

ORIGINAL ARTICLE

Challenges and knowledge gaps facing hemophilia carriers today: Perspectives from patients and health care providers

Megan Chaigneau RN, MSc¹  | Monique Botros BHSc Candidate¹ |Julie Grabell CCRP²  | Wilma Hopman MA, KGH^{3,4}  | Paula James MD, FRCPC²  

¹Queen's University, Kingston, Ontario, Canada

²Department of Medicine, Queen's University, Kingston, Ontario, Canada

³KGH Research Institute, Kingston, Ontario, Canada

⁴Department of Public Health Sciences, Queen's University, Kingston, Ontario, Canada

Correspondence

Paula James, Department of Medicine, Queen's University, Room 2015 Etherington Hall, 94 Stuart Street, Kingston, Ontario K7L 3N6, Canada.
Email: jamesp@queensu.ca

Funding information

Bayer HealthCare, Grant/Award Number: Projects of Excellence

Handling Editor: Dr Neil Zakai

Abstract

Background: Hemophilia carriers experience abnormal bleeding symptoms; however, a lack of awareness about this topic coupled with additional knowledge gaps and barriers leads to suboptimal care for this population.

Objective: The primary objective was to describe the current knowledge gaps and challenges from the perspective of both hemophilia carriers and their health care providers.

Methods: We carried out a mixed methods descriptive study with two population groups between September and December 2020. The hemophilia carrier perspective was obtained through both focus groups and questionnaires, whereas the health care providers perspective obtained via questionnaire sent to the Association of Hemophilia Care Directors of Canada and the Canadian Association of Nurses in Hemophilia Care. Focus groups were analyzed using descriptive thematic analysis and quantitative survey data was also analyzed.

Results: Eleven hemophilia carriers participated along with 19 health care providers (11 physicians, eight nurses). Hemophilia carrier focus group discussions identified four areas representing major challenges or knowledge gaps: (1) negative psychosocial impacts; (2) difficulty determining symptom significance; (3) need for self-advocacy; (4) testing concerns. Survey results from both groups were aligned with the most important topics for ongoing education identified as information on abnormal bleeding symptoms, where to seek treatment, and considerations for heavy menstrual bleeding/menstruation. The majority of both study groups believe obligate or potential carriers should have factor levels checked regardless of age if symptoms of abnormal bleeding occur or before an invasive procedure. However, hemophilia carriers were significantly more in favor of genetic testing under the age of consent than health care providers in all scenarios evaluated.

KEYWORDS

attitudes, delivery of health care, genetic carrier screening, health knowledge, hemophilia, practice, women's health

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Authors. *Research and Practice in Thrombosis and Haemostasis* published by Wiley Periodicals LLC on behalf of International Society on Thrombosis and Haemostasis (ISTH).

Essentials

- Hemophilia carriers experience abnormal bleeding symptoms but receive suboptimal care.
- Mixed methods descriptive study with both carriers and healthcare providers.
- Key knowledge gaps identified on abnormal bleeding symptoms and where to seek treatment.
- Hemophilia carriers favored earlier testing than healthcare providers.

1 | BACKGROUND

Hemophilia is a rare, X-linked bleeding disorder with a classical understanding that males are affected, whereas females are “silent carriers.” Over the past 2 decades, new research has refuted this historical assumption by demonstrating that hemophilia carriers can experience abnormal bleeding.^{1,2} Multiple studies have now clearly demonstrated that carriers of hemophilia experience bleeding symptoms such as menorrhagia, postpartum hemorrhage, excessive postsurgical bleeding, epistaxis, easy bruising, and oral cavity bleeding.^{1,3-7} There is also emerging evidence that hemophilia carriers experience joint issues, both hemarthrosis as well as subclinical joint bleeding.^{8,9} These bleeding symptoms are not exclusive to carriers with low factor levels because studies have shown that even carriers with normal factor levels have excessive bleeding.¹⁰ The variety of ways hemophilia carriership can affect women is reflected in updated nomenclature that classifies carriers according to factor levels and bleeding phenotypes as, women and girls with hemophilia, symptomatic hemophilia carriers, or asymptomatic hemophilia carriers.¹¹ The wide variability in factor levels and bleeding symptoms experienced by carriers creates challenges in determining appropriate assessment and management strategies.¹⁰ Significant knowledge gaps remain about the existence of abnormal bleeding in carriers and, consequently, these patients are often poorly managed and suffer from a reduced quality of life.^{6,12,13}

There is a growing evidence base that women who are carriers of hemophilia have a distinct set of unmet needs that require targeted interventions and initiatives.¹⁴⁻¹⁶ Although our knowledge of abnormal bleeding in carriers has greatly evolved, the remaining barriers result in suboptimal care, missed and untreated bleeding symptoms, and many unidentified hemophilia carriers. The true prevalence of hemophilia carriers is not known but is estimated that for every male with hemophilia there are three to five hemophilia carriers.^{17,18} Of these carriers, approximately one-third will manifest below normal factor levels, classifying them as a woman or girl with hemophilia.^{1,4,11} However, these numbers are not reflected in national and international hemophilia registries, indicating a need to better identify all women and girls affected by hemophilia.¹⁹ For carriers with the rare severe and moderate forms of hemophilia, the age at diagnosis has been found to be significantly delayed in females compared with their male counterparts, despite comparability in age at first manifestation of joint hemorrhage.²⁰

Hemophilia carriers have a distinct set of challenges and needs that are yet to be adequately addressed. To meet these unmet needs, it is crucial to develop a clear and complete understanding of the

current challenges and knowledge gaps facing hemophilia carriers today.

2 | OBJECTIVE

The primary objective of the study was to describe the major challenges and knowledge gaps facing hemophilia carriers from the perspective of both hemophilia carriers and health care providers, with a particular focus on experiences of abnormal bleeding symptoms and carrier testing.

3 | METHODS

Our mixed methods project was carried out from September to December 2020 and used a convergent parallel design where the quantitative and qualitative aspects were conducted simultaneously but analyzed separately.²¹ The qualitative aspect consisted of focus groups with hemophilia carriers, whereas the quantitative aspect included questionnaires completed by both hemophilia carriers and health care providers. The separate results were then merged for interpretation to deepen our understanding of the research question, what are the current challenges and knowledge gaps facing hemophilia carriers today.²¹

A convenience sampling method was used for both study groups. Health care provider participants were recruited via affiliation with the Association of Hemophilia Care Directors of Canada or the Canadian Association of Nurses in Hemophilia Care. Hemophilia carriers were recruited via affiliation with our Inherited Bleeding Disorders Clinic or via hemophilia carrier specific programs organized by Hemophilia Ontario.

Interested carrier participants who met eligibility criteria (self-identified hemophilia carrier, ≥ 18 years, English speaking) were given full study information by email and verbal consent was obtained over the phone. Recruitment goal was 10–15 participants as similar studies found thematic saturation with these numbers.^{16,22}

Organization of carriers into focus groups was based on participant availability with 5–6 carriers per focus group.²³ Each focus group was 1 hour in length and conducted electronically over Microsoft Teams. Focus groups followed a semistructured format with a set of guiding questions that allowed for participant introduced topics to be discussed (Table 1). Focus group transcripts were analyzed via a thematic analysis process to determine key themes.²⁴ Full transcripts were independently coded by two members of the

research team (M.C. and M.B.). Both coding sets were then collated into master coding set and organized into potential themes with supporting data gathered for each theme. Initial themes were rereviewed in relation to coding sets and transcripts before being shared with entire research team to allow for feedback. Ongoing analysis continued to refine specifics of each theme, determine theme names, and select data extract examples.²⁴

Separate questionnaires were completed by the participants of the hemophilia carrier focus groups as well as health care providers (Appendix S1, S2). After focus groups were complete, carrier participants were sent a secure link via email to anonymously complete a carrier-specific questionnaire. All 120 members of Association of Hemophilia Care Directors of Canada and Canadian Association of Nurses in Hemophilia Care were invited by email to complete the health care provider-specific questionnaire anonymously via secure link and given written study information. One reminder email was sent 4 weeks after initial contact.

Although different questionnaires were completed by each study population, multiple identical questions were included to allow for comparison between groups. Survey data were imported into IBM SPSS (version 26.0 for Windows, Armonk, New York, 2019) for statistical analysis. The responses of the three groups to items regarding timing of testing factor VIII (FVIII)/FIX levels for carriers, and

circumstances for genetic testing for those under the age of consent, were compared using the Fisher's Exact test. p values <0.05 were used as the cut-point for statistical significance, and no adjustments were made for multiple comparisons.

Ethics approval was granted by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board before study commencement.

4 | RESULTS

A total of 11 carriers consented to participate in the study. They self-reported their diagnostic information as four obligate carriers and seven nonobligate carriers confirmed with genetic or factor level testing. Carrier participants ranged from 21 to 69 years of age and were affiliated with five different hemophilia treatment centers (HTC) in three different provinces across Canada. All 11 hemophilia carriers also completed the hemophilia carrier questionnaire (Appendix S1). The health care provider questionnaire was completed by 19 health care providers, 11 physicians, and eight nurses.

4.1 | Focus group results

Focus group discussions yielded four areas identified as major challenges or knowledge gaps by hemophilia carrier participants. Supporting quotes for each theme are outlined in Table 2.

4.1.1 | Negative psychosocial impacts

Participants described many negative psychosocial impacts associated with abnormal bleeding symptoms, including increased anxiety, low self-esteem, and missed opportunities/experiences.

TABLE 1 Guiding questions for semistructured focus groups

1. When did you find out that you were a carrier of hemophilia? What type of testing did you receive?
2. Were you ever made aware that carriers of hemophilia can have abnormal bleeding symptoms? If yes, when?
3. Have you ever experienced abnormal bleeding symptoms?
4. Have you faced challenges or obstacles in receiving care related to your hemophilia carrier status?
5. Please describe your experiences with healthcare practitioners, both positive and negative, when seeking care related to your hemophilia carrier status?

TABLE 2 Focus group themes with supporting participant quotes

Theme	Participant Quote
1. Psychosocial impacts of abnormal bleeding	<ul style="list-style-type: none"> • "When I had my period throughout my teens, and experienced symptoms, there was nothing about being a symptomatic carrier, I sort of suffered in silence, and those things at school, anxiety, self-esteem were all certainly affected"
2. Difficulty determining symptom significance	<ul style="list-style-type: none"> • "Even now treatment guidelines for women with bleeding disorders are very vague. It's still very vague, should we be using tranexamic acid or desmopressin... moving forward, I'd like to see some consistency around when I should treat myself"
3. Need for self-advocacy	<ul style="list-style-type: none"> • My GP is old fashioned and didn't believe that I could be symptomatic. It took the [HTC] intervening with my GP to tell her, no, [patient name] can have bleeding as well. It really makes it easier on me because it's hard to advocate for yourself when you're going up against a doctor, because they have the credentials. So, I was blessed to have the support [from the HTC]"
4. Testing concerns	<ul style="list-style-type: none"> • "I'm an obligate carrier of hemophilia B, my parents were always very open and honest, and my factor levels were in the 30s, and that really dictated how I lived my life, the care I received. And I can't imagine my parents not knowing that. If an accident had happened, and you didn't know, it's actually preventative and proactive to know your medical situation... That idea, we're protecting girls by not getting them tested is more harmful"

Abbreviation: HTC, hemophilia treatment center.

These negative impacts were most commonly associated with untreated or unrecognized symptoms, with resolution of the negative impact if proper treatment was received and symptoms improved. Participants who were unaware of their carrier status as young women or were unaware of the link between hemophilia carriership and abnormal bleeding, described more of the negative psychosocial impacts than carriers who grew up aware of their carrier status and the possible implications. Carriers described high anxiety around social events for fear of sudden abnormal bleeding (mostly menstrual bleeding but also epistaxis), and frequently declined to participate in social events or sports teams. Participants who knew their carrier status and were affiliated with an HTC from a young age, described less negative psychosocial impacts and attributed it to prompt treatment for abnormal bleeding symptoms.

4.1.2 | Difficulty determining symptom significance

Participants were often unsure when a given symptom constituted abnormal bleeding and when it was appropriate to seek treatment. They felt that treatment recommendations were “vague” and “not consistent,” which led to confusion as to when they should self-treat with tranexamic acid for example, if they should be waiting for the symptom to resolve, or if they should be consulting with their health-care provider or HTC. They described a tendency to underestimate the severity of their bleeding, which led to a delay in seeking care and receiving treatment. This was partly attributed to the severity of bleeding experienced by the males with hemophilia in their life, which made the bleeding experienced by carriers feel “unimportant” in comparison, even if it was interfering with their daily lives. For some carriers the hesitancy to seek care was also attributed to previous negative experiences where their bleeding symptoms were dismissed by health care providers and so seeking care was seen as “pointless.” This was true even for carriers with below normal FVIII/FIX levels who have mild hemophilia. After a given symptom was treated or a management plan created, carriers expressed both relief and frustration, relief that the symptom was now being treated but frustration that they had not sought care earlier and instead had “suffered in silence.”

4.1.3 | Need for self-advocacy

Participants described multiple encounters with medical professionals who were not aware or did not believe that hemophilia carriers can have abnormal bleeding or abnormal factor levels. Having to advocate for themselves and “prove” the legitimacy of their experiences was frustrating for several of the carrier participants, particularly the women with mild hemophilia. It was described as constantly trying to convince healthcare providers that they are credible and not “lying” or “attention seeking.” One participant described being very grateful when her HTC intervened on her behalf with her primary care provider who “did not believe” that she could be symptomatic despite being a carrier with below normal factor levels who

has mild hemophilia. Participants described how challenging it feels to “go up against a doctor” when trying to advocate for themselves and were very grateful to have support from their HTC which they felt gave them legitimacy. This led to a feeling of “needing to have issues Monday to Friday from 8am to 4pm” so the option of support from the HTC was there.

4.1.4 | Testing concerns

Participants described “inconsistent recommendations” around hemophilia carrier testing (both factor level and genetic testing), instances of testing refusal from health care providers, and situations where delayed testing/diagnosis led to untreated or missed symptoms. Carriers who had learned their carrier status at a young age unanimously felt that growing up with this knowledge was beneficial to them, both because it led to more prompt symptom recognition/treatment and because they were able to gradually incorporate the knowledge and implications into their sense of self. Carriers voiced strong concerns around access to testing for female children. One carrier with mild hemophilia described feeling very supported in her pregnancy and felt that she herself was well taken care of, but after learning the child was female the HTC “immediately stopped caring.” The time between birth and testing of a female child was described as a “forgotten area of care” because there was no plan for any emergency situation that might happen during this time and minimal support is offered. Carriers felt that delayed testing did not “protect” young girls but was “harmful” and they strongly felt that every potential carrier should have the option of factor level testing at a minimum, within the first few years of life.

4.1.5 | Abnormal bleeding symptoms as common link

All four themes can be viewed as interrelated with challenges in one area linked to challenges in the other areas via abnormal bleeding symptoms (Figure 1). For example, participants described how difficulties determining symptom significance led to untreated bleeding symptoms, which then led to negative psychosocial impacts on participant lives such as missed school/work. Likewise, testing concerns were connected to the need for self-advocacy because carriers felt that in the face of real or potential abnormal bleeding symptoms knowing one's carrier status and bleeding risk is necessary to properly advocate for themselves or their child.

4.2 | Survey results

4.2.1 | Carrier results

The majority of hemophilia carrier respondents (9/11) do not feel there are enough resources available for hemophilia carriers and do not find it easy to access up to date information about hemophilia

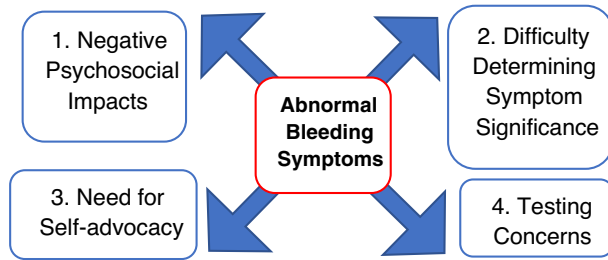


FIGURE 1 Focus group themes

TABLE 3 Carrier views on current resources ($n = 11$)

Question	Yes	No	Unsure
Do you feel there are enough resources out there for hemophilia carriers?	0	9	2
Do you find it easy to access up to date information about hemophilia carriers?	3	8	0

carriers (Table 3). Carriers use a variety of resources to educate themselves, most commonly resources or programming organized by the various hemophilia societies (Canadian Hemophilia Society, World Federation of Hemophilia, National Hemophilia Foundation) and discussions with their health care providers. When asked what was or has been missing from their care, responses echoed the same themes noted in focus groups and highlighted the importance of having care providers that were up to date on the medical issues facing hemophilia carriers, so that their symptoms were addressed and they did not have to advocate for themselves so strongly. They also noted a lack of awareness across medical disciplines that females can have mild hemophilia or be symptomatic carriers, that it wasn't just a disease of men, and asked for specific treatment guidelines.

4.2.2 | Health care provider results

No health care provider respondents disagreed with the statement that hemophilia carriers with normal FVIII/FIX levels can experience abnormal bleeding and that FVIII/FIX levels do not always correlate to severity of bleeding symptoms (Table 4). Health care providers were unanimously in agreement that women and girls with hemophilia and symptomatic hemophilia carriers should be followed at hemophilia treatment centers (19/19 health care provider respondents). When asked which treatments health care providers or their associated clinics prescribe/recommend to hemophilia carriers for treatment of abnormal bleeding symptoms, the majority of health care provider participants responded tranexamic acid (100%), desmopressin (100%), hormone therapy (79%), and factor replacement therapy (63%).

4.2.3 | Priorities for ongoing education

When asked to rank various topics in order of importance for ongoing hemophilia carrier education, responses from both groups were

mostly aligned with the combined top five most important topics being: (1) information on abnormal bleeding symptoms, (2) where to seek treatment, (3) heavy menstrual bleeding/considerations for menstruation, (4) considerations for pregnancy and childbirth, (5) treatment options (Table 5). The main difference in top five rankings between groups was that health care provider rankings also included hemophilia inheritance pattern, whereas carriers rankings also included psychosocial impacts of carrier status.

4.2.4 | Joint beliefs on testing

Identical survey questions were asked of both study groups regarding beliefs around testing that revealed similar results for factor levels testing (Table 6) but significant misalignment around genetic testing (Table 7). The majority of both groups believe factor levels should be checked regardless of age, if symptoms of abnormal bleeding occur or before an invasive procedure. Carriers were more in favor of factor level testing at birth or in the first 5 years of life than health care providers, although the difference between groups was not significant. For the remaining categories, responses of the two groups were very closely aligned with a sizeable minority of both carriers and health care providers in favor of testing in the event of a traumatic accident and prior to menarche. Health care provider responses were nearly identical for both obligate and potential hemophilia carriers in all categories.

When both study groups were asked about the circumstances under which genetic testing for a hemophilia carrier under the age of consent should be considered, hemophilia carriers were significantly more in favor of genetic testing than health care providers in all scenarios (Table 7). The majority of hemophilia carriers believed that a request for genetic testing should occur under the age of consent, when the patient has an upcoming surgical procedure (72.7%), if age of menarche is approaching (72.7%), and with no medical indication but request was made by family (72.7%). Hemophilia carriers were unanimously in support of genetic testing under the age of consent when the patient has symptoms of abnormal bleeding (100%) or symptoms of heavy menstrual bleeding (100%). The majority of health care providers were also in support of genetic testing for potential carriers under the age of consent if patient has symptoms of abnormal bleeding (84.2%) or symptoms of heavy menstrual bleeding (78.9%). However, only 21.1% of health care providers supported genetic testing of either potential or obligate carriers under the age of consent with no medical indication but a family request for testing, compared to 72.7% of carriers supporting testing in this scenario.

5 | DISCUSSION

The themes identified within our focus groups align with previous studies documenting lived experiences, barriers, and challenges of women with bleeding disorders.^{15,16} Women in these studies

Do you agree with this statement?	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Hemophilia carriers with normal FVIII/FIX levels (above 0.40IU/ml (can experience abnormal bleeding symptoms	0	0	3	8	8
In carriers of hemophilia, FVIII/FIX levels do not always correlate with severity of bleeding symptoms	0	0	1	10	8

TABLE 4 Health care provider views on abnormal bleeding in carriers ($n = 19$)

TABLE 5 Ranking of the most important topics for ongoing hemophilia carrier awareness campaigns

	Mean Combined Ranking ^a (0–5 scale)	Mean Health care provider Ranking (0–5 scale)	Mean Hemophilia Carrier Ranking (0–5 scale)
1. Information on abnormal bleeding symptoms	4.24	3.84	4.63
2. Where to seek treatment	4.13	3.53	4.72
3. Heavy menstrual bleeding/considerations for menstruation	4.12	3.79	4.45
4. Considerations for pregnancy and childbirth	4.05	3.74	4.36
5. Treatment options (i.e., antifibrinolytics/tranexamic acid)	3.85	3.42	4.27
6. Hemophilia inheritance pattern	3.79	3.58	4.00
7. Variations in bleeding tendencies for carriers	3.75	3.42	4.09
8. Psychosocial impacts of carrier status	3.74	3.21	4.27
9. General hemophilia information (i.e., types, incidence)	3.53	3.05	4.00
10. Testing considerations (i.e., factor assays and genetic testing)	3.35	3.16	3.54

^aMean combined ranking = (mean health care provider ranking + mean carrier ranking)/2.

described difficulties differentiating between normal and abnormal symptoms, highlighted the need for self advocacy, noted feelings of anxiety and depression, and were often unable to participate in school, work, or recreational activities.¹⁶ Other themes included lack of health care provider awareness, health care provider dismissal of symptoms and limited access to treatment plans, all of which are topics that were brought up in our focus groups by carriers.¹⁵ The negative psychosocial impacts described by our participants is corroborated by reports of hemophilia carriers experiencing inappropriate care and mistrust in the medical system.¹²

The common link of abnormal bleeding symptoms is a natural starting point to addressing all four challenges via increased education and awareness. Multiple interventions are needed including, (1) educational initiatives targeting health care providers outside of hemophilia treatment centres about abnormal bleeding in hemophilia carriers and women and girls with hemophilia, (2) educational initiatives targeting hemophilia carriers themselves to provide clear guidance on what constitutes abnormal bleeding and when to seek care, (3) concrete treatment recommendations for abnormal bleeding symptoms in carriers, and (4) consensus

on testing recommendations for young girls that accounts for the increased bleeding phenotype of hemophilia carriers. These recommendations are supported by similar publications about women and bleeding disorders, calling for educational initiatives at the patient, healthcare provider and community level, and specifically noting awareness of bleeding in hemophilia carriers as an area of particular need.^{15,16}

Our survey findings demonstrate a shift in healthcare provider views towards greater recognition of abnormal bleeding in carriers from previously reported studies. Paroskie et al. found in 2014 that only 51% of health care providers believed carriers with normal FVIII levels could have increased bleeding tendency, whereas our results showed that 84% of health care providers agreed or strongly agreed that carriers with normal FVIII/FIX levels can experience abnormal bleeding symptoms.² Similarly, our findings also demonstrate a potential shift in health provider views toward earlier carrier testing because our results show there are a number of situations where the majority of health care providers are in favor of testing under the age of consent in contrast to previous documentation where 72%

TABLE 6 In your opinion, when should a hemophilia carrier have their FVIII/FIX levels checked? (select all that apply)

	Hemophilia Carrier Responses (n = 11)	Health Care Provider Responses: Obligate Carriers (n = 19)	Health Care Provider Responses: Potential Carriers (n = 19)	Significance: (Fisher Exact Test, 2 -sided)
1. At birth	36.4%	15.8%	15.8%	$p = 0.4$
2. In the first 5 years of life	45.5%	26.3%	26.3%	$p = 0.5$
3. If symptoms of abnormal bleeding occur, regardless of age	81.8%	84.2%	84.2%	$p = 1.000$
4. Before any invasive procedure, regardless of age	63.6%	63.2%	57.9%	$p = 1.000$
5. In the event of traumatic accident, regardless of age	45.5%	47.4%	52.6%	$p = 1.000$
6. Before menarche, regardless of age	36.4%	42.1%	36.8%	$p = 1.000$
7. Only if age of consent has been reached	0%	0%	0%	$p = 1.000$

TABLE 7 In your opinion, under what circumstances should genetic testing for a hemophilia carrier under the age of consent be administered?

	Hemophilia Carrier Responses (n = 11)	Health Care Provider Responses: Obligate Carriers (n = 19)	Health Care Provider Responses: Potential Carriers (n = 19)	Significance: (Fisher Exact Test, 2 -sided)
1. At birth	45.5%	10.5%	0%	$p = <0.001$
2. Patient has upcoming surgical procedure	72.7%	26.3%	10.5%	$p = 0.03$
3. Patient has symptoms of abnormal bleeding	100%	47.4%	84.2%	$p = 0.01$
4. Age of menarche is approaching	72.7%	21.1%	21.1%	$p = 0.01$
5. Patient has symptoms of heavy menstrual bleeding	100%	52.6%	78.9%	$p = 0.05$
6. No medical indication but request has been made by family	72.7%	21.1%	21.1%	$p = 0.03$

Note: Assuming that the request has been made by the patient/family and previous factor level assay was normal.

of health care providers believed testing should only occur after 14 years of age.²

Our results clearly show a parental preference for earlier hemophilia carrier testing compared with health care providers, a finding that has been documented in a number of other studies.^{22,25,26} It is important to recognize the diversity of ways hemophilia affects women and acknowledge the impact an individuals' experience will have on their attitudes and beliefs, particularly those related to testing.^{22,25} A challenge in interpreting our results is that most of our participants reported experiencing a number of bleeding symptoms during childhood or early adolescence, thus placing them within the category of women with hemophilia or symptomatic hemophilia carriers. As such, their personal experiences likely impact their desire for earlier carrier testing, and it is possible that asymptomatic hemophilia carriers would have different beliefs or attitudes regarding the timing of carrier testing.

There is a limited body of evidence on parental views on carrier testing for X-linked disorders in general and even less on hemophilia specifically. What has been published, echoes the results from our focus groups and surveys, with parental motivation for earlier testing centering around trying to do what they feel is best for their child.^{27,28} Parents wanted testing as a means to advocate for their daughters to ensure they would receive appropriate care in the event of abnormal bleeding symptoms.²⁷ Within our focus group discussions, hemophilia carrier participants stated strongly that delaying testing does not "protect" young carriers but can actively "cause harm" because

of missed or ignored bleeding symptoms and delayed treatment. The concept of whether early carrier testing causes harm has been explored with results suggesting that childhood testing does not cause serious harm, whereas also not suggesting a benefit either.²⁸

Historical guidelines on hemophilia carrier testing have often been based on expert opinion and theoretical considerations, rather than empirical evidence examining health care provider and familial experiences or data regarding outcomes.²⁷ Renewed discussion and future research is warranted to establish clear recommendations for the optimal timing of hemophilia carrier testing, acknowledging evolving beliefs, parental views, and updated research on the increased bleeding phenotype of carriers.² An excellent starting point is the recently published European principles of care for women and girls with inherited bleeding disorders, which includes timely and accurate diagnosis for bleeding disorders in women and girls as a principle of care, and calls for a systematic approach to identification and testing of female hemophilia carriers.²⁹

6 | STRENGTHS AND LIMITATIONS

As with most survey-based studies, selection bias is a possible limitation as hemophilia carriers who experience abnormal bleeding symptoms may have been more likely to agree to participate as opposed to those who are asymptomatic. The response rate for the health

care provider survey was low (16%), reinforcing the possibility of selection bias to those health care providers with a previous interest in this topic. Although research team members have some training and experience with qualitative studies, another limitation is that no qualitative methodologist was involved to support interviews and thematic analysis. An additional weakness is the absence of demographic and bleeding related data on the carrier participants (e.g., ethnicity, bleeding score, factor levels), which would shed insight into whether the views expressed are unique to specific subset of carriers. Although the number of hemophilia carrier participants in focus groups was small (11 carriers in two groups), this sample size is in line with other similar qualitative studies that had 11–15 participants.^{16,22} Similarly, our study design of in-depth qualitative work via focus groups, supplemented by questionnaires for both carriers and health care providers, has been used in many similar studies.^{14,15,22,26} Another strength of our study is the wide age range of hemophilia carrier participants, 21–69 years of age, as women's experiences of being a hemophilia carrier has been documented as a process that evolves over time.³⁰ An important consideration to note is that our results relate to the situation in a high resource setting with a specific HTC organization model, publicly funded health care system and represents the Canadian point of view. Lower resource settings or countries with different health care models may have other unique carrier concerns not cited in our study (e.g., financial concerns).

7 | CONCLUSION

Our study adds to the growing body of literature regarding the experience of women with inherited bleeding disorders, highlighting specifically the challenges and knowledge gaps facing hemophilia carriers today. Future projects will focus on the testing concerns identified by carriers and work toward establishing treatment recommendations specific to hemophilia carriers and the abnormal bleeding symptoms they experience.

AUTHOR CONTRIBUTIONS

M. Chaigneau: Project concept and design, data collection, analysis and interpretation of data, critical writing. M. Botros: Data collection, analysis and interpretation of data. J. Grabell: Project design, research support. W. Hopman: Analysis and interpretation of data. P. James: Project concept and design, revision of intellectual content, final approval.

RELATIONSHIP DISCLOSURE

None of the authors have any conflict of interest to declare.

ORCID

Megan Chaigneau  <https://orcid.org/0000-0002-8001-4351>

Julie Grabell  <https://orcid.org/0000-0002-8739-7842>

Wilma Hopman  <https://orcid.org/0000-0002-3023-0080>

Paula James  <https://orcid.org/0000-0003-4649-9014>

TWITTER

Paula James  @james_paulad

REFERENCES

1. Plug I, Mauser-Bunschoten EP, Bröcker-Vriends AH, et al. Bleeding in carriers of hemophilia. *Blood*. 2006;108(1):52-56.
2. Paroskie A, Oso O, DeBaun MR, Sidonio RF Jr. Both hemophilia health care providers and hemophilia a carriers report that carriers have excessive bleeding. *J Pediatr Hematol Oncol*. 2014;36(4):e224-e230.
3. Graham JB, Miller CH, Reisner HM, Elston R, Olive J. The phenotypic range of hemophilia A carriers. *Am J Hum Genet*. 1976;28(5):482-488.
4. Paroskie A, Gailani D, DeBaun MR, Sidonio RF Jr. A cross-sectional study of bleeding phenotype in haemophilia A carriers. *Br J Haematol*. 2015;170(2):223-228.
5. Olsson A, Hellgren M, Berntorp E, Holmström M, Baghaei F. Bleeding phenotype in carriers of haemophilia A does not correlate with thrombin generation. *Haemophilia*. 2015;21(1):e111-e113.
6. Gilbert L, Paroskie A, Gailani D, Debaun MR, Sidonio R. Haemophilia A carriers experience reduced health-related quality of life. *Haemophilia*. 2015;21(6):761-765.
7. Gilbert L, Rollins L, Hilmes M, et al. Haemophilia A carriers demonstrate pathological and radiological evidence of structural joint changes. *Haemophilia*. 2014;20(6):e426-e429.
8. Sidonio RF, Mili FD, Li T, et al. Females with FVIII and FIX deficiency have reduced joint range of motion. *Am J Hematol*. 2014;89(8):831-836.
9. Osooli M, Donfield SM, Carlsson KS, et al. Joint comorbidities among Swedish carriers of haemophilia: a register-based cohort study over 22 years. *Haemophilia*. 2019;25(5):845-850.
10. James P, Mahlangu J, Bidlingmaier C, et al. Evaluation of the utility of the ISTH-BAT in haemophilia carriers: a multinational study. *Haemophilia*. 2016;22(6):912-918.
11. van Galen KP, d'Oiron R, James P, et al. A new hemophilia carrier nomenclature to define hemophilia in women and girls: communication from the SSC of the ISTH. *J Thromb Haemost*. 2021;19(8):1883-1887.
12. Renault N, Howell R, Robinson K, Greer W. Qualitative assessment of the emotional and behavioural responses of haemophilia A carriers to negative experiences in their medical care. *Haemophilia*. 2011;17(2):237-245.
13. Young J, Grabell J, Tuttle A, et al. Evaluation of the self-administered bleeding assessment tool (Self-BAT) in haemophilia carriers and correlations with quality of life. *Haemophilia*. 2017;23(6):e536-e538.
14. Whitaker S, Aiston H, Hung WT, Pink R, Mangles S. Haemophilia Carriers Experience Study (CARES): a mixed method exploration into the experience of women who are carriers of haemophilia. *Haemophilia*. 2021;27:848-853.
15. Arya S, Wilton P, Page D, et al. "They don't really take my bleeds seriously": barriers to care for women with inherited bleeding disorders. *J Thromb Haemost*. 2021;19:1506-1514.
16. Arya S, Wilton P, Page D, et al. "Everything was blood when it comes to me": understanding the lived experiences of women with inherited bleeding disorders. *J Thromb Haemost*. 2020;18(12):3211-3221.
17. Street A, Ljung R, Lavery S. Management of carriers and babies with haemophilia. *Haemophilia*. 2008;14:181-187.
18. CK K, JC L. How many carriers are there? *Haemophilia*. 2010;16(5):842.
19. Maynadie H, Gillet B, Rafowicz A, et al. Girls and women with haemophilia are insufficiently included in registries (abstract 109). Paper presented at: Haemophilia 2020.

20. Di Michele D, Gibb C, Lefkowitz J, Ni Q, Gerber L, Ganguly A. Severe and moderate haemophilia A and B in US females. *Haemophilia*. 2014;20(2):e136-e143.
21. Creswell JW, Clark VLP. *Designing and Conducting Mixed Methods Research*. Sage Publications; 2007.
22. Punt MC, Teela L, Fischer K, et al. A qualitative study on the experiences of haemophilia carriers before, during and after pregnancy. *Haemophilia*. 2021;27:e675-e682.
23. Kreuger RC, Casey MA. *Focus Groups: A Practical Guide for Applied Research*. Vol 1. 5th ed. Ringgold, Inc; 2014:67-68.
24. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101.
25. Thomas S, Herbert D, Street A, Barnes C, Boal J, Komesaroff P. Attitudes towards and beliefs about genetic testing in the haemophilia community: a qualitative study. *Haemophilia*. 2007;13(5):633-641.
26. Dunn N, Miller R, Griffioen A, Lee C. Carrier testing in haemophilia A and B: adult carriers' and their partners' experiences and their views on the testing of young females. *Haemophilia*. 2008;14(3):584-592.
27. Vears DF, Delany C, Massie J, Gillam L. Why do parents want to know their child's carrier status? A qualitative study. *J Genet Couns*. 2016;25(6):1257-1266.
28. Järvinen O, Lehesjoki A-E, Lindlöf M, Uutela A, Kääriäinen H. Carrier testing of children for two X-linked diseases: a retrospective study of comprehension of the test results and social and psychological significance of the testing. *Pediatrics*. 2000;106(6):1460-1465.
29. van Galen K, Lavin M, Skouw-Rasmussen N, et al. European principles of care for women and girls with inherited bleeding disorders. *Haemophilia*. 2021;27(5):837-847.
30. von der Lippe C, Frich JC, Harris A, Solbrække KN. "It was a lot Tougher than I Thought It would be". A qualitative study on the changing nature of being a hemophilia carrier. *J Genet Couns*. 2017;26(6):1324-1332.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Chaigneau M, Botros M, Grabell J, Hopman W, James P. Challenges and knowledge gaps facing hemophilia carriers today: Perspectives from patients and health care providers. *Res Pract Thromb Haemost*. 2022;6:e12783. doi: [10.1002/rth2.12783](https://doi.org/10.1002/rth2.12783)