

## CLINICAL RESEARCH

# Falls and associated complications in adults with haemophilia

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**Risk factors for falls in the general population are frequently identified in patients with haemophilia. Screening for fall risk can help prevent significant injury in populations with high rates of falls and associated complications. We aimed to describe the rates of falls, injurious falls, near falls, and activity restriction due to fear of falling in a population of adults with haemophilia, an inherited bleeding disorder. Subjects completed a questionnaire inquiring about fall history over the previous 12 months at study onset (time 1) and again approximately 12 months later (time 2). In all, 75 patients with haemophilia between the ages of 18 and 85 participated. The annual fall rate was 33% at time 1, and 23% at time 2. 13% of subjects reported recurrent falls. The annual fall injury rate was 15% at time 1, and 16% at time 2. 63 % of subjects reported near falls at time 1, and 49% at time 2. 16% of subjects reported activity restriction due to fear of falling at time 1, and 21% at time 2. Rates of falls, recurrent falls, and fall-related injury in haemophilia patients in this study are similar to or higher than those found in community-dwelling adults aged 65 years and older, although our subjects were younger on average. These high rates were reported across all disease severities. Near falls were common among all subjects and rates of activity restriction were generally lower than those reported in older adults living in the community. Results should be replicated. Haemophilia patients should be questioned about fall history and further research into optimal fall risk prevention in this population is warranted.**

**Keywords:** fall risk, balance, haemophilia, screening

Haemophilia is an X-linked recessive inherited bleeding disorder affecting approximately 1 in 5000 male births worldwide [1]. Patients with haemophilia may have spontaneous and trauma-induced bleeding and, without

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prophylactic replacement therapy, bleeding into large joints is a hallmark of the disease. Haemophilia A and B are to the result of deficiencies of coagulation factors VIII and IX, respectively. Bleeding risk correlates with the degree of deficiency and the disease is categorised by baseline factor activity as severe (<1%), moderate (1-5%) or mild (6-40%). With advances in factor replacement therapy, patients with haemophilia now have near-normal life expectancy.

Risk factors for falls in the general population frequently identified in patients with haemophilia include muscle weakness[2], pain and swelling [3, 4], proprioceptive deficits [5], arthritis [4, 6], and presence of chronic disease [7]. Falls may be particularly dangerous in people with haemophilia due to the risk of bleeding complications [8] and higher prevalence of decreased bone density [9]. Falls are especially concerning in older adults and the haemophilia population is ageing [10]. Studies conducted in other populations with joint disease, such as rheumatoid arthritis, suggest that the negative consequences of falls are not restricted to older people[6]. Research in both children and adults strongly suggests balance deficits and falls are more common in people with haemophilia [5, 8, 11, 12], although sample size has generally been small. Examination of the frequency of falling and associated complications in a population of adults with haemophilia can assist in identifying the scope of the problem.

Screening may be helpful in identifying people at risk of falls before significant injury or dysfunction have occurred [13]. Identification of a "sub-clinical mobility deficit" could be similar to the early identification and treatment of cardiovascular disease risk factors such as high blood pressure or hyperlipidemia [14]. In community-dwelling older adults, falls have been shown to be highly preventable

**Table 1: Subject demographics**

Diagnosis and severity	Number of subjects	Age range in years
All	75	18-85
Haemophilia A	59	18-81
Haemophilia B	21	21-85
Mild	24	18-85
Moderate	17	22-67
Severe	34	21-73

[2, 15, 16], but those at risk must be identified first [17]. In this study, the rates of falls, injurious falls, near falls and activity restriction due to fear of falling in a population of adults with haemophilia were examined.

### Materials and Methods

**Study Subjects:** Subjects, recruited from the Puget Sound Blood Center Haemophilia Care Program between January 11, 2012 and October 9, 2013, were eligible to participate if they had a diagnosis of mild, moderate or severe haemophilia A or B, and were 18 years of age or older. Subjects who had undergone recent orthopaedic surgery were excluded until discharge from outpatient rehabilitation, and until pre-surgery weight-bearing status and activity level were resumed. Additional exclusion criteria included being non-ambulatory, unable to walk 150 feet, unable to follow verbal directions or unable to turn the head and/or change position independently. The study was approved by the University of Washington Institutional Review Board and all subjects gave written informed consent.

**Study Outline:** As part of a larger study on identifying fall risk in adults with haemophilia, subjects filled out a written questionnaire. The questionnaires were administered at the first study visit (time 1) and approximately 12 months later (time 2). Questionnaires were completed at two time points in order to allow evaluation of recurrent falls, to examine the predictive value of the questions and as part of a larger study assessing the screening for fall risk using performance measures. The four questions asked were:

- 'Have you had any falls in the last year?
- 'If yes, did any of these falls result in injury or require treatment?
- 'Have you had any near falls in the last year?
- 'In the last year have you limited your activities, for example what you do and where you go, because you are afraid of falling?

At time 2, subjects were contacted in person, or via telephone, email or postal mail, and again answered the four questions. Demographic data, presented in Table 1, were abstracted from the patient's medical record and included age, diagnosis and haemophilia severity.

**Statistical Analysis:** The rates of subjects reporting falls and other responses were compared across all participants and within severity category. All statistical tests were made by examining 95% confidence intervals. The statistical significance of rates (proportions) compared across

groups were determined by checking whether or not 95% confidence intervals for the group proportions overlapped. Similarly, if the 95% confidence interval of a correlation included zero, it was not deemed statistically significant. Due to small sample size, confidence intervals and statistical significance of differences were calculated via bootstrapping [18]. Each confidence interval is based upon 20,000 bootstrap draws.

### Results

In all, 75 men with haemophilia enrolled in the study and completed the written questionnaire independently at study initiation (time 1). 59 subjects had haemophilia A and 16 had haemophilia B. Approximately 12 months later (time 2), 73 subjects completed the questionnaire, with two subjects lost to follow-up: one was a 36 year-old subject with moderate haemophilia B and one was a 30-year-old subject with severe haemophilia A. Subjects with severe disease were, on average, younger than subjects with moderate or mild disease who enrolled in this study.

At time 1, 25 subjects reported a fall, 11 subjects reported a fall-related injury, 47 subjects reported near falls, and 12 subjects reported activity restriction due to fear of falling, with seven of these subjects also reporting falls. At time 2, 17 subjects reported a fall, 12 subjects reported a fall-related injury, 36 subjects reported near falls, and 15 subjects reported activity restriction due to fear of falling, with seven of these subjects also reporting falls. Most subjects who reported falls also reported near falls (84% at time 1 and 92 % at time 2), but many subjects who reported near falls did not fall (52% at time 1 and 41% at time 2). Results in relation to age and severity of haemophilia are shown in Tables 2 and 3 respectively. Point-biserial correlations between age and any fall ( $r = 0.18$ , bootstrap CI =  $-0.04-0.41$ ) or age and any fall-related injury ( $r = 0.20$ , bootstrap CI =  $-0.03-0.44$ ) were not statistically significant. Due to the wide and overlapping confidence intervals, differences in results across severities of haemophilia were not statistically significant.

### Discussion

In our study we found that falling was common in men with haemophilia, with 33% reporting a fall in the prior year at time 1 and 23% in the subsequent year at time 2. [7, 19, 20]. Although our subjects were younger on average, these rates appear similar to those reported in community-dwelling adults aged 65 and older, which range from 20-25% [7, 20,

**Table 2: Results in relation to age**

	Average/median age (range) in years
<b>All subjects</b>	42.5/40 (18-85)
<b>Mild haemophilia</b>	48.1/51.5 (18-85)
<b>Moderate haemophilia</b>	48.9/52 (22-67)
<b>Severe haemophilia</b>	34.4/32 (21-73)
<b>Subjects reporting fall at time 1 or 2</b>	45.1/43.5 (21-85)
<b>Subjects reporting fall-related injury at time 1 or 2</b>	46.8/49 (21-85)
<b>Subjects reporting activity restriction due to fear of falling at time 1 or 2</b>	51.1/54 (18-81)

21], to 33% [22, 23]. In comparison, annual fall rates reported in subjects with arthritis are higher and range from 30-54% [3, 4, 6, 24, 25]. There is limited research on fall rates in healthy younger adults. One Western Australian study reports annual fall rates ranging from 4-6.3% in adults aged between 25 and 64 [26]. In a different study of adults aged 40 and above with moderate or severe haemophilia, the annual fall rate was 32.4% [11]. In our study, the association between age and falls was not statistically significant, although the lower bound of the correlation confidence interval was near zero. In community-dwelling older adults, increased age is a significant risk factor for falls [27], but in people with rheumatoid arthritis, fall rates and age were not found to be related [6, 25]. Since our sample was entirely male, it is interesting to consider gender differences with respect to fall rates. It has been shown in subjects with rheumatoid arthritis that men fall more frequently than women [6]. We found a recurrent fall rate (subjects who reported falls at both time 1 and time 2) of 13%, while in community-dwelling adults aged 65 and older, recurrent fall rates have been reported to range from 4.75-10% [20, 21].

Reported fall-related injury rates across all enrolled subjects were 15% at time 1 and 16% at time 2. This is similar to annual fall-related injury rates reported in subjects with arthritis, which range from 16-22% [3, 6, 28], and higher than reported in community-dwelling older adults, where annual fall injury rates range from 7-12.5% [7, 20, 29], although our confidence intervals include these rates. Annual fall-related injury rates for younger adults in the community have been reported to range from 1.5-11.5% [26, 29-31]. In another study looking at adults aged 40 and older with moderate or severe haemophilia, the annual fall injury rate across all subjects was reported at 24.3% [11]. In our study, being of increasing age was not consistently associated with fall-related injury across all severities, although again the lower bound of the confidence interval of the correlation was near zero, suggesting a larger sample may have indicated a statistically significant association. Here, the average age of those reporting a fall-related injury was slightly higher (46.8) than the sample as a whole (42.5). In community-dwelling adults aged 65 years and older, fall rates rise with increasing age, but fall-related injury rates are similar among all age groups [19].

Additionally, at time 1 in our study, 63% of the total subject population reported near falls, and 49% at time 2. High rates

of near falls were reported by individuals who had actual falls as well as individuals who did not, with 45% of subjects reporting near falls also reporting actual falls at time 1 and 31% at time 2. There is limited literature on near fall rates, with a wide range of rates reported [32, 33], and its predictive value in terms of future fall risk has not been established.

Reported rates of activity restriction due to fear of falling in our sample were 16% at time 1 and 21% at time 2. These rates are lower than the 38% rate reported in subjects with rheumatoid arthritis [24]. In community-dwelling adults over 65 years of age, rates of activity restriction due to fear of falling are quite variable, ranging from 10-60% [34, 35], and in younger adults from 10-13% [31, 34]. Activity restriction and falls were not strongly related in our study, with 58% of subjects reporting activity restriction at time 1 and 47% at time 2 also reporting falls. Subjects reporting activity restriction were older on average (51.1 years) than the study population as a whole (42.5 years). The relationship between age and activity restriction due to fear of falling in other populations is inconsistent [31, 35]. This may be secondary to measurement issues, which are further discussed below.

There are several limitations in our study. Due to the small sample size, confidence intervals are large and overlap, and no statistically significant differences were noted across severities. It is possible that people who volunteered had an interest in falls due to personal experience, leading to selection bias and a fall rate that is higher than in the haemophilia population as a whole [6]. Without the presence of a control group, we cannot confirm that haemophilia is a risk factor for falls [3, 4]. Since the literature on falls in younger populations is limited, it would be helpful in future research to have a parallel contemporary younger-aged control group for comparison.

There are limitations inherent in the questionnaire. We did not provide subjects with specific definitions of falls or fall-related injuries, and the question on activity restriction due to fear of falling was asked in a general way. This may have helped to capture more falls, injuries and fears, but may have decreased the accuracy due to differing definitions among subjects. We also did not ask about the nature of the fall-related injury, which may help guide the development of interventions. The questionnaire was developed to be used as part of a larger multicentre study assessing the value of brief fall risk screening instruments in the comprehensive clinic setting. In future studies, it may be useful to gather

**Table 3: Results in relation to severity of haemophilia (95% confidence interval)**

	All	Mild	Moderate	Severe
<b>Annual fall rate, Time 1</b>	25/75=33% [23-44%]	10/24=42% [21-63%]	8/17=47% [24-71%]	7/34=21% [9-36%]
<b>Annual fall rate, Time 2</b>	17/73=23% [14-33%]	4/24=17% [4-33%]	5/16=31% [12-54%]	8/33=24% [10-39%]
<b>Recurrent fall rate - Falls at both Time 1 and 2</b>	10/73=13% [7-22%]	3/24=12.5% [4-25%]	3/16=19% [6-40%]	4/33=12% [3-24%]
<b>Annual fall-related injury rate, Time 1</b>	11/75=15% [7-23%]	6/24=25% [8-42%]	2/17=12% [6-29%]	3/34=9% [3-21%]
<b>Annual fall-related injury rate, Time 2</b>	12/73=16% [8-25%]	2/24=8% [4-21%]	4/16=25% [4-47%]	6/33=18% [6-32%]
<b>Annual rate of activity restriction due to fear of falling, Time 1</b>	12/75=16% [8-24%]	6/24=25% [8-42%]	1/17=6% [6-24%]	5/34=15% [3-26%]
<b>Annual rate of activity restriction due to fear of falling, Time 2</b>	15/73=21% [12-30%]	5/24=21% [8-38%]	3/16=19% [6-40%]	7/33=21% [8-36%]

additional information that may affect fall risk, for example joint status, balance impairment and use of prophylaxis.

It is also possible that subjects were influenced by their relationship with the investigators, who were also providing haemophilia care, both in the decision to participate [36] and in the way they responded to the questionnaire at both time points. Although the same questionnaire was used at both time points, it was completed in different ways. At the first study visit, the questionnaire was conducted in the context of the larger study. The visit took 30-60 minutes, and included the consent process and performance and range of motion measures. When repeated 12 months later, the questionnaire was most often conducted by email, postal mail or phone, taking only a few minutes and with minimal contact with the researcher. The time period and mode of administration of the study procedures may affect recall [37, 38]. Recall bias in general may lead to an underestimate of fall rates [3, 28], and retrospective studies tend to underestimate fall rates when compared to prospective research [4]. Subjects may also be more likely to remember injurious falls [39]. It may be important to consider the time period of recall, although the ideal reporting period is unclear [39]. Use of the 12-month recall method has been recommended in fall prevention guidelines [2, 7].

In light of the suggested high fall and fall injury rates noted in men with haemophilia in this and other studies, prevention efforts should be promoted. These may include screening, in-depth evaluation and intervention [2, 15, 27, 40, 41]. The consequences of falling for all populations can be significant on a variety of levels. For example, a recent study demonstrates that 55% of all unintentional injury deaths in adults aged 65 years and older in the US are due to falls [42]. We know that fall risk can be modified in other populations, such as community-dwelling older adults [27, 40, 43]. Fall prevention services have been offered more consistently in older adult populations where fall risk is

more commonly recognised [6]. The authors recommend that clinicians consider incorporating a fall risk screen into the comprehensive assessment of all adult patients with haemophilia, regardless of age, where the high incidence of falls coupled with longitudinal care provided by physical therapists presents an ideal opportunity for the monitoring and prevention of falls [6, 44].

It has been suggested that successful fall prevention requires ongoing effort, as is common in the management of many chronic conditions [7]. Pending results of ongoing multicentre research that may suggest ideal questions, tools or measures to use as a brief screen of fall risk in people with haemophilia, we suggest asking patients about fall history or concerns about falling. We know that in other populations a recent history of falling is a strong, consistent and significant fall risk factor [2, 22, 27], and that many patients do not discuss falls with their healthcare providers [20, 27], making it an important question for us to ask [6]. It is currently recommended by the American and British Geriatric Societies that all adults aged 65 years and older be questioned annually about problems with walking or balance [2]. This recommendation may also be appropriate in adults of all ages with haemophilia, given the similar fall rates across the age span reported in this study.

### Conclusion

In our sample of men with haemophilia, we found that fall and recurrent fall rates were similar to or higher than the fall rates found in community-dwelling adults aged 65 years and older, although the subjects in this study were younger on average. Rates of falls, fall-related injury and recurrent falls did not differ by haemophilia severity or age. Additional research is needed and should confirm these results in a larger sample of patients and across different treatment centres. To maximise the impact of interventions, optimal fall risk screening, assessment and treatment options in this population must also be identified.



## Disclosures

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