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# A scoping review on exercise prescription in hemophilia: A pathway for enhanced mobility and reduced bleeding risk

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## Abstract:

Hemophilia, a genetic disorder characterized by impaired blood clotting, often leads to joint and muscle bleeds, resulting in chronic pain and reduced mobility. Exercise has emerged as a therapeutic intervention to enhance physical capacity and minimize bleeding risks among individuals with hemophilia. The aim of the present scoping review to explore and synthesize the available literature on exercise prescription in hemophilia, focusing on its role in promoting mobility and reducing bleeding complications. A systematic search was conducted across multiple databases, following the Preferred Reporting Items for Systematic reviews and Meta-analyses extension for Scoping Reviews guidelines to identify studies addressing types, intensity, frequency, and safety measures associated with exercise in hemophilia management. Our findings highlight various exercise protocols, including resistance training, aquatic exercises, and low-impact aerobic activities, as effective in improving joint stability, muscle strength, and overall physical function. The review also identifies critical safety considerations, such as personalized exercise intensity and regular monitoring to prevent injury. Although evidence supports the benefits of structured exercise, there remains a need for standardized guidelines specific to hemophilia. Future research should focus on long-term outcomes and individualized exercise regimens to optimize therapeutic gains. This review offers a foundation for healthcare professionals to develop tailored exercise prescriptions, facilitating better mobility, and reduced bleeding risk in hemophilia patients.

## Keywords:

Exercise, hemophilia, mobility, resistance training

## Introduction

Hemophilia is a genetic bleeding disorder characterized by deficiencies in clotting factors, primarily affecting hemophilia A and B, which involve deficiencies in factor VIII and IX, respectively.<sup>[1]</sup> This condition is marked by frequent bleeding episodes, often spontaneous, and recurrent hemarthrosis (joint bleeding), leading to joint damage, muscle atrophy, and

reduced physical function over time.<sup>[2]</sup> The management of hemophilia traditionally centered on prophylactic clotting factor replacement therapies to prevent bleeding episodes and protect joint health.<sup>[3,4]</sup> However, there is an evolving body of research and clinical practice focusing on exercise as a complementary intervention, aiming not only to preserve musculoskeletal health but also to enhance physical functioning, reduce bleeding risk, and improving overall quality of life (QoL) in hemophilic individuals.<sup>[5,6]</sup>

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## Rationale for exercise in hemophilia

Exercise are considered as critical component in the management of many chronic health conditions, contributing to improved cardiovascular health, musculoskeletal strength, and functional independence.<sup>[7,8]</sup> In hemophilia, however, the role of exercise remains complex and somewhat controversial. While physical activity can strengthen muscles surrounding the joints and thus reduce joint bleeding and deterioration, there is an inherent risk of triggering bleeds if exercises are not carefully prescribed and supervised.<sup>[9]</sup> Nonetheless, an increasing number of studies indicate that structured exercise programs – when tailored to individual needs and limitations – may offer substantial benefits.<sup>[10]</sup> Specifically, regular exercise has been associated with improved joint health, enhanced muscle strength, better balance, and an overall reduction in bleeding frequency, potentially mitigating some of the primary complications associated with hemophilia.<sup>[11]</sup>

## Challenges and barriers to physical activity in hemophilia

Despite the recognized benefits of exercise, individuals with hemophilia face unique challenges when it comes to physical activity.<sup>[12]</sup> Fear of injury or bleeding is a significant psychological barrier, often leading to physical inactivity and deconditioning. Furthermore, pain from joint damage and the functional limitations imposed by hemophilia-related arthropathy (joint disease) can limit the range and intensity of exercises that can be safely performed.<sup>[13]</sup> Hemophilia also imposes an economic burden, with regular access to clotting factors and medical care required to manage and prevent bleeds.<sup>[14]</sup> These factors contribute to a sedentary lifestyle among many patients, compounding the risk of musculoskeletal degeneration and decreased functional mobility.<sup>[15]</sup>

From a clinical perspective, healthcare providers may also lack clear guidelines on prescribing exercise for patients with hemophilia, leading to inconsistent advice or hesitancy to recommend physical activity altogether. Therefore, a systematic approach to exercise prescription in hemophilia – considering individual health status, type and severity of hemophilia, and the risk profile of different exercises – is essential. There is a need to develop safe, effective, and adaptable exercise protocols that can enhance mobility and improve patient outcomes without compromising safety. Aerobic exercise, on the other hand, promotes cardiovascular health, endurance, and general physical fitness, which may reduce the risk of obesity – a common comorbidity that exacerbates joint issues in hemophilia.<sup>[16]</sup> Balance and proprioceptive exercises are also integral, as they may improve joint stability and reduce fall risk, which is especially relevant given the fragility of joints affected by recurrent bleeding.<sup>[17]</sup>

## The intersection of exercise, mobility, and bleeding risk reduction

Although exercise may reduce bleeding incidence by strengthening supportive structures around joints, the mechanisms underlying this protective effect are not yet fully understood. Current hypotheses suggest that by enhancing proprioception, joint stability, and overall physical resilience, exercise may reduce the likelihood of bleeds even in patients who experience frequent spontaneous bleeding. Furthermore, regular exercise may contribute to better control over body movements, decreasing the risk of accidental trauma that could lead to bleeds.<sup>[18]</sup>

The aim of the present review is to synthesize the available literature on exercise interventions in hemophilia to provide an evidence-based foundation for exercise prescription tailored to this population.

## Methodology

A scoping review was conducted in accordance with the methodological framework outlined by Arksey and O'Malley and refined by Levac *et al.*<sup>[19]</sup> This approach was chosen to allow a thorough examination of existing literature on exercise prescription for individuals with hemophilia, with specific attention to its impact on mobility and bleeding risk.

## Research question formulation

To guide the review, a specific research question was developed: What types of exercise interventions have been prescribed for individuals with hemophilia, and how do they impact mobility and bleeding outcomes? This question was formulated to capture both the type and effects of exercise interventions in hemophilia populations. By narrowing the focus to studies assessing mobility and bleeding outcomes, authors aimed to identify interventions that specifically target these areas. The research question directed the entire review process, from the identification of relevant studies to data synthesis and extraction.

## Eligibility criteria

Defining eligibility criteria were a critical step in ensuring inclusion of studies that were directly relevant to the review question. Studies were included with the following criteria:

1. Population: Studies had to focus on individuals with hemophilia, regardless of age or severity of the condition. Studies that included a mixed population with other bleeding disorders were excluded unless the results for hemophilia patients were reported separately
2. Intervention: Studies were included if they described exercise interventions explicitly designed or prescribed

for individuals with hemophilia. Interventions could vary from resistance training (RT) to aerobic exercises, physical therapy, and structured exercise programs

3. Outcomes: Studies had to evaluate outcomes related to mobility, bleeding frequency, or other relevant health parameters associated with exercise prescription in hemophilia. Studies that only focused on QoL, psychosocial outcomes, or other unrelated outcomes were excluded
4. Study Design: Randomized controlled trials (RCTs), cohort studies, case-control studies, case series, case reports, and reviews were included to capture a broad scope of evidence. Gray literature and studies that were not peer-reviewed were excluded
5. Language and Date: Studies published in English were included. No date restriction was applied to ensure a comprehensive view of the literature over time.

These criteria were set to ensure a balance between inclusiveness and relevance, allowing for a thorough review of the interventions and outcomes pertinent to the hemophilia population.

### Literature search strategy

A comprehensive and systematic search strategy was employed to locate relevant studies across multiple databases, including PubMed, Scopus, Web of Science, and CINAHL. A combination of keywords and MeSH terms was used to increase the sensitivity of the search. Key terms included "hemophilia," "exercise prescription," "mobility," "bleeding risk," "physical therapy," and "rehabilitation." Boolean operators (AND, OR) were utilized to combine terms and refine results.

A reference management software was used results were compiled in, and duplicates were removed. In addition, a manual screening of reference lists in the included articles was performed to capture relevant studies that may have been missed during the database search.

### Selection of studies

The selection process of studies involved two reviewers who independently screened abstract and titles against the eligibility criteria. After that a full-text review of articles was done that met the initial screening criteria. The two reviewers compared findings after each screening stage, and any disagreements were resolved through discussion. When discrepancies could not be resolved, a third reviewer was consulted to achieve consensus.

The screening process was designed to ensure rigorous selection of studies that directly addressed the research question. This two-step screening allowed for a more

systematic and objective identification of relevant literature, reducing the risk of selection bias.

### Data extraction

To ensure consistency a standardized data extraction form was developed and completeness in capturing relevant study details. The data extraction form included fields for the following information:

- Study characteristics: Information on authors, year of publication, country, and study design
- Participant details: Sample size, age range, severity of hemophilia, and other relevant demographics
- Intervention characteristics: Type, duration, intensity, and frequency of exercise intervention
- Outcomes: Measures of mobility (e.g. gait speed, range of motion [ROM]), bleeding outcomes (e.g. frequency of bleeding episodes, joint bleeds), and other health parameters where applicable
- Conclusion: Summary of the main findings related to the impact of exercise on mobility and bleeding risk.

Two reviewers independently extracted data, and a third reviewer checked all entries for accuracy and consistency. The standardized form helped ensure that the extraction process was both comprehensive and systematic, allowing for a clear overview of study designs, interventions, and outcomes.

### Data analysis and synthesis

Given the heterogeneity of studies in terms of study design, intervention type, and outcome measures, a qualitative synthesis was chosen. Data were analyzed thematically, focusing on patterns related to types of exercise interventions and their effects on mobility and bleeding risk in individuals with hemophilia. The thematic synthesis allowed for identification of the main types of exercise interventions – such as RT, aerobic exercise, and physical therapy – and their respective impact on mobility and bleeding frequency. Results were synthesized to provide a descriptive overview of the types of exercise prescribed for hemophilia patients, including their potential benefits and risks. A narrative approach was employed to summarize findings, as the data did not support a quantitative meta-analysis. Review Manager (RevMan) is Cochrane's software was used to manage data, conduct statistical analyses, and generate forest plots, offering a user-friendly interface to streamline the review process and ensure methodological rigor.<sup>[20]</sup>

### Quality assessment

Although quality assessment is not always necessary in scoping reviews, it was performed in this study to provide context regarding the reliability and rigor of included studies. PEDro scale was used to assess each study's methodological rigor.<sup>[21]</sup>

## Results

### Study selection

A total of 1496 records were identified through electronic databases and registers (1494 from databases and 2 from registers). After removing 596 duplicates, 47 reports were assessed for eligibility. Out of these, 40 reports were excluded based on specific criteria: 10 had an incorrect study design, 15 were case reports, 8 demonstrated insufficient methodology, 3 were news articles, and 4 had demographics that did not meet inclusion criteria. Ultimately, 7 studies met all the criteria and were included in the review, forming the basis for further analysis and interpretation [Figure 1]. Risk of bias graph and risk of bias summary are shown in Figures 2 and 3 RevMan (Review Manager) version 5.4.1 is developed by Cochrane, headquartered in London, United Kingdom.

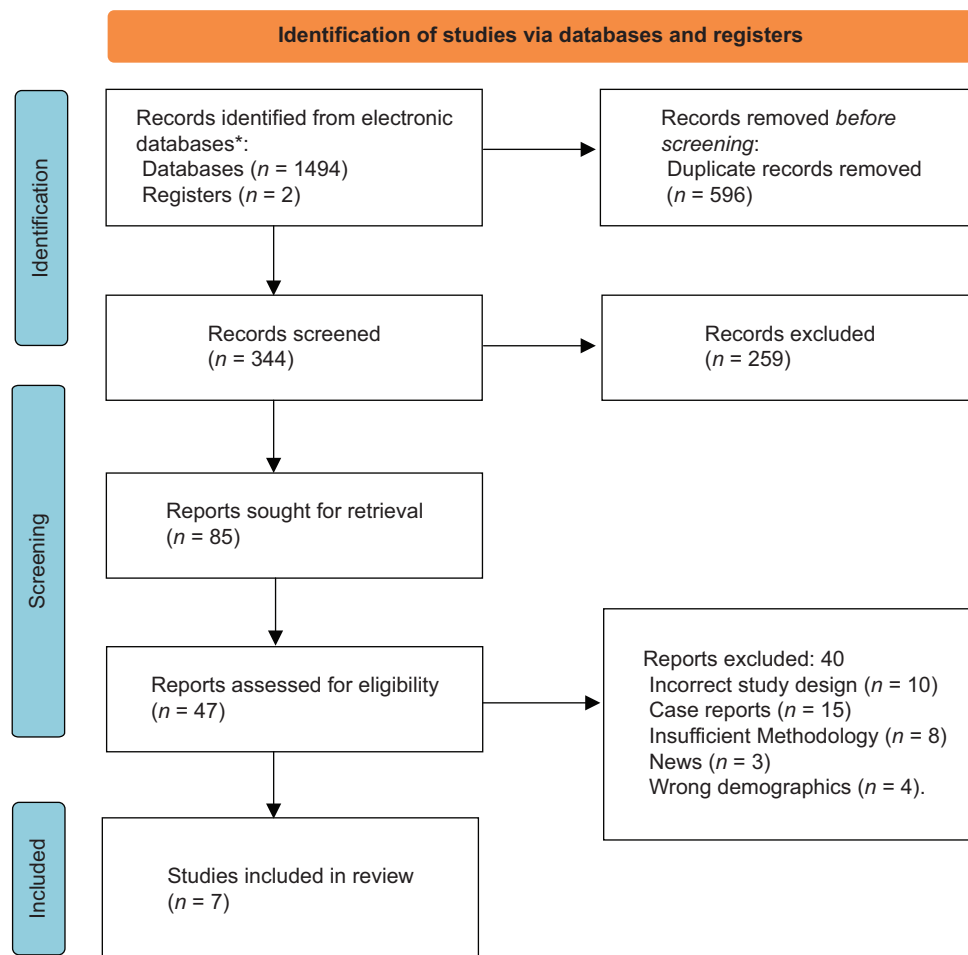
### Key intervention outcomes

An interaction was noted in self-efficacy ( $P = 0.049$ ), exercise adherence ( $P = 0.045$ ), and knee extension strength ( $P = 0.008$ ), indicating different changes between the groups. Main effects were found in exercise

adherence, knee extension strength and ROM, ankle dorsiflexion ROM, Modified Functional Reach Test (mFRT), and 10-m gait time (all  $P < 0.05$ ) from baseline to postintervention. The self-monitoring group showed significantly higher self-efficacy ( $P = 0.018$ ) and exercise adherence ( $P = 0.000$ ) compared to the control, with no differences in physical activity. Their monitoring rate reached 90.3% (62.5%–100%), and no significant changes in pain or bleeding frequency occurred.<sup>[22]</sup>

### Effects of resistance training

On terms of short-term RT after 6 weeks, both the RT and RT pulsed electromagnetic fields resistance training with pulsed electromagnetic fields (RTPMF) groups demonstrated a significant increase in muscle strength (measured by one repetition maximum) for exercises including chest press, shoulder press, scapular retraction, hip flexion/extension/abduction, and knee extension. However, the improvements in these exercises did not significantly differ between the RT and RTPMF groups ( $P > 0.05$ ). At baseline, there were no significant differences in serum measurements among the four groups [Table 1]. Following the 6-week intervention,



**Figure 1:** PRISMA Flow diagram of study selection in review. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71



the absolute change in serum bone-specific alkaline phosphatase levels increased in the RT, RTPEMF, and pulsed electromagnetic fields groups (mean  $\pm$  standard error of the mean:  $25.41 \pm 14.40$ ,  $15.09 \pm 5.51$ , and  $3.23 \pm 5.48$  U/L, respectively) and decreased in the control group ( $-4.73 \pm 2.93$  U/L). These increases were significant in the RT and RTPEMF groups when compared to the control group ( $P = 0.01$  and  $P = 0.05$ , respectively). Serum N-terminal cross-linking telopeptide of collagen type I did not show a significant change in any group. Postintervention, there were also no significant differences among the groups in calcium and phosphorus levels. In addition, there was no significant change in the total alkaline phosphatase level across groups, although in the RT group, this enzyme showed a significant increase compared to baseline ( $P = 0.03$ ).<sup>[23]</sup>

### Ankle arthropathy outcomes

In treating ankle arthropathy in hemophilia, pain, ROM, and gastrocnemius muscle strength and circumference were assessed pretreatment, posttreatment, and after 6 months. Group TM showed significant gains ( $P < 0.05$ ) in muscle circumference and pain reduction, with a marginal strength improvement ( $P = 0.083$ ). Group E improved only in muscle circumference, while the control group showed no change. At 6 months, Group TM maintained pain, strength, and circumference benefits, with a marginal increase in dorsal flexion ( $P = 0.083$ ). Group E maintained muscle circumference improvements, and the control group remained unchanged.<sup>[24]</sup> Aquatic Exercise Therapy is increasingly recognized for its benefits in enhancing muscle strength and joint ROM in hemophilia patients.

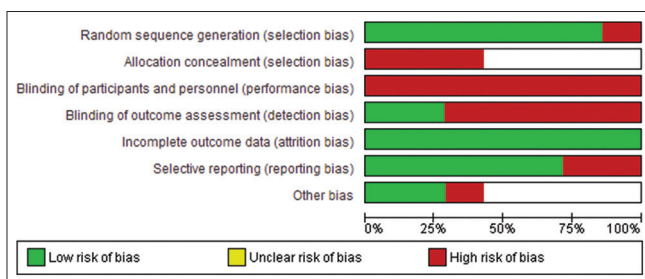


Figure 2: Risk of bias graph

Due to the buoyancy of water, it reduces joint stress and minimizes the risk of bleeding episodes, a common concern in hemophilia.<sup>[25,26]</sup>

### Exercise impact on bone health

In a study comparing mild versus moderate-intensity aerobic walking exercise on bone metabolism markers and hand grip strength in patients with moderate Hemophilia A, the moderate exercise group showed a 32.1% increase in serum calcium levels and a 24.8% improvement in hand grip strength, along with a 22.7% decrease in parathyroid hormone levels. In contrast, the mild exercise group demonstrated a 15.1% increase in serum calcium, a 15% increase in hand grip strength, and a 10.3% reduction in parathyroid hormone. Both groups experienced significant



Figure 3: Risk of bias summary

Table 1: Serum measurements across the four groups<sup>[23]</sup>

Components	RT Group		RTPEMF Group		PEMF group		Control group	
	Baseline	Post Intervention	Baseline	Post Intervention	Baseline	Post Intervention	Baseline	Post Intervention
BALP (U/L)	50.5 $\pm$ 10	75.9 $\pm$ 42.5	38.7 $\pm$ 14.6	53.8 $\pm$ 12.5	51.5 $\pm$ 13.9	54.7 $\pm$ 20.7	47.3 $\pm$ 16.3	42.5 $\pm$ 11.9
NTX (nM)	4.3 $\pm$ 2.5	4.1 $\pm$ 2.9	3 $\pm$ 1.2	3 $\pm$ 0.9	3.3 $\pm$ 1.5	3 $\pm$ 1.0	3.8 $\pm$ 1.4	3.7 $\pm$ 1.4
tALP (U/L)	236 $\pm$ 65	249 $\pm$ 65	239 $\pm$ 42	242 $\pm$ 43	232 $\pm$ 57	247 $\pm$ 76	238 $\pm$ 32	240 $\pm$ 45
Ca (mg/dL)	9.3 $\pm$ 0.3	9.5 $\pm$ 0.2	8.7 $\pm$ 0.3	8.8 $\pm$ 0.2	9.4 $\pm$ 0.4	9.5 $\pm$ 0.4	9.0 $\pm$ 0.4	9.0 $\pm$ 0.4

\*RT, Resistance training; RTPEMF, Resistance Training with Pulsed Electromagnetic Fields; PEMF: Pulsed Electromagnetic Fields; NTX, N-terminal cross-linking telopeptide of collagen type I; BALP, bone-specific alkaline phosphatase; tALP, total alkaline phosphatase; Ca, calcium

**Table 2: Summary of included studies in the review showcasing demographic details and study characteristics**

Author (year)/ research outline	Objective	Sample size	Procedure	Mean age of participants	Conclusion
Goto M <i>et al.</i> (2014) <sup>[22]</sup> /a prospective, controlled, randomized nonblind, comparative study	Impact of self-monitoring home exercise routines for individuals with hemophilia	32	Both groups received personalized exercise guidance to enhance knee function through physical activity. The self-monitoring group was provided with materials, including an activity tracker and a feedback system, enabling them to share updates via the internet and mobile phone. Self-monitoring involved tracking exercise adherence, physical activity levels, bleeding history, and coagulation factor injections	Self-monitoring group - 41.8±8.6 Control group - 43.9±10.7	Home exercise enhanced physical function in hemophiliacs without raising bleeding frequency or pain, and a self-monitoring program may improve exercise adherence, self-efficacy, and knee extension strength
Parhampour B <i>et al.</i> (2013) <sup>[23]</sup> /randomized controlled trial	To evaluate the impact of short-term resistance training and pulsed electromagnetic fields on bone metabolism and joint function in hemophilia patients with osteoporosis	48	The RT group completed 30–40 min of resistance exercises with a placebo pulsed electromagnetic field treatment. The RTPMF group performed the same exercises with fewer repetitions, alongside 30 min of pulsed electromagnetic field exposure. The PEMF group received 60 min of pulsed electromagnetic field exposure at 30 Hz and 40 Gauss	28.23±7.9	Resistance training is beneficial for enhancing bone formation and joint function in patients with severe hemophilia A with osteoporosis
Cuesta-Barriuso R (2014) <sup>[24]</sup> /randomized clinical study	To evaluate the effectiveness of manual therapy and educational physiotherapy in managing ankle hemophilic arthropathy	31	The two physiotherapy programs included one focused on manual therapy with joint traction, passive stretching of the gastrocnemius muscles, and exercises targeting muscle strength and proprioception (manual therapy group), and the other involving educational sessions along with home exercises (educational group). The study duration was 12 weeks	Manual therapy group - 35.36±13.06 Education group - 33.4±14.87 Control group - 37.1±11.59	Manual therapy treatment led to an increase in gastrocnemius circumference and a reduction in pain in patients with ankle hemophilic arthropathy
Feldberg G <i>et al.</i> (2021) <sup>[25]</sup> /single-centre prospective interventional study	The impact of aquatic exercises on enhancing functional capacity in these patient	47	Hydrotherapy protocol following the Halliwick technique was implemented, with patients undergoing therapy in a 9 m <sup>2</sup> pool maintained at a thermoneutral temperature of 33°C–34°C	Swimming - 12.45±5.08 Hydrotherapy - 18.27±11.06	The results indicated that both swimming and hydrotherapy improved physical health in hemophilia patients, but hydrotherapy significantly boosted functional capacity
Von Mackensen S <i>et al.</i> , 2012 <sup>[26]</sup> /randomized controlled trial	To assess how regular aqua-training affects HRQoL, physical performance, bleeding rates, factor use, and orthopedic status in adults with hemophilia over 12 months compared to a nonparticipating control group	28	Patients in the WATERCISE group participated in a 1-h weekly aqua-training program for 12 months, while the control group did not participate	Swimmers - 42.54±13.5 Controls - 39.07±12.3	Aqua-training (WATERCISE) has a beneficial effect on patients with hemophilia
Al-Sharif FA <i>et al.</i> (2014) <sup>[27]</sup> /randomized controlled trial	Impact of mild to moderate intensity treadmill walking on bone metabolism markers and hand grip strength in males with moderate hemophilia A	50	Group A participated in moderate-intensity aerobic exercise training, while Group B engaged in mild-intensity aerobic exercise training	Group A - 38.14±8.32 Group B - 37.97±9.15	Treadmill-based moderate-intensity aerobic exercise training is effective in enhancing bone metabolism markers and hand grip strength in male patients with hemophilia A

Contd...

**Table 2: Contd...**

Author (year)/ research outline	Objective	Sample size	Procedure	Mean age of participants	Conclusion
Cuesta-Barriuso R <i>et al.</i> (2014) <sup>[26]</sup> /randomized controlled trial	Study aimed to assess the effectiveness of two physiotherapy approaches in patients with untreated hemophilic ankle arthropathy	9	Group A - passive mobilization technique and stretching Group B - manual orthopedic therapy	35.7±11.9	Both physiotherapy treatments enhanced the range of motion and reduced pain in patients with ankle arthropathy. No instances of hemarthrosis were observed during the treatment or follow-up phases

RTPEMF=Resistance training with pulsed electromagnetic fields, PEMF=Pulsed electromagnetic fields, WATERCISE

increases in serum calcium and hand grip strength, with significant decreases in parathyroid hormone.<sup>[27]</sup>

### Manual therapy benefits in hemophilia

Manual therapy has shown positive effects on ankle hemophilic arthropathy. Following treatment, Group A showed significant improvements ( $P < 0.05$ ) in plantar and dorsal flexion, eversion, inversion, pain perception, and QoL. Group B also improved in plantar and dorsal flexion, inversion, and eversion ( $P < 0.05$ ). At a 6-month follow-up, both groups maintained these improvements, with no significant changes in ROM or QoL. Both groups experienced further reductions in pain perception ( $P < 0.05$ ) at follow-up, and no ankle hemarthrosis occurred during treatment or follow-up.<sup>[28]</sup> A detailed summary of included articles is summarized in Table 2 and methodological assessment by PEDro scale is tabulated in Table 3.

## Discussion

Exercise, as a carefully controlled intervention, appears to offer substantial benefits in improving joint stability, muscle strength, and overall physical functioning, which are essential in reducing both joint bleeding episodes and the functional impairments often associated with hemophilia. These findings align with emerging perspectives in hemophilia care, which advocate for a multidimensional approach incorporating physical activity as a core component of treatment to promote independence and QoL.

### Benefits of exercise in hemophilia

The review revealed that strength and flexibility exercises, low-impact aerobic activities, and proprioceptive training are generally well-tolerated and confer several benefits without exacerbating bleeding risk.<sup>[12,17,28]</sup> Studies consistently report improvements in joint health and muscular support around joints, particularly the knees, ankles, and elbows—common sites for hemophilia-related complications.<sup>[29-31]</sup> Enhanced joint stability through targeted strengthening is essential in mitigating bleeding risks, as stronger muscles can

better absorb mechanical forces and decrease the strain on joints.<sup>[32]</sup>

Furthermore, improved cardiovascular fitness and endurance from aerobic exercise may reduce fatigue, which can enhance daily functional capacities and reduce fall risk.<sup>[33]</sup> Flexibility and balance training contribute positively by preserving ROM, improving postural control, and decreasing the likelihood of injury, which is critical for people with hemophilia who are prone to joint bleeds due to minor traumas or repetitive use.<sup>[34,35]</sup>

### Safety and monitoring in exercise prescription (risk management strategies)

Exercise prescription in hemophilia requires personalized adjustments and close monitoring to avoid adverse events, especially for patients with severe forms of the disorder.<sup>[36]</sup> The literature emphasizes that proper supervision, ideally by a trained physiotherapist or a hemophilia-specialized healthcare provider, is necessary to ensure safety, particularly during initial training phases.<sup>[37,38]</sup> Regular assessment of joint health and bleeding history is advised to tailor exercise programs, allowing adaptations that can accommodate disease progression or response to treatment.<sup>[39,40]</sup> In addition, prophylactic factor replacement therapy was highlighted as a cornerstone in facilitating safe participation in physical activities. Prophylaxis helps to maintain a baseline level of clotting factors, reducing the risk of spontaneous bleeding episodes and making exercise a safer option for patients with hemophilia.<sup>[41,42]</sup>

### Psychosocial and quality of life improvements

Besides physical health benefits, engagement in regular exercise has demonstrated substantial positive effects on mental health and overall QoL among individuals with hemophilia.<sup>[11,43]</sup> Patients participating in exercise programs report enhanced self-efficacy, reduced anxiety related to movement, and improved social interaction.<sup>[13,44]</sup> As hemophilia often imposes limitations on physical activities, structured exercise interventions can provide

**Table 3: Evaluation of the methodological quality of the included studies**

Author (year)	PEDro criteria**											Total score
	1	2	3	4	5	6	7	8	9	10	11	
Goto M <i>et al.</i> (2014) <sup>[22]</sup>	1	1	0	1	0	0	0	1	1	1	1	7
Parhampour B <i>et al.</i> (2013) <sup>[23]</sup>	1	1	0	1	0	0	1	1	1	1	1	8
Cuesta-Barriuso R (2014) <sup>[24]</sup>	1	1	0	1	0	0	0	1	1	1	1	6
Feldberg G <i>et al.</i> (2021) <sup>[25]</sup>	1	0	0	1	0	0	0	1	1	1	1	6
Von Mackensen S <i>et al.</i> (2012) <sup>[26]</sup>	1	0	0	1	0	0	0	1	1	1	1	6
Al-Sharif FA <i>et al.</i> (2014) <sup>[27]</sup>	1	1	0	1	0	0	0	1	1	1	1	7
Cuesta-Barriuso R <i>et al.</i> (2014) <sup>[28]</sup>	1	1	0	1	0	0	1	1	1	1	1	8

\*\*1. Clearly defined eligibility criteria, 2. Randomized allocation of participants to groups, 3. Concealment of group allocation, 4. Baseline equivalence of groups, 5. Blinding of all participants, 6. Blinding of all therapists administering the interventions, 7. Blinding of all assessors measuring at least one primary outcome, 8. Assessment of at least one primary outcome in over 85% of initially allocated participants, 9. Participants received their assigned treatment or control condition, or data for at least one primary outcome was analyzed, 10. Statistical comparisons between groups, including point estimates, 11. Variability measures for at least one primary outcome. PEDro=Physiotherapy evidence database

a controlled environment where patients feel secure and gain confidence in their physical capabilities.<sup>[45,46]</sup> This reduction in activity-related fear is crucial, as it addresses the often-overlooked psychological burden of living with hemophilia, fostering a sense of normalcy and inclusivity.

### Role of patient education and multidisciplinary collaboration

Patient education is crucial in empowering individuals with hemophilia to understand the benefits and risks of exercise, adhere to tailored regimens, and recognize early signs of joint stress or bleeding. Multidisciplinary collaboration, involving physiotherapists, hematologists, and caregivers, ensures comprehensive care by integrating medical oversight with personalized exercise planning, enhancing mobility while minimizing bleeding risks and complications.

### Gaps in research and limitations of current evidence

Notably, there is a lack of large-scale, RCTs focusing on the long-term effects of specific exercise types on bleeding risk and joint outcomes in hemophilia. Most existing studies are small-scale, limiting the generalizability of their findings. Furthermore, there is limited research on the optimal frequency, intensity, and duration of exercise that balances efficacy with safety, particularly for those with severe hemophilia and recurrent joint bleeds. Another gap is the underrepresentation of certain demographic groups, such as older adults with hemophilia and those from diverse socioeconomic backgrounds, whose access to safe exercise facilities and specialized care may be limited.

### Future Directions and Recommendations

Future research should prioritize high-quality RCTs that explore specific exercise protocols for hemophilia patients of varying severity levels. Longitudinal studies examining the impact of consistent, supervised exercise

on joint integrity and bleeding frequency over extended periods would also be beneficial. Such studies could provide more definitive evidence regarding the safety and efficacy of exercise in this population. In addition, the development of standardized exercise guidelines for hemophilia patients is essential to ensure safe and effective interventions. Collaboration between hematologists, physiotherapists, and exercise scientists could facilitate the creation of tailored exercise prescriptions that address both the physical and psychological needs of hemophilia patients. Guidelines should consider factors such as age, severity of hemophilia, joint status, and previous bleeding history.

### Conclusions

The present scoping review highlights the therapeutic potential of exercise in enhancing mobility, improving QoL, and reducing bleeding risk among hemophilia patients. While promising, current evidence remains limited, underscoring the need for more rigorous research and the development of standardized, evidence-based exercise protocols. As a nonpharmacologic intervention, exercise can play an invaluable role in holistic hemophilia management, complementing pharmacological treatments to improve physical, mental, and social well-being.

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### Conflicts of interest

There are no conflicts of interest.

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