

BMJ Open Feasibility and safety of physical exercise in men with prostate cancer receiving androgen deprivation therapy and radiotherapy: a study protocol

Barbara Bressi ,^{1,2} Cinzia Iotti,³ Maribel Cagliari,⁴ Silvio Cavuto,⁵ Stefania Fugazzaro,¹ Stefania Costi ^{1,4}

To cite: Bressi B, Iotti C, Cagliari M, *et al.* Feasibility and safety of physical exercise in men with prostate cancer receiving androgen deprivation therapy and radiotherapy: a study protocol. *BMJ Open* 2022;**12**:e048854. doi:10.1136/bmjopen-2021-048854

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-048854>).

Received 11 January 2021
Accepted 21 February 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Barbara Bressi;
barbara.bressi@ausl.re.it

ABSTRACT

Introduction Androgen deprivation therapy (ADT) and radiotherapy (RT) increase survival in selected patients with prostate cancer. Nevertheless, the side effects of these therapies are associated with an increased risk of accidental falls and fractures and a decreased quality of life. Preliminary evidence suggests that physical exercise can be a valid strategy to reduce the side effects of ADT and RT in men with prostate cancer. Despite this knowledge, most patients with prostate cancer are insufficiently active, and there is a lack of data on the safety and adherence to the recommended dose of physical exercise. This study protocol is designed to examine the feasibility and safety of a multicomponent experimental physical exercise intervention targeting psychophysical and cognitive functions and the quality of life in this population.

Methods and analysis This is a pilot feasibility study. Twenty-five men currently treated with ADT and RT for prostate cancer will be invited to participate in a 20-week, multicomponent physical exercise intervention, including supervised and unsupervised exercise sessions and meeting the current recommendation for exercise in cancer. The primary outcomes are physical exercise feasibility (recruitment, adherence and drop-out rates) and safety (adverse events related and unrelated to the intervention). The secondary outcomes are muscle strength, balance, fatigue, symptoms of anxiety and depression, cognitive function, quality of life, and patient satisfaction. We will also record the number of accidental falls and fractures occurring during the intervention and at 1 year of follow-up.

Ethics and dissemination The study has received ethics approval from The Area Vasta Nord Local Ethics Committee (Province of Reggio Emilia, 23 June 2020, Number 520/2020/SPER/IRCCSRE). Recruitment began in September 2020 and will be completed in September 2021. The results will be disseminated through scientific journals and conference presentations.

Trial registration number NCT04500080.

INTRODUCTION

Prostate cancer affects approximately 3.7 million people worldwide, ranking first among the most prevalent cancers in the

Strengths and limitations of this study

- This pilot study thoroughly assesses the feasibility and safety of a multicomponent experimental physical exercise intervention for individuals with prostate cancer receiving androgen deprivation therapy and radiotherapy.
- Preliminary data regarding the efficacy of structured, supervised, and unsupervised aerobic, resistance, neuromotor, and impact-loading exercise on the bone health of this population will be provided.
- Both the ecological setting, a community sport facility, and the step-down approach, from supervised to unsupervised physical exercise intervention, should foster the adoption of exercise as daily habits, promoting healthy behaviour.
- The single-group design does not allow for assessment of the efficacy of the multicomponent experimental physical exercise intervention on the bone health outcomes of interest.
- The proposed intervention does not target all the factors associated with lifestyle, such as eating, smoking and alcohol drinking habits, which together with physical exercise, are modifiable behaviours that play a role in cancer prevention.

male population.¹ Curative treatment of locally advanced prostate cancer usually entails radiotherapy (RT) frequently associated with androgen deprivation therapy (ADT).² This type of multimodal treatment is unfortunately associated with a large number of side effects.^{3–4} Previous studies have demonstrated a significant increase in cancer-related fatigue in patients receiving RT, which not only decreases physical well-being but also affects daily activities, cognitive function and quality of life.^{5–7} Furthermore, it is well known that the cardiovascular, metabolic, cognitive and musculoskeletal adverse effects of ADT lead to an increased number of accidental falls and fractures in this population.⁸ Furthermore, since prostate cancer

incidence increases with age,¹ older patients are normally already at a greater risk of frailty due to the presence of other comorbidities that can dramatically affect physical function.⁹ Exercise interventions can prevent a large number of these complications, improving the health and quality of life of individuals with prostate cancer.^{10 11} These exercise programmes should include moderate-high intensity activities that must be performed regularly to maintain exercise-related benefits.^{12 13} A recent systematic review of randomised controlled trials (RCTs) showed that to counteract the negative effects of ADT on bone, multicomponent physical exercise interventions involving aerobic, resistance and impact-loading exercise have been performed.¹⁴ Although these interventions were feasible for most participants in the RCT, those study protocols did not systematically record the adherence rate or adverse events associated with the experimented physical exercise interventions.^{12 13 15} However, these data are fundamental to fostering individual compliance with the recommended dose of exercise.¹² In fact, despite the well-known benefits of physical exercise for cancer survivors,^{12 16} this population is frequently unactive¹⁷ and reports several common barriers to exercise, such as the location or distance to facilities.^{18–20} Furthermore, hospital-based supervised physical exercise interventions can be challenging to implement because they require the use of complex hospital resources.^{18 21 22} This modality does not promote long-term adherence to physical exercise or changes towards a healthier lifestyle, which are considered contemporary health priorities for physical therapy practice.^{23 24}

It is suggested that an intensive lifestyle programme that includes dietary supplements, moderate aerobic exercise, stress management and support group participation may affect the progression of prostate cancer at the early stage.²⁵ Furthermore, a healthier lifestyle seems to be associated with a better health-related quality of life.²⁶

In this regard, we investigated the lifestyle of patients recently diagnosed with prostate cancer, their perceived barriers and facilitators to physical exercise, and motivation to change towards healthier lifestyle.²⁷ Therefore, based on previous research and our descriptive study, we developed a structured experimental physical exercise intervention that combines supervised and unsupervised exercise with a step-down approach. This physical exercise intervention is implemented in a community sports facility and is currently being tested in a small group of patients with prostate cancer receiving ADT and RT for feasibility and safety. Secondary outcomes include muscle strength, balance, fatigue, symptoms of anxiety and depression, cognitive function, quality of life and patient satisfaction. We will also record the number of accidental falls and fractures occurring during the intervention and at 1 year of follow-up. This study protocol describes the experimental physical exercise intervention in detail, with related outcomes, to allow for reproducibility and adaptation to other contexts.

METHODS AND ANALYSIS

Patients and study design

This single group feasibility pilot study was approved by the Comitato Etico dell'Area Vasta Emilia Nord (23 June 2020, Number 520/2020/SPER/IRCCSRE). This study protocol adheres to the recommendation for clinical trials (Standard Protocol Items: Recommendations for Interventional Trials) guidelines (online supplemental file 1), and the study registration data set is shown in [table 1](#).²⁸ Eligible patients are adult men (≥ 18 years) with a histological diagnosis of prostate cancer who are currently treated with ADT and RT and are able to communicate in the Italian language. Participants with musculoskeletal, cardiovascular, psychiatric or neurological disorders that contraindicate exercise will be excluded. All patients referred to RT which are also candidate to receive ADT will be assessed for eligibility. If confirmed, written informed consent will be obtained from all participants, who will be invited to participate in a 20-week structured, supervised and unsupervised, multicomponent physical exercise programme. Patients will be assessed at baseline (T0), at the end of the intervention (T1) and at follow-up, which will occur 12 months from recruitment (T2).

So, the experimental physical exercise intervention will start concomitantly with RT, which lasts about 2 months. As regard to ADT, its duration can vary from 6 to 36 months, and it can begin up to 3 months before patient's enrolment in this study and RT commencement.

Recruitment strategies

Between September 2020 and September 2021, eligible patients treated by the Radiotherapy Unit of Santa Maria Nuova Hospital of Reggio Emilia (Italy) will be given brief, written information about the study by their attending physician (radiotherapist or oncologist). On written consent, patients willing to receive more information will be referred to the Physical Medicine and Rehabilitation Unit and will receive a phone call by a research staff member (physiotherapist), who describes the study aim and modalities to them in detail. Patients who confirm their interest in participating will receive written information and consent forms to participate in the study to be filled out and signed. They will also make the first appointment to provide written consent and to perform the baseline assessment. The patient recruitment process is shown in [figure 1](#), and the example of the patient consent form is provided in online supplemental file 2.

Baseline assessment

In the baseline assessment, demographic, anthropometric, clinical data and physical function data will be collected. Clinical data include the date of diagnosis, tumour stage, time since receiving ADT and RT, and the presence of comorbidities assessed through the Charlson Comorbidity Index.²⁹ Physical function will be measured using a 6 min walk test (6MWT)³⁰ to calculate the intensity of aerobic exercise.

Table 1 Study registration data set

| Data category | Information |
|---|--|
| Primary registry and trial identifying number | ClinicalTrials.gov NCT04500080 |
| Date of registration in primary registry | 5 August 2020 |
| Secondary identifying numbers | 520/2020/SPER/IRCCSRE |
| Source of monetary or material support | Manodori Foundation |
| Primary sponsor | Azienda USL-IRCCS di Reggio Emilia |
| Secondary sponsor | NA |
| Contact for public queries | BB (barbara.bressi@ausl.re.it), SCosti (stefania.costi@unimore.it) |
| Contact for scientific queries | SCosti (stefania.costi@unimore.it), BB (barbara.bressi@ausl.re.it) |
| Public title | Feasibility and Safety of Physical Exercise in Men With Prostate Cancer (PCa_Ex) |
| Scientific title | 'The Feasibility and Safety of Physical Exercise Programme in Men with Prostate Cancer Receiving Androgen Deprivation Therapy and Radiotherapy: a Study Protocol' |
| Countries of recruitment | Italy |
| Health conditions or problems studied | Prostate cancer, androgen deprivation therapy and radiotherapy |
| Intervention | Physical exercise intervention |
| Key inclusion and exclusion criteria | <p>Ages eligible for study: ≥ 18 years Sexes eligible for study: man Accepts healthy volunteers: no</p> <p><i>Inclusion criteria:</i> Adult male patient (≥ 18 years) Histologically documented diagnosis of PCa Undergoing ADT and RT during the study period Willing and able to give written informed consent Able to read and understand Italian language</p> <p><i>Exclusion criteria:</i> Any musculoskeletal, cardiovascular, psychiatric or neurological disorders that contraindicate physical exercise</p> |
| Study type | Interventional Allocation: single group assignment Primary purpose: supportive care |
| Date of first enrolment | April 2021 |
| Target sample size | 25 patients |
| Recruitment status | Recruiting |
| Primary outcomes | Feasibility: recruitment, adherence and drop-out rates Safety: any adverse events related and not related to the intervention |
| Key secondary outcomes | Muscle strength, fatigue, cognitive function, balance, quality of life, anxiety and depression level, and number of falls and fractures Patient's satisfaction: patient feedback via interview with open-ended question |

PCa, prostate cancer.

Experimental physical exercise intervention

The multicomponent experimental physical exercise intervention will last 20 weeks and consists of supervised and unsupervised exercise sessions held three times per week. Following a step-down approach, during the first 8 weeks, all physical exercise sessions will be supervised by a physiotherapist, while during the following 4 weeks, only 1 weekly session will be supervised, whereas the other two will be unsupervised; finally, during the last 8 weeks of experimental physical exercise, all sessions will be unsupervised. Supervised sessions will be conducted in small groups or individually at the Municipal Athletics Field in Reggio Emilia according to scheduled appointments,

whereas the unsupervised sessions can be completed by participants in times, modalities and places of their convenience, providing for them the possibility to access the Municipal Athletics Field.

The multicomponent physical exercise intervention meets the dictates for exercise components, posology (frequency, sets, repetitions, intensity) and progression recommended for healthy adults.³¹ Its components are aerobic, resistance, core muscle stabilisation and neuromotor exercises associated with cognitive tasks. In addition, exercise intervention will include impact-loading exercise to provide an effective bone osteogenic stimulus. This type of exercise has been considered an

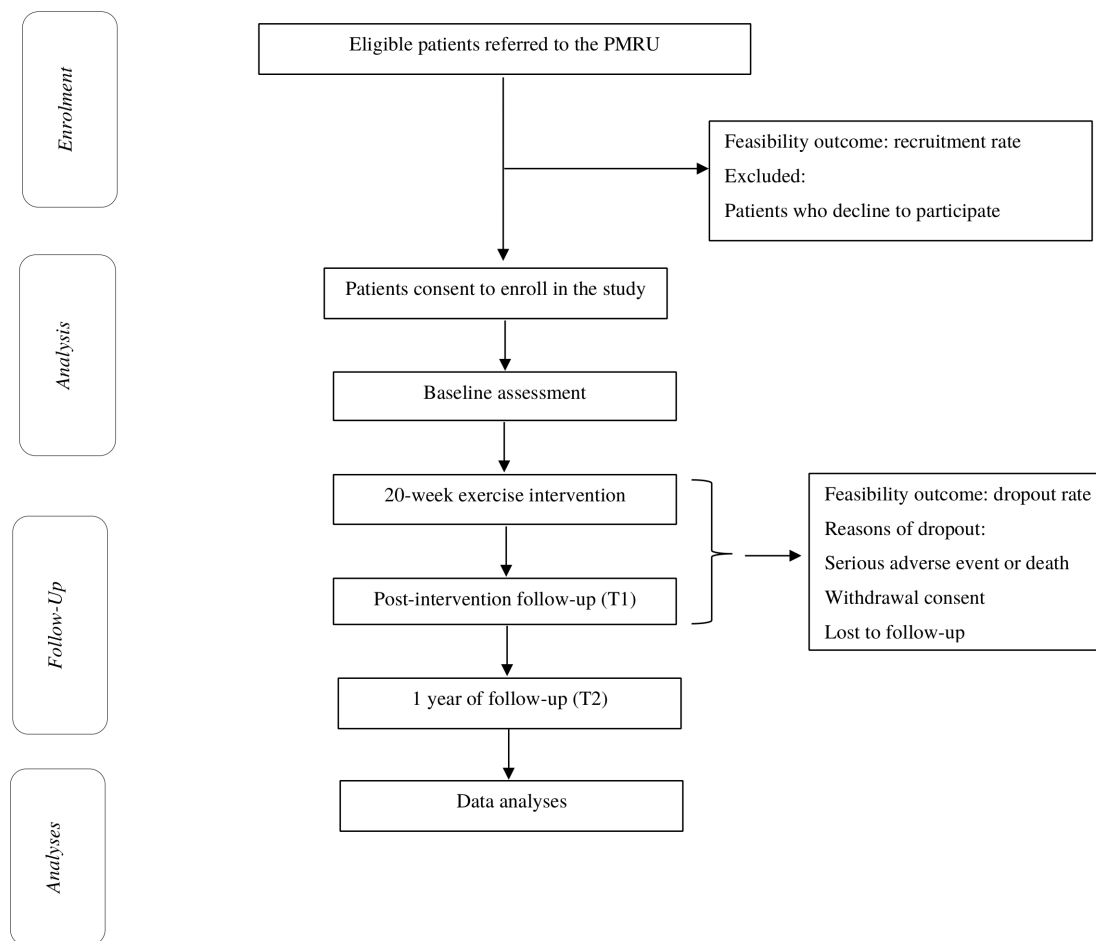


Figure 1 Schematic study flow diagram. PMRU, Physical Medicine and Rehabilitation Unit.

effective strategy to prevent loss of bone mineral density in elderly patients^{32 33} and has been applied in patients with prostate cancer receiving ADT in previous studies.¹⁴ Altogether, the components of this intervention should preserve muscle strength and improve fatigue, balance, and cognitive function,³² and eventually, it should prevent accidental falls and fractures.

The intervention is tailored to individual general health, functional capacity and, as far as possible, preferences.

Supervised physical exercise sessions

Supervised sessions last 1 hour and 15 min and include a period of warm up and cool-down and a combination of the following physical exercise components:

- ▶ Aerobic exercise consists of 20–30 min of aerobic activity at moderate-high intensity, from 60% to 80% of maximum heart rate (% HRmax), previously determined through the 6MWT,³⁰ which is conducted according to the current guidelines.³⁴ To obtain the greatest effects on bone health, the proposed aerobic exercise activities are walking or jogging, depending on individual capacity and habitual or previous experiences of physical activity. The perceived effort will be monitored by the Borg's Rate of Perceived Exertion (RPE) scale to maintain it between fairly light to hard, which corresponds to RPE scores 11–15.³⁵ To ensure

that participants reach the target HR, we will use HR monitors.

- ▶ Progressive resistance exercise consists of strength activity of the major lower and upper extremity muscle groups, using body weight as a load and free weights (resistance bands, dumbbells, anklets with weight, medicine ball). During each session, the goal is to perform four to eight exercises targeting different muscle groups by performing two to four sets of 8–15 repetitions for each exercise. The perceived effort will be measured by the individual using the Borg RPE scale³⁶ (score between 11 and 15). The progression of intensity will be provided, starting the exercises with body weight and gradually increasing the load using free weights.³⁷ Adjustments to load will be made when participants can complete the highest number of specified repetitions (≥ 15 repetitions, see also table 2). Thus, the number of exercises, dose progression (sets, repetitions) and related difficulties (eg, squat depth and/or duration, double task exercises) will be changed during the weeks based on the patient's compliance and performance (see also table 2). For isometric exercises, dose will be incrementally increased by adding free weights, further limb exercise or asking for double task exercise, and/or increasing the duration of exercise from 20 to 60 s.

Table 2 Description of exercise programme and dose progression

| Weeks | 1–4 | 5–8 | 9–12 | 13–16 | 17–20 |
|------------------------------------|---|---|---------------------|---------------------|---------------------|
| Component | Dose | | | | |
| Aerobic exercise | Intensity (% HRmax) Duration | 60%–80% 15–20 min | 60%–80% 20 min | 60%–80% 25 min | 60%–80% 30 min |
| Progressive resistance exercise | Sets Repetitions Difficulties | 2 8–12 Additional free weights, range of motion, number and time* of exercise, additional upper body and/or lower body movements | 2 12–15 8–12 | 3 12–15 8–12 | 4 8–12 8–12 |
| Core muscle stabilisation exercise | Materials Sets Repetitions Difficulties Materials | Free weights (resistance bands, dumbbells, anklets with weight, medicine balls), step 2 8–10 Additional free weights, additional upper body and/or lower body movements and time* of exercise Free weights (resistance bands, dumbbells, anklets with weight, medicine balls), fit ball | 3 10–12 10–12 | 3 12–15 12–15 | 4 12–15 12–15 |
| Neuromotor exercise | Sets Repetitions Difficulties Materials | 2 8–10 Time* of exercise, closing eyes, reducing base of support, introducing unstable support, adding free weights or adding a second cognitive or manual task Free weights (dumbbells, anklets with weight, medicine balls), fit ball, balance board | 2 10–12 10–12 | 3 12–15 12–15 | 4 12–15 12–15 |
| Impact-loading exercise | Sets Repetitions Difficulties Materials | 2 8–10 Additional free weights, introducing multi-directional movement and raising the exercise speed Free weights (dumbbells, anklets with weight, medicine balls), hurdles/hoops/training cone markers, rope, steps | 2 10–12 10–12 | 3 12–15 12–15 | 4 12–15 12–15 |

*Varies from 20 to 60 s and regards isometric exercise and static balance exercise.
% HRmax, per cent maximum heart rate.



- ▶ Core muscle stabilisation exercise consists of postural and trunk stability exercises (eg, strengthening of transverse abdominis and pelvic floor muscles). Participants will perform two core exercises per session in two-four sets of 8–15 repetitions. Sets, repetitions, additional free weights, additional upper body and/or lower body movements and time of exercise from 20 to 60 s will be used to increase the intensity of exercises.
- ▶ Neuromotor exercise consists of balance and functional (coordination) exercises associated with cognitive tasks (eg, counting, adding, subtracting, saying day of weeks) and includes fit ball exercises (eg, knee and contralateral upper limb extension sitting on fit ball), standing balance activities (eg, stand on one leg) and dynamic functional tasks (eg, stop walking balanced on one foot, walking backward). Participants will be asked to complete two to four static and dynamic exercises per session. Static exercises are performed in two-four sets of 20–60 s, while dynamic exercises are performed in two-four sets of 8–15 repetitions. To provide progression, exercises are modified by introducing difficulties (eg, closing eyes, reducing base of support, introducing unstable support, adding free weights, or adding a second cognitive or manual task).
- ▶ Impact-loading exercise consists of jumping, leaping, jumping rope, hopping on one leg, going up and down steps, etc, in other words, exercises that provide impact with the ground using the body weight as a load. Two to four exercises per session will be performed. Training intensity is increased by adding repetitions, additional free weights, introducing multidirectional movement, and raising the exercise speed. To provide a large number of stimuli, several tools will be used.

Also, for core muscle stabilisation, neuromotor and impact-loading exercises, adjustments to load will be made when participants can complete the highest number of repetitions (≥ 15 repetitions) at the target exertion (RPE score between 11 and 15).

A detailed description of exercises, posology, tools and progressivity is available in [table 2](#). Altogether, progressive resistance, core muscle stabilisation, neuromotor and impact-loading exercises are performed for 30–40 min each session.

Unsupervised physical exercise sessions

Unsupervised sessions also consist in all exercise components. In addition to walking or jogging, aerobic exercise can also be performed using bikes, stationary bikes or other aerobic activities based on individual availability and preferences. Regarding the progressive resistance, core muscle stabilisation, neuromotor and impact-loading exercise components, exercises that trade on body weight or with resistance bands that will be provided to patients are taught and suggested to overcome the possible unavailability of appropriate tools. Each activity and exercise will be explained to participants and practised by them during

the supervised sessions. Furthermore, written educational material with instructions and pictures of the exercises will be provided to maximise accuracy of the unsupervised execution. The physiotherapist provides individualised indications regarding the activities to be performed during unsupervised sessions but also supports participants in progressively increasing the exercise workload when the individual perceives an improvement in their functional capacity.

Outcome measures

Primary outcome

Feasibility will be measured through recruitment, adherence and dropout rates.

The recruitment rate is the proportion of eligible individuals referred to the Physical Medicine and Rehabilitation Unit by their treating physician included in the study.

Protocol adherence is the proportion of exercise sessions that are attempted and completed by each participant. The percentage of patients who withdraw from the study and their reason for withdrawal will also be registered.

Safety is measured through the recording of any adverse events related and not related to exercise and its grading for seriousness,³⁸ causality and health consequences by the researcher during the study.

Feasibility and safety are monitored by the physiotherapist through direct inquiry during the first 12 weeks of the programme when supervised sessions are implemented and through a weekly phone call during the last 8 weeks of unsupervised sessions.

Secondary outcomes

Secondary outcome measures include changes in muscle strength, fatigue, cognitive function, balance, quality of life, symptoms of anxiety and depression, number of accidental falls and associated fractures, and participant satisfaction.

Muscle strength

The strength of the major lower and upper extremity muscle groups will be measured with the 10-RM test (extensor muscle group). The 10-RM test assesses the maximum weight that can be lifted for 10 repetitions while maintaining the correct technique. Prior to attempting this test, participants will complete 5 min of aerobic warm-up and 1–2 sets of 15–20 repetitions with a light load. Then, the load will be progressively increased while the number of repetitions will decrease accordingly until only ten repetitions can be completed. A recovery period of 2 min will be provided between each set.^{39 40}

Fatigue

Fatigue will be measured using the Fatigue Severity Scale, a 9-item questionnaire on how fatigue interferes with activities and that rates its severity. The item is scored on a 7-point Likert scale with 1=strongly disagree and 7=strongly agree. The minimum score=9, and the

maximum score=63. A higher score indicates greater fatigue severity.⁴¹

Cognitive function

Cognitive function will be measured using the Mini Mental State Examination (MMSE), a brief cognitive test designed to assess the overall cognitive status of patients. The MMSE tests five areas of mental status (orientation; registration; attention and calculation; recall; language) and is scored on a scale of 30, with adequate cognition for most adults indicated by scores from 24 to 30.⁴²

Balance

Balance will be measured using the Tinetti Performance Oriented Mobility Assessment (POMA). The Tinetti POMA scale is a clinical test used to measure balance and gait abilities. The balance section (POMA-B) consists of 9 items, while the gait section (POMA-G) consists of 8 items. Each item can receive an ordinal score from 0 to 2, where '0' indicates the highest level of impairment and '2' indicates individual independence. The maximum possible total score for POMA-T is 28, for POMA-B is 16, and for POMA-G is 12. A POMA-T cut-off score <19 indicates a high risk of falling.^{43 44}

Quality of life

Quality of life will be measured using the Short Form-12 questionnaire, which consists of twelve items measuring different physical and mental health parameters. Higher scores indicate better physical and mental health.⁴⁵

Anxiety and depression level

Anxiety and depression level will be measured using the Hospital Anxiety and Depression Scale (HADS), a 14-item scale equally distributed across anxiety and depression states. The total score ranges from 0 to 21, with higher scores indicating greater levels of mood disturbances. In patients with cancer, a cut-off score of >9 for the HADS-A and >7 for the HADS-D indicates clinically relevant anxiety and depression levels, respectively.⁴⁶

Accidental falls and fractures

During the intervention, accidental falls and fractures were recorded directly by the physiotherapist who supervised the sessions and performed the weekly phone call and thereafter at the 12month follow-up.

Participant satisfaction

Patient satisfaction will be assessed through a simple structured interview. At the end of the intervention, each participant will be invited to answer the following four open-ended questions that investigate its acceptability:

- ▶ How do you assess the overall experience you have had by participating in this study?
- ▶ Which activities did you like the most?
- ▶ Which activities did you like least?
- ▶ What can be improved in your opinion, or what would you have liked to have been offered?

A summary of the outcome measures and their assessments at follow-up is shown in [table 3](#).

Sample size calculation

No formal sample size requirement is needed for this single-group, pilot, feasibility study. At the Santa Maria Nuova Hospital of Reggio Emilia, nearly 30 patients/year undergo ADT and RT, and we aim to recruit 25 patients during the 12-month recruitment period.

Data analysis

All statistical analyses will be performed by the local Clinical Trials and Statistics Unit of the AUSL-IRCCS of Reggio Emilia. The SAS System or R software will be used according to their availability at the time of data analyses. Descriptive statistics will be reported for feasibility and safety outcomes. For each percentage, the exact two-sided CI will be calculated according to the Clopper-Pearson approach, ensuring a confidence level of at least 95%. In fact, since it is an exact technique, the confidence level typically does not coincide with 95%, the discrepancy for small samples being more noticeable. Adverse events will be described and grouped into homogeneous classes. The data regarding patient satisfaction will be analysed to identify patterns of response and grouped into categories emerging from the data.

Descriptive statistics for secondary outcomes will be reported to inform potential future studies in terms of clinical health outcome measures. For all variables, percentiles, minimum, maximum, mean and SD will be calculated. For the mean, a 95% two-sided CI will be calculated assuming a t distribution. The changing over time of the secondary outcomes will be studied by the analysis of variance for repeated measures.

Concerning the number of accidental falls and fractures, as counts, the CI for the mean will be calculated according to the Poisson distribution. No missing data imputation techniques have been planned, therefore only the available data will be analysed. However, missing data will be appropriately described in their distributional aspects of relevance.

Data management and archiving

The dataset will be stored on a password-protected computer and managed by the Information and Technologies Service (STIT) of the Azienda USL-IRCCS of Reggio Emilia to protect patient privacy and data.

Patient and public involvement

Patients will participate in the study design so that the time and spaces necessary for the home-based intervention can be adapted according to their availability and discretion. Participants may suggest changes related to the frequency and intensity of the sessions and inform the study team about which type of exercises they prefer.

Ethics and dissemination

This study was approved by the Area Vasta Nord Local Ethics Committee of Azienda USL-IRCCS of Reggio

**Table 3** Data collected

| Variables | Data collection method | Data collection points | | |
|-----------------------------------|--|------------------------|----------------|--------------|
| | | Baseline | T1 (20 weeks)* | T2 (1 year)* |
| Primary outcome measures | | | | |
| Feasibility | Recruitment rate Adherence rate Drop-out rate | x | x x | |
| Safety | Number and type of AEs related and not related to intervention | | x | |
| Secondary outcome measures | | | | |
| Muscle strength | Ten repetitions maximum (10-RM) Test | x | x | |
| Fatigue | Fatigue Severity Scale (FSS) | x | x | |
| Cognitive function | Mini Mental State Examination (MMSE) | x | x | |
| Balance | Tinetti Performance Oriented Mobility Assessment (POMA) | x | x | |
| Quality of life | Short Form-12 questionnaire (SF-12) | x | x | |
| Anxiety and depression level | Hospital Anxiety and Depression Scale (HADS) | x | x | |
| Numbers of fall and fractures | Recorded directly by the physiotherapist during the supervised sessions and with weekly phone call during unsupervised session | x | x | x |
| Participant satisfaction | Patient satisfaction | | x | |
| Additional measures | Anthropometry (height, weight, BMI) Demographic data Clinical data Functional capacity (6MWT) | x x x x | x | |

*From baseline.

AEs, adverse events; BMI, body mass index; 6MWT, 6 min walk test.

Emilia (23 June 2020, Number 520/2020/SPER/IRCCSRE), which will also review potential modifications, if any. All patients will provide consent prior to participation. Results will be disseminated through scientific peer-reviewed journals and conference presentations. The expected impact for this study is the development of a useful and acceptable physical exercise programme integrated into the daily routine of patients with prostate cancer receiving ADT and RT.

These results will inform which type of physical exercise is required to improve adherence to the recommended exercise guidelines for cancer survivors and will help researchers plan feasible physical exercise interventions whose efficacy on bone health is to be verified through well-designed RCTs.

Author affiliations

¹Department of Neuromotor Physiopathology and Rehabilitation Medicine, Physical Medicine and Rehabilitation Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy

²PhD Program in Clinical and Experimental Medicine, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Reggio Emilia, Italy

³Department of Oncology and Advanced Technologies, Radiotherapy Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy

⁴Department of Surgery, Medicine, Dentistry and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy

⁵Research and Statistics Infrastructure, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy

Twitter Barbara Bressi @barbara_bressi

Contributors BB, CI, MC, SCavuto, SF and SCosti contributed to study conceptualisation and design and provided input into the development of the protocol. BB, MC and SCosti drafted the manuscript, and all authors revised it critically and approved the final version for publication.

Funding This work is supported by Manodori Foundation, grant number 2019.0062. The Manodori Foundation has no role in study design, data collection, analysis, and interpretation, writing of the manuscript or submission for publication.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Barbara Bressi <http://orcid.org/0000-0001-8014-2591>

Stefania Costi <http://orcid.org/0000-0002-4645-0336>

REFERENCES

- World Health Organization. Cancer today. Available: [https://apps.who.int/iris/bitstream/handle/10665/42451/9241591331.pdf;jsessionid=1F53031C279A57787219D5AF9F7C8332?sequence=1](https://gco.iarc.fr/today/online-analysis-multi-bars?v=2018&mode=cancer&mode_population=countries&population=900&populations=900&key=total&sex=1&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=10&group_cancer=1&include_nmsc=1&include_nmsc_other=1&type_multiple=%257B%2522inc%2522%253Afalse%252C%2522mort%2522%253Afalse%252C%2522prev%2522%253Atrue%257D&orientation=horizontal&type_sort=0&type_nb_items=%257B%2522top%2522%253Atrue%252C%2522bottom%2522%253Afalse%257D&population_group_globocan_id= [Accessed July 29, 2021].
Mohler JL, Antonarakis ES. NCCN guidelines updates: management of prostate cancer. <i>J Natl Compr Canc Netw</i> 2019;17:583–6.
Skolarus TA, Wolf AMD, Erb NL, et al. American cancer Society prostate cancer survivorship care guidelines. <i>CA Cancer J Clin</i> 2014;64:225–49.
Adam S, Koch-Gallenkamp L, Bertram H, et al. Health-Related quality of life in long-term survivors with localised prostate cancer by therapy-Results from a population-based study. <i>Eur J Cancer Care</i> 2019;28:e13076.
Smets EM, Visser MR, Willems-Groot AF, et al. Fatigue and radiotherapy: (B) experience in patients 9 months following treatment. <i>Br J Cancer</i> 1998;78:907–12.
Stone P, Richards M, A'Hern R, et al. Fatigue in patients with cancers of the breast or prostate undergoing radical radiotherapy. <i>J Pain Symptom Manage</i> 2001;22:1007–15.
Feng LR, Espina A, Saligan LN. Association of fatigue intensification with cognitive impairment during radiation therapy for prostate cancer. <i>Oncology</i> 2018;94:363–72.
Edmunds K, Tuffaha H, Galvão DA, et al. Incidence of the adverse effects of androgen deprivation therapy for prostate cancer: a systematic literature review. <i>Support Care Cancer</i> 2020;28:2079–93.
Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. <i>J Gerontol A Biol Sci Med Sci</i> 2001;56:M146–57.
Bourke L, Smith D, Steed L, et al. Exercise for men with prostate cancer: a systematic review and meta-analysis. <i>Eur Urol</i> 2016;69:693–703.
Crawford-Williams F, March S, Goodwin BC, et al. Interventions for prostate cancer survivorship: a systematic review of reviews. <i>Psychooncology</i> 2018;27:2339–48.
Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: consensus statement from international multidisciplinary roundtable. <i>Med Sci Sports Exerc</i> 2019;51:2375–90.
Turner RR, Steed L, Quirk H, et al. Interventions for promoting habitual exercise in people living with and beyond cancer. <i>Cochrane Database Syst Rev</i> 2018;9:CD010192.
Bressi B, Cagliari M, Contesini M, et al. Physical exercise for bone health in men with prostate cancer receiving androgen deprivation therapy: a systematic review. <i>Support Care Cancer</i> 2021;29:1811–24.
Cagliari M, Bressi B, Bassi MC, et al. Feasibility and safety of physical exercise to preserve bone health in men with prostate cancer receiving androgen deprivation therapy: a systematic review. <i>Phys Ther</i> 2021. doi:10.1093/ptj/pzab288. [Epub ahead of print: 23 Dec 2021].
Patel AV, Friedenreich CM, Moore SC, et al. American College of sports medicine roundtable report on physical activity, sedentary behavior, and cancer prevention and control. <i>Med Sci Sports Exerc</i> 2019;51:2391–402.
Thraen-Borowski KM, Gennuso KP, Cadmus-Bertram L. Accelerometer-derived physical activity and sedentary time by cancer type in the United States. <i>PLoS One</i> 2017;12:e0182554.
Ribeiro C, Santos R, Correia P, et al. Resistance training in advanced cancer: a phase II safety and feasibility trial-home versus Hospital. <i>BMJ Support Palliat Care</i> 2020. doi:10.1136/bmjspcare-2020-002230. [Epub ahead of print: 13 Aug 2020]. bmjspcare-2020-002230.
Fox L, Wiseman T, Cahill D, et al. Barriers and facilitators to physical activity in men with prostate cancer: a qualitative and quantitative systematic review. <i>Psychooncology</i> 2019;28:2270–85.
Yannitsos D, Murphy RA, Pollock P, et al. Facilitators and barriers to participation in lifestyle modification for men with prostate cancer: a scoping review. <i>Eur J Cancer Care</i> 2020;29:e13193.
Shea KM, Urquhart R, Keats MR. Physical activity and cancer care in the Atlantic Canadian provinces: an examination of provider beliefs, practices, resources, barriers, and Enablers. <i>J Cancer Educ</i> 2019.
Santa Mina D, Petrella A, Currie KL, et al. Enablers and barriers in delivery of a cancer exercise program: the Canadian experience. <i>Curr Oncol</i> 2015;22:374–84.
Dean E, Skinner M, Myezwa H, et al. Health competency standards in physical therapist practice. <i>Phys Ther</i> 2019;99:1242–54.
Frerichs W, Kaltenbacher E, van de Leur JP, et al. Can physical therapists counsel patients with lifestyle-related health conditions effectively? A systematic review and implications. <i>Physiother Theory Pract</i> 2012;28:571–87.
Ornish D, Weidner G, Fair WR, et al. Intensive lifestyle changes may affect the progression of prostate cancer. <i>J Urol</i> 2005;174:1065–70. discussion 1069–70.
Daubenmier JJ, Weidner G, Marlin R, et al. Lifestyle and health-related quality of life of men with prostate cancer managed with active surveillance. <i>Urology</i> 2006;67:125–30.
Bressi B, Iotti C, Cagliari M, et al. Physical exercise habits, lifestyle behaviors, and motivation to change among men with prostate cancer: a cross-sectional study. <i>Support Care Cancer</i> 2022;13. doi:10.1007/s00520-022-06911-z. [Epub ahead of print: 22 Feb 2022].
Chan A-W, Tetzlaff JM, Gøtzsche PC, et al. Spirit 2013 explanation and elaboration: guidance for protocols of clinical trials. <i>BMJ</i> 2013;346:e7586.
Charlson M, Szatrowski TP, Peterson J, et al. Validation of a combined comorbidity index. <i>J Clin Epidemiol</i> 1994;47:1245–51.
Schmidt K, Vogt L, Thiel C, et al. Validity of the six-minute walk test in cancer patients. <i>Int J Sports Med</i> 2013;34:631–6.
Garber CE, Blissmer B, Deschenes MR, et al. American College of sports medicine position stand. quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. <i>Med Sci Sports Exerc</i> 2011;43:1334–59.
Pinheiro MB, Oliveira J, Bauman A, et al. Evidence on physical activity and osteoporosis prevention for people aged 65+ years: a systematic review to inform the who guidelines on physical activity and sedentary behaviour. <i>Int J Behav Nutr Phys Act</i> 2020;17:150.
Kohrt WM, Bloomfield SA, Little KD, et al. American College of sports medicine position stand: physical activity and bone health. <i>Med Sci Sports Exerc</i> 2004;36:1985–96.
Ats Committee on proficiency standards for clinical pulmonary function laboratories. ats statement: guidelines for the six-minute walk test. <i>Am J Respir Crit Care Med</i> 2002;166:111–7.
Scherr J, Wolfarth B, Christle JW, et al. Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. <i>Eur J Appl Physiol</i> 2013;113:147–55.
Fairman CM, LaFountain RL, Lucas AR, et al. Monitoring resistance exercise intensity using ratings of perceived exertion in previously untrained patients with prostate cancer undergoing androgen deprivation therapy. <i>J Strength Cond Res</i> 2018;32:1360–5.
American College of sports medicine. American College of sports medicine position stand. <i>Progression models in resistance training for healthy adults. Med Sci Sports Exerc</i> 2009;41:687–708.
WHO. Injury surveillance guidelines, 2001. Available: <a href=) [Accessed : July 29, 2021].
- Dos Santos WDN, Siqueira GDdeJ, Martins WR, et al. Reliability and agreement of the 10-Repetition maximum test in breast cancer survivors. *Front Oncol* 2019;9:918.
- Grgic J, Lazinec B, Schoenfeld BJ, et al. Test-Retest reliability of the One-Repetition maximum (1RM) strength assessment: a systematic review. *Sports Med Open* 2020;6:31.
- Ottone M, Pellicciari L, Giordano A, et al. Rasch analysis of the fatigue severity scale in Italian subjects with multiple sclerosis. *J Rehabil Med* 2016;48:597–603.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
- Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. *J Am Geriatr Soc* 1986;34:119–26.



- 44 Faber MJ, Bosscher RJ, van Wieringen PCW. Clinimetric properties of the performance-oriented mobility assessment. *Phys Ther* 2006;86:944–54.
- 45 Ware J, Kosinski M, Keller SD. A 12-Item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–33.
- 46 Annunziata MA, Muzzatti B, Bidoli E, et al. Hospital anxiety and depression scale (HADS) accuracy in cancer patients. *Support Care Cancer* 2020;28:3921–6.