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REVIEW ARTICLE

A clinical practice guideline for primary care physiotherapy in patients with haemophilia

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Abstract

Introduction: As a result of centralisation of haemophilia care to a limited number of intramural settings, many persons with haemophilia have to travel long distances to attend their haemophilia specialised treatment centre. However, regular physiotherapy treatment can be provided by primary care physiotherapists in the person's own region. Due to the rarity of the disease most primary care physiotherapists have limited

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experience with this population. This study aims to provide a clinical practice guideline for primary care physiotherapists working with persons with bleeding disorders.

Method: A list of the most urgent key-questions was derived from a previous study. Literature was summarised using the grading of recommendations assessment, development, and evaluation (GRADE) evidence-to-decision framework. Recommendations were drafted based on four 90 min consensus meetings with expert physiotherapists. Recommendations were finalised after feedback and >80% consensus of all stakeholders (including PWH, physiotherapists, haematologists and the corresponding societies).

Results: A list of 82 recommendations was formulated to support primary care physiotherapists when treating a person with a bleeding disorder. These recommendations could be divided into 13 categories: two including recommendations on organisation of care, six on therapy for adult patients with bleeding disorders and five on therapy adaptations for paediatric care. Therapy recommendations included treatment after a joint- or muscle bleed, haemophilic arthropathy, chronic synovitis, non-haemophilia related conditions and orthopaedic surgery.

Conclusion: An evidence-based practice guideline, based on current evidence from literature and clinical expertise, has been developed for primary care physiotherapists treating a person with haemophilia. To improve care, the recommendations should be implemented in daily practice.

KEYWORDS
clinical practice guideline, haemophilia, physical therapy

1 | INTRODUCTION

Haemophilia is a rare congenital disease which affects a little over one in 10,000 individuals.[1,2] The disease leads to an increased bleeding tendency after surgery, easy bruising and an increased risk of musculoskeletal bleeds.[3] The majority of all bleeds in patients with moderate and severe haemophilia develop in the joints and muscles.[4] As a result of recurrent joint bleeds, a chronic joint disease known as haemophilic arthropathy may develop over time.[5,6] These musculoskeletal manifestations require the involvement of physiotherapists in the multidisciplinary care for persons with haemophilia (PWH) to maintain the desired level of physical functioning.[7] Physiotherapists are involved in rehabilitation after a bleed or surgery, counselling and coaching on sports activities and physical activity, and prevention of musculoskeletal complaints in the long-term.[7] Furthermore, access to physiotherapy treatment is reinforced by the most recent World Federation of Haemophilia (WFH) guideline and the European principles of care for physiotherapy provision in persons with bleeding disorders[8,9]

To enable centres to build more expertise in the management of the disease, treatment for haemophilia in Europe is concentrated in a haemophilia treatment centre (HTC) or a haemophilia comprehensive care centre (HCCC).[10] Access to physiotherapy is a criteria to become a HCCC.[10] As a result of centralisation of haemophilia care, many persons with haemophilia have to travel long distances to attend their treatment centre. In order to overcome this barrier, primary care physiotherapy (i.e., every physiotherapist working outside an HTC) in collaboration with the HTC, can be a realistic alternative for the provision of regular physiotherapy treatment.[9] However, a recent study evaluating the situation in the Netherlands revealed that providing primary care physiotherapy treatment to people with bleeding disorders is challenging due to the rare nature of the disease.[11] Between 37.5% and 43.8% of the primary care physiotherapists who had previously treated a person with haemophilia reported they lacked sufficient knowledge about the bleeding disorder.[11] In addition, 32.1% of persons with haemophilia who had been treated by a physiotherapist in the past felt that their primary care physiotherapist lacked sufficient knowledge about the disease.[11]

The main recommendation to improve primary care physiotherapy for persons with haemophilia is to provide primary care physiotherapists with a clinical practice guideline with general information and guidance about treatment of persons with bleeding disorders.[11] A clinical guideline for physiotherapists working with persons with bleeding disorders in an HTC is already available.[12] However, a specific guideline for primary care physiotherapists is needed, as their role in haemophilia treatment and their background knowledge about the disease are different. The aim for this study is to develop a clinical practice guideline for primary care physiotherapists treating persons with bleeding disorders.

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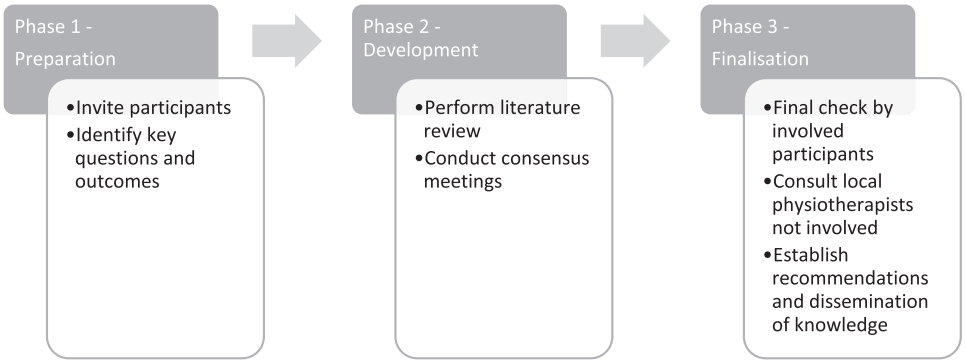

FIGURE 1 Phases of guideline development according to AQUA guidelines.

2 | METHODS

This clinical practice guideline was developed following the GRADE methodology.[13–15] In addition, the authors followed the AQUA guidelines developed by the Dutch National Health Care Institute and the guideline methodology document of the Royal Dutch Society for Physical Therapy.[16,17] The PRISMA reporting guideline was followed during writing of the manuscript.[18] Given the rare nature of the disease, the authors anticipated for a low number of studies and studies with low quality of evidence. To address these limitations, other study designs were included when information from randomised controlled trials or non-randomised controlled trials was lacking. The GRADE approach was applied when sufficient clinical trials were available. The development of the clinical practice guideline consisted of three phases: preparation, development, and finalisation of recommendations (see Figure 1).

2.1 | Participants

Expert physiotherapists and other stakeholders were invited to participate. Expert physiotherapists were eligible if they had more than 5 years working experience with persons with haemophilia in an HCCC. Physiotherapists from the United Kingdom, Ireland, Norway, Sweden and Belgium were invited to take part because the organisation of (physiotherapeutic) care and the treatment of haemophilia in these countries is similar to the situation in the Netherlands. Invited stakeholders included relevant Dutch stakeholders: persons with haemophilia or carers of a child with haemophilia (striving towards maximum variation regarding age and health problems), primary care physiotherapists working with adults, primary care paediatric physiotherapists and representatives of the Dutch Haemophilia Patient Society, the Dutch Society of Haemophilia Treating Physicians and the Royal Dutch Society for Physiotherapy. Persons with haemophilia and carers of a person with haemophilia were eligible to participate if they had accessed physiotherapy treatment for a haemophilia related problem at least once. Primary care physiotherapists were eligible if they had experience with treating at least one person with haemophilia.

2.2 | Phase 1: Preparation—Key questions and outcomes

To guide the development process, key questions and most relevant outcomes were determined. First, key questions were extracted from responses to a survey held in the context of previous research. Subsequently, key questions and outcome measures were finalised based on a consensus approach including a consensus meeting with the expert physiotherapists and a digital survey to both the expert physiotherapists and the stakeholders.

Key questions were included if at least 80% of all participants rated them as important on a 5-point Likert scale. Outcomes were included if at least 80% of all participants rated them as important or critical (i.e., at least four or higher on the nine-point Likert scale), with a maximum of eight outcomes per indication.

2.3 | Phase 2: Development

Development of recommendations is an iterative process based on a systematic literature review and expert and stakeholder consensus during multiple steps.

2.3.1 | Literature review

A total of five literature searches were performed for the following conditions (1) haemophilic arthropathy, (2) joint bleeding, (3) muscle bleeding, (4) chronic synovitis and (5) orthopaedic surgery. Every search string combined the specific condition with physiotherapeutic treatment modalities (e.g., exercise therapy, manual techniques, education). The Electronic Medline database was systematically searched for relevant literature. The search strings used were developed in consultation with an experienced librarian (PW). The full search string for each condition is presented in **Supplementary file 1**. In addition, studies on pathophysiology of joint bleeding and blood related joint changes, guidelines regarding physiotherapy in Osteoarthritis (OA) and muscle bleeds in athletes (without bleeding disorder) were consulted.

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As the research team anticipated for limited evidence, all relevant studies were included regardless of publication date or methodological quality. The research team preferably used data from (randomised) clinical trials. If such studies were unavailable, or if they were only available to a limited extent, the research team also included studies with other study designs (e.g., case studies, expert opinion or preclinical studies).

Data on study design, participants included and study results was extracted by one of the researchers (JB). Trials were summarised in a forest plot using RStudio (version 4.3.1). If no quantitative data was available (e.g., expert opinion or survey based research) a qualitative synthesis of literature was presented. Data was summarised per condition by one researcher (JB). When multiple clinical trials with homogeneous intervention and outcomes data were available a risk of bias analysis was performed, and results were presented using meta-analysis of risk ratio (in case of bleed development) or standardised mean difference (in all other outcome measures).

2.3.2 | Expert consensus

A total of four 90-min online consensus meetings were planned with the expert physiotherapists. During these meetings the summarised literature was presented (JB, MT) and discussed by the expert group. All expert consensus meetings were recorded and transcribed using automated software from Microsoft Teams®. The original audio files were used to check the transcription. One researcher (JB) analysed the consensus meetings, highlighted relevant comments after every meeting and drafted initial recommendations in discussion with MT and MP. The draft recommendations were first shared with the expert physiotherapists using the electronic data capture software Castor. Expert physiotherapists were asked for feedback on the content and text of each individual recommendation. Consensus was reached when at least 80% of expert physiotherapists indicated that the recommendation could be included without changes or only textual changes.

2.3.3 | Stakeholders consensus

Finally, the stakeholder group was requested to provide input on feasibility, useability and clarity of the recommendations. The same data capture software was used and stakeholders were asked to indicate if they wanted to include the statement or if adaptions (textual or content) were needed. Again, a threshold of 80% consensus was used.

2.4 | Phase 3: Finalisation—Determination and development of final products

This final step consisted of combining all recommendations in one comprehensive document. To ensure the recommendations matched the experiences of primary care physiotherapists in daily practice, this final document was shared with primary care physiotherapists not involved in the development of the recommendations. These end-users were asked whether all information was clear and if it was applicable in their situation. In addition, the document was shared with the expert physiotherapists and the stakeholders for a final check and formal approval of the document as a whole.

3 | RESULTS

3.1 | Characteristics of participants

In total 12 physiotherapists with >5 years of experience working in an HCCC agreed to participate. These physiotherapists worked in the Netherlands (4), United Kingdom (3), Ireland (2), Belgium (1), Sweden (1) and Norway (1). Many physiotherapists were involved in care of both children and adults (5), others were only involved in care for either adults (2) or only children (5).

A total of 10 stakeholders participated, including: two persons with haemophilia (aged 22 and 79), one caregiver of a child with haemophilia, two primary care paediatric physiotherapists, two primary care physiotherapists working with adults and representatives from the Dutch Haemophilia Patient Society (1), The Dutch Society of Haemophilia Treaters (1) and The Royal Dutch Society for Physiotherapy (1).

3.2 | Key questions and outcomes

A total of 13 key questions were identified: two on organisation of care, six on treatment in adults with haemophilia and five on children with haemophilia. A total of 26 outcomes in adults and 30 in children were identified as important outcomes to evaluate effect of treatments in haemophilia specific conditions (joint bleed, muscle bleed, chronic synovitis and haemophilic arthropathy). Safety of treatment (i.e., the development of bleeds), ability to perform daily activities and pain were included for both children and adults for all conditions.

3.3 | Literature search and data syntheses

Several literature searches in 2022 and 2023 were performed. A total of 88 studies were included in the development of the guideline; 62 studies were identified by the systematic literature search (17 studies in haemophilic arthropathy,[19–35] 20 in joint bleed,[36–54] 8 in muscle bleed,[40,50,52–57] 10 in chronic synovitis[53,58–66] and 7n in orthopaedic surgery[67–73]). In addition, 11 studies in haemophilic arthropathy without a control group were included[74–84] and 15 other studies (four in haemophilic arthropathy,[85–88] eight in joint bleed,[3,8,89–94] two in muscle bleed[8,95] and one in synovitis[8]). Details about the search strings can be found in **Supplementary file 1**. Details on literature selection is presented in the flowcharts in **Supplementary file 2**. Documents based on the literature were shared with the expert physiotherapists and served as a starting point for the group discussion. Documents shared with the

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expert physiotherapists in preparation of the meetings can be found in **Supplementary file 3**.

3.4 | Recommendations

Based on literature and expert consensus meetings, 81 recommendations were drafted by the research team. Within the subsequent survey, 68 out of 81 reached expert consensus without adaptations. Consensus was reached on 12 recommendations after adjustment by the research team, and one recommendation was the subject of a second discussion at the next meeting. Subsequently, after reaching consensus from the expert physiotherapists, the list of recommendations was sent to the stakeholder group. Of these adapted recommendations, only three out of 82 needed further adaptations to reach consensus by the stakeholders. During the feedback rounds 11 recommendations were added or one recommendation was split into two separate recommendations resulting in a list of total 93 recommendations. The list of recommendations per key question is included in Table 1.

4 | DISCUSSION

An evidence-based consensus clinical practice guideline has been developed to support primary care physiotherapists treating individuals with haemophilia. A comprehensive list of recommendations on 13 relevant key questions were developed. These recommendations are based on information from 88 different studies, and with input from 12 expert physiotherapists and 11 stakeholders. This clinical guideline will enhance primary care physiotherapists to provide high quality care for persons with haemophilia.

In the past, a guideline document for physiotherapists working with people with inherited bleeding disorders in a clinical setting was developed by the Canadian Physiotherapists Working Group.[12] Furthermore, the WFH guideline describes the multidisciplinary care for persons with bleeding disorders, including general statements regarding physiotherapy.[8] In comparison with these earlier statements, in our study we go into detail about the important considerations in the therapeutic process specific for primary care physiotherapist. We provide large amount of detail on different phases of recovery after a bleed, provide recommendations on therapy in case of chronic synovitis and specify which treatment modalities are not recommended. This should provide guidance to primary care physiotherapists with limited experience in treating persons with haemophilia, which would enable them to provide high quality care to patients with this condition. In the current study statements on diagnostic procedures applied by physiotherapists (e.g., diagnosis of a bleed or haemophilic arthropathy) were not included, as the expert group agreed that the diagnostic process should be performed within the HTC and recommendations on diagnostics was therefore deemed less relevant for physiotherapists working outside the HTC.

Methodology in the current study was in concordance with national and international standards.[13–17] The design enabled the research team to combine available information from the existing literature on physiotherapy treatments and the clinical experience of physiotherapists with extensive knowledge and experience of treating adults and children with haemophilia. This allowed the researchers to make recommendations where information from the literature was lacking. As both the expert physiotherapists and the stakeholder group were asked for formal approval of all statements, there is certainty that the recommendations derived through this comprehensive process are supported by more than 80% of all participants involved. Furthermore, by including all relevant stakeholders in the process of development (i.e., persons with haemophilia, primary care physiotherapists and representatives of the patient association, physicians specialised in haemophilia and physiotherapy association), the practice guideline match experiences in daily practice and should be meaningful to all these relevant stakeholders. The current recommendations are based on the available literature in haemophilia. Nevertheless, the authors believe that in the absence of disease-specific recommendations for VWD and other rare bleeding disorders, the recommendations could also inform physiotherapy treatment for these other bleeding disorders. The recommendations are based on consensus meetings with expert physiotherapists from North-western European countries with access to advanced medical treatment and similar delivery of physiotherapy in primary care. It is important to note that not all recommendations may be directly applicable to countries with fewer medical resources or different health care systems. Expert physiotherapists and clinicians working in these countries with limited resources should identify whether the recommendations might be applicable to their setting. Furthermore, future efforts could be made to develop specific recommendations for countries with limited resources, using the current study as a starting point.

Several knowledge gaps were identified during the development of the practice guideline. The researchers found that there were multiple randomised trials of physiotherapy for haemophilic arthropathy and recommendations for this condition could largely be based on the results of these trials. However, information from trials of physiotherapy for joint or muscle bleeding or chronic synovitis was limited. Recommendations for these conditions were therefore based on theoretical evidence, Delphi methods and the opinion of the participating expert physiotherapists. Future research should focus on different regimes of joint loading and exercise prescription with close monitoring after a joint or muscle bleeding to confirm current recommendations. For chronic synovitis, future research should focus on optimal joint loading in case of chronic synovitis and should examine which exercise regimen is safe for the affected joint and effective in preventing joint deterioration.

Future steps in relation to this guideline will focus on dissemination. As previous studies in more common musculoskeletal conditions have shown, it is not a given that guidelines will be used in day-to-day practice.[96–100] The Guidelines International Network (GIN) recommends active dissemination of guidelines to raise awareness of their

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TABLE 1 Complete list of practice guideline recommendations.

Organisation of care

Contact with the haemophilia treatment centre

Situation in which contact between the primary care physiotherapist and the HTC is desired.

All conditions

- Before the start of treatment in primary care, if patients with musculoskeletal complaints report to the physiotherapist without a referral (self-referred).
- If the patient has been referred to the primary care physiotherapist for treatment and does not follow the treatment for no reason provided.
- If there is an inexplicable increase in complaints or complaints develop at other locations.
- If there is no improvement in complaints within the expected period and the desired goals have not been achieved.

For specific conditions

Joint bleeding:

- If there is an increase in pain or swelling and/or a decrease in the range of motion.
- If the bleeding does not recover as expected and/or functional ability does not recover to the desired level.
- If there are recovery impeding factors (e.g., fear of movement, catastrophizing, inadequate coping strategies) that cannot be adequately treated in primary care.

Muscle bleeding:

- If neurological symptoms develop during treatment or there is a suspicion of compartment syndrome, **urgent medical attention is required**. Contact the haemophilia treatment centre immediately and refer the patient to the haemophilia treatment centre.
- If there is an increase in swelling or pain and/or a decrease in the range of motion.
- If muscle function does not recover as expected and/or functional ability does not recover to the desired level.
- If there are recovery impeding factors (e.g., fear of movement, catastrophizing, inadequate coping strategies) that cannot be adequately treated in primary care.

Synovitis:

- if there is a suspicion of bleeding, i.e. if there is an increase in swelling, pain and/or reduced range of motion in the affected joint.

Indication to start primary care physiotherapy

Haemophilic arthropathy

Start physiotherapy treatment for haemophilic arthropathy when:

- The patient needs support with joint complaints that lead or might lead to limitations in daily activities and/or participation
- The patient is unable to achieve or maintain a desired level of independent physical functioning without support of a physiotherapist

Joint bleeding

- Consider not starting local physiotherapy treatment during the acute phase after a joint bleed. A first contact with a local physiotherapist can however be made.
- Consider starting physiotherapy in the sub- and post-acute phase in the following circumstances:
  - If additional musculoskeletal injury (e.g. ligament injury) has been diagnosed with the onset of the bleeding.
  - If there is recurrent bleeding in the same joint and a clear haematological cause is ruled out by the HTC
  - In case of abnormal or delayed recovery back to expected physical baseline
  - If there is an underlying motor problem that impedes recovery from the bleeding
  - If the person wants to return to intense sporting activities or heavy physical labour
  - If there is an expectation that the person in question will need more intensive counselling to return to the desired level, for example in the case of psychosocial determinants influencing recovery and/or significant physical limitations.
- Continue primary care physiotherapy treatment until physical function is back to pre-bleeding status and the functional goals set have been achieved.

Chronic synovitis

The goal of the physiotherapy intervention in the treatment of synovitis is to prevent deterioration of the physical condition, without aggravating the inflammation of the synovial tissue. Treatment is not aimed at reducing the synovial inflammation per se. In the following cases, there is an indication for primary care physiotherapy:

If clear deficits in function of the affected joint or surrounding muscles are identified or if there is a general physical deterioration.

- If the patient needs guidance on gradually increasing joint load over time.
- If the patient wants to return to high-intensity/competitive sports and/or other physically demanding activities.

Muscle bleeding

- Consider not starting local physiotherapy treatment during the acute phase after a muscle bleed. A first contact with a local physiotherapist can however be made.
- Consider initiating primary care physiotherapy during the sub- and post-acute phases in the following circumstances:
  - In case of abnormal or delayed recovery back to expected physical baseline
  - If the pre-bleed (muscle) functioning is considered insufficient and there is therefore a need to improve above this level.
  - If the person wants to return to intense sporting activities or heavy physical labour
  - If there is an expectation that the person in question will need more intensive counselling to return to the desired level, for example in the case of psychosocial determinants influencing recovery and/or significant physical limitations.
- Continue primary care physiotherapy treatment until physical function is back to pre-bleeding status and the functional goals set have been achieved.

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TABLE 1 (Continued)

Orthopaedic surgery

- Consider starting primary care physiotherapy in the preoperative phase to be optimally prepared both physically and mentally, to become familiar with post-operative exercises and/or to practice the use of walking aids.
- Start primary care physiotherapy in all persons with haemophilia after orthopaedic surgery for the same indications as in individuals without a bleeding disorder. Take into account the points of attention described in both the pre- and post-operative phases.

Therapy adult

Arthropathy

General recommendations

- Please note that the patient's load capacity might be lower than expected due to more profound joint damage, multiple affected joints or more (chronic) pain compared to individuals of similar age without haemophilia.
  - Adjust therapy to the individual's load capacity by starting at a lower level.
  - Consider including imaging when it is available to understand the extent of the pathology at the joint level, but keep in mind that imaging and the degree of symptoms a person experiences are only related to a limited degree.
  - Aim to gradually increase the intensity of training as the patient's load capacity improves over time.
- Make sure that the (exercise) therapy is aligned with the patient's goals and pay sufficient attention to the patient's motivation.

Therapy for haemophilic arthropathy

- Offer exercise therapy to all patients with haemophilic arthropathy (see Supplementary file 1 for recommendations on frequency, intensity, timing, and type of exercise therapy)
  - Select functional exercises that include (parts of) activities that patients experience difficulties with in their daily lives, such as walking, climbing stairs or rising from a chair. Aim to improve the ability to perform activities and increase participation and link the exercise therapy to a specific goal which is jointly set in agreement with the patient and ensure that the exercises are specific to achieve this goal.
  - Tailor the treatment to the individual patient (e.g. joint status, multi-joint involvement, overall physical fitness and preferences) in a way they are able to fit the activities into daily life and sustain the increased physical activity in the long term.
  - Aim to enhance self-efficacy with exercise therapy and focus on ways to continue physical activity after guidance diminishes over time.
  - Consider hydrotherapy as an alternative to land-based exercises, for example, for patients with a lot of pain or a lot of functional limitations.
  - When following the treatment with coagulation factors prescribed by the haematologists, there are no indications that exercise therapy causes bleeding.
- Consider manual techniques in patients with haemophilic arthropathy only in addition to exercise therapy or to create conditions necessary to start exercise therapy.
  - Do not use high velocity manual techniques in patients with haemophilic arthropathy.
  - When following the treatment with coagulation factors prescribed by the haematologists, there is no indication that the use of low-intensity, low force manual techniques (i.e. fascial therapy, traction, gentle joint mobilisation) causes bleeding. However, keep in mind that these techniques do not encourage self-management and do not improve self-efficacy.
  - Consider contacting the haemophilia treatment centre if there are any doubts about applying certain manual therapy techniques.
- Information provided to the patient about haemophilia should be provided by healthcare professionals working at the haemophilia treatment centre.
  - Contact the physiotherapist at the haemophilia treatment centre to discuss what information has been provided to the patient regarding disease specific information.
- Do not apply any treatments other than the previously described exercise therapy, additional manual techniques or education. Examples of therapies that are not recommended are TENS, taping, dry needling/acupuncture, shockwave, laser and RICE principles.
  - There is limited evidence for a beneficial effect of these other therapies in haemophilic arthropathy.

Joint bleed

Phases of recovery

After joint bleeding, 3 different phases of recovery can be distinguished. As a complication, chronic synovitis can also develop. It should be noted that every phase could have a longer or shorter duration due to differences between individuals.

- *Acute phase (estimated duration 0–72 hours)*:
  The acute phase is the period in which coagulation should be established. During this phase the formed clot is still vulnerable. Treatment goal within this phase is to support coagulation and form a strong clot that is resilient to forces.The acute phase is characterized by a painful joint, swelling and limitations of range of motion. Changes might be subtle and do not always occur to the same extent.
- *Subacute phase (estimated duration 4–21 days)*:
  In the subacute phase some blood might still be present in the joint cavity and the synovial tissue is hypertrophic and vascularized. Treatment goal within this phase is to start mobilization and to balance the risk of complications due to immobilization with the risk of a re-bleed.
  This phase is characterized by diminished pain and an increase in range of motion of the involved joint. The joint may or may not still be swollen and warm during this phase.
- *Postacute phase (estimated duration > 21 days)*:
  During the post-acute phase blood from the joint cavity is cleared and the joint is able to tolerate full loading. During this phase the joint synovium returns to the pre-bleed status (Note—that for some people this may be a return to an already pathologised synovial layer that is chronically hypertrophic). Treatment goal within this phase is to return to pre-bleed activities and participation.
  The post- acute phase is characterized by complete recovery to the situation before the bleed regarding joint range of motion, swelling, warmth and stability.

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TABLE 1 (Continued)

- *Chronic synovitis (recovery > 3 months)*
  In the case of synovial proliferation (hypertrophy and vascularization of the synovial tissue) prolongs after 3 months, this is classified as chronic synovitis. Chronic synovitis is considered a complication after joint bleeding caused by a vicious circle of joint bleeding and synovial proliferation. In chronic synovitis, the joint appears swollen, but usually not tense, is often painless and slightly warm.

General recommendations for joint bleeding

- Ensure that education on pathophysiology and advice around joint loading are in concordance with the recommendations from the haemophilia treatment centre
  - Contact the haemophilia treatment centre to verify what information has previously been provided to the patient regarding the recovery from a joint bleed.
  - Ask whether the patient has had contact with the haemophilia treatment centre after the onset of the bleeding.
- Take personal factors into consideration when applying interventions and make sure the interventions are appropriate for the individual. Take into account, among other things; age, current and previous functioning, multi-morbidity (including multi-joint arthropathy), cognitive ability, and preferences of the individual.
- Monitor the affected joint during and after treatment and after an increase in load and/or activities.
  - Interventions and weight loading should be relatively pain-free (i.e. not cause more pain than before the bleeding in for example arthropathic joints) and not cause an increase in swelling and/or pain afterwards.
- Look for signs of fear of moving or other psychosocial factors which may inhibit recovery after bleeding.

Therapy in the acute phase (estimated duration 0–72 hours):

- Advise to limit the load on the joint as much as possible, for example by using crutches or a wheelchair (at the lower extremity) or wearing a sling (at the upper extremities)
  - Reducing the load lowers the risk of new bleeding and reduces the risk of bleeding-related cartilage damage.
  - Pay sufficient attention to the impact of the bleeding on daily activities and participation.
- Assess whether the pain is bearable for the person with bleeding.
  - Check that the person is able to control the pain with appropriate pain medication in consultation with the HTC.
  - Cooling (for example by ice application) and the use of transcutaneous electrical nerve stimulation (TENS) may be considered during the acute phase.
- Do not apply other forms of therapy (such as manual techniques or exercise therapy) in this phase.

Therapy in the subacute phase (duration approximately 4–21 days):

- Gradually increase the load on the joint as swelling and pain begin to subside, the range of motion increases, and the patient feels comfortable to begin loading the joint.
  - Gradually increasing joint load is essential to prevent complications caused by immobilization while minimizing the risk of new bleeding.
- Start gentle active exercises aimed at improving the range of motion of the affected joint.
  - Consider supporting the active exercises by applying mild mobilization techniques (supported active mobilization).
  - Avoid end-range of movement as there is the risk of impingement of the synovial tissue.
- Provide functional exercises and activities with the aim of preventing unwanted loss of muscle strength and proprioception.
  - Start light with for example isometric exercises and gradually increase load and include more dynamic exercises.
  - At this stage, do not start with explosive or eccentric exercises and avoid maximum load.
  - Ensure that the function of other joints and muscles is maintained so that deterioration due to a prolonged period of immobilization is minimized or prevented.
- If necessary, consider using tape or bandage to support the affected joint.
- Cooling (for example by ice application) and TENS can be considered at this stage for pain relief in patients with a lot of pain.
- Do not apply other treatment modalities (such as massage, dry needling/acupuncture, shockwave, laser) after joint bleeding.
  - These therapies are not supported by scientific evidence, nor are they supported by expert opinion.

Post-acute phase therapy (estimated duration ≥ 21 days):

- Offer functional exercise therapy with the goal of returning to pre-bleeding levels, both in terms of joint status and in terms of activities and participation.
  - Adjust exercise therapy to fit the individual's goals and abilities (current and pre-bleeding). Tailor therapy and advice to the individual situation with the goal of returning to a level of functioning prior to the bleeding.
  - Gradually increase loading, based on swelling, pain, and joint function.
  - Offer exercises to support proprioception/balance when problems are identified in this area.
- Do not apply other treatments (such as dry needling/acupuncture, shockwave, laser) after a joint bleed.
  - These therapies are not supported by evidence, nor have they been supported by expert opinion

Synovitis

General recommendations for chronic synovitis

- Ensure that education about pathophysiology and activities is consistent with the recommendations of the haemophilia treatment centre
  - Contact the haemophilia treatment centre to find out what information has previously been provided to the patient regarding synovitis.
  - Ask if the patient has been in contact with the haemophilia treatment centre about the synovitis.
- Consider personal factors when prescribing interventions and ensure that interventions are appropriate for the individual, taking into account, among others age, current and previous level of functioning, multi-morbidity (including multi-joint arthropathy) and preferences.
- Carefully monitor the affected joint during and after interventions and after an increase in joint load and/or an increase in activity level.
  - Check for swelling, pain and ROM. Since pain and ROM limitation are generally minimal, swelling usually provides the best clinical indication of the level of synovitis.

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TABLE 1 (Continued)

Therapy for chronic synovitis

- In the early stages, reduce joint loading and activity level. As the swelling subsides, the load and activity level can be gradually increased. The level of activity should be monitored and adjusted according to the degree of swelling of the joint
  - Be aware that it can take several months for synovitis to subside. Any increase in activity should be gradually increased and carefully monitored.
- Provide exercise therapy to patients with synovitis aimed at maintaining joint and muscle function of the affected joint and surrounding muscles (e.g., strength and proprioception) as well as general fitness.
- In individual cases, consider cooling (for example by ice application) to reduce pain.
- Consider using tape, braces or enhanced footwear to support the affected joint and prevent recurrent bleeding and synovial impingement.
- Do not apply other treatments (such as massage, dry needling/acupuncture, shockwave, laser).

Muscle bleed

Phases of recovery

After a muscle haemorrhage, 3 phases of recovery can be distinguished. It should be noted that each phase can last longer or shorter due to, among other things, differences between individuals, trauma mechanism and (time to) treatment. In general, intermuscular haemorrhages take less time to recover than intramuscular haemorrhages.

- *Acute phase (estimated duration 0–72 hours)*:
  The acute phase is the period in which the coagulation must take place. During this stage, the clot formed is still vulnerable. The goal of treatment in this phase is to support clotting. This should eventually form a strong clot that can withstand loading.The acute phase is characterized by pain, swelling, and decreased muscle length. In some cases, there is little restriction of movement, little noticeable swelling, and/or little pain, even though there is intramuscular haemorrhage. The extent of the bleeding does not always correspond to the symptoms experienced and may therefore be underestimated. In some cases, a haematoma may also be visible, although this is not always the case.
- *Subacute phase (estimated duration 4–21 days)*:
  In the subacute phase, the bleeding has stopped and a first clot has formed. However, at the beginning of this phase, the clot is still fragile and therefore caution should be exercised with regard to stretching and contraction of the affected muscle. The goal of treatment at this stage is to begin mobilizing and weigh the risk of complications from immobilization against the risk of new bleeding.
  This phase is characterized by an increase in muscle length and reduced pain of the affected muscle. Reduction of swelling will occur within the sub-acute phase, but improvements in this area may lag behind reductions in pain and increases in muscle length.
- *Postacute phase (estimated duration > 21 days)*:
  During the post-acute phase, the blood in the affected muscle is resorbed. Subsequently, muscle length and strength should return to pre-bleeding function. In the post-acute phase, the risk of rebleeding decreases to pre-bleeding status. The goal of treatment in this phase is to return to pre-bleeding activities and participation. If the load capacity of the affected muscle was limited before the bleeding and there is therefore an increased risk of bleeding, it may be necessary to increase the load capacity of the affected muscle beyond the condition before the bleeding.

General recommendations for muscle bleeding

- Ensure that education on pathophysiology and mobilization is in line with the recommendations of the haemophilia treatment centre.
  - Contact the haemophilia treatment centre to find out what information has previously been provided to the patient regarding the recovery from the muscle bleeding.
  - Inquire whether the patient has had contact with the HTC as a result of the onset of the bleeding.
- Take personal factors into account when prescribing interventions. Ensure that interventions are appropriate for the individual, taking into account age, current and previous functioning, multi-morbidity (including multi-joint arthropathy) and preferences, among other factors.
- Check the affected muscle carefully during and after interventions and after an increase in load and/or activities.
  - Interventions and loading should be relatively painless. They should not lead to a decrease in range of motion and/or cause an increase in pain.
- Be aware of possible neurovascular complications that can accompany muscle bleeding
  - Muscle bleeds may be accompanied by injury to peripheral nerves, resulting in a change in sensation and/or motor function (e.g., compression of the femoral nerve in an Iliopsoas haemorrhage).
  - Muscle bleeds can lead to compartment syndrome. The pressure in the affected muscle can be dangerously high, requiring urgent intervention. Calf and forearm muscles are most often affected.
- Look for signs of fear of moving or other psychosocial factors which may inhibit recovery after bleeding.

Therapy in the acute phase (estimated duration 0–72 hours):

- Avoid stretching the muscle and limit contraction (i.e. avoid (functional) movement against resistance) to reduce the risk of new bleeding. Depending on the muscle affected, this can be done using crutches or a wheelchair for lower extremity muscles or a sling for upper extremity muscles.
- Cooling (for example by ice application) or the use of transcutaneous electrical nerve stimulation (TENS) may be considered to reduce pain during the acute phase.
  - These interventions should only be used as a complement to the other recommendations.
- Do not apply other forms of therapy (such as manual techniques or exercise therapy) in this phase.

Therapy in the subacute phase (duration approximately 4–21 days):

- Increase active exercises of the affected muscle gradually and within the pain threshold, at the moment when the muscle length increases, the pain begins to subside and the patient can start using the affected muscle in a comfortable way.
  - Gradually increasing the exercises is essential to prevent the occurrence of complications due to immobilization and improve resorption, minimizing the risk of new bleeding.
  - Consider antagonistic contraction within relatively pain-free limits to relax the affected muscle, using reciprocal inhibition.

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TABLE 1 (Continued)

- Provide functional exercises and activities to prevent unwanted loss of muscle strength and proprioception.
  - Aim to start functional exercises with only mild resistance.
  - Avoid exercises or activities that require high force or high speed of contraction of the affected muscle.
- Cooling (for example by ice application) or TENS may be considered in individual cases for pain relief in patients with a lot of pain at this stage.
- Do not apply massage therapy after a muscle bleeding
- Do not apply a passive stretch to the affected muscle during this phase to avoid a potential new bleed.
- Do not apply other treatments (such as dry needling/acupuncture, shockwave, laser) after a muscle bleeding.
  - These therapies are not supported by evidence, nor have they been supported by expert opinion

Post-acute phase therapy (estimated duration ≥ 21 days):

- Offer Functional Exercise Therapy to return to pre-bleeding levels or a desired higher level of function, activities, and participation
  - Adjust exercise therapy to individual goals and abilities. Tailor therapy and advice based on pain, range of movement and strength.
  - Offer strength training if a problem in muscle strength is identified. Gradually increase the intensity.
  - Apply pain-free stretches during the post-acute phase if a persistent limitation in muscle length is observed after 6 weeks.
  - Conduct coordination exercises when a problem in this area is identified.
- Do not apply other treatments (such as dry needling/acupuncture, shockwave, laser) after a muscle bleeding.
  - These therapies are not supported by evidence, nor have they been supported by expert opinion

Orthopaedic surgery

In general, the physiotherapy treatment in the pre- and postoperative phase of orthopaedic procedures in people with haemophilia is very similar to that in people without a coagulation disorder. However, there are a number of points to consider when treating individuals with haemophilia.

Points of attention in the pre-operative phase

- Be aware that the baseline condition of someone with haemophilia may be lower than that of someone without haemophilia due to arthropathy in multiple joints and/or advanced arthropathy.
  - Because of this lower baseline condition, the result of prehabilitation may not be the same as in people without haemophilia.
  - If a person is unable to improve the function of the joint to be operated on, focus therapy on improving the patient's general fitness and functioning, familiarizing themselves with post-operative exercises, using walking aids, and/or psychological support.
  - Be aware of possible arthropathy in other joints and avoid overloading the lower extremities, including the knees and ankles. Also adjust the choice of walking aids accordingly.

Points of attention in the postoperative phase

- Be aware to problems related to wound healing. Contact the haemophilia treatment centre if you suspect delayed wound healing.
  - In addition to problems that also occur in the general population, such as infection, haemophilia can also cause delayed wound healing.
- People with haemophilia may experience more pain and swelling in the postoperative period than people without haemophilia. This pain may be associated with the occurrence of bleeding. Contact the HTC if there are concerns about the level of pain, if pain is not well tolerated, or if it interferes with therapy.
- Take into account the potential overloading of other joints during rehabilitation. Adjust the load/exercise therapy and the choice of walking aids if necessary.

Synovectomy

Because radiosynovectomy (treatment of joint inflammation with radioactive material) is a less common procedure in the general population, we provide specific recommendations for the postoperative phase after radiosynovectomy.

- Provide advice on return to activities of daily living in the first 2 weeks after radiosynovectomy. Be cautious with active physiotherapy (e.g., resistance exercises or dynamic exercises) during this time.
- After these two weeks, provide exercise therapy aimed at improving joint function and general fitness if any problems have been identified in this area.
- Take into account the recommendations for therapy in chronic synovitis, such as:
  - Gradual increasing joint load and exercise therapy in which swelling is monitored
  - Apply exercise therapy to improve or maintain joint and muscle function.
  - Do not apply other treatments (such as massage, dry needling/acupuncture, Shockwave, Laser).

Non-haemophilia related problems

In general, the treatment of non-haemophilia-related problems (e.g. musculoskeletal disorders of the spine or Osgood Schlatter) in individuals with haemophilia is similar to the treatment of persons without haemophilia. However, there are a number of points that must be taken into account when treating someone with haemophilia.

- Make sure there are no underlying active haemophilia-related symptoms (i.e. bleeding or joint inflammation) when a person with haemophilia refers themselves to primary care physiotherapy with a musculoskeletal problem.
  - If there is a suspicion of an active haemophilia-related problem, first contact the HTC
- Do not apply techniques with a lot of force (e.g. high velocity mobilization techniques) and/or techniques that may cause soft tissue bruising (e.g. dry needling, shockwave, cupping) without consulting the haemophilia treatment centre.
- Be aware of any multiple joint arthropathy in individuals with haemophilia and adjust treatment accordingly.

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TABLE 1 (Continued)

Children
Points of attention in children
In general the treatment of children with a coagulation disorder is not substantially different from the treatment of adults with this disease. Of course, the age of the child must be taken into account and in many cases parents/guardians must be involved in the treatment. Depending on the age, it will be determined in consultation with the HTC whether the treatment should be carried out by a specialized paediatric physiotherapist or a regular physiotherapist.
Arthropathy • Customize exercise therapy for children with haemophilic arthropathy by adding functional exercises and elements of play. These adaptations must be appropriate for the age of the child. This means challenging children by, for example, throwing a ball, crouching down to pick up toys, or swimming. • Do not use manual techniques in children with haemophilic arthropathy.
Muscle and joint bleeding • Consider adjusting the advice on cooling (for example by ice application) and loading the joint based on the age of the child to improve feasibility. ○ A buggy, stroller or wheelchair can be used on children who cannot use crutches due to their age or motor skills. • Depending on the age of the child, offer exercise therapy in a more functional and playful way. • Provide information that is appropriate for the age of the child and also provide advice to the parents/guardians.
Chronic synovitis • Recommendations for activities and joint loading should be adapted to the age of the child • Adapt exercise therapy in a more functional and playful way for children, depending on the child's age • Consider contacting school and/or sports club about restricting activities/participation in physical education and/or sports.

existence and content among both patients and professionals.[101] In rare diseases like haemophilia, it is important to involve patients and patient organisations to ensure that guidelines are implemented in daily practice. Providing patient-specific information, such as a patient version of the guideline, alongside dissemination strategies for professionals (e.g., educational meetings, easy access to the guideline, or a short video or blog) can enhance the use of recommendations in daily practice.[102,103] In addition, previous studies of physiotherapists' adherence to guidelines have shown that active educational strategies lead to greater uptake of guidelines than passive dissemination alone.[104,105]

5 | CONCLUSION

An evidence-based clinical practice guideline, based on current evidence from literature and clinical expertise, has been developed for primary care physiotherapists treating a person with haemophilia. To improve care, the recommendations should be disseminated to relevant stakeholders and implemented in daily practice.

AUTHOR CONTRIBUTIONS

J. Blokzijl: Conceptualization; data acquisition; data analysis; interpretation of data; writing—original draft. **M.A. Timmer**: Conceptualization; data acquisition; interpretation of data; writing—review & editing; supervision; funding acquisition. **M.F. Pisters**: Conceptualization; interpretation of data; writing—review & editing; supervision, funding acquisition. All authors were involved in data interpretation and review of the paper. All authors approved the final version of the paper.

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CONFLICT OF INTEREST STATEMENT

M. Aspdahl has acted as a paid consultant to Pfizer, Sobi, Novo Nordisk, Roche, CSL Behring and Bayer. P. Loughnane has received Speaker fees from Sobi and Shire, Fees for consultancy work for Sobi, Sponsorship to attend conferences from Sobi and Novo Nordisk and an Investigator Initiated Study grant from Roche. D. Stephensen has received grant/research support from NIHR, EAHAD, Bayer, Novo Nordisk, Pfizer, Roche and Sobi, speaker's bureau from Spark, Roche, Sanofi, Sobi and Takeda. L.F.D. van Vulpen has received research grants form Novo Nordisk and Grifols and performed consultancy for Novo Nordisk and CSL Behring. All fees were paid to the institution. M.A. Timmer has received research grants from Novo Nordisk and Sobi and performed consultancy activities for SOBI, all paid to the institution. Other authors stated that they had no interests which might be perceived as posing a conflict or bias.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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ETHICS STATEMENT

The study was approved by the Institutional Review Board of the UMC Utrecht (IRB number: 22/777).

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