ORIGINAL ARTICLE

Measuring the impact of hemophilia on families: Development of the Hemophilia Family Impact Tool (H-FIT)

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Abstract

Introduction: This study aimed to assess the impact of hemophilia on families, in the context of current and emerging hemostatic therapies, and explore the need for a hemophilia-specific tool targeted at parents of boys aged <4 years. A secondary aim was to develop and validate the new tool.

Methods: Focus groups were conducted with parents of boys with hemophilia and hemophilia health care providers at Canadian hemophilia treatment centers (HTCs) to review the relevance of the Pediatric Quality of Life Family Impact Module (PedsQL-FIM); a novel questionnaire was developed by identifying core themes expressed. This questionnaire, the Hemophilia Family Impact Tool (H-FIT) was validated in a sample of parents of boys with hemophilia relative to the PedsQL-FIM.

Results: Seven focus groups were conducted at four HTCs, generating themes specific to hemophilia not covered by the PedsQL-FIM, suggesting that a new tool be developed (the H-FIT). In the validation phase, 54 parents completed the H-FIT and PedsQL-FIM. The H-FIT had a strong correlation with the PedsQL-FIM across all ages (r = 0.79; *P* < .0001) and a moderate correlation for parents of boys aged <7 years (r = 0.64; *P* = .0007). There was a significant difference between the mean H-FIT

scores for parents of boys using extended half-life factor (68.1; standard deviation [SD]=14.2) compared to standard half-life factor (54.7; SD=18.4; $P = .04$).

Conclusion: A novel, disease-specific tool, the H-FIT, has been developed to measure the impact of hemophilia on families. The H-FIT has good preliminary measurement properties and may be responsive to changes in therapy associated with a decreased burden of administration.

Essentials

- It is important to measure the impact of hemophilia on families in the era of novel therapies.
- This study developed and validated a new tool, the Hemophilia Family Impact Tool (H-FIT).
- The H-FIT was moderately correlated with a generic family impact tool for parents of young boys.
- Initial data suggest that the H-FIT may be responsive to changes in therapy (burden of administration).

1 | INTRODUCTION

For persons with severe hemophilia, regular infusions of clotting factor concentrates (CFCs; i.e., prophylaxis) has been proven to be superior to on-demand/episodic treatment in terms of both joint health outcomes and quality of life.[1,2] As such, long-term prophylaxis started early in life, and ideally before age 3 years, in boys with severe hemophilia, is now recognized as the standard of care to prevent hemophilic arthropathy.[3] Despite the many advances in the treatment of hemophilia, prophylaxis with CFCs still requires regular intravenous access. Given that primary prophylaxis with standard half-life factor VIII (FVIII)/factor IX (FIX) CFCs involves intravenous infusions at least twice weekly—and in the case of hemophilia A, as frequently as every other day—the burden of administration is a significant stressor that falls primarily on parents/caregivers. The advent of longer-acting FVIII/IX CFCs and nonfactor hemostatic therapies allow for less frequent injections that may lead to improved adherence, better health outcomes, and consequently an improved quality of life.

Given this rapidly evolving hemophilia treatment landscape, patient-reported outcome measures (PROMs) are becoming an increasingly important metric in hemophilia research.[4] PROMs in general, and health-related quality of life (HRQoL) in particular, are essential to obtain so as to have a complete understanding of the impact of chronic conditions such as hemophilia and to evaluate the impact of treatments, including efficacy and cost-benefit.[5] Recently, a group of hemophilia health care providers (HCPs) and other experts in the field agreed that measures of HRQoL were important to consider as an outcome measure that should be included in clinical trials.[6]

There are several hemophilia-specific questionnaires that are currently used to measure HRQoL in boys aged <18 years with hemophilia; the Canadian Hemophilia Kids' Life Assessment Tool (CHO-KLAT) and the Quality of Life Assessment instrument for children with hemophilia are the two most commonly used and well-studied tools.[7] These tools have child self-report to measure HRQoL in children aged ≥7 years, and parent-proxy for children aged <7 years.[8] Despite their use of parent-proxy reports for younger children, it is very difficult for parents/caregivers to "get into the head" of a very young child (aged <4 years) and report their HRQoL. This is a period when hemophilia management can be very challenging for the child, the parent(s)/caregivers, and the entire family since it is within this period that primary prophylaxis is optimally introduced and the highest-risk period for inhibitor development. Therefore, we propose a different construct to assess HRQoL in children aged <4 years through measuring the impact of hemophilia on the family.

The impact of hemophilia, or any chronic disease, on a very young child (i.e., aged <4 years) is not an isolated impact. It is generally understood that the ability of a family to adapt and cope with a child with a chronic illness is associated with the health outcomes for the child, a concept that has been well studied in other conditions such cancer[9] and asthma.[10] There is a generic tool that measures the impact of a chronic pediatric condition on the family: the PedsQL Family Impact Module (PedsQL-FIM),[11] but to the best of our knowledge, at the time this study was started, there were no hemophilia-specific family impact tools.

The development of a tool to measure the impact of hemophilia on families would potentially enable clinical and research teams to see and measure the broader impact of a child's therapy sooner, since they would not have to wait for the child to be old enough to self-report. This will become increasingly important in the assessment of emerging hemostatic therapies and allow earlier evaluation of efficacy beyond the traditional physical outcomes such as joint bleeds.

The aim of the present study was to assess the impact of hemophilia on parents/caregivers and families in the context of current and emerging hemophilia therapies, and to explore the relevance of an existing tool (PedsQL-FIM). If the process proved the need for a hemophilia-specific tool, a secondary aim was to develop and validate the new tool within the context of Canadian hemophilia treatment centers (HTCs).

2 | METHODS

This study was conducted in two phases. Phase I was qualitative in nature and explored the impact of hemophilia on families, especially in those aged <4 years, using the PedsQL-FIM as a starting point, to determine if a hemophilia-specific tool is necessary. Phase II was quantitative and assessed the impact of hemophilia on families. Inclusion criteria for both phases were: parents/caregivers of boys with moderate or severe hemophilia (defined as a FVIII/FIX level of ≤5%) between the ages of 0 and 18 years, and experienced health care providers who manage children and/or adults with hemophilia A or B. Parents/caregivers were excluded if their son had (i) mild hemophilia (FVIII/FIX level of >5%), (ii) a history of an inhibitor to FVIII/ FIX (defined as >0.5 Bethesda Units) within the previous 12 months, or (iii) a significant comorbid disease (e.g., hepatitis). All participating centers received ethics approval, and all participants provided informed consent.

2.1 | Phase I

Focus groups were held with parents of boys with hemophilia and hemophilia HCPs in the following locations across Canada: IWK Health Centre in Halifax, Nova Scotia; The Hospital for Sick Children in Toronto, Ontario; Children's Hospital of Eastern Ontario in Ottawa, Ontario; and Hamilton Health Sciences Centre in Hamilton, Ontario. Each group followed a semistructured format, as previously described by Young et al.[12]

The assessment of the impact of hemophilia on families was carried out in conjunction with the assessment of, and revisions to, the CHO-KLAT version 3.0 to maintain its relevance in the era of novel hemostatic therapies.[13] At the end of each focus group, participants were asked to review the items on the PedsQL-FIM to evaluate their relevance through the lens of caring for a child with hemophilia. The PedsQL-FIM is a measure of the impact on the family of caring for a child with a generic chronic condition, and generates a summary score between 0 and 100, with 100 representing the best possible outcome (i.e., the least amount of impact on the family).[11] For this exercise, each of the items from the PedsQL-FIM were displayed on cardstock and participants were asked to vote for the items they felt were most and least relevant. Each participant was given 10 green stickers to vote for the most relevant items and 10 red stickers to vote for the least relevant items, and there were no limits to the number of votes that could be applied to a single item.

Following voting, the group shared thoughts and ideas about their motivation for their voting decisions. Participants were then asked to suggest new items or concepts that they felt are relevant and important to families of boys with hemophilia, not included/covered in the PedsQL-FIM, specifically focusing on managing hemophilia in children aged birth to 4 years. These new items were recorded on cardstock and displayed around the room to encourage continued discussion and development of these new ideas and concepts.

2.2 | Phase I analysis

Phase I analysis was completed primarily by the focus group facilitators (SD, VP, and NY) with the goal of determining if a novel questionnaire is necessary and, if so, to develop the item content for the new tool. The results of the voting by each group were summarized using descriptive statistics. These results were used to inform the relevance of the item content of the PedsQL-FIM to families of boys with hemophilia and to determine if a new tool would provide new or additional information.

After it was determined that a hemophilia-specific tool was required, to develop the item content of the new tool common ideas and themes were identified from across the focus groups and examined using content analysis, based on Charmaz's analysis methods.[14] An expert panel reviewed the proposed wording of the items in the new tool.

Cognitive debriefing was completed with parents of boys with hemophilia at 2 Canadian HTCs to confirm that the intended meaning of the items was understood, that the wording was clear, and that the items were relevant. Thereafter, the final version of the Hemophilia Family Impact Tool version 1.0 (H-FIT) was used for phase II.

2.3 | Phase II

Phase II implemented the newly developed tool, the H-FIT, to a cohort of parents of boys with hemophilia. The phase II cohort did not exclude those who participated in phase I, but was considered a new cohort of parents. To determine the validity, the PedsQL-FIM was also administered, with the a priori hypothesis that the correlation between these two measures would be in the range of 0.4 to 0.6. The sample size required to show that the correlation is in the desired range (α = 0.05; β = 0.20) was a minimum of 19 participants.[15] Demographic information was also collected from each participant. The questionnaires were completed during a single routine clinic visit.

2.4 | Phase II analysis

Phase II data analysis included descriptive statistics to summarize the participant characteristics and the distributions of the H-FIT and the PedsQL-FIM. The distributions of both tools were plotted and assessed for ceiling effects, which are present when ≥15% of respondents achieve the highest possible score.[16] The validity of the H-FIT was assessed by calculating Pearson's correlation coefficient of H-FIT summary scores in relation to the PedsQL-FIM summary scores. The correlation was further examined in exploratory subgroups. First, two different age groups were defined: parents of boys <7 and ≥7 years of age, as 7 is the age at which children are generally able to self-report HRQoL, and therefore where we would expect a divergence of responses.[8] Next, age groups were defined by the clinical study team members to reflect the unique challenges in hemophilia care associated with the different developmental stages: <4 (e.g., diagnosis, initiation

of prophylaxis), 4 to <7 (e.g., starting school, increased activities), 7 to 12 (e.g., increased independence, learning self-administration of therapy), and 13 to 17 (e.g., increased autonomy over health, transition to adult care) years of age. The relationship of the H-FIT score with age of the child was examined using a one-way analysis of variance, and Tukey multiple pairwise comparison was used to determine the difference between H-FIT scores in each age group. Finally, scores from parents of children using extended half-life or standard half-life CFCs were compared using independent sample *t* tests in an exploratory subgroup analysis. Sensitivity analyses were performed to assess the effects of (i) participants who were involved in both phases of the study and (ii) type of caregiver completing the questionnaires.

3 | RESULTS

3.1 | Phase I: Focus groups

Data were obtained from seven focus groups, with a combined total of 43 participants, held in four pediatric HTCs in Canada between October 2017 and April 2018. There were three focus groups with parents of boys with hemophilia (n=23) and four with hemophilia HCPs (n = 20). Twenty-three of the 26 invited parents (88%) participated, of which 16 (70%) had children aged ≥7 years, 4 (17%) had children between 4 and 7 years, and 7 (30%) had children aged <4 years (numbers add to >100%, as 4 parents had more than one child with hemophilia). All of the HCPs who were approached participated in the focus groups.

The duration of the focus groups ranged from 20 to 60 minutes. All participants were given the opportunity to assess the PedsQL-FIM, express their opinions, and engage in active discussion.

The first portion of the focus group was spent reviewing and discussing the items of the PedsQL-FIM. The PedsQL-FIM consists of eight domains covering physical, emotional, social and cognitive functioning, communication, worry, daily activities, and family relationships. A main theme that kept emerging, especially from the parents of younger boys, was that they were unable to differentiate whether they were identifying with some items on the PedsQL-FIM specifically because of their child's hemophilia or simply due to being a parent of a toddler. This was especially true for parents whose only child has hemophilia, as they indicated they have no reference point. Additionally, both parents and HCPs indicated that many of the items, particularly in the physical functioning, cognitive functioning, and daily activities domains were not relevant to them.

The focus groups generated themes specific to hemophilia that were important to parents and HCPs and were not covered by the generic PedsQL-FIM, including stress surrounding treatment administration, guilt resulting from the transmission of hemophilia, and confidence educating others about hemophilia. Overall, the sentiment from both the parents and the HCPs was that while some of the items were potentially relevant, the PedsQL-FIM did not cover issues they felt were important when considering caring for a child

with hemophilia. Based on these discussions and the voting process, we determined that a new tool should be developed to address these important concepts, to enable measurement of the impact on families when caring for a child with hemophilia. This process generated 16 new items to establish the H-FIT. The same answer options and scoring method used for the CHO-KLAT version 3.0[17] were adapted for the H-FIT. Both are scored on a scale of 0 to 100, with 100 representing the best possible score (the least impact of hemophilia on the family). Table 1 outlines the key differences between the PedsQL-FIM and the H-FIT.

Given that the H-FIT is a new tool, cognitive debriefing was conducted with nine parents of boys with hemophilia at two HTCs (IWK Health Centre and The Hospital for Sick Children) in Canada. The ages of their sons with hemophilia ranged from 2 to 16 years. These sessions resulted in the following adjustments: substantial wording changes to one of the questions where the intended meaning was not understood by participants, minor wording changes to one of the questions where a small clarification was made to improve the readability of the question, and a reordering of the questions to space those that are negatively and positively worded. The resulting H-FIT consists of 16 questions and takes approximately 5 to 10 minutes to complete.

3.2 | Phase II: Validation

Fifty-four parents of boys with hemophilia participated in phase II between October 2018 and July 2019. A summary of their baseline characteristics is shown in Table 2. Of the 54 parents, 40 (74%) had sons with severe hemophilia, defined as a baseline factor FVIII/FIX

TABLE 1 Summary of key differences between the Pediatric Quality of Life – Family Impact Module (PedsQL-FIM) and the Hemophilia Family Impact Tool (H-FIT)

	H-FIT	PedsQL-FIM
Number of items	16	36
Physical symptoms of stress	Not included	Included as a subdomain
Cognitive functioning	Not included	Included as a subdomain
Daily activities	Not included	Included as a subdomain
Treatment administration/ burden of administration	Concept covered in 2 questions	Not included
Guilt/worry around functional limitations	Concept covered in 3 questions	Not included
Symptom-specific concerns (ie, bleeding)	Concept covered in 2 questions	Not included
Knowledge/confidence with hemophilia	Concept covered in 2 questions	Not included

level of <1 IU/dL, 11 (20%) had sons with moderate hemophilia, and 3 (6%) did not indicate the hemophilia type or severity of their son's hemophilia. The majority of the boys were on prophylaxis (46/54; 85%) and were being treated with extended half-life (EHL) CFCs (36/54; 67%).

The mean H-FIT score was 64.3 (standard deviation [SD] = 16.1), and the mean score on the PedsQL-FIM was 76.3 (SD = 21.7). Figure 1 shows the distribution of scores for both questionnaires. Of note, the H-FIT had a wider distribution, while the PedsQL-FIM had a strong ceiling effect, with 39% of respondents achieving a score in the highest decile (from 90 to 100).

There were 12 parents (22.2%) who participated in both phases of the study. When excluding these parents, the mean H-FIT score was not statistically different (mean = 65.0; SD = 16.1; $P = .85$). The H-FIT scores were also not significantly different based on the type of caregiver responding to the questionnaires (data not shown). Therefore, all participants are included in the remainder of the analyses.

Overall, the H-FIT had a strong correlation with PedsQL-FIM ($r = 0.79$; $P < .0001$). The H-FIT had a moderate correlation with the PedsQL-FIM for parents of boys aged <7 ($r = 0.64$; $P = .0007$), and a strong correlation for parents of boys aged ≥7 ($r = 0.86$; $P < .0001$; Figure 2).

Figure 3 shows the mean H-FIT score by age of the child. The mean (SD) H-FIT scores were 56.2 (17.0), 64.2 (8.0), 62.7 (19.7), and 71.8 (14.0) for the <4, 4 to <7, 7 to 12 and 13 to 17 age groups, respectively. There was a significant difference between the mean score for the <4 and 13 to 17 age group ($P = .04$). There was also a significant difference between the mean H-FIT scores for parents of boys using EHL CFCs (68.1; SD=14.2) compared to standard half-life (SHL) CFCs (54.7; SD=18.4; $P = .04$), regardless of the age of the child (Figure 4).

4 | DISCUSSION

This study reports on the development, validation, and preliminary measurement properties of a new tool to measure the impact of caring for a child with hemophilia on families, the H-FIT. Focus groups with parents of boys with hemophilia and hemophilia HCPs suggested that the true impact of caring for a child with hemophilia was not captured by the generic measure PedsQL-FIM, supporting the development of a hemophilia-specific tool, the H-FIT. Our initial validation efforts suggest that the H-FIT is valid across the entire pediatric age span, with particular relevance for families with younger children.

The need for a hemophilia-specific measure was further reinforced by the findings of the ceiling effect in the PedsQL-FIM and by the very strong correlation between the H-FIT and PedsQL-FIM in the parents of the older boys. The increasing correlation with age between the PedsQL-FIM and the H-FIT suggests that the PedsQL-FIM was not getting to the crux of matters in the early years, such as burden of administration of treatments, stress around dealing with

TABLE 2 Baseline characteristics of phase II study participants

	Participants (n=54)
Age of child with hemophilia, y, median (range of values)	7 (0.83–17)
Caregiver Type, n (%)	
Mother	40 (74.0)
Father	11 (20.4)
Grandmother	1 (1.9)
Grandfather	2 (3.7)
Hemophilia type, n (%)	
Severe hemophilia A	36 (66.7)
Moderate hemophilia A	6 (11.1)
Severe hemophilia B	4 (7.4)
Moderate hemophilia B	5 (9.3)
Unknown	3 (5.6)
History of an inhibitor to FVIII/FIX, n (%)	11 (20.4)
Current treatment regimen, n (%)	
Prophylaxis	46 (85.2)
On demand	8 (14.8)
Factor type, n (%)	
Standard half-life	15 (27.8)
Extended half-life	36 (66.7)
No treatment received to date	3 (5.5)
Distance from HTC, km, median (range)	50 (7–600)
Custody arrangements, n (%)	
Equally shared, parents live together	30 (55.6)
Equally shared, parents do not live together	3 (5.6)
Child lives with mother only	6 (11.1)
Shared, mainly mother	2 (3.7)
Other	3 (5.6)
Unknown	10 (18.5)
Annual household income, n (%)	
High (>100,000CAD)	19 (35.2)
Middle (<100,000CAD)	20 (37.0)
Low (social assistance/income support)	3 (5.6)
Unknown/prefer not to say	12 (22.2)

Abbreviations: FIX, factor IX; FVIII, factor VIII; HTC, hemophilia treatment center.

the diagnosis, feelings of isolation, and concerns around their child's physical safety and bleeding. Another possible explanation is that over time, as a family becomes more familiar and comfortable with the management of their child(ren)'s hemophilia, the disease-specific issues become less of a concern and align with more generic concerns of caring for a child with a chronic disease.

As new treatments continue to be tested in clinical trials, patient- and family-reported outcomes will become increasingly important to justify the new, often more expensive, treatments. The H-FIT fills a gap in existing measures, by allowing clinicians and
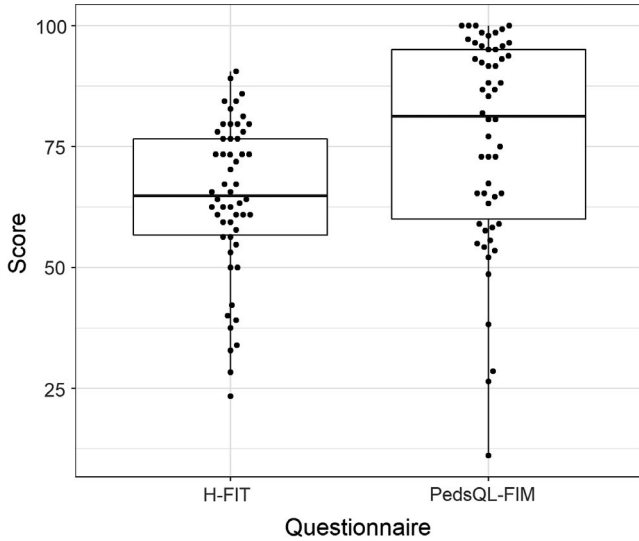
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research & practice
in thrombosis & haemostasis

FIGURE 1 Distribution of Hemophilia Family Impact Tool (H-FIT) and PedsQL Family Impact Module (PedsQL-FIM) scores. The thicker horizontal lines indicate medians; 25th to 75th percentiles are included in the boxes, while the whiskers encompass all values within the 2.5th to 97.5th percentiles. Each point represents an individual score. The PedsQL-FIM suffers from a marked ceiling effect with 39% of respondents achieving a score of >90, while the H-FIT is more normally distributed
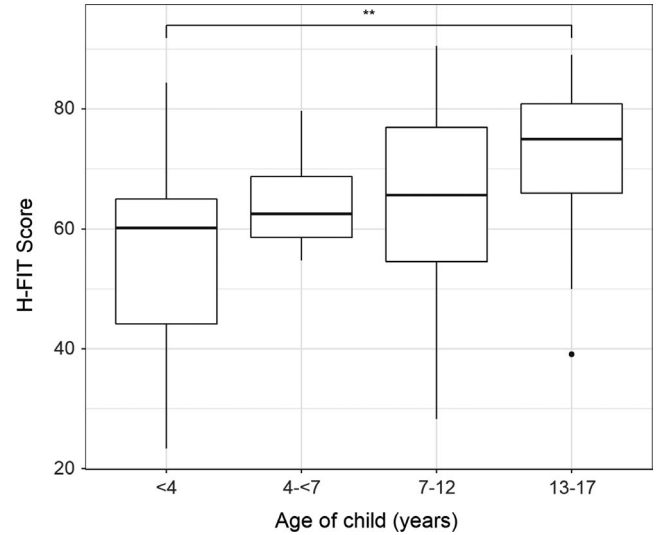

FIGURE 3 Distribution of Hemophilia Family Impact Tool (H-FIT) scores by age of the child. Medians are indicated by the thicker horizontal lines; 25th to 75th percentiles are included in the boxes while the whiskers encompass all values within the 2.5th to 97.5th percentiles; outliers beyond the 97.5th percentile are shown as dots. Group differences denoted with ** are significant at the 0.01 level
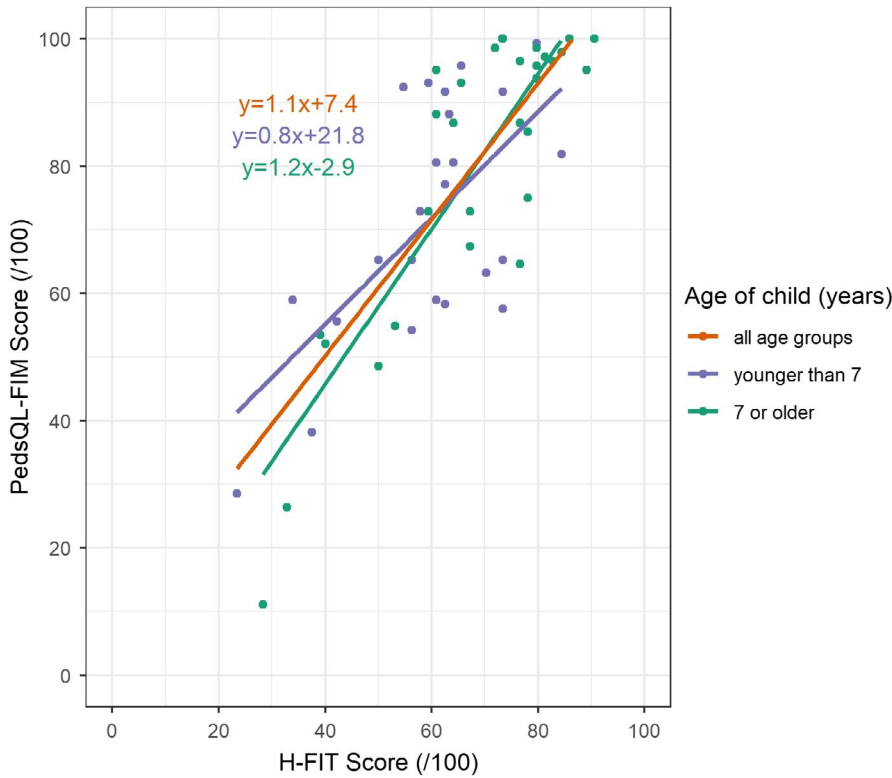
FIGURE 2 Relationship between scores from the Pediatric Quality of Life Family Impact Module (PedsQL-FIM) and the Hemophilia Family Impact Tool (H-FIT)

researchers to measure the impact of hemophilia for the entire pediatric age span, where traditional HRQoL measures can only reliably collect self-reported data from children aged ≥7 years, and as young as 4 years via a parent-proxy report.[12,18] We concede that the impact on the family is a different construct than HRQoL; however, it has been recognized that in the absence of a method to measure HRQoL in very young children, a disease-specific tool to measure the impact on parents caring for a child with a bleeding disorder may provide important information to fill this gap.[19]
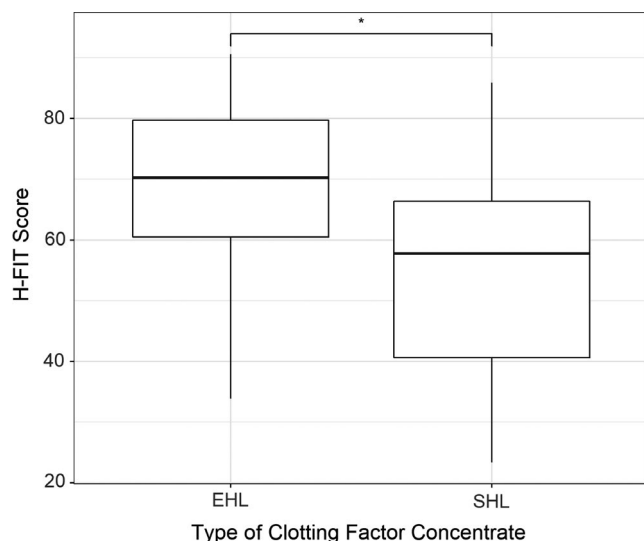
FIGURE 4 Distribution of Hemophilia Family Impact Tool (H-FIT) scores by type of clotting factor concentrate, standard half-life (SHL) or extended half-life (EHL). Medians are indicated by the thicker horizontal lines; 25th to 75th percentiles are included in the boxes, while the whiskers encompass all values within the 2.5th to 97.5th percentiles. Differences denoted with * are significant at the 0.05 level

The preliminary measurement properties show that the H-FIT is valid for the entire pediatric age span, with particular relevance for parents of boys who are aged <4 years. The H-FIT was able to differentiate between the parents of the youngest boys and the parents of the oldest boys, with the parents of the youngest boys reporting a lower score, and therefore a higher impact of hemophilia on their family, with scores increasing as the boys got older. Lower scores for parents of younger boys relative to older boys intuitively makes sense. The impact on the family may decrease with the increasing age of the child(ren) as they begin to assume more responsibility and have more autonomy for their care and management. Further, the correlation of the H-FIT to the PedsQL-FIM was lower for the parents of boys aged <7 years, which may be indicative of the impact of hemophilia-specific challenges around diagnosis, initiation of prophylaxis, strategies for inhibitor eradication (should the need arise, eg, immune tolerance induction therapy), challenging venous access, decisions around central venous access devices, and the adaptation to this new way of life with a child with a severe bleeding disorder, all of which may decrease as the boys get older. We speculate that parents of older boys may experience challenges more similar to other chronic conditions, resulting in higher scores on the H-FIT that are more strongly correlated to the PedsQL-FIM. However, more research is needed in this area to confirm these results.

The H-FIT was also able to differentiate between parents of boys who were using EHL CFCs compared to SHL CFCs, with the former reporting higher scores than the latter. This suggests that a large driver of the impact of a diagnosis of severe hemophilia on families may be the burden of administration and stress around the frequent intravenous administration of CFCs in addition to fears about serious bleeds and/or inhibitor development. Given this large difference in H-FIT scores based on use of SHL versus EHL FVIII/FIX CFCs, we speculate that an even greater difference in scores will be apparent with the use of hemostatic therapies necessitating less frequent and/or different routes of administration such as emicizumab, a therapy that is administered subcutaneously once every 1 to 4 weeks.[20] Although more research is required to test the responsiveness of the H-FIT and its ability to differentiate between factor- and non–factor-based hemostatic therapies, we speculate that using the H-FIT in clinical practice may provide outcome data that can be used by health care payers to justify the use of therapies that have a decreased burden of administration, which are often more expensive. Clinically, results from the H-FIT may also be beneficial in advocating for additional family support resources at the HTC level, such as social work and psychology services.

The results of our study must be interpreted given some possible limitations. The ability of the H-FIT to differentiate between therapies was based on a comparison of two independent groups (boys using EHL vs SHL CFCs). However, it is possible that there could be other differences between these groups that may have impacted their scores, such as personal capacity to cope with caring for a child with a chronic illness. Given that the groups were convenience based, with about twice as many parents/caregivers of boys using EHL than SHL, these interesting exploratory findings need to be confirmed in a future study with a larger sample of parents. Furthermore, since each family was tested only once, there is a chance that families with a child receiving EHL CFCs may have had similar scores even if their child was using SHL CFCs. While this would be less likely, it will be important to test the responsiveness of the H-FIT in a cohort of boys with hemophilia who undergo a switch in therapeutic regimen (e.g., a switch from a SHL factor concentrate to an EHL factor concentrate or from a factor-based hemostatic agent delivered intravenously to a non–factor-based hemostatic agent delivered subcutaneously). Currently, the H-FIT has only been tested and validated in a population of English-speaking Canadian families. While we expect that our results will be generalizable to other countries with access to SHL CFCs, EHL CFCs and nonfactor replacement therapies, additional work will be required to translate and culturally validate the tool for use outside of the Canadian context. This was successfully accomplished with the CHO-KLAT version 2.0,[21] and therefore will be feasible to achieve with the H-FIT.

In conclusion, in this study, a novel, disease-specific tool has been developed to measure the impact of hemophilia on families, the H-FIT. The H-FIT has been shown to be valid, and preliminary data suggest that it will be responsive to changes in therapy as well as the age of the child. Future work should seek to confirm the responsiveness of the H-FIT to changes in therapy, including nonfactor hemostatic therapies, and to adapt the H-FIT for use in different populations globally.

regarding licensure to allow use of the H-FIT and its scoring instructions please contact the Industry Partnership and Commercialization Office at The Hospital for Sick Children (555 University Avenue, Toronto, Ontario M5G 1X8, Canada; e-mail, ipc.requests@sickkids. ca; telephone, +1-416-813-6635).

RELATIONSHIP DISCLOSURE

SD, NLY, VSB, and VEP have a patent on the H-FIT, with royalties paid to The Hospital for Sick Children, NLY, and VEP. VSB reports that he is chair of the International Prophylaxis Study Group, a cooperative study group that is funded by education grants from Bayer Healthcare, Bioverativ/Sanofi, Novo Nordisk, Pfizer, Shire/Takeda, and Spark Therapeutics to The Hospital for Sick Children's "SickKids" Foundation. He has received fees for participation in advisory boards/education events supported by Amgen, Bayer, Novo Nordisk, Pfizer, Roche, and Shire/Takeda and for participation in data safety monitoring boards for Octapharma and Shire/Takeda. He has received investigator-initiated, industry-supported research grants from Novo Nordisk, Bioverativ/Sanofi, and Shire/Takeda. RJK reports receiving speaker and/or consultant fees from Agios Pharmaceuticals Inc., Amgen, Hoffman-LaRoche LTD, Shire Pharma Canada ULC, Novo Nordisk Canada Inc, Octapharma AG, Takeda, and Sanofi-Genzyme. MB has received fees for participation in advisory boards from Roche, Novo Nordisk, and Takeda, and has received grants from Octapharma AG. MC reports having received research support from Bayer, Bioverativ/Sanofi, CSL-Behring, Novo Nordisk, Octapharma, Pfizer, and Shire. He has also received honoraria for speaking/participating in advisory boards from Bayer, Bioverativ/Sanofi, Biotest, CSL Behring, Grifols, LFB, Novo Nordisk, Octapharma, Pfizer, Roche, and Shire. The remaining authors have no disclosures.

AUTHOR CONTRIBUTIONS

SD assisted with the design of the study, conducted data analysis, assisted with data interpretation, and wrote the first draft of the manuscript. NLY designed the study; assisted with data analysis, interpretation, and drafting the manuscript; and critically revised the manuscript. VSB designed the study, assisted with data analysis and interpretation, and critically revised the manuscript. RJK provided study participants, assisted with data analysis and interpretation, and critically revised the manuscript. AKC provided study participants and critically revised the manuscript. CW assisted with data interpretation and critically revised the manuscript. VB provided study participants and critically revised the manuscript. MC provided study participants and critically revised the manuscript. MB provided study participants and critically revised the manuscript. AAKB provided study participants and critically revised the manuscript. VEP designed the study, assisted with data analysis and interpretation, and wrote the first draft of the manuscript. All authors approved the final version submitted for consideration of publication.

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