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Measuring Individual Burden of Illness for Depression among prostate cancer patients

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Abstract

***Objective*: This study aims to develop and test three potential models of Individual Burden of Illness for Depression (IBI-D) in prostate cancer patients.**

***Methods*: Responses to three sets of scales measuring depressive symptoms, functional impairment, and quality of life satisfaction were collected from 191 prostate cancer patients and analysed via principal components analysis to obtain weightings for each of the scales within the three sets of measures. These weightings were then used to form IBI-D Indices, and these were then compared with depressive symptoms alone for their overlap.**

***Results*: Single-factor solutions were found for each of the three IBI-D models, demonstrating generalizability across the three models. Equations based on the loadings of each scale within each IBI-D model, divided by the standard deviation of total IBI-D scores, were used to form IBI-D Indices. Although the correlations between the Patient Health Questionnaire-9 (PHQ9) and each of these IBI-D Indices were statistically significant, between one-quarter and one-fifth of the variance in IBI-D Indices was not accounted for by PHQ9 score alone, demonstrating that the IBI-D Indices provided additional information above that obtainable from a measure of depression alone.**

***Conclusions*: The IBI-D Index can be used to more completely assess the overall effects of depression in prostate cancer patients, the associations between those effects and predictor variables, and the outcomes of intervention studies aimed at decreasing depression (and its effects) in these men.**

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Although prevalence varies according to study samples, diagnostic procedures, and severity, up to 16% of prostate cancer (PCa) patients suffer from clinically significant depression [1] likely to produce adverse side effects such as reduced treatment compliance and impaired decision making [2]. In addition to reducing the patient's chances of recovery [3], depression among PCa patients has been significantly associated with increased emergency room visits (odds ratio (OR) = 4.45, 95% CI), hospitalization (OR = 3.22), outpatient visits (OR = 1.71), and mortality (hazard ratio = 2.06, 95% CI) as well as increased inpatient pharmacy, laboratory, and physiotherapy costs and higher medical and surgical supply costs [4]. In addition, depressed PCa patients are 1.4 times (95% CI) more likely to suicide during the first year after diagnosis than non-PCa men, with the highest suicide rate within 3 months after diagnosis [5]. The accurate assessment of depression and its effects among PCa patients is therefore a priority for psycho-oncology researchers and for clinicians who wish to develop and implement effective interventions to help these men reduce or avoid depression.

However, although there are several valid and reliable self-report scales that may be used to assess depression in PCa patients, almost all of the items in those scales are focused upon the severity, frequency and duration of the symptoms of Major Depressive Disorder as defined by the DSM-V [6], or similar sets of depressive behaviours and experiences. Although it is important to gather such information about the *symptoms* of depression, the effects of those symptoms upon the PCa patient's *overall functioning* and *satisfaction with the quality of his life* are also important factors when planning treatment and are recommended as vital aspects of the overall assessment of depression according to treatment guidelines [7]. A combination measure of depressive symptoms, resultant functional impairment, and satisfaction with quality of life (QoL) can be used to form an Individual Burden of Illness for Depression (IBI-D) Index similar to the measures used to assess the impact of a disease upon society in general, such as Quality of Life Adjusted Years [8] and Disability Adjusted Life Years [9].

In a recent description of the development of such an IBI-D to general depressed patients (i.e. not PCa patients who are also depressed), IsHak *et al.* [10] used principal components analysis (PCA) of three standardized scales that measured major depressive disorder symptoms, functional impairment, and QoL satisfaction to quantify the relative contribution that each of those three factors made

to overall IBI-D. That particular IBI-D was then applied to the data from the Sequenced Treatment Alternatives to Relieve Depression to 'capture the full burden of illness in depression … (and) offer a more accurate metric of recovery' [11, p. 343]. If it were to be focused upon PCa-related effects of depression, such an index might be valuable to researchers and clinicians who work with PCa patients by providing more information than just symptom severity (as is the case with most self-report scales of depression). That information could thereby enable more focused treatment planning that was based on the extent of functional impairment and overall satisfaction with life in addition to depressive symptoms. As well as being a better clinical practice, such an approach is congruent with the development of 'individualized', 'personalized', or 'precision' medicine, which has been recommended as a major research and treatment goal for depression [12]. Therefore, this study used PCa-relevant scales of depression, functional impairment, and QoL to develop an IBI-D Index for depression among PCa patients. Further, because there has only been one report of the development of IBI-D methods to date and that model was not designed to assess IBI-D in PCa patients, three different models of PCa-related IBI-D were developed and compared for their agreement and the contribution they each made to understanding a PCa patient's overall well-being above that available from using a depression scale alone.

Subjects and methods

Subjects

The present sample was recruited as part of a study on male depression and consisted of 187 PCa patients who returned a survey questionnaire that was posted to 410 PCa patients in Southeastern Queensland, Australia in July 2013. Because we wanted to examine the overall role of IBI-D across a range of treatment states as an initial step in investigating the construct with PCa patients, participants were drawn from a cross-sectional sample. Table 1 shows the range of time since diagnosis and treatment states for the sample. All participants had cancers limited to the primary site and regional draining lymph nodes using conventional staging investigations, and they all had received radiotherapy, plus hormone therapy and surgery when required. There were no obvious or significant differences between responders and non-responders according to their medical records.

Materials

Demographic information. A background questionnaire contained the participants' age, living situation, month and year of first diagnosis, present status of their cancer, and previous and current treatments.

Individual Burden of Illness-Depression Indices

Three versions of an IBI-D Index were developed to test for differences across methodologies for assessing IBI-D. The first (IBI-D Index (1)) used the Patient Health Questionnaire-9 (PHQ9; *depression symptoms*, *severity*, and *frequency*), the Work and Social Adjustment Scale (WSAS; *functional impairment*), and the EORTC C30 (*Cancer-related Quality of Life*). The second (IBI-D Index (2)) also used the PHQ9 and the EORTC C30 but substituted the DSM-IV-TR Global Assessment of Functioning (GAF) scale as a measure of *functional impairment*. The third (IBI-D Index (3)) used the PHQ9

Table 1. Demographic data

Variable	Sample characteristics	
Age ($n = 187$)[a]	$M = 69.6$ years (SD = 8.4 years), range = 51 to 86 years	
Time since diagnosis	$M = 26.9$ months (SD = 11.63 month), range = 4 to 84 months	
Past treatments ($n = 187$)[a]		
Radiotherapy	31	16.6%
Surgery	14	7.5%
Hormone therapy	7	3.7%
Combinations	110	58.8%
No treatment	25	13.4%
Current treatment ($n = 187$)[a]		
Radiotherapy	5	2.7%
Surgery	0	0.0%
Hormone therapy	40	21.4%
Combinations	7	3.7%
No treatment	135	72.2%
Present status ($n = 186$)[a]		
Cancer still present, undergoing initial treatment	47	25.3%
In remission (no signs)	128	68.8%
Cancer recurring after previous treatment	11	5.94%

[a]May have given nil or multiple responses.

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and the GAF but substituted the EORTC PR-25 for the C30 because the former is specifically designed to assess QoL in PCa patients. The use of three IBI-D indices was chosen to provide comparisons in IBI-D outcomes when different scales were used to assess functionality and QoL in PCa patients and thus provide some indication of the generalizability of IBI-D indices obtained from these methods as well as the relative contribution each IBI-D Index made above that obtained from a measure of depression alone.

Scales

Depression

The PHQ9 [13] is a measure of the DSM-IV and V-based diagnostic criteria for major depressive disorder [6]. Each PHQ9 item directly reflects one of those diagnostic criteria, and respondents are asked to indicate how often they have 'been bothered by the following problems during the last two weeks' and are provided with four alternative responses ('Not at all', 'Several days', 'More than half the days', and 'Nearly every day'). An additional single item asks how difficult these problems have made it for respondents to 'do your work, take care of things at home, or get along with other people', although this item is not used when scoring the PHQ9. The PHQ9 possesses excellent validity for patients with severe, moderate, and mild depression when assessed against individual clinical interviews and has good internal consistency (Cronbach's alpha) of 0.89 and 0.86 across two samples [13]. Receiver operating characteristics analysis produced an area under the curve of 0.95, confirming the PHQ9's ability to discriminate between depressed and non-depressed persons [13]. Possible scores on the PHQ9 range from 0 to 27 and may be broken down into ranges of minimal depression (0–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), and severe depression (20–27).

Functional impairment

1. The WSAS [14] is a 5-item scale of functional impairment due to an identified problem and was used in the study by IsHak *et al.* [10] referred to previously that developed an IBI-D for the general population. It has internal consistency of 0.807 to 0.942 (Cronbach's alpha) and a correlation of 0.76 with the Hamilton Rating Scale for Depression [14]. Respondents are asked to provide a rating on an 8-point scale (0 = 'no impairment', 8 = 'severe impairment') of how much their problem has impaired their ability to work, manage their home, engage in leisure activities with others, engage in solitary leisure activities, and form and maintain close relationships.
2. The GAF is derived from Axis V of the DSM-IV-TR [15] and provides a 100-point scale for reporting 'the individual's overall level of functioning' (p. 32). The GAF was first developed by Luborsky [16] and later refined [17] for clinical use. Although present in previous editions of the DSM series, the GAF has been omitted from the DSM-V because it was considered to have limitations of consistency in everyday clinical practice. However, it may still be used as a global self-evaluation of a respondent's functionality in the same way as any question stem that uses a Likert scale such as the WSAS, providing that the parameters of the various points on the scale are made clear to respondents. In this study, the same wording for each stage on the scale was used as that in the DSM-IV-TR, and participants were asked to 'Rate your current level of functioning according to the following scale.' Because the GAF has higher scores representing better functioning, the total score was subtracted from 100 to give a score that was in the same direction as the others used to measure IBI-D.

Quality of life satisfaction

(i) The EORTC QLQ C30 is a 30-item QoL scale developed to assess QoL in cancer patients [18]. Items 1 to 28 tap specific aspects of functioning, and items 29 and 30 ask participants about their overall health and QoL (total scores were used in this study). Cronbach's alpha was reported as >0.70 for the C30, and validity was demonstrated by clinical status of 305 cancer patients from 13 nations [18].

(ii) The EORTC PR25 is a similar instrument to the C30 but designed to assess symptoms that are specific to PCa such as urinary, bowel, and sexual symptoms and functioning, and the side effects of hormonal treatment. Data from its administration to 642 PCa patients in 13 nations indicated satisfactory internal consistency of between 0.70 and 0.86. Results from the PR25 were also shown to discriminate between patients defined on their clinical status [19], thus supporting its validity. Items 1 to 7 and 9 to 21 of the PR25 measure specific aspects of PCa-related symptoms. Item 8 refers to incontinence aids, and items 22 to 28 refer to specific issues of sexual performance. Because only 26 participants in the current study reported wearing incontinence aids, this item was deleted from the data analysis to avoid biasing the results. Similarly, items 22 to 28 ask detailed questions about sexual issues, and over 54% of the sample indicated that these items were not applicable to them. These issues are summarized by items 20 and 21 (interest in sex, sexually activity), and therefore items 1 to 21 (except item 8) were used to measure QoL on this scale.

Approval for this study was obtained from the Uniting Health Care Human Research Ethics Committee.

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Results

Demographic data

Table 1 shows the demographic data for the sample. None of the five background variables showed any significant correlation with the scores from any of the scales used to form the three IBI-D Indices.

Calculation of IBI-D-indices

Each of the three IBI-D-Indices was calculated using the *z*-scores from the various instruments described above (*z*-scores were used to reduce the influence of any single scale's score upon the total IBI-D calculation). The *z*-scores for each scale were then entered into three PCAs using direct oblimin rotation. All correlation coefficients were >0.3, the Kaiser–Meyer–Olkin measures of sampling adequacy were greater than the recommended level of 0.6, and the Bartlett's Test of Sphericity was significant for each PCA (Table 2), thus justifying PCA with these data. Although the three scales within each IBI-D Index were significantly correlated (as might be expected with measures of related constructs), the degree of association was not sufficient as to pose a multicollinearity confound.

In each IBI-D Index, an initial single-factor solution was identified (eigenvalues and percent of variances accounted for are shown in Table 2), and inspection of the scree plots and parallel analyses (cutoff eigenvalue = 1.253) also confirmed those single-factor solutions (Table 2). None of the three sets of scales had communalities of <0.551, indicating satisfactory fit between each set of scales. The component loadings were then used to create the following formulas to obtain each IBI-D index as per the method described by IsHak *et al*. [10], in which the component loadings of the three scales were used to weight the *z*-scores of those scale total scores, all divided by the standard deviation of the IBI-D:

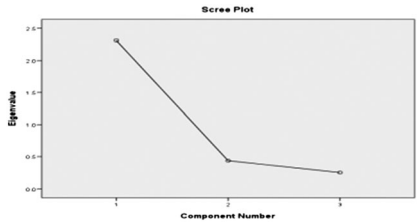
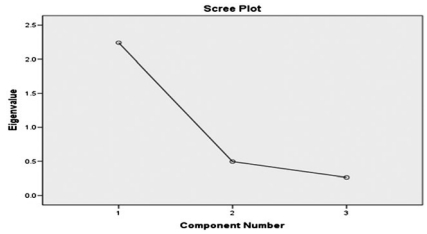
$$\text{IBI-D Index (1)} = [0.880 \times (z\text{PHQ9}) + 0.840 \times (z\text{WSAS}) + 0.912 \times (z\text{C30})]/2.641$$

$$\text{IBI-D Index (2)} = [0.889 \times (z\text{PHQ9}) + 0.806 \times (z\text{GAF Negative}) + 0.894 \times (z\text{C30})]/2.583$$

$$\text{IBI-D Index (3)} = [0.869 \times (z\text{PHQ9}) + 0.785 \times (z\text{GAF Negative}) + 0.742 \times (z\text{PR25})]/1.916$$

Table 3 shows the descriptive statistics for each of the three IBI-D indices, indicating similar distributions of all

Table 2. Principal components analysis outcomes from three Individual Burden of Illness for Depression models

IBI-D Index		Correlation matrices		KMO	Bartlett's Test	Eigenvalues (% variance)	Scree plots
IBI-D (1)		WSAS	C30	0.705	254.135 (3), $p < 0.001$	Factor 1: 2.313 (77.084), factor 2: 0.436 (14.539), factor 3: 0.251 (8.377)	
	PHQ9	0.576	0.736, 0.653				
	WSAS						
IBI-D (2)		GAF	C30	0.693	227.698 (3), $p < 0.001$	Factor 1: 2.241 (74.715), factor 2: 0.495 (16.502), factor 3: 0.263 (8.783)	
	PHQ9	0.554	0.736, 0.566				
	GAF						
IBI-D (3)		GAF	PR25	0.627	121.019 (3), $p < 0.001$	Factor 1: 1.922 (64.060), factor 2: 0.677 (22.564), factor 3: 0.401 (13.376)	
	PHQ9	0.554	0.493, 0.327				
	GAF						

KMO, Kaiser–Meyer–Olkin; IBI-D, Individual Burden of Illness for Depression; WSAS, Work and Social Adjustment Scale; GAF, Global Assessment of Functioning.

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Table 3. Descriptive statistics for three Individual Burden of Illness-Depression (IBI-D) indices

	IBI-D (1)	IBI-D (2)	IBI-D (3)
Mean	−0.0026	−0.0075	−0.0096
Median	−0.2899	−0.2891	−0.3669
Standard deviation	0.937	0.839	1.000
Minimum	−1.79	−1.31	−1.28
Maximum	3.95	3.59	3.98
Skewness	1.412	1.462	1.440
Kurtosis	2.078	2.102	2.017

three Indices and that those distributions were clustered to the lower end of the possible range (skewness) and that the peaks were reasonably normal (kurtosis). These skewness data reflect the largely nonclinical nature of the sample, and the relative homogeneity of the three distributions argues for their interchangeability. That is, the replacement of the functioning and QoL measures did not appreciably alter the results of these indices of overall disease burden from depression among the sample of PCa men.

To determine the extent to which the three IBI-D Indices provided information about these PCa patients that was in excess to that provided by the PHQ9 alone, correlation coefficients between those IBI-D indices and PHQ9 were calculated. For IBI-D (1), the correlation with PHQ9 was 0.872; for IBI-D (2), it was 0.880; and for IBI-D (3), it was 0.887. Although each of these coefficients was statistically significant, the amount of variance in IBI-D (1) not accounted for by the PHQ9 was 24.0%; for IBI-D (2), it was 22.6%, and for IBI-D (3), it was 21.4%. Thus, between one-fifth and almost one-quarter of scores on these IBI-D Indices was not explained by PHQ9 alone, thereby indicating that the addition of the remaining two scales in each IBI-D added to the PHQ9 score and provided an expanded overall description of the burden of disease due to depression that was carried by these patients.

Discussion

The use of assessment data regarding overall functioning and QoL in depressed PCa patients can assist in building a more comprehensive picture of the effects of this psychological disorder in these men than simply symptom frequency and severity of depressive symptoms. As such, this more comprehensive analysis of individual patients can assist in treatment planning and resolution of not only the key symptomatological aspects of depression but also the accompanying effects of those symptoms upon general functioning and the patient's self-evaluation of their QoL. As was noted by IsHak *et al.* [10], this combination of symptoms, functioning, and QoL provides a more comprehensive metric of disease than has been previously reported in studies where such measures have been taken but not included in a single metric [e.g. 20,21]. This provision of a combined measure of all three aspects of depression and its effects allows for more targeted treatments that may then be evaluated for change following treatment rather than simply relying upon symptom reduction *per se*. The IBI-D can also be applied in research settings with PCa patients where it may be that some depressive symptoms are closely related to treatments themselves (such as the effects of hormone therapies) but are a valuable part of an overall PCa treatment regime. These symptoms cannot be ignored simply because they are related to treatment for PCa, and they should be understood as constituting aspects of the depressive state despite their origin in medication (and are thus classified as related to medication in DSM-V). Those symptoms might be understood by patients as an unpleasant side effect of their PCa treatment that, although signifying depressive symptomatology, can be tolerated because of the longer term benefits they may bring to the resolution of PCa. That is, these patients may, via the additional measures incorporated in the IBI-D indices described previously, be able to report that depressive symptoms are present but that functioning and QoL are only marginally affected by those symptoms.

These data were collected from a single treatment centre within a selected social/cultural environment, via self-report scales of depression rather than clinical interviews (although these have been shown to significantly agree), and at a single point in time. Thus, they are limited in generalizability to other settings, populations, and methods. Participants were also self-selected from a postal survey, and IBI-D Index data on non-responders are not available. The choices of scales were based on the criteria of validity and reliability with PCa patients, but other instruments might be substituted in future studies.

However, notwithstanding those common limitations, the results of this study provide the first published information on the ways that an IBI-D Index might be constructed for PCa patients, the equations for three such IBI-D indices, and the amount of extra information that such indices provide beyond that from a scale of depression alone. As such, these findings raise the issue of how best to evaluate PCa patients' depression and suggest a possible method of gathering more comprehensive data on how depression affects these men in addition to how intense and frequent their depressive symptomatology is when they are assessed in clinical or research settings. Further, as reported by IsHak *et al.* in their application of the IBI-D they developed to the Sequenced Treatment Alternatives to Relieve Depression data [11], these IBI-D Indices for PCa patients might be valuable tools to measure the association between factors that have been associated with depression in PCa patients (e.g. marital harmony, hormone therapy, previous depression, anxiety), as well as being an informative outcome measure of the effects of interventions designed to reduce depression in these men.

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Conflict of interest

The authors have declared no conflicts of interest.

References

1. Sharpley C, Christie D. An analysis of the psychometric structure and frequency of anxiety and depression in Australian men with prostate cancer. *Psycho-Oncology* 2007;**16**:660–667.
2. Christie KM, Meyerowitz BE, Giedzinska-Simons A, Gross M, Agus DB. Predictors of affect following treatment decision-making for prostate cancer: conversations, cognitive processing, and coping. *Psycho-Oncology* 2009;**18**:508–514.
3. Thomas B, Thomas I, Nandamohan V, Nair M, Pandey M. Screening for distress can predict loss of follow-up and treatment in cancer patients: results of development and validation of the Distress Inventory for Cancer Version 2. *Psycho-Oncology* 2009;**18**:524–533.
4. Jayadevappa R, Malkowicz S, Chhatre S, Johnson J, Gallo J. The burden of depression in prostate cancer. *Psycho-Oncology* 2011;**21**:1338–1345.
5. Fang F, Keating N, Mucci L, *et al*. Immediate risk of suicide and cardiovascular death after prostate cancer diagnosis: cohort study in the United States. *J Natl Cancer Inst* 2010;**102**:307–314.
6. APA. Diagnostic and Statistical Manual of Mental Disorders-V. American Psychiatric Association: Washington, DC, 2013.
7. APA. Practice guidelines for the treatment of patients with major depressive disorder. American Psychiatric Association; 2010 [cited 2013 Nov 12].
8. Zeckhauser R, Shepard D. Where now for saving lives? *Law Contemp Probl* 1976;**40**:5–45.
9. Murray C. Quantifying the burden of disease: the technical basis for disability-adjusted life years. *Bull World Health Organ* 1994;**72**:429–445.
10. IsHak W, Greenberg J, Saah T, *et al*. Development and validation of the Individual Burden of Illness Index for Major Depressive Disorder (IBI-D). *Adm Policy Ment Health Ment Health Serv Res* 2011;**40**:76–86.
11. Cohen R, Greenberg J, IsHak W. Incorporating multidimensional patient-recorded outcomes of symptoms of severity, functioning, and quality of life in the Individual Burden of Illness Index for Depression to measure treatment impact and recovery in MDD. *JAMA Psychiatry* 2013;**70**:343–350.
12. NIMH. The National Institute of Mental Health Strategic Plan. National Institute of Mental Health: Washington, DC, 2008 [updated August 2008; cited 2013 June 1, 2013]; Available from: http://www.nimh.nih.gov/about/strategic-planning-reports/index.shtml#strategy-objectives.
13. Kroenke K, Spitzer R, Williams J. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;**16**:606–613.
14. Mundt J, Marks I, Shear M, Greist J. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. *Br J Psychiatry* 2002;**180**:461–464.
15. APA. Diagnostic and Statistical Manual of Mental Disorders (4th edn, Text Revision). American Psychiatric Association: Washington, DC, 2000.
16. Luborsky L. Clinicians' judgments of mental health. *Arch Gen Psychiatry* 1962;**7**:407–417.
17. Endicott J, Spitzer R, Fleiss J, Cohen J. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry* 1976;**33**:766–771.
18. Aaronson NK, Ahmedzai S, Bergman B, *et al.* The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;**85**:365–376.
19. van Andel G, Bottomley A, Fosså S, *et al.* An international field study of the EORTC QLQ-PR25: a questionnaire for assessing the health-related quality of life of patients with prostate cancer. *Eur J Cancer* 2008;**44**:2418–2424.
20. Molenaar P, Dekker J, Hendriksen M, Vink A, Schoevers R. Does adding psychotherapy to pharmacotherapy improve social functioning in the treatment of outpatient depression? *Depress Anxiety* 2007;**24**:553–562.
21. Waern M, Rubenwitz E, Runeson B, Skoog I, Wilhelmson K, Allebeck P. Burden of illness and suicide in elderly people: case control study. *Br Med J* 2002;**324**:1355–1358.