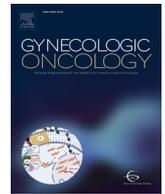




Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Experiences, adherence and satisfaction with a combined exercise and dietary intervention for patients with ovarian cancer undergoing chemotherapy: A mixed-methods study

S. Stelten^a, L.R.C.W. van Lonkhuijzen^b, Y.A.W. Hartman^a, W.J. van Driel^c, R.M. Winkels^d, G.G. Kenter^{b,c,e}, L.M. Buffart^{a,*,1}, M. Hoedjes^{f,1}

^a Radboud University Medical Center, Department of Physiology, Radboud Institute of Health Sciences, P.O. Box 9101, 6500, HB, Nijmegen, Netherlands

^b Amsterdam UMC, University of Amsterdam, Department of Obstetrics and Gynecology, Center for Gynecologic Oncology Amsterdam (CGOA), Meibergdreef 9, 1105 AZ, Amsterdam, Netherlands

^c The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Gynecology, Center for Gynecologic Oncology Amsterdam (CGOA), Plesmanlaan 121, 1066 CX Amsterdam, Netherlands

^d Human Nutrition and Health, Wageningen University and Research, Wageningen, Netherlands

^e Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Obstetrics and Gynecology, Cancer Center Amsterdam, Center for Gynecologic Oncology Amsterdam (CGOA), de Boelelaan 1117, 1081 HV Amsterdam, Netherlands

^f CoRPS - Center of Research on Psychological and Somatic disorders, Department of Medical and Clinical Psychology, Tilburg University, Tilburg, the Netherlands

HIGHLIGHTS

- Patients with ovarian cancer adhered well to a combined exercise and dietary intervention during chemotherapy.
- Participation in the intervention improved patients' fitness, quality of life and recovery after chemotherapy and surgery.
- Patients were generally satisfied with the combined intervention.
- Good intervention adherence, high satisfaction and perceived benefits support successful clinical implementation.

ARTICLE INFO

Article history:

Received 23 December 2021
Received in revised form 11 March 2022
Accepted 13 March 2022
Available online xxxx

Keywords:

Ovarian cancer
Exercise intervention
Dietary intervention
Experiences
Adherence
Satisfaction

ABSTRACT

Objective. This study examined experiences, adherence and satisfaction with a combined exercise and dietary intervention in patients with ovarian cancer and their healthcare professionals (HCPs) as part of the randomized PADOVA trial.

Methods. A mixed-methods approach was used in 24 patients with ovarian cancer receiving first-line chemotherapy who were randomly allocated to a combined exercise and dietary intervention or usual care with counseling sessions post-treatment. Qualitative data on intervention experiences, adherence and satisfaction was collected using semi-structured interviews with patients and their HCPs ($n = 18$ physical therapists; $n = 5$ dietitians). Quantitative data on adherence and satisfaction was collected to provide context to qualitative data.

Results. Exercise relative dose intensity ranged from 36 to 100% (median 72%) and patients attended 33–133% (median 100%) of the prescribed dietary counseling sessions. Patients appreciated guidance on exercise and nutrition and perceived benefits including improved physical fitness, quality of life, peer support and recovery after surgery and/or chemotherapy cycles. Both patients and HCPs were satisfied with the intervention and perceived that participation exceeded prior expectations. Median patient satisfaction score with the intervention was 8.5 out of 10. Suggestions for improving the intervention included further personalization of the number, content and scheduling of the sessions to preferences of patients and HCPs. Patients in the usual care group reported counseling sessions post-chemotherapy to be too little too late.

Conclusions. Patients with ovarian cancer adhered well to the intervention. Numerous perceived benefits of the intervention were reported by patients and HCPs. Good adherence and positive experiences support successful implementation in clinical practice.

© 2022 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

* Corresponding author at: Geert Grooteplein Zuid 10, 6500 HB Nijmegen, the Netherlands.

E-mail address: laurien.buffart@radboudumc.nl (L.M. Buffart).

¹ Shared last author.

1. Introduction

Patients with ovarian cancer may experience negative side effects of cancer and its treatment, such as unintentional weight- and muscle loss, increased levels of fatigue or a decrease in physical function and quality of life [1–8]. Exercise and dietary interventions can positively influence body composition, physical fitness and function and reduce fatigue in patients with cancer during and following treatment [9–16]. Evidence on the benefits of exercise and dietary interventions is mainly based on studies among patients with breast cancer. Generalizability of study results from patients with breast cancer to patients with ovarian cancer is difficult, as ovarian cancer is generally diagnosed at an older age, at a more advanced stage, and has a different treatment trajectory [17]. For patients with ovarian cancer, exercise [18,19] or combined exercise and dietary interventions during chemotherapy have shown to be safe and feasible [20] but adequately powered randomized controlled trials (RCT) evaluating the effectiveness are lacking.

Additionally, information on process evaluation outcomes of an exercise and/or dietary intervention for patients with ovarian cancer during chemotherapy is limited. Process evaluation measures include information on the extent to which physical therapists and dietitians implemented the intervention as intended, reasons for protocol deviations, experiences and satisfaction with the intervention, patients' adherence and reasons for non-adherence, as well as intervention components which did or did not meet the preferences and needs of implementers and patients. Hence, information on process evaluation measures helps to further improve intervention implementation and uptake in clinical practice [21].

We used a mixed-methods approach to assess process evaluation measures during the conduct of the multicenter, randomized Physical Activity and Dietary intervention in OVARian cancer (PADOVA) trial [22] of the first included participants. The PADOVA trial examines the effectiveness of a combined exercise and dietary intervention compared with usual care on body composition, physical function and fatigue as primary outcomes in patients receiving chemotherapy for ovarian cancer. The aim of the current study was to qualitatively examine adherence to and experiences and satisfaction with a combined exercise and dietary intervention in patients with ovarian cancer and their healthcare professionals (HCPs), as well as suggestions for improvement. To support qualitative data, we collected quantitative data on intervention adherence and satisfaction.

2. Methods

2.1. Study design and patient enrollment

Details of the PADOVA trial are presented elsewhere [22]. Briefly, patients with primary epithelial ovarian cancer who are scheduled to undergo first-line (neo)adjuvant chemotherapy were recruited from the Center for Gynecologic Oncology Amsterdam. Exclusion criteria were: prior cancer diagnosis within 5 years; unable to perform basic activities of daily living; contraindication for exercise (e.g. heart failure); cognitive disorder or severe emotional instability; unable to read and/or write Dutch; a life expectancy of less than three months. Patient enrollment started in 2018 and is currently ongoing. After obtaining informed consent and baseline assessment patients were randomly allocated to either a combined exercise and dietary intervention or a usual care group during chemotherapy using a table of random numbers in blocks of four. Randomization was stratified for International Federation of Gynecology and Obstetrics (FIGO) stage (I/II vs III/IV) and chemotherapy regimen (primary surgery followed by adjuvant chemotherapy vs neo-adjuvant chemotherapy followed by interval debulking and adjuvant

chemotherapy). The PADOVA study has been approved by the medical ethical committee of the Amsterdam UMC. The trial is registered in the Netherlands Trial Register (NTR6300).

2.2. Intervention

The exercise intervention included two one-hour moderate-to-high intensity resistance and aerobic exercise sessions per week supervised by a physical therapist at a local physical therapy practice. To ensure adequate training intensity over time, one repetition maximum testing and a steep ramp test was repeated every 3 or 6 weeks respectively, aligning with chemotherapy cycles. Additionally, physical therapists were instructed to adjust training load to a Borg Scale of perceived exertion between 12 and 15. Other adjustments made to the protocol were registered as dose modifications.

The dietary intervention was provided by oncology dietitians once every three weeks during face-to-face sessions at the hospital or by telephone. Counseling was tailored to the nutritional needs of each individual patient according to body composition, nutritional status and dietary intake during chemotherapy. Patients were primarily counseled on preventing weight loss by maintaining sufficient caloric intake, particularly protein intake when they were at risk of malnutrition and on meeting the dietary guidelines set by the World Cancer Research Fund (WCRF) otherwise [23]. The protocol contains one counseling session including self-regulation strategies to maintain adherence to the WCRF recommendations after the end of the intervention.

Patients in the usual care group received usual care during chemotherapy, which did not include structured exercise and/or dietary counseling. After completion of chemotherapy they were offered a maximum of three exercise and three dietary counseling sessions in twelve weeks.

2.3. Data collection and analyses

A mixed-method approach, using both quantitative and qualitative research methods, was used to determine adherence to and experiences and satisfaction with the intervention. Semi-structured interviews were held covering topics including experiences, reasons for (non-)adherence and satisfaction with the intervention (See Supplementary Materials (S1) for the interview guide). A researcher (SS) conducted semi-structured interviews by telephone with both patients and HCPs. In the intervention group, interviews were held directly after completion of the last chemotherapy cycle and in the usual care group interviews were held 12 weeks after completion of chemotherapy and counseling sessions. Interviews were transcribed verbatim and were continued until data saturation was reached (i.e., no new codes emerged in subsequent interviews). Thematic analysis of the interview transcriptions was performed in the original Dutch language, concurrently with data collection and coded in six phases [24] using ATLAS.ti version 8.4:

1. Becoming familiar with the data by reading and re-reading all transcripts (MH, SS).
2. Data-driven, independent open coding of all transcripts (MH, SS).
3. Grouping codes into sub- and main themes. Themes were discussed until consensus was reached (MH, SS), when necessary in consultation with a third researcher (LB).
4. Reviewing and refining (sub)themes until the themes reflected the essence of the complete dataset (MH, SS, LB).
5. Providing names and definitions to all themes. To illustrate the themes, we selected quotes which were translated to English by the authors.
6. Answering the research question using the results from the previous phases.

Quantitative data on demographic and clinical characteristics (i.e. age, FIGO stage and type of treatment) were collected from patients using the baseline questionnaire and medical records. We collected data on the following adherence outcomes (see Table 1 for a detailed description): session attendance, intervention interruption(s), session dose modification, content per dietary session and exercise relative dose intensity (ExRDI) [25] which were registered per session by the physical therapists for the exercise intervention and dietitians for the dietary intervention. Additionally, they registered reasons for non-attendance and protocol adjustments. After completion of the intervention, patients in the intervention group received a questionnaire containing questions on general satisfaction with the intervention.

Descriptive statistics of quantitative data were analyzed using IBM SPSS Statistics 26 and presented as mean and standard deviation (SD), median and interquartile range (IQR) or frequencies (proportions).

3. Results

From February 2018 to October 2019, 120 patients were eligible for participation of whom 108 were invited (See Supplementary Materials (S2) for the flow-chart). Twenty-eight (26%) patients agreed to participate, of whom 15 were randomized to the intervention group and 13 to the usual care group. Three patients from the usual care group and one patient from the intervention group dropped out (S2). Interviews were conducted with 14 patients in the intervention group, 10 patients in the usual care group, 18 physical therapists and 5 dietitians. Interview data was not available for one patient in the usual care group because at the time of the interview the patient indicated not wanting to participate in the exercise- and/or dietary counseling sessions. However, after completion of the study it turned out the patient had participated in the counseling sessions. The interview of another patient was not included in analysis because the dietary- and exercise sessions were amended due to COVID-19 measures. Average age of the patients was 53.7 (SD

10.6) years, 54% were diagnosed with a low FIGO stage, and 71% received chemotherapy in only adjuvant setting (Table 2).

3.1. Intervention group

3.1.1. Adherence to the intervention

Median exercise session attendance was 78% (IQR 68–90) in the intervention group. Main reasons for non-attendance, which was known for 83% of the non-attended sessions, included conflicting hospital appointments (20%), being on holiday (17%) or feeling too ill (14%, Fig. 1). Exercise interruption was reported in 8 out of 14 patients and main reasons for exercise interruption were similar to reasons for non-attendance. Additionally, for two patients exercise interruption was related to the physician's advice to restart the exercise intervention six weeks after surgery instead of at the restart of adjuvant chemotherapy (± 4 weeks post-surgery), according to study protocol.

Patients attended 33–133% (median 100%) of the prescribed dietary sessions. Three patients received additional sessions due to peri-operative nutrition-related problems. Six patients received fewer sessions. This resulted in an intervention interruption in the dietary sessions for four patients. Reasons for fewer dietary sessions were that patients did not experience any nutrition-related problems and/or had no further questions about the dietary guidelines.

Patients and HCPs mentioned that it was easy to adhere to the combined intervention (Table 3).

'It is just very convenient that the researchers searched a physical therapist near my home, and because of this, it doesn't take much effort to adhere.' – patient 1.

Several patients mentioned that they perceived participation in the combined intervention easier than expected. This is in line with comments from their physical therapists who mentioned that the extent

Table 1
Summary of outcome measurements.

Description of outcome	Measurement
<i>Experiences</i> - Sharing experiences of the combined exercise and dietary intervention during or after chemotherapy	Semi-structured interviews ¹
<i>Adherence</i> Session attendance	Semi-structured interviews ¹ Checklist provided by physical therapist and dietitian ²
Intervention interruption	Checklist provided by physical therapist and dietitian ²
Content of dietary sessions	Checklist provided by dietitian ²
Session dose modification	Checklist provided by physical therapist and dietitian ²
Exercise Relative Dose Intensity (ExRDI)	Semi-structured interviews ¹ Checklist provided by physical therapist and dietitian ² Checklist provided by physical therapist ²
<i>Satisfaction</i> - Summary of intervention components that patients appreciated and suggestions for further improvement. - Patient satisfaction with the 1) combined intervention, 2) exercise intervention and 3) dietary intervention rated on a scale from 1 to 10 1 representing 'very bad' and 10 'very good'	Semi-structured interviews ¹ Three self-composed items in questionnaire ³

¹ Semistructured interviews are conducted in patients and their healthcare professionals in the intervention group directly after completion of chemotherapy and for patients and their healthcare professionals in the usual care control group 12 weeks after completion of chemotherapy.

² Checklists are filled in by the physical therapist and/or dietitian during the intervention or counseling sessions.

³ Questionnaire is provided after completion of chemotherapy.

Table 2
Baseline characteristics of participating patients.

	Patients (n = 24)	Intervention group (n = 14)	Usual care group (n = 10)
Age, mean (SD) years	53.7 (10.6)	52.0 (10.6)	56.0 (10.6)
Stage of disease (FIGO), n (%)			
Stage I	7 (29%)	4 (29%)	3 (30%)
Stage II	6 (25%)	3 (21%)	3 (30%)
Stage III	11 (46%)	7 (50%)	4 (40%)
Stage IV	0 (0%)	0 (0%)	0 (0%)
Chemotherapy treatment, n (%)			
Neoadjuvant	7 (29%)	4 (29%)	3 (30%)
Adjuvant	17 (71%)	10 (71%)	7 (70%)

to which patients were able to participate in the exercise sessions exceeded their prior expectations. Physical therapists mentioned they gained knowledge on the exercise possibilities in this group of patients.

'I started the exercise intervention with an open mind, the prescription was clear, but I wondered whether a patient would be able to comply with the protocol, but this turned out to be ok.' – physical therapist.

'I expected it to be heavier, that is because at the time of the cancer diagnosis, a lot of people told me I would not have any energy. However, on the contrary, by participating in the intervention I have experienced I still have a lot of energy.' – patient 2.

'I have learned [from the intervention] that I used to underestimate the physical capabilities of patients and consequently prescribed exercises with a too low intensity.' – physical therapist.

The median ExRDI ranged from 36 to 100% (median 72%, Fig. 2). In total, 31% of the attended sessions were modified (9% of the resistance-, 9% of the endurance- and in 13% both the resistance- and endurance exercises). Resistance exercises were mostly modified by reducing the number of exercises per session (92%). Other modifications were reduction in training load (5%) or a combination of these

modifications (3%). Endurance exercises were always modified by reducing exercise duration. Main reasons for session dose modification in both endurance and resistance exercises were logistic reasons (31%, such as the patient or physical therapist preferring other exercises) or were not specified (32%). Pre-existing physical symptoms (18%) and being too tired (16%) were other reasons for dose modification of resistance or endurance exercises, respectively.

'The exercise sessions were scheduled in line with chemotherapy cycles. When I received chemotherapy on Friday the exercise session was rescheduled from Monday to Wednesday. The content of the specific exercise session after chemotherapy was also adjusted, it was less heavy, for example a shorter distance of rowing.' – patient 3.

Dietary counseling focused on a sufficient calorie and protein intake to prevent weight loss in 61%, WCRF guidelines in 24% and both a sufficient calorie and protein intake and the WCRF guidelines in 15% of all attended sessions (Fig. 3). The content of the counseling sessions was modified for four out of fourteen (29%) patients as information on WCRF guidelines was not provided (reasons unknown). Patients who received less than six dietary sessions and/or did not receive information on the WCRF guidelines were treated by dietitians from the same participating hospital.

Multiple dietitians mentioned they prescribed protein intake in two steps, focusing first on total daily protein intake and then on the minimum of 25 g of protein per meal. In case the first step was difficult to achieve, and it often was, they did not try to achieve the second step. Another modification to the protocol was that dietitians were unable to conduct a body composition measurement in case patients received telephone counseling sessions due to the distance between their home and the hospital. Also, one patient mentioned it was not always possible to adhere to the dietary intervention.

'I was not always able to adhere to the dietary recommendations because other people prepared my meals as I was too tired to cook.' – patient 4.

Both patients and HCPs mentioned positive expectations and experiences with the intervention as intrinsic factors promoting adherence.

'It was hope for a faster recovery that helped me to continue participation in the intervention. I have seen people who have battled a poor

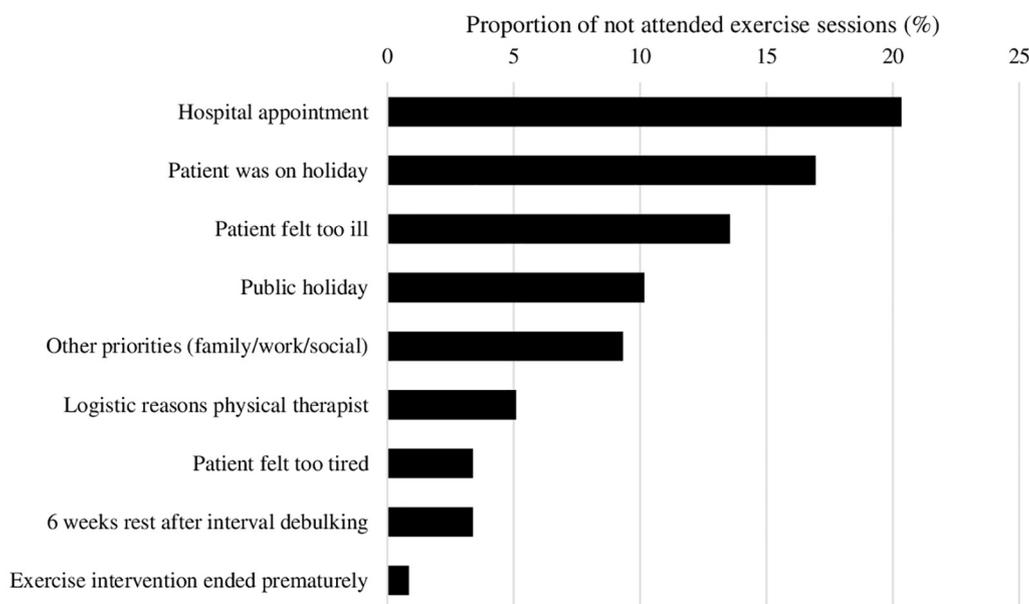


Fig. 1. Reasons for non-attendance of the exercise sessions in the intervention group (n = 14)

Table 3

Overview of interview results on experiences, adherence and satisfaction in patients (n = 14) and healthcare professionals of the combined exercise and dietary intervention during chemotherapy.

Theme	Part of intervention	Who	Subtheme
Experiences			
Perceptions	Combined intervention Exercise intervention	Patients Healthcare professionals Patients	Glad to participate in the intervention Perceived that patients were enthusiastic to participate in the intervention Satisfied with the exercise intervention Appropriate guidance of the physical therapist Appreciation that the physical therapist was specialized in guiding patients with cancer Local physical therapy practice is a safe place to exercise Directly after a chemotherapy cycle or surgery the exercise prescriptions were (too) strenuous Lack of variation in resistance exercises Patients were used to exercise
		Physical therapists	Appreciation to deliver the exercise intervention
Perceived consequences	Dietary intervention	Patients	Satisfied with the dietary intervention Clear and feasible dietary recommendations Easy to get in contact with the dietitian Consultations by telephone are a good alternative for face-to-face sessions to avoid long distance travelling Consultations provided by telephone negatively impacted the patient-dietitian relationship as compared to face-to-face counseling sessions Mismatch between information on nutrition provided by dietitians and knowledge/beliefs of the patients (e.g. due to specific dietary preferences). Patients seemed to appreciate dietary counseling
		Dietitians	Perceived that the intervention helped to recover faster after surgery and chemotherapy cycles
Adherence	Feasibility	Patients	Helped to maintain physical fitness during chemotherapy Perceived that intervention improved quality of life
		Physical therapists	Peer support during group training Structured week schedule Maintenance of physical activity Gain in muscle strength Insights on exercise possibilities in this group of patients Adjustment of care in daily practice due to experiences from delivering the exercise intervention (e.g. increased frequency of steep ramp testing or prescribing a higher training load) Fulfilled that patients experienced positive consequences due to exercise training (e.g. maintenance of physical fitness, strength, energy) Gained knowledge on nutritional intake, especially on protein intake Increased protein intake Perceived that patients achieved their goals (not specified)
Intrinsic factors to continue participation	Combined intervention	Patients	PADOVA protocol was easy to apply because it resembles current daily practice PADOVA protocol is more time consuming than standard care due to for example more frequent exercise testing or having to explain WCRF guidelines Personality trait, i.e. perseverance Enjoyed participation in the (exercise) intervention Experienced or expected advantages of the intervention Similarity with current daily practice
		Healthcare professionals Healthcare professionals	Positive experiences and perceived consequences of the intervention
Extrinsic factors to continue participation	Exercise intervention	Patients	Increased social contact and support Intervention close to a patients' home Agreements with and guidance of healthcare professionals Possibility of flexible appointments with the dietitian Study protocol (e.g. need to fill in study report form) Motivation and effort of patients Easy applicable protocol More frequent sessions (as compared to current practice)
		Healthcare professionals Physical therapists	
Satisfaction	Personal preferences	Dietitians	
		Patients Healthcare professionals	Preference for randomization in intervention group Combined intervention met personal preferences Intervention met personal preferences Pleased with intervention Clear PADOVA protocol Agree with total number, frequency and duration of sessions Dietary intervention did not meet personal preferences or needs in case of a mismatch between information on nutrition provided by dietitians and knowledge/beliefs of the patients (e.g. due to specific dietary preferences)
Expectations	Combined intervention	Patients	No expectations before start of intervention Meeting or exceeding expectations
		Physical therapists	No expectations before start of intervention or expectations were met/exceeded Although insecure at the start, patients proof to be able to comply to the exercise intervention protocol
Expectations	Exercise intervention	Patients	Current standard care for patients with cancer in-hospital focuses on acute care, i.e. prevent or treat malnutrition and to achieve a sufficient daily protein intake.
		Dietitians	

(continued on next page)

Table 3 (continued)

Theme	Part of intervention	Who	Subtheme
Suggested Improvements	Exercise intervention	Patients	At the moment counseling of WCRF guidelines and the protein requirement per meal is not always part of standard care (in-hospital). Some dietitians appreciated to counsel patients in-hospital on healthy nutrition Option to add more variety to the prescribed exercises Once a week PADOVA protocol and once yoga with meditation Possibility to compensate missed sessions (e.g. flexible planning of exercise sessions per week) Extending the duration of the program (until after chemotherapy)
		Physical therapists	Less interim tests, for example once per 6 weeks instead of once per 3 weeks Adding additional exercises for more variety in the exercise protocol to prevent boredom Exercises in alignment with participant personal preferences (functional training) Adding components (e.g. stability-/balance exercises, guidelines for a home-based training when an exercise session is missed, or an additional session is warranted)
	Dietary intervention	Patients	Lower intensity of the resistance exercises to improve feasibility Offering face-to-face dietary consultation close to patients' home Close the gap between information given by dietitians and knowledge/beliefs of patients by for example providing information on alternative diets (e.g. vegan diet) or the influence of nutrition on hormones
		Dietitians	Offer dietary consultations once every 2 weeks instead of once every 3 weeks Amount of sessions should be depending on presence of nutrition-related problems a patient faces. Preference for face-to-face counseling sessions to be able to measure height, weight en body composition in patients Preference to schedule an additional counseling session a few months after completion of the dietary treatment, to be able to repeat the WCRF guidelines Some dietitians would prefer to refer patients to dietitians outside of the hospital for counseling on the WCRF guidelines

fitness level a few years after medical treatment for cancer. It was my biggest fear to recover poorly after chemotherapy. Thus, I had high hopes the exercise intervention would help me recover faster.’ – patient 1.

Personality traits were other intrinsic factors that helped patients adhere to the intervention.

‘I have to finish what I started.’ – patient 2.

Extrinsic factors were agreements with the physical therapist, dietitian or research staff, and social contacts and support.

‘I followed the exercise sessions in a small group of patients, all with oncological symptoms, so you understand and support each other. That is really nice! It is ok to have a bad day, there is no pressure. You do what you can. You can tell your story and can see some other people. Thus socially, it has a very positive effect.’ – patient 5.

3.1.2. Experiences with the intervention

Patients preferred to be randomized to the intervention group. They appreciated the opportunity to participate in the intervention as they experienced positive effects such as an improved quality of life,

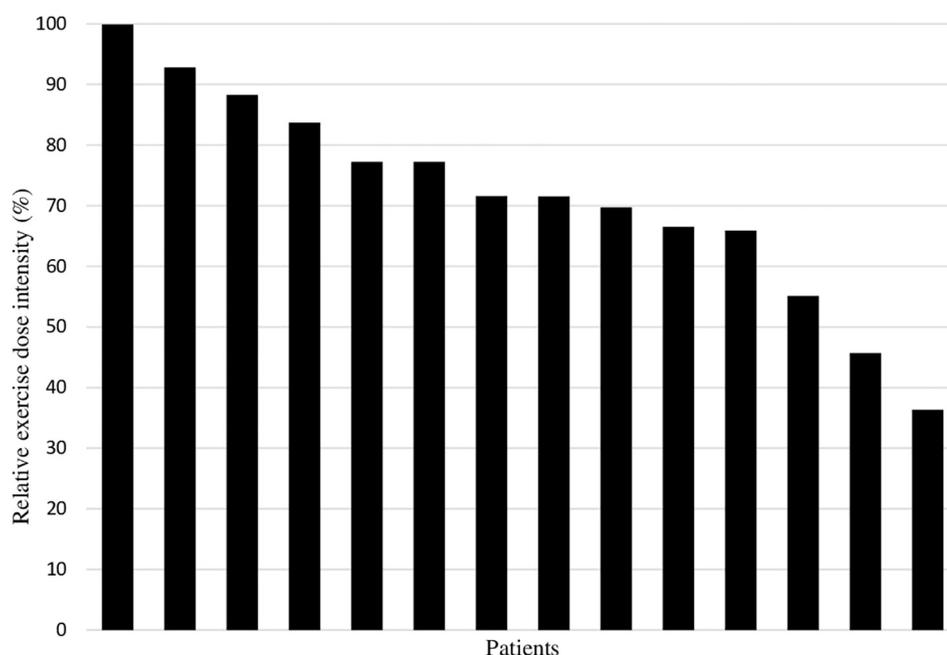


Fig. 2. Relative exercise dose intensity per patient in the intervention group (n = 14)

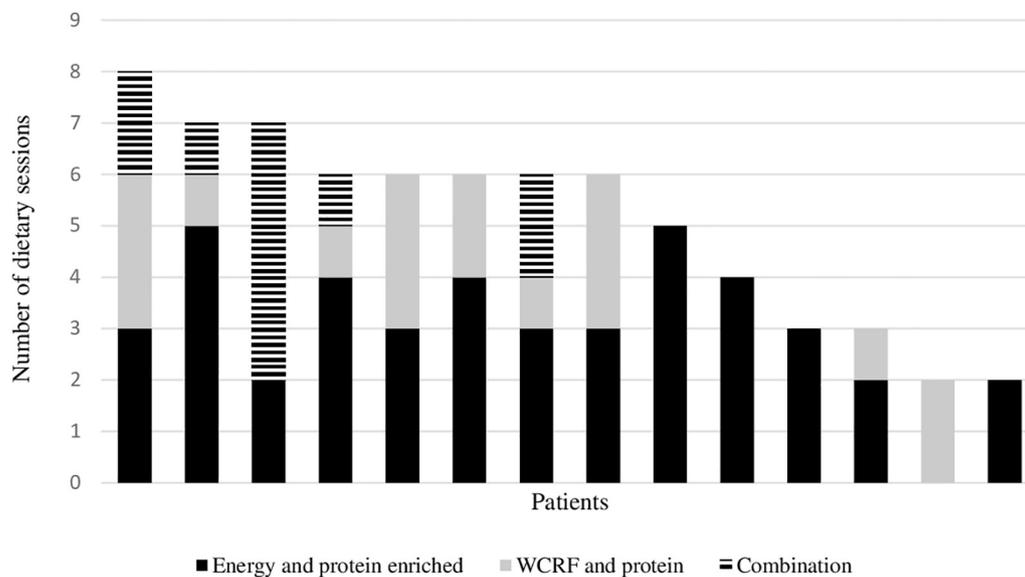


Fig. 3. Attendance to and content of the dietary consultations per patient in the intervention group (n = 14).

maintenance of physical fitness during chemotherapy and that participation in the exercise and dietary sessions helped them to recover faster after surgery and (a cycle of) chemotherapy (Table 3).

'It likely helped me to recover faster, let me say it this way, recovering after surgery and chemotherapy would have probably been harder if I had not received the intervention.' – patient 6.

Also, most HCPs had a positive experience with the intervention as they appreciated the opportunity to deliver the intervention and to experience patients' appreciation.

'It was a great experience to witness a patient's enthusiasm about exercising and gaining energy from the exercise intervention.' – HCP.

HCPs noticed positive results in patients due to the intervention, such as maintenance of physical fitness or strength.

'I found it illuminating to see that a patient could progress so much during chemotherapy using the PADOVA protocol. I now use this protocol in daily practice.' – HCP.

Additionally, patients experienced the local physical therapy practice as a safe location to exercise, and they appreciated the peer support during the group training.

'I appreciate being with peers; you do not need to explain everything.' – patient 5.

'Us peers understand each other.' – patient 4.

Patients reported that they would recommend it to other patients and would like to continue the intervention after completion of the study.

'I have had a very positive experience with the PADOVA exercise and dietary intervention. I would recommend every patient to incorporate this intervention as part of their medical treatment.' – patient 7.

On the other hand, patients indicated that exercise sessions performed shortly after a chemotherapy administration or surgery were particularly difficult to complete because they felt severely fatigued.

'In the first week after chemotherapy the exercise sessions were heavy because I suffered from neuropathy, poor sleep quality and fatigue. In

the second and third week after chemotherapy the exercise sessions felt less strenuous.' – patient 8.

'The exercise sessions felt heavy at the end of chemotherapy treatment, it required a lot of energy to adhere. However, I did it anyway.' – patient 1.

Patients reported to have received clear and feasible dietary advice from the dietitian, and to have gained knowledge on their current and recommended dietary intake, especially their protein intake.

'I have received personalized advice from the dietitian. I have gained more knowledge about my eating pattern and protein intake. My protein intake was too low, so I have learned how to increase my protein intake.' – patient 9.

Patients also mentioned that dietary counseling sessions by telephone were a good alternative for face-to-face sessions avoiding long distance travelling. However, some patients perceived that the telephone counseling sessions negatively impacted the patient-dietitian relationship as compared with face-to-face counseling sessions.

'Due to the telephone consultations, I felt a lack of support. That's why I did not feel like ringing the dietitian whenever I needed support.' – patient 6.

3.1.3. Satisfaction with the intervention

Patients were satisfied with the frequency, duration and content of the exercise and dietary sessions. The majority reported that the combined intervention met their personal preferences and that amendments were not necessary. Patients rated the combined intervention with a median score of 8.5 out of 10 (range 7–10), the exercise intervention with a 9 out of 10 (range 7–10) and the dietary intervention with a 9 out of 10 (range 7–10). Nevertheless, some suggestions to improve the combined intervention were reported during the interviews (Table 3), including more exercise variations per muscle group, and to continue the program after completion of chemotherapy.

'I think you will lose your motivation to exercise when you have to perform the same exercises two times a week for approximately 18 weeks. So, I would suggest adding some variation in the exercises per muscle

group to keep things interesting.’ – patient 10.

Suggestions to improve the dietary intervention included offering face-to-face dietary counseling sessions close to home and offering additional information on alternative diets (e.g. a vegan diet) and on the influence of nutrition on hormone levels.

‘It would have been nice if I had more face-to-face contact with the dietitian. I have only talked to her on the phone. However, face-to-face contact was not possible because I did not want to drive for a long time just to have a 30-minute dietary counseling session. Besides, I was not feeling well due to chemotherapy, there was an intense heat in summer, and I was not allowed to drive due to my reduced vision.’ – patient 4.

Most physical therapists reported to be satisfied with the exercise intervention. Some mentioned that delivering the intervention took extra time as compared to usual care due to more frequent testing and having to adjust the intensity of the program after testing. They mentioned testing every cycle was too often, since they perceived it hard to measure progression in such a short time frame and found it difficult to schedule the test in combination with chemotherapy cycles. Therefore, they recommended to adjust the protocol to testing once every 6 weeks. Other recommendations to improve the exercise protocol were to provide exercise variations to prevent boredom and to offer functional training.

‘.. at this moment endurance training consist of training on a cycle ergometer, this is less important for activities in daily life, like walking.’ – physical therapist.

Most dietitians perceived implementation of the protocol as easy because it was comparable with current daily practice and in line with their personal preferences. For most dietitians the number and frequency of the dietary sessions was sufficient, but they would have preferred the number of sessions to depend on the severity of nutrition-related problems.

‘I have to speak to patients once every three weeks if I want to adhere to the protocol. However, patients are often doing well, which resulted in empty conversations during the dietary counseling sessions. Absence of nutrition-related problems hampered me to speak frequently to patients who were doing well.’ - dietitian.

Dietitians preferred the counseling sessions to be face-to-face, because this positively contributed to building the patient-dietitian relation and it allowed them to measure height, weight and body composition. Some dietitians perceived that counseling on the WCRF guidelines should preferably take place at a local dietetic practice, not in-hospital, as counseling on the WCRF guidelines is not a structural part of in-hospital standard dietary care.

3.2. Usual care group

Three out of ten patients in the usual care group preferred to receive both the exercise and dietary counseling sessions after completion of chemotherapy, four wanted to receive dietary counseling only and three patients only wanted to receive exercise counseling. The patients who did not want to participate in exercise or dietary counseling sessions already received physical therapy (i.e. trial contamination) or dietary counseling sessions (one after referral by the physician during chemotherapy and three found it unnecessary).

‘I did not visit a dietitian because there was no reason for me to do so, as I have tried to live healthy and did not lose weight.’ – patient 11.

‘I did I had no need dietary counseling sessions as the physician referred me to a dietitian during chemotherapy. I did visit a physical therapist after completion of chemotherapy but I did not feel a need to do so,

because I felt rather well, I also started working again and perhaps because there was not much to improve by exercise counseling.’ – patient 12.

The median number of dietary counseling visits was 2.5 (range 1–3). Patients and their dietitians mentioned that more sessions were not needed due to the absence of nutrition-related problems. The median number of exercise counseling sessions was 2 (range 1–3). Some physical therapists added additional sessions to the protocol to further improve fitness or treat pre-existing back problems.

‘At the third counseling session, it appeared that the patient wanted additional counseling sessions after the three sessions prescribed in the protocol. The patient requested additional help to get back to the pre-diagnosis physical fitness level and could not achieve this goal in 2 or 3 counseling sessions. I can imagine some patients are capable of achieving this goal on their own after receiving advice, but this patient required additional guidance from the physical therapist.’ – physical therapist.

Contrary to patients in the intervention group who were intrinsically motivated to adhere to the intervention, patients in the usual care group were extrinsically motivated. They mainly participated in the counseling sessions because it was part of the study protocol. Patients who received exercise and/or dietary counseling sessions had positive experiences. They appreciated the advice from a physical therapist specialized in guiding patients with cancer, and the possibility for telephone counseling sessions with a dietitian instead of face-to-face sessions. Perceived consequences of the exercise intervention included having learned how to maintain energy levels throughout the day and having received exercises targeting various muscle groups and burning of fat mass, which can easily be incorporated in daily life. In addition, patients also experienced positive consequences of the dietary intervention.

‘I have discussed a lot of things with the dietitian about protein and anemia. The dietitian gave advice to help me to regain strength and this helped, I feel better.’ – patient 13.

Several patients in the usual care group indicated that they would have preferred to be randomized to the intervention group.

‘Receiving consultations after completion of chemotherapy is too little too late.’ – patient 12.

4. Discussion

This mixed-methods study examined adherence to and experiences and satisfaction with a combined exercise and dietary intervention during chemotherapy in patients with ovarian cancer. Patients adhered well and reported positive experiences and perceived benefits of participation in the intervention including peer support and improved physical fitness, quality of life and recovery after surgery and between chemotherapy cycles. Both patients and HCPs were generally satisfied with the combined intervention. In both the intervention and the usual care group, patients preferred randomization to the intervention group. Only 33% of the patients in the usual care group wanted to participate in both the exercise and dietary counseling sessions after completion of chemotherapy. Most patients in this group did not want to receive exercise or dietary counseling sessions because they found this too little too late.

The high adherence found in the intervention group contrasted the expectations of both patients and their HCPs, as they reported that they had expected to struggle with adherence. This preconception may have been based on the severe illness and relatively poor prognosis in patients with ovarian cancer as compared to, for example, patients with breast cancer. The 78% attendance to the exercise intervention

we observed, is similar to the attendance reported in studies among patients with (mostly) breast cancer during chemotherapy treatment (63–83%) [26–29] and pilot studies examining home-based low-to-moderate (walking) exercise interventions in patients with ovarian cancer (81%) [18,19]. Also, the high attendance to dietary counseling sessions supports the high attendance (92%) reported in a feasibility study for patients with ovarian cancer receiving adjuvant chemotherapy [20]. We also found that patients with ovarian cancer can comply well to the prescribed exercise type and intensity. Our median ExRDI of 72% was higher than the mean ExRDI of 61% reported in an exercise trial in patients with breast cancer [26]. The high attendance and relatively low number of adjustments to the prescribed protocol may be explained by the use of a systematic approach to tailor the combined intervention to ovarian cancer-specific comorbidities, and disease- or treatment-induced effects [22]. The good adherence holds promise for successful implementation of exercise and dietary support.

The perceived benefits on physical fitness and quality of life reported by patients from the current study are in line with the extensive evidence from RCTs in patients with other types of cancer [16,30,31]. Additionally, our finding that the combined intervention helped patients with ovarian cancer through the different chemotherapy cycles supports findings from a previous concept mapping study among a mixed cancer population that revealed that exercise improved coping with the disease and its treatment [32]. Furthermore, this confirms findings from a previous study in patients with ovarian cancer showing that patients expected that adopting or maintaining a healthy lifestyle would probably help them during treatment [33]. Other positive experiences due to participating in the PADOVA intervention such as receiving quality supervision, peer support, and well-planned structure likely contributed to high satisfaction scores and are in line with findings from previous studies conducted in patients with other types of cancer [28,34,35]. Due to these positive experiences it is important to raise patients' and care providers awareness of and referral to exercise and dietary support during chemotherapy treatment.

Besides the positive experiences and generally high satisfaction with the intervention, our results also present some challenges and suggestions for improvement of the intervention before implementation in clinical practice, after completion of the PADOVA trial. For both the exercise and dietary intervention, patients and their HCPs suggested to individualize the number and content of the exercise and dietary sessions. This is in line with suggestions made in previous studies among patients with breast cancer [28,35]. A specific suggestion for the exercise session was to offer a more flexible exercise session calendar to prevent non-attendance due to a hospital appointment, as this is an important reason for non-attendance [18,26,28,36]. For the dietary intervention, it was suggested by patients to offer face-to-face counseling sessions close to a patients' home. This could be achieved with a national network of oncology dietitians in first line, comparable with that of physical therapists. This suggestion will probably also resolve the problem of not being able to measure body weight and -composition when a counseling session is conducted by telephone and the focus on prevention or treatment of malnutrition mentioned in the interviews by in-hospital dietitians.

With this comprehensive qualitative data collected in a sample of patients participating in a RCT evaluating the effect of a combined exercise and dietary intervention we reached data saturation. We have used quantitative data to support the qualitative data, however because of the small sample size it is not sure if these quantitative results can be generalized to all patients with ovarian cancer. Additionally, the assessment of adherence is limited by the use of logs registered by physical therapists and dietitians. Even though we used standardized checklists that were easy to fill out, the level of detail in which these checklists were completed varied, both at individual and at hospital level. This may have introduced information bias which may have over- or underestimated adherence. In addition, some checklists completed by dietitians lacked detailed information on reasons for not counseling on

the WCRF guidelines and for missed sessions. Therefore, we are not able to conclude that the amount of prescribed dietary sessions should be adjusted. Finally, together with a relatively low response rate, it may be that patients who were more interested in a healthy lifestyle were more likely to participate, as are patients who are younger [37], higher educated [29,38] or diagnosed with a lower FIGO stage [39]. This may hamper generalizability of study findings to all patients with ovarian cancer.

In conclusion, this extensive mixed-methods study, conducted as part of a RCT revealed that patients and their HCPs experienced benefits from participation in the combined exercise and dietary intervention such as peer support and improved fitness, quality of life and recovery after chemotherapy and surgery. Adherence to the combined intervention was high and in general patients were satisfied with the frequency, duration and content of the combined intervention. Suggestions to improve the intervention include further personalization of the number, content and scheduling of exercise and dietary sessions to preferences of patients' and HCPs. Good adherence and positive experiences support successful implementation of the combined intervention in clinical practice together with suggestions to further improve the intervention.

Funding

The PADOVA study is funded by the Dutch Cancer Society, grant number VU 2015–7950. The Dutch Cancer Society was not involved in the design of the study, collection, analysis and interpretation of data, nor in writing the manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Amsterdam UMC (Date 07-11-2018). Additional approval was obtained for the participating hospital.

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Patients signed informed consent regarding publishing their data.

Availability of data and material

Data can be obtained from the corresponding author.

Code availability

Not applicable.

Declaration of Competing Interest

The authors have no relevant financial or non-financial interests to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jgyno.2022.03.011>.

References

- [1] B. Holzner, G. Kemmler, V. Meraner, A. Maislinger, M. Kopp, T. Bodner, et al., Fatigue in ovarian carcinoma patients: a neglected issue? *Cancer*. 97 (6) (2003) 1564–1572.

- [2] V.E. von Gruenigen, H.Q. Huang, K.M. Gil, H.E. Gibbons, B.J. Monk, P.G. Rose, et al., Assessment of factors that contribute to decreased quality of life in gynecologic oncology group ovarian cancer trials, *Cancer*. 115 (20) (2009) 4857–4864.
- [3] V. Meraner, E.M. Gamper, A. Grahmann, J.M. Giesinger, P. Wiesbauer, M. Sztankay, et al., Monitoring physical and psychosocial symptom trajectories in ovarian cancer patients receiving chemotherapy, *BMC Cancer* 12 (2012) 77.
- [4] A.E. Kayl, C.A. Meyers, Side-effects of chemotherapy and quality of life in ovarian and breast cancer patients, *Curr. Opin. Obstet. Gynecol.* 18 (1) (2006) 24–28.
- [5] I.J. Rutten, D.P. van Dijk, R.F. Kruiwagen, R.G. Beets-Tan, S.W. Olde Damink, T. van Gorp, Loss of skeletal muscle during neoadjuvant chemotherapy is related to decreased survival in ovarian cancer patients, *J. Cachexia. Sarcopenia Muscle* 7 (4) (2016) 458–466.
- [6] A. Kumar, M.R. Moynagh, F. Multinu, W.A. Cliby, M.E. McGree, A.L. Weaver, et al., Muscle composition measured by CT scan is a measurable predictor of overall survival in advanced ovarian cancer, *Gynecol. Oncol.* 142 (2) (2016) 311–316.
- [7] M. Mardas, M. Stelmach-Mardas, R. Madry, Body weight changes in patients undergoing chemotherapy for ovarian cancer influence progression-free and overall survival, *Support Care Cancer* 25 (3) (2017) 795–800.
- [8] V.E. von Gruenigen, H.E. Frasure, E.L. Jenison, M.P. Hopkins, K.M. Gil, Longitudinal assessment of quality of life and lifestyle in newly diagnosed ovarian cancer patients: the roles of surgery and chemotherapy, *Gynecol. Oncol.* 103 (1) (2006) 120–126.
- [9] C.S. Padilha, P.C. Marinello, D.A. Galvao, R.U. Newton, F.H. Borges, F. Frajacono, et al., Evaluation of resistance training to improve muscular strength and body composition in cancer patients undergoing neoadjuvant and adjuvant therapy: a meta-analysis, *J. Cancer Surviv.* 11 (3) (2017) 339–349.
- [10] C.W. Cohen, K.R. Fontaine, R.C. Arend, R.D. Alvarez, C.A. Leath III, W.K. Huh, et al., A ketogenic diet reduces central obesity and serum insulin in women with ovarian or endometrial cancer, *J. Nutr.* 148 (8) (2018) 1253–1260.
- [11] C.S. Kampshoff, M.J. Chinapaw, J. Brug, J.W. Twisk, G. Schep, M.R. Nijziel, et al., Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: results of the resistance and endurance exercise after ChemoTherapy (REACT) study, *BMC Med.* 13 (2015) 275.
- [12] H. van Waart, M.M. Stuiver, W.H. van Harten, E. Geleijn, J.M. Kieffer, L.M. Buffart, et al., Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial, *J. Clin. Oncol.* 33 (17) (2015) 1918–1927.
- [13] W. Demark-Wahnefried, M.C. Morey, R. Sloane, D.C. Snyder, P.E. Miller, T.J. Hartman, et al., Reach out to enhance wellness home-based diet-exercise intervention promotes reproducible and sustainable long-term improvements in health behaviors, body weight, and physical functioning in older, overweight/obese cancer survivors, *J. Clin. Oncol.* 30 (19) (2012) 2354–2361.
- [14] M.G. Sweegers, T.M. Altenburg, J. Brug, A.M. May, J.K. van Vulpen, N.K. Aaronson, et al., Effects and moderators of exercise on muscle strength, muscle function and aerobic fitness in patients with cancer: a meta-analysis of individual patient data, *Br. J. Sports Med.* 53 (13) (2019) 812.
- [15] J.K. Vanv, M.G. Sweegers, P.H.M. Peeters, K.S. Courneya, R.U. Newton, N.K. Aaronson, et al., Moderators of exercise effects on cancer-related fatigue: a Meta-analysis of individual patient data, *Med. Sci. Sports Exerc.* 52 (2) (2020) 303–314.
- [16] K.L. Campbell, K.M. Winters-Stone, J. Wiskemann, A.M. May, A.L. Schwartz, K.S. Courneya, et al., Exercise guidelines for Cancer survivors: consensus statement from international multidisciplinary roundtable, *Med. Sci. Sports Exerc.* 51 (11) (2019) 2375–2390.
- [17] K.M. Gil, V.E. von Gruenigen, Physical activity and gynecologic cancer survivorship, *Recent Results Cancer Res.* 186 (2011) 305–315.
- [18] M.J. Newton, S.C. Hayes, M. Janda, P.M. Webb, A. Obermair, E.G. Eakin, et al., Safety, feasibility and effects of an individualised walking intervention for women undergoing chemotherapy for ovarian cancer: a pilot study, *BMC Cancer* 11 (2011) 389.
- [19] D. Mizrahi, C. Broderick, M. Friedlander, M. Ryan, M. Harrison, K. Pumpa, et al., An exercise intervention during chemotherapy for women with recurrent ovarian Cancer: A feasibility study, *Int. J. Gynecol. Cancer* 25 (6) (2015) 985–992.
- [20] V.E. von Gruenigen, H.E. Frasure, M.B. Kavanagh, E. Lerner, S.E. Waggoner, K.S. Courneya, Feasibility of a lifestyle intervention for ovarian cancer patients receiving adjuvant chemotherapy, *Gynecol. Oncol.* 122 (2) (2011) 328–333.
- [21] L.S.A. Linnan, Process evaluation for public health interventions and research. An overview, 2002 (1e edition).
- [22] S. Stelten, M. Hoedjes, G.G. Kenter, E. Kampman, R.J. Huijsmans, L.R. van Lonkhuijzen, et al., Rationale and study protocol of the physical activity and dietary intervention in women with Ovarian cancer (PADOVA) study: a randomised controlled trial to evaluate effectiveness of a tailored exercise and dietary intervention on body composition, physical function and fatigue in women with ovarian cancer undergoing chemotherapy, *BMJ Open* 10 (11) (2020) e036854.
- [23] World Cancer Research Fund / American Institute for Cancer Research, Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Continuous Update Project Expert report, 2018.
- [24] V. Braun, V. Clarke, Using thematic analysis in psychology, *Qual. Res. Psychol.* 3 (2) (2006) 77–101.
- [25] C.M. Fairman, T.S. Nilsen, R.U. Newton, D.R. Taaffe, N. Spry, D. Joseph, et al., Reporting of resistance training dose, adherence, and tolerance in exercise oncology, *Med. Sci. Sports Exerc.* 52 (2) (2020) 315–322.
- [26] J.M. Scott, N.M. Iyengar, T.S. Nilsen, M. Michalski, S.M. Thomas, J. Herndon 2nd, et al., Feasibility, safety, and efficacy of aerobic training in pretreated patients with metastatic breast cancer: a randomized controlled trial, *Cancer*. 124 (12) (2018) 2552–2560.
- [27] L. Witlox, M.J. Velthuis, J.H. Boer, C.N. Steins Bisschop, E.V. Wall, W. Meulen, et al., Attendance and compliance with an exercise program during localized breast cancer treatment in a randomized controlled trial: the PACT study, *PLoS One* 14 (5) (2019), e0215517.
- [28] H. van Waart, L.M. Buffart, M.M. Stuiver, W.H. van Harten, G.S. Sonke, N.K. Aaronson, Adherence to and satisfaction with low-intensity physical activity and supervised moderate-high intensity exercise during chemotherapy for breast cancer, *Support Care Cancer* 28 (5) (2020) 2115–2126.
- [29] C.S. Kampshoff, W. van Mechelen, G. Schep, M.R. Nijziel, L. Witlox, L. Bosman, et al., Participation in and adherence to physical exercise after completion of primary cancer treatment, *Int. J. Behav. Nutr. Phys. Act.* 13 (1) (2016) 100.
- [30] L.M. Buffart, J. Kalter, M.G. Sweegers, K.S. Courneya, R.U. Newton, N.K. Aaronson, et al., Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs, *Cancer Treat. Rev.* 52 (2017) 91–104.
- [31] M.G. Sweegers, T.M. Altenburg, M.J. Chinapaw, J. Kalter, I.M. Verdonck-de Leeuw, K.S. Courneya, et al., Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials, *Br. J. Sports Med.* 52 (8) (2018) 505–513, <https://doi.org/10.1136/bjsports-2017-097891>.
- [32] M.G. Sweegers, L.M. Buffart, W.M. van Veldhuizen, E. Geleijn, H.M.W. Verheul, J. Brug, et al., How does a supervised exercise program improve quality of life in patients with Cancer? A concept mapping study examining Patients' perspectives, *Oncologist*. 24 (6) (2019) e374–e83.
- [33] A.A. Staneva, A.F. Gibson, P.M. Webb, V.L. Beesley, The imperative for a triumph-over-tragedy story in women's accounts of undergoing chemotherapy for ovarian cancer, *Qual. Health Res.* 28 (11) (2018) 1759–1768.
- [34] L.G. Balneaves, C. Van Patten, T.L. Truant, M.T. Kelly, S.E. Neil, K.L. Campbell, Breast cancer survivors' perspectives on a weight loss and physical activity lifestyle intervention, *Support Care Cancer* 22 (8) (2014) 2057–2065.
- [35] K. Vassbakk-Brovold, A. Ja, S. Berntsen, C. Kersten, L. Fegran, Experiences of patients with breast cancer of participating in a lifestyle intervention study while receiving adjuvant chemotherapy, *Cancer Nurs.* 41 (3) (2018) 218–225.
- [36] S.J. Hardcastle, C. Maxwell-Smith, S. Kamarova, S. Lamb, L. Millar, P.A. Cohen, Factors influencing non-participation in an exercise program and attitudes towards physical activity amongst cancer survivors, *Support Care Cancer* 26 (4) (2018) 1289–1295.
- [37] J. Roick, H. Danker, A. Kersting, S. Briest, A. Dietrich, A. Dietz, et al., Factors associated with non-participation and dropout among cancer patients in a cluster-randomised controlled trial, *Eur. J. Cancer Care (Engl.)*. 27 (1) (2018).
- [38] H. van Waart, W.H. van Harten, L.M. Buffart, G.S. Sonke, M.M. Stuiver, N.K. Aaronson, Why do patients choose (not) to participate in an exercise trial during adjuvant chemotherapy for breast cancer? *Psychooncology*. 25 (8) (2016) 964–970.
- [39] R. vdHO Bretveld, M. van der Aa, S. Verboort, Ovarium carcinoom in Nederland, 2019.