



### Prostate Cancer Survivorship: A Systematic Review

Ms Sanchia S Goonewardene<sup>1\*</sup>, Young A<sup>2</sup> and R. Persad<sup>3</sup>

<sup>1</sup>Guys Hospital, Kings College London, UK

<sup>2</sup>University of Warwick, UK

<sup>3</sup>North Bristol NHS Trust, UK

\*Corresponding author: Sanchia S Goonewardene, Guys Hospital, Kings College London, UK, E-mail: [ssg7727@yahoo.co.uk](mailto:ssg7727@yahoo.co.uk)

#### Abstract

**Background:** Due to advances in cancer diagnosis and treatment, the number of prostate cancer survivors is increasing. Yet, with this expanding cohort of patients, very little has been done to develop services.

**Objective:** A systematic review was conducted to explore prostate cancer survivorship issues. This analysis will inform development of interventions.

**Design/setting:** A systematic review was conducted using the following databases from 2000 to May 2015: CINAHL and MEDLINE (NHS Evidence), Cochrane, AMed, BNI, EMBASE, Health Business Elite, HMIC, PschINFO. The papers were retrieved and a quality assessment was conducted using a new tool for survivorship care standards.

**Participants/Interventions/Outcome measurements/Results:** 76 papers met the criteria for inclusion. These specified papers must be on primary research, related to prostate cancer AND Survivorship OR any one of the categories of nutrition, exercise therapy, psychology, treatment outcomes.

**Discussion:** The literature is reviewed and the way forward for survivorship discussed. We also identify possible themes for research.

**Patient summary:** Based on these results, we develop a prostate cancer survivorship care assessment tool and identify areas of practice that can be targeting for further research.

#### Keywords

Prostate Cancer, Survivorship, Patient care, Community based follow-up

Hospital clinics are often overbooked with follow-up patients, with little time available for each patient. Yet few studies or guidelines address the broader, multifaceted aspects of cancer survivorship including self-responsibility and patient empowerment [3].

The Quality, Innovation, Productivity and Prevention (QIPP) transformational programme has been set up by the Department of Health to improve the quality of care the NHS delivers while making up to £20 billion of efficiency savings by 2014-15. One component involves risk profiling of patients, supported by community based teams and developing shared care/decision making. As a result any programme which is set up must do the same. This reflects on the cancer survivorship programme, as the basis of this programme, is risk stratification, according to likelihood of recurrence.

#### Cancer Survivorship

A cancer survivor is any person who has received a diagnosis of cancer from diagnosis until the end of life. Survivorship is defined by Macmillan Cancer Support, [4] a leading UK cancer care and support charity, as someone who has completed initial cancer management with no evidence of apparent disease. According to the National Cancer Institute, cancer survivorship encompasses the “physical, psychosocial, and economic issues of cancer from diagnosis until the end of life.”

Prostate cancer survivors require further investigation as there are concerns current follow-up methods are unsuitable [1]. Due to the growing population of survivors of prostate cancer and the period of austerity for the NHS, patients are not getting the holistic care required during the survivorship phase. Concerns regarding permanent physical, psychosocial, and economic effects of cancer treatment were highlighted by the US Institute of Medicine Report [5]. This defined landmarks for survivorship care: monitoring for recurrence, metastases or side effects and coordination between secondary and primary care.

The unmet needs of cancer survivors, the rising numbers, and pressures to utilise resources efficiently are a significant burden on the health system. These issues have been raised by the National Cancer Survivorship Initiative (NCSI) [1] which highlighted key shifts in attitude towards care.

#### Introduction

Over 2 million people in England have a diagnosis of cancer [1]. Of this, over 250,000 have been diagnosed with prostate cancer [2] and 130,000 people per year die. The Department of Health is spending £750 million on improving earlier diagnosis and prevention of cancer. During the next decade, a rapid increase in the number of new cancer diagnoses as well as a growing number of cancer survivors are predicted.

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The current method of follow-up involved focusing on cancer as an acute disease, with monitoring for recurrence, and no focus on the physical, social, emotional or psychological impact of being a Cancer Survivor. However, there is some debate as to the efficacy of this [1]. Prostate Cancer recurrence can be followed up via PSA, without the actual need to come to clinic. Additionally support for survivorship care has been given from EAU guidelines [6].

Current systematic reviews on prostate cancer survivorship cover a range of topics.

These include symptoms include physical limitations, cognitive limitations, depression/anxiety, sleep problems, fatigue, pain, and sexual dysfunction [7]. This demonstrated cancer survivors can experience symptoms for more than 10 years following treatment. This also highlighted a need for evaluated and managed to optimize long-term outcomes. Another review has highlighted patient requirement for an active part in their healthcare during the survivorship phase [8]. The challenge is in integrating lifestyle support into standardised models of aftercare.

Exercise was found to produce many beneficial effects in the cancer population including improvements in physical function, quality of life, body weight, fatigue levels, and psychological [9]. Physical activity guidelines for cancer survivors suggest that physical activity should be an integral and continuous part of care for all

cancer survivors [9]. This highlighted future studies should focus on identifying clinical, personal, physical, psychosocial, and intervention and self-monitoring and encouraging participants to attempt to generalise behaviours learned in supervised exercise environments [10].

## Method

A systematic review was conducted. The search strategy aimed to identify all references related to prostate cancer, survivorship, specific categories and treatment outcomes. Search terms used were (Prostate cancer OR prostate neoplasms) AND (survivorship OR survivor) OR (support care OR diet therapy OR exercise OR communication) AND (post therapy OR post treatment). Our selection criteria specified papers must be related to Prostate Cancer AND Survivorship. The following databases were screened from 1984 to December 2013: CINAHL and MEDLINE (NHS Evidence), Cochrane, AMed, BNI, EMBASE, Health Business Elite, HMIC, PschINFO. In addition, searches using Medical Subject Headings (MeSH) and keywords were conducted using Cochrane databases. Primary research only was included in the systematic review. Two UK-based experts were consulted in Survivorship care to identify additional studies.

## Eligibility

Studies were eligible for inclusion if they reported primary

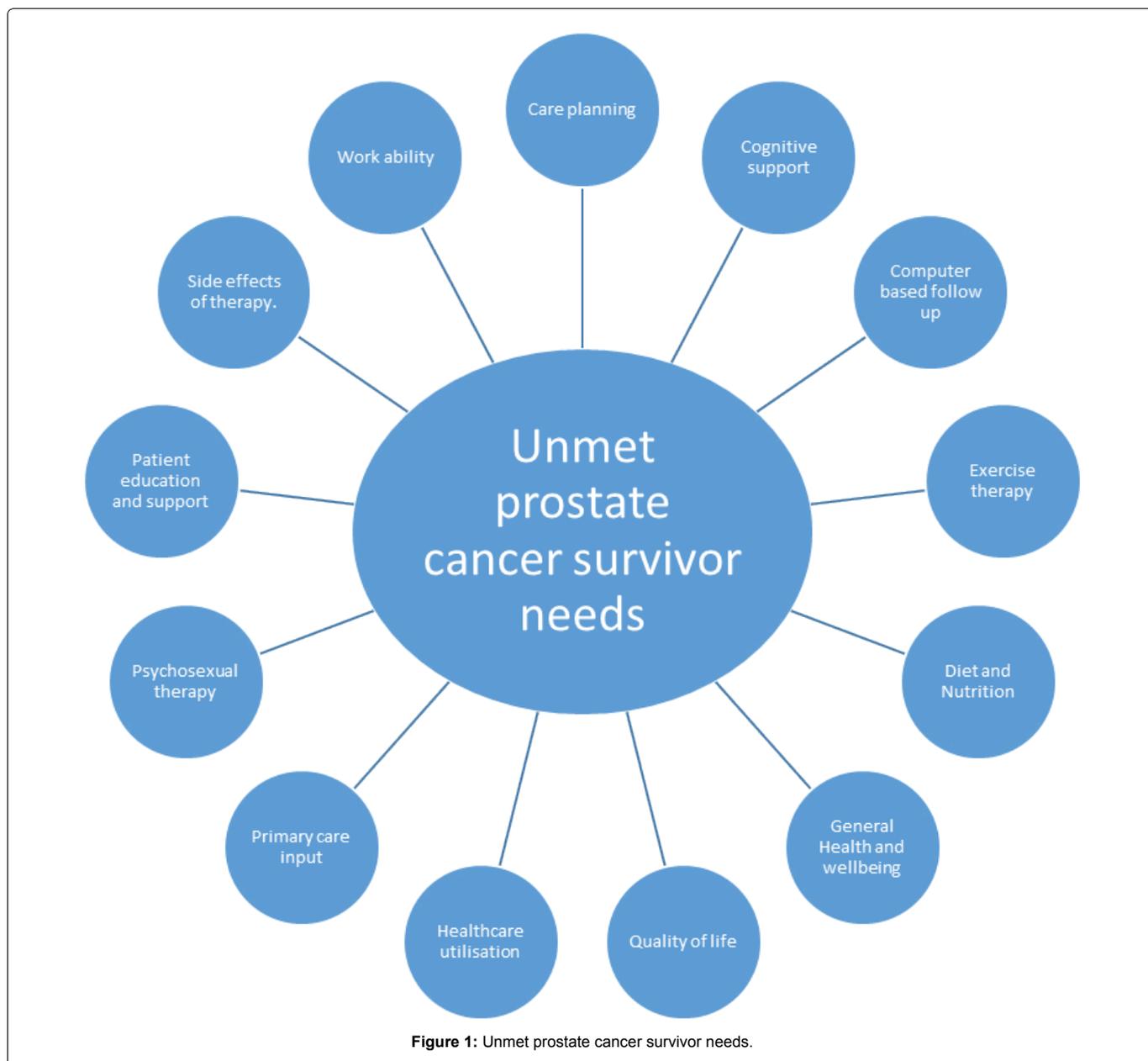


Figure 1: Unmet prostate cancer survivor needs.

research focusing on prostate cancer survivorship related to nutrition, psychology, physical therapy, treatment outcomes and communication and treatment outcomes. Papers were included if published after 1984 and had to be in English. Studies that did not conform with this were excluded

### Selection criteria

Abstracts were independently screened for eligibility by two reviewers and disagreements resolved through discussion or third opinion. Agreement level was calculated using Cohen's Kappa to test the intercoder reliability of this screening process. The PRISMA flow diagram demonstrates the results of the screening and selection process. According to criteria 76 papers were identified.

### Data extraction and quality assessment of studies

Data extraction was piloted by SSG and amended in consultation with the research team. Data extraction included authors, year and country of publication, study aims, setting, intervention aims, number of participants, study methods, intervention components and delivery methods, comparison groups and outcome measures, notes and follow-up questions for the authors. Included studies were quality assessed using Moher et al. [11] for experimental studies, Popay et al. [12] for the action research and qualitative studies. Individual quality assessment tools enabled us to focus on the specific study designs appropriately.

### Results

The search identified 2495 papers (Figure 1). However, only 76 mapped to search terms. 599 were excluded due to not being applicable to the topic. 1761 were duplicates. Of the 75 papers left, relevant abstracts were identified and the full paper obtained, all of which were in English. There was considerable heterogeneity among the included studies therefore a narrative synthesis of the evidence was undertaken. Studies demonstrated a number of problems associated with prostate cancer survivorship care, they did not propose solutions to resolve the issues. What was also demonstrated, was significant fracturing of prostate cancer survivorship care, which was cost inefficient and not properly addressing survivors' needs.

### Characteristics of studies

The systematic review required narrative analysis. Study designs varied and were conducted by a range of members from the multidisciplinary team including specialist nurses, doctors and in addition, researchers. Number of participants: 258139 patients and 330 primary care physicians.

### Risk of bias

These were assessed using Moher et al. [11] 13 studies were of 'C' quality, 27 were of 'A' quality, 35 were of 'B' quality using the criteria of Moher et al. [11]. All studies described withdrawal and dropout rates, including follow-up methodologies, and presented the interventions' outcome results. Blinding was not applicable in any trial. The flow of participants was represented in a consort style diagram in 20 of the studies involved. Allocation concealments of participants were not appropriate and the methods used for each study were. Greater than 80% of participants did provide follow-up data of interest, and outcomes were clearly defined. Only 3 studies had sample size calculated. An adequate summary of results for each outcome was provided, including for non-significant results. Sample results were explicitly defined, as was the method of recruitment and intervention.

### Development and types of interventions, components and delivering of interventions

All studies were complex interventions composed of components acting independently and/or interdependently. Interventions were as follows, below.

- 6 weeks of telephone based cognitive therapy, coping skills training vs. normal care, Campbell, L.C., 2007 [13]

- 7 weeks of group and individual sessions. Outcomes analysed via questionnaire based on Urinary symptoms were measured before the intervention and again after 4 months of follow-up through International Prostate Symptom Scores (IPSS), Faithful S [14]
- Telephone counselling and personalised work book, Kent EE [15]
- Thrice weekly exercise stepping, Outcomes, muscles measurements and mechanical force, Synder DC [16]
- Physical activity measured via accelerometer data and waist circumference over 1 week, Lynch BM [17]
- Telephone analysis examining 7-Day Physical Activity rate, diet history questionnaire, quality of life ; risk for depression ; social support<sup>45</sup>; comorbidity; perceived health; self-efficacy for exercising, Demark-Wahnefried W [18]
- National Health interview survey used to measure outcomes, Elliott J [19]
- Personalised mail intervention, telephone surveys to assess dietary habits at 1 and 2 years , Christy SM [20]
- Intervention: workbook and unit materials, telephone survey, Demark-Wahnefried W [21]
- Point analysis, phone interview, on educational materials, Nesse LE [22]
- Randomised to receive tailored vs none tailored diet and exercise intervention. Analysis on QoL via physical activity recall, Ottenbacher AJ [23]

Outcomes measures ranges from sexual and urinary tract functioning [24] to QoL experiences, short and long term preventative outcomes associated with prostate cancer [25], and examination of primary care physicians views on survivorship [26].

### Discussion of Papers

#### Impact on community based survivorship care

This systematic review clearly highlights the large areas of Survivorship Care that are currently being unaddressed (Figure 2).

#### What patients want

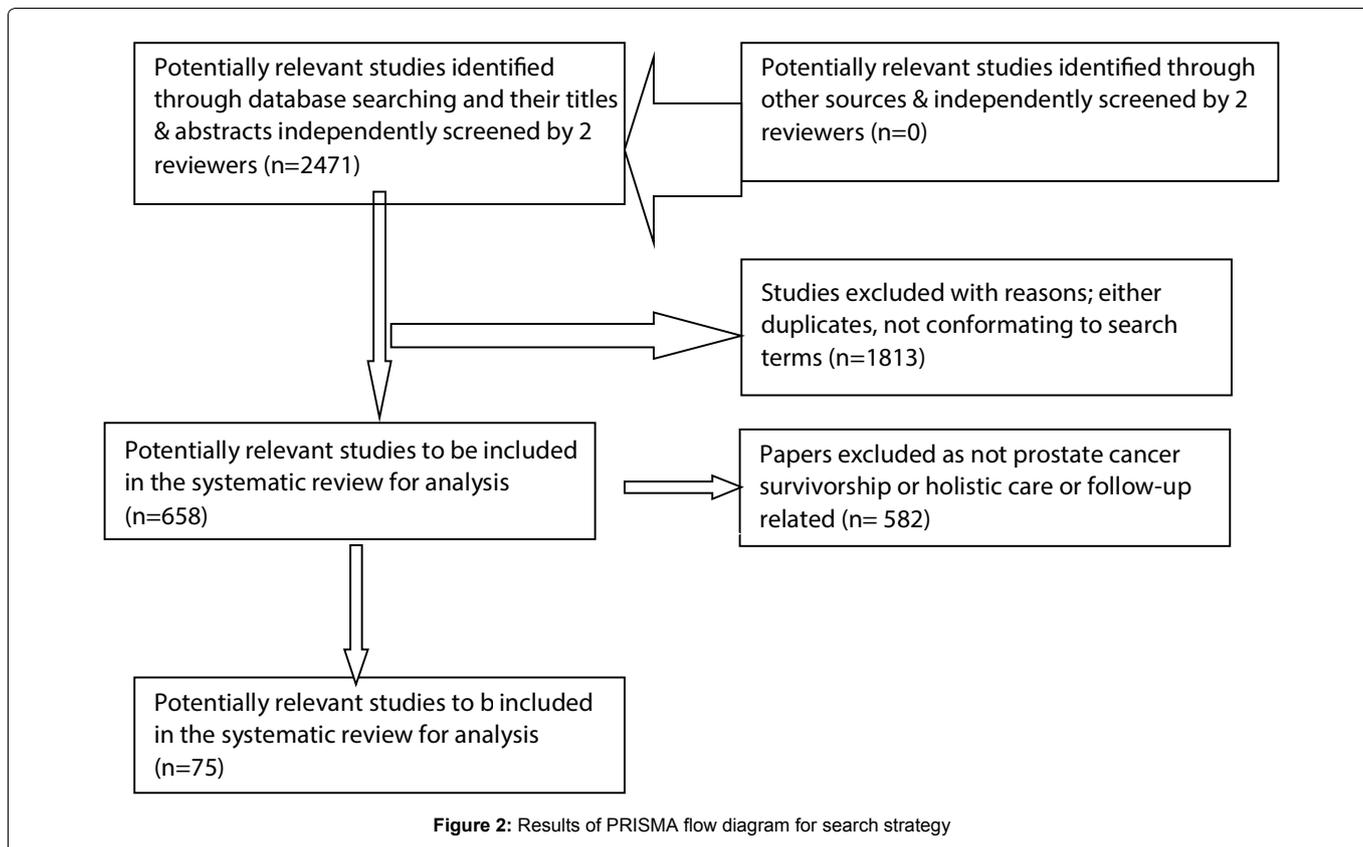
Survivors report few cancer-related symptoms and high QoL Zucca et al. [27]. However some had deteriorated work abilities due to cancer with more problems post therapy [28]. Telephone based interventions are a feasible approach that can successfully enhance coping [29].

#### Psychological impairment and psychotherapy

Many have psychological distress due to cancer and its treatment. These are strongest predictors of depression and can persist with symptom control [30]. Tailored interventions are appropriate and should be considered in these cases. Further research is however required [31]. The psychotherapy input into survivorship care was further confirmed by Biegler [32]. They demonstrated meditation may help to improve cancer-related cognitive dysfunction and alleviate other cancer-related sequelae. Additionally, psychotherapy adds to support future self-management programmes for men surviving prostate cancer [33].

#### Healthcare utilisation

Survivors demonstrate a higher rate of decreased self-rated health, more physical impairment and thyroid diseases, daily use of medication and psychotropics and higher level of anxiety [34]. Increased primary health care use is the result [35,36]. With appropriate information and support in place, PCPs reported being willing to assume responsibility for the follow-up care of adult cancer survivors [26]. Cardiovascular disease risk factors is common, yet not discussed with relevant healthcare teams. This highlights more inter-speciality working is required [37]. Due to the increased demands,



changes in health care, more efficiency, are required to manage increasing demand [38]. The number of physician visits, particularly primary care input, are important factors associated with successful survivorship care [25]. With appropriate information and support in place, multispecialty working together with primary care can manage this cohort [26].

### Cormorbid conditions and side effects of treatment

Survivors suffer sexual, urinary, and bowel dysfunction. Another issues which together with erectile dysfunction, could be addressed by adequate Survivorship care [39]. Increased comorbidities are associated with poorer QOL and higher symptom distress in cancer survivors [40]. Functional status and comorbidity has been shown to decline in the first year post diagnosis [41].

### Social support

This is increasingly important to the prostate cancer survivor and their carer. As a result any programme which is set up, must also be made accessible to the carer/ relative of the survivors [42]. Direct associations are present between perceived support and the use of problem-focused and support-seeking strategies, whereas inverse associations emerged with self-blame, wishful thinking, and avoidance [43]. Healthcare professionals must aim to promote the former.

### Exercise therapy

Exercise interventions have been shown to improve health related quality of life [44]. There are also clear long term health benefits of participating in physical activity programs [45]. Older cancer survivors represent a vulnerable population who we must target and for alteration of health behaviours. This can be a hard-to-reach population [46]. Increasing moderate-to-vigorous activity may assist this population with weight management, however more research is required [47].

This is further supported by the work of Cormie et al. [48]. What was demonstrated was exercise improved fatigue, physical function, risk of comorbid conditions, depression, anxiety and quality of life.

Structured exercise training may improve physical functioning, fatigue, depression and, in total, patients' quality of life [49].

### Health related Qol

Most long-term survivors retrospectively report that cancer either positively influenced their lives or had little long-term impact [50]. Those who express Resentment report that pain, physical deformities, and social isolation significantly reduced their long-term HRQL. This is significant, as it highlights a cohort we need to target.

### Lifestyle interventions

Home-based diet and exercise interventions hold promise in improving lifestyle behaviors however, further research is required [18], and even in older survivors [51] that diet and other lifestyle practices were important predictors of patient QOL [52]. As a cohort, we need to focus on physical, functional and social well-being [19].

### Post treatment care

Despite high levels of satisfaction, discharge of cancer survivors from hospital follow-up could be improved with the provision of additional time, information and support. Better structuring of the final hospital appointment or a review appointment in primary care at this time could help to ensure that discharge from hospital follow-up is managed optimally for cancer survivors [14].

### Psychosexual

Only 43% of men said their partners had encouraged them to find help [22]. This highlights an area of survivorship care which is not properly addressed. This must be corrected to improve sexual rehabilitation in this cohort post therapy.

### Cost effectiveness

None of the studies address cost effectiveness of interventions directly, however one [53], does. This study examined that telephone follow-up is a feasible strategy for or assessing prostate cancer survivor QOL and could provide a low cost, sustainable, and systematic approach to measuring patient-centred outcomes, conducting comparative effectiveness research, and monitoring the quality of prostate cancer care [53].

## Statement of main findings

Our review found a small number of papers of similar research design. All studies reported positive survivorship outcomes or gave further evidence for a way forward. This demonstrates how well adapted the interventions were structured, coupled with the fact that key points were investigated leading to good care. The studies were of moderate quality in relation to the characteristics of their particular design.

Prostate cancer survivors were the focus of these interventions research in all studies. This is a very sizable group, not just in the UK but through the world.

## Strengths and limitations

The search criteria of this review included prostate cancer and survivorship. Interventions of any research design (from a wide range of sources including experts) were assessed and included using the novel survivorship care assessment tool to ensure the inclusion of all relevant interventions previously undertaken in the area. Therefore, this design was robust because previous systematic reviews have limited their search to specific survivorship topics, not looking at survivorship as a holistic package of care. The included studies were assessed for both methodological quality and strength of survivorship care. The review is limited by the different methodological studies. It was a relatively heterogeneous population, indicating the conclusions published are valid. In addition, as only published studies were included, some relevant ongoing studies may have been excluded. The definitions of 'Survivor' have been signposted in this review.

## Findings in relation to other survivorship studies and trends, literature

Concerns regarding permanent physical, psychosocial, and economic effects of cancer treatment were highlighted by the US Institute of Medicine Report [2]. These include impact on life for example, financial, occupational or performance concerns.

The Institute of Medicine produced a report on the focus of survivorship care plans including the chronic effects of cancer, monitoring for and preventing late effects e.g. malignancies, and promoting healthy lifestyles [5]. There is a lack of evidence in this field, with regard to patient follow up and whether it should be led by primary or secondary care, and also a lack of follow up into a patients' wellbeing and quality of life [5]. Survivorship care plans are recommended as an important tool to facilitate communication and allocation of responsibility as part of this [54]. Self-management is part of this, with patient driven assessment of outcomes.

The unmet needs of cancer survivors, the rising numbers, and pressures to utilise resources efficiently [8] are a significant burden on the health system. These issues have been raised by the National Cancer Survivorship Initiative (NCSI) [55] which highlighted key shifts in attitude towards care. The focus is now more on recovery and return to work. This includes personalised approach to individual risk assessment and patient self-management.

The patient consensus meeting (NHS Improvements,) concluded patients are not averse to new approaches to follow-up care and support. However they need to have access to good quality information and rapid access to specialist treatment -should they need it.

An important pre-requisite for survivorship care, is a good insight into the patients' needs and preferences. Providing cancer patients with information about their dis-ease and treatment helps them to make decisions about treatment. In addition they are able to overcome fear, develop realistic expectations, manage side effects and comply with treatment. Individualised information sessions have been associated with lower anxiety, better psychological well-being and higher treatment satisfaction [56]. Continuity and coordination of care is difficult, with many patients unclear about who is responsible for their ongoing survivorship care. However, to date, there has been little consensus on the value and organisation of follow-up [57].

One area which is infrequently addressed is that of sexual dysfunction. This affects many prostate cancer survivors Park et al. [58]. The incidence of varies between 20% and 88% [59]. Changes in body image, pain, and loss of -desire, long-term physical and psychological side effects from cancer treatments can affect sexual functioning.

## Conclusion and recommendations for future

This systematic review has defined landmarks for survivorship care: monitoring for recurrence, metastases or side effects and coordination between secondary and primary care. This has also demonstrated a requirement for further holistic support for patients in the survivorship cohort, which is not being addressed. In addition patients with psychological, emotional, social and financial concerns as well as sexual health concerns were also highlighted as not having their problems addressed leading to poorer quality of life. Since writing this systematic review, based on SSGs recommendation, Prostate Cancer Survivorship and Supportive Care has been added as a section to the EAU congress. This is the way forward.

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