Survivorship and Improving Quality of Life in Men with Prostate Cancer

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Abstract

Context: Long-term survival following a diagnosis of cancer is improving in developed nations. However, living longer does not necessarily equate to living well.

Objective: To search systematically and synthesise narratively the evidence from randomised controlled trials (RCTs) of supportive interventions designed to improve prostate cancer (PCa)-specific quality of life (QoL).

Evidence acquisition: A systematic search of Medline and Embase was carried out from inception to July 2014 to identify interventions targeting PCa QoL outcomes. We did not include nonrandomised studies or trials of mixed cancer groups. In addition to database searches, citations from included papers were hand-searched for any potentially eligible trials.

Evidence synthesis: A total of 2654 PCa survivors from 20 eligible RCTs were identified from our database searches and reference checks. Disease-specific QoL was assessed most frequently by the Functional Assessment of Cancer Therapy-Prostate questionnaire. Included studies involved men across all stages of disease. Supportive interventions that featured individually tailored approaches and supportive interaction with dedicated staff produced the most convincing evidence of a benefit for PCa-specific QoL. Much of these data come from lifestyle interventions. Our review found little supportive evidence for simple literature provision (either in booklets or via online platforms) or cognitive behavioural approaches.

Conclusions: Physical and psychological health problems can have a serious negative impact on QoL in PCa survivors. Individually tailored supportive interventions such as exercise prescription/referral should be considered by multidisciplinary clinical teams where available. Cost-effectiveness data and an understanding of how to sustain benefits over the long term are important areas for future research.

Patient summary: This review of supportive interventions for improving quality of life in prostate cancer survivors found that supervised and individually tailored patient-centred interventions such as lifestyle programmes are of benefit.
1. Introduction

1.1. Cancer survivorship in context

Long-term survival following a diagnosis of cancer is improving in developed nations [1]. Cancer survivor is an umbrella term describing the broad experience of the cancer continuum, that is, “living with, through, and beyond a cancer diagnosis.” This definition was proposed by the National Consortium for Cancer Survivorship in the United States and is echoed by European cancer charities such as Macmillan. The term has evolved and disseminated into clinical practice following high-profile advocates such as Dr. Fitzhugh Mullan who described his own cancer journey from a clinician’s perspective in the New England Journal of Medicine nearly 30 yr ago [2].

Living longer, however, does not necessarily equate to living well. Acceptance that cancer and its treatments can have a negative long-term effect on quality of life (QoL) has been increasing over the past 40 yr. This was first evidenced by the passage of the National Cancer Act in the United States (1971) that promoted research into meeting ongoing postdiagnosis needs. By the early 1980s, new initiatives such as dedicated rehabilitation programmes directed at improving QoL began to emerge [3]. Hence within the survivorship agenda is an implicit undertaking to improve QoL in those diagnosed and treated for cancer. Whereas the concept of QoL is intuitive, it is generally a personal construct and has traditionally been difficult to measure. Reliable measurement and comparison have been improved by the development and validation of generic health-related QoL tools (eg, Short-Form 36 Health Survey, EUROQol five dimensions questionnaire [EQ-5D]), instruments to measure QoL across cancer in general (eg, European Organisation for Research and Treatment of Cancer [EORTC] Quality of Life Questionnaire-Core 36 [QLQ-C30]), cancer-related fatigue (eg, Functional Assessment of Cancer Therapy-Fatigue [FACT-F]), and disease-specific tools (eg, Functional Assessment of Cancer Therapy-Prostate [FACT-P]). EORTC Quality of Life Questionnaire-Prostate Module [QLQ-PR25]).

A review of tools to measure QoL in prostate cancer (PCa) survivors is freely available on the Web [4]. Organised medical care in Europe has typically not been as quick to acknowledge such paradigms in standard health care. For example, the UK government only recognised a lack of focus on the long-term consequences of cancer in its “Improving Outcomes” strategy document in 2010 [5]. In recognition of this, the National Cancer Survivorship Initiative was launched, recommending that cancer be considered analogous to living with a long-term or chronic condition [6]. PCa, in particular, fits this long-term condition paradigm. It is the main global contributor to years lived with cancer disability [7] with an estimated global prevalence of around 4 million men in 2012 [8].

All clinicians treating men with PCa, regardless of stage, need to be aware of the issues that affect QoL in men with PCa, both immediately after diagnosis and treatment and in the many years that follow. The relevance to a urologic audience is that the urologist is often the primary (and indeed may be the only) treating physician; nevertheless, high-quality survivorship requires engagement from all involved in the care of men with PCa. The aim of this paper is to (1) contextualise living with and beyond PCa with a particular focus on adverse events associated with treatment, (2) review the effects of interventions that can improve PCa-specific QoL, and (3) highlight how multidisciplinary teams can address care coordination and symptom management.

1.2. The lived experience of prostate cancer

People surviving cancer are less likely to report favourable QoL than individuals from the general population or patients surveyed from primary care [9]. Cancer survivors are also significantly more likely to report being in average or poor general health (47% of survivors vs 17% of healthy participants) [10]. Nearly half with common cancers (breast, bowel, and prostate) experience additional chronic conditions. Most frequently these are arthritis, heart disease, diabetes, asthma, and osteoporosis [10]. Data from the Surveillance, Epidemiology and End Results Tumour Registry (103 086 men aged 66–84 yr diagnosed with PCa) reported roughly equivalent rates of PCa (7.7%) and cardiovascular (7.2%) mortality [11]. At the population level, risk of PCa death is predicated on numerous factors including the prevalence of prostate-specific antigen (PSA) screening. Advancing age, comorbidity, and adverse effects of treatment for advanced disease are likely key determinants of noncancer mortality.

From a psychological perspective, data from a meta-analysis indicate clinically relevant depression to be present in 17%, 15%, and 18% of men before, during, and after treatment for PCa, respectively. Similarly, clinically relevant anxiety is high with a pretreatment, on-treatment, and post-treatment prevalence reported at 27%, 15%, and 18%, respectively [12]. In advancing disease where medical or surgical castration is utilised, the risk of incident psychiatric illness (composite of depression, dementia, anxiety, insomnia, and psychosis) is up to 26% over a 7-yr follow-up [13]. It is important to note that suicidal intent in PCa survivors is associated with both physical and psychological dysfunction [14]. Hence clinicians should be aware that as many as one in four of their patients could have clinically relevant psychological morbidity.

Without consideration of these data by the clinician responsible for primary treatment, it is easy to imagine that these issues would go unidentified and a number of men would have to endure untreated psychological distress [15]. These data underscore the importance of symptom recognition by the primary treating clinician.

1.3. Adverse effects of anticancer treatment

1.3.1. Radical therapies

The adverse effects of surgery in the form of radical prostatectomy (RP) can be broadly categorised as complications related to function (eg, continence, erectile) or others (eg, anastomotic leak). Reported post-RP urinary incontinence rates range from 5% to 72% [16]. Factors including older age, higher body mass index, increasing comorbidity
index, preoperative lower urinary tract symptoms, greater prostate volume, and the postoperative development of an anastomotic stricture have been associated with an increased risk for persistent incontinence [16–18]. Rates of erectile dysfunction after RP range from 31% to 86% [16] depending on the definition of potency, the population studied, and the time frame evaluated. Factors associated with postoperative erectile function include age, preoperative erectile function, comorbidity status, body mass index, pretreatment PSA, and the extent of nerve sparing performed at surgery [16,19,20].

Nonfunctional complications from RP may arise both in the perioperative period as well as during extended follow-up after surgery. Critical analysis of RP series have collectively found the procedure to be associated with an overall complication rate of approximately 10%, although the vast majority of complications are low grade, most commonly lymphocele/lymphorrhoea and urine leak [21]. Comorbidity status, extent of disease, and surgical approach have been variously associated with perioperative outcomes. Surgeon experience may also be related to complication rates [21].

Prostatic radiotherapy (RT) is most commonly associated with adverse effects around late rectal function/toxicity (ie, increased frequency and urgency of defecation, faecal incontinence, and rectal bleeding) [22]. High-dose RT to the rectal wall can lead to anatomic and functional damage including telangiectasia, mucosal congestion, ulceration, and fibrosis [23] with associated impairment of sensation, compliance, and capacity [24]. Similarly, irradiation of the anal sphincter complex may impair function. As such, compared with RP, RT is more likely to induce declines in bowel function at 2, 5, and 15 yr of follow-up [25]. A critical review of functional outcomes reports that total urinary incontinence and other severe urinary symptoms are rare [26]. However, bothersome storage urinary symptoms are relatively common amongst patients undergoing RT, and some men may also experience fatigue and erectile dysfunction.

1.3.2. Androgen deprivation therapy

Despite its acknowledged anticancer benefits [27–29], androgen deprivation therapy (ADT) is associated with a range of adverse effects in survivors. These were extensively covered in a recent review in European Urology [30]. These include increased fracture risk [31], metabolic consequences, and cardiovascular events [32–36], genital and sexual dysfunction [37,38], fatigue [39], and anaemia [40]. The association between ADT and cardiovascular risk remains controversial and has been discussed elsewhere [33,36,41].

2. Evidence acquisition

A systematic search of the electronic databases Medline (via PubMed) and Embase was carried out from inception to July 2014 to identify interventions targeting PCa QoL outcomes. Medline search terms were prostate cancer [TIAB] AND (quality of life [TIAB]) using a randomised controlled trial (RCT)–only filter. Embase search terms were prostate cancer AND quality of life using an RCT–only filter. Eligible studies known to the authors but not picked up by the database searches were also evaluated for inclusion. We only included supportive interventions that were directed at improving a PCa-specific QoL outcome in men with diagnosed PCa evaluated in a RCT with a usual care comparison. We did not include nonrandomised studies or trials of mixed cancer groups. In addition to database searches, citations for included papers were hand-searched for any potentially eligible trials. Quality appraisal was done according to PCa trial expertise and clinical judgement of the authors (led by L.B.). Results were screened firstly by title, then abstract, and then full text to generate a Preferred Reporting Items for Systematic Reviews and Meta-analysis flow diagram of results [42]. Due to the likely heterogeneity of interventions and the nonstandardised quality appraisal, a narrative synthesis rather than a quantified meta-analysis of data was performed.

2.1. Search results

A total of 22 manuscripts from 20 trials were identified through our searches (Fig. 1) involving 2654 PCa survivors.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Available TNM data</th>
<th>Anticancer treatment</th>
<th>Trial primary outcome</th>
<th>QoL measurement</th>
<th>Intervention (category)</th>
<th>QoL result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ames et al [58]</td>
<td>57</td>
<td>NC</td>
<td>Surgery or RT</td>
<td>NA</td>
<td>FACT-P</td>
<td>Multidisciplinary group education (Educational support)</td>
<td>Unclear</td>
</tr>
<tr>
<td>Bourke et al [55]</td>
<td>100</td>
<td>T3–4</td>
<td>ADT</td>
<td>QoL and blood pressure</td>
<td>FACT-P</td>
<td>Exercise and diet (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Carmody et al [52]</td>
<td>36</td>
<td>NC</td>
<td>Surgery, RT, brachytherapy</td>
<td>NA</td>
<td>FACT-P</td>
<td>Diet (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Cormie et al [47]</td>
<td>57</td>
<td>NC</td>
<td>≥2 mo ADT; previous RT or surgery</td>
<td>NC</td>
<td>QLQ-PR25</td>
<td>Exercise (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Culos-Reed et al [49]</td>
<td>100</td>
<td>NC</td>
<td>≥6 mo ADT</td>
<td>Physical activity behaviour</td>
<td>EPIC</td>
<td>Exercise (Lifestyle)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Dieperink et al [60]</td>
<td>161</td>
<td>T1–3</td>
<td>RT and ADT</td>
<td>EPIC-26 urinary irritative sum score</td>
<td>EPIC-26</td>
<td>Multidisciplinary education (Educational support)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Giesler et al [67]</td>
<td>99</td>
<td>T1a–2c</td>
<td>Surgery, RT, brachytherapy</td>
<td>QoL</td>
<td>PCQoL</td>
<td>Nurse-led enhanced follow-up (Enhanced standard care)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Hack et al [64]</td>
<td>425</td>
<td>T1–4</td>
<td>Surgery, ADT, watchful waiting</td>
<td>NC</td>
<td>FACT-P</td>
<td>Audiotaping consultations (Enhanced standard care)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Lepore et al [59]</td>
<td>250</td>
<td>T1–3</td>
<td>Surgery, RT, brachytherapy, cryosurgery</td>
<td>QoL</td>
<td>UCLA-PCI</td>
<td>Multidisciplinary group education (Educational support)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>McGowan et al [48]</td>
<td>423</td>
<td>NC</td>
<td>Watchful waiting, surgery, RT, chemotherapy, ADT</td>
<td>Physical activity behaviour</td>
<td>FACT-P subscale</td>
<td>Exercise (Lifestyle)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Monga et al [43]</td>
<td>21</td>
<td>NC</td>
<td>RT</td>
<td>NC</td>
<td>FACT-P</td>
<td>Exercise (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Osei et al [63]</td>
<td>40</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>EPIC-26</td>
<td>Online education and support (Educational support)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Overgård et al [65]; Nilsson et al [66]</td>
<td>85</td>
<td>T1c-3 pT2a-T3b</td>
<td>Surgery</td>
<td>Continence status</td>
<td>UCLA-PCI</td>
<td>Pelvic floor training (Enhanced standard care)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Parker et al [68]</td>
<td>159</td>
<td>T1–IV</td>
<td>Surgery</td>
<td>Mood disturbance</td>
<td>UCLA-PCI</td>
<td>One-to-one stress management (Cognitive behavioural)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Pettersson et al [54]</td>
<td>130</td>
<td>T1–3</td>
<td>RT, brachytherapy, proton therapy, ADT</td>
<td>QoL</td>
<td>QLQ-PR25</td>
<td>Diet (Lifestyle)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Segal et al [46]</td>
<td>155</td>
<td>T1–IV</td>
<td>≥3 mo ADT</td>
<td>Fatigue and QoL</td>
<td>FACT-P</td>
<td>Exercise (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
<tr>
<td>Segal et al [45]</td>
<td>121</td>
<td>T1–IV</td>
<td>RT and ADT</td>
<td>Fatigue</td>
<td>FACT-P</td>
<td>Exercise (Lifestyle)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Siddons et al [69]</td>
<td>60</td>
<td>NC</td>
<td>Surgery</td>
<td>NC</td>
<td>PCA-QoL</td>
<td>Group CBI (Cognitive behavioural)</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Templeton et al [62]</td>
<td>55</td>
<td>NC</td>
<td>ADT</td>
<td>NC</td>
<td>FACT-P</td>
<td>Education booklet (Educational support)</td>
<td>Unclear</td>
</tr>
<tr>
<td>Vitolins et al [53]</td>
<td>120</td>
<td>NC</td>
<td>ADT or RT</td>
<td>Hot flash symptoms</td>
<td>FACT-P</td>
<td>Diet and antidepressants (Lifestyle)</td>
<td>Significant effect on QoL</td>
</tr>
</tbody>
</table>

ADT = androgen deprivation therapy; CBI = cognitive behaviour intervention; EPIC = Expanded Prostate Cancer Index Composite; EPIC-26 = Expanded Prostate Cancer Index Composite Short Form; FACT-P = Functional Assessment of Cancer Therapy-Prostate; NA = not applicable; NC = not clear; PCA-QoL = Prostate Cancer Quality of Life Instrument; QLQ-PR25 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Prostate Module; QoL = quality of life; RT = radiotherapy; UCLA-PCI = University of California, Los Angeles, Prostate Cancer Index.

1 T-stage data are referenced as they appear in the original extracted manuscript (some differences due to the US vs European system).
QoL was assessed by questionnaire in all trials involving survivors with T stage 1–4 PCa. Interventions were broadly categorised as lifestyle interventions (10 studies), educational support (5 studies), enhanced standard care (3 studies), or cognitive behavioural approaches (2 studies). Table 1 summarises the included studies.

3. Evidence synthesis

3.1. Lifestyle

3.1.1. Exercise interventions

The past decade has seen growing interest in interventions that improve exercise behaviour and that have been hypothesised to improve clinical outcomes in men with PCa. Early pilot study data (intervention n = 11, control n = 10) showed that in men receiving RT for localised PCa, a directly supervised (by a kinesiotherapist and physician) aerobic exercise training programme, consisting of three sessions of moderate intensity exercise for 8 wk, significantly improved FACT-P scores in the intervention group compared with controls [43]. Crucially, the mean difference between groups (14 points; standard deviation [SD]: 10 points) exceeded the reference range, which suggests clinically meaningful results (ie, 6–9 points) [44]. These effects were not substantiated, however, in a later, larger RCT comparing aerobic (n = 40) or resistance training (n = 40) with usual care (n = 41) in men scheduled to receive RT [45]. This is despite the trial reporting excellent adherence to the interventions with 88% and 83% of the sessions completed in the resistance and aerobic groups, respectively.

The conflicting findings of these trials could be explained by a number of factors. First, the larger study included a wider heterogeneous cohort of men with diagnosed stage I–IV cancers, with around 60% of the overall cohort on ADT. In addition, nearly half of the cohort was already regularly active at baseline, raising the possibility of uncertain incremental gains in these individuals from participating in the trial intervention. Another important difference is in the utilisation of the FACT-P questionnaire. The early pilot trial administered and reported data from a composite of the full Functional Assessment of Cancer Therapy-General questionnaire with the additional FACT-P subscale to give a more informed overview of QoL, whereas the larger RCT reported data from the 12-item subscale only.

In one of the first RCTs of an exercise intervention involving men with PCa, Segal and colleagues [46] randomised men with stage I–IV disease scheduled to receive at least 3 mo of ADT to a 12-wk supervised resistance exercise training programme (n = 82) or a waiting list control group (n = 73). Significant differences in FACT-P mean change scores were reported at 12 wk of follow-up (mean +2 points [SD: 9 points] vs −3 points [SD: 10 points] in the intervention and controls, respectively). Although this does not achieve the suggested clinically relevant threshold, planned exploratory analysis suggested that significant effects were present regardless of curative or palliative treatment intent, or duration of ADT.

Further support for exercise training in men on ADT was recently reported by Cormie and colleagues [47]. Randomising men on ADT for at least 2 mo (with at least 6 mo planned retention) to either a 12-wk supervised aerobic and resistance training programme or usual care produced significant effects on sexual activity as measured by the EORTC QLQ-PR25 tool. Although this represents a novel and potentially important outcome, some caution is warranted due to the limited sample size (exercise n = 29, control n = 27). It should also be noted that there was very little improvement in sexual activity in the intervention group but rather maintenance of baseline activity over the intervention period, compared with controls who reported substantial declines.

Despite some encouraging data from supervised exercise programmes, it is unclear whether such interventions could be readily incorporated into service provision in secondary care. With this in mind, home-based interventions have been utilised as an attempt to recreate some of the clinical benefits while reducing costs and resources associated with supervised programmes. The largest of these trials involved men from all disease stages (described as “local” to “metastatic”) but with most treated radically [48]. Randomisation was to a simple two-page fact sheet on physical activity guidelines for adults (n = 141), self-directed exercise goal setting, barrier identification, and planning (n = 141), or telephone counselling assisted exercise goal setting, barrier identification, and planning (n = 141). After 3 mo of follow-up, no effect on PCa-specific QoL was reported. Critically, only 13.6% of participants in the intervention groups had reported completing the intended goal setting and planning activity, rendering a conclusion of no intervention effect as uncertain. It is also salient to note that recruited participants were already physically active for an average of at least 2 h per week at baseline, raising the potential for ceiling effects of this trial cohort. Home-based approaches in men on ADT have also been attempted with similar null effects on QoL [49]. This trial had a 34% dropout over the 16-wk intervention period, rendering a high risk of bias around these data.

3.1.2. Diet

Modifications to dietary behaviours have generated interest in the research community through potential beneficial impacts on a wide range of clinically relevant outcomes in PCa from disease progression [50] to mitigating the side effects of ADT [51].

A supervised programme of 11 weekly cooking classes (2.5 h each) encouraging the preparation of plant-based meals, fish, and soy and avoiding meat and dairy products reported a significant effect on FACT-P in men with biochemical recurrence after radical therapy [52]. Unfortunately, it is not possible to ascertain whether this difference was clinically meaningful in effect size because no point estimates or measures of variation were included in the article. These data should be regarded as preliminary only, given the small sample (n = 36). Some support for soy supplementation in the diet of men on ADT was reported by Vitolins and colleagues [53] in a trial evaluating soy protein
supplementation (20 g with 160 mg isoflavones; \( n = 30 \)) versus venlafaxine (75 mg once daily; \( n = 30 \)), versus combined soy and venlafaxine (\( n = 30 \)) or milk powder placebo (\( n = 30 \)). The authors reported a significant and clinically relevant difference in FACT-P after 12 wk in men taking soy protein (mean: 113 points; standard error [SE]: 6 points) versus men who did not take soy protein (mean = 104 points; SE: 6 points). Although this is positive, it should be noted that the analysis presented pooled data from both the soy only and soy with venlafaxine arms. Hence it is not possible to untangle the possible effect(s) of each individual intervention.

Other elements of dietary change designed to mitigate adverse effects of radical treatment have not produced improvements in QoL. No significant effect was reported in survivors with stage I–III disease \[54\] scheduled to undergo 7 wk of RT (in combination with either high-dose brachytherapy or proton therapy) who were randomised to receive advice to reduce lactose consumption and choose foods with soluble fibre (\( n = 64 \)) or standard care (\( n = 66 \)). Discrepancies in findings across these three trials could be explained by the different primary treatment regimens in these studies, the impact of pharmacologic agents in combination with diet changes, or could again be a reflection of more intensive intervention delivery in the pilot RCT.

### 3.1.3. Exercise and diet

Recent data from an evaluation of an individually tailored combined exercise and dietary advice intervention demonstrated novel improvements in QoL in men with advanced disease on planned long-term retention on ADT \[55\]. Men were randomised to usual care (\( n = 50 \)) or to receive tapered supervised aerobic and resistance exercise along with dietary advice encouraging reduction of saturated fats and refined carbohydrates and an increase of dietary fibre intake (\( n = 50 \)). Crucially, all participants were not active at baseline, enhancing the generalisability of these data (most men with PCa are not regularly active) \[9\]. Clinically relevant improvements in FACT-P were reported at the end of the intervention at 12 wk of follow-up (\( p = 0.001 \); mean difference: 8.9 points). However, these benefits were not sustained at 6 mo after intervention when support was withdrawn, and notably trial retention dropped from 85% to 68%. These data underscore the importance of support for lifestyle-based interventions directed towards improvement in PCa-specific QoL.

With the supportive evidence from exercise interventions, combining them with dietary advice would appear to be a promising strategy for improving PCa-specific QoL. In addition, exercise interventions could positively affect a range of other important patient outcomes. A systematic review of this topic is currently under way \[56\]. To ensure sustainability of the benefits, ongoing support from dedicated staff and a mix of supervised and independent intervention components is required \[57\]. The treating clinician could play an important role in directly advocating such programmes and arranging referral. These interventions are comparatively low risk to participants. The major obstacle is likely the cost of physical infrastructure (although this need not be based in secondary care; this could be community based) and staff time.

### 3.2. Educational support interventions

Given the numerous adverse effects associated with primary treatment for PCa, the potential impact of clinical applications of educational support has been evaluated using several approaches.

#### 3.2.1. Multidisciplinary approaches

Both pilot (\( n = 57 \)) and larger trial (\( n = 250 \)) results of group-based multidisciplinary interventions (facilitated by health psychologists, medical oncologists, urologists, dieticians, and psychiatrists) reported small benefits on FACT-P outcome (effect size: 0.1) at 6 mo \[58\] or no interaction effect on the University of California, Los Angeles, Prostate Cancer Index (UCLA-PCI) urinary, bowel, or sexual function at 12 mo \[59\] of follow-up. Recent data from Dieperink and colleagues \[60\] are more positive. PCa survivors treated with RT and ADT were assigned to outpatient mixed nurse and physical therapist led counselling (\( n = 79 \)) or usual care (\( n = 82 \)). The nursing component provided psychological support and identified disease-specific problems for the survivor and their spouse, and the physical therapist worked to improve pelvic floor muscle function and general physical activity. The urinary irritative, urinary sum-score and hormonal domains of the Expanded Prostate Cancer Index Composite (EPIC) questionnaire significantly improved in the intervention versus controls at 20 wk of follow-up (effect size: 0.34, 0.4, and 0.19, respectively). This intervention likely succeeded where earlier trials have not, by involving a smaller number of health professionals and allowing more focused tailoring of the intervention. Such approaches were supported by PCa survivors in qualitative investigation following rehabilitation interventions previously \[61\].

#### 3.2.2. Literature provision and online resources

Two pilot trials evaluating provision of an educational booklet or referral to an online support group suggested a positive beneficial effect in disease-specific QoL. However, authors of the booklet evaluation did not report interaction effects or point estimates in their analysis of FACT-P scores, choosing to analyse pre and post test scores separately in the intervention and control group \[62\]. The online support group seemed initially to improve EPIC scores over 6 wk, but these beneficial effects were transient, returning to baseline just 2 wk later \[63\]. Hence there is uncertainty around meaningful clinical benefit from these early data.

As with exercise interventions, the individually tailored approach of Dieperink and colleagues offers promise for PCa survivors. Further independent observations offering supportive data alongside cost-effectiveness evidence is now required.

### 3.3. Enhanced standard care

Enhancing existing features of PCa care could lead to better outcomes for survivors. For example, men who engage and
participate in treatment decision making are considered to experience better satisfaction with overall care. To evaluate if this extended to disease-specific QoL, Hack and colleagues [64] evaluated the provision of audiotapes of treatment consultations with oncologists to men with stage I–IV disease. Men were randomised to no audiotaping (n = 113), audiotaping performed but no tape provided (n = 98), audiotape provided (n = 120), or tape provided on patient request (n = 94). No effect on QoL was reported at 12 wk of follow-up. This large RCT suggests there is no clinical benefit of audiotaping treatment consultations.

Pelvic floor muscle training is an important element of post-RP rehabilitation. Evaluation of enhancing recovery with the aid of a physiotherapist (n = 38) compared with standard care (n = 42) did not result in any disease-specific QoL gains in men with stage I–III disease [65,66]. However, some potential for type II error must be considered in this trial because only 50% of intervention participants attended the physiotherapist-led group training sessions.

Tailored nurse-led initiatives have reported more promising data. Giesler and colleagues [67] designed an intervention to enhance QoL using the “proximal-to-distal” framework (ie, identification of clinical symptoms with the downstream intention affecting life satisfaction). PCa-specific issues (eg, urinary dysfunction, cancer worry, and fatigue) were identified with matched interventional strategies (eg, Kegel exercises for urinary incontinence). Patient-spouse dyads in the intervention arm met once each month for 6 mo with a nurse (twice in person and four times by telephone). At 12 mo of follow-up, improvement in sexual limitation (p = 0.02; effect size: 0.5) and cancer worry (p = 0.03; effect size: 0.51) were reported in the intervention group compared with controls. These data add further support to the evidence for tailored interventions delivered by dedicated staff to improve PCa-specific QoL.

3.4. Cognitive behavioural approaches

Two studies have evaluated cognitive behavioural approaches in survivors with localised disease. The first, larger trial [68] randomised men scheduled to undergo RP to individual sessions of cognitive behavioural stress management (n = 53) with most of the 90-min content focused on relaxation skills and guided imagery, supportive attention (n = 54), or standard care (n = 52). No effect on UCLA-PCI outcomes was reported after up to 12 mo of follow-up. The later, smaller study (n = 60) assessed the potential of a cognitive behavioural group intervention that addressed the psychosocial adjustment of men up to 5 yr post-RP [69]. Disease-specific QoL was evaluated using the PCa QoL scale. The authors indicated that the intervention improved sexual confidence, intimacy, masculine self-esteem, and satisfaction with orgasm in a hierarchical regression. However, it is difficult to understand the clinical relevance of these data because postintervention means and 95% confidence intervals were presented only for the cohort as a whole rather than according to randomisation. As such, it appears that currently little evidence indicates that cognitive behavioural approaches can be recommended in clinical practice for improving PCa-specific QoL.

3.5. Survivorship care coordination and the interface with primary care

Coordination of care for PCa survivors is essential to optimise QoL and promote efficient health care utilisation, although no randomised trials currently examine this in PCa specifically. However, fragmented, poorly coordinated PCa survivorship care may be associated with duplicate services (eg, PSA testing and greater spending), particularly amongst those treated with radical therapy [70]. A lack of agreement regarding roles and responsibilities amongst patients, primary care providers, and specialty care providers during survivorship can exacerbate the issue [71,72]. The Institute of Medicine (IOM) formally recognised the need to address coordination of survivorship care nearly a decade ago by recommending provision of a survivorship care plan. This includes a treatment summary and follow-up care plan for cancer survivors as they transition across the primary/specialty care interface. This standard will require an institution’s cancer committee to develop and implement a process for disseminating comprehensive care summaries and follow-up plans to cancer patients completing treatment with the hope of improving patient-centred care and outcomes. However, the evidence to support formalised cancer survivorship care plan development and provision are mixed, and concerns remain regarding their implementation (eg, reimbursement, maintenance, and contents) [73]. According to a recent nationally representative survey in the United States, primary care providers who received a survivorship care plan from an oncologist were nine times more likely to report survivorship discussions with cancer survivors [71]. However in the same study, <5% of oncology providers routinely issued a written survivorship care plan, and survivorship care discussions amongst primary care providers and patients are still rare.

The American Cancer Society Prostate Cancer Survivorship Care Guidelines [74] support the IOM recommendations that cancer specialists provide survivorship care plans including treatment summary and follow-up recommendations to primary care providers. The guidelines also highlight some practical shared care recommendations to optimise longitudinal PCa survivorship care and QoL. Firstly, they recommend specialist provision of a post-treatment patient-reported measure of side effect burden (eg, the one-page EPIC for Clinical Practice) [75] to primary care providers to facilitate longitudinal self-management and medical management efforts. A second recommendation was the minimum of an annual assessment of late and long-term health-related QoL effects including the psychosocial effects of a cancer diagnosis. A third was interprofessional shared decision making amongst the primary and specialty care providers to tailor roles and responsibilities for central tenets of survivorship care including health promotion, PCa surveillance, screening for second primary cancers, long-term and late effects assessment and management based on the patient’s condition, and resources/expertise in their
primary care setting. The latter is especially important given previous disagreement amongst the primary care and oncology communities regarding survivorship follow-up care coordination and responsibilities [76]. These guidelines were recently endorsed by the American Society for Clinical Oncology with minor modifications.

3.6. Review limitations

This paper specifically targeted RCTs addressing PCa QoL outcomes and found several educational, lifestyle, and behavioural interventions that may improve disease-specific QoL. Other behavioural, medical, and surgical approaches to symptom and side effect management are covered elsewhere [74] and were not the focus of this review. Nevertheless, more work needs to be done in this field to build the high-level evidence base necessary to support men, their partners, and clinicians as they survive PCa. A lack of consistent instrument selection in the included studies makes evidence synthesis challenging with respect to which intervention and instrument outcomes are most relevant to individual survivors (eg, urinary, bowel, sexual, psychosocial, and merits of exercise). Consensus on which instruments are most informative would likely be an informative next step. The FACT-P tool was the most frequently used in the studies included in the present review. A recent international working group advocated the EPIC Short Form for assessing men with localised PCA [77].

3.7. Research recommendations

The treating clinician could play a role in directly advocating supportive programmes to survivors and leading the multidisciplinary team in the referral process. Qualitative evaluation of how some of the interventions covered in this review could be introduced into standard care (eg, in the National Health Service) would be an ideal way to identify barriers and facilitators, and to map roles and responsibilities for care teams looking to deliver evidence-based survivorship care. Multicentre RCTs of such pragmatic complex interventions appear to be the best way of evaluating effectiveness in the long term. Crucially, cost-effectiveness data have not been generated for these programmes and should be collected in parallel during clinical studies. These data will play an important role in the dialogue with commissioners, insurers, and other payers.

4. Conclusions

PCa is the main global contributor to years lived with cancer disability. Primary treatments can often leave men with serious ongoing health problems, both physical and psychological, that adversely affect QoL. Supportive interventions that incorporate direct interaction with specialist health professionals and feature individually tailored prescriptions have shown promise for improving disease-specific QoL. Much of the data in this review comes from lifestyle interventions. Although these data are promising, these programmes are nonstandard for most clinical teams in terms of delivery. Further understanding of how these programmes can be implemented in current practice and how patient engagement and adherence can be maximised is required. These initiatives are likely to be of low risk in terms of potential harm to participants.

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Acquisition of data: Bourke.

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