**Author's response to reviews**

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**Version:** 3  
**Date:** 8 August 2014

**Author's response to reviews:** see over
The Individualized Diet and Exercise Adherence Pilot Trial (IDEA-P) in Prostate Cancer Patients Undergoing Androgen Deprivation Therapy: Study Protocol For A Randomized Controlled Trial

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Abstract

Background. Androgen-deprivation therapy (ADT) is the foundation of treatment for men with metastatic prostate cancer (PC) and is now frequently incorporated into multimodality strategies for the curative treatment of locally advanced PC. Nevertheless, the catabolic effects of ADT result in meaningful adverse effects on physiological and quality of life outcomes which may, in turn, increase risk for functional decline, frailty, cardiovascular disease and metabolic syndrome. Recent evidence demonstrates that lifestyle interventions promoting change in exercise and dietary behaviors is a promising approach, may offset, or even reverse, the adverse effects accompanying ADT. Unfortunately, the limited existing studies of the effects of exercise and dietary interventions targeting PC patients on ADT are characterized by high attrition rates and poor post-intervention maintenance of treatment effects. Consequently, the Individualized Diet and Exercise Adherence Pilot Trial (IDEA-P), is designed to contrast the effects of a lifestyle intervention (LI) designed to promote independent self-management of exercise and dietary behavior with those of a standard care disease management approach (SC) in the treatment of PC.

Methods/Design. A total of 40 PC patients undergoing ADT will be randomly assigned to LI or SC interventions. Outcomes of interest in IDEA-P include changes in self-reported and objectively assessed physical function and physical activity/dietary behavior, body composition, muscular strength, and quality of life. Outcomes will be obtained at baseline, 2 month, and 3 month assessments by trial personnel blinded to participants’ randomization assignment.

Discussion. Findings from this study will establish the feasibility and preliminary efficacy of an innovative LI designed to promote progressively independent self-regulated exercise and dietary behavior change in the treatment of PC patients undergoing ADT.

Trial Registration: NCT02050906 Registered; 1/24/14

Key words: Androgen deprivation, functional limitations, prostate cancer, exercise, diet
Promoting Self-Regulated Exercise and Dietary Behavior Change in Prostate Cancer Patients Undergoing Androgen Deprivation Therapy: Design and Methods of the Individualized Diet and Exercise Adherence Pilot Trial (IDEA-P)

Background.

Despite the well-established therapeutic efficacy of androgen-deprivation therapy (ADT) in the treatment of PC [1], it has become increasingly evident that men on ADT endure lingering adverse effects as a “trade-off” for more effective cancer control and increased longevity. The catabolic effects of ADT result in significant adverse effects including loss of lean muscle mass, increased fat mass, reduced muscle strength, and lower bone mineral density that place men undergoing ADT at greater risk for functional decline and frailty [2-9]. Emerging evidence also suggests that ADT increases risk for cardiovascular disease (CVD) and metabolic syndrome. As prolonged administration of ADT becomes increasingly common, many men will cope with lasting treatment-related side-effects that could meaningfully compromise their physical function and quality of life (QoL). PC is estimated to be the cause of over half a million disability-adjusted life years [10-12]. Thus, defining the feasibility and efficacy of innovative interventions that preserve functional abilities and QoL and attenuate risk for chronic disease are primary clinical considerations for PC patients on ADT [2, 7, 13-17].

Exercise consistently results in improvements in relevant physiologic and patient-reported outcomes across a variety of cancer patients/survivors [10, 18-30]. Findings from recent randomized controlled exercise intervention trials in PC patients undergoing ADT also suggest that exercise yields significant, clinically meaningful improvements in muscular strength, physical function, and QoL [31]. Collectively, these findings provide strong support for the beneficial role of exercise as an adjuvant, supportive care intervention in the treatment of PC patients. Despite the clear benefits accompanying exercise, it is also well established within the
weight management literature that modifying both energy expenditure via increased physical activity and energy intake through changes in dietary behavior is integral to successful behavioral weight management interventions [32-34]. Primary adverse effects of ADT are increases in body fat/weight and decreases in muscle mass/strength, which in turn, place PC patients at increased risk for functional decline, CVD, and metabolic syndrome. Thus, the synergistic benefits of concomitant change in both exercise and dietary behavior could represent an optimal lifestyle intervention approach for offsetting the adverse effects experienced by PC patients during ADT.

Consistent with this position, recent findings revealed that lifestyle interventions combining primarily supervised exercise and dietary advice yielded significant improvements in aerobic fitness, muscular strength, self-reported exercise participation [35], fatigue, quality of life [36], and select body weight related outcomes [37] relative to a standard of care [35,36] or metformin treatment [37] in PC patients undergoing prolonged ADT. Results of these trials are clearly important in that they provide the first evidence of the feasibility and preliminary efficacy of implementing lifestyle interventions combining exercise and dietary modifications in the treatment of PC patients on ADT. Unfortunately, despite these promising findings, 2 of the studies were characterized by high attrition rates of 44% [35] and 32% [36] respectively at post-treatment follow-up. Additionally, in one study, clinically meaningful improvements in quality of life accompanying the 12-week lifestyle intervention were not maintained at 6-month follow-up [36].

The deterioration of benefits accompanying lifestyle interventions have been proposed to be directly related to poor post-treatment adherence to exercise and dietary behavior change [38-40]. Thus, given that adherence to the desired behavior changes are essential determinants of the efficacy of lifestyle interventions, these findings underscore the pressing need to explore novel
approaches to promoting successful adoption and maintenance of independent exercise and dietary behavior among PC patients. It has been proposed that high attrition and poor adherence observed in lifestyle interventions may be attributable to a failure to provide patients with the self-regulatory skills necessary to adopt and maintain independent lifestyle behavior change [40]. One new approach based on social cognitive theory and the group dynamics literature [41], a group-mediated cognitive behavioral (GMCB) lifestyle intervention, has recently produced superior adherence to exercise and dietary behavior change and also yielded significant improvements in a variety of clinically relevant outcomes for PC patients in randomized trials targeting chronic disease patients [40, 42-44]. The GMCB intervention couples exercise and dietary behavior change with self-regulatory skills counseling in order to promote independent maintenance of lifestyle behavior change and sustain intervention-induced improvements in relevant outcomes. Although these findings suggest this approach holds promise for improving the utility of lifestyle exercise and dietary interventions targeting PC patients, the feasibility and efficacy of implementing this approach in the treatment of PC patients undergoing ADT has not been investigated. Therefore, the purpose of the present pilot trial is to examine the feasibility and preliminary efficacy of implementing the GMCB exercise and dietary lifestyle intervention in the treatment of PC patients undergoing ADT.

Methods/Study Design

Overview

The Individualized Diet and Exercise Adherence Pilot Trial (IDEA-P) is a two-arm, single-blind, randomized controlled pilot trial designed to examine the effects of a GMCB lifestyle intervention combining exercise and dietary intervention approaches (LI) relative to those of a standard of care disease management approach (SC) in PC patients undergoing ADT (see Figure 1). Primary objectives of IDEA-P are to determine the feasibility of delivering this
specific LI approach to PC patients on ADT and explore the preliminary efficacy of the LI for improving clinically relevant physiologic and QoL outcomes and the short-term adoption and maintenance of independent, self-regulated exercise and dietary behavior change for men undergoing androgen suppression therapy. A total of 40 PC patients on ADT will be randomly assigned to either the LI (n = 20) or SC intervention (n = 20) arms. Given this is a pilot study, it should be recognized that the target patient accrual does not provide optimal statistical power but is adequate to obtain effect size estimates necessary to inform the design of a subsequent optimally powered randomized controlled lifestyle intervention trial. Assessments of the primary and secondary outcomes will be obtained by study staff who are blinded to treatment arm assignment at baseline, 2 month, and 3 month follow-up screening visits.

**Participant Eligibility**

The inclusion and exclusion criteria are designed to target the recruitment of sedentary PC patients undergoing ADT who are sufficiently healthy to participate in a supervised center-based exercise intervention involving both resistance and aerobic exercise. To be eligible to participate in the IDEA-P trial, volunteers will meet the following inclusion criteria: (a) histologically defined diagnosis of PC based upon pathology reports and staging studies; (b) currently undergoing ADT with a planned course of at least 3 months of continuous therapy; (c) sedentary activity pattern with less than 60 min of structured exercise participation per week during the past 6 months; (d) free of any serious medical condition that precluded safe participation in an exercise program such as coronary artery disease, severe hypertension, peripheral vascular disease, stroke, congestive heart failure, chronic obstructive pulmonary disease, insulin-dependent diabetes, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer, and anemia; (e) consent to participate from the treating oncologist and
primary care physician; (f) willingness to accept randomization and undergo the testing and intervention procedures.

Recruitment and Randomization

Recruitment strategies include direct referral to study investigators from physicians at the Genitourinary Oncology Disease Unit of the James Cancer Hospital and Ohio State University Comprehensive Cancer Center and placement of study-related advertisements and informational brochures in cancer center Oncologists’ offices and Cancer Support newsletters. Volunteers interested in participating in the study completed a telephone screening to verify eligibility. Participants determined to be eligible following the completion of the phone-screening interview are then scheduled for the baseline screening visit. Eligible participants are randomly assigned with equal probability to each of the 2 treatment arms using a 1:1 ratio following the completion of the baseline screening visit. The computer generated randomization allocation sequence is sequentially numbered and sealed in opaque envelopes. The randomization allocation sequence is also concealed from study staff responsible for conducting the baseline assessments.

Informed Consent

Approval of trial protocol and informed consent documents has been obtained from the Ohio State University Cancer Institutional Review Board (Project# 2012 C008) prior to the initiation of recruitment procedures. All participants complete informed consent and Health Insurance Portability and Accountability Act (HIPAA) authorization forms prior to beginning participation in the trial.

Measures

Assessments of all study measures are obtained at baseline, 2-month, and 3-month follow-up screening visits using measures with well established validity and reliability
demonstrated in prior exercise intervention studies [43, 44]. Given that IDEA-P is a single blind pilot trial, the outcome assessments are obtained by trained study personnel that are blinded to participants’ treatment assignment.

Outcome Assessments

Functional Battery

The functional battery includes measures of both self-reported physical function and objective indices of functional performance. Self-reported functional limitations will be measured using the abbreviated Late-Life Function and Disability Inventory (LL-FDI) [45]. Functional Performance will be assessed using 3 valid and reliable timed performance-related mobility tasks: 400 meter walk, stair-climb, and lift and carry task [26, 27, 46, 47]. The 400 meter walk test is completed in a corridor with 2 cones spaced 20 meters apart. Individuals are instructed to walk as quickly as they could and the time to complete 10 laps around the cones is recorded as the performance measure. The stair-climb task involves ascending a set of 8 stairs, turning around on the top of the platform, and then descending. Participants are instructed to complete the task as quickly as they could and performance is measured as the total time (in seconds) necessary to complete the task. The lift and carry test is a simulated common daily activity test involving picking up a 10lb container from a shelf, walking 10 feet around a cone, and returning the container to the starting position on the shelf. Participants are instructed to complete the task as quickly as they can and performance is measured as the total time (in seconds) necessary to complete the task.

Mobility-Related Self-Efficacy

Mobility-related self-efficacy is assessed by asking participants to rate their confidence in successfully completing incrementally more challenging amounts of the 400 Meter Walk and
Stair Climb tasks. For walking self-efficacy, participants are asked to rate their confidence on a 0 (no confidence at all) to 10 (completely confident) scale in completing 2, 4, 6, 8, and 10 laps around the cones without stopping. For both stair climb and lift and carry task self-efficacy, participants rate their confidence in successfully completing 2, 4, 6, 8, and 10 trips on the stairs without stopping. Mobility-related self-efficacy scores are calculated for each task by summing the total, dividing by the total number of ratings, and multiplying by 10 to yield a score ranging from 0 to 100. This hierarchical procedure for assessing mobility-related self-efficacy is consistent with Bandura’s recommendations [41] and has been shown to be valid and reliable in prior exercise intervention trials targeting older adults [48].

Muscular Strength.

Muscular strength will be assessed using standardized one-repetition maximum (1RM) testing protocols for the chest press and leg extension exercises [49, 50]. 1RM tests are the standard by which muscular strength is evaluated and have been found to be safe for older adults. Participants are familiarized with the chest press and leg extension machines and receive instruction on proper form. Participants will begin 1RM testing for each exercise by complete a warm-up set of 4-6 repetitions. Participants will rate the difficulty of the set using a 10-point difficulty scale ranging from 1 (not at all difficult) to 10 (extremely difficult). The participant perceptions of difficulty rating are used to choose the first weight at which a 1 RM test will be attempted. Participant will be asked to lift the weight once and to continue to perform single repetition lifts, separated by at least a 2-min rest interval, until a maximum weight is reached and recorded as the 1RM.

Body Composition
Body composition will be assessed using both the Bod Pod (Life Measurement Inc, Concord, CA) and the dual energy x-ray absorptiometry (iDXA; GE Health Care Lunar, Madison, Wisc) methods. The Bod Pod system uses whole body densitometry to determine body composition (body fat and lean body mass). Whole body densitometry is based on the determination of body mass and body volume, since body density is equivalent to body weight divided by body volume. The Bod Pod has well-established validity and reliability as an assessment of body composition [51]. The iDXA scans were used to determine total body composition as well as percent body fat and fat-free mass for the trunk, arms, legs, android, and gynoid subregions. The iDXA method also has well-established validity and reliability and has been used to assess body composition in prior studies among PC patients on ADT [31].

**Physical Activity and Dietary Behavior**

Assessments of physical activity are obtained using objective and self-report measures. The LIFECORDER EX accelerometer (Suzuken Kenz Inc Limited, Japan) is used to obtain an objective assessment of exercise and physical activity participation. Participants wear the LIFECORDER EX on their right hip attached to either the waistband or belt during all waking hours, except when showering, bathing, or swimming, for 7 consecutive days following the completion of the baseline screening visit. Participants record the times they put on and take off the LIFECORDER EX on a self-monitoring log. The LIFECORDER EX provides assessment of minutes of light, moderate, and vigorous physical activity participation as well as calculating total daily steps taken. Consistent with the metabolic demands for the targeted age group [44], the accelerometer was set for intensity levels of 3-6 METS corresponding to moderate intensity physical activity and > 6 METS corresponding to vigorous intensity physical activity. Self-reported physical activity is assessed using the CHAMPS Questionnaire [52] and the Leisure-Time Exercise Questionnaire (LTEQ)[53]. The CHAMPS is a 41-item measure developed
specifically for the assessment of physical activity in adults 50 years and older. The CHAMPS
measure yields estimates of total minutes of physical activity and energy expended per week in
all physical activities of moderate or higher intensity. The LTEQ measures the self-reported
frequency of exercise participation performed in one’s leisure time during a typical week.
Participants are asked to report the number of strenuous, moderate, and mild bouts of exercise
they perform during an average week. The LTEQ has been shown to demonstrate adequate
reliability and validity in previous research [54]. Dietary behavior is assessed using the food
frequency questionnaire developed by the Nutrition Assessment Shared Resource of Fred
Hutchinson Cancer Research Center and 3 day food records. The FFQ provides a validated
assessment of long term dietary patterns. The three-day diet records provide information on more
recent diet habits and enable us to determine compliance to the weekly dietary goals established
at the group nutrition counseling sessions as well as general dietary changes during the
intervention.

Quality of Life (QoL)

Assessments of global and disease-specific indices of QoL will be obtained using several
valid and reliable scales. The Medical Outcomes Study 36-item Short Form Health Survey (SF-36) [55] is a generic measure of health-related QoL which consists of 2 norm-based composite
scales (mental health and physical health) and 8 subscales (physical functioning, mental health,
role-physical, role-emotional, bodily pain, general health, vitality, and social functioning). The
Satisfaction with Life Scale (SWLS) [56] is a 5-item measure of global life satisfaction. Disease
and function specific QoL measures will include the Functional Assessment of Cancer
Treatment-Prostate survey [57], and the Satisfaction with Function and Appearance (SFA) scale
[46]. The 12-items of the FACT-P scale designed to assess concerns specific to PC patients will
be assessed. The SFA scale is comprised of 6-items that tap one’s satisfaction with their physical
abilities and 3-items assessing satisfaction with their physical appearance. Symptoms of pain and
fatigue will also be assessed. Pain will be measured with the short-form McGill Pain Questionnaire, a valid, reliable 15-item adjective checklist that captures sensory and affective dimensions of pain [58]. Fatigue will be measured with the Brief Fatigue Inventory (BFI) a psychometrically sound 9-item measure that taps disease and treatment-related fatigue severity of cancer patients [59].

**Feasibility Measures.**

Descriptive statistics for assessments of select indicators of trial feasibility including recruitment rates, intervention adherence, adverse events, and retention rates will be calculated prospectively throughout the trial.

**Procedures**

Volunteers expressing an interest in participating in IDEA-P complete a phone screening interview to determine their eligibility for the study. Prior to participation in the trial, participants will complete a baseline screening visit during which assessments of all outcomes are obtained. At the beginning of the baseline screening visit, inclusion criteria will be verified and medical history, informed consent, and HIPAA waiver documents are completed. Participants then complete the functional performance tasks, body composition assessment, 1RM strength testing, followed by the questionnaire assessments. After completion of the questionnaires, participants will be provided verbal and written instructions on how to wear the accelerometer. Participants will wear the accelerometer for the next 7 consecutive days and monitors are returned to trial staff via U.S. postal service. Upon completion of the baseline screening visit, participants are randomly assigned into one of the two treatment arms (LI or SC). Primary care physician and treating Oncologist clearance to exercise will be obtained prior to participation in either the LI or SC treatment arms. Assessments of all outcomes are obtained using the exact same procedures at 2 month and 3 month follow-up screening visits conducted by study staff blinded to participants’ treatment group assignment.
Interventions

Exercise and Dietary Lifestyle Intervention (LI).

The LI involves an 8 week, multi-component approach designed to facilitate exercise and dietary behavior change and promote adherence, independent of study staff, to these behavioral modifications. The exercise component involves a combination of aerobic and resistance exercise performed twice per week. The aerobic exercise stimulus consists of 10-30 minutes of exercise performed at a rating of perceived exertion ranging from 11 (Fairly Light) to 14 (Moderately Hard) on the participant’s choice of a treadmill, stationary cycle, or elliptical trainer. The resistance exercise stimulus involves performing 3 sets of 8RM-12RM at a rating of perceived exertion ranging from 12 (Moderately Hard) to 15 (Hard) of 9 different exercises (leg extension, leg curl, chest press, lat pull-down, overhead press, triceps extension, bicep curl, calf raises, and abdominal crunch). Participants will take 1-2 min rest between each set and all sets will be performed in a symptom limited manner. The exercise prescription is tailored to each individual’s abilities and exercise tolerance/capacity. Consequently, resistance exercise load, volume, and volume-load and aerobic exercise duration and intensity will be guided by participant’s exercise tolerance and gradually increased across the intervention to reach optimal targeted prescription ranges. All exercise sessions will last 1 hour in duration.

GMCB activity counseling component, based upon Social Cognitive Theory, is also integrated with exercise to promote adoption and adherence to independent, self-regulated exercise participation and participant retention. Counseling is delivered via 6 small group sessions (20-30 min in duration) conducted once per week immediately following a center-based exercise session during months 1-2. Participants also receive 4 brief (20-min) individualized activity counseling sessions conducted via phone calls in months 1-3. Specific content of this component includes the promotion of group identity and social norms for activity; self-monitoring; goal setting; barrier problem solving; fostering social support; reducing sedentary
time. The purpose of activity-related behavioral counseling component of the LI arm is to instruct PC patients undergoing ADT on the use of self-regulatory skills necessary to adopt and maintain exercise, and through the use of the group as an agent of behavioral change, facilitate motivation to develop and implement these behavioral skills in order to successfully plan and participate in increasing frequency of independent exercise and physical activity participation. A basic principle underlying these contacts and their sequencing is one of gradually weaning participants from the dependency on staff and the group program toward independent self-regulation of exercise. This process is one of a phased increase in the ratio of personal responsibility in conjunction with a phased decrease in staff, group and clinic dependency. Thus, in contrast to most approaches in traditional exercise interventions, the present approach places an emphasis on the regulation of behavior and social problem solving barriers to promote independent exercise participation.

To foster the practice/mastery of the newly acquired exercise and behavioral skills and prevent participants from becoming dependent on the expertise of exercise staff to remain physically active, supervised center-based exercise decreases from 2 sessions per week in weeks 1-6 to 1 supervised sessions/week in weeks 7-8 of the intervention. During weeks 7-8, participants have the goal of completing one center-based exercise session independent of study staff supervision during each week. During month 3, participants will have the goal of completing two center-based exercise sessions independent of study staff supervision. Participants will be provided free access to the center-based exercise facility during all its standard operating hours during weeks 7-12. While the facility is supervised by trained fitness staff members during this time, the participants will have no supervisory contact with the study staff during these independent exercise sessions. The advantages of the approach integrating counseling and the titration away from staff supervision is it helps participants actively apply their developing exercise and behavioral skills to exercise independently while also
concomitantly providing them access to the study’s exercise facility to facilitate completion of
the independent exercise sessions during weeks 7-12 and allows us to evaluate uptake of
independent exercise adherence from in months 2-3.

The dietary component of the LI includes 10 (30-min) nutritional counseling sessions
with a registered dietitian. The first 8 counseling sessions will be conducted once/week
immediately following a center-based exercise session during months 1-2. The 2 remaining
sessions are conducted via biweekly phone calls during Month 3. The specific dietary objectives
are consistent with the Therapeutic Lifestyle Changes recommended in the Adult Treatment
Panel III Report of the National Cholesterol Education Program [60] and the American Institute
of Cancer Research [61]. The nutrition intervention encourages reductions in portion size and
caloric and fat consumption together with a gradual transition from an animal-based diet to a
more plant-rich diet while still incorporating animal foods including milk and meat with an
emphasis on monitoring food proportion and portion size. Specific goals of the dietary
component include: (a) reduction in energy intake by 500-1000 kcal per day; (b) reduction in
total fats to 25-30%, saturated fats to 7%, and protein to 15% of total calories; (c) increase in
fruit and vegetable consumption to 5 servings per day; (d) intake of 3 or more servings per day of
whole grains per day and a gradual increase to at least 25 grams of dietary fiber per day. The
nutrition counseling uses the GMCB and motivational interviewing approaches that have been
demonstrated to be an effective approach to promote behavior change in chronic disease [43] and
cancer patients [58, 59] previously. The nutrition counseling also builds upon many of the
cognitive-behavioral self-management strategies utilized in the exercise intervention including
self-monitoring, building self-efficacy, goal setting, and anticipating and overcoming barriers to
dietary behavior change.

Standard of Care (SC) Intervention
Men randomized to the SC arm receive usual PC treatment, standard disease management education, as well as educational literature describing the American Institute of Cancer Research dietary and physical activity guidelines. To equate contact between treatment arms to levels consistent with similar, contemporary lifestyle intervention trials [62, 63], 20-min phone contacts delivered by Genitourinary Oncology clinic staff focusing on routine aspects of PC self-management will be conducted biweekly with men in the SC arm. As an incentive to promote retention across the trial, men randomized to standard of care will also receive 2 supervised exercise training sessions and dietary counseling sessions following the completion of the 3 month assessment. Men will complete assessments of all outcomes scheduled at baseline and months 2 and 3.

Statistical Analysis

The primary hypotheses of the IDEA-P trial are: (1) the LI intervention will be a safe, well-tolerated intervention that yields acceptable recruitment, adherence, retention, and adverse event rates (2) the LI intervention will result in superior improvements in physical function, muscular strength, body composition, and QoL relative to the SC intervention; and (3) the LI intervention will successfully promote adoption and short-term maintenance of independent, self-regulated exercise and dietary behavior change at 3 month follow-up. Differences in the longitudinally gathered outcome data collected at 2 and 3 month follow-up assessments will be individually standardized by baseline values and evaluated using a weighted repeated measures analysis of variance statistical model adjusting for the effects of age and gender. All analyses will be conducted according to the intention to treat principle with last value carried forward imputation methods used to account for missing data. As noted previously, the target patient accrual does not provide optimal statistical power but is adequate to obtain effect size estimates
necessary to inform the design of a subsequent optimally powered randomized controlled lifestyle intervention trial.

Discussion

The IDEA-P trial is a single-blind, two arm randomized controlled pilot trial evaluating the feasibility and preliminary efficacy of a GMCB lifestyle intervention approach combining individualized exercise and dietary modification and behavioral self-regulatory skills counseling in the treatment of PC patients undergoing ADT. Given the integral role of ADT in PC treatment, there is a critical need to determine the benefits of supportive care approaches for reducing the adverse effects accompanying ADT. The synergistic benefits of lifestyle interventions combining exercise and dietary behavior change may be a particularly beneficial adjuvant treatment approach for offsetting the adverse effects experienced by PC patients during ADT. Although recent findings suggest lifestyle interventions combining exercise and dietary advice approaches yield significant improvements in clinically relevant outcomes for PC patients undergoing ADT [35-37], some of these studies have been characterized by high attrition rates [35-36] and poor-post intervention maintenance of treatment effects [36]. Consequently, these findings suggest that novel approaches for improving successful adherence to independent self-regulation exercise and dietary behavior change are warranted.

The proposed pilot trial is innovative from both research and clinical practice perspectives. From a research perspective, IDEA-P is innovative in that it expands knowledge from existing studies of the benefits of lifestyle exercise and dietary interventions in PC patients on ADT [35-37]. Notably, it is the first to determine the feasibility and efficacy of implementing a group-based LI that has been effective in promoting both successful maintenance of independent exercise and dietary behavior change and superior changes in relevant functional and QoL outcomes in other chronic disease patients [40, 42, 43] among men PC on ADT. There are also other methodological aspects of IDEA-P that make it innovative from extant PC
research. For example, implementing the theory-based activity and dietary behavioral counseling to promote behavior change expands on the primarily psycho-educational advice-based approaches used in prior studies. Furthermore, whereas prior investigations have relied exclusively on self-reported physical activity assessments, which consistently overestimate exercise and physical activity participation, the present study is the first to include a more accurate objective measure of physical activity. Collectively, these features make IDEA-P unique from prior or on-going lifestyle interventions targeting men on ADT. From a clinical perspective, we believe determining the feasibility, safety, and preliminary efficacy of implementing this LI intervention approach in men on ADT will have meaningful future implications for clinical practice for PC patients. Results of this feasibility study will inform the design of larger randomized controlled lifestyle intervention trials. If findings from larger scale efficacy trials demonstrate meaningful benefits of implementing this lifestyle exercise and dietary intervention in the treatment of PC patients on ADT, such results could provide the evidence necessary to alter current standard of care practices towards the inclusion of exercise and dietary interventions in the routine clinical treatment of PC patients.

Although findings from the IDEA-P trial could yield meaningful implications for the role of lifestyle interventions as an adjuvant behavioral approach for the treatment of PC patients, there are select study limitations that should be acknowledged. Given this is a pilot trial intended to determine safety, feasibility, and preliminary efficacy of delivering the group-based behavioral LI during ADT, the sample size does not provide sufficient power to detect meaningful differences in all relevant outcomes of interest. Additionally, there are clearly other clinically relevant outcomes, such as select biomarkers of PC and chronic disease that may be favorably influenced by the LI that are not assessed in the present pilot trial.

In summary, determining the feasibility and preliminary efficacy of the LI relative to the effects of SC could have significant implications for the treatment of PC patients on ADT.
Findings from the present pilot trial will also provide effect size estimates necessary to inform the design of subsequent, large scale definitive LI efficacy trial, the results of which would fill a critical gap in knowledge addressing the utility of implementing exercise and dietary modification in the treatment of PC patients undergoing ADT.

_Trial Status._ The IDEA-P trial is active with patient recruitment and intervention delivery currently ongoing.

**Abbreviations:** ADT: Androgen Deprivation Therapy; PC: Prostate cancer; IDEA-P: Individualized Diet and Exercise Adherence Trial-Pilot; LI: Lifestyle intervention; SC: Standard of care; CVD: cardiovascular disease; QoL: Quality of life; GMCB: Group-mediated cognitive behavioral; LL-FDI: Late Life Function and Disability Inventory; IRM: One repetition maximum; iDXA: dual energy x-ray absorptiometry; LTEQ: Leisure time exercise questionnaire; FFQ: Food frequency questionnaire; SF-36: Short form health survey; SWLS: Satisfaction with life scale; SFA: Satisfaction with function and appearance scale; FACT-P: Functional assessment of cancer treatment-prostate scale; BFI: Brief fatigue inventory; HIPAA: Health insurance portability and accountability act;

_Acknowledgements_

Support for the present study is provided by National Cancer Institute Grant # R03 CA16296901

_Competing Interests_

The authors declare that they have no competing interests.

_Author Contributions_

BCF, SKC, EG, and JMTA conceived the study. BCF, SKC, and EG participated in the design of the study. BCF, EG, ARL, and CS are conducting the study. BCF and ARL wrote the manuscript. All authors read and approved the final manuscript.
3. References


Figure Legend

Figure 1. Design of the IDEA-P trial