

# A Cross-National Survey of People Living with Hemophilia: Impact on Daily Living and Patient Education in Central Europe

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**Background:** Information about the impact of hemophilia on daily living and information preferences for patients and their caregivers in Central Europe has been limited.

**Methods:** This cross-national survey was conducted between April 1 and October 15, 2020 and utilized a self-administered questionnaire to collect data (Typeform™) from people living with hemophilia in Bulgaria, Croatia, Czech Republic, Hungary, Slovakia and Slovenia. The questionnaire included 22 questions regarding difficulties in daily life and preferences for receiving hemophilia-related information. Respondents were stratified into two main groups, people with hemophilia (PwH) or their caregivers (CPwH). Results were analyzed using descriptive statistics.

**Results:** Of the 364 respondents, 232 were PwH (63.7%) and 132 were CPwH (36.3%). In total, 70.3% of hemophilia patients/caregivers responded that they are kept sufficiently informed about life with hemophilia, with 68.0%, 59.1% and 56.3% of respondents obtaining information from their physicians, patient associations and via digital media (internet and social media), respectively. However, 97.8% of respondents expressed an interest in additional information, particularly new hemophilia treatment options (62.1%), which in contrast to other topics was indicated most frequently by both patients and caregivers in all six countries. Most frequent difficulties in everyday life with hemophilia were identified as mobility problems (41.8%), unexpected bleeding (38.5%), pain (35.4%), and uncertainty with what they can or cannot do (25.0%). During the 2020 COVID-19 pandemic, 52.5% of respondents reported that they did not experience any major change in daily living with hemophilia.

**Conclusion:** Based on our Central European survey, hemophilia mostly affects peoples' lives by causing mobility difficulties, unexpected bleeding, pain and uncertainty in daily activities. Although the majority of respondents reported being educated about hemophilia, most PwH and CPwH respondents sought additional information, highlighting the need for continuous personalized patient education to cope with present challenges.

**Keywords:** Central Europe, cross-national survey, hemophilia, patient preference, information sources

## Plain Language Summary

### What Was Known Before

Differences exist between countries in Eastern Europe and Western Europe in terms of Hemophilia Treatment Centers (HTCs), healthcare systems and infrastructure, and socio-economic conditions. Data in the literature is lacking about how such differences may impact

the level of patient education and information preferences for individuals living with hemophilia in Central Europe.

## What Does This Study Add

This cross-national survey addresses the gap in knowledge by providing data on perceived disease interference in everyday life, self-reported level of disease education, and health information-seeking behavior from people with hemophilia and their caregivers living in six Central European countries.

## Interpretation

Survey results indicate that the most frequently reported concerns of patients and their caregivers in Central Europe relate to mobility/movement problems, unexpected bleeding, pain, and uncertainties about daily activities, followed by difficulties with travel, administering medication and other issues. Notably, the majority of respondents reported being well or very well informed about their condition. However, most respondents still requested additional information about living with hemophilia and the latest scientific developments, highlighting the need for ongoing and personalized patient education.

## Introduction

Improvement of treatment outcomes and quality of life for people with hemophilia (PwH) has been in focus for decades.<sup>1,2</sup> Yet, despite implementation since 2008 of the European Principles of Hemophilia Care (EPHC),<sup>1</sup> management practices, treatment access and patient education still vary in different European regions.<sup>3</sup> The 2020 European Hemophilia Consortium (EHC) survey revealed that Western Europe has benefitted more from improvements made due to EPHC implementation compared to Eastern Europe.<sup>3</sup> Access to different types of hemophilia care, including at-home treatments and prophylaxis, was also higher among Western European countries compared with Eastern European countries.<sup>3</sup> Notably, the European Hemophilia Network (EUHANET) reported that countries with the lowest number of Hemophilia Treatment Centers (HTCs) tend to be in Eastern Europe.<sup>4</sup> To ensure continuing improvements in hemophilia care across Central and Eastern Europe, it is important to recognize how variations in access to treatment and information about the condition can impact everyday life for PwH and their caregivers (CPwH).

The World Federation of Hemophilia (WFH) recently published updated guidance on hemophilia management.<sup>2</sup> One key recommendation is that health professionals are now encouraged to involve patients in treatment decisions, recognizing patients as experts with a unique knowledge of their own health and their preferences for treatments,

health states and outcomes.<sup>2</sup> However, for informed decision-making, it is important to consider the level of patient education about their disease state, including their perceived burden of disease and available strategies to cope with present difficulties. Hughes et al aimed to evaluate the everyday life of 51 PwH in five Western European countries, including their behavior and experiences related to their condition, their treatment, the challenges they face and ways to manage their condition.<sup>5</sup> The study highlighted that despite recent advances in hemophilia care, PwH still face multiple everyday challenges and uncertainties, which was something considered by PwH as a normal part of the condition through all life stages.<sup>5</sup> This data substantiates the need for a more personalized approach to patient education and care, to address misplaced notions of normality and uncertainty by allowing PwH to be better informed about their protection from unexpected bleeds, and how that should translate into patient health behavior.<sup>5</sup>

In a Central European community with diverse socioeconomic conditions and health care systems, data on level of health education and information preferences for PwH in Central European is scarce. Furthermore, with the introduction of modern monitoring technologies,<sup>6</sup> and novel extended half-life clotting factors and nonfactor replacement therapeutics,<sup>7,8</sup> it is becoming increasingly important that PwH and their caregivers are sufficiently informed about how their present and future challenges can be adequately addressed with relevant solutions and strategies, to make better and informed treatment and health behavior choices. Therefore, this study aimed to collect data on the level of PwH and CPwH health education and health information-seeking behavior from six Central European countries, to identify perceived disease interference in everyday life, patient information preferences and acquisition, as well as to better understand how the coronavirus disease 2019 (COVID-19) outbreak has impacted people with hemophilia and their caregivers across Central Europe.

## Methods

A self-administered questionnaire was developed by national experts in collaboration with six national hemophilia patient association representatives across six European Union member states (Croatia, Czech Republic, Slovenia, Slovakia, Bulgaria and Hungary). The survey was originally developed in English and translated into each local language. The questionnaire was uploaded to Typeform™ survey platform (Barcelona,

Spain). Additionally, a paper version of the questionnaire was prepared and partially used in Slovenia due to local community preference. This study anonymously collected information preferences and subjective opinions so did not fall under the scope of the Declaration of Helsinki in the represented countries, therefore no Institutional Review Board (IRB) or Ethics Committee (EC) approval was required. General Data Protection Regulations (GDPR) and other national and European Union legislative practices and principles were ensured. Participation in the survey was voluntary, and patients were informed about the survey and its objectives prior to their involvement.

Between April 1 and October 15, 2020, national hemophilia patient associations distributed a link to an electronic survey platform or posted paper versions to all current members. The questionnaire consisted of 22 questions regarding challenges in daily life, level of patient education, and preferences for receiving hemophilia-related information: questions 1–4 relate to the respondents, eg “how old is the hemophilia patient you take care of?”; questions 5–6 relate to COVID-19 impact on aspects of daily life, eg “what kind of help would you appreciate in this time of COVID-19 crisis?”; questions 7–8 relate to level of patient health education, eg “how well are you informed about living with hemophilia and its latest scientific developments?”; questions 9–10 relate to acquisition/sources of information, eg “which Social Media do you use frequently?”; questions 11–15 relate to how hemophilia affects everyday life, eg “what are the main difficulties caused by hemophilia you experience in day-to-day life?”; and questions 16–22 relate to contact with physician/HTC, eg “in the case of a typical visit to your hemophilia physician, how long is the average time spent with the physician?”. Completed anonymized paper versions of the questionnaire were entered into Typeform<sup>TM</sup> online survey jointly by two professionals experienced in healthcare quantitative research methods. Database lock and analysis was performed by Seesame s.r.o. (Bratislava, Slovakia). All results were analyzed using descriptive statistics, and no formal comparison of groups was planned and so was not performed.

## Results

### Study Respondents

A total of 364 respondents were stratified into two main groups, people living with hemophilia (PwH) or caregivers of people living with hemophilia (CPwH). The majority of PwH (81.9%) were adults aged >25 years whereas most CPwH were parents/legal guardians of children or young

PwH (80.3% CPwH responded on behalf of children and young people aged ≤25 years; 50.0% CPwH responded on behalf of children aged ≤12 years). Overall, 62.1% of all respondents (226/364) were aged >25 years. Of the respondents, 73.9%, 15.1% and 11.0% had severe, moderate and mild hemophilia, respectively, and 18.4% had current inhibitors. [Table 1](#) summarizes the characteristics of all respondents.

### Level of Patient Education and Health Information Preferences

Respondents were asked how well informed they felt they were about living with hemophilia, including how knowledgeable they were about the latest scientific developments. Overall, 70.3% of respondents reported that they were very well or well informed (ie sufficiently informed) about living with hemophilia and the latest scientific developments. Results were consistent across all countries, and between both PwH and CPwH ([Figure 1](#)).

In order to assess source preferences for obtaining health information, respondents were asked to report their sources for obtaining information about living with hemophilia and gaining knowledge about the latest scientific developments ([Figure 2](#)). Overall, the most common information sources were physicians (68.0%), patient associations (59.1%) and digital media (internet and social media; 56.3%). There was no difference in information preferences and acquisition between PwH and CPwH ([Figure 2](#)).

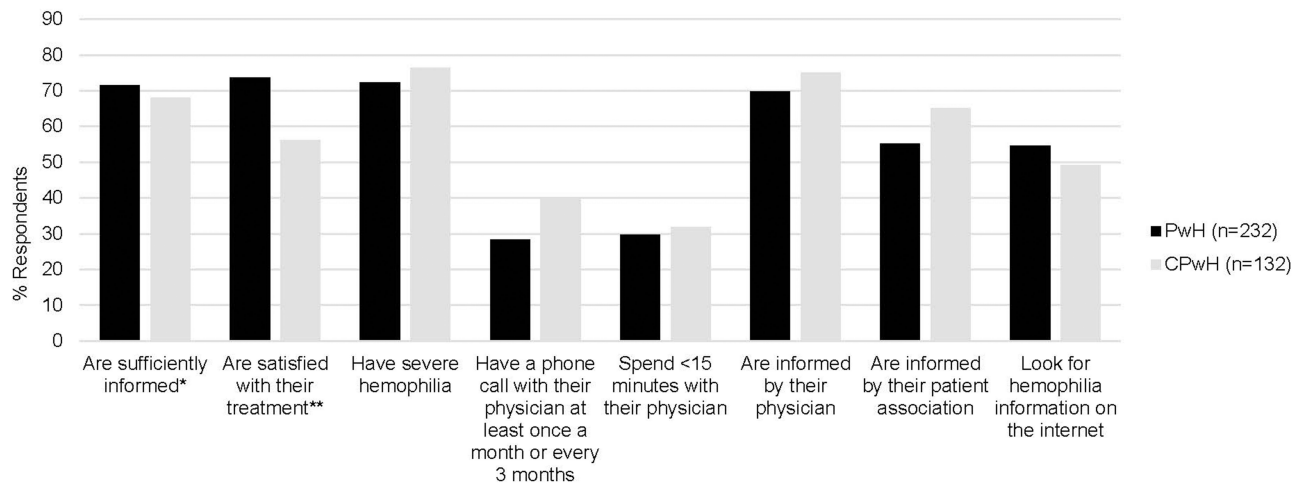
Respondents reported that they were sufficiently informed regardless of whether digital media was one of their information sources or not (73.0% vs 67.0%, respectively). The most frequented social media sites for information acquisition were reported by respondents as Facebook (66.5%), YouTube (49.2%), Facebook messenger (45.0%) and Instagram (19.2%). Use of digital media as a health information source was similar between respondents aged ≤25 years and >25 years (55.1% vs 57.1%, respectively), but approx. 2-fold higher in respondents from the Czech Republic than those from Bulgaria (73.6% vs 35.8%, respectively) (data not shown).

Regarding follow-up visits with physicians, 14.8%, 54.7% and 30.5% of respondents reported that consultations typically last >30 mins, 15 to 30 minutes and <15 mins, respectively. In order to ascertain whether the duration of physician visit impacts respondent health education level, the profile of respondents that spend <15 mins with their physician was determined ([Supplementary Figure](#)

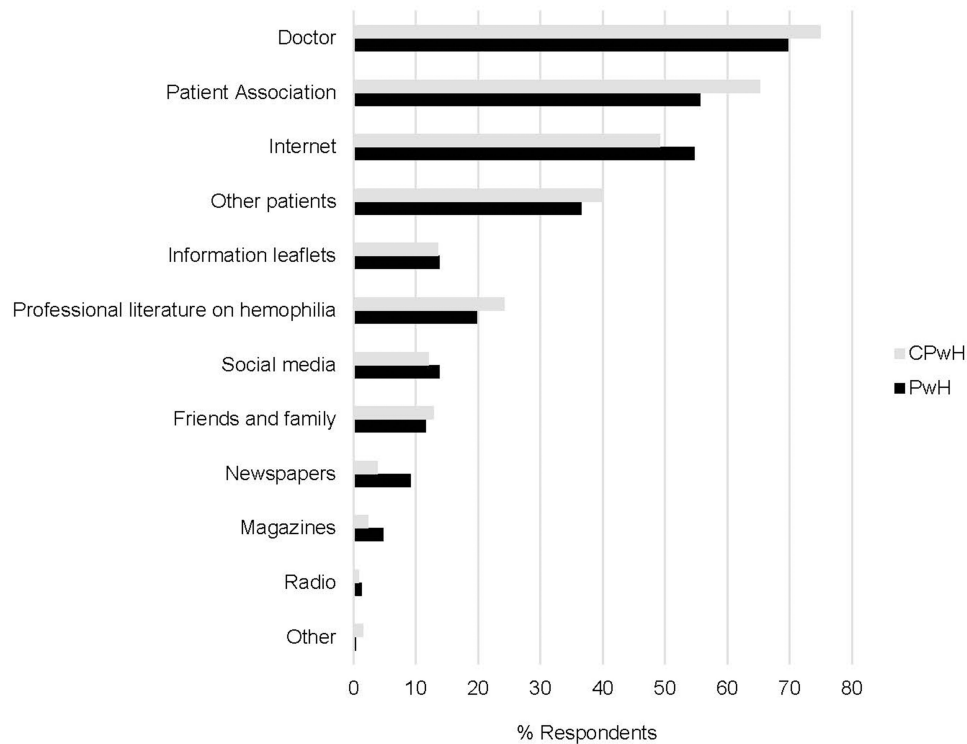
**Table 1** Respondent Characteristics

Country	Bulgaria n=53		Croatia n=33		Czech Republic n=87		Hungary n=50		Slovakia* n=84		Slovenia n=57		All N=364	
	PwH	CPwH	PwH	CPwH	PwH	CPwH	PwH	CPwH	PwH	CPwH	PwH	CPwH	PwH	CPwH
No. of respondents, n (%)	20 (37.7%)	33 (62.3%)	20 (60.6%)	13 (39.4%)	56 (64.4%)	31 (35.6%)	37 (74.0%)	13 (26.0%)	54 (64.3%)	30 (35.7%)	45 (78.9%)	12 (21.1%)	232 (63.7%)	132 (36.3%)
Age range, n (%):														
0–6 years	0 (0.0%)	8 (24.2%)	0 (0.0%)	2 (15.4%)	0 (0.0%)	17 (54.8%)	0 (0.0%)	4 (30.8%)	0 (0.0%)	5 (16.7%)	0 (0.0%)	2 (16.7%)	0 (0.0%)	38 (28.8%)
7–12 years	1 (5.0%)	7 (21.2%)	0 (0.0%)	7 (53.8%)	1 (1.8%)	3 (9.7%)	0 (0.0%)	2 (15.4%)	0 (0.0%)	7 (23.3%)	2 (4.4%)	2 (16.7%)	4 (21.7%)	28 (21.2)
13–25 years	12 (60.0%)	15 (45.5%)	3 (15.0%)	2 (15.4%)	7 (12.5%)	8 (25.8%)	2 (5.4%)	6 (46.2%)	1 (1.9%)	6 (20.0%)	3 (6.7%)	3 (25.0%)	28 (12.1%)	40 (30.3%)
26–49 years	5 (25.0%)	3 (9.1%)	11 (54.5%)	0 (0.0%)	21 (37.5%)	3 (9.7%)	14 (37.8%)	0 (0.0%)	36 (66.7%)	12 (40.0%)	15 (33.3%)	3 (25.0%)	102 (44.0%)	21 (15.9%)
> 50 years	2 (10.0%)	0 (0.0%)	6 (30.0%)	2 (15.4%)	27 (48.2%)	0 (0.0%)	21 (56.8%)	1 (7.7%)	17 (31.5%)	0 (0.0%)	25 (55.6%)	2 (16.7%)	98 (42.2%)	5 (3.8%)
Age group, n (%)														
≤25 years	43 (81.1%)		14 (42.4%)		36 (41.4%)		14 (28.0%)		19 (22.6%)		12 (21.1%)		138 (37.9%)	
>25 years	10 (18.9%)		19 (57.6%)		51 (58.6%)		36 (72.0%)		65 (77.4%)		45 (78.9%)		226 (62.1%)	
Current inhibitors, n (%)	1 (5.0%)	7 (21.2%)	4 (20.0%)	2 (15.4%)	11 (19.6%)	5 (16.1%)	5 (13.5%)	1 (7.7%)	12 (22.2%)	15 (48.3%)	2 (4.4%)	2 (16.7%)	35 (15.1%)	32 (24.3%)
Severity of hemophilia, n (%):														
Mild	3 (15.0%)	3 (9.1%)	2 (10.0%)	4 (30.8%)	7 (12.5%)	1 (3.0%)	10 (27.0%)	0 (0.0%)	6 (11.1%)	0 (0.0%)	6 (13.3%)	1 (8.3%)	34 (14.7%)	9 (6.8%)
Moderate	0 (0.0%)	10 (30.3%)	2 (10.0%)	2 (15.4%)	11 (19.6%)	3 (9.7%)	7 (18.9%)	1 (7.7%)	4 (7.4%)	6 (20.0%)	6 (13.3%)	0 (0.0%)	30 (12.9%)	22 (16.7%)
Severe	17 (85.0%)	20 (60.6%)	16 (80.0%)	7 (53.8%)	38 (67.9%)	27 (87.1%)	20 (54.1%)	12 (92.3%)	44 (81.5%)	24 (80.0%)	33 (73.3%)	11 (91.7%)	168 (72.4%)	101 (76.5%)

**Note:** \*Age groups for Slovakia were defined as 0–6, 7–12, 13–18, 19–49 and 50+ years.  
**Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.



**Figure 1** Health education level of respondents. \*Sufficiently informed = well or very well informed about living with hemophilia and the latest scientific developments; \*\*satisfied with treatment = in the last year, I have been satisfied with my treatment/the patient I take care of has been satisfied with their treatment. **Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.



**Figure 2** Health information sources. **Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.

S1). Despite spending <15 minutes with their physician, two-thirds of respondents (66.7%) reported that they remained sufficiently informed (Supplementary Figure S1). For all patients that were sufficiently informed, physician follow-up visits lasting <15 minutes were more common for people with hemophilia aged >25 years

compared with those aged <25 years (66.7% vs 40.6%, respectively) (data not shown). Notably, of respondents spending <15 mins with their physician during follow-up visits, 64.0% reported that their physician remained one of their main information sources (Supplementary Figure S1).

A total of 356/364 respondents (97.8%) reported being interested in additional information regarding different aspects of life with hemophilia. [Figure 3](#) shows the top 5 additional information most frequently identified by PwH and CPwH. New treatment options and technologies allowing easier administration were identified by 62.1% and 41.8% of respondents, respectively. In a separate multiple-choice question, respondents were able to indicate their satisfaction in terms of quality of life and present treatment in the past year, and whether they were informed about new treatment options during the past six months. Within this question, 68.1% of respondents reported being overall satisfied with their current treatment (data not shown), 45.9% of respondents reported being overall satisfied with their quality of life, and 42.0% of respondents reported that they were not informed about new treatment options during the past six months (see [Supplementary Tables S1](#) and [S2](#), respectively).

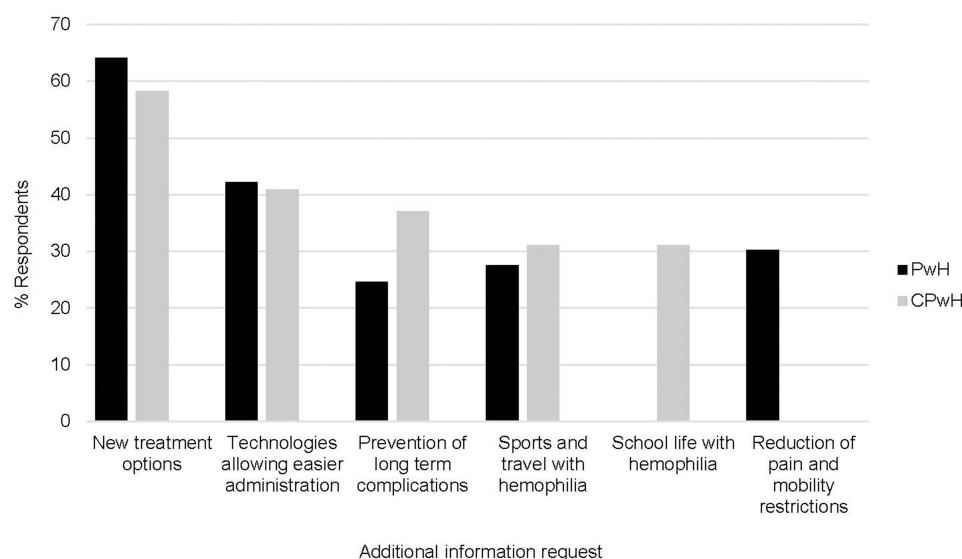
## Respondent Main Difficulties in Day-to-Day Life Caused by Hemophilia

Participants in the survey were given multiple-choice questions and asked to select/list any possible difficulties that were present at the time of the survey, as well as to indicate by how much various day-to-day aspects are impacted by hemophilia, using a 5-point Likert scale. The multiple-choice questions asked about how much hemophilia generally affects their life, as well as more specific areas of daily living. Respondents reported mobility problems (41.8%), sudden/unexpected bleeding (38.5%), pain (35.4%) and uncertainty about what

I can/cannot do (25.0%) as the most common day-to-day difficulties in life caused by hemophilia ([Figure 4](#)). However, the aforementioned difficulties were reported differently by PwH and CPwH: PwH more frequently reported motion/mobility problems (53.4%), pain (39.2%), sudden/unexpected bleeding (36.6%) and uncertainties in daily activities (22.0%), while CPwH more frequently referred to sudden/unexpected bleeding (41.7%), uncertainty about what I can and cannot do/uncertainty what the patient can and cannot do (30.3%), pain (28.8%) and travel (25.0%) ([Figure 4](#)).

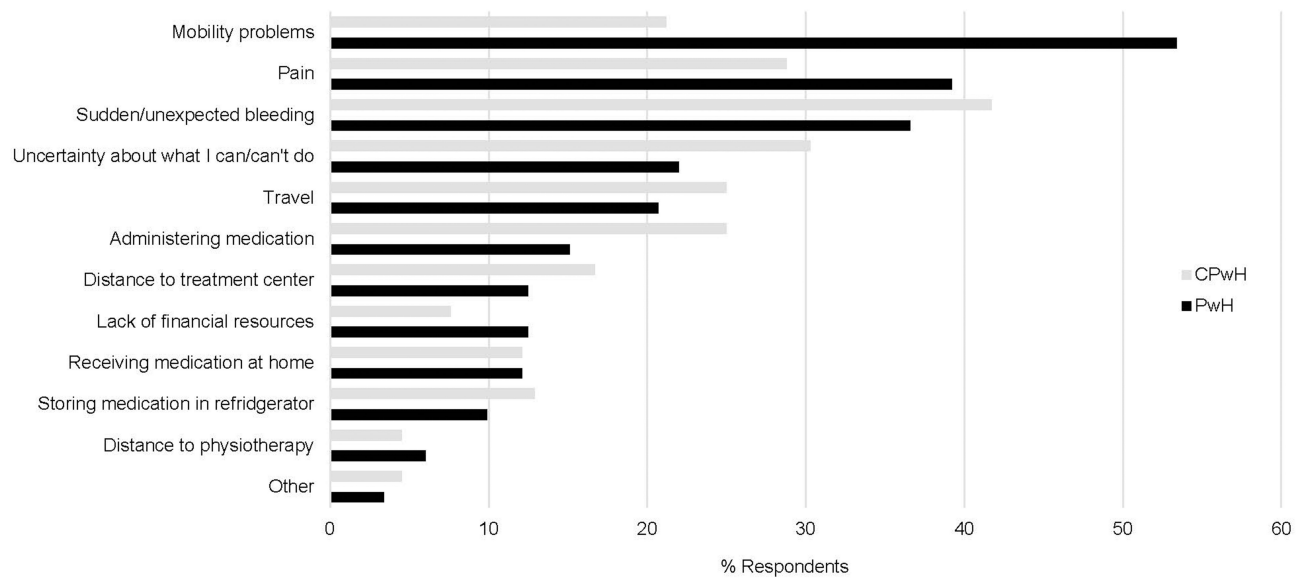
When asked specifically about the level of impact of hemophilia on education/work life, ability to find partner, family life, daily routines and happiness in general, moderate to severe impact was reported by 25–41% of the respondents, suggesting that more than half of respondents find ways to cope with the limitations regarding the above mentioned day-to-day aspects (see [Supplementary Tables S4-6](#) and [S8-9](#)). On the other hand, more than half of respondents reported moderate to severe impact on their mobility or choice of hobbies (see [Supplementary Tables S3](#) and [S7](#)), consistent with the frequent selection of mobility/motion problems, pain, unexpected/sudden bleeding and uncertainties of what I can/cannot do/uncertainties about what the patient can/cannot do, as shown in [Figure 4](#).

Interestingly, when responding to the general question about how much the disease interferes with everyday life, approximately twice more PwH and CPwH respondents with severe or moderate hemophilia tended to report a moderate to severe impact on average compared to



**Figure 3** Most common additional hemophilia information requested by respondents.

**Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.



**Figure 4** Main difficulties in day-to-day life caused by hemophilia. **Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.

mild hemophilia respondents (65.4% and 69.9% vs 30.2%, respectively, [Figure 5](#)).

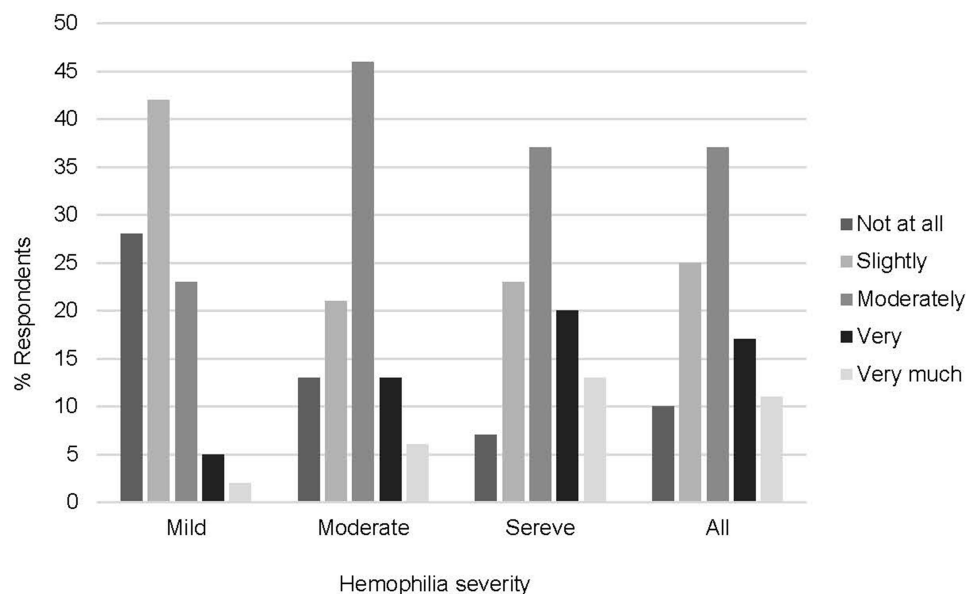
### Impact of COVID-19 on Living with Hemophilia

Approximately half of PwH and their caregivers (52.5%) reported no major change in living with hemophilia during the first wave of the COVID-19 pandemic (March/April 2020) ([Figure 6](#)). A small proportion of respondents (12.9%) reported experiencing anxiety and mental pressure living

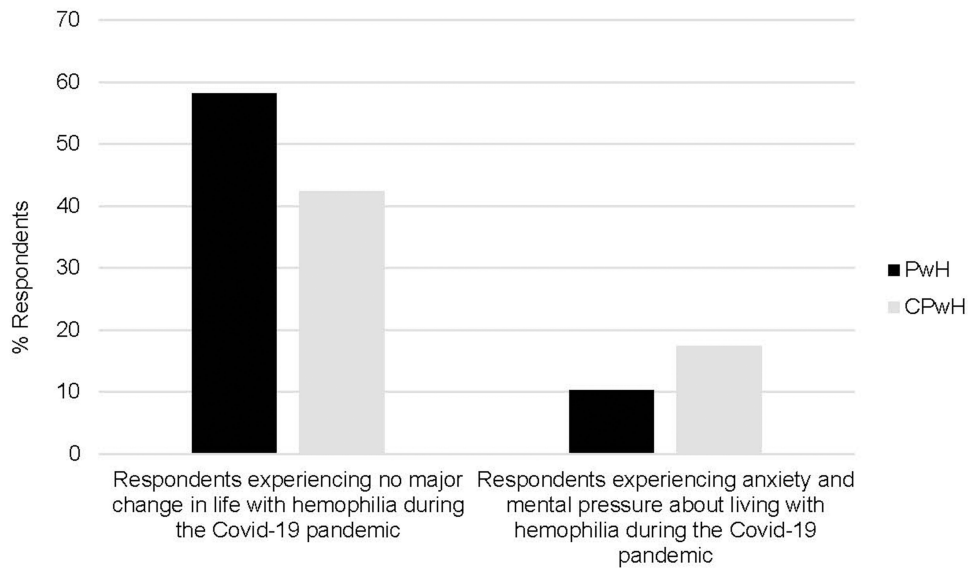
with hemophilia during the COVID-19 pandemic. [Figure 7](#) reveals that the most frequent help requested by respondents during the COVID-19 pandemic is consistent between PwH and CPwH. Overall, the impact for respondents of COVID-19, ie no big change vs big change, was not dependent on digital media activity (55.0% vs 45.0%, respectively).

### Discussion

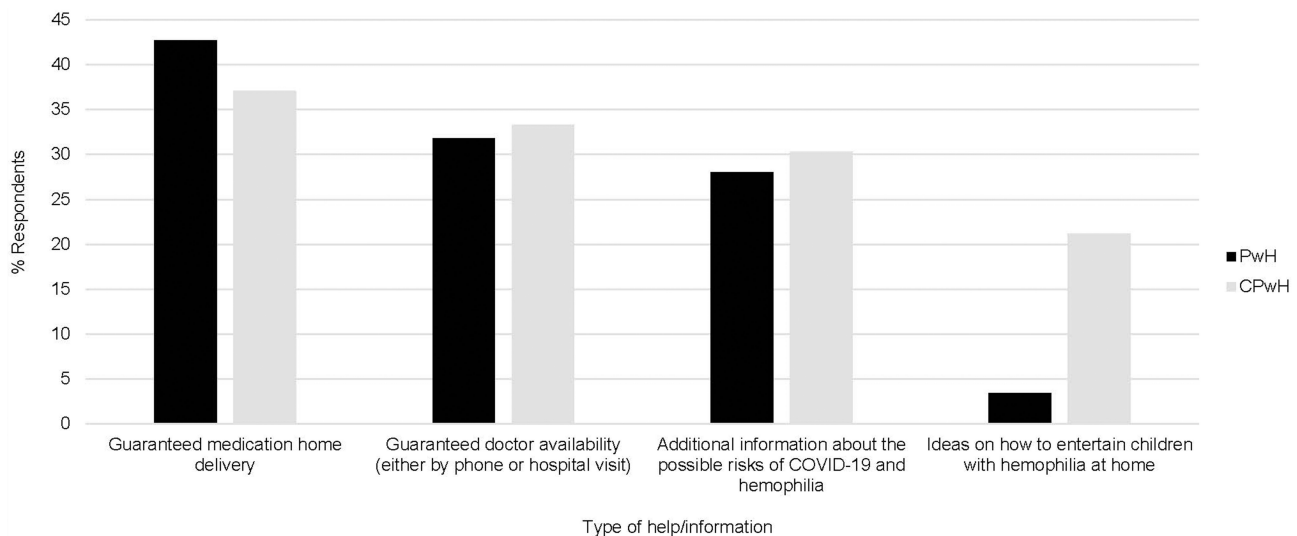
This survey of 364 people living with hemophilia is, to the best of our knowledge, the only study to report on



**Figure 5** Interference of hemophilia in daily living, stratified by disease severity (mild, moderate or severe hemophilia).



**Figure 6** Impact of COVID-19 on respondents living with hemophilia. **Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.



**Figure 7** Type of help/information most frequently requested by respondents during the COVID-19 pandemic. **Abbreviations:** CPwH, caregivers of people with hemophilia; PwH, people with hemophilia.

hemophilia impact on everyday life, patient education preferences and health information behavior in Central Europe.

Most of the respondents in our study were adults with severe hemophilia, which according to the literature, represents approximately one-third of people living with hemophilia in Europe.<sup>9,10</sup> The proportion of respondents with diagnosed inhibitors in our survey (18.4%) is much higher than reported in the recent European CHES (Cost of Hemophilia in Europe: a Socioeconomic Survey) study

(4.5%).<sup>11</sup> It is well established that inhibitor development is more common in people with severe hemophilia, and is also a major complication of hemophilia treatment; children with hemophilia present with inhibitors before the age of 9 years in approximately half of cases.<sup>12–14</sup> Although both CHES and our study included mostly severe patients, the CHES study included only adult patients (aged ≥18 years).<sup>11</sup> In contrast, 50% of survey responses from CwPH were based on children aged ≤12 years, which may partly attribute for the increased number



of respondents reporting inhibitors in our study. Another possible reason could be that PwH who experience problems with their treatment are perhaps more likely to respond to a survey about their treatment and patient education level.

Health information sought from different sources by people with hemophilia may influence the quality of healthcare rendered as well as affecting treatment decision-making.<sup>15</sup> Our results for PwH are consistent with recent reports for the general European population, that physicians are the preferred first source of health information by most people.<sup>15</sup> The second and third most commonly used health information sources in our study were patient associations and digital media (internet plus social media), respectively. New digital technologies have become increasingly important in the daily lives of many people worldwide.<sup>16</sup> As a result, the traditional physician–patient relationship is being challenged with the steady growth in the use of the internet for health information access in Europe over the last two decades.<sup>16,17</sup> Similar to our study, previous health information-seeking behavior studies show that although the internet is utilized by many individuals, healthcare professionals remain the most common and trusted source of information.<sup>18</sup> Other sources of patient information such as radio, newspapers, magazines, internet, and friends/family are used by individuals to supplement information provided by healthcare professionals.<sup>18</sup> According to recent European statistics, more than 50% of EU citizens routinely use the internet to seek health information,<sup>19,20</sup> and the majority are young adults.<sup>19,21</sup> Our result, showing that 56.3% of respondents use digital media sources for obtaining patient information, is consistent with previous reports,<sup>20</sup> and corresponds to levels of internet access and broadband connectivity in Europe.<sup>16</sup> A significant proportion of respondents in our study are not yet taking full advantage of digital media as a health information source, which may be due to several different factors such as age, gender and socioeconomic status.<sup>22,23</sup> On the other hand, the use of the internet did not appear to impact on PwH education level as respondents reported being sufficiently informed regardless of whether digital media was used as a source of patient information. Nevertheless, considering emerging health monitoring technologies enabling telemedicine such as Florio<sup>®</sup> HAEMO,<sup>6</sup> digital prudence is becoming more important to enable efficient treatment monitoring and communication with HTCs.

The daily challenges faced by people with hemophilia and their caregivers can have a significant negative impact on well-being, as well as psychosocial functional status.<sup>24</sup> The Haemophilia Experiences, Results and Opportunities (HERO) study in North America reported severe pain interference in approximately 30% of PwH aged >30 years,<sup>25</sup> while results from the HERO survey in Brazil revealed that 64% of adult male PwH have moderate/severe pain,<sup>26</sup> both based on analysis of the standardized EuroQOL five dimensions questionnaire (EQ-5D). Analysis by O'Hara et al of young adults (aged 18–35 years) treated with primary prophylaxis in the CHES survey, showed that 73% of respondents had at least one bleed event in past 12 months. In addition, mean EQ-5D assessment showed that 38% of primary prophylaxis respondents had moderate/severe pain, and 31% reported moderate/severe anxiety/depression.<sup>27</sup> Since the CHES survey was performed before broader access to novel extended half-life (EHL) factors and subsequent nonfactor replacement therapies, which were demonstrated to similarly reduce the annualized bleeding rate for patients,<sup>28,29</sup> it would be important to repeat population-wide screening of these issues currently.

Clotting factor replacement therapy has been the mainstay of hemophilia treatment worldwide for many years, both prophylactically and to treat bleeding.<sup>2</sup> However, bioengineering technologies have led to the rapid expansion of therapeutic options with extended half-lives, increased efficacy and reduced consumption.<sup>30</sup> The availability of diverse therapies from EHL concentrates and nonfactor hemostatic strategies to emerging gene therapy has increased the complexity of hemophilia care and necessitates re-education for PwH and CPwH.<sup>30–32</sup> In our study, the majority of respondents (approximately two thirds), both PwH and CPwH, reported to be sufficiently informed about living with hemophilia and the latest scientific developments. Approximately two-thirds of respondents in the survey also reported that they were satisfied with their treatment over the past 12 months. Healthcare providers and the hemophilia community should therefore recognize the benefits of effective health education in improving patient satisfaction, compliance and outcomes,<sup>33</sup> and particularly the availability of personalized health education as well as adequate and complete information for patient association platforms and digital sources.

Despite the majority of respondents reporting being generally well informed about the latest scientific

developments in hemophilia, nearly all respondents expressed an interest to receive additional information, mainly about new treatment options and technologies allowing easier administration. Of note, administration of medication was less often indicated as a common difficulty by the respondents in the survey (18.7%), with both PwH and CPwH placing more emphasis on difficulties concerning motion and mobility issues, unexpected bleeding, pain and uncertainty in daily activities. This aspect becomes especially important for personalizing patient education since, for example, an increased focus on easier mode of administration for recent nonfactor therapies may not always be at the center of day-to-day challenges for PwH. Conversely, personalized factor replacement therapy, supported by an established safety and efficacy profile during past decades and modern digital monitoring applications, may provide more certainty via rapid adaptation of factor levels for daily activities, and thus be more suitable at addressing the more frequently reported challenges pertaining to mobility. These complex considerations require careful education of PwH and their caregivers for informed and shared decision-making.

During the months of April and May 2020, when most of the responses in our survey were being collected, the novel coronavirus pandemic (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was widespread across Europe.<sup>34</sup> The COVID-19 pandemic's disruption of healthcare has been particularly challenging for patients with rare diseases, such as hemophilia. A recent survey of the Rare Barometer Programme by EURODIS (Rare Diseases Europe) reported that 9 in 10 patients with a rare disease have experienced interruptions in the care they receive due to the COVID-19 pandemic.<sup>35</sup> For example, almost 7 in 10 reported that their appointments with their general practitioners or specialists have been cancelled.<sup>35</sup> Six in 10 patients declared that interruptions of care related to the COVID-19 pandemic are detrimental to their health or the health of the person they care for, and 7 in 10 patients reported negative effects on wellbeing.<sup>35</sup> In our survey, more than half of PwH and their caregivers reported no major change in living with hemophilia during the COVID-19 pandemic, with only approximately 1 in 3 respondents reporting that they were living with anxiety and mental pressure about their condition as a result of the COVID-19 pandemic. The low proportion of respondents with anxiety and mental pressure during COVID-19 may be attributed to an increase in home delivery of treatment medications in some countries,

eg Czech Republic, and home self-treatment by patients, as per the EPHC recommendations and further endorsed by the European Association for Hemophilia and Allied Disorders (EAHAD) and EHC during the COVID-19 pandemic.<sup>1,36</sup> Respondents identified that guarantee of medication home delivery and physician availability would be most helpful during the COVID-19 pandemic. Compared with PwH, almost six times as many CPwH reported needing additional help with activities to entertain children with hemophilia at home. This result is not that surprising since 50% of CPwH respondents care for children with hemophilia vs <2% of PwH respondents who were children aged  $\leq 12$  years.

Several study limitations should be considered when interpreting the results. First, the survey questionnaire used was designed for the purposes of the study but was not subjected to rigorous psychometric and clinimetric testing; in contrast, the HERO<sup>25,26</sup> and CHES studies<sup>27</sup> both used the standardized EQ-5D domain analysis. Items for our questionnaire were based on expert opinion as well as from the literature but did not include any standardized assessment of the validity, reliability and responsiveness of the questionnaire. This may have resulted in redundant or missing items and some respondent misperception for some questions and scaling. Since the sample size was relatively small and no formal statistical comparison was performed, the significance of reported differences remains unclear and results should be interpreted with caution. Second, the survey covered six Central European countries which are considerably heterogeneous with respect to the standards of hemophilia care, including per capita consumption of factor VIII (FVIII) and IX (FIX).<sup>37,38</sup> Strengths of the study include the involvement of a meaningful sample of participants from six different countries in Central Europe. In addition, the study included patients who were receiving a variety of different hemophilia treatments, of different ages, and with different disease severity. Patients were recruited through the hemophilia patient associations, so selection was random (through mailings to all members) with less chance of bias.

## Conclusions

This study collected data on hemophilia impact on daily living and patient education level of PwH and their caregivers from six Central European countries. The most frequent difficulties in everyday life for people living with hemophilia were indicated to be mobility problems, unexpected bleeding, pain, and uncertainties

in daily activities impacting the choice of hobbies. Overall, the majority of respondents were well or very well informed about living with hemophilia and about the latest scientific developments. Despite being generally well informed, nearly all PwH and their caregivers expressed an interest in additional information regarding new treatment options, highlighting the need for personalized health education adapted to present challenges on an ongoing basis. This study may also help provide a better understanding of how the COVID-19 pandemic is affecting people with hemophilia and their caregivers across Central Europe, with approximately half of respondents reporting no major impact during the first wave of the outbreak.

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## Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in revising the article critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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