

ORIGINAL ARTICLE

Clinical haemophilia

The SLIM study—Shared medical appointments to change lifestyles of overweight people with haemophilia: A randomized multiple baseline (n-of-1) design

Marcel A. L. Hendriks^{1,2}  | Johanna W. M. van Wanroij³ | Britta A. P. Laros-van Gorkom³ | Maria W. G. Nijhuis-van der Sanden² | Thomas J. Hoogeboom²

¹Department of Health Innovations and Technology, Research Group Empowering Healthy Behaviour, Fontys University of Applied Sciences, Eindhoven, the Netherlands

²Radboud Institute for Health Sciences, IQ Healthcare, Radboud university medical center, Nijmegen, the Netherlands

³Department of Haematology, Radboud university medical center, Nijmegen, the Netherlands

Correspondence

Thomas J. Hoogeboom, Geert Grooteplein 21, 6525 EZ Nijmegen, the Netherlands.
Email: Thomas.hoogeboom@radboudumc.nl

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Abstract

Introduction: People with haemophilia suffer from haemophilic joint disease that may result in physical inactivity and overweight. Shared medical appointments (SMAs) might help limit the consequences of haemophilic arthropathy. SMAs are group meetings supervised by one or more healthcare professionals that can be utilized to improve lifestyle.

Aim: To evaluate the feasibility and efficacy of SMAs in people with haemophilia to improve physical activity and eating habits.

Methods: A multiple baseline single-case design was used. Overweight people with haemophilia were eligible to participate. Seven weekly SMAs were conducted using multiple behavioural change techniques to improve physical activity and eating habits. Feasibility of SMAs was evaluated using (a) dropout rate, (b) occurrence of adverse events (AEs), (c) adherence rate and (d) patient satisfaction. During 13 weeks, physical activity was measured daily and eating habits were measured three times per week. The efficacy of SMAs was determined using randomization tests and visual data inspection.

Results: Out of the six men participating in the study, one participant dropped out. No study-related AEs occurred. The adherence rate of SMAs was 80%, and participants reported to be 'very satisfied' with the SMAs. Randomization tests and visual analyses demonstrated (statistical) improvements in physical activity ($p = .03$). No effect was found in self-reported eating habits ($p = .55$).

Conclusion: Shared medical appointments are feasible in people with haemophilia and appear to improve physical activity. The effect on improving eating habits could not be established. Scientific replication of our approach is warranted to confirm or refute the merit of SMAs in people with haemophilia.

KEYWORDS

behaviour therapies, dietary habits, group therapy, Hemophilia, physical activity, self-management

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1 | INTRODUCTION

People with haemophilia are at risk of getting trapped in a vicious circle of deteriorating health and increasing risk of cardiovascular diseases (CVDs).^{1,2} Repeated joint bleeds can lead to haemophilic joint disease, causing patients to experience pain and difficulties in moving.^{3,4} This discomfort and the fear of new bleeds in already damaged joints may lead to physical inactivity.^{3,5} Physical inactivity may, in turn, result in weight gain,⁶ which then further increases the pressure on joints resulting in more bleeds and increased haemophilic arthropathy.⁶⁻⁸

Breaking this vicious circle might be possible by improving the physical activity and eating habits in people with haemophilia.^{4,9} To do so, in the Netherlands, these people are referred to a physical therapist and/or dietician.^{4,9} Alas, these lifestyle treatments are frequently monodisciplinary and thus lack a shared goal, potentially resulting in cost-inefficient care.^{4,9-12} Shared medical appointments (SMAs) might be an effective care model to structure the fragmented care for people with haemophilia.^{11,12}

In SMAs, people receive a combined treatment approach in a group setting supervised by one or more healthcare professionals including patient education, physical examination and clinical support.^{11,12} During the appointments, two effective approaches are combined as follows: group peer support, which promotes self-management through learning from others' experiences, and clinical one-on-one care, which adds personal accompaniment.¹¹⁻¹³ We hypothesized that SMAs might improve the physical activity and eating habits and break the vicious circle of decline in people with haemophilia. Therefore, the primary aims of this study were to evaluate the feasibility and efficacy of SMAs in people with haemophilia on physical activity and eating habits. Secondary, aims were to assess the efficacy of SMAs on weight, blood pressure, functional mobility, activity level, pain, patient-specific complaints, kinesiophobia and motivation.

2 | METHODS

2.1 | Design

Since haemophilia is a rare chronic disease, we decided to utilize a randomized, concurrent, multiple baseline single-case design.¹⁴ This design allows systematic manipulation of relevant variables to evaluate intervention effects for individual participants.¹⁵ To do so, participants are measured repeatedly over a period of time including a baseline phase where no manipulation takes place, which is taken as a control. By applying multiple baselines of varying length and multiple measures per participant, observed effects of the treatment can be distinguished from effects due to chance.^{15,16} Participants completed repeated measures during a (a) baseline phase A (2-4 weeks), (b) an intervention phase B (7 weeks) and (c) a postintervention phase A' (2-4 weeks). The start and also the duration of phase A is staggered at random across individuals resulting in different durations of phase A, see Figure 1. A sample size of four to eight

participants is common for this design and results in sufficient statistical power.^{15,17,18} Taking into account the possibility of dropouts, at least six participants were intended to be included in this study. The power was confirmed by calculating the minimum achievable *p*-value using the number of permutations of measures per study phase, $[(1/2016840)]$ results in $p < .01$.^{16,19}

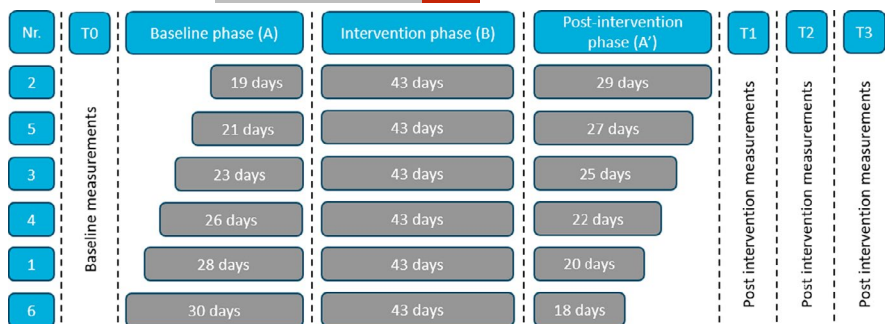
The study protocol was reviewed and approved by the Medical Ethical Committee of the Radboudumc Nijmegen (protocol number 2016-2415). To ensure sufficient rigour, the study was monitored by a clinical study monitor of the Radboudumc Nijmegen. This study is reported according to the Consolidated Standard of Reporting Trials (CONSORT) 2010 statement extended with reporting N-of-1 trials (CENT) 2015.²⁰

2.2 | Participants

Adult males diagnosed with haemophilia A, B or factor VII deficiency at the Haemophilia treatment centre in the Radboudumc Nijmegen were eligible to participate in the study. The inclusion criteria were as follows: (a) age between 18 and 80 years, (b) body mass index (BMI) ≥ 25 kg/m², (c) at least one lifestyle risk factor on the cardiovascular risk management (CVRM) questionnaire and (d) willing to change their lifestyle. Participants were excluded if they: (a) had another coagulation disorder or (b) used anticoagulants because of an increased risk of bleeding. Participants were recruited by their haemophilia nurse specialist during regular control visits or by phone. Those who gave oral consent received the information letter and had the opportunity to ask questions regarding participation. After giving written informed consent, people were randomly assigned a starting point directly after screening by the principal researcher using opaque sealed envelopes.

2.3 | Intervention

The seven SMAs of 2 hours per session took place weekly at the Radboudumc. A haemophilia nurse specialist, two physical therapists, two dieticians and a psychologist (sessions 3 and 6) were supervising the SMAs. The main goal for SMAs was to achieve and maintain a healthier lifestyle by improving physical activity, eating habits and corresponding motivation through behavioural change. Behavioural change techniques used were as follows: goal setting; social support; pros and cons; problem-solving; monitoring of behaviour; and information about health, social and environmental consequences.^{21,22} In the first SMA, every participant had two intake sessions to set their first small and easy achievable goals in their own context on physical activity (physical therapist) and eating habits (dietician). The content of the other six SMAs was not predetermined but was flexible and dependent on the requests of the participants. A standard element of each of the six meetings was reflecting on the personal goals; participants were challenged to adjust the goals if necessary or create new goals if goals were achieved. The last ten minutes of every appointment were used to determine the



Nr.: Participant number, T0: Baseline, T1: five weeks after B, T2: three months after B, T3: one year after B

FIGURE 1 Staggered phase start and duration of the SLIM study including participant allocation and measurements

content of the next SMA. The final content of the SMAs is displayed in the results.

2.4 | Feasibility

The feasibility of the intervention was evaluated using (a) dropout rate with corresponding reason for dropout, (b) occurrence of adverse events (AE), (c) adherence rate noted during the intervention period and (d) patient satisfaction after the intervention measured on a 7-points Likert scale using the second question of the global perceived effects (GPE), see Appendix A.²³

2.5 | Outcome measures

2.5.1 | Primary outcome measures

The primary outcomes, physical activity and eating habits, were measured repeatedly. To measure physical activity, a pedometer (Fitbit Zip) was used. The Fitbit Zip recorded daily steps during all phases of the study (91 measures) and is reported to be the most reliable and valid consumer pedometer.²⁴ Participants were asked to wear the pedometer all day except during the night and if the pedometer could get wet. The principal researcher collected the daily step counts at the start of phase B, weekly in phase B and at the end of phase A'. To measure self-reported eating habits, a visual analogue scale (VAS) was used constructed by the authors of this study: 'How healthy have you eaten in the past 2 days?', see Appendix B. Participants completed the VAS digitally in a secured data entry platform (Castor) three times a week in all phases of the study (39 measures). Although more reliable tools were available to measure eating habit, we chose the VAS to minimize the burden of repeatedly completing the measures over time to avoid participants dropping out of the study.

2.5.2 | Secondary outcome measures

Participants monitored pain in rest, pain during physical activity, patient-specific complaints, kinesiophobia and motivation for both improving physical activity and eating habits using seven VAS, see Appendix B. For safety reasons, coagulation factor usage was

monitored. Participants completed these measures 3 times per week throughout all phases of the study, resulting in 39 measures. Of the seven VAS, five VAS originated from validated questionnaires. The Dutch Patient-Specific Complaints, the Tampa Scale of Kinesiophobia and the Patient Activation Measure were, respectively, used to measure patient-specific complaints, kinesiophobia and motivation on maintaining improved physical activity and eating habits.²⁵⁻²⁸ Two VAS measures originated from consensus among the authors to measure pain in rest and pain during physical activity.

At baseline (T0), 5 weeks (T1), 3 months (T2) and 1 year after the last SMA meeting (T3), weight, blood pressure, coagulation factor use, kinesiophobia (TSK questionnaire), functional mobility (the Timed Up and Go [TUG] test) and daily functioning (Haemophilia Activity List [HAL]) were measured by the haemophilia nurse specialist and physical therapist. Moreover, at T0 participants' age, length, haemophilia type and severity and at T1 the GPE were measured by the haemophilia nurse specialist. Cut-off points were specified for each measure to determine clinical relevance. These points were as follows: (a) 3% reduction for weight, (b) if blood pressure was above 140/90 and got below 140/90, (c) if the Tampa scale score was higher than 37 a decrease in this score below 37, (d) a decrease of 3.4 seconds for the TUG and (e) an increase of 10.21% on the HAL.^{26,29-32}

2.6 | Data collection and analysis

All data were entered into the data entry program Castor EDC. Twenty per cent of the data entered by the principal researcher were checked by the clinical study monitor. Since the statistical analyses do not allow missing data, mean imputation was conducted.³³ Descriptive statistics were used to describe the participants at baseline and to assess feasibility.

The repeated measures were analysed visually using the 2-SD band method.^{18,34} A 2-SD band was calculated using phase A and was graphed through phases B and A'. If two or more measures from phase B or A' consecutively exceeded the 2-SD band, the result was considered clinically relevant.^{18,34} In addition, randomization tests for multiple baseline single-case designs were conducted for the repeated measures and the seven secondary VAS outcome measures.³⁴ The null hypothesis states that there is no effect between phase A and phases B and A'. The significance level for the randomization test is set at $\alpha = .05$. The visual analyses were conducted

using Stata/IC 15.0, and the randomization tests were conducted using R version 3.5.1 with the SCRT-R package.

Finally, a sensitivity analysis was conducted to assess the robustness of the outcomes regarding the mean imputation. This was done considering the worst-case scenario using Minmax imputation.³³ Additionally, sensitivity analyses were conducted in case of AE which may have influenced the results.

3 | RESULTS

3.1 | Participants

Thirty-one males with haemophilia were eligible to participate. Twenty-five did not participate for the following reasons (a) not interested, (b) a language barrier, (c) already training and (d) did not have a consultation at the hospital for over a year or were not contacted because of travel distance. In total, six males gave written consent to participate in the study. One participant dropped out of the study after 2 weeks of intervention due to lack of time and motivation for the SMAs and was excluded from the analyses. The participant flow is depicted in Figure 2. Table 1 presents the characteristics of the study participants.

3.2 | Shared medical appointments

All seven SMAs were completed as planned. The content of the SMAs consisted of education (transferring knowledge from professional to

participant), exploration (experiencing healthy behaviour) and evaluation (reflection on assignments and personal goals), see Table 2. Topics expected by healthcare professionals to be relevant but not requested by the participants were 'eating and special occasions' and 'eating and social environment'.

3.3 | Feasibility of the intervention

There were no adverse events related to the intervention. However, participant 2 fell in baseline phase (A) during a walk in the snow and had an elective total replacement knee surgery, unrelated to the fall, at the beginning of phase A' resulting in no daily steps but did not dropout of the study. The average adherence rate of SMAs was 80%, see Table 1. Reasons for missing appointments were (a) too busy with work ($n = 3$), (b) birthday party ($n = 1$), (c) holiday ($n = 1$) and (d) forgot the appointment ($n = 1$). The participants reported being 'very satisfied with the treatment' with a median score of 2 (range 1–4) on the GPE. Moreover, evaluation showed that participants appreciated the contribution of the dietician, and would have liked organized follow-up meetings to keep motivation high.

3.4 | Primary outcomes

Our primary outcome measures were daily steps and self-reported eating habits and are depicted in Figures 3 and 4, respectively, and in Table 3. In daily steps, 3% of data was missing due to malfunctions of the pedometer. The missing data were considered to be missing completely at random. The randomization test on physical activity between phase A and phases B and A' was statistically significant ($p = .03$). This effect was confirmed by the 2-SD band method, which showed clinically relevant increases in daily steps in participants 1 and 6 in phases B and A' and participant 4 in phase A', see Figure 3. The randomization test on eating habits between phases was not statistically significant ($p = .552$). This was confirmed by the 2-SD band method, which showed no clinically relevant improvements in self-reported eating habits except in participant 2, who showed improvements in phase A', see Figure 4.

3.5 | Secondary outcomes

Means and standard deviations of our primary outcomes are depicted in Appendix D. Randomization tests for secondary effectiveness outcome measures were not statistically significant: physical activity motivation ($p = .825$), eating habit motivation ($p = .809$), pain in rest ($p = .142$), pain during physical activity ($p = .254$), patient-specific complaint question 1 ($p = .760$), patient-specific complaint question 2 ($p = .511$) and kinesiphobia ($p = .321$). Coagulation factor usage stayed within reasonable limits; only participant 2 increased his factor usage in phase A (fall in the snow) and phase A' (total knee replacement) by a maximum of 7500 and 44,500 units per day, respectively.

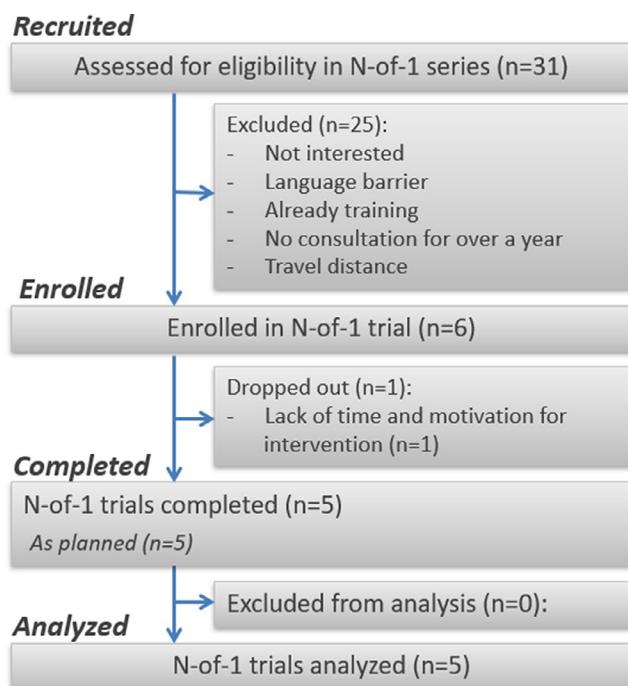


FIGURE 2 Flow chart of enrolment [Colour figure can be viewed at wileyonlinelibrary.com]



Participant	Age (years)	BMI (kg/m ²)	Haemophilia type	Severity of haemophilia	Adherence rate SMA n (%)
1	64	29.61	A	Mild	7 (100%)
2	59	38.88	A	Severe	7 (100%)
3 ^a	48	33.32	A	Mild	2 (28.57%)
4	30	34.16	B	Mild	6 (85.71%)
5	41	30.58	A	Mild	5 (71.43%)
6	51	35.56	Factor VII	Severe	3 (42.86%)

Abbreviation: BMI, body mass index.

^aDropped out.

TABLE 1 Baseline characteristics of study participants

SMA	Content	Healthcare professionals
1	Information about the program, intake physiotherapist and dietician and sharing personal goals.	HNS, PT, RD
2	Education: 1) Why you need to do physical exercise?, 2) What is healthy exercise behaviour?, and 3) What food is considered healthy?	HNS, PT, RD
3	Education: 1) How to maintain behavioural change?, 2) Advantages and threats of vegetables, meat and eating regularly.	HNS, PT, RD, Psych
4	Education: How to achieve a healthy lifestyle? A success story of an Expert by Experience. Exploration: Swimming for people with haemophilia (physical activity).	HNS, PT, RD, EBE
5	Education: 1) How can you exercise with regards to your haemophilia? and, 2) How to read nutrition labels? Evaluation: Did you find local exercise initiatives? Education: what is healthy exercise behaviour?	HNS, PT, RD
6	Education: 1) What kind of eater type are you? Exploration: What are suitable home exercises to do circuit training? Evaluation: Did you find local exercise initiatives?	HNS, PT, RD, Psych
7	Education: How to read nutrition labels? Evaluation: What is your future perspective?	HNS, PT, RD

TABLE 2 Final content of the SMAs and attending healthcare professionals

Abbreviations: EBE, expert by experience; HNS, haemophilia nurse specialist; Psych, psychologist; PT, physical therapist; RD, registered dietician; SMA, shared medical appointment.

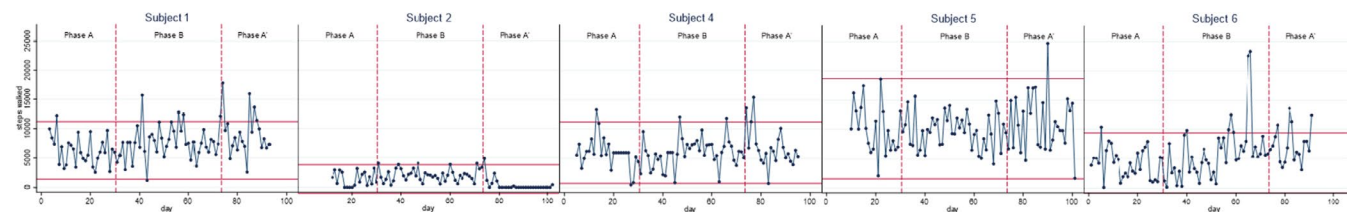


FIGURE 3 Visual analysis using the 2-SD band method (horizontal red lines) for daily step count in the five participants. The two SD bands were calculated using the data from phase A per participant

3.6 | Pre- and postintervention measures

Our secondary outcome measures had 6% missing data. Seven measures indicating weight decrease, five measures indicating a decrease in blood pressure and one measure indicating an increase in haemophilia activity level were considered clinically relevant. No relevant changes were found in the TSK questionnaire and the TUG test. Table 4 depicts baseline and postintervention measures for every participant.

3.7 | Sensitivity analyses

Sensitivity analyses were conducted to check the robustness of the primary outcomes regarding the mean imputation method for the daily steps and the AEs of participant 2. Using the Minmax imputation method, the randomization test on daily steps was not statistically significant ($p = .122$). This was confirmed by the 2-SD band method, which showed no improvements in daily steps that

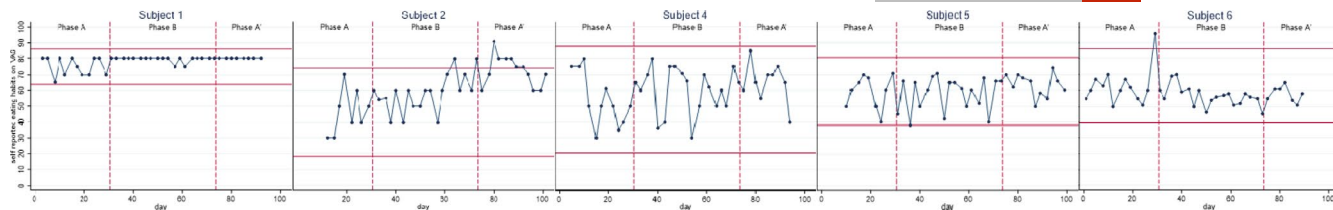


FIGURE 4 Visual analysis using the 2-SD band method (horizontal red lines) for self-reported eating habits in the five participants. The two SD bands were calculated using the data from phase A per participant

TABLE 3 Mean and standard deviation of physical activity and eating habit outcomes per participant and study phase

Participant	Phase A		Phase B		Phase A'	
	PA	EH	PA	EH	PA	EH
1	6257 (2481)	75 (6)	7642 (2810)	79 (2)	9070 (3609)	80 (0)
2	1402 (1212)	46 (14)	2081 (1046)	58 (12)	373 (1008)	73 (10)
4	5961 (2610)	54 (17)	5997 (2436)	61 (14)	6842 (3285)	65 (13)
5	10134 (4291)	59 (11)	9702 (2903)	58 (11)	11116 (4981)	64 (7)
6	4271 (2546)	63 (12)	6004 (4829)	56 (6)	7323 (3037)	58 (5)

Note: Numbers are given in mean (SD).

Abbreviations: EH, eating habits measured on a visual analogue scale (0–100); PA, physical activity measured in daily steps.

TABLE 4 Baseline and postintervention measures

Participant	Follow-up	Weight [Kg] (difference to T0 in %)	BMI [kg/m ²]	BP [mm/Hg]	TSK	TUG [sec]	HAL [%]
1	T0	87.6	29.61	143/76	30	5.58	100.0
	T1	79.4 (-9,4)	26.84	126/81	42	5.23	100.0
	T2	79.8 (-9,0)	26.97	120/84	32	4.76	100.0
	T3	82.1 (-6,3)	27.75	124/79	—	5.58	100.0
2	T0	123.2	38.88	136/83	50	9.96	45.7
	T1	115.4 (-6,3)	36.42	133/67	42	21.33	32.1
	T2	119.0 (-3,4)	37.56	124/64	48	9.03	22.3
	T3	121.0 (-1,8)	38.19	132/74	52	7.25	39.0
4	T0	114.4	34.16	137/95	27	6.10	96.8
	T1	111.0 (-2,6)	33.15	135/89	34	5.83	99.3
	T2	112.6 (-1,6)	33.62	137/82	29	5.23	95.5
	T3	120.0 (4,9)	35.83	137/92	29	5.59	92.4
5	T0	105.8	30.58	119/73	42	6.45	73.8
	T1	101.2 (-4,4)	29.25	121/77	38	4.68	77.0
	T2	100.4 (-5,1)	29.02	129/81	37	5.00	85.4
	T3	—	—	—	—	—	—
6	T0	111.4	35.56	134/89	46	7.05	48.8
	T1	111.6 (0,2)	35.62	128/81	49	6.53	58.9
	T2	112.0 (0,5)	35.75	163/91	45	6.68	52.0
	T3	115.8 (3,9)	36.96	126/88	50	6.94	50.8

Note: Bold values are considered clinically relevant compared with baseline

Abbreviations: BMI, body mass index; BP, blood pressure (systolic BP/diastolic BP); HAL, Haemophilia Activity List; HR, heart rate; TSK, Tampa Scale of Kinesiophobia; TUG, Timed up and Go.

were considered clinically relevant except in participant 1 in phase A' and participant 6 in phases B and A' (Appendix C). Moreover, a clinically relevant decrease in daily steps was observed in participant 1 in phase B. Excluding participant 2 from the analysis, the randomization test on the daily steps and self-reported eating habits were statistically significant ($p = .049$) and not statistically significant ($p = .437$), respectively, and thus confirmed our planned analysis.

4 | DISCUSSION

This study aimed to evaluate the feasibility and efficacy on physical activity and eating habits of SMAs in people with haemophilia. The results suggest the intervention was feasible in terms of dropout rate ($n=1$), AEs (none), adherence rate (80%) and patient satisfaction (very satisfied). Furthermore, the results suggest SMAs might be effective in increasing physical activity levels (however not robust), but we were not able to detect improving eating habits, nor did we find improvements in pain in rest, pain during physical activity, patient-specific complaints, kinesiophobia, motivation, functional mobility and daily functioning. We did, however, find clinically relevant decreases in weight and blood pressure.

Multiple studies investigated the efficacy of SMAs in other populations.^{12,35} A systematic review in people with diabetes type 2 shows SMAs decrease glucose level, cholesterol and blood pressure.¹² In our study, we found positive results for physical activity. However, unlike our expectations, we did not find improvements in eating habits.¹² This can be explained by differences in the content of the SMAs, duration and the study population. In RCTs included in the review, the content consisted mostly of behaviour change in eating habits. The duration of SMAs in people with diabetes ranged from every 3 weeks to every 3 months during at least 6 months but mostly over a year.¹² In contrast, in our study, seven weekly SMAs focussed both on physical activity and on eating habits. Possibly, the behaviour change in eating habits in this study was too superficial. Therefore, research is recommended on SMAs to improve eating habits in people with haemophilia taking into account all basic components of the behavioural change wheel from Michie.²² Moreover, people with diabetes type 2 differ in clinical picture from people with haemophilia. In diabetes type 2, adopting a healthy lifestyle can decrease the burdens of the disease, as it can reduce or even abolish the use of medication. In contrast, for people with haemophilia, a healthy lifestyle cannot reduce medication use, but only prevent the complications of haemophilia.

In our study, we found several clinically relevant improvements. After 5 weeks, we found decreased weight in three participants and decreased blood pressure in two participants. Regarding the visual analysis, these improvements can be explained by an increase in steps (participant 1) and improved eating habits (participant 2). However, this effect did not last 1 year after the intervention, indicating that SMAs failed to achieve a long-term behavioural change.

Our study had a number of strengths and limitations. A strength was the utilization of the multiple baseline design, as this design made it possible to assess the efficacy of the SMAs in a limited sample.^{15,16} A limitation of this design is that it is especially useful for demonstrating immediate intervention effects.³⁶ The SMA intervention aims to change lifestyles, which is considered time-consuming.³⁷ Another limitation is that we measured eating habits with a self-constructed VAS which was the least burdensome way to measure eating habits in order to prevent missing data and drop-outs. Still, it appeared to be suboptimal since participants' knowledge of what healthy eating habits are was limited at the start of the study causing an unreliable baseline. Perhaps future research can monitor eating habits using a multiple-day diet diary or app. Furthermore, measuring patient satisfaction with one question might have been too limited to fully grasp the concept of patient satisfaction. Finally, the external validity of single-case designs is limited compared with RCTs.³⁸ On the other hand, the internal validity is strong due to the large number of repeated measures per participant.

Given the positive findings of SMAs in this and other studies, we recommend future researchers to continue studying the feasibility and efficacy of SMAs in other chronic diseases.^{12,35} The prevalence of chronic diseases is increasing due to the enhanced life expectancy; attention must be paid to healthcare costs. Therefore, the demand for improving self-management is becoming more recognized especially in people with chronic diseases.^{11,39} Furthermore, we recommend that healthcare professionals start monitoring the progress of their patients more carefully and keep evaluating the efficacy of their own interventions. Our data clearly show that outcomes can fluctuate on a daily basis. In order to get a complete understanding of a patient's health problem and response to treatment, we strongly recommend the use of daily measures to reflect on with the patient.⁴⁰

5 | CONCLUSION

Shared medical appointments are feasible in people with haemophilia and seem to have a small positive effect on the level of physical activity, weight and blood pressure. We were not able to detect improved eating habits. Scientific replication of our approach is warranted to confirm or refute the merit of SMAs in people with haemophilia. Furthermore, the content of the SMAs and the measurement procedures should be adapted for future programmes. Moreover, healthcare professionals are advised to monitor the progress of their patients carefully and keep evaluating the efficacy of the treatment.

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DISCLOSURES

The authors stated that they had no interest which might be perceived as posing a conflict or bias.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Marcel A. L. Hendriks  <https://orcid.org/0000-0001-5853-1160>

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APPENDIX A

GLOBAL PERCEIVED EFFECT QUESTIONNAIRE

Global Perceived Effect (GPE-DV)

The Global Perceived Effect (GPE) is used to measure the patient's opinion of recovery. The GPE consists of 2 items that must be answered on a 7-point scale. The scale runs from fully recovered to worse than ever. The following questions are central:

1. "To what extent have you recovered from your symptoms since the start of treatment?"
 - Fully recovered
 - Much improved
 - Slightly improved
 - No change
 - Slightly deteriorated
 - Much deteriorated
 - Worse than ever
2. How satisfied are you with your treatment?
 - Absolutely satisfied
 - Very satisfied
 - Somewhat satisfied
 - Neither satisfied nor dissatisfied
 - Slightly dissatisfied
 - Seriously dissatisfied
 - Absolutely dissatisfied

APPENDIX B

SLIM-QUESTIONNAIRE INCLUDING ACCOUNTABILITY

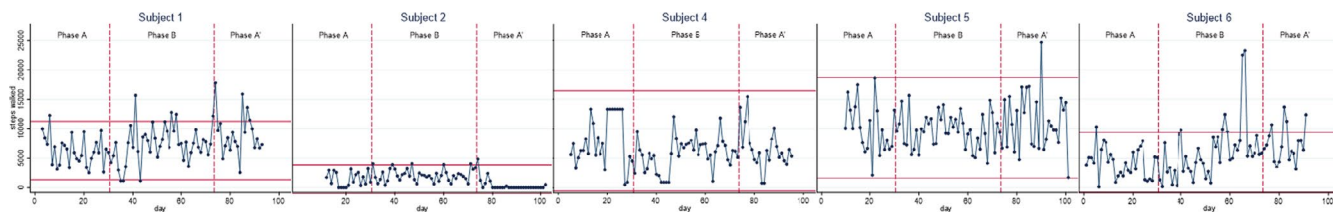
SLIM questionnaire [Translated from Dutch]

This questionnaire consists of 10 questions. You will see a line drawn for each question. The intention is that you put one dash on this line to indicate what applies to you.

Example: If you have little pain at rest at the moment, put the dash more on the left part of the line in question 1. If you are currently in a lot of pain, move the dash to the right. The more pain you have, the further you place your dash to the right. You answer the other questions in the same way.

Question	Source
1. How much pain do you currently have while resting? _____ No pain at all Unbearable pain	Visual Analogue Scale pain
2. How much pain do you currently have while moving? _____ No pain at all Unbearable pain	Visual Analogue Scale pain
3. How much difficulty do you have with (1) _____ No effort at all Impossible	Patient specific complaints question 1
4. How much difficulty do you have with (2) _____ No effort at all Impossible	Patient specific complaints question 2
5. How healthy have you eaten in the past two days? _____ Completely unhealthy Completely healthy	SLIM- study team
6. I'm afraid that I might injury myself if I exercise. _____ Totally disagree Totally agree	TSK questionnai re
7. I am confident that I can maintain lifestyle changes in physical activity even during times of stress. _____ Totally disagree Totally agree	Short Patient Activation Measure question 13
8. I am confident that I can maintain lifestyle changes in eating habits even during times of stress.. _____ Totally disagree Totally agree	Short Patient Activation Measure question 13
9. How many units of blood clotting medication have you used in the last 24 hours?	SLIM- studyteam
10. How many units of blood clotting medication have you used in the last 48 hours?	SLIM- studyteam

APPENDIX C



Visual analysis using the 2-SD band method (horizontal red lines) for daily step count in the five participants. The two SD bands were calculated using the data from phase A per participant. Missing data are imputed using Minmax imputation.

APPENDIX D

MEAN AND STANDARD DEVIATION OF SECONDARY OUTCOMES PER PARTICIPANT AND STUDY PHASE

Note

Participant	Measure	Phase A	Phase B	Phase A'
1	PA motivation	76 (36)	86 (2)	85 (0)
	EH motivation	72 (29)	80 (2)	70 (28)
	Pain in rest	0 (0)	0 (0)	0 (0)
	Pain during PA	1 (3)	0 (0)	0 (0)
	PSK nr.1	0 (0)	0 (0)	0 (0)
	PSK nr.2	0 (0)	0 (0)	0 (0)
	Kinesiophobia	0 (0)	0 (0)	0 (0)
	2	PA motivation	50 (0)	50 (0)
EH motivation		50 (0)	50 (0)	50 (1)
Pain in rest		22 (19)	24 (6)	55 (18)
Pain during PA		32 (21)	38 (5)	68 (16)
PSK nr.1		55 (14)	50 (7)	69 (12)
PSK nr.2		55 (14)	69 (12)	88 (7)
Kinesiophobia		70 (12)	77 (6)	79 (4)
4		PA motivation	63 (10)	68 (8)
	EH motivation	55 (7)	61 (6)	64 (10)
	Pain in rest	0 (0)	3 (8)	4 (7)
	Pain during PA	4 (6)	12 (13)	13 (9)
	PSK nr.1	59 (14)	53 (12)	43 (15)
	PSK nr.2	57 (9)	47 (11)	48 (14)
	Kinesiophobia	0 (0)	3 (15)	0 (0)

Participant	Measure	Phase A	Phase B	Phase A'
5	PA motivation	42 (18)	34 (2)	39 (5)
	EH motivation	36 (2)	35 (3)	40 (4)
	Pain in rest	9 (11)	6 (2)	7 (4)
	Pain during PA	8 (8)	5 (3)	9 (11)
	PSK nr.1	15 (18)	11 (5)	26 (8)
	PSK nr.2	17 (16)	10 (5)	27 (7)
	Kinesiophobia	51 (10)	35 (3)	25 (5)
6	PA motivation	56 (5)	53 (2)	61 (2)
	EH motivation	52 (8)	54 (1)	52 (4)
	Pain in rest	11 (5)	16 (7)	21 (3)
	Pain during PA	33 (13)	39 (11)	42 (6)
	PSK nr.1	100 (0)	100 (0)	100 (0)
	PSK nr.2	100 (0)	100 (0)	100 (0)
	Kinesiophobia	82 (7)	77 (8)	73 (7)

Measures are on a visual analogue scale (0–100). Numbers are given in mean(SD). Abbreviations: EH, eating habits; nr., number; PA, physical activity; PSK, patient-specific complaint.