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Lessons learnt from a process evaluation of an exercise intervention in patients treated with autologous stem cell transplantation

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This paper describes the process evaluation of an 18-week supervised exercise programme in 50 patients treated with high-dose chemotherapy followed by autologous stem cell transplantation. The intervention included 30 exercise sessions with six resistance exercises and interval training. We evaluated the context, dose delivered and received, and patients' and physiotherapists' satisfaction with the intervention. Ninety-two per cent of the patients trained within 15 km of their home address, with an average session attendance of 86%. Most patients trained at the prescribed intensity for four of the six resistance exercises, but the dose delivered and received of the two remaining resistance exercises and interval training could not be determined. Both patients and physiotherapists highly appreciated the programme (score of 8.3 and 7.9 out of 10 respectively). This process evaluation provided valuable lessons for future trials: (1) It is possible to deliver supervised exercise training to this patient group in local physiotherapy practices; (2) to determine dose received all intervention components should be standardised; and (3) to optimise data collection, all study materials should be tested more extensively prior to the start of the intervention.

KEYWORDS
autologous stem cell transplantation, exercise programme, haematologic malignancies, process evaluation

1 | INTRODUCTION

High-dose chemotherapy followed by autologous stem cell transplantation (auto-SCT) is currently the preferred treatment for patients with multiple myeloma in first line and aggressive lymphoma in first or second line (Sureda et al., 2015). Although auto-SCT improves survival of these malignancies (Copelan, 2006), a substantial part of SCT survivors may experience deficits in their quality of life (Mosher, Redd, Rini, Burkhalter, & Duhamel, 2009; Pidala, Anasetti, &

Trial Register: The study was registered at the Netherlands Trial Register (NTR2341)

Jim, 2010). Frequent long-term difficulties mentioned by Dutch survivors include problems with physical fitness and fatigue (Braamse et al., 2014).

Previous systematic reviews reported that exercise may have beneficial effects on physical fitness and fatigue in patients treated with SCT for a haematologic malignancy (Persoon et al., 2013; van Haren et al., 2013). In contrast to our hypothesis, in the EXercise Intervention after Stem cell Transplantation (EXIST) randomised controlled trial (RCT), we found no significant beneficial effects of an 18-week supervised moderate-to-high intensity exercise programme on physical fitness and fatigue when compared to usual care (Persoon et al., 2017). Physical fitness and fatigue improved from baseline to first follow-up in both the exercise and control group, but no significant between-group differences in effects were found. It is currently unclear whether this complex patient population—in terms of variability in side effects and co-morbidities—was able to adhere to the exercise prescription. A suboptimal adherence to the prescribed exercise intervention may have contributed to the lack of significant between-group differences in our study, in addition to suboptimal timing of intervention delivery and/or contamination in the control group (Persoon et al., 2017).

Several investigators have recommended to report more information about the adherence to the exercise prescription (Campbell, Neil, & Winters-Stone, 2012; Hacker & Mjukian, 2014; Winters-Stone, Neil, & Campbell, 2014). This information is vital to better understand study findings and to translate beneficial interventions effectively into clinical practice (Campbell et al., 2012; Kuehl et al., 2016; Winters-Stone et al., 2014). Conducting a process evaluation as part of an effectiveness trial is valuable in this respect. In general, process evaluations enable evaluation of the actual implementation of, and exposure to an intervention and may help to explain why an intervention was effective or not (Craig et al., 2008; Hulscher, Laurant, & Grol, 2003). Furthermore, process evaluation results can inform future optimisation of the intervention (Craig et al., 2008; Hulscher et al., 2003).

To gain more knowledge on whether the exercise intervention was implemented as intended in the EXIST trial, we conducted a process evaluation to describe the context in which the intervention took place (i.e. environmental factors that could have influenced the intervention implementation (Linnan & Steckler, 2002)), the intervention dose (i.e. the frequency, intensity, type and time/duration; the so-called FITT factors of the performed exercises), and the patients' and physiotherapists' satisfaction with the intervention. The results of this process evaluation resulted in lessons learnt for future multicentre RCTs.

2 | METHOD

The study and intervention methods of EXIST have been described elsewhere (Persoon et al., 2010, 2017). Shortly, EXIST was a multicentre RCT that evaluated the effectiveness of a supervised moderate-to-high intensity exercise programme compared with a usual care control group on physical fitness and fatigue in patients recently treated with auto-SCT. The study procedures were approved by the Medical Ethics Committee of the Academic Medical Center (AMC, Amsterdam) and by the boards of the eight other participating hospitals.

Patients were eligible for EXIST if they were treated with auto-SCT for multiple myeloma or lymphoma 6–14 weeks earlier, provided they had sufficiently recovered from treatment (Hb > 10.5 g/dl, platelets > 80 × $10^{9/}$l), were able to undergo exercise testing, and able to participate in an exercise intervention. In case patients were treated with consolidation chemotherapy or radiation therapy following the auto-SCT, they were included 2–6 weeks after ending this treatment. At first, eligibility was evaluated by the treating haematologist, the ward doctor, the transplantation coordinator and/or the nurse practitioner in the participating hospital. After the patients provided written informed consent, the registration form was mailed to the study team, and an appointment was made for a sports medical assessment. The sports physician usually did not have the results of imaging, but could ask for additional information when necessary. After confirmation of eligibility by a sports physician, patients were randomly assigned to the exercise intervention or usual care control group. This process evaluation focuses on the intervention group only.

2.1 | Exercise intervention

The intervention programme was supervised by physiotherapists who preferably had experience with the supervision of exercise in cancer survivors or in patients with a chronic disease, and who worked in well-equipped local physiotherapy practices within a 15 km range of the patients home or work address. The physiotherapists were reimbursed by the project funding. After a patient had been allocated to the intervention group, the study team contacted a physiotherapy practice and checked the suitability of the training equipment, instructed the physiotherapist and provided him/her with the study materials. These materials included the report of the sports physician, the intervention manual and the training log. The report of the sports physician included a brief summary of the patients' medical history (patient reported), sports history, risk factors for cardiovascular diseases and the patients' current physical, social and psychological status. Furthermore, it included the results of the cardiopulmonary exercise test and when already available, the results of the DXA scans (bone mineral density). In case of physical limitations, the sports physician sometimes made small adaptations to the exercise prescription.

The intervention programme consisted of an 18-week supervised resistance exercise and interval training programme and five counselling sessions aiming to improve compliance with the exercise programme and to stimulate patients to pursue a physically active lifestyle (Persoon et al., 2010, 2017). Exercise sessions lasted 60 min and took place twice a week in week 1–12, and once a week in week 13–18. Depending on the opportunities in the physical therapy practices, exercise sessions could be private or group-based with up to four patients (generally with other diagnoses and not participating in EXIST) per physiotherapist. The counselling sessions were planned in week 1, 4, 10, 12 and 18. Some physiotherapists were able to implement the 5–15 min sessions during the exercise sessions, while others made separate appointments next to the exercise sessions.

TABLE 1 Process evaluation components and their outcome measures

Component	Outcomes	Assessment
Context		
	Number of physiotherapy practices and physiotherapists	The number of participating physiotherapy practices and the number of physiotherapists who delivered the intervention
	Availability of equipment	Number of physiotherapy practices with insufficient equipment for protocol execution
	Travel distance	The shortest possible route by car from the patients' home to the physiotherapy practice.
	Group size	Mean group size over the attended exercise sessions. Two attended exercise sessions with missing data allowed
		The number (%) of patients that had private exercise sessions for ≥80% of the exercise sessions
Dose delivered and received		
Overall	Exercise sessions attended	Number (%) of exercise sessions attended, specified by the physiotherapist
		Reasons for not attending the exercise sessions
		The number and percentage of patients that attended ≥80% of the exercise sessions
	Counselling sessions attended	Number (%) of sessions attended, specified by the physiotherapist
		Reasons for not attending the counselling sessions
		The number and percentage of patients that attended ≥80% of the counselling sessions
Resistance exercises	1-RM tests performed for the four standardised exercises	Median number of 1-RM test performed
		Reasons for not performing or not adequately performing the 1-RM test
	Number of sets of the four standardised exercises performed	(25-(exercise sessions in which exercise was not performed + cancelled exercise sessions))*2. Two exercise sessions with missing data allowed
		Reasons for not performing the exercise
	Mean intensity for the four standardised exercises in week 1–12 and in week 13–18	Averaged (resistance achieved/1-RM). Only patients who attended >12 (week 1–12) and/or >3 (week 13–18) exercise sessions were included in analyses. Two attended exercise sessions with missing data allowed.
Interval training	Number of steep ramp tests performed	Median number of steep ramp tests performed
	Number of patients with changes to interval intensity or frequency of training	Number (%) of patients who did not follow the intervention training protocol for at least 2 exercise sessions
Satisfaction (patients)		
Exercise programme	Overall appreciation	Overall mark for the programme (1 = very bad, 10 = very good)
	Number of exercises per training	1 item (1 = far too little, 5 = far too much)
	Intensity of the exercises	1 item (1 = far too heavy, 5 = far too light)
	Quality of the physiotherapist	1 item (1 = completely satisfied, 5 = completely dissatisfied)
	Appreciation with training location	1 item (1 = completely satisfied, 5 = completely dissatisfied)
	Worthiness of time investment	1 statement: '*The exercise sessions were worth the time investment*' (1 = completely agree, 5 = completely disagree)
	Enjoyment of exercise sessions	1 statement: '*I enjoyed the exercise sessions*' (completely agree, 5 = completely disagree)
Counselling programme	Usefulness of the programme	1 item (1 = useful, 5 = useless)
	Amount of attention for active lifestyle	1 item (1 = far too less, 5 = far too much)
Overall	Strengths of the programme	3 entry options
	Weaknesses of the programme	3 entry options
	Suggestions for improvements	1 open-ended question

(Continues)

TABLE 1 (Continued)

Component	Outcomes	Assessment
Satisfaction (physiotherapists)		
Exercise programme	Appreciation	Overall mark for the programme (1 = very bad, 10 = very good)
	Strengths of the programme	3 entry options
	Weaknesses of the programme	3 entry options
	Suggestions for improvements	1 open-ended question
Counselling programme	Appreciation	Overall mark for the programme (1 = very bad, 10 = very good)
Overall	Would the physiotherapist recommend patients to follow this intervention	1 open-ended question
	Intervention protocol	1 statement: '*the intervention programme was clear*' (1 = completely agree, 5 = completely disagree)
	Communication and support	2 statements: '*I was satisfied about the communication with and support by the study team*' and '*I was satisfied about the communication with and support by the sport physician*' (1 = completely agree, 5 = completely disagree)
	Training logs	1 statement: '*Filling out the trainings logs was easy*' (1 = completely agree, 5 = completely disagree)

The resistance exercises included four standardised exercises (vertical row, leg press, bench press and pull over). In the first 12 weeks, two times 10 repetitions were completed at 65%–80% of the indirectly determined one repetition maximum (1-RM; the maximal resistance that can be moved in one contraction in a controlled manner with good posture). From week 13 onwards, the resistance was reduced (35%–40% 1-RM) and the number of repetitions was increased to 20 per set. In addition, the programme included lunges and either sit-ups or abdominal crunches using an exercise machine. The frequency and intensity of the abdominal crunches were equal to those of the standardised exercises. For the lunges and the sit-ups, the protocol included the performance of two sets of 0.7 times the maximal number of repetitions. These exercises were less standardised and sometimes substituted due to injuries. For instance, the sit-ups/abdominal crunches were not prescribed in case of osteoporosis or back injuries. Because of the resulting variation in exercise performance, we focused on the four standardised exercises for the dose delivered and received.

The interval training included two sets of 8 min of cycling at alternating intensities. Exercise intensity was determined using the maximal short exercise capacity (MSEC; the maximal workload) assessed during the steep ramp test (De Backer et al., 2007). With this test the subject started cycling at a work load of 25 W for 30 s, and subsequently the load was increased by 25 W every 10 s until exhaustion. During the interval training sets, blocks of 30 s at 65% of MSEC were alternated with either blocks of 60 s at 30% MSEC (week 1–8) or 30 s at 30% MSEC (week 9–18). The indirect 1-RM measurements and the steep ramp test were performed every 4 weeks to adjust the training load accordingly. These tests could be re-administered during a regular training session in case the training load was deemed too high or too low, and were also performed in week 18 to assess patients' improvements during the intervention programme.

In order to monitor training progression, the physiotherapists were asked to keep a training log and to email the log to the study team after every 4 weeks of training. The physiotherapist could contact the sport physician and/or the study team in case of questions, problems (e.g. in case of an inadequate training intensity) or injuries.

2.2 | Outcomes

We assessed the context in which the intervention took place, the dose delivered and received and patients' and physiotherapists' satisfaction with the intervention (Table 1).

2.2.1 | Context

The context includes the environmental factors that could have influenced intervention implementation (Linnan & Steckler, 2002) (Table 1).

2.2.2 | Dose delivered and received

In line with the definitions provided by Linnan and Steckler (Linnan & Steckler, 2002), we define dose delivered as the amount of the intended intervention components that were provided, and dose received as the extent to which participants actively engage and/or use the materials or recommended resources. We merged these two components and assessed session attendance and the compliance to exercise FITT factors (Table 1).

Session attendance at the exercise and counselling sessions was retrieved from the training logs and the associated correspondence between the study team and the physiotherapist.

For the four standardised resistance exercises, we determined per exercise (1) the median number and percentage of 1-RM tests performed and the reason for non-compliance; (2) the number and percentage of exercise sessions in which the exercises were performed and the reasons for non-compliance; and (3) the average intensity as expressed as the mean of the ratio between resistance achieved and the 1-RM value per exercise in week 1–12 and in week 13–18.

Using the training logs, we registered the number of correctly executed steep ramp tests (from which the median number was calculated) and the reasons for not performing the steep ramp tests. To gain insight into the compliance with the interval training protocol, we registered the number and calculated the percentage of patients for whom deviations from the protocol during ≥2 exercise sessions were reported. The precise nature of the protocol deviations could not be determined since the training logs lacked details regarding the performed frequency, intensity and duration of the interval training.

2.2.3 | Satisfaction

The patients' and physiotherapists' satisfaction with the intervention was assessed post-intervention using study specific satisfaction questionnaires that included predominantly open-ended questions, 10-point numeric rating scales and 5-point scales (Table 1).

Physiotherapists who supervised more than one participant filled out the questionnaire once, and in case more than one physiotherapist supervised a participant, the questionnaire was sent to the contact person of the study team.

3 | RESULTS

Fifty-four of the 109 (50%) patients who participated in EXIST were randomly allocated to the intervention group. Four of these intervention patients were lost to follow-up due to disease relapse or progressive disease and were excluded from this evaluation. Of the remaining 50 patients, 29 (58%) were men and 27 (54%) were diagnosed with multiple myeloma (Table 2). One adverse event was directly related to the intervention programme, i.e. a patient strained a calf muscle, but he recovered from this injury within the intervention period and was able to continue with the programme.

TABLE 2 Baseline demographics and clinical characteristics of the 50 patients who followed the exercise intervention

Gender, male, *n* (%)	29 (58)
Age, median (range), years	53 (20–67)
Married/living together, *n* (%)	42 (84)
Higher education level, *n* (%)	14 (28)
Sports history, yes[a], *n* (%)	30 (60)
Cancer type, *n* (%)	
MM	27 (54)
(N)HL	23 (46)
Time since auto-SCT, median (range), days	71.5 (42–275)
Remission status after auto-SCT, *n* (%)	
CR	35 (70)
VGPR/PR	15 (30)
Hb (g/dl)[b], median, range	11.8 (9.5–14.8)
Co-morbidity	
Neuropathy, *n* (%)	12 (24)
Musculoskeletal disorders, *n* (%)	35 (70)
Cardiovascular disease or risk factors	19 (38)
Respiratory disease, *n* (%)	7 (14)
Other, *n* (%)	10 (20)

MM, multiple myeloma; (N)HL, (non-)Hodgkin lymphoma; auto-SCT, autologous stem cell transplantation; CR, complete response; VGPR, very good partial response; PR, partial response/remission.
[a]Participating in sports at least once a week before diagnoses/relapse.
[b]Haemoglobin levels older than 21 days were excluded (*n* = 9), as blood values can change quickly after recent auto-SCT.

3.1 | Context

3.1.1 | Number of physiotherapy practices and physiotherapists

In total, 42 physiotherapy practices participated and at least 75 physiotherapists delivered the intervention (number of physiotherapist unknown for nine patients). The physiotherapist of six practices supervised more than one participant.

3.1.2 | Availability of equipment

Four physiotherapy practices did not have a cycle ergometer suitable for conducting the steep ramp test. One of these practices was substituted by another practice, and the other three practices were supplied with an ergometer.

For 18 (36%) patients, substitutions or adjustments were made to one or more resistance exercises because of unavailability of resistance exercise machines (for instance, the vertical row was replaced by the low row or seated row). In six patients, the intensity of one or more resistance exercises was restricted by the resistance range of the exercise machines or by the absence of sufficiently heavy dumbbells. One practice used machines with hydraulic resistance, which impeded the determination of training intensity.

3.1.3 | Travel distance

The median travel distance between the patients' home or work address and their physiotherapy practices was 2.6 km (range = 0.04–19.2). Four (8%) patients had a travel distance >15 km.

3.1.4 | Group size

Group size varied widely between exercise sessions and within patients. The median group size was 2 (range = 1–4). Eleven (22%) patients mainly (>80%) had private sessions. Median group size was unknown for 17 (34%) patients due to missing data for ≥2 sessions.

3.2 | Dose delivered and received

3.2.1 | Session attendance

For two (4%) patients, the exercise logs and associated correspondence were missing. For three (6%) additional patients, the number of counselling sessions was not reported. The remaining patients attended on average 25.8 (*SD* = 3.8) of the 30 (86%) prescribed exercise sessions and 4.4 (*SD* = 0.9) of the 5 (89%)

TABLE 3 Dose received of the four standardised resistance exercises by the 50 patients

	Vertical row	Leg press	Bench press[a]	Pull over[b]
Median number of 1-RM tests performed (max 5 per patient)				
Performed, median (range) per patient[c]	4 (0–5)	4 (0–5)	4 (0–5)	3.5 (0–5)
Missing logs/values, *n* with ≥1 test (% of tests prescribed)[d]	6 (6)	7 (6)	16 (6)	8 (8)
Not performed, *n* with ≥1 test (% of tests prescribed)[d]				
Non-attendance	21 (11)	21 (11)	21 (11)	21 (11)
Inadequate execution/ equipment	12 (12)	13 (12)	7 (8)	12 (12)
Injuries	5 (4)	5 (5)	5 (4)	7 (6)
Physiotherapist decided not to change resistance	5 (2)	4 (2)	5 (2)	3 (1)
Other	8 (3)	9 (4)	8 (3)	9 (4)
Number of exercise sessions with exercises performed (max 25 per patient)				
Performed, median (range)[c]	22 (10–25)	22 (4–25)	22 (8–25)	22 (0–25)
Missing logs/values for ≥2 sessions, *n* (% of sessions prescribed)[d]	13 (13)	13 (13)	13 (14)	15 (15)
Not performed, *n* (% of sessions prescribed)[d]				
Non-attendance	38 (13)	38 (13)	38 (13)	38 (13)
Injuries	4 (2)	6 (3)	5 (2)	6 (5)
Other	9 (2)	6 (1)	2 (0)	2 (0)
Intensity achieved, n (%)				
Week 1–12, patients with >12 valid exercise sessions	36 (72)	33 (66)	37 (74)	29 (58)
Prescribed intensity (65%–80% of 1-RM)	29 (81)	32 (97)	32 (86)	22 (76)
<65% of 1-RM	6 (17)	1 (3)	4 (11)	6 (21)
>80% of 1-RM	1 (3)	—	1 (3)	1 (3)
Week 1–13, patients with >3 valid exercise sessions	18 (36)	18 (36)	17 (34)	18 (36)
Prescribed intensity (35%–50% of 1-RM)	18 (100)	18 (100)	14 (82)	16 (89)
<35% of 1-RM	—	—	1 (6)	2 (11)
>50% of 1-RM	—	—	2 (12)	—

[a]Or chest press.
[b]Or flies.
[c]Patients with missing values/training logs excluded.
[d]Percentage missing or not performed tests/exercise sessions of the total number of prescribed tests/sessions for all patients.

prescribed counselling sessions. The number of patients attending ≥80% of the training and counselling sessions was 36 out of 48 (75%) and 39 out of 45 (87%) patients respectively. Most frequently reported reasons for not-attending the exercise sessions were injury or illness (34%, *n* = 19), holiday (27%, *n* = 17) and session took place after follow-up assessments (19%, *n* = 16). Reasons for not attending the counselling sessions were: session took place after follow-up assessment (55%, *n* = 14), illness of the patient (31%, *n* = 5), judged as not needed (7%, *n* = 1) and holiday (7%, *n* = 1).

3.2.2 | Resistance exercises

1-RM tests

The median number of 1-RM tests conducted per patient was 3.5 for the pull over and 4 for the other three exercises (Table 3). Test performance of the 1-RM test was inadequate in 6%–11% of the prescribed tests because patients reached the maximum number of repetitions allowed (>16) or 'achieved' the same number of repetitions for every test (i.e. 5 or 10). Four (8%) patients did not perform one or two interim test moments and the previous 1-RM values were used to determine training intensity. No explanation was given for this deviation from the protocol. In these cases, the maximal 1-RM was considered unknown and training intensity of the subsequent exercise sessions could not be determined. In six patients (12%), the physiotherapists substituted the final test session for a normal training, and consequently the values of the 1-RM tests were lacking (Table 3).

Frequency

The frequency of exercise sessions could be calculated for approximately 70% of the patients and was a median of 22 out of 25 (Table 3).

Intensity

The training intensity achieved in week 1–12 on the pull over, the leg press, vertical row and bench press could be calculated for respectively 58%, 66%, 72% and 74% of the patients. The proportion of these patients who trained at the prescribed intensity ranged from 76% for the pull over and 97% for the leg press. For week 13–18, we were able to calculate the intensity achieved in ≥3 of the 4 protocolled exercise sessions of 35% of the patients (Table 3).

3.2.3 | Interval training

Steep ramp tests

Patients performed a median of 4 tests (range 0–5). The number of steep ramp tests performed was unknown for 7 out of 50 (14%) patients (6% of the prescribed tests) due to missing training logs or values. Of the total number of prescribed tests, 20% (n = 32) were not performed or not performed on time, of which 1% (n = 2) was related to injuries and 4% (n = 3) of the prescribed tests were performed inadequately.

Interval training protocol

For 28 (56%) patients, it was reported that they did not fully comply with the interval training protocol in ≥2 exercise sessions. In the majority of these patients (n =23, 82%), the training load had to be reduced. Unfortunately, due to incomplete recording and log books, and substantial variation in the methods used to lower the interval training dose (e.g. early termination, lower workload, endurance training instead of interval training), it was impossible to determine the dose delivered and received in more detail.

3.3 | Satisfaction

Forty-seven (94%) patients and 34 (81%) physiotherapists filled out the satisfaction questionnaire. Patients and physiotherapists appraised the exercise programme with an 8.3 and 7.9 out of 10 respectively. About 86% of the physiotherapists would advise other patients treated with auto-SCT to follow this exercise programme. However, a substantial proportion of the physiotherapists (47%) was not satisfied with the communication with and support by the sports physician (Table 4). Both patients and physiotherapists were satisfied about the method for training progression (Table 5). Patients also frequently mentioned personal benefits, including perceived physical improvements (n = 20, 43%) and regaining their daily routine (n = 19, 40%). The physiotherapists reported more frequent on technical aspects of the intervention than patients, such as the choice of exercises (n = 17, 50%). Negative aspects mentioned by patients and physiotherapists were the high intensity and the lack of variation in exercises.

TABLE 4 The patients' and physiotherapists' satisfaction with the intervention programme

Patients (n = 47)	
Moderate-to-high intensity exercise programme	
Overall appreciation, mean (*SD*)[+,a]	8.3 (0.9)
Number of exercises, n (%)[a]	
Too few	4 (8.7)
Just right	38 (82.6)
Too many	4 (8.7)
Intensity of the exercises, n (%)[b]	
Too high	5 (11.9)
Just right	33 (78.6)
(Much) too low	4 (9.5)
Appreciation with training location, median (range)*	1 (1–4)
Quality of the physiotherapist, median (range)*	1 (1–4)
Worthiness of time investment, median (range)[*,c]	1 (1–4)
Enjoyment of exercise sessions, median (range)*	1 (1–4)
Counselling programme	
Usefulness of the programme, median (range)[*,c]	2 (1–5)
Amount of attention, n (%)[d]	
(much) to little	10 (23.3)
Just right	33 (76.7)
Physiotherapist (n = 36)	
Appreciation with the exercise programme, mean (*SD*)[+,d]	7.9 (0.7)
Appreciation with the counselling programme, mean (*SD*)[+]	7.7 (0.9)
Would the physiotherapist recommend patients to follow this intervention? N (%)[e]	
Yes	24 (85.7)
Some	4 (14.3)
Clearness of the intervention protocol, median (range)*	1 (1–5)
Communication with, and support by the study team, median (range)*	1 (1–4)
Communication with and support by the sports physician, median (range)[*,c]	3 (1–5)
Easiness of filling out the training logs*	2 (1–4)

[+]1 = very bad, 10 = very good.
*1 = completely agree.
5 = completely disagree.
Missing in [a]n = 1.
[b]n = 5.
[c]n = 2.
[d]n = 4.
[e]n = 6.

TABLE 5 Positive and negative aspects of the intervention and suggestions for improvements

Category	Patients (*n* = 47) Aspect (3 max per patient)/ suggestion	*N* (%) who mentioned aspect/ suggestion	Physiotherapists (*n* = 34) Aspect (3 max per therapist)/suggestion	*N* (%) who mentioned aspect/suggestion
Positive aspects[a,d]	Marked physical improvements	20 (43)	Use of steep ramp test and 1-RM tests to set intensity/training progression	17 (50)
	Gain daily routine/ motivating	19 (40)	The choice of exercises (targeting all muscle groups/both aerobic and resistance exercises)	17 (50)
	The design of the training programme	17 (36)	Improved physical fitness	10 (29)
	The supervision by the physiotherapist(s)	16 (34)	Study materials (EXCEL sheet/manual)	9 (26)
	Feeling better/satisfied	10 (21)	Improved self-confidence	8 (24)
	Overall improvements	8 (17)	Duration of the training programme	4 (12)
	Social aspects	6 (9)	Other	9 (26)
	Other	10 (21)		
Negative aspects[b,e]	Intensity was too high	14 (30)	Intensity was too high	16 (47)
	Boring, no variation of exercises	12 (26)	Boring, no variation of exercises	7 (21)
	Physical complaints	6 (13)	Exercise were static/isolated/not ADL specific/not functional	5 (15)
	Intervention programme too short	5 (11)	Risk on injuries/risk of too much overload	5 (15)
	Logistical problems	4 (9)	Difficulties with supervision	6 (18)
	The experienced obligation	2 (4)	Impossibility to adapt programme	5 (15)
	Other	6 (13)	Parts of the programme not evidence based	3 (6)
	No (other) negative points	14 (30)	Other	12 (35)
Suggestions for improvements[c,f]	More variations in (resistance) exercises	6 (13)	More variation	7 (21)
	More/diversify aerobic exercises	5 (11)	Adapt intensity	6 (18)
	Decrease (interval) training intensity	4 (9)	More aerobic exercises	4 (12)
	More individualisation in programme design	2 (4)	Adjust or used different tests to set intensity	4 (12)
	Other	8 (17)	Adjust programme to individual patient	2 (6)
	No suggestions	14 (30)	Other	2 (6)
			No suggestions	6 (18)

[a]Thirty-six of 141 possible aspects missing/not given.
[b]Fifty-six of 141 possible aspects missing/not given.
[c]Eleven of 51 possible suggestions missing. Four patients gave two different suggestions.
[d]Twenty-eight of 102 possible aspects missing/not given.
[e]Forty-three of 102 possible aspects missing/not given.
[f]Six of 37 possible suggestions missing. One physiotherapist gave two and another three suggestions.

4 | DISCUSSION

In the current process evaluation of a supervised moderate-to-high intensity exercise intervention offered to patients who had undergone auto-SCT, we studied the context in which the intervention took place, the dose delivered and received and the patients' and physiotherapists' satisfaction with the intervention. The context and satisfaction were good, and session attendance was satisfactory. The intensity (week 1–12) and frequency were specified for the majority of the patients (~70%) for four of the six resistance exercises, and were considered appropriate. There was, however, considerable variation in the performance of the two less standardised resistance exercises (i.e. lunges and the abdominal crunches/sit-ups), which hampered us to include them in the ratings for dose delivered and received. In addition, there were indications that for a substantial part of the patients the training load of the interval training was too high during at least a part of the training programme, but we were unable to precisely study the dose delivered and received of this component due to the lack of detailed information about the frequency, intensity and duration in the training log.

Given the above, we believe that it is not evident, but it cannot be ruled out that an inadequate compliance is partly responsible for the lack of significant effects in the EXIST study. We previously hypothesised that the lack of significant effects may also be related to a suboptimal timing of the intervention delivery or to contamination in the control group (Persoon et al., 2017). Notwithstanding these hypotheses, given the lack of significant effects, it is not recommended to add the intervention in its current form to the usual care of patients recently treated with an auto-SCT. However, as systematic reviews reported beneficial effects of exercise on physical fitness and fatigue in cancer patients (Cramp & Byron-Daniel, 2012; Jones et al., 2011; Padilha et al., 2017; Strasser, Steindorf, Wiskemann, & Ulrich, 2013), exercise interventions may still be considered as valuable treatment options. Therefore, we believe that the lessons learnt in our study might still be highly valuable for future exercise interventions in cancer patients.

The most important lessons learnt during the performance of this process evaluation were that (1) it was possible to deliver the supervised exercise intervention in local physiotherapy practices near the patient's home or work address, (2) to adequately rate the dose delivered and received all the components of the intervention should be standardised, and (3) all study materials, and specially the training log, should be further rigorously pretested prior to the start of the study to reduce the risk of losing important information about the implementation of the intervention.

4.1 | Context

Our study shows that it is possible—in the Dutch setting—to deliver a supervised exercise intervention at physiotherapy practices within 15 km from the patient's home or work address. In the Netherlands, everyday travel distances are mostly short and physiotherapy is highly accessible. The mean travel distance to the nearest physiotherapist is for instance approximately 1.5 min by car (volksgezondheidzorg.info, 2017). Still, not all physiotherapy practices are able to deliver the exercise intervention, as not all practices have the required exercise equipment. The limited travel distance may have been beneficial for the participation, as travel distance has been identified as a barrier to participating in supervised exercise intervention studies (Gollhofer et al., 2015; van Waart et al., 2015). However, to achieve this limited travel distance, we had to include many physiotherapy practices which all treated only small numbers of patients, resulting in inter-patient variation in training equipment, intervention delivery and/or reporting.

4.2 | Dose delivered and received

The average session attendance of 86% found in our study was good and comparable to that reported by a previous study that evaluated an outpatient exercise programme among patients treated with auto- or allogeneic SCT (Knols et al., 2011).

We learnt that we were able to apply the exercise principles progression and continuous overload (Campbell et al., 2012; Winters-Stone et al., 2014) in the intervention programme by incorporating regular evaluation moments. The 1-RM and steep ramp tests were generally adequately performed. Likewise, the results of the 1-RM tests were considered appropriate to identify training intensity throughout the programme. This is an important finding, as these principles have not always been correctly applied in previous studies (Campbell et al., 2012; Persoon et al., 2013; Winters-Stone et al., 2014). In the EXIST study, we did not specifically recruit patients with low physical activity and/or physical fitness levels. However, as the physical fitness of the patients after auto-SCT was compromised (Persoon et al., 2016), there was room for improvement in fitness levels in this patient population.

The current exercise programme had been studied among patients with other cancer types (De Backer et al., 2007, 2008) and the intensity of the interval training was prescribed based on the patients' individual fitness level assessed by the steep ramp test. As the training load was reduced in at least some of the training sessions in about half of the patients, the programme might have been too challenging and/or the steep ramp test might have been not accurate enough in estimating the correct training load in this patient population. Kampshoff et al. (Kampshoff et al., 2016) reported lower compliance to the endurance interval training than resistance exercise in a previous study evaluating a comparable training programme, and suggested that the steep ramp test may be less accurate to prescribe the intensity for the interval training than the 1-RM tests for prescribing training intensity of the resistance exercises. Our recent analyses showed that the test can accurately assess aerobic fitness at a group level, but may overestimate aerobic fitness in individual patients with low fitness and underestimate it in patients with high fitness (Stuiver et al., 2017). Still, given its good feasibility and short duration, we have suggested to use the results of the steep ramp test in combination with the Borg score for prescribing exercise intensity in individual patients (Stuiver et al., 2017).

We have no indication that the missing of data was systematic, as the missingness in our study was likely mainly caused by incomplete recording and log books, and variation in exercise performance. Our results indicate that in order to adequately determine the dose delivered and received, all prescribed exercises should be standardised as much as possible. Additionally, before the start of the intervention, the possible difficulties (i.e. a lack of adequate training equipment, frequent musculoskeletal problems) should be identified and solutions should be outlined. Still, under real-life circumstances, complete standardisation in delivering an intervention programme among a diverse patient population—in terms of variability in side effects and co-morbidities (including the frequent musculoskeletal problems)—will remain difficult. For instance, we allowed some patients to train closer to home at a physiotherapy practice without all the necessary equipment for all exercises, rather than asking them to travel further to a practice that was better equipped. Also, in some cases, adaptations to exercises due to musculoskeletal problems of the patient or due to unsuitability of equipment were made after the start of the programme. Such variation in exercise performances complicates the assessments of the dose delivered and received, but it does not necessarily imply reduced quality of the exercise programme.

In addition to the need for standardisation of the prescribed exercises, the results indicate that more extensive pre-testing of process evaluation materials is warranted to avoid variations in interpretation of instructions or questions, and to prevent a loss of information necessary for the process evaluation. In order to minimise the burden, it is also important that physiotherapists are able to complete the training logs quickly and easily. In this study, we used a study specific EXCEL file, and although most physiotherapists agreed with the statement in the satisfaction questionnaire that filling out the training logs was easy, still about one quarter of the physiotherapists responded neutrally or even disagreed. In future studies it may be worth considering linking the training log to the patient record systems used by physiotherapists. Furthermore, advances in the design of exercise equipment, i.e. the further incorporation of information technology, might facilitate the setup of the equipment and the monitoring of the dose received.

Finally, further studies could incorporate regular monitoring of the returned training logs and frequent contact with the physiotherapists to support completeness of logs. However, this may reduce the comparability to the real-life setting.

4.3 | Satisfaction

Overall, patients and physiotherapists were satisfied with the exercise programme. Patients perceived improvement in physical fitness and valued the fact that they regained a daily routine. The use of scheduled testing throughout the intervention to ensure adequate training intensity and progression was well received by the physiotherapists. Negative aspects of the intervention mentioned by the patients and physiotherapists were the high intensity and the lack of variation. This is in line with a cross-sectional study on exercise preferences among patients with non-Hodgkin's lymphoma that found that the majority of patients had a preference for moderate intensity exercise and for different activities each session (Vallance, Courneya, Jones, & Reiman, 2006).

5 | CONCLUSIONS

The implementation of the moderate-to-high intensity exercise programme evaluated in the EXIST study was satisfactory for most components. It was possible to deliver the exercise intervention in local physiotherapy practices near the patients' home address and both patients and physiotherapists were satisfied with the intervention. The dose delivered was adequate for the four standardised resistance exercises, but could not be assessed for the two less standardised resistance exercises and the interval training. Therefore, to accurately assess the dose delivered and received, future studies should strive for maximal standardisation of the exercise intervention, and should further pre-test their study materials to reduce the risk of missing important information necessary for conducting a process evaluation.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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