Depression, Anxiety, and Their Association to Health-Related Quality of Life in Men Commencing Prostate Cancer Treatment at Tertiary Hospitals in Cape Town, South Africa

Hayley Irusen, MMedSc1, Pedro Fernandez, PhD1, Andre Van der Merwe, PhD1, Sharain Suliman, PhD2, Tonya Esterhuizen, MSc3, John Lazarus, MD4, Jeannette Parkes, MD5, and Soraya Seedat, PhD6

Abstract

Background: Comorbid depression and anxiety in men with localised prostate cancer (CaP) largely go undiagnosed and untreated and their effects on health-related quality of life (HRQOL) in men with CaP should not be underestimated. We examined the prevalence of depression and anxiety and its association with HRQOL in men about to commence treatment for CaP and the differences between treatment groups, radical prostatectomy (RP) and radiation therapy (RT).

Method: One hundred and seven participants from a longitudinal prospective observational study assessing depression, anxiety and HRQOL in men with localised CaP (DAHCaP), were used in this cross-sectional analysis. Data were collected shortly before participants were scheduled to receive their treatment. The Centre for Epidemiologic Studies Depression Scale (CES-D), the State Trait Anxiety Inventory (STAI), the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the European Organisation for Research and Treatment in Cancer Quality of Life questionnaire (EORTC QLQ-C30) and (EORTC QLQ-PR25) were used in this analysis.

Results: Symptoms of depression pre-treatment were noted in 39.3%, state anxiety 28%, trait anxiety 31.4% and prostate cancer anxiety in 12.1% of participants. Statistically significant correlations (P ≤ .05) with the CES-D and a cluster of symptoms on the EORTC QLQ-C30 domains for Global Health (rs = .35), fatigue (rs = .38), pain (rs = .32), dyspnoea (rs = .28), insomnia (rs = .30) and finance (rs = .26) and EORTC QLQ-PR25 domains for urinary symptoms (rs = .43), bowel (rs = .43) and hormone replacement therapy (HRT) (rs = .41) were observed. Statistically significant correlations were also noted between the STAI-S and EORTC QLQ-C30 and EORTC QLQ-PR25. No statistically significant difference was noted between treatments.

Conclusion: More men were depressed than anxious with significant associations with HRQOL prior to commencement of treatment. CaP treatments should focus not only on the prevailing indisposition but include a psychooncological and HRQOL assessment at pre-treatment in high-risk individuals.

1Department of Urology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa
2Department of Psychiatry, Stellenbosch University and SA MRC Genomics of Brain Disorders Unit, Cape Town, South Africa
3Biostatistics Unit, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa
4Department of Urology, Groote Schuur Hospital, University of Cape Town, South Africa
5Department of Radiation Oncology, Groote Schuur Hospital, University of Cape Town, South Africa
6Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

Corresponding Author:
Hayley Irusen, MMedSc, Department of Urology, Faculty of Medicine and Health Sciences, Stellenbosch University, Francie van Zijl Dr, Parow, Cape Town 7500, South Africa.
Email: phirusen@sun.ac.za

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).
Introduction

Cancer is potentially a life-threatening disease involving aggressive treatments that may pose a challenge for patients psychologically. Prostate cancer (CaP) was the second most frequent and fifth leading cause of death worldwide among men in 2020.1 In South African (SA) men CaP is the commonest cancer and the second leading cause of death (13%)2 with a lifetime risk of 1 in 16 for developing the disease.3

This study was conducted within the framework of the public health care service in SA. Mayosi et al, 2014 estimated that the public health care sector in SA provided medical care to approximately 40 million uninsured individuals accounting for about 84% of the population and funded by the government.4 The per capita spend for health care at state funded facilities in SA was estimated at $140 which is 10 times lower compared to private health care.4 Many of these institutions face critical staff shortages, as was illustrated by the collapse of oncology services in one of the country’s 9 provinces, KwaZulu Natal, in 2017, making work onerous for those committed to giving the best medical care to the public.5,6

A key proposition regardless of the challenges experienced by health care teams is to be alert to the psychological (depression and anxiety) needs of men with CaP and its association with HRQOL. If left untreated, psychological impairment comes at great personal and institutional cost. For instance, this has been shown to be associated with increased resource utilization and higher mortality.7-9

The prevalence of depression and anxiety in patients with cancer is substantially higher than that of the general population,10 making a compelling argument for men with CaP at risk to be identified early and managed appropriately. Hartung et al, 2017 observed that in individuals with cancer, the odds of being depressed was 5 times more than that of the general population,11 while Caruso et al, 2016 in their 2016 review, highlighted that depression was 2 to 3 times more frequent in men with CaP compared to the general population. An earlier study by the Johansson group,12 using a self-developed scale, measured depression and anxiety at 43% and 49%, respectively, while a meta-analysis of men with CaP, estimated the prevalence of depression and anxiety prior to treatment at 17.27% and 27.04%, respectively.13

There has been growing interest in the interrelationship between psychological dysfunction and HRQOL. An analysis examining pain in CaP patients found that those without pain had a better HRQOL, and lower levels of depression and anxiety.14 Similarly, men with lower urinary tract symptoms (LUTS) were depressed and anxious with a poorer quality of life.15 However, HRQOL is a multidimensional construct that includes physical, role functioning, social and psychological aspects of well-being and functioning.16 Studies have found that depression and anxiety affect many of the HRQOL domains.17,18 The latter comprise symptom clusters or constellations and was defined by Dodd et al, 2001, as 3 or more concurrent symptoms that are related to each other and may or may not have the same etiology. Cheng and Lee, 2011, established that pain, fatigue, insomnia and mood disturbances was common in elderly patients receiving treatments for cancer and that this cluster affected their quality of life.

In SA, the prevalence of mood and anxiety disorders in the general population was observed at 9.7% and 15.8%, respectively.19 Although psycho-oncological studies of CaP have been increasing elsewhere, few, if any, have explored depression, anxiety and HRQOL in South African men diagnosed with CaP. Our aims were to estimate: (1) depression and anxiety in men with localised CaP (2), the association between depression and anxiety to HRQOL, (3) whether there were differences in depression, anxiety and HRQOL between those receiving RT and RP prior to receiving treatment.

Method

Study Sample

We used baseline data obtained between June 2019 and February 2022 from 107 participants recruited into an ongoing prospective observational study examining depression, anxiety and HRQOL undergoing curative treatments for histologically diagnosed localised prostate cancer (DAHCaP) for this cross-sectional analysis. (Figure 1) Any individual fulfilling the inclusion criteria and about to receive either Radical Prostatectomy (RP) or External Beam Radiotherapy (RT) was included. Consecutive sampling was used.

Description of Setting and Procedures

Participants were recruited from the 2 academic centres Tygerberg Hospital (TBH) and Groote Schuur Hospital (GSH) in the Western Cape, SA. Study data were collected pre-treatment (when participants were scheduled to come into hospital) and then twelve weekly for a year. We used demographic data, the Centre for Epidemiologic Studies Depression scale (CES-D), the State-Trait Anxiety Inventory-State (STAI-S), the State-Trait...
Anxiety Inventory-State (STAI-T), the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), the European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and (EORTC QLQ-PR25) in this analysis. Validated self-administered questionnaires were used. Those who were unable to complete the self-administered validated questionnaire were assisted by the researcher. Study documents were available in English, Afrikaans and isiXhosa, the primary languages in this region.

Prior to the commencement of the study, clinicians involved in screening of participants were presented with an overview of the protocol. Exclusion criteria were hypogonadism, androgen deprivation treatment (ADT) or evidence of metastases.23,24 Men with a confirmed diagnosis of hypogonadism with associated low mood were excluded. 25 Similarly, any participant on ADT was excluded as its effect on mood has been recognised.26

Men with either low or intermediate risk of localised CaP as per the D’Amico classification were invited by the treating clinician to participate in the study.27 The D’Amico Classification is as follows: Low-risk: Prostate Specific Antigen (PSA) ≤ 10, Gleason Score (GS) ≤ 6 and clinical stage T1-T2a. Intermediate risk: PSA between 10 and 20, GS 7 or clinical stage T2b and High risk: PSA > 20, GS ≥ 8 or clinical stage T2c-3a.28 High risk participants were excluded as ADT is often prescribed in these patients.29

Cognitive deficits in the elderly co-occur with depression and include impairment of episodic memory, speed of processing information, executive function and visuospatial ability.30 Eligible participants underwent a pre-eligibility screening test for cognitive impairment (CI) using the 6 Item Screening (SIS) CI test.31,32 Participants with 2 or fewer errors were invited to continue their participation. Those with a positive screen for CI were advised to visit their nearest clinic for further assessment.

Written informed consent was obtained from all eligible participants. The study was approved by Health Research Ethics Committees (HREC) of Stellenbosch University (S19/01/019) and University of Cape Town (UCT) (418/2019). Research principles outlined by the Helsinki Declaration, SA Good Clinical Practice Guidelines and the SA Research Medical Research Council (SAMRC) Ethical Guidelines for Research were followed.

The Mini International Neuropsychiatric Interview (M.I.N.I.) was used as a diagnostic instrument to assess participants for a range of psychiatric disorders such as depression, anxiety, substance use disorders, obsessive compulsive disorders etc. and was administered by a trained rater,33 although these data are not reported here. Participants with obsessive compulsive disorder, alcohol and substance use disorders, for example, as assessed on the MINI, were excluded.

Quality checks were undertaken for missing data both on the paper and electronic version stored on REDCAP, a secure web application for managing surveys. All study data belonging to participants were de-identified using a personal identification number (PIN). The reporting of the study conforms to the STROBE guidelines.34

---

**Figure 1.** Flow diagram of study population. RP, Radical Prostatectomy, RT, Radiation Treatment.
Measures

Demographic and Clinical Variables are shown in Table 1. The Centre for Epidemiologic Studies Depression Scale (CES-D) is a 20 item self-reported scale used to measure symptoms of depression-the sum of which determines the total score. A CES-D score of ≥16 indicated symptoms of depression. Responses reflect the frequency of feelings and behaviours over the past 7 days and were rated on a 4-point scale ranging from 0 (rarely or none of the time) to 3 (most or all of the time). Items number 4, 8, 12 and 16 were reverse scored, and once corrected, an overall score was calculated by summing the scores; higher scores suggest greater levels of depressive symptoms.

The State Trait Anxiety Inventory (STAI) is made up of 2 separate scales and measures state anxiety (STAI-S) and trait anxiety (STAI-T). STAI-S consists of 10 anxiety-absent items (reversed items) and STAI-T comprises 9 anxiety-absent (reversed items). Scores for each range between 20 to 80. STAI-S items assessed the intensity of current feelings (1 = not at all, 2 = somewhat, 3 = moderately so, and 4 = very much so) and STAI-T assessed the frequency of feelings in general (1 = almost never, 2 = sometimes, 3 = often, and 4 = almost always). A cut-off of ≥39 was used to detect clinically significant symptoms. A higher cut-off ≥54 was also applied in this sample as has been suggested as a cut-off for older individuals.

The Memorial Anxiety Scale for Prostate Cancer (MAX-PC) is an eighteen-item questionnaire with a 4-point Likert-type scale. The scale can be scored in its entirety by summing all the items or summary scores and can be grouped into CaP anxiety (11 items), prostate specific antigen (PSA) anxiety (3 items), or fear of recurrence (FOR) (4 items). It consisted of eighteen items with 4 responses and a score range between 0 to 3; a cut-off of ≥27 was used. The total scores ranged between 0 to 54.

The European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-C30) comprises thirty items covering 5 functional scales, 3 symptom scales, 6 symptom items and 2 items on global HRQOL (Table 2). The scores are calculated by averaging items within the scales and transforming average scores linearly so that they range from 0 to 100. On this scale, we used a ≥20 score difference as particularly significant, ≥10 score difference as clinically significant. Scores can detect a higher (“better”) level of functioning and a higher (“worse”) level of symptoms.

The European Organisation for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ-PR25) assesses CaP symptoms and its treatments. Questions are grouped into 4 symptom scales, 2 functional scales and 5 conditional questions ie, sexual function, conditional on being sexually active (4 questions) as well as a question on use of an incontinence aid (Table 3). All items and scale scores of the

Table 1. Demographic and Clinical Variables.

|                          | RP (%) (n = 49) | RT (%) (n = 58) | Total (%) (n = 107) | P value |
|--------------------------|----------------|----------------|--------------------|---------|
| Age in years (Median, IQR)| 61 (57-66)     | 64 (61-69)     | 63 (59-68)         | .016    |
| Race                      |                |                |                    | .134    |
| Black                     | 8.2            | 20.7           | 15.7               |         |
| Mixed ancestry            | 81.6           | 65.5           | 72.9               |         |
| Caucasian                  | 10.2           | 13.8           | 12.1               |         |
| Education                 |                |                |                    | .919    |
| Primary School            | 22.4           | 25.9           | 24.3               |         |
| High School               | 61.2           | 58.6           | 59.8               |         |
| Tertiary Education        | 16.3           | 15.5           | 15.9               |         |
| Employment Status         |                |                |                    | .602    |
| Formally Employed         | 14.3           | 22.4           | 18.7               |         |
| Unemployed/Retrenched     | 22.4           | 19.0           | 20.6               |         |
| Retired/Pensioner         | 49.0           | 50.0           | 49.5               |         |
| Casual Worker             | 14.3           | 8.6            | 11.2               |         |
| Marital status            |                |                |                    | .213    |
| Life Partner              | 79.9           | 69.0           | 73.8               |         |
| No Life Partner           | 20.4           | 31.0           | 26.2               |         |
| History of Smoking        | 89.8           | 75.9           | 82.2               | .060    |
| History of Alcohol        | 93.9           | 81.0           | 86.9               | .050    |
| Medical History           |                |                |                    |         |
| Asthma                    | 2.0            | 6.9            | 4.7                | .236    |
| Heart Disease             | 20.4           | 25.9           | 23.4               | .507    |
| High Blood Pressure       | 65.3           | 63.8           | 64.5               | .871    |
| Diabetes                  | 18.4           | 20.7           | 19.6               | .763    |
QLQ-PR25 were linearly transformed to a 0 to 100 scale with parameters for clinical significance described as above.  

### Statistical Analysis

The IBM SPSS version 27 (IBM Corp. Released 2020, IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp) was used. Scales were summarised using median and inter-quartile ranges by treatment group. Non-parametric Mann-Whitney tests were used to compare distributions of scale scores between groups. Statistical difference was set at $P < .05$.

### Results

One hundred and seven men were included, 49 (RP) and 58 (RT). There was no group difference on demographic and clinical variables except for age, with more participants being younger in the RP group ($P = .016$) and a higher reported history of alcohol use in the RP group ($P = .050$) (Table 1). Approximately 3 quarters (72.9%) of the sample self-reported being of Mixed Ancestry, 15.7% Black and 12.1% Caucasian. Under half (49.5%) were retired/pensioners and 73.8% indicated they had a life partner. Many had received a high school education (59.8%) and

---

### Table 2. EORTC QLQ-C30 Pre-Treatment Scores Compared to Reference Values.

|                      | RP (n = 49)                        | RT (n = 58)                        | Baseline Reference Values |
|----------------------|-----------------------------------|-----------------------------------|--------------------------|
|                      | Median (25th, 75th Percentile)    | Median (25th, 75th Percentile)    | Median (IQR)             | Effect Size**, P-value |
| **Global Health QOL**| 85.71 (71.43, 92.86)              | 85.71 (71.43, 100.00)             | 75 (50, 83.3)            | .01, .924              |
| **Functional Scales**|                                  |                                   |                          |                         |
| Physical Functioning | 30.00 (25.00, 35.00)              | 30.00 (25.00, 35.00)              | 100 (80,100)             | .08, .418              |
| Role Functioning    | 25.00 (25.00, 37.50)              | 25.00 (25.00, 37.50)              | 100 (83,3,100)           | .02, .823              |
| Emotional Functioning| 31.25 (25.00, 43.75)              | 31.25 (25.00, 43.75)              | 83.3 (58,3,100)          | .02, .861              |
| Cognitive Functioning| 25.00 (25.00, 37.50)              | 25.00 (25.00, 37.50)              | 83.3 (83,3,100)          | .06, .527              |
| Social Functioning  | 25.00 (25.00, 37.50)              | 25.00 (25.00, 37.50)              | 100 (66,7,100)           | .03, .795              |
| **Symptom Scales/Items** |                                  |                                   |                          |                         |
| Fatigue             | 33.33 (25.00, 41.67)              | 33.33 (25.00, 50.00)              | 22.2 (0, 44.4)           | .0, .992               |
| Nausea              | 25.00 (25.00, 25.00)              | 25.00 (25.00, 25.00)              | 0 (0, 33.3)              | .04, .694              |
| Pain                | 37.50 (25.00, 50.00)              | 25.00 (25.00, 50.00)              | 0 (0, 33.3)              | .03, .724              |
| Dyspnea             | 25.00 (25.00, 25.00)              | 25.00 (25.00, 25.00)              | 0 (0, 33.3)              | .03, .753              |
| Insomnia            | 50.00 (25.00, 75.00)              | 25.00 (25.00, 50.00)              | 0 (0, 33.3)              | .15, .112              |
| Appetite            | 25.00 (25.00, 25.00)              | 25.00 (25.00, 25.00)              | 0 (0, 33.3)              | .07, .498              |
| Constipation        | 25.00 (25.00, 25.00)              | 25.00 (25.00, 25.00)              | 0 (0, 33.3)              | .13, .180              |
| Diarrhoea           | 25.00 (25.00, 25.00)              | 25.00 (25.00, 25.00)              | 0 (0, 33.3)              | .0, .996               |
| Finance             | 25.00 (25.00, 50.00)              | 25.00 (25.00, 50.00)              | 0 (0, 33.3)              | .0, 1.000              |

A higher score for a functional scale represents healthy functioning and a higher symptom scale/item represents a higher level of symptom expression. A difference of ≥10 is considered a clinically significant difference and ≥20 as particularly significant. Ref. Values used are baseline values pre-treatment for Age (60-69)*40 **43.

### Table 3. EORTC QLQ-PR25 Pre-Treatment Scores.

|                      | RP (n = 49)                                  | RT (n = 58)                                  | Effect Size**, P-value |
|----------------------|---------------------------------------------|---------------------------------------------|-----------------------|
|                      | Median (25th, 75th Percentile)               | Median (25th, 75th Percentile)               | Effect Size**, P-value |
| **Symptom Scales**   |                                              |                                              |                       |
| Urinary Symptoms     | 40.63 (34.38, 34.38)                         | 37.50 (28.13, 46.88)                        | .17, .073             |
| Incontinence Aid     | 25.00 (25.00, 25.00)                         | 25.00 (25.00, 25.00)                        | .02, .861             |
| Bowel Symptoms       | 25.00 (25.00, 31.25)                         | 25.00 (25.00, 31.25)                        | .13, .166             |
| *HRT Symptoms        | 29.17 (25.00, 37.50)                         | 29.17 (25.00, 37.50)                        | .08, .393             |
| **Functional Scales**|                                              |                                              |                       |
| Sexual Activity      | 62.50 (50.00, 75.00)                         | 50.00 (25.00, 75.00)                        | .12, .201             |
| Sexual Functioning   | 56.25 (43.75, 68.75)                         | 50.00 (43.75, 62.50)                        | .14, .161             |

A higher score for a functional scale represents healthy functioning and a higher symptom scale/item represents a higher level of symptom expression. Reference values were not available at the time of writing. HRT, Hormone replacement therapy.

---
15.9%, a tertiary education. The median age (years) of the sample was 63 (IQR: 59 to 68) and per treatment group, RP 61 (IQR: 57 to 66) and RT 64 (IQR: 61 to 69) ($P = .016$). The median income/month in United States Dollars (USD) was $268.55 (IQR: 127.56 to 604.25) and per treatment group, RP $248.53 (IQR: 126.95 to 469.97) and RT 305.63 (IQR: 214.84 to 806.05).

Approximately forty percent of the sample scored ≥16 (CES-D), with 44.9% in the RP and 34.5% in the RT group although the group difference was not statistically significant. The median CES-D score was 13 (IQR: 11 to 18) per treatment group was RP 15 (IQR: 10 to 19) and RT 13 (IQR: 11 to 18).

There were significant correlations between depression and a cluster of HRQOL symptoms. We observed the following statistically significant low to moderate correlations between the CES-D and the EORTC QLQ-C30 and EORTC QLQ-PR25. There was an inverse correlation between EORTC QLQ-C30 and CES-D for Global Health ($r = - .35$, $P < .01$) with those with poor Global Health being more depressed. Positive correlations between CES-D and EORTC QLQ-C30 for fatigue ($r = .38$, $P < .01$); pain ($r = .32$, $P < .01$), dyspnoea ($r = .28$, $P < .01$), insomnia ($r = .30$, $P < .01$) and finance ($r = .26$, $P < .01$) was noted. The following statistically significant correlations between the CES-D and EORTC QLQ-PR25 were also observed, urinary ($r = .43$, $P < .01$), bowel ($r = .43$, $P < .01$), and HRT symptoms ($r = .41$, $P < .01$).

Twenty-eight percent of men scored above the ≥39 cut off (STAI-S) and per treatment: 30.6% (RP) and 25.9% (RT) for state anxiety and was non-significant between treatment groups. As the median age of the sample was 63 years, we analysed the data using the higher ≥54 cut off and 3.7% scored above this. The median STAI-S score was 29 (IQR: 23 to 41). Likewise, the median score per treatment group was RP 31 (IQR: 24 to 43) and RT 28 (IQR: 23 to 41).

The following statistically significant low to moderate correlations between the STAI-S and EORTC QLQ-C30 were observed; a statistically significant negative correlation with Global Health ($r = - .48$, $P < .01$) which implied that those with poor Global Health were more anxious; statistically significant positive correlations between the STAI-S and EORTC QLQ-C30 for pain ($r = .35$, $P < .01$), fatigue ($r = .47$, $P < .01$), dyspnoea ($r = .37$, $P < .01$), insomnia ($r = .30$, $P < .01$) and finance ($r = .42$, $P < .01$) were also noted. The following statistically significant correlations between the STAI-S and EORTC QLQ-PR25 were observed with urinary ($r = .29$, $P < .01$), bowel ($r = .39$, $P < .01$) and HRT symptoms ($r = .33$, $P < .01$) symptoms.

Under a third (31.4%) scored above ≥39 for trait anxiety (STAI-T) and 30.6% (RP) and 25.9% (RT) per treatment group. The median trait score was 32.50 (IQR: 26 to 41). Likewise, the median score per treatment group was RP 32 (IQR: 26 to 40) and RT 33 (IQR: 26 to 42). There was a statistically significant correlation between the STAI-S and STAI-T ($r = .39$, $P < .01$).

Just over ten percent (12.1%) reported CaP anxiety (MAX-PC) while anxiety per treatment group was reported as RP (14.3%) and RT (10.3%). The median score for the sample was 13 (IQR: 11 to 20) and similarly per treatment group median scores were RP 13 (IQR: 11 to 22) and RT 14 (IQR: 12 to 19). The median scores per treatment group for CaP anxiety, PSA anxiety and FOR were as follows; RP: CaP anxiety 4 (IQR: 0 to 14); PSA anxiety 0 (IQR: 0 to 0); FOR 8 (IQR: 5 to 12) and RT: CaP anxiety 3 (IQR: 0 to 8); PSA anxiety 0 (IQR: 0 to 0); FOR 9 (IQR: 6 to 12). There was no statistical difference between treatments.

Higher scores on the EORTC QLC-C30 and PR25 on the function scale indicates better functioning; however, a higher score on the symptom scale denotes worse symptoms. Our analysis for HRQOL showed that there was no statistically significant difference at baseline between treatment groups on the EORTC QLC-C30 and EORTC QLC-PR25. However, compared to the baseline reference values for the EORTC QLC-C30 using a 10-point difference and RT 64; $P = .016$) and a history of alcohol use ($P = .050$). We found that 39.3% of our sample had symptoms of depression, 28% state anxiety, 31.4% trait anxiety and 12.1% CaP anxiety. Compared to an earlier SA prevalence study examining common mental disorders by Herman 2009, some participants (12.1%) were anxious about their CaP as observed on the MAX-PC, with RT participants reporting fear of their cancer returning. Similar findings were noted in a recent systematic review in CaP patients done by James et al, 2022. About a third of the men had trait anxiety suggesting a predisposition to anxiety. Our values for

Discussion

No significant differences in demographic or clinical variables between treatment groups were observed, apart for age (RP, 61 and RT 64; $P = .016$) and a history of alcohol use ($P = .050$). We found that 39.3% of our sample had symptoms of depression, 28% state anxiety, 31.4% trait anxiety and 12.1% CaP anxiety. Compared to an earlier SA prevalence study examining common mental disorders by Herman 2009, the prevalence of anxiety and depression in men with CaP is much higher compared to the general population.

A greater percentage of participants reported anxiety in the RP group. A recent study found that men due to undergo RP were anxious from the time of diagnosis to when they received treatment. Some participants (12.1%) were anxious about their CaP as observed on the MAX-PC, with RT participants reporting fear of their cancer returning. Similar findings were noted in a recent systematic review in CaP patients done by James et al, 2022.
depression and anxiety correspond well with the meta-analysis done by Watts 2014.14 No difference in depression, anxiety and CaP anxiety between treatment groups was observed.

There were statistically significant correlations between depression, state anxiety and a cluster of symptoms on both the EORTC QLQ-C30 (Global Health, fatigue, pain, dyspnoea, insomnia, and finance) and EORTC QLQ-C25 (urinary symptoms, bowel, and HRT). Untreated depression and anxiety have been shown to lower HRQOL and are associated with multiple HRQOL domains47,48 and are referred to as clusters as identified by Dodd et al, 2001. Baden and colleagues,40 2020 estimated that 1 in 13 CaP survivors will experience the pain-fatigue-depressive symptom cluster, which if attended to, may help improve HRQOL. This is supported by findings from a randomised clinical trial examining mediating factors on HRQOL, which showed that pain, fatigue, anxiety and depression had a negative effect.50 Similarly, a recent Swiss CaP survivorship study concluded that the pain, fatigue and depression cluster was associated with a poorer HRQOL.51 An analysis of factors predicting the quality of life in men with CaP, established mental health as a predictor.52,53 Seeman et al, 2018 showed that depressive symptoms had a significant negative effect on the QOL of men with CaP.54 We were unable to account for the correlation between the CES-D and STAI-S with HRT symptoms despite participants not being exposed to ADT. It is possible that this may in part be attributed to late onset hypogonadism (LOH).55 However as both clinical and biochemical features are required to be present for a diagnosis of LOH and in the absence of biochemical evaluation we cannot make this determination.56

Interestingly, we found more participants symptomatic for depression (38.9%) than anxiety (28.3%), consistent with findings made by others.16,48,57 This corroborates earlier studies, which suggest the existence of a paradoxical relationship between anxiety and depression in older patients with CaP, ie, while depression appears to increase with age, anxiety decreases.58-60 It has been proposed that physiological and psychological processes such as decreased emotional responsiveness, increased emotional control and psychological immunization are reasons why older individuals with cancer may have less anxiety and more depressive symptoms and may need more consideration.51 Decreased anxiety in older adults with CaP have been supported by a recent study examining the effect of COVID 19 anxiety on state anxiety.62

Outcomes examining the relationship between depression and anxiety in older adults with CaP have been inconsistent and it has been suggested that brevity, acceptability and coverage of instruments used to measure the parameters under review, the depressive condition under evaluation and the type, stage and phase of the cancer may explain some of the variability in outcomes.12 Furthermore, it has been suggested that the variance in estimates may be attributed to whether the interview was done by a trained psychiatrist (13%) or self-reported (4%-49%).63,64 In addition, the wide range of estimates may in part, also, be due to the fact that the measurement of depression and anxiety in patients with cancer is challenging because of the overlapping symptomatology for both conditions that include fatigue, weight loss, sleep disturbance, loss of appetite and anxiety.46,59

The baseline HRQOL QLQ-C30 scores of our sample, juxtaposed with the baseline reference values for men between 60-69 years of age pre-treatment, are comparatively different. Our participants in both treatment arms rated themselves much better on the Global Health Related QOL on the EORTC QLQ-C30 but reported worse functioning and having more symptoms compared to the reference values. The latter appears to be supported by a study from SA examining contributors to HRQOL which suggested that those from disadvantaged backgrounds have a worse HRQOL.65 It is worth noting the reference values used were obtained using pooled data from clinical and epidemiological studies and participants included in such studies may lend themselves to recruitment bias and possibly explain some of the differences.66 Population demographics may also have contributed to the differences with participants from a lower socio-economic setting included in this analysis. We found that RP participants reported better sexual activity on the EORTC QLQ-PR25 compared to RT group (Table 3). These results point to the likelihood that comparatively, the RP patient were younger (P = .016), and this is in agreement with findings made by Kurian 2018.67

The evidence from this analysis, although self-reported, has several clinical implications not only from an individual context but from a clinical services perspective. Firstly, Walker et al,68 2014 found that major depression was common in patients attending cancer clinics and most go untreated; particularly at risk were people that were socially deprived. Second, a meta-analysis drawn from 76 studies (176 863 patients) confirmed that the relative risk of mortality increased by 17% in patients with depression compared to those without.69 Thirdly, the prevalence of sub-clinical depressive symptoms in the elderly has a significant impact on functioning and warrants clinical intervention.70 Finally, a diagnosis of depression was associated with increased visits to the emergency room, hospitalizations and outpatient visits.7 Similarly within the SA context, it was noted that mental disorders are not only linked to other health conditions but are amongst the costliest medical disorders in terms of the projected health expenditure needed to treat them.8 It should be noted that some authors have argued for alternative CES-D cut-points. For instance, a systematic review which synthesized studies evaluating the accuracy of the CES-D as a screening tool for depression in the general population suggested a cut-point of 20.71 As our study included older individuals with CaP a ≥16 cut-off was used.72

In conclusion, our findings suggest that SA men with CaP are ostensibly depressed and or anxious, both of which are associated with a cluster of symptoms characterized by a decreased HRQOL even before commencing treatments.
Notably we found more men with CaP reported being depressed rather than anxious.

The ramification of untreated anxiety and depression in SA men with CaP may be at an untold cost to both the individual and attending health care provider. In a recent overview of depression in CaP, Sharpley’s group have strongly recommended that screening and a detailed diagnosis of depression should be included as part of urological clinical practice. Given the benefit of an extended life, CaP treatments should not only focus on the prevailing indisposition but include a psycho-oncological and HRQOL evaluation of high-risk individuals thereby ensuring that those years can be purposeful.

The following are possible limitations. Participants attended a publicly funded specialist facility in SA, and therefore these results should not be generalised to other groupings (such as those with access to private health care facilities). As the data used was based on a single time point directionality could not be determined and change in wellbeing could therefore not be assessed. The tools used in this analysis were self-reported validated tools and therefore the reported prevalence may be higher than an interview-based study. Caution should be exercised when interpreting and generalising results given the sample size. Men with known hypogonadism were excluded from the study and therefore the influence of hypogonadism on depression, anxiety and HRQOL could not be ascertained. Participants were screened for cognitive dysfunction and those with cognitive impairment on screening were excluded. Depression and cognitive impairments are known to co-occur, especially in older adults. Inclusion of men with depression at baseline yet exclusion of those with cognitive impairment at may have contributed to sampling bias. Despite this, we believe the following to be the strengths of this study. The data was collected prior to commencement of treatments on urological functioning and symptom status to reduce the likelihood of recall bias. This study has enhanced our understanding of the psychological and HRQOL status of SA men embarking on treatment for CaP and the interrelationship between depression, anxiety and HRQOL. It also provides a springboard for the longitudinal work we are in the process of investigating.

**Future Direction**

These finding highlights the importance of clinicians recognizing depression and anxiety in men commencing treatment for CaP and its negative effect on a cluster HRQOL symptoms and managing appropriately prior to commencement of treatment for CaP. Future work should focus on collaborative care models that integrate multidisciplinary teams to improve access to psychological treatments and should be incorporated into treatment protocols for these patients.

**Acknowledgments**

Thank you to the study participants. We are also grateful to Dr H. Burger, Dr F. Cassim and Dr D. du Plessis for their insights and comments. Sincere thanks to the staff at the Departments of Urology and Radiation Oncology at Tygerberg Hospital and Groote Schuur Hospital, Cape Town, South Africa, and finally our gratitude to Miss K. Kleinhaps for her help on the study.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Ethical Approval**

Ethical approval for the study was obtained from Stellenbosch University (S19/09/019) and the University of Cape Town (418/2019). In addition, research principles outlined by the Helsinki declaration, SA Good Clinical Practice Guidelines and the MRC Ethical Guidelines for Research were followed.

**Funding**

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Research Foundation Thuthuka Grant (No. 117798). The funders were not involved in the design, analysis or writing of this report. A supplemental grant was received from the Harry Crossley Foundation.

**ORCID iDs**

Hayley Irsen [https://orcid.org/0000-0003-0489-0218](https://orcid.org/0000-0003-0489-0218)
Pedro Fernandez [https://orcid.org/0000-0002-8728-9032](https://orcid.org/0000-0002-8728-9032)
Andre van der Merwe [https://orcid.org/0000-0002-2006-8331](https://orcid.org/0000-0002-2006-8331)
Sharain Suliman [https://orcid.org/0000-0001-5510-3128](https://orcid.org/0000-0001-5510-3128)
John Lazarus [https://orcid.org/0000-0003-2417-8332](https://orcid.org/0000-0003-2417-8332)

**References**

1. Sung H, Ferlay J, Siegel RL et al., Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3): 209-249. doi:10.3322/caac.21660.
2. Babb C, Urban M, Kielkowsk D, Kellett P. Prostate Cancer in South Africa: Pathology Based National Cancer Registry Data (1986–2006) and Mortality Rates (1997–2009). Prostate Cancer. 2014;2014:1-9. doi:10.1155/2014/419801.
3. Cancer Association South Africa. Men & Cancer. Mens Health. [https://cansa.org.za/mens-health/](https://cansa.org.za/mens-health/). Published 2022. Accessed June 8, 2022.
4. Mayosi BM, Benatar SR. Health and Health Care in South Africa — 20 Years after Mandela. N Engl J Med. 2014;371(14): 1344-1353. doi:10.1056/NEJMsr1405012.
5. Gray A, Vawda Y. Health Legislation and Policy. South African Health Review 2018. Durban: Health Systems Trust. [http://www.hst.org.za/publications/Pages/SAHR2018](http://www.hst.org.za/publications/Pages/SAHR2018) (2018).
6. Malakoane B, Heunis JC, Chikobvu P, Kigozi NG, Kruger WH. Public health system challenges in the Free State, South Africa: A situation appraisal to inform health system strengthening. *BMC Health Serv Res*. 2020;20(1):58. doi:10.1186/s12913-019-4862-y.

7. Jayadevappa R, Malkowicz SB, Chhatre S, Johnson JC, Gallo JJ. The burden of depression in prostate cancer. *Psycho Oncol*. 2012;21(12):1338-1345. doi:10.1002/pon.2032.

8. Stein DJ, Seedat S. From research methods to clinical practice in psychiatry: Challenges and opportunities in the developing world. *Int Rev Psychiatr*. 2007;19(5):573-581. doi:10.1080/09540260701563536.

9. Gomella LG, Johannes J, Trabulsi EJ. Current prostate cancer treatments: Effect on quality of life. *Urology*. 2009;73(S suppl L):S28-S35. doi:10.1016/j.urology.2009.03.003.

10. Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. *BMJ*. 2018;361:k1415. Published online. doi:10.1136/bmj.k1415.

11. Hartung TJ, Bra¨hler E, Faller H, et al. The risk of being depressed is significantly higher in cancer patients than in the general population: Prevalence and severity of depressive symptoms across major cancer types. *Eur J Cancer*. 2017;72:46-53. doi:10.1016/j.ejca.2016.11.017.

12. Caruso R, Nanni MG, Ribà M, et al. Depressive spectrum disorders in cancer: Prevalence, risk factors and screening for depression: A critical review. *Acta Oncol* (Madr). 2017;56(2):146-155. doi:10.1080/0284186X.2016.1266090.

13. Johansson E, Steineck G, Holmberg L, et al. Long-term quality-of-life outcomes after radical prostatectomy or watchful waiting: The Scandinavian Prostate Cancer Group-4 randomised trial. *Lancet Oncol*. 2011;12(9):891-899. doi:10.1016/S1470-2045(11)70162-0.

14. Watts S, Leydon G, Birch B, et al. Depression and anxiety in prostate cancer: A systematic review and meta-analysis of prevalence rates. *BMJ Open*. 2014;4(3):1-9. doi:10.1136/bmjopen-2013-003901.

15. Gerbershagen HJ, Özgür E, Straub K, et al. Prevalence, severity, and chronicity of pain and general health-related quality of life in patients with localized prostate cancer. *Eur J Pain*. 2008;12(3):339-350. doi:10.1016/j.ejpain.2007.07.006.

16. Coyne KS, Wein AJ, Tubaro A, et al. The burden of lower urinary tract symptoms: Evaluating the effects of LUTS on health-related quality of life, anxiety and depression: EpiLUTS. *BJU Int*. 2009;103(3):4-11.

17. Orbell S, Schneider H, Esbitt S, et al. Health-Related Quality of Life. *Encyc Behav Med*. 2013:929-931. doi:10.1007/978-1-4419-1005-9_753. Published online.

18. Hays RD, Wells KB, Sherbourne CD, Rogers W, Spritzer K. Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. *Arch Gen Psychiatr*. 1995;52:11-19.

19. Wells KB, Sherbourne CD. Functioning and utility for current health of patients with depression or chronic medical conditions in managed, primary care practices. *Arch Gen Psychiatr*. 1999;56:897-904.

20. Dodd MJ, Miaskowski C, Paul SM. Symptom clusters and their effect on the functional status of patients with cancer. *ONF*. 2001;28(3):465-470.

21. Cheng KK, Lee DT. Effects of pain, fatigue, insomnia, and mood disturbance on functional status and quality of life of elderly patients with cancer - 1-s2.0-S1040842810000594.pdf. *Crit Rev Oncol Hematol*. 2011;78:127-137.

22. Herman AA, Stein DJ, Seedat S, Heeringa SG, Moomal H, Williams DR. The South African Stress and Health (SASH) study: 12-month and lifetime prevalence of common mental disorders. *S Afr Med J*. 2009;99(5):339-344.

23. Higano CS. Side effects of androgen deprivation therapy: Monitoring and minimizing toxicity. *Urology*. 2003;61(2 suppl L):32-38. doi:10.1016/S0090-4295(02)02397-X.

24. McKay RR, Feng FY, Wang AY, Wallis CJD, Moses KA. Recent advances in the management of high-risk localized prostate cancer: Local therapy, systemic therapy, and biomarkers to guide treatment decisions. *Am Soc Clin Oncol Educ B*. 2020;40:e241-e252. doi:10.1200/esdbk_279459.

25. Wang C, Nieschlag E, Swdolf R, et al. Investigation, treatment and monitoring of late-onset hypogonadism in males. *Int J Androl*. 2009;32(1):1-10. doi:10.1111/j.1365-2605.2008.00924.x.

26. Dinh KT, Reznor G, Muralidhar V, et al. Association of androgen deprivation therapy with depression in localized prostate cancer. *J Clin Oncol*. 2016;34(16):1905-1912. doi:10.1200/JCO.2015.64.1969.

27. Mottet N, Cornford P, van den BRCN, et al. EUA-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. *Eur Assoc Urol*. 2021:1-211. Published online. http://www.uroweb.org/fileadmin/tx_eauguidelines/2005/Pocket/Prostate_Cancer.pdf.

28. Hernandez DJ, Nielsen ME, Han M, Partin AW. Contemporary Evaluation of the D’Amico Risk Classification of Prostate Cancer. *Urology*. 2007;70(5):931-935.

29. Gunner C, Gulamhusein A, Rosario DJ. The modern role of androgen deprivation therapy in the management of localised and locally advanced prostate cancer. *J Clin Urol*. 2016;9(2 suppl l):24-29. doi:10.1177/2054158616654048.

30. Koenig AM, Bhalla RK, Butters MA. Cognitive functioning and late-life depression. *J Int Neuropsychol Soc*. 2014;20(5):461-467. doi:10.1017/S1355617714000198.

31. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care*. 2002;40(9):771-781. doi:10.1097/01.MLR.0000024610.33213.C8.

32. Ramlall S, Chippis J, Bhigjee A, Pillay B. Screening a heterogeneous elderly South African population for cognitive impairment: The utility and performance of the Mini-Mental State Examination, Six Item Screener, Subjective Memory Rating Scale and Deterioration Cognitive Observee. *Afr J Psychiatr*. 2013;16(6). doi:10.4314/apysj.v16i6.57.

33. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric
34. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Ann Intern Med.* 2007;147(8):573-577. doi:10.7326/0003-4819-147-8-200701160-00010.

35. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977;1(3):385-401. doi:10.1177/014662167700100306.

36. Miller WC, Anton HA, Townson AF. Measurement properties of the CES-D scale among individuals with spinal cord injury. *Spinal Cord.* 2008;46(4):287-292. doi:10.1038/sj.sc.3102127.

37. Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care Res.* 2011;63(suppl 11):467-472. doi:10.1002/acr.20561.

38. Kvaal K, Ulstein I, Nordhus IH, Engedal K. The Spielberger State-Trait Anxiety Inventory (STAI): The state scale in detecting mental disorders in geriatric patients. *Int J Geriatr Psychiat.* 2005;20(7):629-634. doi:10.1002/gps.1330.

39. Roth A, Nelson CJ, Rosenfeld B, et al. Assessing anxiety in men with prostate cancer: Further data on reliability and validity of the Memorial Anxiety Scale for prostate cancer (MAX-PC). *Psycho.* 2006;47(4):5-6.

40. Jurys T, Smolka M, Dzierzawa-Kloza M, Stepanik M, Burzynski B. EORTC QLQ-C30 and EORTC QLQ-PR25 — tools for assessing the quality of life of men suffering from prostate cancer. *Oncol Clin Pract.* 2022;18(1):1-7. doi:10.5603/OCP.2021.0040.

41. Gamper EM, Musoro IJ, Coens C, et al. Minimally important differences for the EORTC QLQ-C30 in prostate cancer clinical trials. *BMC Cancer.* 2021;21(1):1-8. doi:10.1186/s12885-021-08609-7.

42. Giesinger JM, Loth FLC, Aaronson NK, et al. Thresholds for clinical importance were established for interpretation of the EORTC QLQ-C30 in clinical practice and research. *J Clin Epidemiol.* 2020;118:1-8. doi:10.1016/j.jclinepi.2019.10.003.

43. Waraich P, Goldner EM, Somers JM, Hsu L. Prevalence and incidence studies of mood disorders: A systematic review of the literature. *Can J Psychiatry.* 2004;49:124-138. doi:10.1177/0706743704050100206.

44. Irusen H, Burger H, Fernandez PW, et al. Decisional conflict is associated with treatment modality and not disease knowledge in South African Men with prostate cancer: Baseline results from a longitudinal prospective observational study. *Cancer Control.* 2022;29:1-8. doi:10.1177/10732748221082791.

45. James C, Brunckhorst O, Eymech O, Stewart R, Dasgupta P, Ahmed K. Fear of cancer recurrence and PSA anxiety in patients with prostate cancer: A systematic review. *Support Care Cancer.* 2022;30(7):5577-5589. doi:10.1007/s00520-022-06876-z.

46. De Sousa A, Sonavane S, Mehta J. Psychological aspects of prostate cancer: A clinical review. *Prostate Cancer Prostatic Dis.* 2012;15(2):120-127. doi:10.1038/pcan.2011.66.

47. Johansson R, Carlbring P, Heedman Å, Paxling B, Andersson G. Depression, anxiety and their comorbidity in the Swedish general population: Point prevalence and the effect on health-related quality of life. *PeerJ.* 2013;2013(1):1-15. doi:10.7717/peerj.98.

48. Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. *Psycho Oncol.* 2010;19:734-741.

49. Baden M, Lu L, Drummond FJ, Gavin A, Sharp L. Pain, fatigue and depression symptom cluster in survivors of prostate cancer. *Support Care Cancer.* 2020;28(10):4813-4824. doi:10.1007/s00520-019-05268-0.

50. Charalambous A, Giannakopoulou M, Bozas E, Paikousis L. Parallel and serial mediation analysis between pain, anxiety, depression, fatigue and nausea, vomiting and retching within a randomised controlled trial in patients with breast and prostate cancer. *BMJ Open.* 2019;9:1-10. doi:10.1136/bmjopen-2018-026809.

51. Adam S, Thong MSY, Martin-diener E, et al. Identifying classes of the pain, fatigue, and depression symptom cluster in long-term prostate cancer survivors — results from the multi-regional Prostate Cancer Survivorship Study in Switzerland (PROCAS). *Support Cancer Care.* 2021;29:6259-6269.

52. Bellardita L, Rancati T, Francesca M, et al. Predictors of health-related quality of life and adjustment to prostate cancer during active surveillance. *Eur Urol.* 2013;64:30-36.

53. Monahan PO, Champion V, Rawl S, et al. What contributes more strongly to predicting QOL during 1-Year recovery from treatment for clinically localized prostate cancer: 4-weeks-posttreatment depressive symptoms or type of treatment? *Qual Life Res.* 2007;16:399-411. doi:10.1007/s11136-007-9123-9.

54. Seemann T, Pozzobom F, Vieira MCS, Boing L, Machado Z, Guimarães Acde A. Influence of symptoms of depression on the quality of life of men diagnosed with prostate cancer. *Revista Brasileira de Geriatria e Gerontologia* 2018;21(1):70-78. doi:10.1590/1981-22562018021.170114.

55. Haarburger D. *Hypogonadism in the Elderly Male,* 2017. https://www.ampath.co.za/storage/74/pathechat-34-hypogonadism-in-the-elderly-male.pdf

56. Wang C, Nieschlag E, Swerdlow R, et al. Investigation, Treatment, and Monitoring of Late-Onset Hypogonadism in Males: ISA, ISSAM, EUA, EAA, and ASA Recommendations. *Eur Urol.* 2009;55:121-130.

57. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. *Lancet Oncol.* 2011;12(2):160-174. doi:10.1016/S1470-2045(11)70002-X.

58. Weiss Wiesler TR, Nelson CJ, Tew WP, et al. The relationship between age, anxiety, and depression in older adults with...
cancer. *Psycho Oncol*. 2015;24(6):712-717. doi:10.1002/pon.3638.

59. Nelson CJ, Weinberger MI, Balk E, Holland J, Breitbart W, Roth AJ. The chronology of distress, anxiety, and depression in older prostate cancer patients. *Oncol*. 2009;14(9):891-899. doi:10.1634/theoncologist.2009-0059.

60. Jorm AF, Windsor TD, Dear KBG, Anstey KJ, Christensen H, Rodgers B. Age group differences in psychological distress: The role of psychosocial risk factors that vary with age. *Psychol Med*. 2005;35(9):1253-1263. doi:10.1017/S0033291705004976.

61. Jorm AF. Does old age reduce the risk of anxiety and depression? A review of epidemiological studies across the adult life span. *Psychol Med*. 2000;30(1):11-22.

62. Irusen H, Burger H, Fernandez PW, Esterhuizen T, Suliman S, Seedat S. COVID-19 related anxiety in men with localized prostate cancer at tertiary hospitals in the Cape Town, South Africa. *Cancer Control*. 2021;28:1-6. doi:10.1177/10732748211024239.

63. Walker J, Holm Hansen C, Martin P, et al. Prevalence of depression in adults with cancer: A systematic review. *Ann Oncol*. 2013;24(4):895-900. doi:10.1093/annonc/mds575.

64. Krebber AMH, Buffart LM, Kleijn G, et al. Prevalence of depression in cancer patients: A meta-analysis of diagnostic interviews and self-report instruments. *Psycho Oncol*. 2014;23(2):121-130. doi:10.1002/pon.3409.

65. Jelsma J, Ferguson G. The determinants of self-reported health-related quality of life in a culturally and socially diverse South African community. *Bull World Health Organ*. 2004;82(3):206-212.

66. Scott NW, Fayers PM, Aaronson NK, et al. EORTC QLQ-C30 Reference values. *QolEortcOrg*. 2008;(July):1-427. https://www.eortc.org/app/uploads/sites/2/2018/02/reference_values_manual2008.pdf

67. Kurian CJ, Leader AE, Thong MSY, Keith SW, Zeigler-Johnson CM. Examining relationships between age at diagnosis and health-related quality of life outcomes in prostate cancer survivors. *BMC Publ Health*. 2018;18(1):1060. doi:10.1186/s12889-018-5976-6.

68. Walker J, Hansen CH, Martin P, et al. Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: A cross-sectional analysis of routinely collected clinical data. *Lancet Psychiatr*. 2014;1(5):343-350. doi:10.1016/S2215-0366(14)70313-X.

69. Pinquart M, Duberstein PR. Depression and cancer mortality: A meta-analysis. *Psychol Med*. 2010;40(11):1797-1810. doi:10.1017/S0033291709992285.

70. Wittayanukorn S, Qian J, Hansen RA. Prevalence of depressive symptoms and predictors of treatment among U.S. adults from 2005 to 2010. *Gen Hosp Psychiatr*. 2014;36(3):330-336. doi:10.1016/j.genhosppsych.2013.12.009.

71. Vilagut G, Forero CG, Barbaglia G, Alonso J. Screening for Depression in the General Population with the Center for Epidemiologic Studies Depression (CES-D): A systematic review with meta-analysis. *PLoS One*. 2016;11(5):e0155431. doi:10.1371/journal.pone.0155431.

72. Saracino RM, Weinberger MI, Roth AJ, Hurria A, Nelson CJ. Assessing depression in a geriatric cancer population. *Psycho Oncol*. 2017;26(10):1484-1490. doi:10.1002/pon.4160.

73. Sharpley CF, Christie DRH, Bitsika V. Depression and prostate cancer: Implications for urologists and oncologists. *Nat Rev Urol*. 2020;17:571-585.