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Chapter 3

Psychological and Social Factors influencing Patients’ Treatment Selection for Localised Prostate Cancer


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1. Introduction

Prostate cancer is the most common form of cancer in men in the United Kingdom (UK). A quarter of all new cases of cancer diagnosed in men are prostate cancers. In 2009, over 40,000 cases of prostate cancer were reported in the UK and more than 10,000 men die from the disease each year [1]. Prostate cancer is also a major concern worldwide. Its highest incidence rates are found in Australia and New Zealand with its lowest in South-Central Asia [2].

The rate of men being diagnosed with prostate cancer has significantly increased worldwide in recent decades [3]. This is likely due to the prostate-specific antigen test being performed among younger men and resulting in the majority of men being diagnosed with localised prostate cancer (LPCa) [4, 5]. These men are usually presented with treatment options, which most commonly include: (1) active surveillance (i.e., regular monitoring of disease activity for those intended to be treated with subsequent curative treatment), (2) radical prostatectomy, (3) external beam radiation therapy, and (4) brachytherapy, and are asked to consider and select their preferred treatment. The situation that patients with LPCa face is somewhat unique. They have to decide between treatments because there is no substantial evidence to suggest that one treatment modality differs from other treatments, in terms of overall survival rate [6, 7]. However, there are considerable differences in the side-effects associated with each treatment option.
2. Treatment side-effects and their psychological impact

Men confronted with this treatment decision often need to take into consideration a range of factors, including the potential physical side effects of treatments and their psychological, social and emotional consequences. For example, patients being treated with radical therapies can experience severe side-effects, such as urinary incontinence (UI) and erectile dysfunction (ED), as a result of treatment. UI symptoms can persist years after treatment [8] and this can have an impact on all aspects of an individual’s functioning. Men with UI often avoid social situations due to the risk of their incontinence becoming apparent to other people. They can feel embarrassed by their inability to self-control their bodily functions and by the lack of empathy from other people within social situations [9].

Relatively little research has been conducted to examine the relationship between ED and psychological morbidity among men with prostate cancer. Nevertheless, ED has been reported to have a profound effect on a patient’s quality of life post-treatment. Nelson et al. [10] examined the relationship between depressive symptoms and erectile function. A group of men, who did not receive any treatment for their prostate cancer, completed self-report questionnaires measuring anxiety and depression symptoms and erectile function approximately 4-years post-diagnosis. Erectile dysfunction was found to be a significant predictor of depression independent of other influential factors of depression, such as anxiety and marital status. This finding suggests that men can experience lasting psychological effects from their disease. Another study by Nelson et al. [11] examined men’s responses to ED affecting their sexual function and their adjustment to diminished erections after having undergone a radical prostatectomy. These men completed self-report questionnaires measuring erectile function and sexual satisfaction pre-operatively, 12 and 24 months post-operatively. The findings revealed that sexual satisfaction decreased after surgery with patients feeling ashamed and embarrassed by their difficulty to perform sexually with their partners. Sexual dissatisfaction persisted over the period of 24-months, even in men who reported good erectile function post-operatively. Thus, it appears that men do not seem to adjust well to the consequences of their treatment.

ED is a condition which not only affects the individual but also affects couples. There have been differences in the perceptions held by men with ED due to treatment for prostate cancer and their partners. Men with ED have reported an “all or nothing” approach to their sexual relationship with their partner; in that if they are unable to ‘perform’ sexually then it is pointless to engage in sexual contact. This can lead to men withdrawing from intimate contact with their partners causing strain on the relationship [12]. Women partners have reported to be less concerned about treatments to help the physical functioning of their partners with ED, and are more focused on finding alternative ways to maintain intimacy and sexual stimulation [13].

The option of active surveillance as a management plan for LPCa can also affect the quality of life of men diagnosed with the disease. Although no active treatment is administered, active surveillance can have a psychological impact. Qualitative studies have provided some insight into the experiences of living with prostate cancer. For instance,
Hedestig et al. [14] conducted interviews with patient with untreated LPCa and analysed the interview transcripts using in-depth qualitative narrative analysis. Their findings revealed that men perceived their disease as life-threatening, experienced uncertainty, fear and worry about their cancer progression, and a repressed sense of manhood due to sexual dysfunctions.

3. Personal beliefs and treatment selection

The decision on a treatment modality for LPCa could, therefore, be described as a challenging one requiring patients to weigh up a range of physical and psychological outcomes of treatments. Indeed, it has been shown that patients can experience decision-related distress at diagnosis, which can persist over time and lead to poorly informed treatment decisions [15]. The difficulties associated with making a treatment choice can be further magnified by patients making their decisions based on their personal beliefs. These personal beliefs can help patients construct a mental representation about their disease and its treatment, which can guide their adjustment to their disease. Such beliefs are of particular importance to treatment decisions when there is great uncertainty around the long-term effects of treatment.

Extensive research has found that personal beliefs can predict a range of outcomes, including quality of life, help-seeking behaviour and treatment adherence [16-18]. These beliefs have also been shown to affect treatment choice, mainly by way of selecting between conventional treatment and complementary and alternative medicines (CAM) for conditions, such as chronic pain, hypertension, and both localised and advanced prostate cancer [19-22]. These studies reported that patients who used CAM were more likely to hold negative beliefs about their illness (i.e., that their illness was chronic and that they had little personal control over its management); and about conventional treatments (i.e., believed the treatments would result in significant undesirable side-effects). In contrast, patients who were less likely to favour CAM held positive beliefs about their illness and its treatment (i.e., believed the condition was not severe and would easily be controlled with conventional treatment). Indeed, patients’ positive beliefs about their illness were also shown to increase the likelihood of choosing generic rather than branded medicines, as well as reduce the amount of drugs they consumed to manage their conditions [20, 23].

It is not well-understood how patients, who are diagnosed with LPCa and offered conventional treatments, make sense of their disease and their treatment decisions through examining personal beliefs. Patients with LPCa can make treatment decisions that may not necessarily be in accordance with the treatment-related information provided by urologists [24]. Thus, patients may choose a treatment based on confounding information derived from their own experience and from other sources available to them. By gaining a better understanding of patients’ personal beliefs may help both patients and urologists make more informed decisions about treatments.
4. A systematic review of the literature

An initial scope for existing literature reviews in prostate cancer research yielded two reviews [25, 26]. The more recent review [26] was conducted five years ago and restricted its search period to a 14 year time span, used a small number of literature databases and only searched for original, peer-reviewed studies to explore broadly the personal (not just beliefs specifically) and external factors pertaining to the decision-making process of patients. It concluded that there is a general lack of understanding about the role of patients’ beliefs in treatment selection and that this was an area worthy of enquiry. Our aim was, therefore, to provide an updated review on factors influencing treatment selection for LPCa, as well as specifically examine the literature pertaining to patients’ personal beliefs about LPCa and/or its treatments.

A systematic search of the literature was conducted in electronic databases to retrieve relevant published papers from 1980 – 2010, which included: MEDLINE (1950-present); CINAHL; ScienceDirect and CancerLIT (PubMed). Searches were conducted by exploding and combining the medical subject term ‘prostate cancer’ and free-text words, such as ‘beliefs, cognitions, choices, treatment options’. A language restriction was not set whilst searching for the papers.

Non-scholarly literature was searched using the following charity databases: The Prostate Cancer Charity (Jan-April 2010) and Cancer Research UK. The following Government websites were also searched: World Health Organisation (WHO) and the National Institute of Health and Clinical Excellence (NICE). The Networked Digital Library of Theses and Dissertations was searched for theses discussing relevant work and studies.

The reference lists of literature reviews were hand-searched and key authors identified from the search procedure were contacted for any other relevant studies.

The studies retrieved from the literature searches were screened against the inclusion criteria, which included: (i) samples of men diagnosed with, and being treated for, LPCa, and (ii) studies examining patients’ beliefs about their LPCa and treatment options. All study designs except reviews, opinion papers and single case studies, were considered for inclusion into the present review.

The titles and abstracts of the references yielded from the search procedure were screened against the inclusion criteria. The full text of the potentially relevant papers were retrieved and read for consideration into the review. The papers that met the inclusion criteria were assessed for their methodological quality.

5. Synthesis of findings

The search procedure yielded ten papers, which are summarised in Tables 1 and 2. It was inappropriate to combine findings statistically to produce meaningful outcomes. This was
partly due to the small number of quantitative studies identified for inclusion into the review. Primarily, the assessment of the included studies revealed there to be many methodological differences that existed between the studies. This made it difficult to pool studies to determine the effect of perceptions on treatment selection. Therefore, a qualitative synthesis of the findings was undertaking with studies being grouped according to treatment modality and those factors affecting decision-making. Statistical findings from the quantitative studies were used to support the observed findings from the qualitative studies.

5.1. Beliefs underpinning treatment selection for localised prostate cancer

5.1.1. Radical prostatectomy

Patients' beliefs and other influences in selecting to undergo a radical prostatectomy were clearly reported in nine of the studies [27-35]. Many of the patients perceived their cancer as a localised problem and that the most tangible and definitive method of curing or preventing the disease from spreading was to remove the tumour [27-29, 31, 35]. These findings were also replicated in three of the quantitative studies, which reported that beliefs about the effectiveness of surgery and complete tumour removal were statistically associated with selecting surgery [33-35]. Surgery would also allow for surgeons to be more informed about the nature and extent of the cancer and would provide the patients with more information about their disease [27, 28]. Surgery was considered to have the best evidence base in terms of its efficacy in combating cancer compared to other curative treatment options [31, 32]. Overall, patients believed surgery to be the best and most effective form of treatment. This corresponds with current treatment rates, which show that the majority of patients with LPCa opt for surgery [36].

5.1.2. External beam radiation therapy and brachytherapy

External beam radiation therapy (EBRT) was regarded by most patients as being an inferior treatment option to a radical prostatectomy. This was based on their belief that EBRT provided uncertainty surrounding its ability to cure their cancer [27, 28, 30, 31] through treatment administered externally to the body. Unlike a radical prostatectomy, EBRT was believed to disadvantage the patient by being time-consuming and disruptive to daily life with severe consequential side-effects [27, 28]. Interestingly, some of these side-effects were mistaken for side-effects associated with chemotherapy (e. g., hair loss, weight loss, vomiting) [27, 28, 30]. It appeared that when patients selected EBRT as their preferred treatment, it was to avoid the negative effects of surgery, i. e., being less invasive and resulting in fewer side-effects [31, 35]. These beliefs were similar to those held by patients who selected brachytherapy as their preferred treatment. However, like a radical prostatectomy, brachytherapy was believed to provide a ‘direct’ and, therefore, more effective and convenient form of treatment to cure their cancer [31, 34].
5.1.3. Active surveillance / watchful waiting

The terms ‘watchful waiting’ were used in some of the papers along with the other active treatment options. Watchful waiting usually refers to a less intense management plan where palliative care is usually provided. These options were rarely considered by patients as a management option for their cancer. They were typically rejected due to patients’ fear about the cancer spreading [31, 33] and their need to be “doing something” active to combat their prostate cancer [28, 31]. Holmboe and Concato [31] suggested that other possible explanations for patients rejecting watchful waiting included fear of death or the inability to monitor cancer progression. Patients who opted for active surveillance perceived their cancer as ‘a very small growth’ and a common disease among men as they get older. These men were accepting of the uncertainty surrounding their disease progression and believed it would be best to endure the severe side-effects of curative treatment only when it was evident that treatment was required [37]. However, this willingness to accept active surveillance as a management option appeared to occur in men whose urologists advocated the view that the disease was not severe and would progress slowly [37].

<table>
<thead>
<tr>
<th>Study Ref</th>
<th>Authors, year, &amp; study location</th>
<th>Design</th>
<th>Characteristics of sample</th>
<th>Major findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>Denberg et al. (2006) Denver, USA</td>
<td>Perspective cohort (follow-up 6-8 months) using semi-structured interviews</td>
<td>20 men newly diagnosed with LPCa considering treatment options Age range 53-80 years 70% (white); 25% (African American); 5% (Latino)</td>
<td>40% perceived surgery as a definitive treatment Surgery offered crucial knowledge about tumour 55% perceived surgery as undesirable regarding invasiveness</td>
</tr>
<tr>
<td>28</td>
<td>O’Rourke (1999) North Carolina, USA</td>
<td>Perspective cohort (follow-up 3 &amp; 12 months) using couple &amp; individual semi-structured interviews</td>
<td>18 men newly diagnosed with LPCa who have made a treatment decision 18 spouses recruited Mean age 67.6 (range 52-78 years) (patient) Mean age 62.1 (range 49-74 years) (partner) 13% white (patient), 5% African American; 72% white, 28% African American (spouse)</td>
<td>Couples believed cancer is only curable through surgery Perceived uncertainty about radiotherapy regarding efficacy &amp; outcome Men more concerned about side-effects than wives</td>
</tr>
<tr>
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<td>[29]</td>
<td>O'Rourke &amp; Germino. (1998) North Carolina, USA</td>
<td>Retrospective cross-sectional study using unstructured focus groups</td>
<td>11 men diagnosed with LPCa, who have made a treatment decision 6 spouses recruited Age range 58-72 years (patients) Age range 51-64 years (spouses) 99% white; 1% African American</td>
<td>Surgery perceived as a first line choice Prior bias toward surgery due to perceived association with cure Radiotherapy perceived inferior to surgery due to its efficacy &amp; side-effects</td>
</tr>
<tr>
<td>[30]</td>
<td>Steginga et al. (2002) Queensland, Australia</td>
<td>Cross-sectional study using semi-structured interviews</td>
<td>108 men diagnosed with LPCa considering curative treatment options Mean age 62 years (range 39-80 years) Ethnicity not specified</td>
<td>47% described other patients’ treatment experiences used in their decision-making 34% held lay belief that surgery was the best way to cure their cancer 12% were uncertain about radiotherapy as a way to cure their cancer</td>
</tr>
<tr>
<td>[31]</td>
<td>Holmboe &amp; Concato. (2000) New Haven, USA</td>
<td>Cross-sectional study using interviews with open-ended questions</td>
<td>102 men newly diagnosed with LPCa, who have made a treatment decision Mean age 66.4 years Majority white (89%)</td>
<td>Majority influenced by external information (i.e., 30% for physician recommendation) Classified likes &amp; dislikes of treatments Removal of tumour &amp; evidence of efficacy as main likes for surgery Fear of future consequences was the most common reason to reject watchful waiting</td>
</tr>
<tr>
<td>[37]</td>
<td>Davison et al. (2009) Vancouver, Canada</td>
<td>Retrospective cross-sectional study using interviews with semi-structured interviews</td>
<td>25 men with low-risk prostate cancer on active surveillance Mean age 66 years (range 48-77 years) Majority white (92%); 8% South Asian</td>
<td>Men perceived their cancer as a common disease &amp; exaggerated the potential incidence Realised treatment might be necessary, but viewed as “a grey zone”</td>
</tr>
</tbody>
</table>

Table 1. Description of the Qualitative Studies included in the Systematic Review
<table>
<thead>
<tr>
<th>Study ID reference</th>
<th>Authors, year, &amp; study location</th>
<th>Design</th>
<th>Characteristics of sample</th>
<th>Major findings</th>
</tr>
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<tbody>
<tr>
<td>[32]</td>
<td>Hall et al. (2003) Virginia, USA</td>
<td>Retrospective cross-sectional study using self-report questionnaires developed from literature review &amp; clinical impressions</td>
<td>351 men with LPCa treated with surgery or brachytherapy Mean age 62±5 years (radical prostatectomy); 66±8 years (brachytherapy); 70±7 years (combination of brachytherapy &amp; radiotherapy) Ethnicity not specified</td>
<td>42.9% brachytherapy patients &amp; 97.5% radical prostatectomy patients chose treatment based on evidence shown to cure the cancer. Side-effects were an important motivator. Urologists were the most important source of information and a major factor in decision-making process.</td>
</tr>
<tr>
<td>[33]</td>
<td>Zeliadt et al. (2010) USA</td>
<td>Cross-sectional study using self-report questionnaires developed from preliminary focus groups &amp; cognitive interviews</td>
<td>198 newly diagnosed patients considering surgery only &amp; patients considering other treatment options Mean age 63 years 72% white, 11% black, 16% Hispanic/Asian (surgery); 68% white, 26% Black, 6% Hispanic/Asian (other options)</td>
<td>Treatment efficacy influenced preference for surgery. Personal burden influenced nonsurgical options.</td>
</tr>
<tr>
<td>[34]</td>
<td>Gwede et al. (2005) Florida, USA</td>
<td>Cross-sectional study using questions derived from previous study</td>
<td>69 men diagnosed with LPCa, who have made a decision about treatment Mean age: 57.7 years (range 39.6-71.1) (surgery); 65.2 years (range 45.7-89.2) (brachytherapy) 86.5% (surgery); 97% (brachytherapy) white</td>
<td>Cure and complete tumour removal were the main motivations for surgery (74%). Brachytherapy related to quality-of-life issues.</td>
</tr>
<tr>
<td>[35]</td>
<td>Teramoto et al. 2006 Kamogawa, Japan</td>
<td>Cross-sectional study using self-report questionnaires</td>
<td>51 men diagnosed with LPCa treated with radical prostatectomy or external beam radiation therapy Overall mean age: 68.2 (range 56–75 years) Japanese sample</td>
<td>Physician was the major factor influencing treatment decisions in both treatment groups (&gt;90%). Family and others was a more important factor for patients undergoing surgery than patients undergoing radiation therapy. Surgery was desired for cancer control. Radiation therapy favoured concerning side-effects.</td>
</tr>
</tbody>
</table>

Table 2. Description of the Quantitative Studies included in the Systematic Review
5.1.4. The role of urologists and partners in informing patient beliefs

The recommendations made by urologists emerged in many of the papers [28, 29, 31-33, 37] as being influential in shaping patients’ beliefs regarding their treatment choice. A high percentage of patients (48-65%) said they would select the treatments recommended by their urologist [30, 32]. Consequently, seeking a second opinion was unnecessary serving only to delay treatment and provide potentially more conflicting information to process [27, 28].

Partners, who often experience considerable emotional distress themselves on hearing the diagnosis [25, 38], have also been found to exert an important influence on patients’ beliefs. Three studies reported the role of the partners to be a source of information or a mediator in helping men to process their treatment information [27, 32, 34]. However, it was also reported in two studies that, ultimately, it is the patients themselves who reported ownership of their treatment decision [29, 37].

5.1.5. The role of patients’ information seeking behavior in informing beliefs

Another major factor influencing patients’ beliefs was their own information-seeking behaviour. Patients and their partners are often actively engaged in learning about their treatment options, side-effects and the background of their urologists [29]. The evidence suggested that they made use of a variety of resources, including health care professions (HCPs) (i.e., urologists, radiation oncologist), the internet, books, magazines, friends and family [27, 29, 30, 32, 34, 37]. Processing such large amounts of advice and potential contradictory information was suggested to be an explanation for the misconceptions about treatments reported by the patients (i.e., associating the effects of chemotherapy with radiotherapy) [27, 30].

5.1.6. The role of other patients’ treatment experiences in informing patient beliefs

In four studies, there was evidence that patients [27, 28, 30, 33] and their partners used the experiences of other people with cancer in their decisions about treatment. Denberg et al. [27] described that these experiences influenced patients’ beliefs regarding LPCa, its treatment and treatment side-effects. Steginga et al. [30] reported that 47% of men described considering other people they knew (not just those with prostate cancer), who had negative experiences with cancer or cancer treatment, in their decision-making. O’Rourke [28] reported that comparisons with other patients, who had a positive outcome from treatment, were mostly related to surgery and that comparisons were usually made between friends and family members, who had undergone surgery and were making a good recovery. It has been suggested that patients may pay more attention to the experiences of other patients with cancer than to the risk information presented to them by their urologists and specialist nurses [27]. The reliability of their findings was supported by the quantitative findings of Zeliadt et al. [33], who reported a statistically significant association between the experiences from other patients and treatment selection for patients who only considered surgery as a viable treatment.
6. Discussion

The findings synthesised in the present review have demonstrated that patients select a treatment or management option based on their beliefs about their cancer, the perceived effectiveness of the treatment and their beliefs regarding the side-effects of the treatment. With regards to the present findings, the majority of patients select active surveillance because of their belief that their cancer was not aggressive, selected to undergo a radical prostatectomy because they believed it to be most effective at curing their cancer, and selected EBRT because of the reduced risk of side-effects. A range of factors external to the patient, which inform these beliefs, were also identified. These included the patients’ high regard of the urologists’ treatment recommendation, the emotional distress experienced by partners, the various modes of seeking information about treatments, and other peoples’ experiences of treatment.

It is, however, also very clear that the evidence base on patients’ beliefs in the context of LPCa remains limited. This is an area in need of high quality prospective studies to gain a greater understanding of the factors that influence treatment decisions. This understanding could help develop interventions designed to support men in these decisions and to assist with their long-term adjustment to prostate cancer and its treatment.

The limited evidence that has been synthesised in this review does, however, enable some clear recommendations to be made how this area of research and, ultimately, clinical practice may move forward. In particular, it is clear that the existing findings relate well to two theoretical frameworks, which have been developed to understand patients’ beliefs regarding illness and treatment; and which have also been the basis of therapeutic interventions [39, 40]. These are the self-regulatory model (SRM) [41, 42] and the Necessity Concerns Framework (NCF) [17, 43]. The SRM describes that individuals’ personal beliefs allow them to make sense of their disease and enable them to reach their illness goals (e. g., in LPCa these could be survival, reducing the risk of side effects, etc.). These beliefs cluster around 5 domains: (1) identity (the way patients describe their disease and its symptoms); (2) cause (what caused the disease); (3) timeline (how long the disease is going to last); (4) consequence (how will the disease and/or its treatment affect me?); and (5) controllability (whether the disease is believed to be preventable, curable, or controllable). Similarly, the NCF also focuses on personal beliefs, but those specifically related to treatment. Previous research has shown that patients’ beliefs regarding treatment tend to focus on two domains: beliefs regarding how necessary/important the treatment is to their future well-being and beliefs regarding concerns (i. e., what are the potential adverse consequences of the treatment?).

There was clear evidence in the studies included in this review of the beliefs specified by both the SRM and NCF. For example, patients believed their cancer to be a mass within the body (akin to identity beliefs) and that removing this mass would cure their cancer (akin to controllability beliefs). Similarly, patients believed curative treatment would offer them the best outcome in terms of survival (akin to necessity beliefs) because their cancer could potentially re-occur (akin to concern beliefs). Furthermore, the importance of factors external to the patient in shaping their beliefs is also specified by the SRM. Thus, it was suggested that
the results of this review provide strong evidence to support the use of these theoretical frameworks in future research.

7. Recommendation for health care

It is clear that the use of patients’ beliefs in their decisions on a treatment modality has led them to base their decisions on misconceptions rather than on evidential information. HCPs may need to challenge misinformed beliefs held by patients to help them make more informed decisions regarding their treatment. In order to make more conclusive recommendations for health care practice, further research is required to establish the extent to which personal beliefs alter treatment selection.

8. Recommendations for further research

The majority of the studies included in this review used a qualitative approach. Such methods explore a topic area in-depth and provide a descriptive account of findings. While this approach can provide very rich data in specific domains, these data are not intended to be generalisable. Thus, quantitative studies (preferably with prospective designs) are required in the future to ascertain, not only the salient beliefs influencing treatment choices but also, how these beliefs affect long-term adjustment to the disease and its treatment.

With regards to the studies which employed quantitative methodologies, none used standardised and validated measures for examining illness or treatment beliefs. Two of the quantitative studies [32, 34] developed their measures of beliefs from previous published work. The remaining study developed its measure from preliminary focus groups and interviews [33]. It could be suggested that further validation of these measures is required before any strong conclusions can be drawn.

The time at which illness and treatment beliefs were measured is another shortcoming of the included studies. Some of the studies included those patients who had already made a treatment decision or who had already started treatment. This may have affected the reliability of the findings due to the potential bias of patients recalling what they believed about their illness and its treatment at these times in the treatment process. Prospective designs involving the assessment of beliefs before a treatment choice is made would offer a more robust approach.

A further limitation concerned the majority of the patient samples being predominantly white and from North America. Therefore, the experiences of other groups, such as men of Afro-Caribbean origin in whom the risk of prostate cancer is greater, were not represented. Further research is required across a range of ethnic and cultural groups.
9. Conclusion

The present review has revealed that our understanding of the role played by the personal beliefs of men regarding their LPCa and its treatment is still limited. The existing evidence has been dominated by qualitative methods, cross-sectional designs and the use of non-validated instruments. However, it is also clear from existing findings that the adoption of the SRM and NCF, with their associated validated instruments, could provide a greater understanding of the factors that influence treatment decisions. Further research using psychological frameworks could also help develop interventions to support men in their treatment decisions, and assist with their long-term adjustment to LPCa and its treatment.

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