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Incidence, Structure and Interrelationships of Subsyndromal Depression Symptomatology in Prostate Cancer Patients

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Abstract

Background: Although it has similar disease burden effects as Major Depressive Episode, Subsyndromal Depression (SSD) has not yet been examined in prostate cancer (PCa) patients.
Objective: To describe the prevalence of SSD, its symptom components, and relationships between those components, in a sample of PCa patients.
Methods: 507 Australian PCa patients completed Zung Self-rating Depression Scale (ZSDS). The DSM-IV-TR 10 criteria for Major Depressive Episode were defined and used to detect SSD.
Results: SSD occurred in 17.5% of the sample. Worthlessness and guilt, diminished ability to think or concentrate, and anhedonia were the most common symptoms reported. Anhedonia and concentration difficulties were the most powerful predictors of overall depressive status.
Conclusion: Because of SSD's damaging effects upon patients' functioning and quality of life, it may be valuable to assess this form of depression in PCa patients and use the presenting symptomatology as potential goals for treatment planning (German J Psychiatry 2013; 16(3): 95-102).

Keywords: cancer; oncology; prostate; depression; subsyndromal depression

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Introduction

Prostate cancer (PCa) patients experience distressing levels of depression (Kronenwetter et al., 2005; Kunkel et al., 2000; Sharpley et al., 2008) that are above those for non-PCa age-peers (Couper et al., 2006), and those depressed PCa patients have greater frequency of admission to emergency treatment, hospitalization, outpatient visits and death (Jayadevappa et al., 2011). The most common yardsticks for depression is Major Depressive Episode (MDE) as defined via the DSM-IV-TR (APA, 2000) or scores on standardised scales of depression, such as the Beck Depression Inventory (BDI) (Beck et al., 1961), the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) or the Zung Self-rating Depression Scale (ZSDS) (Zung, 1965), which have cutoff scores indicating if patients are suffering depression that is "clinically significant" or "requiring treatment". A recent review of 56 diagnostic validity studies indicated that several self-report instruments (including the BDI, HADS and ZSDS) "showed promise" (p. 151) as valid measures of DSM-IV-TR-based MDE in cancer populations (Mitchell et al., 2012). While not a substitute for clinical interviews for diagnostic and treatment purposes, self-reports may suffice for research studies with large samples (Fountoulakis et al., 2007).

A formal diagnosis of MDE requires the presence of at least five of the DSM-IV-TR criteria (see Table 1), including criteria 1 and 2 (depressed mood, anhedonia). However, another form of depression called subsyndromal depression (SSD) requires only two of the symptoms for MDE (Judd et al., 1994). The exact definition of SSD was "at least two or more current depressive symptoms, present for most or all of the time, lasting for at least 2 weeks, in individuals who

Table 1: Content analysis of SDS items and DSM-IV-TR criteria for Major Depressive Episode

DSM-IV Criteria for Major Depression (must have at least 5 during a 2-week period, including 1 or 2)	SDS (20 items)
1. Depressed mood for most of the day and on most days	1, 3, 14
2. Diminished pleasure or interest in most activities	6, 18, 20
3. Significant change in weight or appetite	5, 7
4. Insomnia or hypersomnia	4
5. Psychomotor agitation or slowing	9, 13, 15
6. Fatigue or loss of energy	10
7. Feelings of worthlessness or excessive, inappropriate guilt	17
8. Diminished ability to think or concentrate, indecisiveness	11, 16
9. Recurrent thoughts of death or suicide	19
10. Symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning	12
SDS items not addressing DSM-IV-TR criteria	2, 8

did not meet criteria for major depression or dysthmia" (Judd et al., 1996, p. 1411). (It is important to note that SSD requires any two MDE criteria, whereas Minor Depressive Disorder requires at least one of the two key symptoms of depressed mood or anhedonia to be present.)

Judd et al. reported "No large consistent differences in impairment" between patients with MDE and those with SSD across eight domains of functioning (Judd et al., 1996); both depressive groups suffering significantly more than participants with no symptoms of MDE (Judd et al., 1998). The incidence and effects of SSD are particularly relevant in older persons who have SSD because they also have a 5.5-fold chance of developing MDE within one year compared to people who have none of the symptoms of MDE at all (Lyness et al., 2006), and show significantly greater levels of psychological disability, hopelessness and death ideation (Chopra et al., 2005). Other data suggest that elderly SSD patients "are as ill as those with minor or major depression (in terms of) medical burden" (Lyness et al., 2007, p. 214) but is prevalent, underdiagnosed, and undertreated (Goldney et al., 2004; Vanitallie, 2005).

Judd et al. (1997) proposed that SSD might occur in persons with no previous history of depression but who have suffered from a major stressor event, such as receiving a diagnosis of cancer, which is "one of life's most disturbing and dispiriting events" (2003; p. 283). However, to date, there have been no published studies of the incidence and structure of SSD in PCa patients. Therefore, this paper reports on a study designed to assess the incidence of SSD in a sample of PCa patients, to explore the symptom profiles of PCa patients who presented with SSD, and to determine if SSD was related to age, treatment type and cancer status.

Materials and Methods

Subjects

From 965 PCa patients in Brisbane, Australia, who were invited by letter to participate, 508 (52.6%) completed usable questionnaires. All participants had cancers limited to the primary site and regional draining lymph nodes using conventional staging investigations. Treatments included radiotherapy, plus hormone therapy (HT) and surgery. Other inclusion criteria were: (i) the diagnosis of prostate cancer was proven histologically; (ii) all of the treatment options were properly considered by patients via discussion with their GP, a radiation oncologist and a urologist; and (iii) patients were included regardless of the type of HT they had been prescribed. Unwillingness to participate in the study was the only exclusion criterion

Instruments

Background questionnaire: age, living situation, time since diagnosis, treatments received and continuing, present status of their cancer.

Depression: The Zung Self-Rating Depression Scale (SDS) (Zung, 1965) is a standardised paper and pencil test of depression that is one of the three most popular self-report scales for assessing depression (Fountoulakis et al., 2007), and has been used in studies of depression in PCa patients (e.g., Sharpley et al., 2009a; Sharpley et al., 2009b). The SDS was developed from factor analytic studies of the syndrome of depression which underlie the DSM definition (APA, 2000) and includes items for all of the current DSM-IV-TR criteria for Major Depressive Episode (MDE) (see Table 1). Although some reports ask respondents to rate their depression symptoms on the SDS for shorter lengths of time than is used for MDE (i.e., 2 weeks), that decision is "arbitrary" according to the SDS's author (Zung, 1965), and may be adjusted to match the two-week period used for the MDE in the DSM-IV-TR. Therefore, in the present study (as in many previous studies of depression in PCa samples using the SDS), respondents were asked to indicate the frequency "during the last two weeks" of each of the depressive symptoms contained in the 20 items of the SDS by answering in one of four possible ways: "None or a little of the time", "Some of the time", "Good part of the time", or "Most or all of the time". Raw scores range from 20 to 80, with higher scores being indicative of more severe depression. The SDS has split-half reliability of .81 (Zung, 1965), .79 (DeJonge and Baneke, 1989) and .94 (Gabrys and Peters, 1985), and internal consistency (alpha) of .88 for depressed patients and .93 for non-depressed patients (Schaefer et al., 1985), and as .84 and .83 for previous PCa samples (Sharpley et al., 2009b; Sharpley and Christie, 2007). The SDS is superior to the MMPI Depression Scale and the Beck Depression Inventory for assessing depression in male psychiatric inpatients (Schaefer et al., 1985) and has sensitivity of 93% in predicting depression validated via clinical interview among older

Table 2: Background variables

Variable	Mean	SD	Range	
Age	67.87yr	6.99	26-87	
Time since diagnosis	17.93 mo	10.15 mo	0-219 mo	
Living situation	Wife/ partner N (%)	Widowed N (%)	Separated/ divorced N (%)	Never married N (%)
	451 (85.6)	25 (4.7)	34 (6.5)	17 (3.2)
Treatments received (may have received more than one treatment category)	Radio-therapy N (%)	Surgery N (%)	Hormone therapy N (%)	No treatment N (%)
	246 (34.7)	121 (17.2)	179 (25.3)	161 (22.8)
Treatments continuing (*n* = 442)	104 (23.5)	10 (2.3)	170 (38.5)	158 (35.7)
Current PCa status (n = 507)	Under Treatment 286 (50.4)	Remission 192 (37.9)	Recurring 29 (5.7)	

patients (Agrell and Dehlin, 1989). Scores of 40 or above indicate the presence of "clinically significant depression" (Zung, 1973, p. 335). SDS raw scores were used in this study.

Depression symptoms: The 10 criteria for MDE that are listed in the DSM-IV-TR were examined, and the first and second authors (both experienced clinical psychologists in assessing and diagnosing MDE) separately and independently (i.e., without knowledge of each other's ratings during the rating period so as to avoid any bias from that source) allocated each of the 20 SDS items to these 10 criteria. Inter-rater agreement was 100% for this task and the resultant allocation of SDS items to the MDE criteria is shown in Table 1.

Procedure

Participants were recruited by nurses or administration assistant (not the authors) via informal advertisements and verbal invitation to participate in a study about "how you have experienced prostate cancer". After agreeing to participate, patients completed the survey questionnaires individually and anonymously. The questionnaires were stored in a secure location before coding for subsequent data analysis. Ethical approval for this study was obtained from the Wesley Human Research Ethics Committee, Brisbane. All participants gave written consent to take part in the study.

Results

Demographic data

Table 2 presents the background data for the sample. None of these background variables correlated significantly with SDS scores.

Psychometric data

Reliability (Cronbach's alpha) for the SDS was .84, allowing further analysis (Anastasi, 1982). Mean SDS score was 34.92 (SD = 8.81), range = 20 to 66/80. The 5% trimmed mean was 34.58, discounting outlier effects. Skewness, kurtosis, boxplot inspection and examination of the Normal Q-Q Plot and Detrended Normal Q-Q Plot indicated normality. 152 (28.9%) patients fulfilled Zung's (Zung, 1973) criteria for clinically significant depression.

Incidence of SSD

Table 3 presents the mean, SD, median, and ranges for each of the sets of SDS items which comprised the 10 MDE criteria. Because an SDS raw score equal to or greater than 40 (out of a possible score of 80) is an indicator of "clinically significant" depression (Zung, 1973), a 50% score on any of the sets of SDS items that comprise the 10 MDE criteria might also be accepted as indicative of a clinically significant score on each of those criteria. Such a 50% score would equate to 2.0 out of the maximum score of 4.0 for the mean

Table 3: Descriptive data for MDE criteria subsets of SDS items

Criteria	1	2	3	4	5	6	7	8	9	10
Mean	1.422	1.776	1.502	1.801	1.383	1.837	1.786	1.915	1.012	1.057
SD	.504	.941	.643	.952	.484	.886	1.034	.949	.405	.251
Median	1.333	1.50	1.0	2.0	1.333	2.0	1.0	1.50	1.0	1.0
Low	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
High	4.0	4.0	4.0	4.0	3.67	4.0	4.0	4.0	4.0	3.0
Clinically significant	127	219	159	274	84	311	237	255	38	29
% clin. sign.	23.9	41.7	29.9	51.6	15.8	58.6	44.7	48.0	7.2	5.5

values that were used to calculate the SDS item(s) scores for the 10 MDE criteria. Using this criterion, the incidence and percent of clinically significant scores for each of the MDE criteria is shown at the base of Table 3. Using that index of clinicity, 27.7% of the sample did not have a score of 2.00 or above on any of the 10 MDE criteria, 17.3% scored above 2.0 for at least one of the MDE criteria, 14.0% did so for two MDE criteria, 11.2% for three MDE criteria, 11.0% for four MDE criteria, 11.8% for five MDE criteria, 3.7% for six MDE criteria, 2.0% for seven MDE criteria, 1.0% for eight MDE criteria, and 0.4% for nine MDE criteria. These data suggest that, at least according to the yardstick of a 50% score or above on the relevant subset of SDS items comprising each MDE criterion, 46.2% of the sample had scores on at least two of the MDE criteria at a level that that could be considered indicative of clinical significance and might therefore be classified as having SSD.

However, this metric refers to the SDS criteria for clinical significance and not to Judd et al.'s original 1994 requirement (1994) mentioned above that "two or more" but less than 5 of the symptoms of MDE are present "most or all of the time" (Judd et al., 1994). Therefore, further analysis was based upon a score of 4.00 (i.e., "most or all of the time") on the relevant set of SDS items for each MDE criterion. This is the highest rating response possible for participants to give on the SDS and could be accepted as indicative of their rating themselves as suffering extremely on the particular SDS item(s). From that classification, 63.4% of participants did not report any of the MDE symptoms at the 4.0 level of intensity, 17.7% of participants reported one of the MDE criteria at an intensity of 4.0, 9.3% reported two MDE criteria at the most severe intensity, 4.7% reported three MDE criteria at severe intensity, 3.5% reported four MDE criteria at severe intensity, 0.6% for five MDE criteria at that intensity, and 0.4% each for six and eight MDE criteria respectively. In order to eliminate any possible participants who may have met the criteria for MDE, the latter two categories of participants (i.e., those who had 5, 6 or 8 MDE criteria) were not counted when determining the frequency of SSD. Therefore, only participants who had at least 2 but less than 5 MDE criteria were counted (9.3% + 4.7% + 3.5%), giving a total of 17.5% of participants who qualified for a diagnosis of SSD.

By comparison, all 5 participants who had an average score equal to "most or all of the time" for the 3 SDS items which tapped MDE criteria 1 (Depressed mood) also met the full criteria for MDE. However, of the 181 participants who reported that they experienced the 3 SDS items which tapped MDE criteria 2 (Anhedonia) at an average of "most or all of the time", only 7 (3.86%) also met the full criteria for MDE. Only one participant met both of the MDE criteria for Depressed mood and Anhedonia and also met the full MDE criteria. Thus, 5.1% (5 + 7 = 12) of the sample met the criteria for MDE.

Structure of SSD symptom profiles

The frequencies of the 10 MDE criteria for the 53 PCa patients who fell into the SSD category are shown in Figure 1, and indicate that the most common MDE criteria were 7, 8, and 2. Apart from relatively lower frequencies of MDE criteria 4 and 6, there were only very small incidences of the remaining five MDE criteria. Table 4 shows these data broken down across the SSD patient subgroups according to the number of MDE criteria reported. Table 4 also includes the mean frequencies for each of the 10 MDE criteria for patients who reported two MDE and three MDE symptoms respectively (which were significantly similar ($r = .841$, $p < .01$)), as well as the incidence of each MDE criterion for the patients who scored more than three MDE symptoms. It is apparent that the relative greater frequencies of MDE criteria 7, 8 and 2, and (although lower) MDE criteria 4 and 6

Figure 1: Frequency of 10 MDE criteria for all participants with SSD

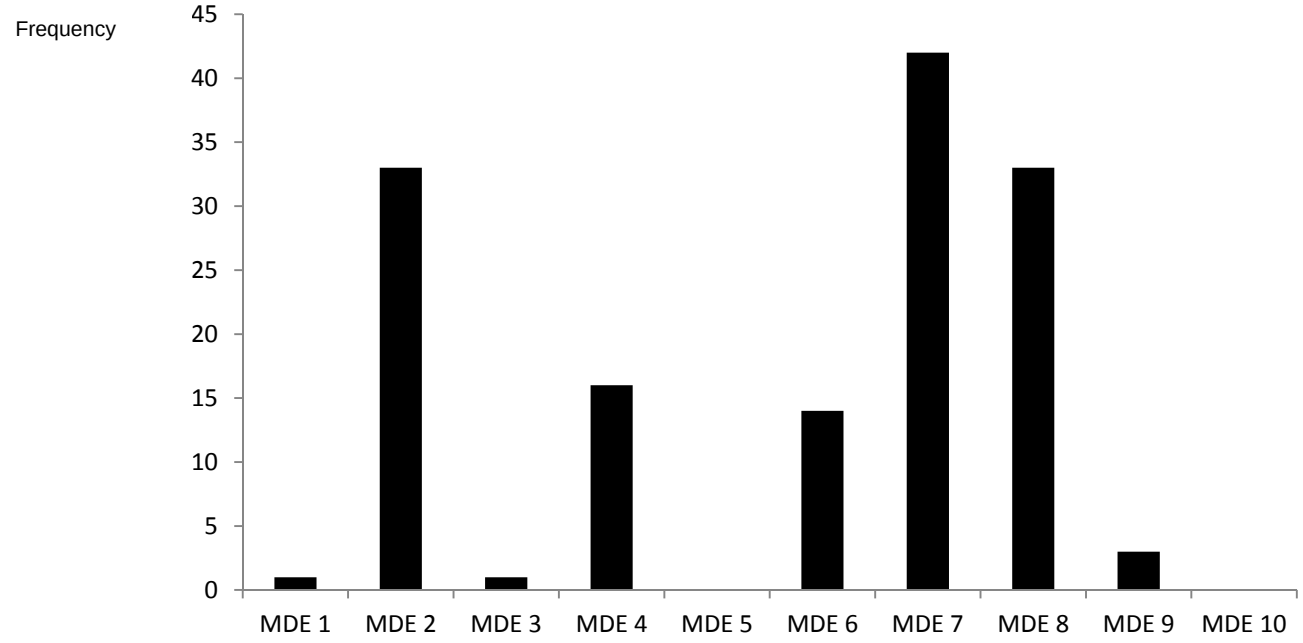

Table 4. Frequencies of MDE criteria across SSD categories

SSD Category/ MDE criterion	MDE symptoms				
	2 *n*=22	3 *n*=28	4 *n*=1	5 *n*=1	6 *n*=1
Criterion 1	0 (0)	0 (0)	0	0	1
Criterion 2	6 (0.27)	24 (0.86)	1	1	1
Criterion 3	0 (0)	1 (0.04)	0	0	0
Criterion 4	8 (0.36)	5 (0.18)	1	1	1
Criterion 5	0 (0)	0 (0)	0	0	0
Criterion 6	6 (0.27)	6 (0.21)	1	0	1
Criterion 7	14 (0.64)	25 (0.89)	1	1	1
Criterion 8	10 (0.45)	22 (0.79)	0	1	0
Criterion 9	0 (0)	1 (0.04)	0	1	1
Criterion 10	0 (0)	0 (0)	0	0	0

over all the other MDE criteria that was shown for all SSD patients in Figure 1 are also consistent across all levels of SSD severity, and identify this subgroup of MDE symptoms as the key aspect of SSD in this sample.

Relationships between SSD criteria and overall depression

Criteria 7, 8, 2, 4 and 6 had mean scores that were within 0.139 (or 3.48% of the possible maximum score of 4) of each other. This suggests some degree of cohesiveness in the way that the sample responded to these SDS items (and the MDE criteria which they comprise). There were two other sets of relatively cohesive mean scores: those for items 9 (1.012) and 10 (1.057) (within 0.045, or 1.125% of each other); and those for items 5 (1.383), 1 (1.422) and 3 (1.502), which were within 0.119 (2.98%) of each other. The correlation matrix for the 10 MDE criteria is shown in Table 5 and suggests that many of the relationships between the 10 MDE criteria were statistically significant. However, with a large sample, the likelihood of obtaining significant correlations is increased, and it is salutary to determine the strength of the relationships by reference to the amount of variance accounted for by each correlation rather than its statistical significance alone. As a yardstick, those correlations which accounted for more than 10% of the variance in scores have been underlined, and provide a more informative way of interpreting the matrix.

Linear regression using the total SDS score minus items 2 and 8 (which were not included in the allocation to MDE criteria: Table 1) as the dependent variable and combined scores for the relevant SDS items for the respective MDE criteria 1 to 10 as the predictor variables produced an R square of .979 ($F(10, 503) = 2{,}304.00$, $p < .001$). Examination of the Beta weights (standardised coefficients) showed that MDE criteria 8 (.303) and 2 (.267) were the most powerful predictors of the reduced SDS total score, but that all the remaining MDE criteria also significantly explained that dependent variable. When hierarchical regression was applied to these data, MDE criteria 2 and 8 accounted for 78.2% of the variance in the DV, MDE criteria 3 and 5 explained an extra 12.40% of the variance in the abbreviated SDS total score, and MDE criteria 1, 4, 6, 7, 9 and 10 explained only another 7.4% of the variance in the DV. On this basis, it may be concluded that anhedonia and concentration difficulties were the most powerful MDE criteria in explaining the overall depressive status of these men, followed by significant weight or appetite change and psychomotor agitation or slowing. Other MDE criteria (depressed mood, sleeping problems, fatigue, feeling worthless, thoughts of death or suicide and impairment in daily functioning) were less influential in explaining the overall abbreviated SDS scores of these men. All assumptions were met for each regression analysis.

MDE symptoms and age, treatment type and cancer status

Pearson correlation coefficients for age of the men in the sample and their scores of each of the MDE criteria were nonsignificant. However, there was a significant direct correlation between age and number of MDE criteria on which patients scored 4.0 (i.e., "most or all of the time") ($r = .107$, $p < .05$), but this relationship explained less than 2.00% of the variance and so should be considered meaningless. MANOVA on those treatments which have been shown to influence mood (radiation therapy, hormone therapy), plus the cancer status of patients (i.e., cancer present, cancer in remission), revealed that there were no significant effects on any of the MDE criteria scores by any of the independent variables, nor any significant interactions; there were also no significant effects on number of MDE criteria on which patients scored 4.0 for any of the independent variables.

Table 5: Correlation matrix for 10 MDE criteria

Criteria	1	2	3	4	5	6	7	8	9	10
1		.604*	.279*	.251*	.380*	.262*	.548*	.530*	.459*	.241*
2			.357*	.135*	.249*	.210*	.755*	.632*	.338*	.167*
3				-.008	.081	.084	.339*	.337*	.023	.105
4					.373*	.368*	.117	.150*	.218*	.111
5						.406*	.218*	.264*	.389*	.294*
6							.145*	.136*	.170*	.139*
7								.630*	.296*	.138*
8									.195*	.128*
9										.201*

* $p < .01$

Assumptions of homogeneity and equality of variance were met for these analyses. When classified into subgroups of patients who met Judd et al.'s (Judd et al., 1994) criteria for SSD (i.e., experiencing two or more MDE symptoms "most or all of the time"), Chi-square analysis showed no significant differences in proportions of patients who were currently receiving radiation therapy, whether their cancer was in remission or remained, or whether they were above or below the mean age of the sample.

Discussion

The first finding of note is that, using Judd et al.'s (Judd et al., 1996; Judd et al., 1994) definition of SSD as two or more symptoms of MDE but less than required for that disorder, over 17% of this sample could be thus described, which is almost twice the rate of 9.9% of older patients in primary care reported by Lyness et al. (1999) and greater than the 15.2% of similar patients reported by Grabovich et al. (Grabovich et al., 2010). While the data from the current study cannot conclude that SSD is a direct outcome of PCa per se (there was no significant correlation between PCa disease severity and SSD score), the fact that these men showed rates of SSD that were nearly twice those for a similarly-aged sample that was in primary care provides some initial support that PCa (like any cancer) may contribute to depression in patients. The rate of MDE in the present sample was 5.1%, which is above the rate of less than 4% reported for men aged 55 years and over in Australia (Henderson et al., 2000). Bearing in mind the previous findings that SSD is associated with significant decreases in quality of life, and that levels of psychological distress may be comparable to those experienced by patients with MDD or MDE, these results support the argument made by some other authors that SSD warrants increased attention by health care providers, and extends that comment to include PCa patients. As mentioned earlier in this paper, no previous studies have been published on SSD in PCa patients, and the present findings could be an indicator of the value of further examination of this kind of depression among this population.

Of similar relevance to the planning and provision of psychosocial treatment options to PCa patients with SSD is the finding that the most common symptom profiles of PCa patients that met the criterion for SSD were concerned with feelings of worthlessness and/or guilt, reduced pleasure in most things, and impaired thinking. Although requiring further examination in other samples of PCa patients, these results suggest potential therapy targets that may be checked with individual patient depression symptom profiles and then used to develop strategies which are focussed upon patients' self-esteem, anhedonia and cognitive confusion and impairment. Also relevant to this process are the somatic symptoms of fatigue and sleeping problems. Although these can be related to the kinds of treatment which PCa patients may undergo (e.g., radiotherapy has been associated with increased fatigue in patients who receive it), there was no significant statistical indicator that the fatigue experienced by this sample was a function of treatment or cancer status, thereby justifying a focus upon fatigue as an outcome of psychological factors and amenable to psychosocial interventions. When examined via regression analysis, anhedonia and cognitive impairment explained the greatest percentage of variance on the abbreviated SDS score, reinforcing the importance of these symptoms as potential psychosocial treatment targets for PCa patients with SSD.

There are some limitations to this study. First, there was no age-matched non-cancer patient sample to make direct comparisons with, requiring a comparison with population-based data. There are some limitations in making such comparisons since the two samples are, by definition, different in that only one has been identified by cancer (whereas cancer will occur within the population data but not be identified as such in depression prevalence data for that population). Second, among any sample of men age 68 years, it is to be expected that depression will be high (O'Connor, 2006). Further, the prevalence of threatening diseases also is higher among older persons, and hence it might be expected that SSD would accompany that prevalence also. However, as noted in the Results, there were no significant correlations between SSD and any of Background variables, including age. In fact, the Pearson correlation coefficient between age and SDS total score (from which SSD status was derived) was $r = .001$, suggesting that age did not play a part in the SSD status of the participants in this study. Third, the sample was restricted in time, culture and geography, and further investigations of the existence and nature of SSD in other PCa populations and at specific periods after initial diagnosis will be valuable in determining the generalisability of the current findings. Fourth, despite the SDS being well-validated in previous studies of depression, possessing satisfactory reliability and having been used with previous samples of PCa patients, it is only one method of detecting the presence of SSD. Finally, although almost all studies of mood disorders in cancer populations refer to "depression", there is an argument for considering a portion of those cases as Adjustment Disorders if they do not fully meet the criteria for Major Depressive Disorder.

Notwithstanding those limitations, these are the first reported data from an examination of SSD in a sample of PCa patients, and the initial findings suggest that further consideration of this form of depression in this population is warranted. Further, the structure of SSD as being reflective of reduced patient self-esteem, anhedonia, and cognitive difficulties provides an initial framework for further investigation of SSD in this population, and also suggests some potential goals and behavioural targets that might be relevant in the delivery of psychosocial treatments for men with PCa who suffer from some of the symptoms of MDE but who do not meet the requirement for the number of symptoms needed to qualify for that diagnosis.

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