

PATERSON, C., ROBERTS, C., KOZLOVSKAIA, M., NAHON, I., SCHUBACH, K., SARA, S., SAYNER, A.M., DE ABREU LOURENCO, R., TURNER, M., CHAN, R.J., LAM, T., WOO, H. and TOOHEY, K. 2022. The effects of multimodal prehabilitation interventions in men affected by prostate cancer on physical, clinical and patient reported outcome measures: a systematic review. *Seminars in oncology nursing* [online], 38(5), article 151333. Available from: <https://doi.org/10.1016/j.soncn.2022.151333>

The effects of multimodal prehabilitation interventions in men affected by prostate cancer on physical, clinical and patient reported outcome measures: a systematic review.

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2022

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Title: The effects of multimodal prehabilitation interventions in men affected by prostate cancer on physical, clinical and patient reported outcome measures: A systematic review

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Declarations

The authors received no specific funding for this work

Conflicts of interest/Competing interests: none to declare

Ethics approval: not applicable

Consent to participate: not applicable

Consent for publication: not applicable

Abstract

Objective: To synthesise existing evidence on the effects of multimodal prehabilitation interventions in men affected by prostate cancer on physical, clinical and patient reported outcome measures.

Data sources: A systematic review was conducted according to the PRISMA 2020 Statement Guidelines. Electronic databases (Medline, Embase, CINAHL and Cochrane CENTRAL and clinicaltrials.gov) were searched using key search terms. Articles were assessed according to pre-specified eligibility criteria. Data extraction and quality appraisal was conducted. The findings were integrated in a narrative synthesis.

Conclusion: Of the 5863 publications screened, 118 articles were assessed in full-text and 17 studies met the pre-screening eligibility criteria. There were a range of study designs which included: randomised controlled clinical trials (n=11), quasi experimental (n=4), cohort (n=1), and case series (n=1), covering a total of 1739 participants. The prehabilitation interventions included: physical activity, peer support, pelvic floor muscle training, diet, nurse-led prehabilitation, psychological, and prehabilitation administration of phosphodiesterase-5 inhibitors.

Implications for nursing practice: Significant heterogeneity existed in the prehabilitation intervention programs for men affected by prostate cancer in terms of the composition, duration, method of administration, and the outcomes measured to quantify their impact. This systematic review has identified that multimodal prehabilitation interventions are an emerging area for practice and research among men affected by prostate cancer. Importantly, there has been a lack of focus on the inclusion of partners as critical companions during this distressing phase of the cancer care continuum. For the moment, all members of the multidisciplinary team caring for people affected by prostate cancer are encouraged to use the findings in this review to inform holistic models of care.

Key words: prehabilitation, prostate cancer, systematic review, multimodal, physical, clinical, patient report outcome measures

Introduction

Prostate cancer is the most prevalent type of cancer in men and represents a significant health problem worldwide ¹. Radical treatments for localised prostate cancer include surgery and radiotherapy ² and can be associated with a negative impact on patients' quality of life ³ and psych-social outcomes ⁴. To improve overall quality of life and patient outcomes, an important clinical question remains about "when" is the most opportune time to introduce recovery-optimising behaviours and strategies ⁵. Cancer prehabilitation is defined as a process on the continuum of care that occurs between the time of a cancer diagnosis and the beginning of acute treatment ⁶. It is hypothesised that prehabilitation offers a clinical route to improving the patients' physical and psychological status and may buffer (moderate) treatment-related deconditioning between the time of diagnosis to post-treatment recovery ⁷. Prehabilitation includes physical and psychological assessments that establish baseline functioning and identifies impairments that can impact on cancer treatment-related morbidity, as well as provide targeted interventions to optimise overall well-being prior to treatment ⁶.

Internationally, there is a growing recognition to include prehabilitation models of care in the cancer pathway with recent recommendations highlighting its value ⁸. However, efficacy evidence that prehabilitation translates into better long-term outcomes for men affected by prostate cancer is unclear ⁵. To date, there have been various systematic reviews on the topic of prehabilitation prior to surgical treatment in other cancer groups including colorectal ^{9,10}, lung ¹¹, breast ¹², and mixed cancer groups ^{13,14}. Therefore, there is an important clinical need to take stock of the evidence to understand the impact of prehabilitation interventions for men affected by localised prostate cancer opting for radical therapy. There is a growing interest in other cancer treatments and modes of prehabilitation, which include: exercise, psychological, nutritional, pelvic floor exercises, and sexual prehabilitation ⁸. This timely systematic review will critically review the impact of different modalities of prehabilitation interventions on health outcomes in men affected by localised prostate cancer opting for radical treatment. This review will address the following clinically focussed research question:

- In men affected by localised prostate cancer, what are the effects of prehabilitation interventions on post-treatment outcomes including physical functioning, clinical and patient reported outcomes?

Materials and Method

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement ¹⁵, see Supplementary Table 1. The systematic review was registered with PROSPERO 2019 CRD42019139872 and followed an a priori protocol.

Types of studies

Inclusion

All randomised or quasi-randomised trials conducted in men affected by localised prostate cancer (opting for any primary active treatment modality) that compared prehabilitation intervention(s) to standard care (or another prehabilitation intervention/modality) were included. Given the anticipated dearth of RCTs in the clinical area, this review also included all single arm prospective case series of prehabilitation interventions.

Exclusion

Any animals or in vitro experiments. Case reports, reviews, commentaries, editorials, and conference abstracts and studies published in languages other than English.

Types of participants

Inclusion

All adults (≥ 18 years) with localised prostate cancer irrespective of modality of primary active treatment. Participants who received any form of prehabilitation either in the home or hospital setting.

Exclusion

All men treated for salvage prostatectomy/radiotherapy and men on active surveillance and/or watchful waiting (ie. non-curative treatment).

Types of interventions

Inclusion

Prehabilitation is defined as a single- or multi-modality intervention that could include any of the following: physical exercise, nutritional support, patient education, psychological therapy, pelvic floor muscle training, interventions to facilitate sexual functioning (e.g. use of PDE-5 inhibitors, vacuum pump device, etc) and peer support ¹⁶. The control is defined as those participant's receiving usual care as defined in the clinical pathway.

Types of outcome measurements

Inclusion

Identification of objective physical function, clinical and patient-reported outcomes described at post-treatment completion.

Physical function measurements: physical tests to measure fitness, functional capacity, pulse wave velocity, 6 Minute Walk Test, 30 second sit to stand test, blood pressure and pulse wave velocity.

Clinical outcomes: urinary incontinence (number of pads/weight of incontinence pads), sexual function, oncological outcomes (Prostate Specific Antigen, Gleason Score, histopathology), complications, blood loss, length of hospital stay, post-treatment mobilisation, post-treatment pain, re-admission rate within 90 days, mortality and RTOG/EORTC Late Radiation Morbidity.

Patients reported outcomes: health-related quality of life (HRQoL), disease-specific HRQoL, anxiety and depression, coping, and self-management self-efficacy.

Exclusion

Prehabilitation studies with no post-treatment outcomes.

Literature search

The CINAHL, ClinicalTrials.gov, Cochrane CENTRAL (Database of Systematic Reviews and Central Register of Controlled Trials) Medline, and Scopus databases were searched for all relevant publications. See **Supplementary Table 2** for exemplary searches. The search architecture used a wide range of keywords and subject headings to increase the sensitivity and inclusiveness of the searches. Pre-screening eligibility criteria were applied to all records identified. All records were managed using Endnote software and uploaded to Covidence systematic review software for de-duplication and screening of records.

Data collection and analysis

Following de-duplication, two review authors *independently* screened the titles and abstracts of identified records for eligibility. The full-text papers of all potentially eligible records were retrieved and screened independently by two review authors using a data extraction form, linking together multiple records of the same study in the process. Any disagreements were resolved by discussion or through consulting a third review author.

Assessment of risk of bias in included studies

The assessment of the risk of bias of each study, considering the issues of randomisation, allocation concealment, blinding, completeness of outcome data, selective reporting and any other potential bias were considered across all the included studies. The assessment tool was developed as part of a Health Technology Assessment ¹⁷ and has been used in previous cancer care systematic review publications ^{4,18}. The appraisal tool assessed a range of designs including: RCTs, non-randomized controlled studies, cohort, case-control, other observational studies (for example, interrupted time series, case series, cross-sectional designs) and were classified as “low”, “unclear” and “high” risk according to the criteria specific to each study design. Some items in the quantitative assessment tool are only relevant to

RCT's; therefore a “non-applicable” item option was available for other research designs. The appraisal tool has 17 items and three levels of quality assessment ranging from two to zero.

Data extraction and management

Two review authors independently extracted outcome data. Study characteristics were extracted by one review author and checked by a second review author for accuracy across all publications. A data extraction form was developed and piloted before its use.

Data extracted included a 'characteristics of included studies' table with the following: study design; countries and institutions where the data were collected; dates defining start and end of patient recruitment and follow-up; whether there was an *a priori* protocol or analysis plan; participant demographic and clinical characteristics, prehabilitation intervention, definition of standard of care, follow-up protocol; withdrawals; physical, clinical and patients reported outcomes; the numbers of participants who were included in the study; losses and exclusions of participants, with reasons; study funding sources; ethical approval; and power calculation.

Data synthesis

It was not possible to conduct a meta-analysis because of the large heterogeneity across the studies included. This review completed tabulation of primary research studies and used of narrative synthesis to generate findings. Specifically, this involved data reduction (subgroup classification by domain of prehabilitation, with results tabulated), data comparison (identifying patterns and themes through clustering and counting and making contrasts and comparisons) and conclusion drawing and verification (synthesis of subgroup analysis to inform a comprehensive understanding of the topic, verified with the primary source of data for accuracy).

Findings

Of the 5863 publications screened, 118 articles were assessed in full-text and 17 studies met the pre-screening eligibility criteria (**Fig 1**).

Fig 1 PRISMA Flow Diagram

The studies were conducted in a range of countries which included: Australia (n=5), Canada (n=2), Italy (n=1), Korea (n=1), The Netherlands (n=2), Sweden (n=1), United Kingdom (n=1), and the United States of America (n=4), see **Table 1** for an overview of the included studies. Across the included studies the sample sizes ranged from 28 to 310, with a total of 1739 participants in this review. There were a range of study designs which included: randomised controlled clinical trials (n=11), quasi experimental (n=4), cohort (n=1), and case series (n=1), see **Table 2** for the results of the quality assessment. The majority of the prehabilitation study participants included men affected by localised prostate cancer being treated by radical prostatectomy, with the exception of several studies which included mixed treatment groups (surgery and brachytherapy) ¹⁹, and (neoadjuvant androgen deprivation therapy and radiotherapy or brachytherapy) ^{20,21}. One study ²² did not report on the clinical characteristics of the study participants. All the studies delivered prehabilitation interventions among men affected by localised prostate cancer opting for radical prostatectomy, but most authors did not report on the approach to radical surgery (open, laparoscopic or robotic) and the surgical techniques in nerve-sparing or non-nerve sparing approaches which might have impacted on the study outcomes.

Prehabilitation Interventions

Broadly, there were several classifications of prehabilitation interventions identified across the 17 studies, see **Table 3**. These interventions included physical activity ^{23,24}, peer support ^{22,25} pelvic floor muscle training ²⁶⁻³¹, diet ^{32,33} nurse-led prehabilitation ^{19,20,34}, psychological ³⁵ and prehabilitation administration of phosphodiesterase-5 inhibitors ²¹. Heterogeneity existed in the prehabilitation intervention programs for men affected by prostate cancer in terms of the composition, duration, method of administration, and the outcomes measured to quantify their impact see **Supplementary Table 3**. Furthermore, across the included studies there was a notable lack of reporting in relation to adherence and fidelity outcomes. Nine studies did not report on planned intervention adherence or fidelity assessment methods, including how this was to be assessed and by whom, or if

Table 1. Overview of the included studies

| Author and Year | Purpose | Sample size, mean age (SD, years), gender | Participants (cancer stage, Gleason score, treatment) | Response rate | Design | Time points | Data collection tools |
|---------------------------------------|---|--|---|--|--------------------------------------|---|---|
| Au, et al. 2019 Canada | To explore whether prehabilitation is associated with differences in physical activity during the postoperative inpatient stay and the week after discharge in men undergoing abdominal surgery | Sample size: primary study n=86 however, n=42 were provided with accelerometers (due to limited number). Mean age: Intervention (I): 61.4 (±7.8) Control (C): 58.4 (±6.1) | Cancer stage: T1 (I: n=0 / C: n=1) T2 (I: n=7 / C: n=11) T3 (I: n=12 / C: n=7) Gleason Score: 7 (I: n=17 / C: n=16) 8 (I: n=0 / C: n=2) 10 (I: n=2 / C: n=1) Treatment: Robot-Assisted (I: n=14 / C: n=16) Open: (I: n=5 / C: n=3) | n=38/42 (90%) I: n=19 C: n=19 | Randomised controlled clinical trial | Prehab 4-8 weeks prior to RP surgery. T1: Inpatient. Day 1 postop for 24-h period (starting 8am) T2: Outpatient. First day of discharge for 7 days (starting 8am) | Wrist-worn accelerometers (Actiwatch 2, Philips Healthcare, Respironics, USA). |
| Chambers et al. 2013 Australia | Assess the feasibility of peer intervention for couples where the man was preparing for prostate cancer surgery. | Sample size: n=10 (peer support volunteers) / n=20 (couples) Mean age: Peer support: 66.2 years (SD 7.5) Couples: Men 61.9 years (SD 6.3) / Women 55.8 years (SD 7.7); p<0.01 Gender: peer support = male Couples = male / female (heterosexual couples only) | Cancer stage: not disclosed, aside from requiring a diagnosis of localised prostate cancer to participate. Gleason Score: Not reported Treatment: Not reported other than RP | Couples that completed all sessions n=17/20 (85%) | Quasi experimental study | Couples: Baseline: recruitment T1: 3 months post-surgery T2: 6 months post-surgery | Peer support: Peer focus group (audiotaped and transcribed verbatim) Couples: Working Alliance Inventory; IES-R; Sexuality needs subscale of the Supportive Care Needs Survey; PTGI |
| Crowe et al. 2018 Australia | To determine the effect on viewing an animated pelvic floor model on participants' ability to correctly perform PFM exercises prior to RP. | Sample size: n=51 (I: n=23 / C: n=28) Mean age: I: 62.0 (SD 7.63) years. (P=0.78) C: 61.75 (SD 7.18) years | Cancer Stage: does not state specifically. Only mentions localised PCa Gleason Score: Not reported Treatment: Robot-assisted: n=47 (92%) Open: n=4 (8%) | 105 approached (45 declined / ineligible). 60 enrolled. 9 withdrew. n=51/60 (85%) | Randomised controlled clinical trial | Baseline: prior to physiotherapy assessment (which occurred between 1 day to 4 weeks prior to surgery) T1: 1 month following RP T2: 3 months following RP | EPIC-26; Study diary; 6-item, non-validated questionnaire (re: info they received about PFM exercising); PFM assessment (TPUS and DRE) |
| Dalais et al. 2004 Australia | To determine the effects of diets rich in heat-treated (HT) soy grits and HT soy grits and linseed compared with a control diet low in soy and linseed on the biochemical markers of prostate cancer who were scheduled to undergo radical prostatectomy. | Sample size: n=28 (Soy: n=8 / Soy and Linseed: n=10 / Wheat: n=8) Mean age: Soy: 61.7 (±5.1) / Soy and Linseed: 58.4 (±4.9) / Wheat: 60.5 (±5.2) | Cancer stage: Not reported Gleason Score: Soy: 6.50 (±0.85) Soy and Linseed: 5.75 (±0.90) Wheat: 5.71 (±1.38) Treatment: RP | 38 referred. 32 eligible. n=28/32 (87.5%) | Randomised controlled clinical trial | Baseline: pre-study T1: follow up (1 day before surgery) Duration of intervention days: Soy: 23.2 (±3.2) Soy and Linseed: 27.4 (±3.6) Wheat: 22.2 (±3.1) | Pre-study visit: Blood and urine samples (urinary isoflavone and lignan concentrations, biochemical markers, urinary creatinine, PSA and free PSA, testosterone, sex hormone-binding globulin, free androgen index, dihydrotestosterone); physical measurements (BMI); Validated food frequency questionnaire (Anti-Cancer Council of Victoria, Carlton Australia) 1 day before surgery: Blood and urine samples repeated |
| Dijkstra-Eshuis et al. 2015 | To investigate the effectiveness of preoperative PFMT with biofeedback on Stress Urinary | Sample size: n=121 <i>Allocations:</i> PFMT with Biofeedback (n=65) Control (n=56) <i>Follow up:</i> | Cancer stage: T1: n=34 (31.5%) T2: n=74 (68.5%) Gleason Score: | Allocated: n=121 Followed-up: | Randomised controlled clinical trial | Baseline: Preoperatively (this period lasted ~4 weeks for intervention group) T1: 6 weeks postop | Preop: KHQ; IPSS and 24-hour bladder diary; PeLFI; |

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| The Netherlands | Incontinence (SUI) and on Quality of Life (QoL) in men scheduled to undergo a LARP. | PFMT with biofeedback (n=64) Control (n=56) <i>Analysis:</i> PFMT with biofeedback (n=56) Control (n=46) Mean age: 63.7 years (SD ±5.3) | 5: n=2 (1.6%) 6: n=50 (40.7%) 7: n=40 (32.5%) 8: n=10 (8.1%) 9: n=7 (5.7%) Treatment: No nerve sparing: n=52 (48.1%) Unilateral: n=22 (20.2%) Bilateral: n=34 (31.5%) | n= 120/121 (99%) Analysed: n=102/121 (84.3%) | | T2: 3 months postop T3: 6 months postop T4: 9 months postop T5: 1 year postop | <i>Pelvic Floor Examination:</i> anal visual inspection and digital palpation, as well as biofeedback registration with rectal probe Post-op (6 weeks / 3,6,9,12 months): KHQ, IPSS, 24-hr bladder diary and 24-hr pad test 12 months post-op: In addition to above post op data collection the PeLFIs and Pelvic Floor exams completed again. |
| Demark-Wahnefried et al. 2017 USA | To explore whether weight loss favourably affects tumour biology and other outcomes in overweight men opting for radical prostatectomy. | Sample size: n=40 Mean age: 60.1 (6.3) | Cancer stage: Not reported Gleason score: Not reported Treatment: RP (not detailed which approach). | N=97 screened N=38 refused participation. N=20 weight loss intervention N=20 wait-list control. | Feasibility Randomised controlled clinical trial | Baseline: At the time of recruitment. Time 2: not clearly reported. 50 days on the protocol. | Clinical measurements: body fat and lean mass, Vo2, RAND-36, Prostate Cancer Index, Physical Activity Recalls (7-day) Circulating biomarkers Tumour biomarkers |
| Dubbelman et al. 2012 The Netherlands | The recovery of urinary continence after radical retropubic prostatectomy (RRP), comparing the effect of physiotherapist guided PFME's, with guidance by an instruction folder only. | Sample size: n=66 PG-PFME (physio guided PFME) n= 33 F-PFME (info folder only PFME) n=33 Mean age: Not reported Median age = 64 years. | Cancer stage: Not reported Gleason Score: Not reported Treatment: Open RRP. Nerve sparing was performed depending on pre-operative and intra-operative assessment of the extent of disease. Bladder neck spared in 21/66 patients. <i>Bilateral nerve sparing:</i> n=21/66 <i>Unilateral nerve sparing:</i> n=16/66 <i>Non-nerve sparing:</i> n=28/66 (one surgical approach unknown) | n=66 (no mention of dropouts – appears all were followed up) | Randomised controlled clinical trial | Baseline: before surgery T1: 26 weeks after catheter removal. | Urodynamic measurements: Brown-Whickham Method, modified by Griffiths (to measure UPP – Urethral Pressure Profilmetry). Continence: 1-hr and 24-hr pad tests |
| Hawkins et al., 2017 USA | To determine whether combining a computer-based support with a human cancer mentor would benefit men affected by prostate cancer before treatment and into survivorship. | Sample size: 310 Mentor only intervention n=105, Comprehensive health enhancement support system (CHESS) intervention n=103, CHESS + Mentor n=102 Mean age: 60 years | Cancer Stage: stage 1 or 2. Gleason score: Not reported Treatment: Not reported | Total of 461 patients invited, 147 declined, 4 were excluded. | Randomised controlled clinical trial | Time 1: baseline within 2 months of diagnosis, T2: 2 weeks, T3: 6 weeks, T4: 12 weeks, and T5: 24 weeks. | Postal questionnaire WHOQOL, EPIC, FACT-P, cancer Information Competence, Social Support, Health Care Competence, COPE, Bonding scale |
| Hirschhorn, et al. 2014 Australia | To assess the effect of a multicomponent theory-based intervention, incorporating patient information guides, an evidence summary, audit and feedback processes and a provider directory, in the | Sample size: <i>Pre-intervention - Public Hospital:</i> Patients undergoing RP n=51 Patients consenting to survey n=42 <i>Pre-Intervention – Private Hospital:</i> Patients undergoing RP n=125 Patients consenting to survey n=101 <i>Post-Intervention – Public Hospital:</i> Patients undergoing RP n=26 | Cancer stage: Not reported Gleason Score: Not reported Treatment: Radical Prostatectomy (second private site had a new robot assisted RP) | Patients that returned surveys <i>Overall Response Rate:</i> 139/232 (60%) | Cohort (before and after) study | Surveys: mailed 3 months post-surgery Practice Audits: month by month data Patient Information Guides: When first scheduled for RP. Audited from at monthly intervals from April 2012 | Survey (demographic, receipt of PFMT before and after surgery, satisfaction with treatment for UI) ICIQ-UI Short form The RAND 36-item short form Health Survey (SF-36) |

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| | provision / receipt of pre-operative pelvic floor muscle training (PFMT) among patients undergoing radical prostatectomy. | Patients consenting to survey n=17 <i>Post-Intervention – Private Hospital:</i> Patients undergoing RP n=166 Patients consenting to survey n=73 Mean age: 63yrs (SD 7) | | | | Audit Feedback (newsletters and presentations): 3-month intervals from May 2011- Aug 2012. | |
| Kinsella et al. 2011 UK | To assess whether the demonstration of erectile management techniques to patients before RP influenced treatment choice and, ultimately, regret. | Sample size: n=82 (I: n=41 / UC: n=41) *UC = usual care Mean age: I: 60.6 (±5.5) years /UC: 61.5 (±6.8) years (p=0.54) | Cancer stage: T1 (I: n=16 / UC: n=14) T2 (I: n=25 / UC: n=27) Gleason Score: 6 (I: n=22 / UC: n=25) 7 (I: n= 19 / UC: n=16) Treatment: Robot-Assisted Prostatectomy or Laparoscopic Radical Prostatectomy with expectation of nerve sparing Some men withdrew from RP and opted for Brachytherapy | I: n=33/41 (80.5%) UC: n=40/41 (97.5%) | Quasi experimental study | Baseline: pre-treatment T1: 3 months T2: 6 months T3: 9 months T4: 12 months (follow-ups done at 3 monthly intervals) | IIEF-5; HADS; 2 item regret questionnaire |
| Kim 2011 Korea | To explore a self-care nursing intervention among men affected by prostate cancer undergoing radical prostatectomy. | Sample size: 69 N=35 intervention group N=34 control group Age: Below 60 years old n=14, 61-70 years n=42, over 70 years n=13 | Cancer stage: T2 n=57, T3 n=12 Gleason score: 6 n=25, 7 n=31, >8 n=11. Treatment: RP | Not reported. | Quasi experimental study | Baseline: before surgery and 2 months follow-up. | Self-as-Career Inventory (self-care agency) Quality of Life FACT-P |
| Manley et al. 2016 Australia | To evaluate the effect of pelvic floor muscle (PFM) assessment and training before and after robot-assisted laparoscopic radical prostatectomy (RARP) in improving PFM strength and urinary incontinence. | Sample size: n=98 Mean age: 64yrs | Cancer stage: pT2: n=63 (65%) pT3a: n=28 (29%) pT3b: n=6 (6.2%) Gleason Score: 6: n=9 (9.2%) 3+4: n=60 (61%) 4+3: n=19 (19%) 8+: n=10 (10%) Treatment: RARP using same robot and same technique of anastomosing - maximising urethral length. Nerve-sparing technique performed on all men regardless of age. | n=98/115 (85.2%) 7 didn't have assessment at 4 days following catheter removal. 10 men did not have assessment at 4 weeks post catheter removal | Case series | Baseline: pre-op T1: 4 days post catheter removal T2: 4 weeks post catheter removal | PFM assessments / DRE / Trans-abdominal ultrasound / physio record of whether patient requiring incontinence pads or pull-ups |
| Parker et al. 2009 USA (Texas) | To assess the short-term and long-term efficacy of a presurgical stress management intervention at reducing mood disturbance and improving quality of life (QOL) in men undergoing radical prostatectomy (RP) for prostate cancer | Sample size: n=159 Stress Mgt (SM) n=53 Supportive Attention (SA) n=54 Standard Care (SC) n=52 <i>1 week before surgery:</i> SM (n=48) / SA (n=54) / SC (n=50) <i>Day of surgery:</i> SM (n=48) / SA (n= 52) / SC (n= 50) <i>6 weeks post-surgery:</i> SM (n=31) / SA (n=39) / SC (n=36) <i>6 months post-surgery:</i> SM (n=37) / SA (n=38) / SC (n=32) <i>12 months post-surgery:</i> SM (n=32) / SA (n=37) / SC (n=32) Mean age: SM – 59.8 (SD 6.9) / SA – 60.7 (SD 7.2) / SC – 60.9 (SD 5.9) | Cancer stage: 1 (SM: 6=12% / SA: 7=13% / SC:7 =13%) 2 (SM: 35=69% / SA: 42=79% / SC:39=75%) 3 (SM: 10=19% / SA: 4=8% / SC: 6=12%) Gleason Score: Not reported Treatment: Non-nerve sparing: (SM:14=28% / SA: 11=22% / SC: 12=25%) Nerve sparing: (SM: 32=64% / SA: 33=66% / SC: 34=39%) Nerve Graft: (SM: 4=8% / SA: 6=12% / SC: 3=6%) | 221 men approached. 164 consented and completed baseline ax n= 159/164 (96.9%) <i>final numbers at 1-month post-surgery:</i> SM: n=32/53 (60.3%) SA: n=37/54 (68.5%) SC: n= 32/52 (61.5%) | Randomised controlled clinical trial | All assessments completed at each time point aside from the morning of surgery. Due to time limitations only one was performed the day of surgery. Baseline Ax: 1 month before surgery T1: 1 week before surgery T2: day of surgery T3: 6 weeks post-surgery T4: 6 months post-surgery T5: 12 months post-surgery. | POMS; IES; SF-36; PCI |

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|----------------------------------|---|--|--|---|--|---|--|
| Santa Mina et al. 2018 Canada | To assess feasibility of a multi-centre RCT examining home-based prehabilitation versus a control condition in men undergoing radical prostatectomy. | <p>Sample size: Baseline: n=86 (PREHAB: n=44 / CON: n=42) T1 (pre-op) PREHAB: n=38 / CON: n=35 T2 (4 weeks post-op) PREHAB: n=37 / CON: n=34 T3 (12 weeks post-op) PREHAB: n=34 / CON: n=32 T4 (26 weeks post-op) PREHAB: n=33 / CON: n=28</p> <p>9 and 21 participants withdrew between baseline and surgery and 26 weeks follow up, respectively. 4 participants did not undergo surgery (dropouts)</p> <p>Mean age: I: 61.2yrs (SD 8.0) C: 62.2yrs (SD 6.9)</p> | <p>Cancer stage: 0 (PREHAB: 0 / CON: 1) T1 (I: 0 / C: 1) T2 (I: 16 / C: 18) T3 (I: 26 / C: 21) Missing (I: 2 / C: 1)</p> <p>Gleason Score: 7 (I: 31 / C: 30) 8 (I: 0 / C: 6) 9 (I: 6 / C: 2) 10 (I: 6 / C: 3) Unknown (I: 0 / C: 1) Missing (I: 1 / C: 0)</p> <p>Treatment: Surgery Robot-assisted (I: 34 / C: 32) Open (I: 8 / C: 8) Unknown: (I: 2 / C: 2)</p> | <p>Recruitment rate: 86/185 (46.5%) PREHAB: 25% CON: 33%</p> <p>Exercise I: 27/38 (69.2%) met min requirements</p> <p>Pelvic Floor I: 36.8% C: 38.9% achieved pre-op training prescriptions</p> | Multicentre randomised controlled clinical trial | <p>Mean wait time for RP days: I: (75 ± 29) C: (80 ± 34)</p> <p>Baseline; T1: 1 week pre-surgery; T2: 4 weeks post-op; T3: 12 weeks post-op; T4: 26 weeks post-op</p> | 6MWT; grip strength; elbow flexion and extension; WC; BF%; BMI; accelerometry; FACT-P; PORPUS; FACT-F; HADS; PDI; IPSS; IIEF; CHAMPS |
| Sundberg et al. 2017 Sweden | To evaluate the effect on symptom burden as well as health-related quality of life when using the application for real-time symptom assessment and management during adjuvant radiotherapy for localised prostate cancer | <p>Sample size: T1-Baseline: (I: n=66 / C: n=64) T2-End of tx: (I: n=59 / C: n=56) T3-3 months: (I: n=60 / C: n=55)</p> <p>Mean age: for all patients was 69yrs (52-82yrs) I: 69 (SD 5.8) / C: 69 (SD 6.2)</p> | <p>Cancer stage: 1 (I: 16 – SD 24 / C: 18 – SD 28) 2 (I: 29 – SD 44 / C: 25 – SD 39) 3 (I: 17 – SD 26 / C: 20 – SD 31) Missing (I: 4 – SD 6 / C: 1 – SD 2)</p> <p>Gleason Score: 6 (I:10 – SD 15 / C: 5 – SD 8) 7 (I: 28 – SD 42 / C: 36 – SD 56) 8 (I: 13 – SD 20 / C: 13 – SD 20) 9 (I: 14 – SD 21 / C: 7 – SD 11) 10 (I: 1 – SD 2 / C: 1 – SD 2) Missing (I: Nil / C: 2 – SD 3)</p> <p>Treatment: Neoadjuvant HT (I: 50 – SD 76 / C: 40 – SD 62) EBRT (I: 20 – SD 30 / C: 22 – SD 34) High Dose Rate Brachytherapy (HDR) with EBRT (I: 46 – SD 70 / C: 44 – SD 66)</p> | <p>Eligible cohort: n= 130/186 (69.89%) I: n= 66/107 (61.68%) C: n= 64/79 (81%)</p> | Non-randomised controlled clinical trial | <p>T1: Baseline T2: After end of treatment - EBRT treated for 8 weeks / HDR & EBRT treated for 5 weeks T3: 3 months after treatment.</p> | EORTC QLQ-C30; EORTC QLQ-PR25; SOC (A questionnaire measuring health literacy was also used (the health literacy index was categorised from a tested scale) |
| Tienforti et al. 2012 Italy | To evaluate the efficacy of one session of preoperative biofeedback (BFB), in reducing the incidence, duration and severity of post prostatectomy urinary incontinence (PPUI) and in improving the quality of life (QoL) of patients undergoing RP. | <p>Sample size: n=32 I: n=16 C: n=16</p> <p>Mean age: I: 64yrs (52-74yrs) C: 67yrs (60-74yrs)</p> | <p>Cancer Stage: T1c (I: 1 / C: 0) T2a (I: 2 / C: 1) T2b (I: 1 / C: 0) T2c (I: 8 / C: 10) T3a (I: 4 / C: 2) T3b (I: 0 / C: 1) Not evaluated (I: 0 / C: 2)</p> <p>Gleason Score: 6 (I: 7 / C: 5) 7 (I: 7 / C: 8) Not evaluated (I: 2 / C: 3)</p> <p>Treatment: Nerve sparing Monolateral (I: 4 / C: 3) Bilateral (I: 3 / C: 1) Pelvic lymphadenectomy (I: 8 / C: 11)</p> | <p>38 screened. 34 eligible. n=32/34 (94.11%) n = 16 in each group</p> <p>1 x withdrawal from the intervention and the control due to procedural intolerance and surgical complication, respectively.</p> | Prospective, single centre, randomised controlled clinical trial | <p>Baseline: 1 day prior to RP; all followed up for a period of 6 months. Intervention: monthly intervals Control: 1, 3 and 6 months after catheter removal</p> | ICIQ-UI; ICIQ-OAB; UCLA-PCI; IPSS-QoL |

| | | | | | | | |
|------------------------------|--|---|---|--------------|--|--|-----------------------|
| Zelevsky et al., 2014 USA | To explore the effect of sildenafil citrate (sc) on sexual function in men before radiotherapy | Sample size: C: n=77, I: n=125 Mean age: C: 65 years< n=55, >65 years n=27, I: 65 years< n=83, >65 years n=42 | Cancer Stage: Not reported Gleason Score: C: 6 n=44, 7 n=29, 7> n=4, I: 6 n=75, 7 n=47, >7 n=3 Treatment: C: EBRT n=17, brachytherapy n=33, EBRT +ADT n=27; I: EBRT n=25, brachytherapy n=57, EBRT+ADT n=43 C: ADT no n=69, yes n=8, I: no n=112, yes n=13 | Not reported | Double-blind, placebo controlled trial | Baseline before radiation treatment, 3, 6, 9, 12, 18 and 34 months | I-PSS, SF -36, IIEF-6 |
|------------------------------|--|---|---|--------------|--|--|-----------------------|

Abbreviations: ADT (Androgen Deprivation Therapy), BF% (body fat percentage), BMI (Body Mass Index), CHAMPS (Community Healthy Activities Model Program for Seniors), COPE (Brief COPE Scale), DRE (Digital Rectal Examination), EPIC-26 (Expanded Prostate Cancer Index Composite), EORTC QLQ-C30 (European Organisation for Research and Treatment [EORTC] Quality of Life Questionnaire), EORTC QLQ-PR25 (EORTC Quality of Life Questionnaire for Prostate Cancer), FACT-F (Functional Assessment of Cancer Treatment-Fatigue), FACT-P (Functional Assessment of Cancer Treatment-Prostate), HADS (Hospital Anxiety and Depression Scale), IES-R (The Revised Impact of Events Scale), IES (The Impact of Event Scale), IIEF (International Index of Erectile Function Scale), IPSS (International Prostate Symptom Score), ICIQ-UI (International Consultation on Incontinence Questionnaire on Urinary Incontinence), ICIQ-OAB (International Consultation on Incontinence Questionnaire-Overactive Bladder), IPSS-QoL (International Prostate Symptom Score-Quality of Life), KHQ (Kings Health Questionnaire), PTGI (Post-Traumatic Growth Inventory), PFM Assessment (Pelvic Floor Muscle Assessment), PCI (The University of California, Los Angeles, Prostate Cancer Index), PCS (Prostate Cancer Subscale), PDI (Pain Disability Index), PeLFIs (Pelvic Floor Inventories), PORPUS (Patient-Oriented Prostate Utility Scale), POMS (Profile of Mood States), RP (Radical Prostatectomy), UCLA-PCI (University of California, Los Angeles – Prostate Cancer Index), SOC (Sense of Coherence Scale), SF-36 (The Medical Outcomes Study (36 item short form survey), TPUS (Real-time Transperineal Ultrasound), WHOQOL (World Health Organisation Quality of Life Scale), WC (Waist Circumference), 6MWT (6-Minute Walk Test).

Table 2. Results of Quality Assessment

| Quantitative Studies | Item number of check list | | | | | | | | | | | | | | | | |
|--------------------------------|---------------------------|---|---|---|-----|-----|-----|---|---|-----|-----|----|----|----|-----|-----|----|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
| Au et al. 2019 | 2 | 2 | 1 | 2 | 1 | 0 | 0 | 2 | 1 | 0 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| Chambers et al. 2013 | 2 | 2 | 2 | 1 | N/A | N/A | 1 | 2 | 2 | N/A | 1 | 2 | 2 | 2 | 2 | 1 | 2 |
| Crowe et al. 2018 | 2 | 2 | 2 | 0 | 2 | 0 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| Dalais et al. 2004 | 2 | 2 | 2 | 1 | 1 | 0 | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| Demark-Wahnefried et al., 2017 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| Dijkstra-Eshuis et al. 2015 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | N/A | 1 | 2 |
| Dubbelman et al. 2012 | 2 | 2 | 0 | 0 | 1 | 0 | N/A | 2 | 2 | 0 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| Hawkins et al. 2017 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 |
| Hirschhorn et al. 2014 | 2 | 2 | 2 | 1 | N/A | N/A | 2 | 2 | 2 | N/A | N/A | 2 | 2 | 2 | 1 | N/A | 1 |
| Kinsella et al. 2011 | 2 | 2 | 2 | 2 | 1 | N/A | 2 | 2 | 2 | 0 | 1 | 2 | 1 | 2 | 1 | 1 | 2 |
| Kim 2011 | 2 | 1 | 1 | 0 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| Manley et al. 2016 | 2 | 2 | 0 | 1 | N/A | N/A | 0 | 2 | 2 | N/A | 1 | 1 | 2 | 0 | 1 | 1 | 1 |
| Parker et al. 2009 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | N/A | 2 | 2 |
| Santa Mina et al. 2018 | 2 | 2 | 1 | 2 | 1 | 0 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 1 | 2 |
| Sundberg et al. 2017 | 2 | 2 | 2 | 2 | N/A | N/A | 0 | 2 | 1 | N/A | 2 | 2 | 2 | 2 | 0 | 1 | 2 |
| Tienforte et al. 2012 | 2 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | N/A | 1 | 2 |
| Zeilefsky et al., 2014 | 2 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 |

Item number check list key*: 1 is the hypothesis/aim/objective clearly described, 2 is the study design well described and appropriate, 3 method of patient/control group selection clearly described, 4 characteristics of the patient/control group clearly described, 5 were patients randomised to the intervention group, 6 was randomisation/allocation concealed, 7 characteristics of patients lost to follow-up clearly described, 8 intervention clearly described, 9 main outcome measures clearly described, 10 was an attempted made to blind those measuring the primary outcome of the intervention, 11 population characteristics adequately described and controlled, 12 main findings clearly described, 13 methods of analysis appropriately and clearly described, 14 estimates of variance reported for main results, 15 analyses adjusted for different lengths of follow-up, 16 data analysed according to intention to treat principle, 17 conclusions supported by the results

*Three levels of assessment quality scores

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|--------------------------|
| Low risk of bias (2) |
| Unclear risk of bias (1) |
| High risk of bias (0) |

Table 3. Overview of the prehabilitation interventions

| Author and Year | Purpose | Intervention |
|-------------------------------|--|---|
| Exercise | | |
| Au et al. 2019 | To explore whether prehabilitation is associated with differences in physical activity during the postoperative inpatient stay and the week after discharge in men undergoing radical prostatectomy. | <p>Intervention: Individualised home-based, moderate intensity aerobic and resistance exercises prescribed and demonstrated shortly after consenting to surgery. Provided with exercise bands, mat and stability ball in addition to a manual detailing exercise prescription with supporting behaviour change strategies. Participants also received information and coaching on pelvic floor exercises prior to surgery.</p> <p>Control: Received the same pelvic floor exercises and were given a book on maintaining healthy lifestyle after diagnosis. No further exercise support.</p> <p>Wrist-worn accelerometers were provided shortly after surgery (either in post-anaesthetic care unit or on admission to ward) with instructions to wear the device for at least 1 week after discharge. Inpatient data captured over 24-h period and outpatient over 7-day period after discharge.</p> |
| Santa Mina et al. 2018 | To assess feasibility of a multi-centre RCT examining home-based prehabilitation versus a control in men undergoing radical prostatectomy. | <p>Intervention: Individualised total-body exercise (60 minutes, unsupervised, home-based, moderate-intensity 3-4 days per week); Pelvic floor exercise regime; Lifestyle support book, provided with an exercise manual and online videos, resistance bands, stability ball, and yoga mat. Participants were also provided with a heart rate monitor.</p> <p>Control: Pelvic floor exercise regime; lifestyle support book and completion log.</p> <p>Participants in both groups completed logbooks and communicated (via phone) weekly with the study team to facilitate and monitor compliance.</p> |
| Peer Support | | |
| Chambers et al. 2013 | To assess the feasibility of peer intervention for couples where the man was preparing for radical prostatectomy. | <p>Intervention: Received 12 hours of training via lectures, workshops, role plays and practical demonstration. Topics covered: communication skills, adjustment to cancer, managing treatment effects, sexuality and research procedures. Guided by a manuscript and used a web-based data management system providing online guides required them to indicate which sessions and components were delivered and when. Monthly group supervision including case discussion and adherence to protocol.</p> <p>Couples Intervention: Psychoeducation including couple communication and supporting each other, stress management and challenging negative beliefs about cancer, aging and sexuality, education to manage treatment side effects and sexuality (expression of affection and non-demanding sexual touch), choosing treatment for erectile dysfunction.</p> <p>8 intervention sessions via telephone (2 prior to surgery, 3 fortnightly calls commencing two weeks post-surgery and 3 calls at 10, 16- and 22-weeks post-surgery). Audio-visual resource and participant workbook with self-help materials also provided.</p> |
| Hawkins et al., 2017 | To determine whether combining a computer-based support with a human cancer mentor would benefit men affected by prostate cancer before treatment and into survivorship. Clinical profile of the participants are not reported. | <p>Intervention arms:</p> <p>Telephone and e-mail Information Support from a Trained Cancer Mentor: Cancer information mentor telephoned the participants weekly for first month, twice during the second month and once a month for 4 months.</p> <p>Web-based System of Information and Support (CHES): online website resource which provided information, communication and support related to prostate cancer issues.</p> <p>Combined intervention: Mentor + CHES combination of both interventions.</p> |
| Pelvic Floor Exercises | | |
| Crowe et al. 2018 | To determine the effect on viewing an animated pelvic floor model on participants' ability to correctly perform pelvic floor muscle (PFM) exercises prior to radical prostatectomy. | <p>Intervention: Provided with DVD of animated pelvic floor instruction, divided into visual chapters with Australian voiceover (9.5 mins in length). Included basic anatomy and physiology of male urogenital system; focussing on pelvic floor, information about why surgery may affect continence; internal views of pelvic floor during PFM contraction and external visual cues for participants, showing correct PFM contraction. Diaries returned to physiotherapists at their PFM assessment. Participants underwent (physiotherapy) PFM assessment pre-operatively (between 1 day / 4-weeks prior to surgery). Only provided with feedback once contractions were complete. Performed PMF contractions standing and lying down. Real-time Transperineal Ultrasound assessment was performed in crook lying. Then participants placed on left side (lying) for Digital Rectal Examination. Following assessments, the physiotherapist provided pelvic floor education and further education and treatment.</p> <p>Control: Received a DVD about prostate cancer only, with no information about PFM exercise.</p> <p>All participants given a study diary to complete. Had to record all occasions of watching study DVD and frequency of performing PFM exercises. Also, if they received any PFM instruction and from who.</p> |
| Dijkstra-Eshuis et al. 2015 | To investigate the effectiveness of preoperative PFMT with biofeedback on Stress Urinary Incontinence and on Quality of Life in men scheduled to undergo a robotic prostatectomy. | <p>Preoperatively: Both groups were seen by a pelvic floor physiotherapist and were provided with an explanation of relevant anatomy and physiology. All had pelvic floor examination (rated as strong, normal, weak or absent). No instruction on how to perform PFM contraction was provided and no written information was provided.</p> <p>Intervention: Received 1 weekly 30 min session of PFMT preoperatively for 4 weeks. Given toilet behaviour instructions and biofeedback assisted behavioural training using exercises comprising maximum voluntary contractions (MVCs) - endurance, relaxation and coordination with abdominal breathing. Feedback and verbal instruction used to teach patients how to control pelvic floor. Number and type of contractions were selected to improve coordination and motor control. If necessary intra-anal electrical stimulation was used to make patients aware of pelvic floor muscles.</p> |

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| | | <p>Patients advised to practice in various positions 2 x daily until surgery and given advice on how to integrate into daily activities. Also told to resume postop after catheter removal. Written instructions – 2 x sets of 30 contractions daily during abdominal breathing with one breath between each contraction.</p> <p>Control: Received written pelvic floor muscle exercises immediately after catheter removal (7-10 days postoperatively)</p> <p>Postop: All participants from both groups received PMFT with biofeedback and/or electrostimulation if they were still incontinent 6 week postoperatively.</p> |
| Dubbelman et al. 2012 | The recovery of urinary continence after radical prostatectomy, comparing the effect of physiotherapist guided PFME's, with guidance by an instruction folder only. | <p>Pre-operatively: All men were instructed in PFME, but intensity varied depending on intervention type.</p> <p>Intervention: Received the pelvic floor educational folder, as well as receiving intensive guidance by a physiotherapist. Post-operatively this group received a max of 9 x 30 minutes sessions after surgery with a physiotherapist.</p> <p>Control: Received an information folder only. Contained information about urogenital tract anatomy, consequences of operation and exercises to strengthen pelvic floor.</p> |
| Hirschhorn et al. 2014 | To assess the effect of a multicomponent theory-based intervention, incorporating patient information guides in pre-operative pelvic floor muscle training (PFMT) among patients undergoing radical prostatectomy. | <p>Receipt of PFMT: Pre-operative and/or post-operative. Provided by physio and/or nurse and included 1:1 training.</p> <p>Practice Audits: Clinical sites provided month-by-month data on patients that received pre-operative PFMT; and post-operative PFMT (not having been seen preoperatively).</p> <p>Intervention: Patient Information Guides: Distributed to patients when scheduled for RP and provided information on how to do PFM exercises and covered 'what is PFMT'; 'When should I start PFMT'; 'Where can I get help / advice about PFMT'. Audits conducted monthly to ascertain guide use, replacements required and overall referral patterns.</p> <p>Evidence Summary: 2-page summary of RCT supporting pre-operative PFMT for men undergoing RP. It was presented at a urology clinic service meeting and copies distributed to and discussed in person with local urologists. Newsletters outlining study progress were produced 3-monthly and distributed to local stakeholders.</p> <p>Provider Directory: Hard-copy directory of local providers of PFMT for men was produced. Included links to online directories of PFMT. Distributed to potential referrers of men to PFMT.</p> |
| Manley et al. 2016 | To evaluate the effect of pelvic floor muscle (PFM) assessment and training before and after robot-assisted laparoscopic radical prostatectomy (RARP) in improving PFM strength and urinary incontinence. | <p>Intervention: A 2-hour continence physiotherapist consultation was provided to men pre-operatively. Three separate assessments were conducted to evaluate correct activation, squeeze pressure, reflex activation and endurance: (1) perineal pelvic floor muscle assessment anteriorly, (2) Digital rectal exam (DRE) to evaluate the external sphincter (EAS) and puborectalis, (3) real-time trans-abdominal ultrasound assessment.</p> <p>Patient as well as partner / family / friend were educated about anatomy and were guided on how to perform exercises. Strength, reflex action, coordination and endurance training exercises were individualised according to assessment findings and provided to practice daily (before and after surgery).</p> <p>Postoperatively: Patients seen again at 4 days and 4 weeks postop, at which they had a strength assessment and were provided with ongoing education and exercise programs. All PFM assessments repeated postop with exception of DRE (due to possible pain and discomfort).</p> |
| Tienforti et al. 2012 | To evaluate the efficacy of one session of preoperative biofeedback (BFB), combined with an assisted, low-intensity postoperative programme of pelvic floor muscle training (PFMT) in reducing the incidence, duration and severity of post-prostatectomy urinary incontinence (PPUI) and in improving the quality of life (QoL). | <p>Intervention: Day before radical prostatectomy participants were provided with supervised training session with BFB; anatomy and physiology education of lower urinary tract and pelvic floor; wrong execution corrected among the participants was corrected.</p> <p>Following catheter removal – supervised session with biofeedback was provided. Oral and written instructions on pelvic floor contractions and a structured programme of exercises (3 sets daily, 10 minutes each of 5 seconds contraction then 5 seconds relaxation) performed at home lying, sitting and standing. Exercise frequency was recorded in a training diary. Monthly visits were provided after removing the catheter with 20 minutes assisted biofeedback at each visit. The intervention continued until the participants no longer needed use of containment pads.</p> <p>Control: Standard care, no formal education on PMFT. After catheter removal participants only received only oral and written instructions from urologist on pelvic floor exercises to be completed at home (3 x sets daily for 10 minutes) until recovery of continence. No training diary used.</p> |
| Diet | | |
| Dalais et al. 2004 | To determine the effects of diets rich in heat-treated (HT) soy grits and HT soy grits and linseed compared with a control diet low in soy and linseed on | <p>Intervention: Participants asked to consume 4 slices of bread daily until the day of surgery. Only difference between study groups was the type of grain in each bread.</p> <p>Soy group: 50g of HT soy grits.</p> |

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| | the biochemical markers of prostate cancer who were scheduled to undergo radical prostatectomy. | <p>Soy and Linseed group: 50g of HT soy and 20g of linseed.</p> <p>Placebo: pearled wheat bread.</p> <p>Daily isoflavone levels achieved in 4 slices of the phytoestrogen bread = 117mg. Heat treatment (HT) was used to reduce bitterness and antinutritional factors associated with raw soy.</p> |
| Demark-Wahnefried et al. 2017 | To explore whether weight loss favourably affects tumour biology and other outcomes in overweight men opting for radical prostatectomy. | <p>Weight loss intervention: Reduced caloric intake by 1000 kcal. Education provided by registered dietician and followed up semi-weekly face-to-face. Exercise physiologists provided education of aerobic PA for an addition 250 kcal deficit.</p> <p>Wait-listed control: counselled weekly by dieticians on food sources.</p> |
| Nurse-led models of care | | |
| Kinsella et al. 2011 | To assess whether the demonstration of erectile management techniques to patients before RP influenced treatment choice and, ultimately, regret. | <p>Intervention: All patients attended a clinic and were counselled by one of two prostate cancer nurse specialists. Verbal and written information was provided about surgery, morbidities (incontinence, erectile dysfunction [ED]) and follow-up care including open access to ED clinic. Participants were invited to attend an educational session on physiology and psychology of ED post treatment; practical demonstration of vacuum therapy and injections (with opportunity to practice techniques) and access to psychologist specialising in sexual dysfunction before treatment and for 12 months following.</p> <p>Postoperatively: Following catheter removal (10th post-operative day) surgical patients prescribed 20mg tadalafil on alternate days. Those with reduced erectile function 8 weeks later (despite PDE5 inhibitor) were started on pump or injections under nurse supervision.</p> |
| Kim 2011 | To explore a self-care nursing intervention among men affected by prostate cancer undergoing radical prostatectomy. | Intervention: Series of nurse led educational sessions on pelvic floor exercises and biofeedback, containment pads usage, education on diet, coping strategies, symptom management, wound care, catheter care, erectile dysfunction education prior to radical prostatectomy. |
| Sundberg et al. 2017 | To evaluate the effect on symptom burden as well as health-related quality of life when using the application for real-time symptom assessment and management during adjuvant radiotherapy for localised prostate cancer | <p>Intervention: Patients equipped with a smartphone. Given thorough instructions on how to use app with the opportunity to send test report under supervision. Participants were provided a checklist and phone number for technical support. Asked to send daily reports when they felt unwell for entire period during radiotherapy treatment (5-8 weeks) and 3 weeks after completion of radiotherapy. Patients advised alerts were monitored office hours only. Reminder message sent if report was not submitted. Contact nurses viewed reported symptoms and contacted patient to discuss.</p> <p>Questions addressed occurrence, frequency and distress level, regarding bladder (n=4) and bowel (n= 4) function, fatigue, pain, anxiety, distress, sleep, flushing and other (open ended questions with ability to write a message). A clinical risk assessment model was embedded to assess alerts (yellow = often and nurse contacted same day / red = very often and nurse made contact within the hour).</p> <p>Patients could also view self-care advice (with links to relevant websites) based on their own symptom history graphs over time.</p> |
| Psychological | | |
| Parker et al. 2009 | To assess the short-term and long-term efficacy of a presurgical stress management intervention at reducing mood disturbance and improving quality of life (QOL) in men undergoing radical prostatectomy (RP) for prostate cancer | <p>Intervention groups: Stress Management (SM): Pre-surgery: 2 x 60-90 min individual sessions with Clinical Psychologist and a stress management guide that expanded on session. Cognitive behavioural therapy in nature with 60% of time focussed on relaxation (diaphragmatic breathing and guided imagery). Given audiotapes to practice at home. Second session was imaginal exposure of the day of surgery and discussion of fears about cancer, surgery and learned problem focussed coping strategies. Day of Surgery: 2 x brief booster sessions with a clinical psychologist. One the morning of (before surgery) and then 48 hours after surgery to reinforce relaxation and coping.</p> <p>Supportive Attention (SA): Pre-surgery: 2 x 60-90 min individual sessions with clinical psychologist. Included detailed medical psychosocial and medical History in semi-structured interview format. Psychologist provided empathy and used reflective listening. Day of Surgery: 2 x brief boosters with clinical psychologist. One the morning of (before surgery) and then 48 hours after surgery discussing experiences leading up to surgery and their hospital stay.</p> <p>Standard Care (SC): No meetings with clin psych. Received routine medical care.</p> |
| Sexual Function | | |
| Zelevsky et al., 2014 | To explore the effect of sildenafil citrate on sexual function in men before radiotherapy | Intervention: Participants were given 50mg sildenafil citrate 3 days before starting external beam radiotherapy. Participants were received androgen deprivation therapy (ADT) and radiotherapy were given 50mg SC within 1 months of starting ADT. |

additional strategies were planned to maintain or improve fidelity outcomes. Only four studies (24, 25, 25, 33) provided information in relation actual intervention adherence or fidelity in relation to the extent to which the intervention was delivered as planned. This observation is important because without a complete published description of interventions, members of the cancer care multidisciplinary team and patients cannot reliably implement effective interventions.

Physical Activity

Only two studies ^{23,24} included prehabilitation exercise interventions among men affected by localised prostate cancer receiving radical prostatectomy. The interventions had similarities in that they both provided physical activity, which was home-based, unsupervised, and were moderate in intensity after the participants provided their consent to surgery. They also included written educational materials, exercise bands, mats, and stability balls as part of the exercise intervention delivery [23, 24]. These two studies also included educational support for pelvic floor exercise instruction but neither study measured clinical outcomes to assess the impact on urinary continence.

While these studies had similarities in the intervention, they measured different outcomes. The first study ²³ identified that the participants in the prehabilitation exercise intervention group had higher physical activity levels in the in-patient setting post-operatively compared to the control group (difference of 117.5, SD 57.8 minutes of activity, $p < 0.05$). However, no statistically significant differences between the study groups were observed for physical activity minutes in the home-setting or for the 6-minute walk test ²³. Both studies did not observe any difference in the length of hospital stay ^{23,24}. The second study identified statistically significant differences for the six-minute walk test at four weeks, reduced body fat percentage at four and 12 weeks, greater grip strength, smaller waist circumference and lower body mass index at 26 weeks post-operatively compared to the control group. Furthermore, the participants in the prehabilitation intervention reported reduced anxiety scores prior to surgery and at 26 weeks post-operatively ²⁴. There were no differences in the number or grade of surgical complications between the prehabilitation group and the control group ²⁴.

Peer support

Two studies^{22,25} evaluated the impact of a peer support prehabilitation intervention. One study explored peer support among couples prior to radical prostatectomy²⁵, whereas the other study did not report on the clinical characteristics of the participants but that peer support was delivered to men affected by prostate cancer only (no partners) prior to definitive treatment²². The peer support interventions were different in content, model of delivery and assessment of study outcomes. The first study [22] delivered a couples-based peer support intervention and involved prostate cancer peer volunteers who received a 12-hour training programme which covered the following topics: communication, adjustment to cancer, managing treatment side-effects, sexuality, and considerations for research procedures. The peer support intervention was delivered to 20 couples over eight sessions via the telephone at two calls prior to surgery, three fortnightly calls that started two weeks post-surgery, and three calls at 10, 16 and 22 weeks post-surgery²⁵. The peer volunteers described a sense of altruistic motivations to give something back and felt that they had something experiential to offer couples affected by prostate cancer. However, both the volunteers and the participants described that the tele-mode of delivery meant that it was difficult to establish a good rapport and this was particularly challenging when navigating sexual well-being conversations.

The Peer Support for Couples study²⁵ identified a number of effects over time from baseline (pre-surgery) and three months post-surgery for improvements in intrusion ($p=0.042$), avoidance ($p=0.014$), total impact of event scale ($p=0.036$), new possibilities ($p=0.035$) and appreciation of life ($p=0.026$). Psychological distress in men and partners decreased over time, but in contrast unmet sexual needs increased²⁵. Some caution needs to be taken in the interpretation of these results in the absence of a control group in this study design²⁵. The other study²² aimed to test whether a computer-based support program and support from a cancer mentor would improve quality of life related outcomes compared to either intervention alone. Overall, the combined intervention condition had few and disparate results. Statistically significant improved scores were reported for higher functional well-being at three months, positive coping at six months and on bonding scores at both six weeks and six months in favour of the combined intervention²².

Pelvic Floor Muscle Training

A total of six studies²⁶⁻³¹ explored the impact of prehabilitation pelvic floor muscle training. All of the studies provided involvement of a registered physiotherapist, with the exception of one study²⁹ where the pelvic floor muscle training was delivered by a qualified nurse or physiotherapist. The intervention content and recommended frequency and intensity of the pelvic floor muscle prescriptions across all the studies differed. One study²⁶ used an animated DVD to provide education on pelvic floor muscle training, and the participants were provided with tailored feedback during 1:1 assessments with qualified physiotherapists following real-time transperineal ultrasound and digital rectal examinations at one, to four weeks, prior to surgery.

One study²⁷ elsewhere provided very specific pelvic floor exercise prescriptions which consisted of one minute of rest, ten maximum voluntary contractions lasting three seconds with maximum effort, three maximum endurance contractions lasting 30 seconds with a Valsalva manoeuvre, each task was separated by one minute of rest. Other studies did not report on the frequency or duration of the pelvic floor muscle exercise prescriptions which makes the interpretation challenging for translation to clinical practice²⁷⁻³⁰. One study²⁷ also used intra-anal electrical stimulation to make patients aware of how to effectively engage the pelvic floor muscles. Most of the studies tailored individual pelvic floor muscle training feedback on a 1:1 basis to the participants following physical examination by a qualified physiotherapist using both real-time transperineal ultrasound assessment and digital rectal examinations²⁷⁻³⁰ ranging from 30 minutes to 2-hour appointments prior to, and after surgery. In keeping with the heterogeneity of intervention content and mode of delivery, the study outcome measures were also diverse which makes the clinical interpretation of the study findings problematic, and some caution should be taken.

Outcomes assessed across the studies included the following, 1) the ability to perform pelvic floor contractions correctly^{26,30}, 2) confidence in ability to perform pelvic floor exercises²⁶, 3) satisfaction with educational materials^{26,29}, 4) urinary continence rates²⁶⁻³¹, 5) changes in urethral pressure²⁸, and 6) quality of life outcomes^{26,27,29,31}. The results across the studies reported mixed results on the study

outcomes which is not surprising given the significant clinical heterogeneity in the definitions used for urinary continence across the suite of included studies. Adopting consensus-based approaches to the definition of urinary continence is vitally important in the clinical trial setting for clinicians and researchers to fully understand the impact and clinical value of prehabilitation pelvic floor exercise prescriptions. The following definitions of urinary continence outcomes were reported across the studies: 1) no leakage at all on a 24-hour pad test at 1 year post-operatively ²⁷, 2) loss of <4 gram of urine on 24-hour pad test and <1 gram of urine on the 1-hour pad test ²⁸, 3) no use of continence aids at 4-weeks post catheter removal, 4) ICIQ-UI score of 0, with one study using EPIC ²⁶ and the other study used ICIQ-UI short-form ²⁹ but neither study provided a cut-off score for urinary continence classification.

Given these important considerations, it is not surprising that there were mixed outcomes for the impact of prehabilitation pelvic floor exercises among men affected by prostate cancer. One study reported no differences in the participants ability to perform pelvic floor muscle exercises correctly when comparing those participants who received instruction via a DVD alone compared to those participants that received instruction with a DVD and 1:1 feedback with a qualified physiotherapist ²⁶. The majority of the studies did not observe statistically significant differences between the intervention groups and control groups for urinary continence rates ²⁶⁻²⁹ post-surgery, with the exception of only two studies who reported favourable outcomes over time for prehabilitation pelvic floor exercises ^{30,31}.

Noteworthy, three studies ^{27,29,31} assessed the impact of prehabilitation pelvic floor muscle training interventions on quality-of-life outcomes and all of the studies reported that there were no statistically significance differences over time. Factors found to be associated with incontinence rates post-surgery included a low maximum urethral closure pressure, nerve-sparing and bladder neck sparing ²⁸, age and pelvic floor muscle strength prior to surgery ³⁰. From a clinical standpoint, other factors which may have an impact on the continence recovery of these participants was the clinical skill and learning curve of the operating surgeon, which were not acknowledged in any of the studies.

Diet and Tumour Biomarkers

Two studies ^{32,33} explored the impact of prehabilitation dietary modifications on prostate cancer biomarkers and quality of life outcomes among men affected by localised prostate cancer opting for radical prostatectomy. The first randomised controlled trial of n=26 participants aimed to determine the effects of a diet rich in phytoestrogens on prostate cancer biomarkers in the presurgical setting ³². The study design consisted of the following study groups 1) Soy group: 50 grams of heat-treated (HT) soy grits, 2) Soy and Linseed Group: 50 grams of HT soy and 20 grams of linseed, and 3) Control Group: pearled wheat bread. The results identified that the HT soy vs placebo (wheat) group showed statistically significant difference for total PSA (-12.7% vs 40%, p=0.02) and free total PSA ratio (27.4% vs 15.6%, p=0.01). HT soy grits and HT soy grits and linseed also showed differences in free/total PSA ratio (27.4% vs -10%, p=0.007). Thus, these results may suggest that a dietary manipulation containing 50 grams of HT soy grits daily in the presurgical setting may have favourable effects on biomarkers for prostate cancer. However, caution must be taken given the small sample size and these are only indicative findings of prostate cancer biomarkers which might not actually translate to reduced tumour aggressiveness or indeed overall survival.

The second randomised control trial ³³ of n=40 participants tested the impact of whether a prehabilitation weight loss intervention favourably affected tumour markers and quality of life outcomes. The intervention consisted of a reduced caloric intake by 1000 kcals and educational support by a registered dietician and exercise physiologist twice weekly. Participants were instructed to perform aerobic physical activity aiming for an additional deficit of 250 calories. The control group received weekly counselling from a registered dietitian on food sources only. There were no statistically significant differences in weight loss or physical activity levels between both the study groups. The only quality of life subscales that demonstrated statistically significant improvements were on the vitality and erection function subscales in favour of the intervention group. Interestingly, this study reported increased tumour proliferation rates in the weight loss intervention arm, on the contrary to the study hypothesis ³³. This was a small study which has raised more clinical questions particularly around the impact of rapid weight loss on prostate cancer biology prior to definitive treatment.

Nurse-Led Models of Prehabilitation

Three studies explored the impact of nurse-led prehabilitation interventions among men affected by prostate cancer opting for radical prostatectomy^{19,34} and men receiving radical radiotherapy²⁰. The studies were conducted in a range of countries which provides insights into various nurse-led prehabilitation models in the UK¹⁹, Sweden²⁰ and Korea³⁴, but very much in its infancy. All of the studies were quasi experimental in design and aimed to test the impact of supported self-management interventions for erectile dysfunction¹⁹, multimodal supportive care intervention to optimise holistic self-care agency³⁴ and real-time symptom assessment and supported self-management using a smartphone technology²⁰. All studies used different patient reported outcome measures and similarly the interventions varied in content and delivery, but central to all the nurse-led interventions was supporting the individual man's self-management capabilities and rehabilitation.

The first study of n=83 participants tested whether the demonstration of erectile management techniques among men prior to radical prostatectomy influenced decisional regret, anxiety and depression, and sexual function¹⁹. The results identified that there was reduced levels of decisional regret at 1-year post-surgery in favour of the intervention group ($p=0.03$), and erectile dysfunction was the reason for regret among all the participants. A further important clinical finding was that the Hospital Anxiety and Depression Scale scores were lower in the intervention group compared to the control at 3, 6, 9, 12 months¹⁹. While sexual function scores were higher in the intervention group at 6- and 9-months post-operative but lost statistical significance at 12 months between both study groups.

The second study of n=69 participants³⁴ explored a self-management educational intervention among men prior to radical prostatectomy. The educational programme included nurse led sessions on pelvic floor exercises and biofeedback, containment pad usage, education on diet, coping strategies, symptom self-management, wound care, catheter care and erectile dysfunction education prior to radical surgery. The results identified improved scores of self-care agency and quality of life in favour of the intervention. However, there was no statistically significant change in self-care activity/behaviours among the study participants in both groups.

The third study ²⁰ of n=130 participants evaluated the effects of a real-time symptom assessment and nurse-led supported self-management intervention among men undergoing radiotherapy. The participants were asked to send symptom reports each day and/or anytime that they felt unwell during radiotherapy treatment and for a further three weeks following the completion of treatment. The smartphone technology had an integrated clinical risk model that triggered timely alerts to the nurse. The nurse could view the participants' symptom history and contact the patient to discuss a supported self-management plan. Patients in the intervention group also had access to a self-care library. Overall, the study results demonstrated that the intervention group reported lower levels of nausea and fatigue at the end of radiotherapy compared to the control group. Those in the intervention group had significantly less symptom burden for emotional functioning, insomnia, and urinary-related symptoms at the end of treatment, with sustained benefits across these quality of life domains at three months after completion of treatment compared to the control group ²⁰.

Psychological

Only one randomised controlled trial ³⁵ of n=159 explored the short- and long- term efficacy of a prehabilitation stress management intervention aimed at reducing mood disturbances and improving quality of life among men undergoing radical prostatectomy. The intervention was delivered by a clinical psychologist and consisted of the following study conditions: 1) stress management group, 2) supportive attention group, and 3) control group. Quality of life and mood assessments were conducted at one month before surgery, one week before surgery, the morning of the surgery, six weeks after surgery, and six and 12 months after surgery. There were a range of clinically meaningful findings which may demonstrate the efficacy of a stress management intervention on short- and longer-term mood and quality of life outcomes. Results identified that the stress-management intervention before surgery reduced mood disturbances before surgery and enhanced general aspects of physical quality of life up-to one year after surgery ³⁵.

Prehabilitation phosphodiesterase-5 inhibitors

A randomised control trial ²¹ of n=202 participants explored the efficacy of sildenafil citrate on sexual function in men treated by radiotherapy. The intervention included 50mg of sildenafil citrate three days before starting external beam radiotherapy, and participants treated by neoadjuvant androgen deprivation therapy (ADT) and radiotherapy commenced 50mg sildenafil citrate within one month of starting ADT. The results identified that at 12 months erectile function (EF) scores were better in the intervention arm compared to the placebo (p = 0.018), with overall improved satisfaction with EF (p = 0.027). However, no lasting significant differences were observed at 24 months between both study arms. Moreover, no other differences were observed in urinary or quality of life measures between groups at any time point ²¹.

Discussion

This systematic review set out to identify the impact of prehabilitation interventions in men affected by prostate cancer on physical, clinical, and patient reported outcome measures following primary active treatment. This review has made an important contribution which has underscored that significant heterogeneity in prehabilitation models of care exist for men affected by prostate cancer in terms of the mode of administration, duration, and outcome measures used to quantify their impact. This has important implications for practice and in the future design of clinical trials in prehabilitation prostate cancer models of care.

The adoption of core outcome sets ³⁶ in clinical trials are needed to enable standardisation of study outcomes to foster a clear and robust understanding of the empirical evidence on short- and longer-term outcomes in this patient group. While there are prostate cancer clinical trial core outcome set (COS) recommendations (36), these are largely bio-medical in nature, except for disease-specific health-related quality of life outcomes, which are suitable for prehabilitation clinical trials. This review has identified significant heterogeneity of study outcomes in relation to 1) physical function assessments, 2) clinical assessments and 3) patients reported outcomes measures. There was a total of 57 different

outcomes used across the prehabilitation studies, which underscores the current challenges in this field. Future recommendations to address this issue would be to conduct future consensus-based methodology research to develop agreement in the COS for prehabilitation clinical trials.

The composition of the prostate cancer prehabilitation interventions were largely unimodal which included exercise, peer support, pelvic floor exercises, diet, psychological, sexual, or multimodal nurse-led interventions. Importantly, none of the studies within these broad classifications of intervention type measured similar physical, clinical or patient reported outcomes. Likewise, the duration of the prehabilitation intervention prior to radical treatment needs to be considered because largely the prehabilitation intervention durations were not reported as mainstay across most of the included studies. This is an important predictor of outcomes because interventions delivered over two weeks, will not have comparable outcomes with interventions delivered over six weeks in relation to time effects and wait-times for surgical lists. Given that the types of interventions varied and a lack comprehensive reporting across the studies it was difficult to determine the therapeutic validity and efficacy (for example, measures of cardiorespiratory fitness and postsurgical outcomes such as mortality, length of stay, postsurgical complications, or readmission rates) following prehabilitation interventions in this current review. A recent systematic review (40) assessed ‘prehabilitation exercise interventions’ before all urologic cancer surgery using the Consensus on Therapeutic Exercise Training (CONTENT) scale to assess the therapeutic validity and efficacy. In keeping with recommendation to develop prostate cancer prehabilitation COS, we also need agreement on the appropriate outcomes to adjudicate prostate cancer prehabilitation clinical efficacy.

When developing prehabilitation programs health care professionals must ensure that all care remains person-centred to address existing unmet needs ^{4,5,16}. Many of the studies examined the effect of a unimodal intervention. While this is a useful way to look at the impact of a single intervention, clinical practice is usually a combination of different interventions to address the individual’s person-centred care needs. To-date, there is a dearth of research which has explored how multimodal prehabilitation interventions afford support to partners, as crucial companions in cancer recovery ³⁷. Often the support of a spouse, carer or other significant person can make a difference in how well a man affected by

prostate cancer copes during their rehabilitation journey³⁸. Further research is needed to understand the needs of the dyad during the prehabilitation phase. Spouses are usually expected to provide support with decision making, recalling information at medical appointments and even with transportation.

The cost of medical care is steadily rising and becoming a major factor in health care planning, and there are significant issues faced by these men around financial toxicity³⁹. None of the studies included in this review provided any data concerning the cost of providing different types of prehabilitation interventions, and noteworthy, no studies identified the cost-effectiveness of such models of cancer care. This limitation is partly due to the difficulty in costing some interventions, and the psychosocial impact of interventions can be even more problematic to analyse from a financial standpoint. We would strongly recommend that future prehabilitation trials embed a cost-effectiveness component in their study designs, particularly if we are to allocate otherwise scarce cancer care resources to earlier in the treatment pathway.

The last recommendation would be that future research considers the potential value of wearable sensors and mobile devices to capture real-time self-management [41, 42, 43] and home-based interventions as part of prehabilitation. Studies such, as Santa Mina [24], demonstrated the potential value of this application, but further research is needed. With the global policy call to transition cancer care out of hospital and into the community, as observed during the COVID-19 pandemic [44, 45] and the persuasive added value of wearable technologies, this is an important area for future research.

Limitations

Despite this review following a clear, rigorous and transparent review process there are a number of limitations to point out. This review included studies which were published in the English language only, and as such may have excluded publications in other languages which might have omitted important information. However, the review did represent evidence from a range of international countries. One of the major challenges of this review was synthesising evidence from heterogeneous study designs and methodologies, and our findings are constrained due to the methodological limitations of the primary studies included. This review has enabled a broad summary of the evidence in relation

to prehabilitation in prostate cancer which has provided some clinical practice recommendations and facilitated refinement of the future research directions.

Conclusion

This systematic review has identified that multimodal prehabilitation interventions is an emerging area for practice and research in prostate cancer. It makes an important contribution which underscores that significant heterogeneity in prehabilitation models of care exist in terms of the mode of administration, duration, and outcome measures used to quantify their impact. Importantly, there has been a lack of focus on the outcomes of including partners as critical companions during this distressing phase of the cancer care continuum. Due to limitations within the individual studies and the infancy of the research there is limited knowledge about the cost-effectiveness of such interventions. In the meantime, all members of the multidisciplinary team caring for people affected by prostate cancer are encouraged to use the findings of this review to inform holistic models of care.

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Supporting Information

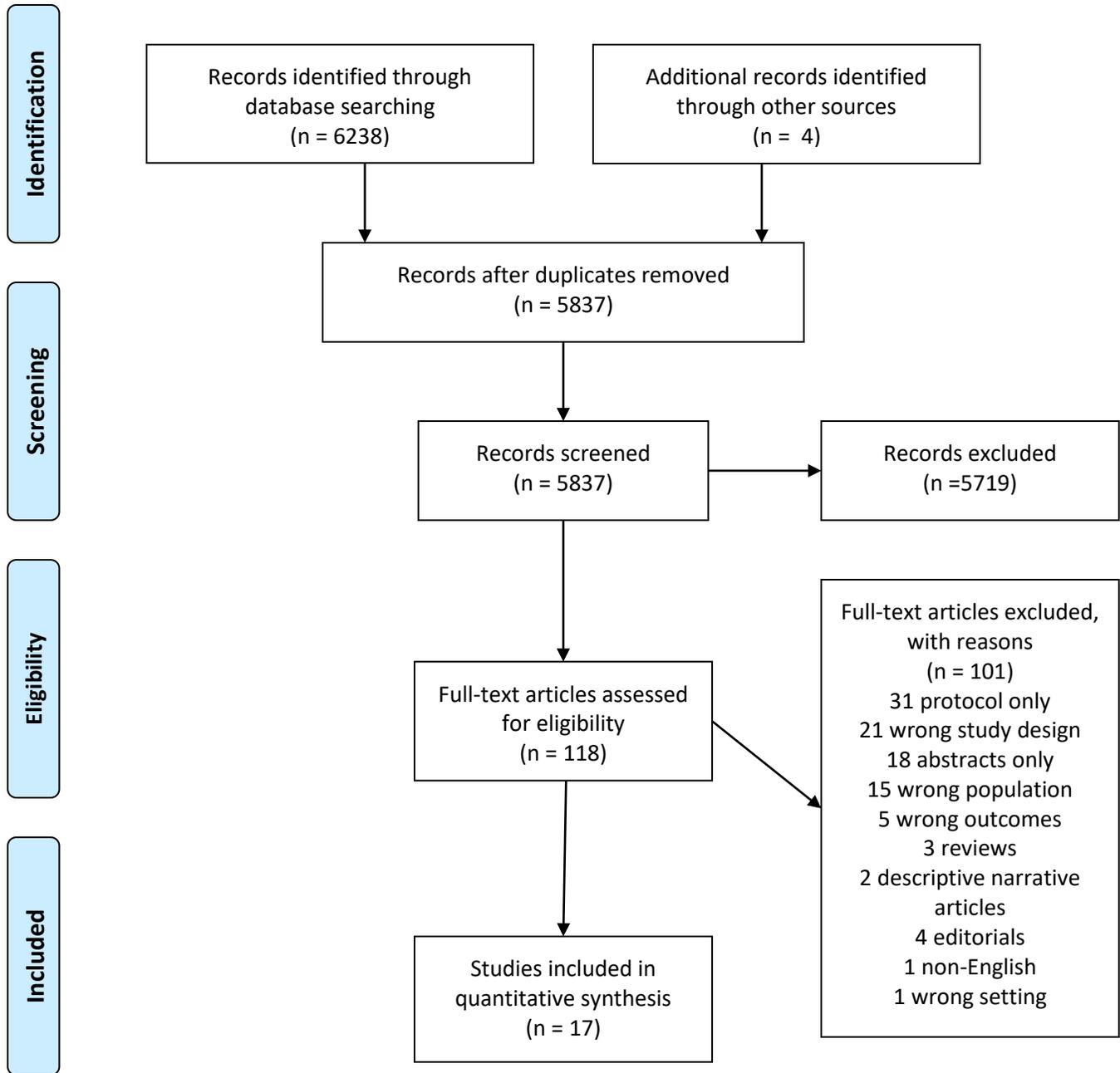
S1 Table. Example of Database searches

S2 Table. Overview of Study Findings

S3 Table. Completed PRISMA Checklist



Fig 1 PRISMA Flow Diagram



Supplementary Table 1. PRISMA checklist

| Section/topic | # | Checklist item | Reported on page # |
|------------------------------------|----|---|----------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both | 1 |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 3 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 5 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 6 and 7 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 6 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 6 and 7 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 8 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Supplementary tables |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Figure 1 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 8 and 9 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 8 and 9 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 9 |
| Section/topic | # | Checklist item | Reported on page # |

| | | | |
|-------------------------------|----|--|-----------|
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 6 and 9 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 9 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 9 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 9 |
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 10 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 10 and 11 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 10 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 10 - 18 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 11-15 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 10 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 18-21 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 20 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 21 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 1 |

Supplementary Table 2: Example of database searches

| Database: Cumulative Index to Nursing and Allied Health Literature (CINAHL) | | | |
|---|---|---|--------------|
| Symbols used in this document: | | | |
| MH = Main Heading or "CINAHL Heading" | | | |
| + = Explodes the "CINAHL Heading" | | | |
| " " finds a phrase | | | |
| Asterisk (*) = truncates stem of a word | | | |
| n5 = finds words within 5 words of each other | | | |
| ? = wildcard that finds alternate spellings of a word | | | |
| Search # | Concept/Explanation | Search Terms/Strategy | # of Results |
| #1 | "Population" – Men affected by prostate cancer | (MH "Prostatic Neoplasms+") OR "prostatic neoplasm*" OR (cancer n5 prostate) OR "prostate cancer" OR "prostatic cancer" OR "prostatic carcinoma" | 32,844 |
| #2 | "Intervention" - Prehabilitation | prehabilitation OR prehab OR "pre-operative rehabilitation" OR "peri-operative rehabilitation" OR exercise* OR nutrition* OR food OR education OR psychological OR "pelvic floor" OR "sexual intervention*" OR "peer support" | 1,136,916 |
| #3 | "Outcomes of interest" | (MH "Urinary Incontinence+") OR Incontinen* OR bladder OR urinary OR "sexual function*" OR "sexual dysfunction*" OR "sexual problem*" OR "sexual difficult*" OR "oncological outcome*" OR PSA OR "gleason score*" OR histopathology OR complication* OR "blood loss" OR "loss of blood" OR (MH "Length of Stay") OR "length of stay" OR mobili?ation OR pain OR re-admission OR readmission OR mortality OR death OR morbidity OR "quality of life" OR HRQoL OR anxiety OR depression OR cope OR coping OR self-management OR self-efficacy | 1,440,584 |
| #4 | Outcome of prehabilitation interventions on men affected by prostate cancer | #1 AND #2 AND #3 | 2,215 |
| #5 | English language limiter | | 2,177 |

| Database: ClinicalTrials.gov | | | |
|------------------------------|--------------------------------------|--|--------------|
| Search # | Concept/Explanation | Search Terms/Strategy | # of Results |
| #1 | Prostate Cancer – Prehabilitation | <p>“Condition or disease”: Prostate Cancer</p> <p>“Other terms”: prehabilitation OR prehab OR “pre-operative rehabilitation” OR “peri-operative rehabilitation” OR exercise* OR nutrition* OR food OR education OR psychological OR “pelvic floor” OR “sexual intervention*” OR “peer support”</p> <p>“Age Group”: Adult (18-64) and Older Adult (65+)</p> | 543 |

| Database: Cochrane Library | | | |
|--|---|--|--------------|
| Symbols used in this document: | | | |
| MH = Main Heading or "MeSH Heading" | | | |
| + = Explodes the "MeSH Heading" | | | |
| " " finds a phrase | | | |
| Asterisk (*) = truncates stem of a word | | | |
| NEAR = finds words within 6 words of each other | | | |
| ? = wildcard that finds alternate spellings of a word | | | |
| Search # | Concept/Explanation | Search Terms/Strategy | # of Results |
| #1 | | (MH "Prostatic Neoplasms+") | 4,968 |
| #2 | | "prostatic neoplasm*" OR (cancer NEAR prostate) OR "prostate cancer" OR "prostatic cancer" OR "prostatic carcinoma" | 13,157 |
| #3 | "Population" – Men affected by prostate cancer | #1 OR #2 | 13,576 |
| #4 | "Intervention" - Prehabilitation | prehabilitation OR prehab OR "pre-operative rehabilitation" OR "peri-operative rehabilitation" OR exercise* OR nutrition* OR food OR education OR psychological OR "pelvic floor" OR "sexual intervention*" OR "peer support" | 254,974 |
| #5 | | (MH "Urinary Incontinence+") | 1,965 |
| #6 | | (MH "Length of Stay") | 6,802 |
| #7 | | Incontinen* OR bladder OR urinary OR "sexual function*" OR "sexual dysfunction*" OR "sexual problem*" OR "sexual difficult*" OR "oncological outcome*" OR PSA OR "gleason score*" OR histopathology OR complication* OR "blood loss" OR "loss of blood" OR "length of stay" OR mobilization OR pain OR re-admission OR readmission OR mortality OR death OR morbidity OR "quality of life" OR HRQoL OR anxiety OR depression OR cope OR coping OR self-management OR self-efficacy | 571,944 |
| #8 | "Outcomes of interest" | #5 OR #6 OR #7 | 571,944 |
| #9 | Outcome of prehabilitation interventions on men affected by prostate cancer | #3 AND #4 AND #8 | 1,269 |
| | Exclude protocols, editorials and clinical answers | | 1,244 |
| Note - 1,244 results include 113 systematic reviews and 1131 trials. | | | |

| Database: MEDLINE | | | |
|---|---|---|--------------|
| Symbols used in this document: | | | |
| MH = Main Heading or "MeSH Heading" | | | |
| + = Explodes the "MeSH Heading" | | | |
| " " finds a phrase | | | |
| Asterisk (*) = truncates stem of a word | | | |
| n5 = finds words within 5 words of each other | | | |
| ? = wildcard that finds alternate spellings of a word | | | |
| Search # | Concept/Explanation | Search Terms/Strategy | # of Results |
| #1 | "Population" – Men affected by prostate cancer | (MH "Prostatic Neoplasms+") OR "prostatic neoplasm*" OR (cancer n5 prostate) OR "prostate cancer" OR "prostatic cancer" OR "prostatic carcinoma" | 157,240 |
| #2 | "Intervention" - Prehabilitation | prehabilitation OR prehab OR "pre-operative rehabilitation" OR "peri-operative rehabilitation" OR exercise* OR nutrition* OR food OR education OR psychological OR "pelvic floor" OR "sexual intervention*" OR "peer support" | 2,922,134 |
| #3 | "Outcomes of interest" | (MH "Urinary Incontinence+") OR Incontinen* OR bladder OR urinary OR "sexual function*" OR "sexual dysfunction*" OR "sexual problem*" OR "sexual difficult*" OR "oncological outcome*" OR PSA OR "gleason score*" OR histopathology OR complication* OR "blood loss" OR "loss of blood" OR (MH "Length of Stay") OR "length of stay" OR mobili?ation OR pain OR re-admission OR readmission OR mortality OR death OR morbidity OR "quality of life" OR HRQoL OR anxiety OR depression OR cope OR coping OR self-management OR self-efficacy | 5,941,548 |
| #4 | Outcome of prehabilitation interventions on men affected by prostate cancer | #1 AND #2 AND #3 | 5,093 |
| #5 | English language limiter | | 4,850 |

| Database: SCOPUS | | | |
|---|---|--|--------------|
| Symbols used in this document: | | | |
| TI:AB_ + searching the Title and Abstract fields | | | |
| " " finds a phrase | | | |
| Asterisk (*) = truncates stem of a word | | | |
| w/5 = finds words within 5 words of each other | | | |
| ? = wildcard that finds alternate spellings of a word | | | |
| Search # | Concept/Explanation | Search Terms/Strategy | # of Results |
| #1 | "Population" – Men affected by prostate cancer | TI:AB "prostatic neoplasm*" OR (cancer w/5 prostate) OR "prostate cancer" OR "prostatic cancer" OR "prostatic carcinoma" | 141,784 |
| #2 | "Intervention" - Prehabilitation | TI:AB prehabilitation OR prehab OR "pre-operative rehabilitation" OR "peri-operative rehabilitation" OR exercise* OR nutrition* OR food OR education OR psychological OR "pelvic floor" OR "sexual intervention*" OR "peer support" | 3,176,551 |
| #3 | "Outcomes of interest" | TI:AB Incontinen* OR bladder OR urinary OR "sexual function*" OR "sexual dysfunction*" OR "sexual problem*" OR "sexual difficult*" OR "oncological outcome*" OR PSA OR "gleason score*" OR histopathology OR complication* OR "blood loss" OR "loss of blood" OR "length of stay" OR mobilization OR pain OR re-admission OR readmission OR mortality OR death OR morbidity OR "quality of life" OR HRQoL OR anxiety OR depression OR cope OR coping OR self-management OR self-efficacy | 4,838,977 |
| #4 | Outcome of prehabilitation interventions on men affected by prostate cancer | #1 AND #2 AND #3 | 2,475 |
| #5 | English language limiter | | 2,000 |

Supplementary Table 3. Overview of Study Findings

| Author and Year | Study outcomes | Physical function assessments | Clinical assessments | Patient reported outcome measurement | Adherence/Fidelity | Findings |
|------------------------|---|--|--|---|--|--|
| | | | | | Exercise | |
| Au et al. 2019 | Physical activity levels during post-operative inpatient stay and 1-week following discharge relative to participation in prehabilitation prior to radical prostatectomy. | Accelerometry (Actiwatch 2, Philips Healthcare, Respironics, wrist worn). | Not measured. | Not measured. | Planned strategies for adherence/fidelity: Not reported Actual (extent to which the intervention was delivered as planned): Not reported. | Mean inpatient physical activity: <i>Prehab</i> : 442.5 ± 40.2 <i>Control</i> : 324.0 ± 40.2 (mean difference = 117.5 ± 57.8 min; 95% CI [0.04, 235.0], p<0.05). Mean daily physical activity during 1-week post-discharge: <i>Prehab</i> : 448.4 ± 31.2 <i>Control</i> : 491.4 ± 31.2 (mean difference 42.6 ± 44.9 min; 95% CI [-134.0, 48.7]). 6MWT: No statistically significant correlations between mean 6MWT change or length of stay with mean in- and outpatient physical activity minutes. No statistical difference between both groups for LoS. |
| Santa Mina et al. 2018 | Home based exercise: adherence was defined as achieving the minimum of the prescribed exercise range for moderate intensity aerobic and resistance training. Pelvic floor: adherence was defined as achieving the total volume of contractions relative to the prescribed volume. Both measured through logbook completed by research coordinator during weekly communication. Operative and in-patient outcomes were ascertained via chart review and included: LoS and surgical complications. | Physical Activity: 6MWT; grip strength; elbow flexion and extension; CHAMPS Body composition: BMI; WC; BF% Inpatient, post-op & 1 wk post discharge: accelerometry | Post-Op Complications: Prehab: n=18 Control: n=14 Hospital stay was similar in both groups. | HRQOL: FACT-P and PORPUS, IPSS, IIEF, PDI Fatigue: FACT-F Anxiety / Depression: HADS Physical Activity: CHAMPS | Planned strategies for adherence/fidelity: Adherence to the home-based exercise program and pelvic floor exercises (PREHAB and CON) were measured through a logbook completed by the research coordinator during weekly communication. Adherence to the total-body exercise (PREHAB) and pelvic floor training prescription (PREHAB and CON) was assessed by dividing the total training volume completed by the minimum training volume prescribed. Adherence to the homebased exercise program was defined as achieving the minimum of the prescribed exercise range for moderate intensity aerobic and resistance training. Adherence to pelvic floor exercise regimen was defined as achieving the total volume of contractions relative to the prescribed volume. Actual (extent to which the intervention was delivered as planned): Twenty-seven of 38 (69.2%) PREHAB participants met the minimum requirements of their individualized, home-based exercise prescriptions. 36.8% and 38.9% of PREHAB and CON participants achieved the preoperative pelvic floor training prescriptions and the difference was not significant. | Prehab had significantly greater 6MWT at 4 weeks post-op 20 minutes greater than the minimal clinically important difference (MCID) of 19 minutes (38.68 ± 13.89; p=0.005). However, at 26 weeks post-op there was no statistically significant difference between groups (24.2m, p=0.087). Prehab demonstrated reduced body fat percentage compared to the control prior to surgery, also at 4- and 12-weeks post-op (despite similar baseline levels) (1.26% ± 0.38, 1.01% ± 0.38, and 1.48% ± 0.39, respectively; p<0.01) Prehab had greater grip strength (4.4kg ± 1.92, p=0.022), lower waist circumference (1.34 ± 0.60, p=0.022) and lower BMI (0.48kg/m ² ± 0.16, p=0.003) at 26 weeks post-op Prehab showed statistically significant and clinically important reductions in anxiety levels prior to surgery (1.49 ± 0.70, p= 0.035) and at 26wks post-op (1.59 ± 0.71, p=0.025). Control group had greater erectile function than prehab at 4 weeks post RP (3.83 ± 1.33, p=0.004) but not at any other time. |
| | | | | | Peer Support | |
| Chambers et al. 2013 | Acceptability of the study protocol to peer volunteers and to couples | Not measured. | Not measured. | Therapeutic Alliance: Working Alliance Inventory | Planned strategies for adherence/fidelity: Session delivery was monitored closely by the project manager to support treatment fidelity. Ongoing monthly group supervision included case discussion and review of adherence to the protocol. | Peer Support: 3 x themes: a personal congruence with research; feeling that the research approach had merit; wanting to show peer support was an effective model. Peers described altruistic motivations by wanting to give back and personally feeling they had something unique to offer due to personal experience. |

| | | | | | | |
|-------------------------------|--|---------------|---|---|---|--|
| | (Therapeutic Alliance). Psychological outcomes and unmet needs of the couples (psychological distress, sexual supportive care needs and benefit finding). | | | Psychological Distress: IES-R Sexual Supportive Care Needs: Sexuality needs subscale of the Supportive Care Needs Survey Benefit Finding: PTGI | Actual (extent to which the intervention was delivered as planned): Of all couples recruited, 85% (17) completed all sessions. | Peers found sexuality discussions unfamiliar with couple discussion challenging to manage. Tele-based contact made it hard to establish rapport and working within the structured protocol conflicted with their common sense or lay model of support on basis of personal experience. Positives – personal growth, steep but rewarding learning curve, gaining more compassion, wisdom, insight, and different perspectives on life. Couples-Therapeutic Alliance: Did not differ between patients / partners and did not change over time. Scores higher for bond than task (p=0.001) and goal (p=0.000). On average pre-treatment calls were longer than post-treatment (M=35.9mins; SD 21.2 vs (M=26.1 mins; SD 11.9; p=0.08). Management of erectile dysfunction was explicitly discussed in 30% of pre-treatment and 37% of post-treatment calls. Couples-Adjustment Outcomes: Time effects were evident with improvements from baseline and 3 months post-treatment for intrusion (p=0.042), avoidance (p=0.014), total IES-R (p=0.036), new possibilities (p=0.035) and appreciation of life (p=0.026). With a trend for PTGI total scale scores (p=0.054). Decrease in partner distress between baseline and 3-months post-surgery (intrusion p=0.005; avoidance p=0.003; IES-R total p=0.002). Sexuality and supportive care needs increased between baseline and 3 months post-surgery (p=0.002). Psychological distress in men and partners decreased over time, more so for partners who were more distressed at baseline. By contrast unmet sexual needs increased. |
| Hawkins et al., 2017 | Not clearly detailed. Quality of life outcomes Cancer information competence, social support, health care competence, coping and bonding. | Not measured. | Not measured. | Quality of life: WHOQOL, EPIC, Coping: Brief Cope, Emotional and Functional well-being: FACT-P, 5-Item Cancer Information Competence, 6-Item Social Support Scale, 5-Item Healthcare Competence, 5-Item Bonding Scale | Planned strategies for adherence/fidelity: The mentor calls were audio recorded and reviewed frequently by the project director during the early months of intervention and less frequently thereafter to ensure adherence to the protocol. Actual (extent to which the intervention was delivered as planned): Not reported. | The combined intervention group scored statistically significantly higher for functional well-being at 3 months, on positive coping at 6 months and on bonding at both 6 weeks and 6 months. The interventions did not produce the expected benefits to the study participants on the primary and secondary outcomes. |
| Pelvic Floor Exercises | | | | | | |
| Crowe et al. 2018 | Ability to correctly perform a PFM contraction assessed by both digital rectal examination and trans-perineal ultrasound (by a blinded physio). Questionnaires to evaluate urinary continence (at | Not measured. | TPUS: to determine movement of anorectal angle, antero-cranial lift of bladder neck, posterior movement of external urethral sphincter and length of hold. DRE: assessed for anterior movement of puborectalis, lift | EPIC-26; Study diary; questionnaire (satisfaction with PMF exercise information received). | Planned strategies for adherence/fidelity: All participants were given a study diary to complete. They were instructed to record all occasions of watching their study DVD and the frequency of performing the PFM exercises. Actual (extent to which the intervention was delivered as planned): Nine of the 60 participants enrolled withdrew from the study, leaving 51 evaluable participants – 28 in the control group and 23 in the intervention group. Reasons for withdrawal were varied and included anxiety around forthcoming surgery (3 participants), feeling stressed by involvement in the study (1), | Ability to perform PFM contraction correctly: No statistically significant between each group assessed by both DRE and TPUS ($c^2[1]=0.53$, $p=0.58$). Viewing PMF contraction animated model did not predict successful performance, even after controlling for days PFM information and age ($p=0.063$) Confidence in ability to perform PFM contraction: 65% of intervention and 52% of control indicated they felt “extremely confident” or “quite confident” that they could perform PFM contraction prior to physiotherapy assessment. Satisfaction with information: Completed by 18 members of intervention and 25 members of control. Majority of the intervention |

| | | | | | | |
|------------------------------------|--|----------------------|--|-------------------------------|--|---|
| | <p>baseline, 1- and 3-months post-RP).</p> <p>Satisfaction with PFM information received (completed prior to physiotherapy assessment).</p> | | <p>of the PFM, complete relaxation of the PFM and length of hold.</p> | | <p>deciding against proceeding with RP (1), failing to make physiotherapy assessment appointment (1), declining any study follow up (1), and no stated reason (2).</p> | <p>group (n=22, 95%), found information provided in PF animation "extremely easy" or "quite easy" to understand. Control group reported they wanted more information.</p> <p>Urinary incontinence: There were no statistically significant differences between groups on EPIC-26 at baseline. Overall, urinary function among the control group was lower but failed to reach statistical significance (p=0.092). The intervention group did not display statistical significance in mean urinary incontinence at 3 months (F [1,35] =0.18, p=0.68)</p> <p>PFM Exercise information received: Nearly half n=51 (49%) reported they didn't receive any verbal information about PFM exercise from specialist and n=10 (20%) reported didn't receive any written information.</p> <p>Participants who reported they were given PFM information were more likely to receive from nurses (74%) than doctors (23%)</p> |
| <p>Dijkstra-Eshuis et al. 2015</p> | <p>Urinary continence (defined as no leakage at all on a 24-hr pad test) at 1-year post op.</p> <p>Quality of Life (measured using PeLFIs, KHQ and IPSS)</p> | <p>Not assessed.</p> | <p>Continence: 24-hr pad test.</p> | <p>QoL: KHQ; PeLFIs; IPSS</p> | <p>Planned strategies for adherence/fidelity: Not reported</p> <p>Actual (extent to which the intervention was delivered as planned): Not reported.</p> | <p>Interim analysis after 122 patients, 1 year postoperatively showed that there was no advantage for men in the treatment group on continence outcomes.</p> <p>Only 1 patient received electrostimulation preoperatively to make the participant aware of pelvic floor musculature.</p> <p>No significant differences between the intervention group and control group in terms of incidence of SUI and QoL for KHQ and IPSS 6 weeks, 3,6,9 months and 1-year post op (P>0.05)</p> <p>At 1-year post op a total of 22.8% of patients were still incontinent.</p> <p>Researchers halted the trial prematurely because interim analysis showed no benefit for the intervention group.</p> <p>When applying a stringent definition of continence, preop sessions of PFMT with biofeedback are not effective in improving the recovery of continence and QoL after a LARP.</p> |
| <p>Dubbelman et al. 2012</p> | <p>Recovery of continence after RRP (measured by 1-hr and 24-hr pad tests). Continence was defined as a loss of <4g urine on the 24-hr pad test and of <1g on the 1-hr pad test.</p> <p>The effect of RRP on the urethral sphincter function and its relation to post radical prostatectomy incontinence (PPRI); and the effect of the intensity of PFME on the urethral sphincter function as measured by</p> | <p>Not assessed.</p> | <p>Continence: 1-hr and 24-hr pad tests</p> <p>Urethral Sphincter Function: Urethral Pressure Profilometry -UPP (Maximum urethral closure pressure – MUCP and Functional Profile length – FPL)</p> | <p>Not assessed.</p> | <p>Planned strategies for adherence/fidelity: Not reported</p> <p>Actual (extent to which the intervention was delivered as planned): Not reported.</p> | <p>19/66 (28.7%) of men had regained continence 6 months post RP.</p> <p>Changes of Urethral Pressure Profile after operation: There was a median relative decrease in FPL and MUCP of 64% and 41% of all participants. Compared to those that were still incontinent after 6 months, the MUCP of men who regained continence was significantly higher both before and after RP.</p> <p>Of the men who regained continence, 13/19 (68%) had a preoperative MUCP ≥53.1cm H₂O; of those who did not regain continence, 28/47 (60%) had a MUCP <53.1cm H₂O.</p> <p>Effect of Intensity of PFME on Urethral Profile Parameters: There were no significant differences in the changes in UPP between F-PFME and PG-PFME groups. However, there was a (counterintuitive) trend toward a higher relative decrease of MUCP in PG-PFME group (45% vs 36% respectively, p=0.05).</p> <p>Bladder and Nerve Sparing: Nerve sparing, and bladder neck sparing showed a trend towards a positive effect on the relative decrease of the MUCP (P=0.085 and P=0.066 respectively).</p> |

| | | | | | | |
|------------------------|---|---------------|--|---|---|---|
| | Urethral Pressure Profilometry (UPP). | | | | | <p>Non-nerve sparing approach (OR: 0.0149, P=0.007) and bladder neck sparing (OR: 4.586, P=0.021) were prognostic factors for a higher relative decrease of the MUCP after RRP.</p> <p>MUCP seems to be the most important prognostic factor for persistent PRPI. It was found that pre-and post-prostatectomy MUCP was significantly lower in persistently incontinent men compared to men who regained continence. However, the relative decrease in MUCP was almost identical in both groups. So, a low preop MUCP seems to predispose to persistent incontinence.</p> |
| Hirschhorn et al. 2014 | <p>The efficacy of a multicomponent, theory-based intervention in provision / receipt of preop PFMT among men undergoing RP.</p> <p>To compare postoperative outcomes (incontinence, satisfaction with treatment, QoL) of patients receiving preoperative PFMT with those not receiving it.</p> | Not assessed. | ICIQ-UI short form | The RAND 36-item Short Form Health Survey (SF-36) | <p>Planned strategies for adherence/fidelity: Not reported</p> <p>Actual (extent to which the intervention was delivered as planned): Not reported.</p> | <p>Satisfaction Data: <i>'How satisfied are you with the treatment you received (for leakage of urine)?'</i> A significantly higher proportion of post-intervention respondents (37/48 = 77%) than pre-intervention respondents (41/70 = 59%) were satisfied with the treatment they received (P=0.048)</p> <p>A significantly higher proportion of respondents receiving preop PFMT (54/69 = 78%) than respondents not receiving preop PFMT (24/49 = 49%) were satisfied with treatment (P=0.002)</p> <p><i>'How satisfied are you with the effect of your treatment (for leakage of urine)?'</i></p> <p>No significant difference in the proportion of all respondents satisfied with the effect of treatment pre-intervention (40/70 = 57%) vs post-intervention (35/48 = 73%); P=0.119)</p> <p>A significantly higher proportion of respondents receiving preop PFMT (50/69 = 72%) than respondents not receiving preop PFMT (25/49 = 51%) were satisfied with the effect of treatment (P=0.021)</p> <p>Practice Audits: Significant increase in mean (SD) number of patients provided with preop PFMT post-intervention Pre: 12.1 (3.6) patients/month, Post: 16.7 (3.7) patients/month P=0.018</p> <p>Increase in private hospital patients provided with PFMT Pre: 11.1 (3.8) pts / mth Post: 15.7 (4.2) pts / mth P=0.027. But no significant difference in the mean number of public hospital patients.</p> <p><i>Continence Outcome Data:</i> No significant difference in the mean (SD) ICIQ sum scores for all respondents pre vs post-intervention Pre: 7.8 (5.6) vs Post: 7.0 (5.4); P=0.368</p> <p>Respondents receiving preop PFMT had significantly lower mean (SD) ICIQ sum scores than respondents not receiving Pre-op PFMT. <i>Pre-op PFMT:</i> 6.2 (5.0) <i>Post-op PFMT:</i> 9.2 (5.8) P<0.001</p> <p>No significant differences of QoL domains, p<0.05.</p> |
| Manley et al. 2016 | <p>To improve PFM strength.</p> <p>To improve urinary continence (continence was defined as requiring no use of continence aids at 4-week post catheter removal assessment)</p> | Not assessed. | PFM assessment / DRE / Trans-abdominal ultrasound / continence aids used | Not assessed. | <p>Planned strategies for adherence/fidelity: Not reported</p> <p>Actual (extent to which the intervention was delivered as planned): Not reported.</p> | <p>PMF strength preop: Strong: n=77 (79%), moderate: n=12 (12%), Weak: n=9 (9%)</p> <p>PMF strength postop: Only a small number of men with strong PMF preop were not as strong 4 weeks post catheter removal (18.2%). Of the 21 patients who could increase PMF from preop levels, 15 (71.4%) did so by 4 weeks, while balance remained at baseline level. Younger age significantly predicted strength improvement from day 4 to 4 weeks postop (OR, per one year younger = 1.14, p=0.029)</p> <p>No tumour characteristics significantly predicted change over time.</p> <p>Incontinence: 41/83 (49.4%) were continent and 42/83 (50.6%) were incontinent at 4-week post catheter removal. PFM strength correlated</p> |

| | | | | | | |
|--------------------------------|---|---------------|--|--|---|---|
| | | | | | | with continence ($p<0.01$) however, preop strength was not associated with continence at 1 month ($p>0.4$) Increasing age had stronger effect in predicting incontinence in men with baseline moderate and weak PFM strength (OR=1.83, $p=0.07$) than in men with strong preop PFM strength (OR=1.05, $p=0.3$). |
| Tienforti et al. 2012 | Self-reported recovery of continence 6 months after catheter removal. Continence was strictly defined as an ICIQ-UI score of 0. The number of incontinence episodes per week, number of pads used per week, OAB symptoms and impact of incontinence of QoL | Not assessed. | Continence: ICIQ-UI; ICIQ-OAB; number of pads per week; UCLA-PCI score | QoL: IPSS-QoL | Planned strategies for adherence/fidelity: Exercise frequency was recorded in a training diary. Actual (extent to which the intervention was delivered as planned): Not reported. | Continence: The difference between groups was statistically significant at each reported follow up time. In the intervention group continence (ICIQ-UI = 0) was achieved by six, eight and ten patients at 1, 3 and 6 months, respectively. In the control group only one patient achieved continence. The number of incontinence episodes and pads per week were significantly lower for patients in intervention group. <i>Number of incontinence episodes per week:</i> 3 months (I: 3.84 vs C: 14), 6 months (I: 2.72 vs C: 13.06) <i>Number of pads per week:</i> 3 months (I: 1.50 vs C: 6.25), 6 months (I: 1.31 vs C: 4.625) QoL: Patients in the intervention group reported lower IPSS-QoL scores (better QoL) than those in the control at all follow up times but the different was not statistically significant $P>0.05$. |
| Diet | | | | | | |
| Dalais et al. 2004 | The effect of a diet rich in phytoestrogens on biochemical markers in men diagnosed with prostate cancer. Mean changes in urinary excretion of phytoestrogens, PSA, and free/total PSA ratio from baseline to after intervention. | Not assessed. | Blood and urine samples (urinary isoflavone and lignan concentrations, PSA, free/total PSA ratio, testosterone, sex hormone-binding globulin (SHBG), dihydrotestosterone, free androgen index, creatinine (daidzein; genistein; enterolactone) | Food frequency questionnaire (Anti-Cancer Council of Victoria) | Planned strategies for adherence/fidelity: To assess patient compliance, urinary isoflavone and lignan concentrations were determined by high-performance liquid chromatography. Actual (extent to which the intervention was delivered as planned): Not reported. | No statistically significant differences at baseline between the 3 study groups for clinical and demographic characteristics (Groups: Soy, Soy and Linseed, and Wheat). Soy group: Statistically significant increase in urinary excretion of genistein and daidzein. Soy and Linseed group: Statistically significant increase in urinary excretion of genistein, daidzein and enterolactone. Placebo: no change Heat-treated soy vs placebo (wheat) group showed statistically significant difference for total PSA (-12.7% vs 40%, $p=0.02$) and free total PSA ratio (27.4% vs 15.6%, $p=0.01$). Heat-treated soy grits and Heat-treated soy grits and linseed: free/total PSA ratio (27.4% vs -10%, $p=0.007$). Free androgen index: HT soy vs HT soy and Linseed (16.4% vs -15.5%, $p=0.04$). Results suggest a dietary manipulation containing 50g of HT soy grits daily will have favourable effects on biomarkers for PCa. |
| Demark-Wahnefried et al., 2017 | Feasibility and fidelity outcomes. Pre-Post differences on body mass and composition, energy intake, PA, physical functioning, quality-of-life, serum biomarkers, lymphocytic gene expression, tumour markers. | Not assessed. | Body fat and mean mass, Vo2, biomarkers | RAND-36, Prostate Cancer Index and Physical Activity Recalls | Planned strategies for adherence/fidelity: Designed as a feasibility trial, the primary aims were attainment of the following benchmarks: (1) enrolment of 40 participants within 2 years; (2) >80% retention; (3) adherence, defined as completion >70% of contact sessions; and (4) safety, defined as the absence of serious adverse events in the intervention arm. Actual (extent to which the intervention was delivered as planned): This trial achieved 85% retention, 95% adherence, and documented no serious adverse events; the accrual target also was achieved but required six additional months. | Changes in scores for the weight loss intervention versus the control arm for respectively: Weight: -4.7 (SD 3.1) kgs vs - 2.2 (4.4) kgs $p>0.05$. Caloric intake: - 500 (SD 636) vs -159 (SD 600) kcal per day $p<0.05$ PA: +0.9 (SD3.1) vs 1.7 (SD 4.6) MET hours per day $p>0.05$, Vitality: +5.5 (SD7.14) vs -1.8 (SD8.1), $p<0.05$, Testosterone: +55 (SD 86) vs -48.3 (SD 203) ng dl, Sex-hormone-binding globulin: +14 (SD14.6) vs + 1.8 (7.6) nmol, $P<0.01$, Leptin: - 2.16 (SD 2.6) vs -0.03 (3.75), $p<0.05$, |

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| | | | | | | Ki67 proliferation rates 5.0 (2.5, 10.0) vs 0.0 (0.0, 2.5), $p<0.01$. Overall, mixed results on biomarkers because of weight loss among men affected by prostate cancer in the prehabilitation setting. |
| Nurse led models of care | | | | | | |
| Kinsella et al. 2011 | Reduce long-term (treatment decision) regret. Regret was determined if over the previous 4 weeks the patient had wished he could change his mind about his treatment choice at least some of the time, or indicated that he felt that he would have been better off if he had received another treatment. | Not assessed. | Not assessed. | HADS; 2 item regret questionnaires. IIEF-5 (sexual function) | Planned strategies for adherence/fidelity: Not reported. Actual (extent to which the intervention was delivered as planned): Not reported. | Regret: 8 men (19.5%) in UC group expressed regret at 1-year compared to 1 man (2.5%) in the intervention group ($p=0.03$). ED was cited as reason for regret in all men. HADS: Significantly lower in the intervention group at all postop time points ($P<0.01$) Possible selection bias however, patients self-selected treatment. IIEF: Before treatment scores were identical for both groups ($P=1.0$). 3 months: following treatment, there were no significant score differences. 6, 9 and 12-months: Intervention group patients had significantly higher IIEF scores at 6 & 9 months for RP group. 12-months postop no significant difference on the IIEF-5 scores between usual care or RP intervention group ($p>0.05$) |
| Kim 2011 | Self-care agency scores. Quality of life and self-care activities. | Not assessed. | Not assessed. | FACT-P, The Self-as-Career Inventory, Self-Care Activity | Planned strategies for adherence/fidelity: Not reported. Actual (extent to which the intervention was delivered as planned): Not reported. | Self-care agency in intervention group 145.14 pre-surgery vs 149.28 3 months post-surgery vs, control group 145.29 prior to surgery and 144.76 post surgery, $p<0.01$. Self-care activity scores in the intervention group was 30.39 vs 29.64 in the control group, $p>0.05$. Quality of life scores in the intervention group was 107.32 before surgery and 105.79 after surgery, compared to the control group of 102.53 points before the surgery and 95.10 after the surgery, $p<0.01$. |
| Sundberg et al. 2017 | Early detection, reporting and management of symptoms and concerns during treatment for prostate cancer. To reduce symptom burden and improve HRQoL (emotional function, insomnia, urinary symptoms). | Not assessed. | Not assessed. | EORTC QLQ-C30; EORTC QLQ-PR25; SOC | Planned strategies for adherence/fidelity: Not reported. Actual (extent to which the intervention was delivered as planned): Not reported. | Demographics and clinical characteristics were balanced between groups, except control group which had statistically lower level of education. Findings suggest Interaktor could be an efficient mHealth tool for facilitating supportive care needs during cancer treatment. CG: Significantly decreased global QoL ($p=0.015$) and role ($p=0.004$) as well as emotional ($p=0.026$) and social ($p=0.004$) functioning. Participants reported increased fatigue ($p=0.001$) and insomnia ($p=0.005$) Both IG and CG reported significant increase of diarrhoea, urinary symptoms and sexual activity during radiotherapy treatment. CG: significantly worse emotional functioning at end of RT ($p=0.002$) & 3 months later ($p=0.26$) compared to the intervention group. High levels of fatigue ($p=0.047$) and nausea ($p=0.038$) at end of treatment were experienced in the control group. Insomnia and urinary symptoms more frequently reported at end of treatment ($p=0.005$ / $p=0.005$) and 3 months later ($p=0.035$ / $p=0.038$). IG: rated emotional functioning ($p=0.007$), insomnia ($p=0.004$) and urinary related symptoms ($p=0.003$) better at T2 (end of radiotherapy compared to the control group). |

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| | | | | | | SOC was a significant predictor in the dependent scales, except for nausea at T2. IG rated better emotional functioning and fewer problems with sleep and urinary symptoms than CG did at the end of treatment. |
| Psychological | | | | | | |
| Parker et al. 2009 | Assess short-term (preoperative and perioperative) effects of intervention. Assess the long-term (6 weeks, 6 and 12 months after surgery) effects of the intervention. | Not assessed. | Urine samples (to measure cortisol and catecholamine levels) Bloods (to measure immune function) These were not reported on in the current article. Medical charts reviewed for diagnosis, disease stage, surgical technique, and PSA levels. | Adjustment and QoL measures: POMS; IES; SF-36; PCI | Planned strategies for adherence/fidelity: Not reported. Actual (extent to which the intervention was delivered as planned): Not reported. | Findings demonstrate the efficacy of a brief presurgical stress management intervention in improving short and long-term outcomes. Short-term effects (1 week before and morning of surgery): IES scores - no statistically significant group differences or changes over time. Mood disturbance - significant group differences – SM, 8.2 (0.92); SA, 9.8 (0.91); SC, 11.9 (0.99); p=0.02 SM group: Post hoc analyses showed that men had significantly less mood disturbance than did men in the SC group (p=0.006). No other group comparisons reached significance. Long-term effects (6 weeks, 6 months, and 12 months post-surgery): IES scores – no significant group changes over time long-term (all Ps > 0.05 – no data shown). PCS (physical component summary) scores: Significant group differences: SM, 50.9 (1.3); SA, 48.8 (1.2); SC, 46.1 (1.3); p=0.004; 6 weeks: 47.2 (1.09) / 6 month: 49.6 (1.10) and 12 months: 49.0 (1.10); p=0.02. SM group: post hoc analyses indicated the men had significantly higher PCS scores than SC group (p=0.0009) MCS (mental component summary) scores: No statistically significant group differences over time. Prostate Specific QoL: No significant group differences by time interactions. For most scales it declined from baseline to 6 weeks and 6 months after surgery, then improved by 12 months after surgery. Significant changes over time for: Urinary function, urinary limitation, urinary bother, and sexual function - all (P<0.0001). Cancer worry (P<0.004). |
| Sexual Function | | | | | | |
| Zelevsky et al. 2014 | Primary outcome was to determine whether prophylactic use of SC prevented loss of spontaneous EF at 24 months after treatment. Secondary outcomes were urinary function, quality of life and satisfaction with EF. | Not assessed. <i>Penile duplex doppler studies were not performed.</i> | Not assessed. | Quality of life: SF-36, IPSS, IIEF | Planned strategies for adherence/fidelity: Participants were asked to keep a daily pill diary to document adherence. Actual (extent to which the intervention was delivered as planned): Not reported. | At 12 months EF scores were better in the intervention arm compared to the placebo (p = 0.018), with overall improved satisfaction with EF (p = 0.027). No lasting significant differences observed at 24 months between both study arms. No other differences were observed in urinary or quality of life measures between both groups. |

Abbreviations: ADT (Androgen Deprivation Therapy), BF% (Body Fat Percentage), BMI (Body Mass Index), CHAMPS (Community Healthy Activities Model Program for Seniors), DRE (Digital Rectal Examination), ED (Erectile Dysfunction), EPIC-26 (Expanded Prostate Cancer Index Composite), EORTC QLQ-C30 (European Organisation for Research and Treatment [EORTC] Quality of Life Questionnaire), EORTC QLQ-PR25 (EORTC Quality of Life Questionnaire for Prostate Cancer), FACT-F (Functional Assessment of Cancer Treatment-Fatigue), FACT-P (Functional Assessment of Cancer Treatment-Prostate), HADS (Hospital Anxiety and Depression Scale), IES-R (The Revised Impact of Events Scale), IPSS (International Prostate Symptom Score), IIEF (International Index of Erectile Function Scale), KHQ (Kings Health Questionnaire), LoS (Length of Hospital Stay), PA (Physical Activity), PDI (Pain Disability Index), PeLFIs (Pelvic Floor Inventories), Prehab (Prehabilitation), PFM Assessment (Pelvic Floor Muscle Assessment), PCI (The University of California, Los Angeles, Prostate Cancer Index), PTGI (Post-Traumatic Growth Inventory), PSA (Prostate Specific Antigen), POMS (Profile of Mood States), PORPUS (Patient-Oriented Prostate Utility Scale), Post-op (post-operatively), PPUI (Post-Prostatectomy Urinary Incontinence), RP (Radical Prostatectomy), SF-36 (The Medical Outcomes Study (36 item short form survey)), SF (Sense of Coherence Scale), 6MWT (Six-Minute Walk Test), SHBG (Sex Hormone-Binding Globulin), TPUS (Real-time Transperineal Ultrasound), UCLA-PCI (University of California, Los Angeles – Prostate Cancer Index), UPP (Urethral Pressure Profilometry), WC (Waist Circumference).