

Interventions for prostate cancer survivorship: A systematic review of reviews

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Abstract

Objectives: To systematically review the evidence for interventions addressing key domains of the American Cancer Society (ACS) and American Society of Clinical Oncology (ASCO) Prostate Cancer Survivorship Care Guidelines: health promotion, surveillance, physical side effects, psychosocial management, and care-coordination.

Methods: We conducted a systematic review of systematic reviews and meta-analyses of interventions targeting ACS/ASCO guideline domains. All titles and abstracts were independently assessed for inclusion based on predetermined criteria. Relevant data were extracted and assessment of methodological quality performed.

Results: Forty-four systematic reviews of interventions targeting ACS prostate cancer guideline domains were included for review. Exercise and psychosocial interventions were effective for improving men's survivorship outcomes in the domains of health promotion, physical side effects, and psychosocial management. Across the domains evidence quality varied and there was a limited diversity of participants. No reviews of interventions addressing surveillance and cancer care coordination were identified.

Conclusions: There are substantive knowledge gaps in prostate cancer survivorship research that are a barrier to real improvements in men's outcomes across the breadth of the survivorship experience. A targeted research and implementation agenda in prostate cancer survivorship is urgently needed if we are to meet the current and future burden of this disease on individuals, families, and communities.

Keywords: cancer, oncology, interventions, prostate cancer, randomized controlled trial, survivorship, systematic review

Prostate cancer is the most commonly diagnosed cancer among men in developed countries, with over 1.1 million men diagnosed each year worldwide¹. Advances in treatment have led to significant increases in survival rates, with over 90% of men diagnosed with prostate cancer living at least five or more years^{2,3}. Although advances in treatment mean that men are surviving longer, they may not be surviving well. A substantive group of men with prostate cancer experience heightened psychological distress⁴ and unmet needs in psychological and sexual supportive care are common^{5,6}. Disease and treatment side effects include fatigue⁷, erectile dysfunction, and incontinence⁸, sarcopenia⁹, and increased risk of cardiometabolic disease¹⁰, with these patient populations characterised by a high prevalence of overweight/obesity and insufficient physical activity that may contribute to poorer quality of life¹¹. Men with prostate cancer also have an increased risk of suicide that is especially evident in the first twelve months after diagnosis and in men with advanced disease^{12,13}. Thus, addressing the unique and long term needs of prostate cancer survivors is critical to quality oncology care.

The importance of survivorship care was first formally recognised by the Institute of Medicine in 2005¹⁴. In 2014 the American Cancer Society (ACS) published specific *Prostate Cancer Survivorship Care Guidelines*, which were subsequently endorsed by the American Society of Clinical Oncology (ASCO)^{15,16}. These guidelines aim to promote comprehensive follow-up care, optimal health, and quality of life for men with prostate cancer with five key domains for action: health promotion; surveillance for prostate cancer recurrence and screening for second primary cancers; management of long-term physical side effects; psychosocial management; and care coordination. The guidelines recommend survivors maintain a healthy weight by limiting high-caloric foods; engage in regular physical activity including weight-bearing exercises; consume a diet high in fruits, vegetables, and whole grains; avoid or limit alcohol consumption; and avoid smoking tobacco. In order to monitor for prostate cancer recurrence, it is recommended that Prostate Specific Antigen (PSA) levels are assessed every 6 to 12 months for the first five years after treatment, and a digital rectal examination is performed annually¹⁷. As prostate cancer survivors may be at increased risk of bladder or colorectal cancers, survivors need to be monitored and symptoms referred for thorough evaluation to detect any second primary cancers early¹⁸. The guidelines highlight the importance of assessing and managing long-term side-effects such as anaemia, bowel dysfunction, sexual dysfunction, and cardiometabolic risks, tailored for the type of cancer treatment received^{15,16}. Additionally, survivors should be routinely screened using the Distress Thermometer¹⁹ at various stages of the cancer pathway, with patient-reported quality of life recorded at diagnosis and annually thereafter as part of survivorship care²⁰. In order to improve care-coordination, it is advised that cancer specialists provide all prostate cancer survivors with a survivorship care plan, incorporating both treatment summaries and clinical follow-up recommendations for primary care practitioners^{15,16}.

The ACS survivorship care domains and corresponding guidelines were developed using a combination of expert consensus and an evidence synthesis which was largely observational, based on small sample sizes, and with great variability in methodologies¹⁵. In addition, according to the ACS process, these guidelines need to be revised every 5 years¹⁵. Thus, it is timely to investigate the evidence presented in systematic reviews that relate to prostate cancer survivorship care. Specifically, there is a need to synthesise the evidence regarding the overall effectiveness of various intervention types, identify conflicting evidence, and determine whether this can sufficiently inform improved guidelines for targeting care across the survivorship domains for men with prostate cancer. Accordingly, we undertook a systematic review of the

evidence for interventions addressing key domains of the American Cancer Society (ACS) and American Society of Clinical Oncology (ASCO) Prostate Cancer Survivorship Care Guidelines: health promotion, surveillance, physical side effects, psychosocial management, and care-coordination. Key objectives were to identify systematic reviews about interventions that map to these survivorship domains and evaluate the extent of evidence available to support specific approaches.

Methods

Systematic reviewing methods were used to identify existing reviews rather than original research. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist to guide the conduct and reporting of this review ²¹.

Search strategy

Electronic searches were conducted in the Cochrane Database of Systematic Reviews, the Database of Abstracts and Reviews of Effects, CINAHL, Scopus, PsycInfo, and PubMed, using the search strategies in Appendix A. Key terms related to “prostate cancer”; AND “intervention” OR “RCT” or “trial” or “program”; AND “survivorship” OR “quality of life” OR “side effects” OR “surveillance” OR “healthy lifestyle” OR “care-coordination”; AND “review”. Searches were conducted from inception to 27th July 2018, and limited to English language. The search was not date limited. After duplicates were removed, two authors independently screened the title and abstract of each citation and then retrieved potentially eligible articles for full text review. Any queries were resolved through discussion with the wider research team. Inter-rater agreement on eligible articles was calculated, with Cohen’s κ of 0.83 indicating near perfect agreement between authors (FCW, NR). Additional hand searching of reference lists of included studies was also conducted.

Eligibility criteria

Systematic reviews or meta-analyses examining trial studies which assessed the effectiveness of an intervention in comparison to control conditions on any outcome within a prostate cancer survivorship domain were eligible for inclusion. All titles and abstracts were independently screened, and relevant reviews were retrieved and assessed for inclusion. Any disagreement within this process was resolved through discussion within the team. Inclusion criteria were organised in accordance with the patient, intervention, comparison, outcome (PICO) reporting structure ²¹. Review articles were included if they focused on populations of adult prostate cancer survivors, or where a subset of included studies investigated adult men with prostate cancer; evaluated controlled or uncontrolled trials of interventions for prostate cancer survivors; and focused on survivorship outcomes within the five domains. We excluded reviews that reported on general cancer populations or trials of mixed cancer groups, interventions that were conducted pre-diagnosis, and studies focusing on clinical or medical anti-cancer treatment only.

Data extraction and analysis

From each eligible systematic review or meta-analysis, data was extracted relating to authors, year, objectives, participants, intervention types, outcome variables, quality assessment, and authors’ conclusions. The reviews varied in whether they grouped studies according to intervention types (e.g. exercise interventions to improve a range of outcomes), outcomes (e.g.

any intervention to improve quality of life), or both (e.g. exercise interventions to improve quality of life). Findings were summarised according to the survivorship domain that was the outcome of interest within each review article. Reviews which addressed outcomes within more than one survivorship domain were therefore summarised in more than one category. From this, a narrative synthesis of the conclusions of reviews published within the last five years (since the guidelines release) about intervention effectiveness was undertaken. Additionally, a summary table was created to describe the quantity and quality of the evidence across each of the domains. No statistical analyses or meta-analyses were conducted. Appraisal of individual component studies was beyond the scope of this synthesis, as these were the aims of the original systematic reviews and meta-analyses.

Quality Assessment

Each systematic review was critically appraised using a modified checklist from the Database of Abstracts of Reviews of Effects (DARE). The checklist was used to assess the reliability and validity of included review articles²². To be included in the current synthesis, reviews had to meet at least five of the seven criteria **provided in Figure 1**. In order to assess the quality of the overall body of evidence within each domain, we relied on review authors' conclusions regarding the quality of interventions within each review. These are summarized within the presentation of results.

Results

Overall, the search identified 902 articles. After removal of duplicates and title and abstract screening, 63 articles were examined in greater detail. Of these, 46 unique systematic reviews met the inclusion criteria, however 2 were excluded after quality assessment, leaving 44 review articles in the current synthesis (Figure 2). Overall the included review articles reported on a total of 548 studies; however, this included only 212 unique studies as there was significant overlap between review articles in the same domains. The reviews varied considerably in inclusion criteria and objectives. The majority of reviews were of high methodological quality, meeting all seven criteria on the DARE checklist (n=27, 61%). The most common issues reducing review quality were not involving more than one author in each stage of the review process, and not assessing the quality of the primary studies. Appendix B presents the main characteristics of each included review.

Coverage of domains

Overall, the majority of systematic reviews reported on outcomes relating to psychosocial management (n = 23), health promotion (n = 19) and physical side effects (n = 17). No reviews investigated care-coordination as a primary outcome, however, three review articles reported on interventions targeting individual's self-efficacy, uncertainty, and knowledge regarding care which could be considered a proxy for care-coordination. No articles were located that systematically reviewed interventions designed to improve surveillance for recurrent cancer or screening for other primary cancers. Eleven of the included reviews (25%) conducted a meta-analysis for some or all of the primary studies, while for the majority of reviews this was not possible due to considerable heterogeneity across studies.

Participant characteristics

The majority of included reviews focused on a broad population of men diagnosed with prostate cancer, including men with any stage of cancer, and undergoing any treatment type. Two reviews excluded men with advanced stage of disease due to the different treatment and outcome pathways^{23, 24}. Additionally, eight of the included reviews focused only on men undergoing androgen deprivation therapy (ADT)²⁵⁻³², while three focused only on those undergoing radical prostatectomy³³⁻³⁵, undertaking an evaluation of the effect of exercise interventions on differing treatment-related side effects and adverse events. For the reviews investigating interventions to assist men undergoing ADT, seven reviews focused on body composition, weight gain, and cardiometabolic risk outcomes, while one review focused on depression, anxiety, and quality of life²⁵. For men undergoing radical prostatectomy, the reviews focused on physical symptoms known to cause common side effects including erectile dysfunction and incontinence. Further regarding the populations of interest in the current reviews, only one review focused on ethnic minority populations in America³⁶, while one other review included three studies addressing ethnicity as a mediator³⁷.

Intervention characteristics

The included reviews reported on a range of individual intervention types, classified primarily into exercise, nutrition, psychosexual or psychosocial approaches. Exercise interventions consisted of aerobic training, resistance training, flexibility exercise, unsupervised physical activity, pelvic floor or sphincter training, and qigong. Nutrition interventions included structured diet regimes (such as low-fat, high-fibre) or dietary modification, dietary counselling, individual supplements, or any combination. Psychosocial interventions were defined as interventions involving one of the following components: psychosexual, education, cognitive-behavioural, relaxation, supportive counselling, peer support, and communication, and were often multi-modal.

Narrative synthesis

To address the second research question regarding the effectiveness of interventions in addressing singular domains of survivorship, the combined findings and conclusions of review articles published within the last five years are summarized in a narrative synthesis. Twenty-eight of the review articles (63%) were published after 2013, with the overall conclusions from the body of evidence presented in Table 1. Nine review articles assessed the effectiveness of exercise interventions on a range of outcomes across multiple domains of survivorship, thus these reviews are included in the synthesis more than once.

Health promotion

Eleven review articles focused on health promotion outcomes, investigating the impact of nutrition and exercise interventions on body weight, body composition, physical activity levels, and PSA levels. Reviews in this domain of survivorship reported on nutrition (n=4), exercise (n=10), or combination (n=3) interventions which included aerobic and/or resistance training, diet, and dietary supplements. No review reported on individual studies which investigated outcomes related to smoking, or alcohol consumption. Reviews investigating evidence relating to exercise interventions generally reported higher quality bodies of evidence than reviews of combination or nutrition interventions. Overall, the reviews included in the health promotion domain suggest that there is strong, high-quality evidence of the effectiveness of exercise interventions, with inconclusive evidence for nutrition interventions.

Five reviews reported that exercise interventions, such as aerobic and resistance training, could be effective in improving physical activity levels^{27, 28, 30, 38, 39}. One review of diet and exercise interventions reported reductions in body weight⁴⁰, with diet having more effect on weight loss than exercise alone. One review reported the efficacy of exercise interventions to preserve and improve lean body mass particularly in the setting of ADT²⁷, while another review reported no effect in other parameters of body composition³¹. There was some evidence that particular diets and supplements can impact prostate cancer progression. Nutrition interventions which were reported to stabilise or decrease serum PSA levels tended to be low in fat, and include plant-based supplements (pomegranate, flaxseed, lycopene, and soy)^{41, 42}; however, soy supplementation did not improve any outcomes in one review³¹. The overall impact of nutrition interventions on PSA levels could not be reliably estimated due to limited, and low-quality trials.

Surveillance

No review articles were retrieved which reported on interventions to improve rates of surveillance for second primary cancers and monitoring for recurrence.

Physical side effects

Sixteen systematic review articles reported on interventions aiming to alleviate ongoing physical side effects of prostate cancer treatment in the survivorship period, including fatigue, muscle strength, peak oxygen intake, bone health, cardiovascular fitness, sexual function, and incontinence. Reviews in this domain of survivorship reported on exercise (n=12), exercise combined with diet (n=1), and other complex intervention types (n = 3). Overall, the body of evidence addressing the physical side effects of prostate cancer with exercise interventions was reported to be high quality.

Five reviews suggested that a combination of aerobic and resistance training delivered during or after treatment for prostate cancer survivors could be effective in improving cardiorespiratory fitness, and peak oxygen capacity, with resistance training demonstrating improvements to muscular strength^{27-29, 32, 43}. Exercise interventions were less effective in improving other markers of cardiovascular health such as lipid profile, blood pressure, glucose and cardiometabolic risk among men undergoing ADT^{27, 28, 31, 32}. Very few appropriately designed studies included long-term duration (e.g. 12 months duration) and implementation of osteogenic specific exercise programs (e.g. impact loading) on outcomes of bone health and as a result, limited information exists on the effects of exercise on bone mineral density. Evidence from seven reviews reported that exercise interventions including aerobic or resistance training, qigong, or exercise in combination with healthy diet, may significantly reduce symptoms of fatigue^{27, 28, 30, 44-47}, while one review did not have sufficient data for analysis²⁹. One review also investigated the effectiveness of psychosocial interventions, such as cognitive-behavioural therapy and education, and indicated that these may have positive effects on cancer-related fatigue⁴⁵. For incontinence outcomes, one review reported that preoperative pelvic floor training did not improve the time to incontinence above and beyond the benefits of pelvic floor exercise post-operatively³³, while another reported that pre-operative pelvic floor exercise improves early continence but not long-term continence rates in men after radical prostatectomy³⁵. One review reported that pelvic floor interventions showed significant improvements on urinary symptoms both with and without biofeedback, with only three trials examining the effects on sexual function and self-esteem⁴⁸. One review reported improvements in sexual bother, sexual confidence, and sexual satisfaction from interventions utilising psycho-educational, peer support,

and cognitive-behavioural group interventions⁴⁹. Exercise interventions were reported to have a borderline positive effect on sexual activity but no effect on sexual function⁵⁰.

Psychosocial management

Eighteen included systematic reviews reported on interventions which aimed to improve the psychosocial effects of cancer and treatment for prostate cancer survivors, predominantly focusing on quality of life, depression, anxiety, and mental health outcomes. Reviews in this domain of survivorship reported on the effectiveness of psychosocial (n=5), exercise (n=9), or nutrition (n=3) interventions.

Five reviews reported on the effectiveness of psychosocial interventions on outcomes including quality of life, depression, anxiety, and distress^{23,49,51-53}. Reviews with a narrower scope reported no significant effect of supportive care interventions on quality of life or depression outcomes^{23,51}. Two reviews which focused only on depression or anxiety reported that psychosocial strategies have a short-term benefit, particularly peer support and psychotherapy rather than education, but this was not sustained over time^{52,53}. One review reported small improvements in some aspects of health-related quality of life, however it was uncertain whether these were clinically important improvements as the evidence base was of low quality⁵¹. Finally, one comprehensive review with a broader scope included 56 RCTs, and reported that combinations of cognitive behavioural, health professional communication, psychoeducation, and peer support interventions were most commonly applied and effective in improving decision-related distress, mental health, and health-related quality of life outcomes⁴⁹.

Evidence from eight reviews suggested that aerobic and resistance exercise interventions show some benefit in improving health-related quality of life outcomes, both during and after treatment, particularly with supervised interventions^{28,30,31,44,46,50,54,55}. Other reviews reported an unclear impact of exercise on quality of life⁴⁷, or insufficient data for analysis^{27,29,33}. The effect of healthy eating on quality of life was also inconclusive as reported in one review³¹. Exercise interventions were reported to have no impact on depression or anxiety outcomes⁴⁶, or again there was insufficient data available²⁵.

Care-coordination

No reviews investigated interventions that target care-coordination. Two supportive and psychosocial care reviews published in the last five years described interventions to improve self-efficacy and coping which may be a proxy for care-coordination^{23,51}. These reviews found little evidence for effectiveness in improving self-efficacy or coping in men with prostate cancer. Nevertheless, no reviews were identified in this study that examined professional or system-led interventions to improve care coordination for prostate cancer survivorship.

Discussion

Current evidence supports the effectiveness of exercise and psychosocial interventions for improving men's prostate cancer survivorship outcomes in the domains of health promotion, physical side effects, and psychosocial management. However, evidence quality is varied and inconsistent/absent or poor for specific topics within these domains such as diet, sexual well-being, reduction of alcohol and tobacco consumption. No evidence was found for effective approaches to surveillance and care-coordination. Few studies addressed the needs of high need and vulnerable patients; or considered population-based implementation. It is clear that there are

significant knowledge gaps in prostate cancer survivorship that will be a barrier to real improvements in men's outcomes across the breadth of the survivorship agenda.

Exercise interventions are effective at improving cardiorespiratory fitness, muscular strength, fatigue, incontinence, physical activity levels and quality of life in men diagnosed with prostate cancer, with some evidence on preserving/improving lean mass but with inconsistent reports on other parameters of body composition. There is inconclusive evidence for nutrition interventions slowing progression of disease, although dietary changes can assist with weight loss. Psychosocial interventions incorporating peer support, cognitive-behavioural therapy, and tailored supportive care elements are effective in improving quality of life and mental health, reducing depression and anxiety and decision-related distress. However, there are differences in results across reviews that likely relate to the review approach and currency as well as the need for interventions to respond to differences in men's clinical context, background, sociodemographic and cultural circumstances, and personal resources.

The lack of systematic reviews investigating monitoring for prostate cancer recurrence, and surveillance of other primary cancer types may be due to an absence of interventional research examining this within survivorship. Several reviews have focused on interventions which aim to increase the uptake of PSA testing to screen for prostate cancer, and assess the effect on incidence and diagnosis rates⁵⁶⁻⁵⁹; but limited studies have investigated interventions designed to target PSA testing after diagnosis. Follow-up testing and ongoing surveillance is an important aspect of survivorship care, helping to detect recurrence and monitor for diagnosis of other primary cancers, and is of particular importance for patients undergoing active surveillance¹⁵. The monitoring guidelines in the ACS/ASCO framework are based on expert consensus, and while experts agree that routine monitoring is necessary, the exact intervals and recommendations for surveillance varies depending on clinical and treatment factors, and continue to evolve⁶⁰. Research from America, Australia, and Europe has reported that many men undergoing active surveillance may not be adhering to the recommended surveillance protocols, with between 13 and 30% of patients not adhering to PSA and biopsy testing guidelines in the first 2 years post-diagnosis⁶¹⁻⁶³. Evidence suggests that exercise interventions can delay the transition to active therapy in men undergoing active surveillance, and current randomised controlled trials underway to investigate further^{64,65}. Until data is routinely collected and reported on individuals' adherence to routine monitoring and surveillance guidelines, for those undergoing active surveillance, ADT and other treatments, it cannot be determined whether other interventions are necessary. Thus, this remains a neglected survivorship domain in the literature which requires further attention.

There was no review evidence relating to the care-coordination domain of survivorship. The ACS guidelines recommend that all patients are given a survivorship care plan by the treating specialist, and that specialists and primary care providers discuss the care plan components and are involved in shared care¹⁵. However, care plans are not routinely provided to patients^{66,67}, and the extent to which prostate cancer patients in particular are receiving care plans remains unclear. Interventions to overcome barriers to the use of survivorship care plans, and encourage shared care between oncology specialists and primary care providers need to be identified. There is evidence to suggest that patient navigation and nurse-led interventions may be effective in coordinating care during early diagnosis and treatment phases of breast, thyroid, and gastro-intestinal cancer⁶⁸⁻⁷¹, but trials among men with prostate cancer post-diagnosis have not yet been conducted. Future research is needed to examine the extent to which nurse

navigation interventions may be effective in assisting with survivorship care planning, or care-coordination, for men with prostate cancer.

In terms of assessing the effectiveness of interventions for specific patient groups, evidence was again limited. Only one included review, published in 2012, focused on minority ethnic populations³⁶. Prostate cancer survivors with lower income, less education and from non-white populations have poorer quality of life and a lower likelihood of survival compared with higher-income, more educated, and white prostate cancer survivors^{72, 73}. Yet, there is a lack of targeted interventions to address survivorship outcomes for men of minority ethnic backgrounds, those living in rural areas, and gay and bisexual men diagnosed with prostate cancer as much of the published research is based on the experience of well-educated, heterosexual, white men^{73, 74}. Additionally, there was a lack of focus in the included reviews on addressing survivorship care interventions for men undergoing treatments other than radical prostatectomy or androgen deprivation therapy. Few studies addressed the needs of men with advanced prostate cancer, despite the fact that men with advanced disease are known to experience high distress⁷⁵. Broadening the focus, and developing appropriate interventions targeting a variety of patient groups is essential to promote equity in survivorship care. Health policy makers and health service providers need to work with researchers to ensure that appropriate survivorship care can be delivered to all men with prostate cancer, regardless of individual characteristics or circumstances.

The current ACS guidelines in the domain of health promotion are broad and non-specific, recommending that prostate cancer survivors engage in at least 150 minutes of physical activity each week and eat a diet high in fruits, vegetables, and whole grains¹⁵. For nutrition interventions, evidence relating to particular diets and supplements is still inconclusive, and no recommendations can be made regarding the use of any nutritional intervention for managing PSA levels until further high-quality trials are conducted. From the current review there is high-quality evidence to suggest that targeted exercise-based interventions have a positive effect on physical activity, muscle strength, quality of life, urinary incontinence, and fatigue. While exercise interventions may show improvements in outcomes across the domains of health promotion, physical side effects, and psychosocial management, the focus needs to shift towards recommendations for the specific problems men with prostate cancer face, such as resistance exercise to increase loss of muscle mass associated with treatments⁷⁶. We propose that the guidelines need to be updated to reflect information matched to the particular needs of individual men.

Although there was evidence to support the use of psychosocial interventions involving peer support, cognitive-behavioural, psychotherapy, and communication to improve quality of life and mental health outcomes, there was less support for simple education or information provision interventions. A clear understanding of which components of psychosocial interventions are both effective and acceptable for men with prostate cancer is a priority. Trial quality in this area could be improved by attention to statistical power, use of consistent outcome measures, and by targeting patients at most need⁴⁹. In this regard, the application of stepped or tiered care models where intervention is matched to the depth of needed, and stepped up when required through the use of regular screening and assessment is a needed future direction⁷⁷.

Future research is needed to examine the acceptability and effectiveness of exercise and psychosocial interventions in more diverse populations, and strategies to support optimal translation into routine clinical practice are needed. In a controlled trial, the benefits of specific

exercise regimes compared to usual care can be clearly tested; however, there is limited evidence of these interventions being scaled effectively to reach large sections of the population in real-world settings. For such interventions to be successfully implemented population-wide, this relies on strategies for motivating men to engage in self-directed exercise. This may be particularly difficult for men who have not previously exercised or who experience physical constraints or side effects. An intervention that involved 6 months of supervised exercise followed by 6 months of self-directed exercise showed that men were able to preserve improvements in cardiorespiratory fitness, physical function, muscle strength and self-reported physical functioning that took place within the first 6 months⁷⁸, providing a potential strategy to overcome the self-motivation issue. Again, for psychosocial interventions which have been shown to be effective in a controlled trial environment, further understanding of how these can be implemented into practice is required, as limited work has investigated the feasibility of scaling to larger populations. Future trials also need to assess how to sustain intervention effects over a longer follow-up period. Thus, there is work to be done before translating targeted interventions suited to the diverse range of patients who are diagnosed with prostate cancer into practice⁷⁹.

Study limitations

This synthesis of systematic reviews provides an overview of current evidence on the effectiveness of a variety of interventions on health and wellbeing outcomes across the five domains of prostate cancer survivorship. By bringing together evidence from extensive previously published literature, this synthesis provides insight into the current state of research in the area, however, there are some limitations which need to be acknowledged. The reviews of interest included a wide variety of intervention types, study designs, and outcomes measures, making it challenging to compare and to identify similar themes across different reviews. Additionally, the reporting of quality assessments was also lacking in some cases, and many included reviews provided a narrative synthesis rather than a meta-analysis, and did not report odds ratios or effect sizes due to the heterogeneity of primary studies. The search terms and search logic were not overseen by a certified medical librarian, and although a thorough search of pertinent databases was conducted by two authors, we also cannot guarantee that some relevant reviews may not have been located.

Clinical implications

This review highlights the need for contemporary prostate cancer survivorship interventions that address all relevant survivorship domains, with an integrated or multicomponent approach that builds synergies between approaches. Methods for developing, testing and implementing complex interventions are now well described⁸⁰, and the application of these will help ensure feasibility for implementation at scale is a priority. Men with prostate cancer often experience long term decrements in quality of life and psychological wellbeing as a result of their cancer experience. Long term survivorship care that is responsive to their specific concerns is crucial.

Conclusions

The five domains of the ACS Prostate Cancer Survivorship Care Guidelines provide a framework for comprehensive follow-up care and optimal health and quality of life for men with prostate cancer. Without high quality evidence, solutions to improving outcomes among prostate cancer survivors will continue to be obscured to clinicians, researchers and policy-makers. While

there is evidence for the effectiveness of exercise and psychosocial interventions for men with prostate cancer in three of the five domains, methods for successfully scaling these interventions to large populations are not well described, nor is the optimal approach to tailoring for specific needs well understood. In addition, for surveillance and care coordination, review evidence is absent and this must serve as a concern for all interested in the welfare of men with prostate cancer and their families. Recent advances in prostate cancer treatment and care have led to increased survival for men with prostate cancer. Our review highlights the need for survivorship interventions to be developed, tested and proven at a similar pace to the rate of progress in anti-cancer therapies. Priority therefore needs to be given to research that identifies ways to provide an effective range of interventions to meet the survivorship needs of men with prostate cancer.

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Conflict of interest statement

The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest, in the subject matter or materials discussed in this manuscript.

References

1. Ferlay J, Soerjomataram I, Ervik M, et al. Globocan 2012: Cancer incidence and mortality worldwide Lyon, France: International Agency for Research on Cancer; 2014 [Available from: <http://globocan.iarc.fr>. (accessed [16/01/2015])]
2. Australian Institute of Health and Welfare. Cancer in Australia 2017. Canberra: AIHW; 2017.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA: Cancer J Clin*. 2018;68(1):7-30.
4. Watts S, Leydon G, Birch B, et al. Depression and anxiety in prostate cancer: A systematic review and meta-analysis of prevalence rates. *BMJ Open*. 2014;4(3).
5. Smith DP, Supramaniam R, King MT, et al. Age, health, and education determine supportive care needs of men younger than 70 years with prostate cancer. *J Clin Oncol*. 2007;25(18):2560-2566.
6. Steginga SK, Occhipinti S, Dunn J, et al. The supportive care needs of men with prostate cancer (2000). *Psychooncology*. 2001;10(1):66-75.
7. Hofman M, Ryan JL, Figueroa-Moseley CD, et al. Cancer-related fatigue: The scale of the problem. *Oncologist*. 2007;12(Supplement 1):4-10.
8. Stanford JL, Feng Z, Hamilton AS, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: The prostate cancer outcomes study. *JAMA*. 2000;283(3):354-360.
9. Smith MR, Saad F, Egerdie B, et al. Sarcopenia during androgen-deprivation therapy for prostate cancer. *J Clin Oncol*. 2012;30(26):3271-3276.
10. Choong K, Basaria S. Emerging cardiometabolic complications of androgen deprivation therapy. *Aging Male*. 2010;13(1):1-9.
11. Galvão DA, Newton RU, Gardiner RA, et al. Compliance to exercise-oncology guidelines in prostate cancer survivors and associations with psychological distress, unmet supportive care needs, and quality of life. *Psychooncology*. 2015;24(10):1241-1249.
12. Smith DP, Calopedos R, Bang A, et al. Increased risk of suicide in new south wales men with prostate cancer: Analysis of linked population-wide data. *PloS One*. 2018;13(6):e0198679.
13. Dalela D, Krishna N, Okwara J, et al. Suicide and accidental deaths among patients with non-metastatic prostate cancer. *BJU Int*. 2016;118(2):286-297.
14. National Research Council. From cancer patient to cancer survivor: Lost in transition. Washington: Academies Press; 2005.
15. Skolarus TA, Wolf AM, Erb NL, et al. American cancer society prostate cancer survivorship care guidelines. *CA Cancer J Clin*. 2014;64(4):225-249.
16. Resnick MJ, Lacchetti C, Bergman J, et al. Prostate cancer survivorship care guideline: American society of clinical oncology clinical practice guideline endorsement. *J Clin Oncol*. 2015;33(9):1078-1085.
17. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guideline in oncology: Prostate cancer US: NCCN; 2013 [Available from: nccn.org/professionals/physician_gls/pdf/prostate.pdf. (accessed [13/07/2018])]
18. American Cancer Society. Guidelines for the early detection of cancer US: ACS; 2018 [Available from: <https://www.cancer.org/healthy/find-cancer-early/cancer-screening-guidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html>. (accessed [13/07/2018])]

19. Chambers SK, Zajdlewicz L, Youlden DR, et al. The validity of the distress thermometer in prostate cancer populations. *Psychooncology*. 2014;23(2):195-203.
20. Singh J, Trabulsi EJ, Gomella LG. The quality-of-life impact of prostate cancer treatments. *Curr Urol Rep*. 2010;11(3):139-146.
21. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ*. 2009;339.
22. Centre for Reviews and Dissemination. Database of abstracts of reviews of effects (DARE) York, England: Centre for Reviews and Dissemination; [Available from: <https://www.ncbi.nlm.nih.gov/pubmedhealth/about/DARE/>. (accessed [04-05-2018])]
23. Moore TH, King AJ, Evans M, et al. Supportive care for men with prostate cancer: Why are the trials not working? A systematic review and recommendations for future trials. *Cancer Med*. 2015;4(8):1240-1251.
24. Miles CL, Candy B, Jones L, et al. Interventions for sexual dysfunction following treatments for cancer. *Cochrane Database Syst Rev*. 2007(4).
25. Chipperfield K, Brooker J, Fletcher J, et al. The impact of physical activity on psychosocial outcomes in men receiving androgen deprivation therapy for prostate cancer: A systematic review. *Health Psychol*. 2014;33(11):1288-1297.
26. De Backer IC, Schep G, Backx FJ, et al. Resistance training in cancer survivors: A systematic review. *Int J Sports Med*. 2009;30(10):703-712.
27. Gardner JR, Livingston PM, Fraser SF. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: A systematic review. *J Clin Oncol*. 2014;32(4):335-346.
28. Hasenoehrl T, Keilani M, Sedghi Komanadj T, et al. The effects of resistance exercise on physical performance and health-related quality of life in prostate cancer patients: A systematic review. *Supp Care Cancer*. 2015;23(8):2479-2497.
29. Keilani M, Hasenoehrl T, Baumann L, et al. Effects of resistance exercise in prostate cancer patients: A meta-analysis. *Supp Care Cancer*. 2017;25(9):2953-2968.
30. Moe EL, Chadd J, McDonagh M, et al. Exercise interventions for prostate cancer survivors receiving hormone therapy: Systematic review. *Am J Sports Med*. 2017;2(1):1-9.
31. Teleni L, Chan RJ, Chan A, et al. Exercise improves quality of life in androgen deprivation therapy-treated prostate cancer: Systematic review of randomised controlled trials. *Endocr Relat Cancer*. 2016;23(2):101-112.
32. Yunfeng G, Weiyang H, Xueyang H, et al. Exercise overcome adverse effects among prostate cancer patients receiving androgen deprivation therapy: An update meta-analysis. *Med*. 2017;96(27).
33. Wang W, Huang QM, Liu FP, et al. Effectiveness of preoperative pelvic floor muscle training for urinary incontinence after radical prostatectomy: A meta-analysis. *BMC Urol*. 2014;14:99.
34. Lassen B, Gattinger H, Saxer S. A systematic review of physical impairments following radical prostatectomy: Effect of psychoeducational interventions. *J Adv Nurs*. 2013;69(12):2602-2612.
35. Chang JI, Lam V, Patel MI. Preoperative pelvic floor muscle exercise and postprostatectomy incontinence: A systematic review and meta-analysis. *Eur Urol*. 2016;69(3):460-467.

36. Sajid S, Kotwal AA, Dale W. Interventions to improve decision making and reduce racial and ethnic disparities in the management of prostate cancer: A systematic review. *J Gen Intern Med.* 2012;27(8):1068-1078.
37. Cockle H, Hearne J, Faithfull S. Self-management for men surviving prostate cancer: A review of behavioural and psychosocial interventions to understand what strategies can work, for whom and in what circumstances. *Psychooncology.* 2010;19(9):909-922.
38. Finlay A, Wittert G, Short CE. A systematic review of physical activity-based behaviour change interventions reaching men with prostate cancer. *J Cancer Surviv.* 2018.
39. Hallward L, Patel N, Duncan LR. Behaviour change techniques in physical activity interventions for men with prostate cancer: A systematic review. *Health Psychol.* 2018.
40. Mohamad H, McNeill G, Haseen F, et al. The effect of dietary and exercise interventions on body weight in prostate cancer patients: A systematic review. *Nutr Cancer.* 2015;67(1):43-60.
41. van Die MD, Bone KM, Emery J, et al. Phytotherapeutic interventions in the management of biochemically recurrent prostate cancer: A systematic review of randomised trials. *BJU Int.* 2016;117 (Suppl 4):17-34.
42. Hackshaw-McGeagh LE, Perry RE, Leach VA, et al. A systematic review of dietary, nutritional, and physical activity interventions for the prevention of prostate cancer progression and mortality. *Cancer Causes & Control.* 2015;26(11):1521-1550.
43. Beaudry RI, Liang Y, Boyton ST, et al. Meta-analysis of exercise training on vascular endothelial function in cancer survivors. *Integr Cancer Ther.* 2018;17(2):192-199.
44. Baguley BJ, Bolam KA, Wright ORL, et al. The effect of nutrition therapy and exercise on cancer-related fatigue and quality of life in men with prostate cancer: A systematic review. *Nutrients.* 2017;9(9).
45. Larkin D, Lopez V, Aromataris E. Managing cancer-related fatigue in men with prostate cancer: A systematic review of non-pharmacological interventions. *Int J Nurs Pract.* 2014;20(5):549-560.
46. Vashistha V, Singh B, Kaur S, et al. The effects of exercise on fatigue, quality of life, and psychological function for men with prostate cancer: Systematic review and meta-analyses. *Eur Urol.* 2016;2(3):284-295.
47. Horgan S, O'Donovan A. The impact of exercise during radiation therapy for prostate cancer on fatigue and quality of life: A systematic review and meta-analysis. *J Med Imag Rad Sci.* 2018;49(2):207-219.
48. Kim K, Kim JS. Intervention for patient reported urinary symptoms in prostate cancer survivors: Systematic review. *J Cancer Surv.* 2017;11(5):643-654.
49. Chambers SK, Hyde MK, Smith DP, et al. New challenges in psycho-oncology research iii: A systematic review of psychological interventions for prostate cancer survivors and their partners: Clinical and research implications. *Psychooncology.* 2017;26(7):873-913.
50. Bourke L, Smith D, Steed L, et al. Exercise for men with prostate cancer: A systematic review and meta-analysis. *Eur Urol.* 2016;69(4):693-703.
51. Parahoo K, McDonough S, McCaughan E, et al. Psychosocial interventions for men with prostate cancer: A cochrane systematic review. *BJU Int.* 2015;116(2):174-183.
52. Newby TA, Graff JN, Ganzini LK, et al. Interventions that may reduce depressive symptoms among prostate cancer patients: A systematic review and meta-analysis. *Psychooncology.* 2015;24(12):1686-1693.

53. Chien CH, Liu KL, Chien HT, et al. The effects of psychosocial strategies on anxiety and depression of patients diagnosed with prostate cancer: A systematic review. *Int J Nurs Stud*. 2014;51(1):28-38.
54. Menichetti J, Villa S, Magnani T, et al. Lifestyle interventions to improve the quality of life of men with prostate cancer: A systematic review of randomized controlled trials. *Crit Rev Oncol Hematol*. 2016;108:13-22.
55. Bourke L, Boorjian SA, Briganti A, et al. Survivorship and improving quality of life in men with prostate cancer. *Eur Urol*. 2015;68(3):374-383.
56. Ilic D, O'Connor D, Green S, et al. Screening for prostate cancer: An updated cochrane systematic review. *BJU Int*. 2011;107(6):882-891.
57. Djulbegovic M, Beyth RJ, Neuberger MM, et al. Screening for prostate cancer: Systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2010;341.
58. Jepson RG, Forbes CA, Sowden AJ, et al. Increasing informed uptake and non-uptake of screening: Evidence from a systematic review. *Health Expect*. 2001;4(2):116-130.
59. Weller DP, Patnick J, McIntosh HM, et al. Uptake in cancer screening programmes. *Lancet Oncol*. 2009;10(7):693-699.
60. National Comprehensive Cancer Network (NCCN). Nccn guidelines version 4.2018 - prostate cancer USA: NCCN; 2018 [Available from: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. (accessed [09/03/2018])]
61. Evans MA, Millar JL, Earnest A, et al. Active surveillance of men with low risk prostate cancer: Evidence from the prostate cancer outcomes registry–victoria. *Med J Aust*. 2018;208(10):439-443.
62. Luckenbaugh AN, Aufferberg GB, Hawken SR, et al. Variation in guideline concordant active surveillance followup in diverse urology practices. *J Urol*. 2017;197(3 Pt 1):621-626.
63. Bokhorst LP, Alberts AR, Rannikko A, et al. Compliance rates with the prostate cancer research international active surveillance (prias) protocol and disease reclassification in noncompliers. *Eur Urol*. 2015;68(5):814-821.
64. Galvao DA, Taaffe DR, Spry N, et al. Enhancing active surveillance of prostate cancer: The potential of exercise medicine. *Nat Rev Urol*. 2016;13(5):258-265.
65. Galvao DA, Hayne D, Frydenberg M, et al. Can exercise delay transition to active therapy in men with low-grade prostate cancer? A multicentre randomised controlled trial. *BMJ Open*. 2018;8(4)
66. Birken SA, Mayer DK, Weiner BJ. Survivorship care plans: Prevalence and barriers to use. *J Cancer Educ*. 2013;28(2):290-296.
67. Blanch-Hartigan D, Forsythe LP, Alfano CM, et al. Provision and discussion of survivorship care plans among cancer survivors: Results of a nationally representative survey of oncologists and primary care physicians. *J Clin Oncol*. 2014;32(15):1578-1585.
68. Robinson-White S, Conroy B, Slavish KH, et al. Patient navigation in breast cancer: A systematic review. *Cancer Nurs*. 2010;33(2):127-140.
69. Dohan D, Schrag D. Using navigators to improve care of underserved patients. *Cancer*. 2005;104(4):848-855.
70. Lee T, Ko I, Lee I, et al. Effects of nurse navigators on health outcomes of cancer patients. *Cancer Nurs*. 2011;34(5):376-384.
71. Gilbert JE, Green E, Lankshear S, et al. Nurses as patient navigators in cancer diagnosis: Review, consultation and model design. *Eur J Cancer Care*. 2011;20(2):228-236.

72. Hall SE, Holman CDAJ, Wisniewski ZS, et al. Prostate cancer: Socio-economic, geographical and private health insurance effects on care and survival. *BJU Int.* 2005;95(1):51-58.
73. Singh GK, Williams SD, Siahpush M, et al. Socioeconomic, rural-urban, and racial inequalities in us cancer mortality: Part i—all cancers and lung cancer and part ii—colorectal, prostate, breast, and cervical cancers. *J Cancer Epidemiol.* 2011.
74. Kleinmann N, Zaorsky NG, Showalter TN, et al. The effect of ethnicity and sexual preference on prostate-cancer-related quality of life. *Nature Reviews Urology.* 2012;9(5):258.
75. Chambers SK, Foley E, Clutton S, et al. The role of mindfulness in distress and quality of life for men with advanced prostate cancer. *Qual Life Res.* 2016;25(12):3027-3035.
76. Galvao DA, Taaffe DR, Spry N, et al. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: A randomized controlled trial. *J Clin Oncol.* 2010;28(2):340-347.
77. Schofield P, Chambers S. Effective, clinically feasible and sustainable: Key design features of psycho-educational and supportive care interventions to promote individualised self-management in cancer care. *Acta Oncol.* 2015;54(5):805-812.
78. Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation. *Eur Urol.* 2014;65(5):856-864.
79. Editorial. Exercise and cancer treatment: Balancing patient needs. *Lancet Oncol.* 2018;19(6):715.
80. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: The new medical research council guidance. *Int J Nursing Studies.* 2013;50(5):587-592.

Table 1. Narrative synthesis of high-quality reviews published in the last five years

Domain	Health Promotion	Surveillance	Physical side effects	Psychosocial management	Care-coordination
ACS Guidelines	Counsel survivors to achieve and maintain healthy weight, and avoid or limit alcohol and tobacco products.	Measure serum PSA every 6 to 12 months, and perform annual DRE.	Assess and manage long-term treatment related side effects.	Identify, treat, and manage ongoing psychosocial effects.	Cancer specialists should provide all prostate cancer patients with a survivorship care plan.
Number of reviews	11	0	16	18	2
Outcomes	Physical activity (n=5) Body weight and composition (n=7) PSA (n=2)		Cardiorespiratory fitness and physical function (n=5) Fatigue (n=8) Incontinence (n=2)	QoL (n=12) Depression (n=5) Anxiety (n=2)	Self-efficacy (n=2)
Summary of findings	Both aerobic and resistance exercise demonstrate increases in overall physical activity levels. Exercise interventions were reported to preserve/improve lean mass with inconsistent effects on other parameters of body composition. Diet interventions were reported to achieve significant weight loss. Individual nutrition interventions also showed some small positive impacts on PSA levels, particularly plant-based supplements, but overall there was inconclusive evidence of the effectiveness of diet interventions on PSA levels.		Both aerobic and resistance exercise demonstrate improvements in cardiorespiratory fitness, muscle strength, and physical function. Aerobic training interventions showed improvements in peak oxygen uptake, while resistance training showed improvements in muscle strength. Exercise interventions were reported to have inconsistent effects on markers of cardiovascular health such as lipid profile, blood pressure and glucose. Limited information exists on the impact of exercise and bone health in men with prostate cancer.	Combinations of education, cognitive behavioural, peer support, and communication components within psychosocial interventions were found to be the most commonly utilized and effective. Multi-modal psychosocial interventions were described as effective for decision-related distress, mental health, and domain-specific and health-related quality of life. Psychosocial interventions also appear to have short-term benefit on depression and anxiety, particularly when isolating the peer support and psychotherapy components. Exercise interventions including aerobic or resistance training predominantly report improvements in QoL outcomes, particularly supervised aerobic and resistance training. Aerobic and resistance training exercise interventions reported no effect on depression or anxiety outcomes.	Reviews relating to care-coordination outcomes were not identified. Limited evidence was found for psychosocial interventions targeting self-efficacy and coping, which may serve as a proxy in this domain.
Quality of evidence	The bodies of evidence from exercise interventions were predominantly rated as high quality and low risk of bias, while nutrition interventions were of poorer methodological quality.		Evidence was predominantly rated as high quality with only one review of psychosocial interventions rating the body of evidence as low quality.	Psychosocial intervention evidence was rated as low to moderate in most reviews. Exercise intervention evidence rated as moderate to high quality, and low risk of bias.	No reviews on care coordination identified.

Figure 1. Methodological quality checklist (adapted from Database of Abstracts of Reviews of Effects)

1. Is there a well-defined research question?
2. Is there a defined search strategy?
3. Were inclusion/exclusion criteria reported?
4. Were the included studies synthesized?
5. Are the primary study designs and number of studies clearly stated?
6. Was the quality of the included studies assessed?
7. Has more than one author been involved at each stage of the review process?

Figure 2. Flow diagram of included studies

