Original Article

Sports participation and sports injuries in Dutch boys with haemophilia

Olav Versloot1 | Merel A. Timmer1 | Piet de Kleijn1 | Marleen Schuuring2 | Casper F. van Koppenhagen3 | Janjaap van der Net2 | Kathelijn Fischer1

1Van Creveldkliniek, University Medical Center Utrecht, Utrecht, The Netherlands
2Center for Child Development, Exercise and Physical Literacy, University Children’s Hospital, University Medical Center, Utrecht, The Netherlands
3Physical Medicine and Rehabilitation, University Medical Centre, Utrecht, the Netherlands

Correspondence
Olav Versloot, Van Creveldkliniek (C01.428), PO Box 85500, 3508 GA Utrecht, The Netherlands.
Email: o.versloot@umcutrecht.nl

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Introduction: Sports participation in children with hemophilia is generally considered to be associated with increased injury risk, which is generally considered highest in severe hemophilia.

Aim: To assess sports participation according to age and severity in children with hemophilia and its association with sports injuries.

Methods: In a retrospective single-center study, sports participation, injuries, and bleeding data from three consecutive annual clinic visits were collected for young patients with hemophilia (PWH, aged 6-18). Sports in categories 2.5 and 3 of 3 according to the National Hemophilia Foundation classification were considered high-risk. Groups were compared using chi-square testing.

Results: 105 PWH (median age: 13(IQR 10-14); 53% severe; bleeding rate: 1/y) were identified; three were unable to perform sports and were excluded. The majority of PWH (77%) played sports weekly, of which 80% high-risk sports. Sports participation (median 3.0x/wk), and the proportion of injured PWH was similar in severe (42%) and non-severe (33%) PWH. Sports injuries were rare (65% no injuries in 3 years, median 0/y (IQR 0-1)). Annually, PWH did not report more injuries (15%) than age-matched boys (28%). Sports injuries were not associated with frequency and type of sports.

Discussion: This retrospective study showed high sports participation (including high-risk sports) and low injury rates. Sports participation was similar across severities and injury rates were not higher than among the general population. Injuries were not associated with frequency or type of sports. A prospective study with objective assessment of sports participation and injuries is warranted to confirm these findings and avoid recall bias.

Keywords
children, hemarthrosis, sports injuries, sports participation
INTRODUCTION

Hemophilia is an inherited, chronic hematological disease in which patients have decreased levels of clotting factor VIII (hemophilia A, FVIII) or IX (hemophilia B, FIX). At this moment, there is no cure. Hemophilia severity is classified as severe (<1% FVIII/FIX), moderate (1%-5%) or mild (5%-40%).1 Low clotting factor levels can cause spontaneous or traumatic bleeds, including joint bleeds. These joint bleeds can lead to hemophilic arthropathy if not managed appropriately.2 Accordingly, patients with hemophilia (PWH) are at an increased risk of reduced social participation (work, education, and sports). PWH were traditionally discouraged to participate in sports because of the assumed increased bleeding risk due to body contact or joint trauma. The introduction of prophylactic therapy3 has drastically improved the opportunity to participate in sports for PWH, making it a patient relevant outcome.

Participation in sports is essential for children,4 both with and without hemophilia. As in other chronic health conditions (eg, rheumatoid arthritis, cerebral palsy, and cystic fibrosis),5-8 participating in sports has been associated with numerous positive effects in children with hemophilia: improved endurance, increased strength and proprioception,9-11 conservation of muscle mass and bone density,11-13 reduced bleeding risk,10,14 as well as improved health-related quality of life,15 social development16 and physical literacy.17 However, independent of hemophilia, sports participation, especially in high-risk (HR) sports, increases the risk of injuries or bleeds.18-20 Due to this increased injury risk, parents, and care-givers may still be reluctant toward sports participation, potentially limiting children with hemophilia in achieving an active lifestyle.21,22

Previous studies have reported that Dutch children with hemophilia are just as active as their peers,21,23,24 but information on type and intensity of sports participation and the associated injury risk with regard to age or severity remains limited.

Two American studies with one-year follow-up failed to show an association between participation in (high-impact) sports and an increased injury risk in children with hemophilia.25,26 A detailed Australian study showed a transient increase in bleeding risk in children and adolescents with moderate and severe hemophilia after vigorous physical activity but the absolute increase in bleeding risk was small.27 A nationwide cross-sectional study in Finland reported higher sports injury risk in adolescents with a chronic health condition (eg, asthma, diabetes, and joint pain) than in the general population.28

The primary aim of this study was to assess sports participation according to age and severity in Dutch children with hemophilia over a 3-year period. As a secondary aim, the association between sports participation and the number of sports injuries was assessed.

MATERIALS AND METHODS

2.1 Design and setting

This single-center, retrospective study was performed at the van Creveldkliniek (University Medical Center (UMC) Utrecht) in 2018. At our clinic, patients are assessed annually in a structured multidisciplinary clinic (eg, physician and physiotherapist), including routine assessment of sports participation, bleeds, and injuries. Sports participation (regular planned sports) and, injuries were self-reported; bleeds were extracted from the infusion logs and hospital files. Injury data were cross-checked with hospital files. All data were entered in the patient file during the annual multidisciplinary clinic visit. Data from the three most recent annual multidisciplinary visits were extracted anonymously from electronic patient files. The study was approved by the IRB of UMC Utrecht (approval number: 18-265). Informed consent was waived because the data were collected anonymously.

2.2 Participants

The participants of this study were children with hemophilia A or B who were 6-18 years during their three most recent
annual clinic visits (range: 2011-2018). Patients with current inhibitors or neurological disability were excluded. Due to the low number of patients with moderate hemophilia, patients with moderate and mild hemophilia were grouped as “non-severe”.

2.3 | Data collected

Sports participation characteristics (active in organized sports at least once weekly (yes/no), active in HR sports at least once weekly (yes/no), number and type of sports, weekly frequency), number of bleeds and number of sports injuries were collected from the three most recent annual clinic visits. Infusion logs included bleeding data and were completed mostly by parents. Sports were defined as “all forms of physical activity which, through casual or organized participation aim at expressing or improving physical fitness and mental well-being, forming social relationships or obtaining results in competition at all levels.”29 Participation in school physical education classes was not considered. Sports injuries were defined as any injury as a result of participation in sport resulting in the need for any form of medical treatment, including infusion of clotting factor concentrate with or without concomitant treatment such as physiotherapy, taping, braces, crutches etc. Joint bleeds were defined as any complaint located in peripheral synovial joints (ankles, knees, elbows, shoulders, hips, or wrists) requiring treatment with clotting factor concentrate. A muscle bleed was defined as “an episode of bleeding into a muscle, determined clinically and/or by imaging studies, generally associated with pain and/or swelling and loss of movement over baseline”.1 Bleeds reported included both bleeds related as well as unrelated to sports. Weekly sports frequency (times/week) was recorded. Sports were categorized into five risk categories according to the classification of the US National Hemophilia Foundation (NHF).30 A selection of sports and their risk categories are displayed in Table S1. These runs from 1 (safe) via 1.5 (safe to moderate risk), 2 (moderate risk), 2.5 (moderate risk to high risk) to 3 (high risk). Category 1 contains low impact sports with a low collision risk like walking and swimming, while sports in category 2.5 (eg, football) and category 3 (eg, rugby) are considered to be HR-sports.30 Sports categorized across multiple categories were classified as the average risk category (eg, 2.5 for football). The highest category in which participants were involved in was used to test the association of sports participation with injuries and/or bleeds. In case of participation in sports of different risk categories, patients were classified into the highest risk category. Sports participation was collected for each annual clinic visit and was analyzed and presented per year.

The collected data of PWH were compared to the sports participation and sports injury data of Dutch general population (GP).31,32 These data are collected bi-annually by a standardized Dutch questionnaire and were collected online or by phone. Participants were asked to provide a maximum of 4 sports they performed. In order to compare these groups, similar age groups were created: 6-12 and 12-18 years. Data on injuries in the GP was collected from a nationwide injury registry.33

2.4 | Statistics

Sports participation and HR-sports participation according to age and hemophilia severity (severe vs. non-severe) were tested by means of Pearson’s chi-square tests. Age groups of 6-11 and 12-18 years were created in order to compare results to the Dutch general population.32 Associations between hemophilia severity and HR-sports and between sports participation and the number of sports injuries were tested using Pearson’s chi-square tests.

All results were presented as median values with interquartile range (IQR) with 95% confidence intervals (CI) where appropriate. Statistical significance levels were set at 5% (P < .05). The statistical analysis was performed using SPSS statistical software, version 25 (IBM corp., Armonk, NY).

3 | RESULTS

3.1 | Participants

Originally, 105 patients with hemophilia (PWH) were identified. Three patients were excluded due to epilepsy, cerebral palsy, or a current inhibitor, leaving 102 eligible patients. Patient characteristics are shown in Table 1. In total, 86% had hemophilia A, and 53% had severe, 5% moderate and 42% mild hemophilia. Because of the low number of patients with moderate hemophilia (n = 5), patients with moderate and mild hemophilia were grouped as “non-severe” to be able to assess differences in PWH with no clotting factor activity and PWH with some, but insufficient factor activity.34

Median age of the participants was 13 years (IQR 11-15). Continuous prophylaxis was used by all severe and 2 moderate patients. A total number of 187 bleeds were reported during follow-up. These bleeds were reported by 69 (68%) patients, with 33 PWH (32%) not reporting any bleeds during follow-up. The median bleeding rate was 1 bleed/3 years (range: 0-8). PWH with bleeds reported a median of 2.7 bleeds/3 years (range: 1-8).

During a median follow-up of 3 years (year 1:100%; year 2:99%; year 3:93%) a total of 287 person-years were collected. Due to shifting age distributions, the number of patients aged 6-18 varied during the three years of data collection. Due to these reasons, group sizes varied for each year: n = 102,
3.2 | Sports participation

3.2.1 | Participation

Sports participation and injuries according to year and severity is shown in Figure 1. Overall, 87/102 (85%) of PWH played sports at any time during the follow-up period. Due to switching between sports and overlapping activities within PWH, sports participation was presented per year (1; 2; 3).

Per year, 77% of PWH participated in a total number of 37 different sports at some time during the study, including 70/87 (80%) participating in HR-sports. Sports participation remained consistent during the three-year follow-up (year 1:73/102 (72%), year 2:76/98 (78%), year 3:74/89 (83%); P = .65). The majority (59%) played one sport, 13% played two sports and 1% three sports. A median weekly frequency of 3 (IQR 2-3) was reported.

Within the risk categories, “moderate risk to high risk” (NHF 2.5) was the most frequently reported category (75%). This seems to be particularly based on the high number of participants (49%) playing football.

3.2.2 | Sports participation according to age

Average annual sports participation (6-11yrs.: 94% (CI 83-98) vs. 12-18yrs.: 84% (CI 71-91); P = .13) and HR-sports participation (81% (CI 72%-88%) vs. 76% (CI 66%-83%), P = .91) were similar between age groups for the entire follow-up period (see Table S2). The highest reported risk category was similar in both age groups (median 2.5 (IQR 2.5-2.5) vs. 2.5 (IQR 2.5-2.5), P = .39).

3.2.3 | Sports participation compared to the general population

Sports participation was similar for Dutch boys with hemophilia and their healthy peers. An average of 77%, (CI 72%-82%) of PWH played sports, compared to 74% (CI 73%-75%) in the age-matched GP.31 Participation in HR sports was similar as well, at 74% (CI 68%-80%) in PWH, compared to 64.5% (CI 60%-69%) in GP. Sports participation according to age was similar as well (6-11 years: 75% PWH vs. 65% GP; 12-18 years: 74% PWH vs. 76% GP).35

Type of sports chosen according to age is shown in Table 2. Boys with hemophilia and age-matched healthy children preferred different sports, as did different age groups. Football was the most popular sport in both PWH and the general population. In addition, the top three included swimming and judo among PWH, and fitness and field hockey in the general population.35

3.2.4 | Sports participation according to hemophilia severity

Sports participation, bleeding, and injuries during follow-up according to hemophilia severity are shown in Table 3. Sports participation was similar in patients with severe and non-severe hemophilia (severe vs. non-severe: 76% vs. 72% (P = .64) for year 1, 73% vs. 78% (P = .55) for year 2, and 76% vs. 73% (P = .56) for year 3, respectively). HR-sports participation was similar for patients with severe and non-severe hemophilia (72% vs. 82% (P = .57), 68% vs. 83% (P = .12), 77% vs. 79% (P = .59), respectively). Weekly sports frequency was similar for patients with severe and non-severe hemophilia (median 3.0 times/week (IQR 2.0-3.8) vs. 3.0 (IQR 3.0-3.0), P = .30) and remained stable throughout the follow-up. Patients with severe and non-severe hemophilia reported similar highest NHF categories (median 2.5 (IQR 2.0-2.5) vs. 2.5 (IQR 2.5-2.5); P = .12). This could be due to the high overall number of patients playing football (NHF = 2.5; severe: 44% (CI 31%-57%), non-severe: 56% (CI 42%-69%); P = .21) in both groups.
Sports injuries were rare: 56 sports injuries were reported by 33 (38%) PWH, resulting in a median of 1.7 injury/PWH in three years and 0 (IQR 0-1; range: 0-7) injuries/year. Although the majority of injuries (34/56) were reported by patients with severe hemophilia, injury rates were not associated with severity: both the number of patients with injuries (severe: 20/48 (42%) vs. non-severe: 13/39 (33%)) and the number sports injuries per PWH (median 0 (IQR 0-1) vs. 0 (IQR 0-1); $P = .63$) were similar in severe and non-severe patients. The proportion of PWH reporting was not higher than the GP (14.9% vs. 28.0%).

Hemophilia severity, increased training frequency, higher risk category, nor age differences were associated with an increase in sports injuries. Playing football was not associated with increased injury risk. In PWH playing football, injury

FIGURE 1  Sports participation (1A) and sports injuries (1B) in the general population and in young Dutch PWH
Bleeds were reported more frequently than sports injuries. The results of the study show that even with prophylactic treatment, more PWH with severe hemophilia reported bleeds than PWH with non-severe hemophilia (year 1: 55% vs. 26%; year 2: 49% vs. 39%; year 3: 39% vs. 21% bleeds), reaching statistical significance in year 1 and 2 ($P < .05$) only (Table 3). The proportion of PWH reporting bleeds was similar in those actively involved and those not involved in both sports (39% vs. 37%) and HR sports (38% vs. 43%).

### DISCUSSION

#### 4.1 Principle findings

PWH reported high sports participation (77%), of which 74% participated in HR sports. Sports participation was similar to the general population and across hemophilia severity. Dutch boys with hemophilia preferred different sports than children in the general population.

Sports injuries were rare (38% of PWH during 3-year follow-up, median 0 (IQR 0-1) injury/year), and were not associated with hemophilia severity, (high-risk) sports participation, weekly frequency, risk category or age. PWH did not report more sports injuries than the GP.

#### 4.2 Strengths and limitations

This was a retrospective study which analyzed data routinely provided by children with hemophilia and their parents over their last three clinic visits. The lack of a standardized collection method could have led to information bias in the data and potential overestimation of sports participation and underestimation of sports injuries. Although no gold standard for self-reporting of sports participation exists, using a standardized questionnaire as the Modifiable Activities Questionnaire would improve the accuracy of the data.
(MAQ)\(^{38,39}\) might be one way of improving sports participation assessment. The MAQ was recently validated in a Dutch population\(^{40}\) and has been used in studies with PWH before.\(^{19,24}\)

Duration of sports activities was not included in this study, as this is known to be difficult to estimate by participants.\(^{41}\) Collecting data prospectively with an objective tool, such as accelerometers,\(^{36,42}\) are expected to result in less variation and more reliable estimates of duration and intensity of PA. The analysis of sports injuries was limited to the number of sports injuries during the studied period. Data on severity, location, and injury mechanism of the injury were unavailable in the current data set and confirms the need for prospective studies with regards to injury studies.\(^{43}\)

### 4.3 | Comparison with other studies

This study showed high sports participation by young Dutch PWH, similar to the general Dutch general population.\(^{33}\) Previous studies in Dutch,\(^{23,24}\) British,\(^{15}\) Australian,\(^{19}\) Irish\(^{44}\) and Israeli\(^{45}\) PWH already reported high participation in PWH. These were cross-sectional studies, most of them\(^{19,23,24,44,45}\) only reporting being active in sports or not. Maximal follow-up was three months.\(^{45}\) The current study included weekly sports frequency as exposure measure and a three-year follow-up. The study by Khair et al\(^{15}\) included weekly sports frequency (79% at least twice weekly). Median weekly frequency was calculated from published data and seemed to be slightly lower (median 2 (IQR 2-3)) than in the current study, with 79% sporting at least twice weekly.\(^{15}\)

This study had a three-year follow-up, which allowed for a more reliable assessment of sports participation and explore the association with age. Only four studies\(^{25-27,45}\) assessed the association between sports participation and sports injuries. Tiktinsky et al excluded patients under prophylaxis.\(^{45}\) This hampers a comparison with the current study. Ross et al,\(^{26}\) McGee et al\(^{25}\) and Broderick et al\(^{27}\) studied sports and injuries and/or bleeds. Ross et al and McGee et al reported similar bleeding rates during 1- and 3-year follow-up. Ross et al reported no association between the impact of sports and injuries in 37 boys with severe hemophilia receiving prophylaxis during a one-year follow-up.\(^{26}\) McGee et al included all severities and showed no association between sports injuries and being engaged in organized sports.\(^{25}\) Broderick et al included 104 boys with moderate and severe hemophilia. They reported more bleeds (median 3/y) and an transient, increased relative bleeding risk (OR: 3) after PA with a follow-up of up to 1 year.\(^{27}\)

This study was the first to assess self-reported sports injuries in Dutch PWH. In comparison, Schmikli et al performed a nationwide cross-sectional sports injury study in the Netherlands.\(^{33}\) With a 3-month recall-period, 28% of boys below 18 reported at least one injury. No follow-up was involved in this study. Although frequently assumed, PWH in the present study did not report a higher injury rate than age-matched Dutch boys. The exact reason for this difference cannot easily be given: PWH might be more cautious when playing sports, but recall bias could have underestimated the number of reported injuries as well.

### 4.4 | Perspective

Individualizing hemophilia treatment includes counselling on (the risks of) sports injuries. Although studies in the general population have reported that sports injury risk is associated with type of sports,\(^{46-49}\) and intensity,\(^{18,20,27}\) this was not observed in the present cohort. Even a low number of joint injuries could lead to significant joint damage.\(^{2}\) Both data from the present study and previous studies suggest that playing sports is relatively safe in young PWH. However, we were unable to identify any studies containing data on adult PWH. Injury risk is expected to be higher in young adults,\(^{33}\) especially for contact sports such as football. In addition, injury risk may depend on physical fitness, physical literacy and/or motor proficiency as well. Ideally, these factors should be assessed and taken into account when performing sports counselling, but first their impact needs to be addressed in future studies.

### 4.5 | Conclusion

This study assessed sports participation with regard to age and severity and the association with sports injuries in PWH. Sports participation among PWH (77%) was similar to the general population). Sports injuries were reported by 38% of patients in a 3-year period. Neither sports participation nor the number of sports injuries was associated with disease severity or age. Active involvement in sports or HR sports was not associated with a higher proportion of bleeds. In addition, the association between clotting factor activity levels, sports injuries and bleeds should be considered. To be able to address clinical issues and provide adequate counselling at patient level, more detailed data on sports injury risk factors is needed. For this purpose, future studies should rely on objective, prospective data, instead of patient reported retrospective outcome.

### CONFLICTS OF INTEREST

OV has reported no interests which might be perceived as posing a conflict or bias. MT has reported no interests which might be perceived as posing a conflict or bias. PK received support from NovoNordisk. MS has reported no interests which might be perceived as posing a conflict or bias. CvK
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AUTHORS’ CONTRIBUTION
OV, KF, and JN were involved in the design of the study. OV analyzed the data and wrote the paper. All authors were involved in data interpretation. All authors reviewed and approved the final version of the paper.

ORCID
Olav Versloot https://orcid.org/0000-0003-0748-1364
Merel A. Timmer https://orcid.org/0000-0003-1910-999X
Janjaap van der Net https://orcid.org/0000-0003-2606-5104
Kathelijn Fischer https://orcid.org/0000-0001-7126-6613

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