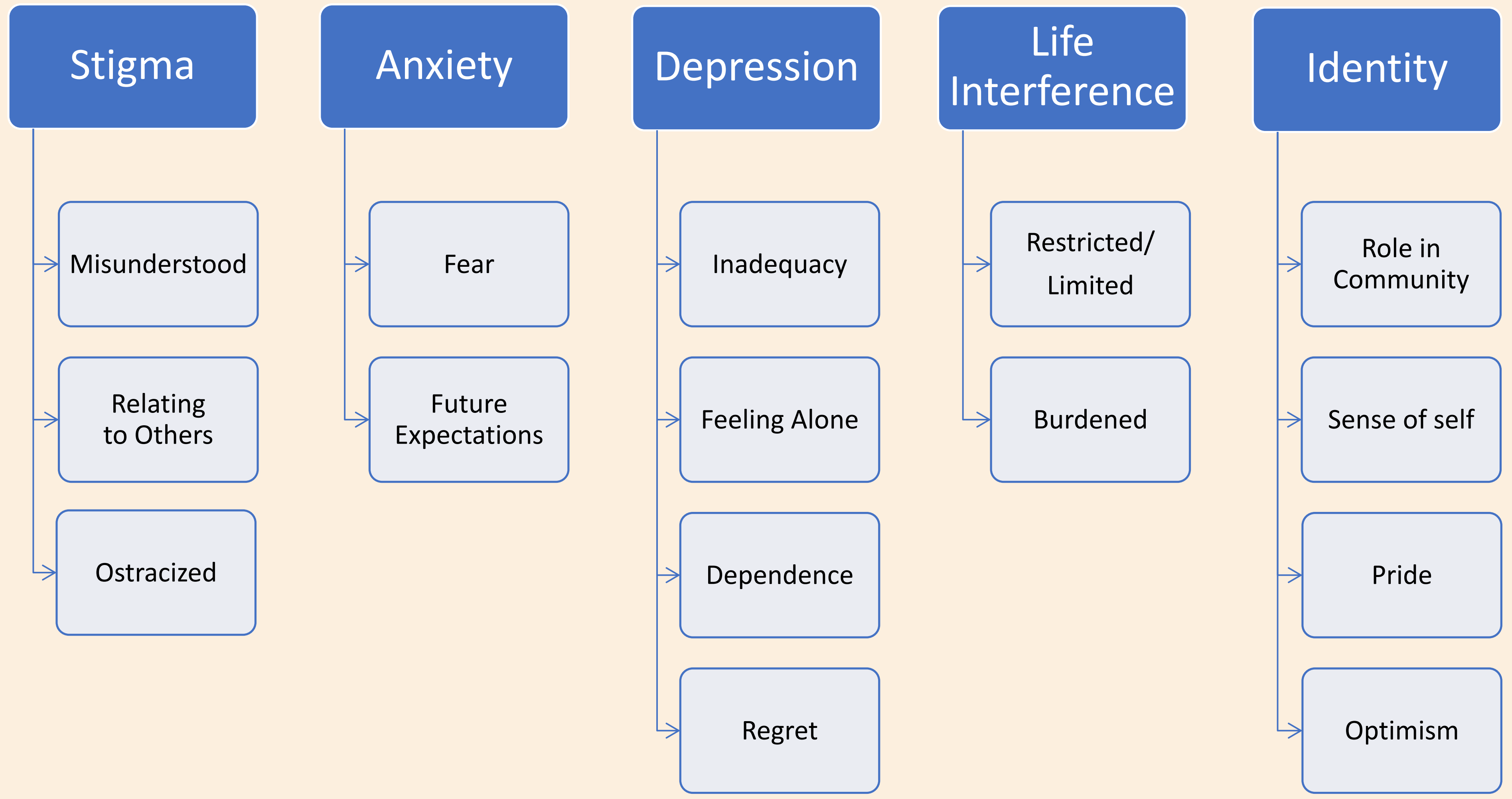
- I feel tied to my hemophilia treatment regimen.
- I feel upset about missing opportunities because of my hemophilia.
- My hemophilia is always in the back of my mind.
- Hemophilia keeps me from being able to fulfill the roles I expect to be able to do.

Section 2. Gene Therapy Specific Items

- I worry about potential side effects of gene therapy for hemophilia.
- I am concerned that I may lose my identity as a person with hemophilia after I receive gene therapy.
- I am happy about getting gene therapy.

The PROM has two sections: a general mental health outlook section that focuses on hemophilia and uses the term "treatment" generally, not specifying gene therapy, and a gene-therapy specific section to be used in GT clinical trials. Instructions on the PROM state to "Select the answer that represents how much you agree with the following statements." The five-point answer scale is "Very much," "Quite a bit," "Somewhat," "A little bit," or "Not at All," plus "Not Applicable."

Figure 1. Domains and Concepts of the coreHEM MH Conceptual Framework



When refining the framework based on findings from the CE interviews, "Concerns about the Future" and "Concerns about Treatment" were combined as "Future Expectations," and "Inclusion in the Disease Community" became "Role in Community." Examples of sub-concepts added (not shown) included "Accidents and Traumatic Bleeds," "Hiding A Bleed," and "Economic/Political Outlook [for treatment access]"

CONCLUSIONS

A content-validated instrument will soon be available for use as an exploratory outcome in hemophilia GT clinical trials and real-world settings. Its use will allow for collection of MH outlook data, meeting the needs of the value framework and helping fulfill the intentions of the COS.

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coreHEM mental health

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