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ORIGINAL ARTICLE

# The experiences and attitudes of hemophilia carriers around pregnancy: A qualitative systematic review

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## Abstract

**Background:** Hemophilia carriers (HCs) face specific psychosocial challenges related to pregnancy, caused by their inherited bleeding disorder. Optimal support from healthcare providers can only be realized by exploring medical and psychological healthcare requirements.

**Objective:** To review all published evidence on the experiences and attitudes of HCs regarding reproductive decision-making, prenatal diagnosis, pregnancy, childbirth, and puerperium to provide an accessible overview of this information for health care providers.

**Study selection:** Cochrane library, PubMed/MEDLINE, EMBASE, CINAHL, and PsycINFO were searched for original qualitative data. Two authors performed study selection, risk-of-bias assessment, data extraction, and data analysis through meta-summary. The extracted themes were discussed within the research team.

**Findings:** Fifteen studies with an overall moderate quality were included. The following findings were identified: (a) Quality of life of family members with hemophilia influences reproductive decision-making; (b) Genetic counselling is generally considered useful; (c) The development of a specialized carrier clinic is considered valuable; (d) HCs describe prenatal diagnosis as beneficial yet psychosocially challenging; and (e) noninvasive prenatal diagnosis and preimplantation genetic diagnosis are predominantly considered beneficial. These findings are limited by the overall moderate quality of included studies and the possibly partly outdated results in the current era of hemophilia treatment.

**Conclusions:** Available qualitative literature on HCs around pregnancy focuses on genetic counselling and prenatal diagnosis. Future studies are needed on the experiences and needs of HCs through pregnancy and puerperium as well as in light of emerging hemophilia diagnosis and treatment options.

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KEYWORDS

Hemophilia A, Hemophilia B, inherited blood coagulation disorders, qualitative research, reproduction, systematic review, von Willebrand Diseases

## 1 | INTRODUCTION

Inherited bleeding disorders include a diverse group of conditions resulting in impaired blood coagulation, with symptoms varying from mild bleeding after trauma or surgery to spontaneous joint or muscle bleeds and life-threatening complications.[1,2] Hemophilia A and B result in factor VIII and factor IX deficiencies, respectively.[3] Despite the X-linked recessive inheritance pattern, women who are carriers of the genetic defect (hereinafter referred to as hemophilia carriers [HCs]) may also experience significant bleeding symptoms because of low factor levels resulting from skewed X-chromosome inactivation.[4,5]

These congenital disorders have a significant medical and psychological impact on the different reproductive stages of HCs.[6] The possibility of transmitting the genetic defect to offspring complicates reproductive decision-making and introduces the option of preimplantation diagnosis and, during later stages, prenatal diagnosis.[7-9] Prenatal diagnostics are primarily used to guide obstetric management and to enable parents to be psychologically prepared for raising an affected child.[10-12] In families with severe hemophilia, prenatal diagnosis is sometimes performed with the aim of terminating a pregnancy in the case of an affected child.[13-15] Transmission of genetic disorders may lead to feelings of guilt and self-blame in parents.[9,16] Furthermore, hemostatic challenges are faced during childbirth as HCs have an increased risk of excessive bleeding after delivery and affected neonates are at risk of perinatal bleeding complications, including intracranial hemorrhage.[17-21] A multidisciplinary approach to preparing an individual management plan for delivery and the puerperium is required to diminish these risks.[22-24]

A recent European patient survey highlighted the significant barriers faced by women with congenital bleeding disorders regarding reproduction.[25] One of their main findings was the importance of improving education for healthcare providers. Therefore, to facilitate psychosocial support for HCs who wish to get pregnant, the aim of this systematic review is to provide an overview of all published evidence on the attitudes and experiences of HCs concerning reproductive decision-making, prenatal diagnosis, pregnancy, childbirth, and the puerperium.

**Essentials**

- Insight in Haemophilia carriers (HCs) healthcare requirements around pregnancy is needed to provide optimal care.
- We identified 15 papers in the literature on HC experiences and attitudes related to pregnancy.
- Extracted themes, partly outdated, mainly focus on genetic counselling and prenatal diagnosis.
- New studies are needed on current experiences and needs of HCs during all reproductive stages.

## 2 | METHODS

### 2.1 | Protocol

This qualitative systematic review was conducted according to the Cochrane methodology,[26] the PALETTE framework,[27] and PRISMA guidelines.[28]

### 2.2 | Review question

The review aims to answer the following question: "What are the experiences and attitudes of HCs with/toward reproductive decision-making, prenatal diagnosis, pregnancy, childbirth, and puerperium?"

### 2.3 | Eligibility criteria

Qualitative and mixed-method studies, including interviews, focus group discussions, case studies, and open-ended questionnaires, regarding the subjective experiences of HCs surrounding pregnancy were eligible. During the early stages of conducting this review, von Willebrand disease (VWD) was also included, but because of the availability of only one qualitative study of low quality on VWD and the differences in inheritability and pathophysiology, this congenital bleeding disorder was omitted.[29] Inclusion criteria consisted of: (a) women with inherited VWD or HCs; (b) a description of their experiences and needs; and (c) in the context of reproductive decision-making, prenatal diagnosis, pregnancy, childbirth, and puerperium. Only articles written in English or Dutch were eligible. Studies on women with acquired VWD or acquired hemophilia, studies with solely quantitative data, and studies on hemophilia complicated by HIV/AIDS or hepatitis were excluded. Additionally, conference abstracts and studies with insufficient or unclear information were excluded.

### 2.4 | Information sources and search

The search included papers published up to 23 October 2019 in the following electronic databases: the Cochrane library, PubMed/MEDLINE, EMBASE, CINAHL, and PsycINFO. Each search string

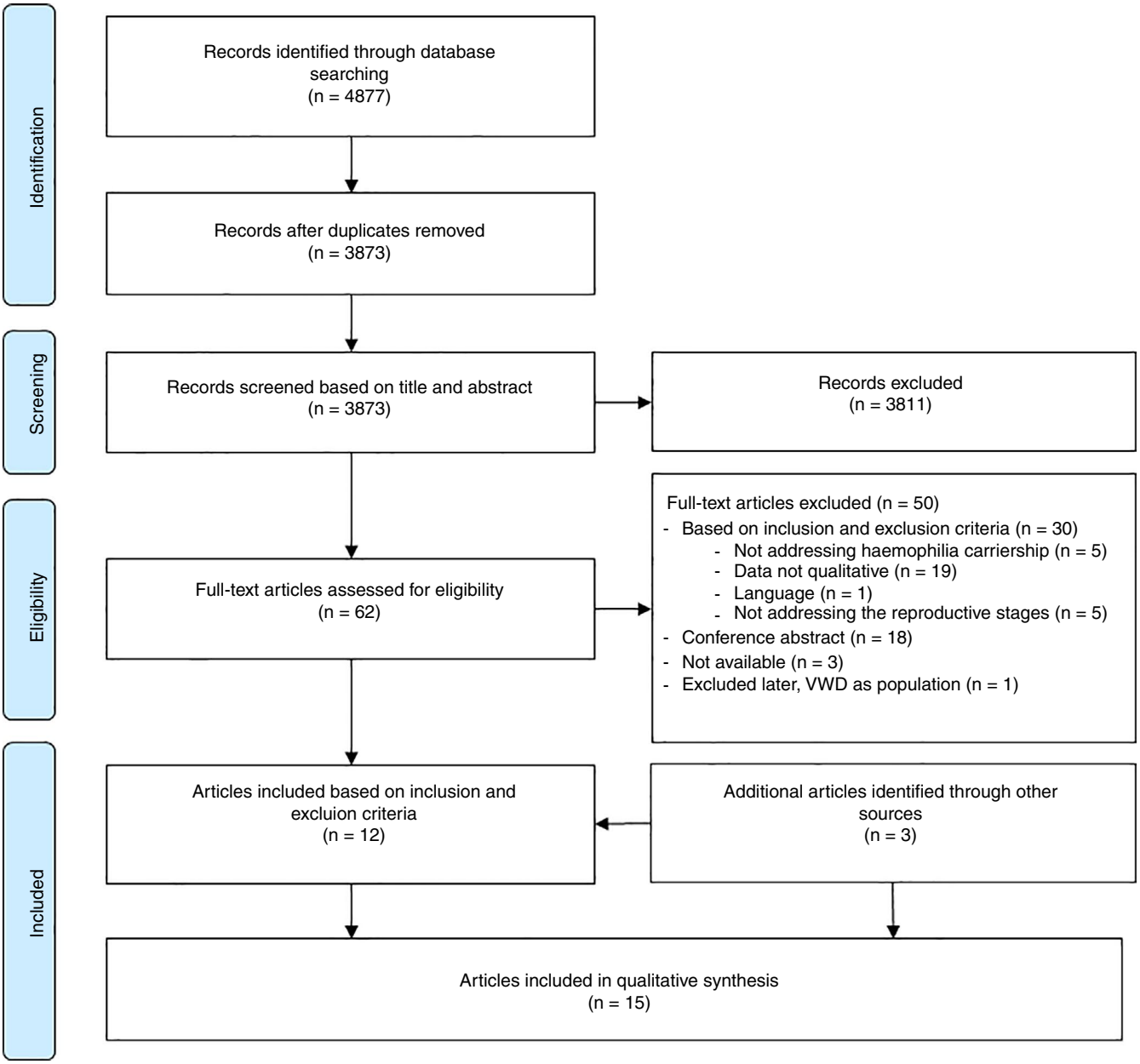


**FIGURE 1** Prisma flowchart for identifying eligible studies. Other sources include manual searching of the reference lists

used predefined search terms (title and abstract) and MeSH/Emtree terms related to qualitative study design, bleeding disorders, and reproductive phases (full search is provided in Appendix S1). No restrictions were applied. This search also included women with VWD.

## 2.5 | Selection and appraisal of studies

After combining the search results, duplicates were removed by Mendeley reference software and by hand. All potential articles were independently screened by two authors (T.A., M.P.), first based on title and abstract and later on full text. In cases of unresolved disagreements during the screening process, a third reviewer was consulted (K.G.). The reference lists of the included articles were searched to identify missed studies.

## 2.6 | Data collection and analysis

A standardized data extraction tool was developed with the following main components: study design, study aims, number of participants, HC characteristics, data collection methods, data analysis techniques, and reported themes. One author (T.A.) conducted the data extraction and a second author (M.P.) checked the complete data extraction for accuracy. In cases of disagreement, the senior authors (L.S., K.G.) were consulted to reach final agreement.

**TABLE 1** Overview of included articles

| Author (year) | Topic | Methods | Participants | Main results |
|---|---|---|---|---|
| Boardman (2019)[35] | Views toward genetic screening | Interviews<br>Grounded theory analysis | 3 HCs in the United Kingdom | HCs stated that hemophilia is not "life limiting," which resulted in negative attitudes toward genetic screening, particularly if associated with TOP. Another HC supported prenatal genetic screening to aid obstetrical care and the emotional preparation for having an affected child. |
| Evans (1979)[33] | Attitudes toward fetoscopy and amniocentesis | Interviews<br>Data analysis unclear | 29 HCs in the United Kingdom | HCs either decide not to have any more children, mostly because of anxiety about having an affected child, or to have more children regardless of the risk of having an affected child and are against TOP. |
| Gillham (2015)[15] | Factors influencing use of reproductive decision-making, genetic counselling, PND | Interviews<br>Thematic analysis | 17 HCs in South Africa | Genetic counselling was experienced as helpful to those HCs who had attended. Lack of awareness of bleeding and genetic risks. Wish for a dedicated carrier clinic. |
| Kadir (2000)[44] | Attitudes and experiences toward reproductive decision making, PND and TOP | Interviews<br>Data analysis unclear | 197 HCs in the United Kingdom | Reproductive decision-making was mainly affected by experiences of hemophilia within the family. Hemophilia was a reason for TOP, affected by religious beliefs. Factors affecting reproductive decision-making were counselling at the center and awareness of PND options. Women chose not to have children to avoid passing on hemophilia because of previous experiences with hemophilia or to the stress of PND. |
| Leuzinger-Bohleber & Teising (2012)[41] | Experiences and attitudes towards reproductive decision-making, PND, and TOP | Case study<br>Data analysis unclear | 1 HC in Germany | Reproductive decision-making was experienced as extremely burdensome: in particular, the decision regarding continuation of pregnancy or TOP following a positive finding during PND. |
| Lewis (2012)[32] | NIPD, benefits and disadvantages | Interviews<br>Thematic analysis | 19 HCs in the United Kingdom | NIPD was preferred because of technical aspects (avoiding miscarriage), timing (perceived control, early re-engagement, normalization of pregnancy, and peace of mind) and enhanced decision-making (stepwise approach). Minor disadvantages were debated including concerns about increased bonding at a time in pregnancy when miscarriage risk is high. |
| Lewis (2012)[34] | NIPD, experiences and preferences for service delivery | Interviews<br>Thematic analysis | 19 HCs in the United Kingdom | The reasons for using NIPD in HCs were to prepare for the possible outcome of an affected child and to provide the right care and medical attention during birth. The safety and timing of the test were seen as the most important aspects of NIPD. The importance of receiving the information and results from a specialist health care provider is highlighted. |
| Ljung (1987)[45] | Attitudes toward and experiences with genetic counselling, PND, and medical system | Interviews<br>Data analysis unclear | 29 HCs in Sweden and Denmark (same as Tedgard et al (1989)) | HCs wished to be educated on their options in reproductive decision-making and PND. Emotional support can be provided by other women with experience of PND as well as the family doctor. |
| Markova (1984)[38] | Views and experiences of genetic counselling, reproductive decision-making and PND | Interviews<br>Data analysis unclear | 29 HCs in Scotland and Canada | HCs showed interest in genetic counselling for information and advice. Prenatal testing and TOP were considered unacceptable in cases of hemophilia. |
| Morris (2015)[42] | Experiences with genetic counselling and reproductive decision-making | Focus groups<br>Thematic analysis | 1 HC in South Africa | Genetic counselling is difficult to understand. Genetic counselling was experienced as informative. |
| Smurl (1984)[39] | PND | Case study<br>Data analysis unclear | 1 HC in the United States of America | HC stated multiple reasons to not perform PND: experience with satisfactory quality of life within family, family willingly and self-sacrificially accepting responsibilities of hemophilia in the family and feeling fetal movements. |

(Continues)

**TABLE 1** (Continued)

| Author (year) | Topic | Methods | Participants | Main results |
|---|---|---|---|---|
| Tedgard (1989)[37] | Experience of PND (amniocentesis and fetal blood sampling) and pregnancy | Interviews<br>Data analysis unclear | 29 HCs in Sweden and Denmark (same as Ljung et al (1987)) | Prenatal diagnostics were experienced as distressing, resulting in serious mental and psychosomatic symptoms. Abortion/miscarriage after PND was experienced as psychologically difficult. Women with an unaffected fetus still experienced pregnancy as difficult. A need for psychological support was felt before and after PND. |
| Thomas (2007)[43] | Attitudes and experience with genetic testing, pregnancy, and the puerperium | Interviews<br>Thematic analysis | Unknown number of HCs in Australia | Women were unsure about who needs genetic testing. Some women wish for more accessible and user-friendly genetic testing. TOP was only considered by women if inhibitors were present within the family. Strong religious beliefs were described in this study. |
| VanderMeulen (2019)[36] | Experience with, understanding of, and attitudes toward postpartum bleeding | Interviews<br>Qualitative descriptive analysis | 1 HC in Canada | HC was desensitized to heavy vaginal bleeding because of her heavy menstrual bleeding. As a result, she would only consider postpartum bleeding abnormal if heavier than a heavy period. |
| von der Lippe (2017)[40] | Experience of reproductive decision-making and PND | Interviews<br>Inductive thematic analysis | 16 HCs in Norway | HCs experienced guilt and sorrow during reproductive decision-making. Women experienced more sadness than anticipated when expecting an affected son. |

*Note:* Participants include only those relevant to our research question.

Abbreviations: HCs, hemophilia carriers; NIPD, noninvasive prenatal diagnosis; PND, prenatal diagnosis; TOP, termination of pregnancy.

Data analysis was performed according to the meta-summary methods by Sandelowski.[30] Codes from the included articles were analyzed and organized into newly developed categories. These categories were analyzed and concept themes were constructed. The concept themes and original codes were compared and final themes were discussed within and assigned by the research team (T.A., M.P., K.G., L.S.). The narrative synthesis of the results will be presented for each reproductive phase in chronological order from becoming pregnant up to the puerperium.

### 2.7 | Assessment of methodological quality

Methodological quality was determined using risk-of-bias assessment and carried out independently by two authors (T.A., M.P.) using a self-developed scoring system based on the Critical Appraisal Skills Programme (CASP) Qualitative Checklist.[31] In this scoring system, each of 10 questions can be answered on a 2-point scale (0-2 points). The quality of studies was classified as *high* (16-20 points), *moderate* (12-15), or *low* (0-11).

## 3 | RESULTS

In total, 4877 articles were obtained after removing duplicates. Title and abstract screening resulted in 62 eligible articles, after which 15 articles were included in this review (Figure 1, Table 1).[15,32-45] Themes identified were divided according to each reproductive phase (Table 2). Most studies addressed HCs' experiences with reproductive decision-making and prenatal diagnosis. Five studies were published wherein data on experiences of pregnancy, childbirth, and puerperium were also described.[15,36,37,40,43]

### 3.1 | Critical appraisal

Results of the appraisal of methodological quality are shown in Table 3. Of the included studies, eight were classified as *high*, three as *moderate*, and four as *low*. Overall, methodological components were scarcely described (no report on researcher–participant relation in 11 articles; data analysis insufficiently described in seven articles). On the contrary, project aims and justification of the choice of qualitative methods were provided in 14 and 13 articles, respectively.

### 3.2 | Narrative synthesis of results

#### 3.2.1 | Becoming pregnant

The decision to become pregnant or not to have children was strongly influenced by women's experiences with hemophilia in their families.[15,39,40,44] Women whose family members with hemophilia experienced a satisfactory quality of life more readily accepted

**TABLE 2** Identified attitudes and experiences of hemophilia carriers surrounding pregnancy

| | | Attitudes | Experiences |
|---|---|---|---|
| Reproductive decision-making | Becoming pregnant | Experience within the family influences decision-making[15,35,38,41,43,44]<br>Wish for informed reproductive decisions together with specialized health care providers[15,38,43]<br>Importance of hemophilia disclosure within the family[15] | Knowing about the possibility of having an affected child is difficult[40] |
| | Genetic counselling | Meaning and purpose difficult to understand beforehand[15,38]<br>Unanimous interest in genetic counselling[15]<br>Personalization of counselling (eg, tailored information, peer support)[38,45] | Useful and informative[15,38,43,44]<br>Increased awareness of potential risks leads to concerns and can be overwhelming[38,40, 43] |
| | Prenatal diagnosis (PND)<br>a) In general | Quality of life of affected family members influences HCs' decisions on PND[35,43]<br>Experiences of PND of family members influences the choice of PND[15,39,40]<br>Preferred to take place early in pregnancy[32,39]<br>Felt as beneficial for obstetrical care and emotional preparation for having an affected child[34,35,43] | HCs who had experienced PND before, would choose it again in subsequent pregnancies[37]<br>Negative diagnosis evoked happiness and relief[32,37,41]<br>Positive diagnosis evoked sadness, disappointment, and concern about subsequent decisions[37,41,43] |
| | b) NIPD | NIPD was valued as easy and safe, yet the impact of the result is acknowledged[32,34] | Early timing was appreciated[32,34] |
| | c) Invasive testing | Confidence in reliability of the result[37] | Visualization of the fetus, risk of miscarriage, and waiting period between testing and hearing the results were distressing[32] |
| | d) PGD | PGD was received positively, except by HCs with fundamental objections (eg, religious/ethical beliefs)[43] | Unknown |
| | Termination of pregnancy (TOP) | Experiences in the family with hemophilia influence decision-making[15,41]<br>Generally, HCs do not consider hemophilia as severe enough for TOP[15,43] | Strong emotional reactions, including guilt and powerlessness[37,41] |
| Pregnancy and delivery | Pregnancy | Importance of professional and emotional support[37] | Worry and uncertainty[40] |
| | Childbirth | Uncertainty of maternal bleeding risks during childbirth[15]<br>Fear of doctors not providing the correct treatment during childbirth[40] | Unknown |
| | Puerperium | Desensitization to postpartum vaginal blood loss from heavy menstrual bleeding[36] | Diagnosis of an affected child evoked grief and guilt[43] |

Abbreviations: HCs, hemophilia carriers; NIPD, noninvasive prenatal diagnosis; PGD, preimplantation genetic diagnosis; PND, prenatal diagnostics; TOP, termination of pregnancy; unknown, no data available on this topic in the included studies.

hemophilia as being part of their lives and were more likely to wish to have children of their own.[15,35,39,40]

> … this is not a life limiting condition, in either sense of the word, and you know, my dad, although his health has suffered has, you know, he's rally driving, he's done sea sailing he's, you know, this isn't something that makes you stop living your life, it will be a part of our boy ….
>
> Hemophilia carrier from the United Kingdom[35]

On the contrary, women who had seen a significant impact of hemophilia on the quality of life of family members were less likely to want to have children themselves, more concerned about passing on hemophilia, and more worried about the consequences of having an affected child.[43,44] Some women decided not to become pregnant as they did not want to go through the stress of genetic testing.[33,44] Overall, women wished to be able to make informed reproductive decisions.[43]

> I am fine with being a carrier, but I don't plan to have children with haemophilia. I sound harsh but it is the severity not the actual condition that worries me.
>
> Australian potential hemophilia carrier[43]

Disclosure by the family of the potential to be an HC before pregnancy was valued.[15,43] Other HCs expressed that they did not feel

**TABLE 3** Critical appraisal of included studies

| Author (year) | Was there a clear statement of the aims of the research? | Is a qualitative methodology appropriate? | Was the research design appropriate to address the aims of the research? | Was the recruitment strategy appropriate to the aims of the research? | Was the data collected in a way that addressed the research issue? | Has the relationship between researcher and participants been adequately considered? | Have ethical issues been taken into consideration? | Was the data analysis sufficiently rigorous? | Is there a clear statement of findings? | How valuable is the research? | Score | Quality |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Boardman (2019)[35] | Y | Y | U | Y | Y | Y | Y | Y | Y | High | 19 | High |
| Evans (1979)[33] | Y | Y | N | N | N | N | N | N | Y | Moderate | 7 | Low |
| Gillham (2015)[15] | Y | Y | U | Y | Y | N | Y | U | Y | High | 16 | High |
| Kadir (2000)[44] | Y | Y | N | N | Y | N | U | N | Y | Low | 9 | Low |
| Leuzinger-Bohleber & Teising (2012)[41] | Y | N | N | N | N | N | U | N | U | Low | 4 | Low |
| Lewis (2012)[32] | Y | Y | Y | Y | Y | N | Y | U | Y | High | 17 | High |
| Lewis (2012)[34] | Y | Y | Y | U | Y | N | Y | U | Y | High | 15 | High |
| Ljung (1987)[45] | Y | Y | U | Y | Y | U | N | N | Y | Moderate | 13 | Moderate |
| Markova (1984)[38] | Y | Y | U | Y | Y | N | Y | N | U | Moderate | 13 | Moderate |
| Morris (2015)[42] | Y | Y | Y | Y | Y | Y | Y | Y | Y | High | 20 | High |
| Smurl (1984)[39] | U | U | N | N | N | N | N | N | U | Low | 2 | Low |
| Tedgard (1989)[37] | Y | Y | U | Y | Y | N | Y | N | Y | Moderate | 14 | Moderate |
| Thomas (2007)[43] | Y | Y | Y | Y | Y | N | Y | U | U | High | 16 | High |
| VanderMeulen (2019)[36] | Y | Y | U | Y | Y | U | U | Y | Y | High | 17 | High |
| von der Lippe (2017)[40] | Y | Y | U | Y | Y | N | U | Y | Y | High | 16 | High |

*Note:* Scoring system based on the Critical Appraisal Skills Programme (CASP) Qualitative Checklist.[31] Answers can be as follows: Y (= yes, 2 points), U (= uncertain, 1 point) and N (= no, 0 points). Classification (self-developed because of absence of CASP classification in the literature): high quality (16-20 points), moderate quality (12-15 points) and low quality (0-11 points).

isolated during reproductive decision-making because of their exposure to hemophilia in the family.[43] Knowledge of the possibility of having an affected child was experienced as difficult.[40]

> It is not being a carrier that's difficult, what's difficult is when you find yourself in a situation where it has a consequence.
>
> Norwegian hemophilia carrier[40]

### 3.2.2 | Genetic counselling

The meaning and purpose of genetic counselling was difficult for HCs to understand.[15,38] Once understood, there was a vast interest in receiving genetic counselling.[15,38] A specialized clinic for information on prenatal diagnosis, reproductive decisions, and risks would aid HCs during reproductive phases.[15,38] Preferences for the structure of the counselling differed, so the extent of information provision, neutral information vs advice, and the provision of peer support should be voluntarily chosen by each HC.[38,45]

> I would like my own clinic day (…) I still have so many questions about genetic risk, health risk and the future risks to my son.
>
> South African hemophilia carrier[15]

Women who received genetic counselling experienced it as useful.[15,38,43,44] These women were more aware about prenatal diagnosis, yet this knowledge also led to concerns and feelings of being overwhelmed.[38,40,43]

### 3.2.3 | Prenatal diagnosis in general

Choices regarding prenatal diagnosis are again based on experiences with the clinical severity of hemophilia within the family and prenatal diagnosis experiences of family members.[15,39-41] Those women who did not choose prenatal diagnosis had often seen satisfactory experiences with hemophilia and readily accepted hemophilia as part of their lives, or opted out of prenatal diagnosis due to religious beliefs.[15,35,40,44]

> We were offered amniocentesis to check if [the baby had] haemophilia so [I] can make my choice, but [we] said no. We would accept what were given.
>
> South African hemophilia carrier[15]

Women tended to be concerned about the consequences of prenatal diagnosis, especially the potential risks of the procedure and the choices to be made when results became known.[32,35,41,43] Prenatal diagnosis was believed to be beneficial for obstetrical care and emotional preparation for having an affected child.[34,35,43] Women preferred testing to take place early in pregnancy, when no fetal movements were yet felt and pregnancy was not visible. HCs appreciated prenatal diagnosis as it facilitated subsequent decision-making.[32,39,41]

Women who had experience with prenatal diagnosis would opt for it again during subsequent pregnancies.[37] Confirmation of expecting a healthy child was received with happiness and relief.[32,37,41] The diagnosis of an affected child resulted in sadness, disappointment, and a burden of subsequent decisions.[37,40,41,43]

> Is it morally right to get a child with a serious disease, now that we could avoid it?
>
> Norwegian hemophilia carrier[40]

### 3.2.4 | Noninvasive prenatal diagnosis

Women were positive about noninvasive prenatal diagnosis (NIPD) for fetal sex determination because of the ease of the procedure (both practical and psychological) and its safety in comparison to invasive testing.[32,34] They valued the possibility of a stepwise approach to decision-making.

Early timing was important, allowing for practical and psychological preparation, providing peace of mind, allowing re-engagement with their pregnancy, and control during early stages of pregnancy.[32] For those with a female fetus, early normalization of pregnancy was achieved. However, those with a male fetus experienced anxiety early on and disengagement with the pregnancy, and postponed announcement of their pregnancy if invasive testing would be the next step.[32] Despite the low burden of the procedure, women still acknowledged the important consequences of this test.[32] Nevertheless, all HCs still rather wanted to know the sex of the fetus as soon as possible as it allowed for timely preparation.[32] As one HC described:

> It made you worry more, but then good worry because you had that knowledge, if you see what I mean.
>
> English hemophilia carrier[32]

### 3.2.5 | Invasive testing

Invasive testing (amniocentesis, chorionic villus sampling, and fetal blood sampling) was seen as an opportunity to make a decision on continuation or termination of pregnancy (TOP) based on the knowledge of having an affected child in addition to knowing the sex of

the fetus.[43] However, seeing the fetus during invasive testing was thought to be distressing[32]:

> I think that it's quite a difficult situation, actually being able to see what's going on while the actual test is being done.
>
> English hemophilia carrier[32]

Women experienced invasive testing as distressing because they were concerned about the risks for the fetus and in some cases their own risk.[37] The time spent waiting for the result was described as distressing and had a significant influence on their daily lives. Many HCs described feeling worried, experiencing sleeping problems, and having (psycho)somatic symptoms during this period.[37]

HCs whose pregnancy ended in miscarriage after prenatal testing reported strong emotional feelings and (psycho)somatic symptoms, despite it being unclear whether invasive testing was the cause of the miscarriage.[37] One HC felt guilty because a healthy child had to die because of her fear of having a hemophilic child, which made her feel powerless and furious.[41]

### 3.2.6 | Preimplantation genetic diagnosis

HCs were positive about the possibility of preimplantation genetic diagnosis (PGD), except for HCs who rejected PGD based on religious beliefs. Furthermore, HCs were mostly neutral toward embryo selection, but were against the destruction of remaining embryos.[43]

### 3.2.7 | Termination of pregnancy

TOP was regarded as an individual decision by HCs.[43] Family experiences with hemophilia influenced this decision: those with positive experiences felt that hemophilia does not justify TOP, that hemophilia is not severe enough and that the disease is manageable[15,38,40,43]:

> Why do they talk about that [termination]? Is that an issue?
>
> Norwegian hemophilia carrier[40]

Some women preferred not to become pregnant again or to leave the outcome to chance rather than choose TOP in the case of an affected child.[15] Women with negative family experiences supported TOP.[41] Yet, these women still experienced TOP as difficult and felt guilty about their decision.[41] Women expressed the need for professional psychological support after TOP.[37] Religious beliefs played an important role in decisions around TOP.[43]

### 3.2.8 | Pregnancy

HCs reported pregnancy with a bleeding disorder as difficult and fearful.[37,40] Furthermore, HCs whose pregnancies with healthy fetuses continued after prenatal diagnosis described their pregnancies as difficult and felt they needed professional emotional support.[37] No further information was available on this topic.

### 3.2.9 | Childbirth and puerperium

No data were available on childbirth. Women were uncertain about the peripartum bleeding risks[15] and feared that doctors would not provide the right treatment.[40]

One HC reported feeling desensitized to vaginal blood loss because of her heavy menstrual bleeding. In case of abnormal postpartum bleeding, she stated being more likely to believe the blood loss to be normal in contrast to bleeding from surgical wounds.[36] Another HC reported feelings of grief and guilt during the puerperium when her child was diagnosed with hemophilia, knowing that her son had inherited this from his mother.[43]

## 4 | DISCUSSION

In the past decade, there has been increased interest in the psychosocial aspects of bleeding disorders. Most of the literature focuses on coping strategies and health-related quality of life of male hemophilia patients or experiences of caregivers for children with hemophilia,[46,47] but interest in the psychosocial situation of HCs regarding the different female reproductive stages is growing.[48-51] This systematic review provides the first overview of the available literature on HCs' experiences with and attitudes toward the phases surrounding pregnancy. The majority of the included qualitative studies focus on reproductive decision-making and prenatal diagnosis. Data on pregnancy, childbirth, and puerperium are limited.

A central theme is the effect of family experience on each reproductive phase. Women who had close experiences with severe hemophilia were more likely to choose options that prevented passing on hemophilia. In contrast, women whose family members with hemophilia experienced a satisfactory quality of life more readily accepted that the disease could be part of future generations. Women advocated for a specialized carrier clinic with expertise on HCs to enable informed reproductive decision-making. This is in line with the results from the patient survey from Noone et al in underlining the importance of educated health care providers to provide optimal psychosocial support.[25] Additional results in this review show that there is a significant (research and patient) interest in genetic counselling. Although there has been a focus on invasive testing in the past, new NIPDs are promising for lowering the extensive burden of invasive testing.[52] During several phases of pregnancy, women highlighted the emotional burden, which continued even after receiving the news that the expected child was unaffected.

When comparing the qualitative study on women with VWD to the findings in our systematic review, overlapping themes were discovered. Women with VWD wish for health care providers to be informed about their bleeding disorder and its consequences, and explicitly highlighted the value of specialized health care provision.[29] As in HCs, the bleeding disorder causes worry and uncertainty during pregnancy.[29,40] Although the underlying mechanism of inheritance and the pathophysiology of the disorder are different from hemophilia, similar psychosocial challenges seem to be faced by women with VWD, albeit based on a single low-quality study.

The conclusions of this review are based on an extensive search of multiple medical and psychological databases, with all review stages conducted by two authors. This review is limited by the overall quality of the included studies (being "moderate"). Late pregnancy, childbirth, and puerperium were rarely addressed. In past decades, there has been a significant improvement in the treatment of hemophilia,[14,53,54] a substantial innovation in genetic testing,[55] and an increase in the awareness of the consequences of inherited bleeding disorders in women.[24,46] Therefore, the findings described in the four articles published before 1990 may not be applicable to current attitudes and experiences in countries where medical care has progressed. Furthermore, cultural and socioeconomic differences between high-income countries (nine studies) and low- and middle-income countries (two studies) are important to acknowledge because the quality and availability of care differ correspondingly. Nevertheless, inclusion of all contexts (time and location) allowed us to reflect on a wider variety of settings.

## 5 | CONCLUSION

The emotional burden women experience during reproductive decision-making and the need for timely preconceptional counselling is evident. However, a marked need is also revealed for continued support during prenatal diagnosis and the period *after* prenatal diagnostics up to childbirth and the postpartum period in the case of an affected child. Scarce qualitative data have been published on HCs during pregnancy, childbirth, and puerperium and on women with VWD during all reproductive stages. Future qualitative studies are needed to gain insight into the experiences and attitudes of these women, especially during the later stages, to optimize the quality of reproductive health care for this population.

### CONFLICT OF INTEREST

The authors have no competing interests.

### AUTHOR CONTRIBUTIONS

M.C. Punt designed and performed the research, analyzed and interpreted the data, and wrote the manuscript. T.H. Aalders designed and performed the research, analyzed and interpreted the data, and wrote the manuscript. K.P.M. van Galen and L.H. Schrijvers designed the research, analyzed and interpreted the data and critically reviewed the manuscript. K.W.M. Bloemenkamp, M.H.E. Driessens and K. Fischer interpreted the data and critically reviewed the manuscript. All authors gave their consent to the final version of the manuscript.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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