

Characterising prostate cancer patients undergoing androgen deprivation therapy: Is there a group of men more at risk of cognitive changes? A Cross-sectional Study

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1. BACKGROUND AND RATIONALE

Although androgen deprivation therapy (ADT) yields significant clinical and survival benefits in prostate cancer patients, it has been associated with cognitive side-effects and even the development of dementia (Cherrier & Higano, 2019). While the severity of cognitive changes may vary greatly, it nonetheless may negatively impact on quality of life. Despite evidence supporting the role of androgens and its metabolites in modulating cognition, the research surrounding ADT-induced cognitive impairment appears to be mixed (Durdiakova et al., 2011). Serious clinical implications have arisen from population studies and meta-analyses proposing that ADT may increase the risk of developing dementia (e.g., Kim et al., 2017; Robinson et al., 2019). Given that ADT is often prescribed over prolonged periods, elucidating inconsistencies in whether the therapy gives rise to cognitive side-effects is critical in providing best practice clinical care to support clinicians, patients with prostate cancer and their families.

Some studies have suggested that there may be a certain group of men within the prostate cancer population who may be more vulnerable to ADT-induced cognitive changes (e.g. Cherrier et al., 2009; Green et al., 2002; Jenkins et al., 2005; Plata-bello et al., 2019). Identifying this subset group may explain some of the inconsistencies in the research. Moreover, determining the characteristics of this group and predictors of ADT-induced cognitive decline may help clinicians identify patients at risk of abnormal cognitive changes and provide support to them and their families. There is limited research attempting to characterise those demonstrating an accelerated cognitive decline.

Demographic Variables Associated with Cognitive Functioning

A recent study by Plata-bello et al. (2019) found patients with lower education were more susceptible to age-related cognitive decline than those with higher education. While this difference between high- and low-education levels was also evident in participants without prostate cancer, it was more pronounced in patients undergoing ADT. Education level tends to indicate one's level of cognitive reserve (Tucker & Stern, 2011). Theories of cognitive reserve suggest that individuals with higher cognitive reserve are more able to withstand the negative impacts of brain damage (i.e. demonstrate less severe clinical symptoms) (Stern, 2002). There is evidence implicating that cognitive reserve may be able to mitigate the adverse impact of white matter lesions on cognition, providing support for the theory (Brickman et al., 2011). In terms of the impact of ADT on the brain, patients with low cognitive reserve may be more susceptible to

the decline in the neuroprotective effect of androgens. This theory of cognitive reserve may also explain some of the inconsistencies in the research regarding ADT-induced cognitive decline. For instance, study samples with lower education (10-11 years; Green et al., 2004; Yang et al., 2015) demonstrated more observable cognitive impairments than samples with higher education levels (e.g. 16 years; Alibhai et al., 2010). Moreover, the 'protective' effects of education may not occur equally across all ethnic groups, given potential differences in accessibility, acculturation and other factors (Díaz-Venegas et al., 2016).

As most prostate cancer diagnoses occur in men over 65 years old, this population is already at increased risk of cognitive dysfunction due to normal ageing (McHugh, Root, Nelson & Morris, 2018). While the research remains inconsistent, some studies suggest that ADT may accelerate the cognitive ageing process, as elderly patients are more likely to experience ADT-induced cognitive decline (Jayadevappa et al., 2019; Tae et al., 2019).

Other important demographic variables that may influence cognitive functioning include marital status, occupation, residential area and bilingualism or multilingualism. In terms of partner status, older men cohabitating with a partner were less likely to demonstrate abnormal cognitive decline than those who were single, separated or widowed (Feng et al., 2014; Håkansson et al., 2009). This finding may reflect the impacts of having greater intellectual and social stimulation that is inherent in dyadic relationships. Occupations with higher complexity have also been found to be associated with better later-life cognitive functioning, even when the effects of education and early-life cognitive ability were taken into account (Smart et al., 2014). Moreover, residential area may also impact cognitive status as differences have been found between rural and urban settings (Xiang et al., 2018). Furthermore, the ability to speak another language has been found to preserve cognitive functioning, attention, cognitive control and efficient neural processing, with some studies suggesting that it may even delay dementia (Gold et al., 2013). Overall, many of these demographic factors have not been extensively explored in previous research examining the relationship with ADT and cognitive functioning. Examining demographic factors alone, however, is insufficient, rather the complex interplay of various factors should be taken into consideration.

Disease- and Treatment-related Variables Associated with Cognitive Functioning

Various disease- and treatment-related variables may impact cognitive functioning and also explain some of the disparities underlying the research. For instance, men having undergone

surgery may experience deleterious impacts of anaesthesia, with older populations being more susceptible (Jim et al., 2010). Other side-effects arising from treatment (e.g. sleep changes, fatigue, hot flushes, etc.) may also adversely impact cognitive functioning directly or indirectly. Moreover, many studies (e.g. Alibhai et al., 2010) exploring ADT-induced cognitive impairment fail to mention the type of ADT drug and how it was administered (e.g. intermittent, continuous, injections, tablets, combined, etc.). There may be differential drug effects on cognition (Green et al., 2004). Furthermore, cognitive ADT-associated effects may be associated with ADT duration (Nead et al., 2017). Therefore, these disease- and treatment-related variables may be important predictors of ADT-induced cognitive dysfunction.

Other Medical Variables Associated with Cognitive Functioning

There is strong evidence that vascular risk factors (e.g. hypertension, diabetes, coronary artery and peripheral vascular disease) elevate the risk of abnormal cognitive changes (Duron & Hanon, 2008; Esme et al., 2018). Medication other than ADT may also affect cognitive function as drugs treating vascular conditions (e.g. antiplatelet & statins) may have protective effects (Tae et al., 2019). Additionally, neurological events (e.g. strokes, seizures, head trauma etc.) and family history of neurocognitive diseases are important factors needed to be considered in assessing predictors of abnormal cognitive decline.

Psychosocial and Lifestyle Variables Associated with Cognitive Functioning

Negative affective changes (e.g. depression, irritability, anxiety, fatigue, etc.) are often reported in men undergoing ADT (Cherrier & Higano, 2019). These changes may negatively impact cognitive functioning and/or be a response to the effects of ADT. Depression, for example, has been reliably associated with cognitive impairment, although the causal direction is unclear (Rock et al., 2014). Nonetheless, assessing men's mood is clinically important as the concomitant occurrence of cognitive complaints and depressive symptoms in older adults has been shown to predict dementia in a number of studies (Babulal et al., 2016; Byers & Yaffe, 2011).

Social and lifestyle variables (e.g. physical activity, smoking, alcohol intake, diet, etc.) can also have a substantial impact on cognitive functioning. In a recent meta-analysis, greater social support and larger social networks in older adults were associated with higher levels of global cognition (Kelly et al., 2017), whereas, poor social functioning was associated with poorer global cognition. Although the direction and nature of the association between social support and

cognitive functioning is unclear, investigating the social functioning of men diagnosed with prostate cancer may provide helpful insights when characterising groups of men at risk of cognitive changes.

Physical exercise and a diet characterised by a high intake of vegetables, fruits, legumes, whole grains and low in saturated fats, have demonstrated protective effects on cognitive health (Christie et al., 2017; Richard et al., 2018). Whereas, smoking and excessive alcohol consumption are associated with accelerated cognitive deterioration in older men (Sabia et al., 2012; Sabia et al., 2014). Moreover, differences between patients' intellectual engagement (e.g. reading, problem-solving activities, playing musical instruments, etc.) may also provide insight into men's cognitive functioning (Staff et al., 2018; Verghese et al., 2003). These lifestyle variables have not been explored in men undergoing ADT experiencing cognitive difficulties. Many of these variables are modifiable and recommendations may help clinically manage patients with cognitive complaints.

1.1. AIMS

The study will consist of two parts: Part 1 consisting of a cross-sectional survey, and Part 2 consisting of a semi-structured interview. The aims for Part 1 of the study are to:

- 1) Quantitatively determine whether there are distinct biopsychosocial profiles of men with prostate cancer on ADT that explain differences in cognitive functioning.
- 2) Determine whether the biopsychosocial profile members differ according to socio-demographic, medical, intrapersonal and interpersonal variables.
- 3) Determine whether the identified profiles also differentiate cognitive functioning in prostate cancer patients not undergoing ADT and age-matched controls without prostate cancer.
- 4) Determine whether a difference exists in the prevalence of cognitive problems between prostate cancer patients on ADT, patients without ADT and age-matched controls without prostate cancer.

The aim for Part 2 of the study is to examine in-depth through qualitative methodology the nature and impact of ADT-associated cognitive changes on these men's and their partner's lives and the types of cognitive change. Overall, by understanding the characteristics of prostate

cancer patients experiencing cognitive problems from hormone therapy, it can help clinicians better identify and provide support to patients and their families.

2. STUDY PLAN AND PROCEDURES FOR CROSS-SECTIONAL STUDY (PART 1)

2.1. Design

This is a cross-sectional survey, with an invitation for subject and their partners to participate in qualitative substudy (Part 2 of study).

2.2. Participants

Only men over 17 years old, who are able to read and speak English sufficiently well to respond to written questions and provide consent and have access to an electronic device will be included for the study. There will be three groups of participants:

- i) Men diagnosed with prostate cancer, who are currently undergoing ADT;
- ii) Men diagnosed with prostate cancer, who have are on ‘watchful waiting’;
- iii) Age-matched men without a prostate cancer diagnosis.

G*Power (Erdfelder et al., 1996) analysis estimates a minimum sample size of 150 participants (50 in each group) to achieve a medium effect size with a power of .8, alpha of .05 and 6 estimated covariates in an ANCOVA investigating differences in rates of cognitive problems between the groups. Given a lack of consensus surrounding sample size calculation for Latent Profile Analysis (LPA), ‘rule of thumb’ estimates of 10 subjects per variable indicate that at least 50 participants are required for distinct profiles to occur in an LPA with 5 profile variables (Bentler & Chou, 1987). Therefore, at least 150 participants are required in total with 50 in each individual LPA of the 3 participant samples.

For the non-cancer age-matched control sample, we will recruit men between the ages of 55 to 75, which is consistent with 1 standard deviations around average age of prostate cancer diagnosis in Australia ($M=65.4$, $SD=9.6$; Ruseckaite et al., 2016).

2.3. Recruitment

Participants will be provided with a hyperlink to the online survey, which will contain information about the study and a consent page. Participants must consent electronically before being able to complete the survey. They will be recruited through three methods:

1. By health clinics or healthcare professionals;
2. Email invitation to men and women (who may have partners eligible for recruitment) listed on research registers (e.g., Pathfinder, Register4, etc.);

3. Prostate cancer-related social media channels (such as Facebook, Twitter, the Men's Shed);
4. By word of mouth.

All eligible people enrolled into the study will be entered into a participants' registration database. Each participant will be allocated a unique study number, which will be used to identify them on all study documentation.

2.4. Withdrawal from the study

Participants will complete a survey on one occasion only. They will be free to discontinue participation in the study at any time, but their data will remain as part of the study unless they explicitly withdraw consent for use of their data.

2.5. Data collection

The demographic, treatment-related, medical details will be obtained directly from participating men (see Appendix A for the questionnaires) Self-reported questionnaires detailed below will be used to investigate patients' self-perceived cognitive status and lifestyle factors.

- The Functional Assessment of Cancer Therapy- Prostate (FACT-P; Appendix B) is a widely-used measure specifically developed for men with prostate cancer to assess their health-related quality of life (Esper et al., 1997). It contains subscales examining: physical well-being, social/family well-being, emotional well-being, functional well-being and additional concerns (e.g. feelings of manliness, urination, aches and pains). Reflecting on their experience in the past week, patients rate on a five-point scale (from 0 = 'not at all' to 4 = 'very much') the frequency of 39 statements (e.g. 'I have a lack of energy'). Due to redundancy, the emotional well-being scale was removed from questionnaire.
- The Functional Assessment of Cancer Therapy-Cognitive Subscale (FACT-cog, version 3; Appendix C) is a measure of perceived cognitive function developed from oncologist and patient input (Wagner et al., 2009). It consists of a four-factor structure: perceived cognitive impairments, comments from others, perceived cognitive abilities and impact on quality of life. Reflecting on their experience in the past week, patients rate on a five-point scale (from 0 = 'never'/'not at all' to 4 = 'several times a day'/'very much') the frequency of 37 statements (e.g. 'my thinking has been slow').

- Cognitive Functioning Scale from the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; Appendix D) assesses one's difficulties with attention and memory. Subjects rate on a 4 point scale the extent to which they have experienced cognitive difficulties within the last week.
- The Fear of Cancer Recurrence-short form (FCR4, Appendix E; Humphris et al., 2018) is a 4-item questionnaire assessing concerns, fears and worries related to the possibility of cancer progressing or returning. Each item is rated on a Likert scale ranging from 0 (not at all or never) to 4 (a great deal or all the time). The rating for each item is summed to form a total score
- A brief dietary questionnaire developed by Dr. Heather Francis measuring the number of times someone consumes a type of food (e.g., vegetables, fruits, etc.) in a week (Appendix F).
- The 6-item version of Need for Cognition Scale (NCS-6, Appendix G; Lins de Holanda Coelho et al., 2018) is an assessment of one's tendency for intellectual engagement. Participants rate how characteristic each statement applies to them, rated on a Likert scale ranging from 0 (extremely uncharacteristic) to 4 (extremely characteristic).
- The International Physical Activity Questionnaire (IPAQ, Appendix H; Booth, 2000) contains 7 items assessing the type and amount of physical activity and time spent sitting people did in the last 7 days.
- The short-form version of the Depression Anxiety Stress Scales (DASS-21, Appendix I; Lovibond & Lovibond, 1995) is a 21-item self-report questionnaire with three subscales: depression, anxiety and stress consisting of 7 items each. Items are scored on a scale from 0 = 'did not apply to me at all' to 3 = 'applied to me very much'.
- The State Self-Compassion Scale – Short Form (Neff et al., 2020; Appendix J) contains 6 questions assess how one responds to painful or difficult situations, measured on a 5-point Likert scale (1 being 'Not at all true for me' to 5 being 'Very true for me').
- Impact of COVID-19 will be assessed using 3 questions (Appendix K).

Estimated time required for all questionnaires is around 20-30 minutes. The questionnaires will be completed electronically (via an internet-based tool) either during a clinic visit or at home.

2.6. Statistical considerations

To address the first aim: are there distinct biopsychosocial profiles of men with prostate cancer on hormonal therapy? We will use Latent Profile Analysis (LPA), which is a person-centred statistical approach used to identify homogeneous, mutually exclusive groups (or ‘profiles’) that exist within a heterogeneous population. In our research, we hypothesise that there will be subgroups of men with prostate cancer who are more vulnerable to cognitive side-effects from hormone therapy. We sought to identify the biopsychosocial characteristics that underlie these men using LPA. The selection of variables we will include in these analyses were based on theoretical models and previous literature on predictors of subjective and objective cognitive functioning (Green et al., 2005; Plata-bello et al., 2019). These variables include education level, treatment side-effects/physical well-being, social/family well-being, healthy lifestyle habits (diet and exercise) and psychological wellbeing. To ensure that we create a parsimonious profile, we will select one measure from each family of variables that correlates most highly with our variable of interest – cognitive functioning. To this end, we will develop a profile with five variables drawn from each of the families. Potential covariates include time since diagnosis, medical comorbidities, age and self-reported impact of COVID measure. We will use an exploratory method of determining the number of profiles in the hormone therapy group. We will evaluate the relative fit using the Bayesian Information Criterion (BIC) and the Aikake Information Criterion (AIC). Entropy will be computed to estimate the distinctiveness of the identified profiles from one another. Interpretability and parsimony will be considered in selecting the optimal model. To determine whether cognitive functioning differs between the identified profiles, ANCOVA will be used to examine whether there are significant differences between the profiles on cognitive functioning.

To address our second aim examining whether the identified profiles differ across several biopsychosocial characteristics, ANCOVA and chi-squared analyses will be used to compare other biopsychosocial characteristics between the profiles extracted from above. These include:

- Sociodemographic factors:
 - Marital status
 - Employment status
 - Regional vs urban
 - Language (i.e., multilingualism)

- Medical factors:
 - Prostate cancer type (early or localised/ locally advanced/ metastatic)
 - Treatments: ADT, surgery, radiation, others
 - Medical comorbidities
- Intrapersonal factors
 - Functional well-being
 - Need for cognition
 - Self-compassion

To address our third aim, we will perform the same LPA forcing these profiles in the prostate cancer control group and non-cancer control group. In this way, we can determine whether these profiles are unique to patients on hormone therapy and whether these different profiles may provide additional information about cognitive functioning (e.g., is there a particular group that is most associated with poor cognitive functioning?).

To address our fourth aim examining the prevalence of cognitive problems our groups, an ANCOVA will be conducted comparing levels of cognitive problems in prostate cancer patients on hormone therapy, prostate cancer controls and noncancer age-matched controls. Further post-hoc tests will be conducted examining whether:

- Men with prostate cancer on hormone therapy experience greater cognitive problems than noncancer age-matched controls
- Men with prostate cancer on hormone therapy experience cognitive problems over and above the effect of cancer of cognition (i.e., men with prostate cancer and not on hormone therapy).
- Men with prostate cancer and not on hormone therapy experience greater cognitive problems than noncancer age-matched controls (i.e., examining the effect of prostate cancer on cognition).

We plan to use Bonferroni correction. We anticipate at least 0.4 standard deviation (SD) difference between self-reported cognitive functioning in men with prostate cancer on hormone therapy versus noncancer controls. Previous research specifies that difference of at least .4 SD is considered to reflect a minimum clinically meaningful indicator of poor cognitive functioning in previous research (Cheung et al., 2014).

Treatment of missing data

Missing data will be imputed with maximum likelihood (ML) estimates.

3. STUDY PLAN AND PROCEDURES FOR THE QUALITATIVE SUBSTUDY (PART 2)

3.1. Design

There is limited information on how men perceive the relationship between ADT and cognitive impairment, and how these cognitive changes impact their and their partner's lives. In order to understand the types of cognitive difficulties, a qualitative approach to data collection and analysis will be employed. This method will enable in-depth insights into the perspectives and experiences of the men and their partners.

3.2. Sample size

The number of interviews planned for men and their partners is around 15 to 20 each, with a maximum total sample size of 40. Interviews will continue until data saturation is reached and this may be before the minimum number of interviews for both men and their partners is achieved. Data saturation is defined as three consecutive interviews with no new themes identified. Additionally, there may be 2-4 interviews conducted for member-checking purposes to ensure consistency, clarity and validity of the identified themes.

3.3. Recruitment

The participants in the substudy will be drawn from those participating in the main survey and have consented online (by providing their details) to be contacted about participating in an interview. Participants who have endorsed problems with their cognition on the survey (i.e., reported side-effect, responses on FACT-cog or EORTC QLQ-C30 cognitive functioning scale) will be selected. The partners will also be recruited through the men with consent provided. Information about the study may be also emailed to participants at their request.

3.4. Procedure

Interviews will be conducted via telephone at a time that is convenient to the participant. All participants will be provided with a detailed written participant information statement, which will be included in the online survey, prior to agreeing to take part in the study. Verbal consent will be obtained and recorded as part of the interview. The semi-structured interviews are expected to last between 20-60 minutes. All interviews will be audio-recorded and transcribed by the researcher and volunteers. Volunteer transcripts will be checked by the researcher. Men and

their partners will be interviewed separately, without the other partner present to ensure the privacy of their responses.

Should the participant become distressed during the interview, the researcher will stop the interview and offer support. Interviews only continued with participants' agreement once distress passed. Participants will be referred to relevant support lines (e.g. Cancer Council Support Line, Beyond Blue Support Line and Lifeline) or back to their treating clinicians. They will be reassured that they can withdraw at any stage from the research.

Thematic analysis (Braun & Clark, 2006) will be used to examine the data and identify themes. Patients' and their partners' responses to more detailed questionnaires regarding the patients' cognitive difficulties will be examined. At the conclusion of the study, participants' data will be deidentified with their contact details kept separately in another source.

3.5. Semi structured interviews

Interviews will be guided by a semi-structured interview schedule and various questionnaires (see Appendix M). Topics discussed using the interview schedule will include but are not limited to:

- When changes to cognition were first noticed;
- The kinds of cognitive difficulties experienced (i.e., spatial navigation, processing speed, etc.);
- Circumstances where the difficulties were more pronounced;
- Impact of these difficulties on quality of life;
- Exploring certain responses to questionnaire and survey answers;

3.6. Data analysis

The verbatim transcripts of the interviews will be coded with themes identified using the framework method (Gale et al., 2013). This method allows in-depth explorations of how patients and their partners perceive the factors associated with the patient's cognitive difficulties. It also has the ability to integrate an inductive and deductive approach. The stages of the framework method include: transcription of the interview, familiarisation with the data, coding the data, developing a working analytical framework, applying the framework to the transcript, charting the data into the framework matrix and interpreting the data. Methodological rigor will be maintained through the acknowledgement of reflectivity, review of transcripts, response-driven inquiry, team debriefing, member-checking, iteration of the interview guide and

auditability. The questionnaires will be scored accordingly to the recommended guidelines provided by their manuals.

4. DATA MANAGEMENT

All the data will be collected on a secure password-protected database and Macquarie University's cloud-based storage system. The data will be deidentified with a separate file containing the details of the participants. Deidentified data may be made publicly available in an online repository, as this is becoming a more common practice for journal publication.

5. ETHICAL, REGULATORY AND ADMINISTRATIVE ISSUES

The study will be performed in accordance with the "NHMRC National Statement on Ethical Conduct in Human Research" (Commonwealth of Australia, 2007- Updated May 2015) and the principles laid down by the 18th World Medical Assembly (Helsinki 1964) and amendments at subsequent World Medical Assemblies. No participants will be identified in any reports, and information identifying individual subjects will be removed from the data set prior to analysis.

5.1. Human Research Ethics Committee (HREC) Oversight

The study must be approved by the relevant HREC prior to commencing recruitment.

5.2. Informed Consent

Online written information about the study (both Part 1 & 2) will be provided to all participants (see Appendix L). This information and consent form will be contained in the hyperlink for the survey. This information can also be emailed to the participants at their request. Participants will not be able to access the survey without initially providing consent. Consent for participation in the study (both Part 1 & 2) will be obtained electronically from every patient.

Specific information and consent forms will be available online for the qualitative substudy at the same time as the survey information and consent form, whereby participants agree to be contacted by leaving their details. As the telephone interview (Part 2 of the study) does not require to the participant and researcher to meet face-to-face, we will audio-record the consent to participate in the interview at the start of the phone call. Some participants (i.e., partners of the patients) may only be providing oral consent.

5.3. Confidentiality

Confidentiality of patients in the study will be strictly ensured. Macquarie University will be the coordinating centre and will hold a separate secure database will be set-up containing contact details of those people agreeing to participate to ensure follow-up and any qualitative interviews are completed according to the protocol. Patient identification numbers will be generated here and used in a separate database containing the data generated by the study (this second database will not contain any other identifying information of participants).

6. SITES

The study will actively recruit patients across Australia. Participants will be recruited through participating healthcare professionals in their private rooms/clinics, public and private hospital clinics and online. Specific prostate cancer research registers will be contacted and asked to circulate information to people registered with them.

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APPENDIX A

1. What is your date of birth? (dd/mm/yyyy):	
2. What is your marital status?	<input type="checkbox"/> Single <input type="checkbox"/> Married/De facto/Partnered <input type="checkbox"/> Separated/Divorced <input type="checkbox"/> Widowed
3. What is your highest level of schooling completed?	<input type="checkbox"/> Did not complete year 10 <input type="checkbox"/> Completed year 10 <input type="checkbox"/> Completed year 12 <input type="checkbox"/> Vocational studies (e.g., TAFE) <input type="checkbox"/> Undergraduate degree or equivalent <input type="checkbox"/> Postgraduate degree or equivalent
4. What is your employment status?	<input type="checkbox"/> Full-time <input type="checkbox"/> Part-time <input type="checkbox"/> Looking for employment <input type="checkbox"/> Self-employed <input type="checkbox"/> Carer <input type="checkbox"/> Retired, Date (dd/mm/yyyy):
5. What type of work do/did you do?	<input type="checkbox"/> Professional, technical and managerial occupations <input type="checkbox"/> Clerical and sales occupations <input type="checkbox"/> Service occupations <input type="checkbox"/> Agricultural, fishery, forestry and related occupations <input type="checkbox"/> Processing occupations (e.g., food, textiles, metals, plastic) <input type="checkbox"/> Machine trades occupations <input type="checkbox"/> Benchwork occupations (e.g., assembling and repair of products) <input type="checkbox"/> Structural work occupations (e.g., construction related) <input type="checkbox"/> Other
6. If you are CURRENTLY WORKING, please answer the following questions: (if not, go to question 7)	
After commencing treatment for your prostate cancer:	
i. Did you notice any changes to your ability to work?	<input type="checkbox"/> No <input type="checkbox"/> Yes, provide some details: _____
ii. Have you been able to perform your work duties at the same level as before?	<input type="checkbox"/> No <input type="checkbox"/> Yes
iii. Have you decreased your hours at work?	<input type="checkbox"/> No <input type="checkbox"/> Yes

7. If you are RETIRED, please answer the following questions: (if not, go to question 8)

i. Did you retire before or after commencing treatment?

Before

After

ii. Did the side-effects of your treatment lead to an early retirement for you?

No

Yes

8. Do you have any children?

No

Yes

If YES:

i) How many?

ii) Do they live with you?

No

Yes

9. What is your country of birth?

10. Postcode:

11. Do you speak any other languages other than English?

No

Yes, what languages?

12. What type of prostate cancer do you have?

Early or localised (cancer cells have grown but have not spread beyond the prostate)

Locally advanced (cancer has spread outside the prostate gland into nearby parts)

Metastatic prostate cancer (cancer has spread to distant parts of the body)

13. Date of diagnosis (**dd/mm/yyyy**):

14. Most recent Prostate Specific Antigen (PSA) level: _____ng/mL Date (**dd/mm/yyyy**):

15. Select the treatments for prostate cancer you have received:

Active Surveillance sometimes called ‘Watch & Wait’

Surgery

Type:

Radical prostatectomy (removal of prostate gland and some of the surrounding tissue)

Surgical castration or orchiectomy (removal of the testicles to reduce the production of testosterone by the body)

Other: _____

Date:

Radiation therapy

Type:

External beam radiation (beams of radiation are focused on the prostate gland from a machine outside the body)

Brachytherapy (pellets of radioactive material are inserted through the skin in the area between the scrotum and anus and into the prostate.)

Other: _____

Date:

Hormone therapy (Tick or cross the boxes below)

	Monthly injections	Four-monthly injections	Six-monthly injections	Intermittent injections (depending on your PSA levels)	Tablet form
Abiraterone (Zytiga)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Apalutamide (Erleada)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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Bicalutamide (Casodex)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Darolutamide (Nubeqa)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Degarelix (Firmagon)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Enzalutamide (Xtandi)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Flutamide (Eulexin)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Goserelin (Zoladex)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Histrelin (Vantas)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ketoconazole (Nizoral)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Leuprolide (Lupron, Eligard)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nilutamide (Nilandron)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Triptorelin (Trelstar)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Other treatments for prostate cancer: _____

16. Have you experienced these SIDE-EFFECTS following treatment:

i) Changes in thinking (e.g., memory, attention, etc.)	<input type="checkbox"/> No	<input type="checkbox"/> Yes
iii) Sleep changes	<input type="checkbox"/> No	<input type="checkbox"/> Yes
iv) Mood changes	<input type="checkbox"/> No	<input type="checkbox"/> Yes
v) Tiredness that does not go away with rest	<input type="checkbox"/> No	<input type="checkbox"/> Yes
vi) Reduced libido	<input type="checkbox"/> No	<input type="checkbox"/> Yes

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vii) Erection problems	<input type="checkbox"/> No	<input type="checkbox"/> Yes
viii) Loss of muscle strength	<input type="checkbox"/> No	<input type="checkbox"/> Yes
ix) Weight gain	<input type="checkbox"/> No	<input type="checkbox"/> Yes
x) Hot flushes	<input type="checkbox"/> No	<input type="checkbox"/> Yes
xi) Breast changes (e.g., growth, tenderness, etc.)	<input type="checkbox"/> No	<input type="checkbox"/> Yes
xii) Loss of bone density	<input type="checkbox"/> No	<input type="checkbox"/> Yes
xiii) Others _____		

OTHER MEDICAL DETAILS

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17. Do you have a heart condition?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
18. Do you have diabetes?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
19. Do you have high blood pressure?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
20. Do have sleep apnoea?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
21. Have you ever had any form of a condition that affects the brain (encephalitis, meningitis, epilepsy, dementia, Parkinson's etc.)?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
22. Has anyone in YOUR FAMILY been diagnosed with condition that affects the brain (encephalitis, meningitis, epilepsy, dementia, Parkinson's etc.)?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
23. Have you ever been knocked unconscious for more than 5 minutes?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
24. Have you ever been diagnosed with a learning disability?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
25. Were you born more than 1 month premature?	<input type="checkbox"/> No	<input type="checkbox"/> Yes
<p>26. Have you been under general anaesthesia in the past year?</p> <input type="checkbox"/> No <input type="checkbox"/> Yes, please indicate the month of the most <u>recent</u> occasion:		
<p>27. Have you had a STROKE?</p> <input type="checkbox"/> No <input type="checkbox"/> Yes, please indicate the year of the most <u>recent</u> occasion:		
<p>28. Have you had a SEIZURE or FITS (where you have blacked out)?</p> <input type="checkbox"/> No <input type="checkbox"/> Yes, please indicate the year of the most <u>recent</u> occasion:		
<p>29. Have you ever been diagnosed with a mental health condition? (e.g., anxiety, depression, etc.)</p> <input type="checkbox"/> No <input type="checkbox"/> Yes, outline your condition(s): _____		
<p>30. Do you smoke OR have you ever smoked?</p> <input type="checkbox"/> No <input type="checkbox"/> Currently smoking <input type="checkbox"/> Stopped smoking		

31. Have you ever smoked more than a total of 100 cigarettes (5 packs) in your life?

- Yes No

32. How often do you drink alcohol?

- I do not drink alcohol**
 Everyday
 A few times a week
 A few times a month
 A few times a year

33. Have you ever used illegal drugs? (e.g., marijuana, heroin, cocaine, etc.)

- I have never used illicit drugs**
 Once
 A few times
 Regularly

34. Describe any other medication (not for prostate cancer) you are taking and what is it treating:

APPENDIX B

FACT-P

Below is a list of statements that other people with prostate cancer have said are important. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

<u>PHYSICAL WELL-BEING</u>		Not at all	A little bit	Some-what	Quite a bit	Very much
1	I have a lack of energy	0	1	2	3	4
2	I have nausea	0	1	2	3	4
3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4	I have pain	0	1	2	3	4
5	I am bothered by side effects of treatment	0	1	2	3	4
6	I feel ill	0	1	2	3	4
7	I AM FORCED TO SPEND TIME IN BED	0	1	2	3	4
<u>SOCIAL/FAMILY WELL-BEING</u>		Not at all	A little bit	Some-what	Quite a bit	Very much
1	I feel close to my friends	0	1	2	3	4
2	I get emotional support from my family	0	1	2	3	4
3	I get support from my friends	0	1	2	3	4
4	My family has accepted my illness	0	1	2	3	4
5	I am satisfied with family communication about my illness	0	1	2	3	4

6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
7	<i>Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box <input type="checkbox"/> and go to the next section.</i>					
8	I am satisfied with my sex life	0	1	2	3	4

By circling one number per line, please indicate how true each statement has been for you during the past 7 days.

	<u>FUNCTIONAL WELL-BEING</u>	Not at all	A little bit	Some-what	Quite a bit	Very much
1	I am able to work (include work at home)	0	1	2	3	4
2	My work (include work at home) is fulfilling	0	1	2	3	4
3	I am able to enjoy life	0	1	2	3	4
4	I have accepted my illness	0	1	2	3	4
5	I am sleeping well	0	1	2	3	4
6	I am enjoying the things I usually do for fun	0	1	2	3	4
7	I am content with the quality of my life right now	0	1	2	3	4
	<u>ADDITIONAL CONCERNS</u>	Not at all	A little bit	Some-what	Quite a bit	Very much
1	I am losing weight	0	1	2	3	4
2	I have a good appetite	0	1	2	3	4
3	I have aches and pains that bother me	0	1	2	3	4
4	I have certain parts of my body where I experience pain	0	1	2	3	4

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5	My pain keeps me from doing things I want to do	0	1	2	3	4
6	I am satisfied with my present comfort level	0	1	2	3	4
7	I am able to feel like a man	0	1	2	3	4
8	I have trouble moving my bowels	0	1	2	3	4
9	I have difficulty urinating	0	1	2	3	4
10	I urinate more frequently than usual	0	1	2	3	4
11	My problems with urinating limit my activities	0	1	2	3	4
12	I am able to have and maintain an erection	0	1	2	3	4

APPENDIX C

FACT-Cog Version 3

Below is a list of statements that other people with your condition have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	<u>PERCEIVED COGNITIVE IMPAIRMENTS</u>	Never	About once a week	Two to three times a week	Nearly every day	Several times a day
1	I have had trouble forming thoughts	0	1	2	3	4
2	My thinking has been slow	0	1	2	3	4
3	I have had trouble concentrating	0	1	2	3	4
4	I have had trouble finding my way to a familiar place	0	1	2	3	4
5	I have had trouble remembering where I put things, like my keys or my wallet	0	1	2	3	4
6	I have had trouble remembering new information, like phone numbers or simple instructions	0	1	2	3	4
7	I have had trouble recalling the name of an object while talking to someone	0	1	2	3	4
8	I have had trouble finding the right word(s) to express myself	0	1	2	3	4
9	I have used the wrong word when i referred to an object	0	1	2	3	4
10	I have had trouble saying what I mean in conversations with others	0	1	2	3	4

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11	I have walked into a room and forgotten what I meant to get or do there	0	1	2	3	4
12	I have had to work really hard to pay attention or I would make a mistake	0	1	2	3	4
13	I have forgotten names of people soon after being introduced	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

		Never	About once a week	Two to three times a week	Nearly every day	Several times a day
1	My reactions in everyday situations have been slow	0	1	2	3	4
2	I have had to work harder than usual to keep track of what I was doing	0	1	2	3	4
3	My thinking has been slower than usual	0	1	2	3	4
4	I have had to work harder than usual to express myself clearly	0	1	2	3	4
5	I have had to use written lists more often than usual so I would not forget things	0	1	2	3	4
6	I have trouble keeping track of what I am doing if I am interrupted	0	1	2	3	4
7	I have trouble shifting back and forth between different activities that require thinking	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	<u>COMMENTS FROM OTHERS</u>	Never	About once a week	Two to three times a week	Nearly every day	Several times a day
1	Other people have told me I seemed to have trouble remembering information	0	1	2	3	4
2	Other people have told me I seemed to have trouble speaking clearly	0	1	2	3	4
3	Other people have told me I seemed to have trouble thinking clearly	0	1	2	3	4
4	Other people have told me I seemed confused	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	<u>PERCEIVED COGNITIVE ABILITIES</u>	Not at all	A little bit	Some-what	Quite a bit	Very much
1	I have been able to concentrate	0	1	2	3	4
2	I have been able to bring to mind words that I wanted to use while talking to someone	0	1	2	3	4
3	I have been able to remember things, like where I left my keys or wallet	0	1	2	3	4
4	I have been able to remember to do things, like take medicine or buy something I needed	0	1	2	3	4
5	I am able to pay attention and keep track of what I am doing without extra effort	0	1	2	3	4
6	My mind is as sharp as it has always been	0	1	2	3	4
7	My memory is as good as it has always been	0	1	2	3	4

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8	I am able to shift back and forth between two activities that require thinking	0	1	2	3	4
9	I am able to keep track of what I am doing, even if I am interrupted	0	1	2	3	4
	<u>IMPACT ON QUALITY OF LIFE</u>	Not at all	A little bit	Some-what	Quite a bit	Very much
1	I have been upset about these problems	0	1	2	3	4
2	These problems have interfered with my ability to work	0	1	2	3	4
3	These problems have interfered with my ability to do things I enjoy	0	1	2	3	4
4	These problems have interfered with the quality of my life	0	1	2	3	4

APPENDIX D

Cognitive Functioning Scale from the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)

For each item below, please circle one (1) number per line.

During the past week:

	Not at all	A little bit	Quite a bit	Very much
Have you had difficulty in concentrating on things like reading a newspaper or watching television?	0	1	2	3
Have you had difficulty remembering things?	0	1	2	3

APPENDIX E

The Fear of Cancer Recurrence-short form (FCR4, Humphris et al., 2018)

For each item below, please circle one (1) number per line.

	Not at all	A little	Sometimes	A lot	All the time
I am afraid that my cancer may recur	1	2	3	4	5
I am worried or anxious about the possibility of cancer recurrence	1	2	3	4	5
How often have you worried about the possibility of getting cancer again	1	2	3	4	5
I get waves of strong feelings about the cancer coming back	1	2	3	4	5

APPENDIX F

DIETARY QUESTIONNAIRE

Think about the food you've eaten over the past year. Remember breakfast, lunch, dinner and eating out. Please select the option that best describes how often you have consumed each of the following food or drink items.

		Less than 1 time per month	2-3 times per month	1-2 times per week	3-4 times per week	5+ times per week
1	Fruit	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	Vegetables	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	Wholegrains and cereals (including brown rice)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	Dairy products (natural, no added sugar)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5	Protein foods (lean white or red meat, eggs, tofu, legumes/beans)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	Sugar-sweetened soft drinks	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7	Sweet foods (e.g. cakes, pastries, chocolate, lollies)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8	Food from a takeaway or fast-food restaurant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

APPENDIX G

The 6-item version of Need for Cognition Scale (NCS-6, Lins de Holanda Coelho et al., 2018)

For each sentence below, please CIRCLE how uncharacteristic or characteristic this is for you personally.

		Extremely uncharacteristic	.	.	.	Extremely characteristic
1	I would prefer complex to simple problems.	0	1	2	3	4
2	I like to have the responsibility of handling a situation that requires a lot of thinking.	0	1	2	3	4
3	Thinking is not my idea of fun.	0	1	2	3	4
4	I would rather do something that requires little thought than something that is sure to challenge my thinking abilities.	0	1	2	3	4
5	I really enjoy a task that involves coming up with new solutions to problems	0	1	2	3	4
6	I would prefer a task that is intellectual, difficult and important to one that is somewhat important but does not require much thought.	0	1	2	3	4

APPENDIX H

IPQ

The following questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous activities that you did in the last 7 days . Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.				
1	During the last 7 days , on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?	days per week	<input type="checkbox"/> No vigorous activity → Skip to question 3	
2	How much time did you usually spend doing vigorous physical activities on one of those days?	hours per day	minutes per day	<input type="checkbox"/> Don't know/ not sure
Think about all the moderate activities that you did in the last 7 days . Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.				
3	During the last 7 days , on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.	days per week	<input type="checkbox"/> No vigorous activity → Skip to question 5	
4	How much time did you usually spend doing moderate physical activities on one of those days?	hours per day	minutes per day	<input type="checkbox"/> Don't know/ not sure
Think about all the time you spent walking the last 7 days . This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.				
5	During the last 7 days , on how many days did you walk for at least 10 minutes at a time?	days per week	<input type="checkbox"/> No vigorous activity → Skip to question 5	

6	How much time did you usually spend walking on one of those days?	hours per day	minutes per day	<input type="checkbox"/> Don't know/ not sure
<p>The last question is about the time you spent sitting on weekdays during the last 7 days. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.</p>				
7	During the last 7 days , how much time did you spend sitting on a week day ?	hours per day	minutes per day	<input type="checkbox"/> Don't know/ not sure

APPENDIX I

DASS-21

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all - NEVER

1 Applied to me to some degree, or some of the time - SOMETIMES

2 Applied to me to a considerable degree, or a good part of time - OFTEN

3 Applied to me very much, or most of the time - ALMOST ALWAYS

		Never	Sometimes	Often	Almost always
1	I found it hard to wind down	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (e.g., excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I found it difficult to work up the initiative to do things	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I experienced trembling (e.g., in the hands)	0	1	2	3
8	I felt that I was using a lot of nervous energy	0	1	2	3
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting agitated	0	1	2	3
12	I found it difficult to relax	0	1	2	3
13	I felt down-hearted and blue	0	1	2	3
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15	I felt I was close to panic	0	1	2	3
16	I was unable to become enthusiastic about anything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3

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19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life was meaningless	0	1	2	3

APPENDIX J

State Self-compassion scale

HOW I FEEL TOWARDS MYSELF RIGHT NOW

Think about a situation you are experiencing right now that is painful or difficult. It could be some challenge in your life, or perhaps you are feeling inadequate in some way. Please indicate how well each statement applies to how you are feeling toward yourself right now as you think about this situation, using the following scale:

		Not at all true for me				Very true for me
1	I'm giving myself the caring and tenderness I need.	1	2	3	4	5
2	I'm obsessing and fixating on everything that's wrong.	1	2	3	4	5
3	I'm remembering that there are lots of others in the world feeling like I am.	1	2	3	4	5
4	I feel intolerant and impatient toward myself.	1	2	3	4	5
5	I'm keeping things in perspective.	1	2	3	4	5
6	I feel like I'm struggling more than others right now.	1	2	3	4	5

APPENDIX K

COVID-19 questions

For the following questions, please circle the number that best corresponds to your views:

1. How much is COVID-19 affecting your life?										
0 No affect at all	1	2	3	4	5	6	7	8	9	10 Severely affects my life
2. How concerned are you about COVID-19?										
0 Not at all concerned	1	2	3	4	5	6	7	8	9	10 Extremely concerned
3. How much does COVID-19 affect you emotionally? (e.g., does it make you angry, scared, upset or depressed?)										
0 Not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 Extremely affected emotionally

APPENDIX L

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Chief Investigator's / Supervisor's Name & Title: Prof. Kerry Sherman

Characterising prostate cancer patients undergoing hormone therapy: Is there a group of men more at risk of cognitive changes? A Cross-sectional Study

Information for Participants

You are invited to take part in this research study because you either:

- have been treated for prostate cancer.
- do not have prostate cancer.

Research studies include only participants who choose to take part. Before deciding whether or not to take part in this study, it is important that you read and understand the information below. It tells you why we are doing the study, what is involved in it, and any benefits or risks associated with taking part. It also describes your right not to participate or stop taking part in the study at any time. Please ask a member of the study staff to explain anything you do not understand. Make sure all your questions have been answered to your satisfaction before you decide whether or not to participate. Please take your time to make your decision. You can discuss it with your friends and family.

Purpose

The purpose of this study is to learn more about men's experiences with hormone therapy and their cognitive functioning. The results of this study will help us to develop better information resources and tools to support men making decisions about treatment for prostate cancer and those who are undergoing hormone therapy.

Who is conducting the study?

The study is being conducted by Lorna Huang (lorna.huang@hdr.mq.edu.au) to meet the requirements of a Doctor of Philosophy (PhD) degree under the primary supervision of Prof. Kerry Sherman (Kerry.Sherman@mq.edu.au) Deputy Head Department of Psychology. Other associate supervisors include: Dr. Heather Francis, Prof. Howard Gurney, Prof. David Gillatt and

A/Prof. Haryana Dhillon. This research is endorsed by the Australian and New Zealand Urogenital Prostate Cancer Trials Group (ANZUP).

How many people will take part?

Around 150 people who, like you, have or have not been diagnosed with prostate cancer will take part in this study.

What is involved?

If you are interested in taking part in this study, you will be asked to consent to taking part by ticking the ‘yes’ box on the questionnaire. To be eligible for study participation you need to be:

- Over 17 years old;
- Able to read and speak English sufficiently well to respond to written questions;
- Able to provide consent;
- Fit one of three categories:
 - i) diagnosed with prostate cancer, who are currently undergoing hormone therapy;
 - ii) diagnosed with prostate cancer, who have are on ‘watchful waiting’ or ‘active surveillance’;
 - iii) without a prostate cancer diagnosis.

When you have consented, you will fill out a form that asks some questions about:

- You and your life generally
- Diagnosis and treatment
- Health
- Cognition
- Mood
- Intellectual engagement

We will ask you to fill out the online or paper survey one time only. It will take you about 20-30 minutes to fill out the form.

If you and your partner are willing to talk about your experiences further, there is an opportunity to participate in an optional online or telephone interview. Continue reading for more information.

Information about your cancer treatment (if applicable)

You will need to provide some details about your prostate cancer and the treatment you had with your treatment team.

Optional Interview

If you are experiencing cognitive difficulties, we are particularly interested in speaking with you in more detail. We would also like to invite your partner to talk about his/her opinions about any cognitive changes seen in you due to prostate cancer. You and your partner will be compensated for your time with a gift voucher worth \$100 AUD (\$50 each).

If you and your partner are interested in taking part in the interview, you can provide your details (i.e., name, phone number, email address) in the survey. If you are not interested in participating in the interview, please do not provide your details.

A member of the research team may contact those who have provided their details and organise a time to conduct the interview. You have the opportunity to opt out at any time, if you no longer want to participate. Not all participants who have provided their details will be contacted.

The interview will happen with a member of the research team. Your talk with them will be recorded. After the interview is over, the recording will be transcribed (written out exactly as it was recorded) to allow us to go over what was said in detail after. The discussion will be guided by some questions about your experience. The topics we will ask about will include:

- Any cognitive changes you have experienced;
- The types of cognitive changes;
- Impact of these changes on your life.

The interview can be done over the phone, and it will be at a time that suits you. It will take between 30 – 60 minutes of your time, one time only.

If you are interested in doing the interview now but change your mind later, you can let us know that you no longer want to take part when we call. Changing your mind will not affect your treatment, relationship with the medical team, or participation in other parts of the study.

How long will my involvement take?

Both the survey and the interview will take up no more than 1 to 1½ hours of your time in total. The survey being around 20-30 minutes and the optional interview being around 30 -60 minutes.

What will happen to information collected about me?

Information received from you will be accessed and stored by the researchers at Macquarie University. The information will be stored in the secure electronic study database at Macquarie university. The database is protected by passwords, so only people with approval can access it. Any paper surveys you fill out will be scanned and stored on the server, the paper copies will be destroyed by secure shredding. This information will be used to work out the study results.

It will not be possible for anyone to identify you by looking at the database that has your answers to the survey and health information. The information we collect about you will be stored using a code to identify you. Your name, address and contact details will not be stored with your information. The information collected will be kept for at least seven years; when the information is destroyed it will be done securely. The deidentified data collected from the study may be made publicly available in an online repository (as it is becoming a common practice when publishing in scientific journals).

Risks & Benefits

There are no known risks associated with the study. However, you may find the survey questions raise things you had not thought about before. Some people may find the questions upsetting. If this occurs, you can talk to a member of the research team to discuss your concerns. You may alternatively wish to talk to one of the people in your treatment team or your GP.

Taking part in this study will not change your treatment or follow-up with your treating doctor in any way. Taking part in the study may not be of direct benefit to you, but the knowledge gained from this study will help with understanding the best way to care for people with prostate cancer.

What are the costs?

Taking part in this study will not change any of the usual costs of your medical care. You will not be paid for taking part in online or paper survey. If you choose to participate in the online or telephone interview, you will be compensated for your time (see ‘Optional Interview’ section for more details).

What about confidentiality?

Any information or personal details gathered in the course of the study are confidential, except as required by law. Only project researchers will have access to the data. Identifying information will be kept securely. Identifying information will never be included in a publication of the research. There is no intention that the data will be made available for use in future Human Research Ethics Committee-approved projects.

What are your rights as a participant?

The decision to take part in this study is your own. You may choose not to take part or may leave the study at any time. Deciding not to take part or deciding to leave the study later will not affect your care or treatment.

You will be told about new information that may affect your health, welfare, or willingness to stay in this study.

Questions

If you would like to know more about the study at any stage, please feel free to contact Lorna Huang on lorna.huang@hdr.mq.edu.au

Ethics Approval

This study has been approved by the Macquarie University Human Research Ethics Committee.

What you are agreeing to?

By agreeing to participate in this study you are acknowledging that you have read and understood the information above and any questions you have asked have been answered to your satisfaction. You acknowledge that you are agreeing to participate in this research, knowing that you can withdraw from further participation in the research at any time without consequence.

You acknowledge that you will be able to download a copy of this form to keep.

If you have any reservations or concerns about any ethical aspect of your participation in this research, you may contact the Committee through the Director, Research Ethics & Integrity (telephone: (02) 9850 7854; email: ethics@mq.edu.au). Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.

This is an online study. You are under no obligation to participate and will not be given the study URL until you have signed up for the study. In order to sign up for the study, you must agree to the terms of participation noted in the information and consent form.. You are free to stop the survey at any stage.

What can I do if I would like to speak more about my feelings?

If you would like to receive emotional support or further discuss your experiences, Cancer Council Support Line (13 11 20) or Lifeline Counselling Service (phone number 13 11 14) can provide more help. These services are provided free of charge.

PARTICIPANT CONSENT FORM

I,
[name] have read and understood the Information for Participants on the above named research study.

I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the health professionals involved.

I freely choose to participate in this study and understand that I can withdraw at any time.

I also understand that the research study is strictly confidential.

I hereby agree to participate in this research study.

Yes No

Email address to send this information to: _____
Email confirmation: _____

I agree to be contacted about the study interview:

Yes No

Contact number: _____

Email address: _____

My partner agrees to be contacted about the study interview:

Yes No

Contact number: _____

Email address: _____

Participant name:
.....

Participant signature:
.....

Date:
.....

APPENDIX M

Semi-structured interview guide

Hello, _____, How are you going?

I'm here today to understand your perspectives on the impacts of the treatment you've undergone for prostate cancer on your cognition. I just want to remind you that this interview will take around 30-60 minutes of your time. I will be recording and transcribing the interview. It is currently being recorded right now. However, all your information will be confidential and de-identified at the end of the study. Participation is voluntary, and you can withdraw from the study at any time without giving a reason. Are you happy to continue?

Do you have any other questions?

For men with prostate cancer:

Cognitive problems	
<p>I know you have endorsed a number of concerns with your thinking abilities on the survey, what are you main concerns with your thinking?</p> <ul style="list-style-type: none"> • Ask for examples <ul style="list-style-type: none"> ○ Impact on life (e.g., have these difficulties prevented you from doing some of the things you would like to do?) ○ Impact on family life, social life, work? Driving? Future plans? Finances? ADLs? ○ Impact on confidence? • Can you pinpoint when it's generally more worse? Are there times when its better? • When did you or others first notice these concerns? (before/after treatment) <p>You mentioned how you have difficulties _____ after commencing treatment, did you also notice changes to:</p> <ul style="list-style-type: none"> • Memory (e.g., taking in info, forgetting, needing cues to remember) • Working memory (e.g., keeping track of finances, mental calculations) • Attention (easily distracted? Multi-tasking) • Executive functioning (organising, planning, problem-solving, figuring ways to judge different demands of life) • Processing speed (taking you slower to do things) • Language (word-finding, any difficulties understanding or expressing yourself) • Visuospatial (e.g., navigating – reading maps, orienting yourself around the place) • Personality? (e.g., more irritable etc.?) 	
Mood/sleep	
<ul style="list-style-type: none"> • Cognitive changes impacting mood • Mood impacting cognition • History of low mood/anxiety? Ever received a diagnosis or seen a psychologist? • Sleep 	
Coping	
<p>What are some things you do to help manage your cognition? Mood?</p> <ul style="list-style-type: none"> • Cognitive strategies? • Social life? • Activities to keep brain active? • Activities to improve mood? 	

<ul style="list-style-type: none"> • Are you apart of any support groups? Sharing concerns with treating doctor or prostate cancer nurse? 	
Future support	
<ul style="list-style-type: none"> • Have you seen anyone about your concerns with your cognition? • What kind of support would you like? • Would you be interested in taking part of an intervention designed to support cognitive functioning? 	
Is there anything else you think would be important for us to know?	

Ending

Thank you for sharing your insights today! I really appreciate it.

Note: flag anyone who is 'moderate' on DASS-21

I noticed on the survey that you've discussed having concerns about your mood. Are you seeing anybody for these concerns? It may be helpful to share this with your GP so they can work together with you in getting you proper psychological help. They can offer a subsidised mental health care plan. You can also call your prostate cancer nurse, Cancer Council Support Line (13 11 20) or Lifeline Counselling Service (phone number 13 11 14), who can also can provide help.

Partner- Semi-structured interview guide

Cognitive problems	
Have you noticed any changes to your husband/partner's thinking abilities?	
<p>What are your main concerns with his thinking abilities?</p> <ul style="list-style-type: none"> • Ask for examples <ul style="list-style-type: none"> ○ Impact on life (e.g., family life, social life, work? Driving? Future plans? Finances? ADLs?) ○ How do these difficulties affect you? • Can you pinpoint when it's generally more worse? • When did you first notice these concerns? (before/after treatment) <p>You mentioned how he has have difficulties with _____ after commencing treatment, did you also notice changes to:</p> <ul style="list-style-type: none"> • Memory (e.g., taking in info, forgetting, needing cues to remember) • Working memory (e.g., keeping track of finances, mental calculations) • Attention (easily distracted? Multi-tasking) • Executive functioning (organising, planning, problem-solving, figuring ways to judge different demands of life) • Processing speed (taking you slower to do things) • Language (word-finding, any difficulties understanding or expressing yourself) • Visuospatial (e.g., navigating – reading maps, orienting yourself around the place) • Personality? (e.g., more irritable etc.?) 	
Mood/sleep	
<ul style="list-style-type: none"> • Cognitive changes impacting mood? • Mood impacting cognition? • History of low mood/anxiety? 	

• Sleep?	
Coping	
What are some activities he engages in that help him do to help manage HIS cognition? Mood?	
<ul style="list-style-type: none"> • Cognitive strategies? • Social life? • Activities to keep brain active? • Activities to improve mood? 	
Sharing concerns with treating doctor or prostate cancer nurse?	
Future support	
<ul style="list-style-type: none"> • What kind of support would you like him to help him with his cancer journey? • What kind of support would you like? • Are you apart of any support groups? 	
Is there anything else you think would be important for us to know?	

Ending

Thank you for sharing your insights today! I really appreciate it.

I noticed on the survey that you've discussed having concerns about your mood. Refer to Cancer Council Support Line (13 11 20)