


# Screening for Emotional Disorders in Patients With Cancer Using the Brief Symptom Inventory (BSI) and the BSI-18 Versus a Standardized Psychiatric Interview (the World Health Organization Composite International Diagnostic Interview)

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**BACKGROUND:** Given the adverse consequences of psychiatric and psychosocial morbidity on the quality of life for patients with cancer, prompt detection of psychological symptoms is mandatory. The authors examined the properties and accuracy of the Brief Symptom Inventory (the 53-item version [BSI] and the 18-item version [BSI-18]) for the detection of psychiatric morbidity compared with the World Health Organization Composite International Diagnostic Interview (CIDI) for International Classification of Diseases-10th Revision psychiatric diagnoses. **METHODS:** A convenience sample of 498 patients with newly diagnosed cancer who were recruited in cancer outpatient services participated in the CIDI interview and in BSI and BSI-18 assessments. **RESULTS:** The prevalence of psychiatric morbidity was 39.75%. When participants were classified as cases using the BSI standard case rule, agreement with the CIDI was potentially acceptable (sensitivity, 72.7%; specificity, 88.7%). In contrast, the accuracy of the BSI-18 in identifying cases was poor according to the standard case rule, with very low sensitivity (29.3%) (misclassification rate, 28.7%). By using a first alternative case-rule system (a BSI-18 global severity index [GSI] T-score  $\geq 57$ ), sensitivity marginally improved (45%), whereas a second alternative case-rule system (a GSI T-score  $\geq 50$ ) significantly increased sensitivity (77.3%). In receiver operating characteristic curve analysis, a further cutoff GSI T-score  $\geq 48$  exhibited good discrimination levels (sensitivity, 82.3%; specificity, 72.4%). There were some differences in GSI cutoff T-scores according to the International Classification of Diseases-10th Revision diagnosis and sex. **CONCLUSIONS:** The BSI appeared to have acceptable diagnostic accuracy compared with a standardized psychiatric interview. For the BSI-18, it is mandatory to use alternative case-rule systems, to identify patients with psychiatric morbidity. *Cancer* 2018;124:2415-26. © 2018 American Cancer Society.

**KEYWORDS:** cancer, consultation-liaison psychiatry, diagnostic accuracy, psychiatric morbidity, psycho-oncology, screening.

## INTRODUCTION

Since the Psychosocial Collaborative Oncology Group (PSYCOG) multicenter study, which was carried out more than 30 years ago in the United States on 215 outpatients with newly diagnosed cancer,<sup>1</sup> a number of other investigations in several countries, such as Australia,<sup>2,3</sup> Belgium,<sup>4</sup> Germany,<sup>5,6</sup> Italy,<sup>7</sup> Spain,<sup>8</sup> and the United Kingdom,<sup>9</sup> have confirmed a prevalence of psychiatric morbidity of approximately 35% to 40%, as assessed using either standardized, semistructured interviews (eg, the World Health Organization [WHO] Composite International Diagnostic Interview [CIDI] from the International Classification of Diseases [ICD]) or structured interviews (eg, the Structured Clinical Interview [SCID] from the Diagnostic and Statistical Manual for Mental Disorders [DSM]). The rates of depression, anxiety, and adjustment disorders<sup>10</sup> among patients with cancer, are higher than those in general population controls,<sup>11</sup> with negative consequences in reducing patients' coping abilities, quality of life, adherence to treatment, response to primary chemotherapy, and wish to live.<sup>12</sup> Consequently, guidelines have been developed by several cancer agencies and national cancer-control institutions worldwide that have stressed the need to routinely screen patients with cancer for psychological disorders and emotional distress, for example, using distress as the sixth vital sign,<sup>13,14</sup> within a whole person-centered cancer-care approach.<sup>15-19</sup>

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Although structured and semistructured psychiatric interviews are considered the gold standard in terms of establishing psychiatric morbidity, such interviews are not easily applicable in routine cancer care for several reasons, including the time needed to administer the interview to each individual patient, low awareness/confidence by nonspecialists of the medical team, and the perception that this is not their specific role.<sup>20</sup> Therefore, several short and ultra-short psychometric tools have been validated to be applied in oncology. However, ultra-short tools (eg, the 1-item National Comprehensive Cancer Network Distress Thermometer [DT]) cannot be used alone to diagnose depression, anxiety, or distress in patients with cancer because of their low specificity.<sup>21-23</sup> Other instruments (eg, multi-item scales) have been assessed as adequate for screening purposes (namely, to rule out those who do not have a diagnosis) but not for case-finding purposes in confirming clinical caseness.<sup>24-26</sup> Furthermore, brief screening tools usually tend to target 1 dimension, such as depression, leaving others, such as irritability, interpersonal sensitivity, suicidality, obsessive thoughts, or anxiety, unaddressed.

Among the self-administered tools, the Brief Symptom Inventory (BSI), which was derived from the longer 90-item Symptom Check-List-90 R (SCL-90-R) and consists of 53 items, is a more complete instrument and covers a series of psychological symptoms (eg, phobic anxiety, depression, irritability, interpersonal sensitivity, psychoticism). The BSI has been the focus of several studies in patients with cancer and has exhibited good levels of sensitivity and specificity compared with other psychometric tests (rather than more accurate structured psychiatric interviews).<sup>27-29</sup> The shorter 18-item version of the BSI (the BSI-18), also has been introduced as a more easily administered version for use in busy oncology clinics.<sup>30</sup> A 3-dimensional factorial structure (ie, somatization, anxiety, and depression) was identified both in adult survivors of childhood cancer<sup>31</sup> and in patients with breast cancer<sup>32</sup> and pancreatic cancer,<sup>33</sup> supporting the structural validity of the BSI-18. When examined for screening purposes, compared with other psychometric tools as gold standards, the BSI-18 was identified as superior to the DT among outpatients with cancer<sup>34</sup> and long-term survivors of cancer<sup>35</sup>; however it was inappropriate for detecting cases,<sup>36</sup> exhibiting lower sensitivity compared with the expanded SCL-90 questionnaire.<sup>37,38</sup>

A strong limitation of current research is that very few data are available regarding the case-finding properties of the BSI-18 compared with a formal psychiatric assessment, which indeed is the reference gold standard for

diagnosis, rather than the other psychometric tools used in most studies to examine accuracy in detecting caseness. With respect to this, a recent study of 250 young adult cancer survivors indicated that the BSI-18 had good overall concordance with the SCID psychiatric interview for making diagnoses according to the DSM, but the recommended cutoff scores failed to identify the majority of patients with psychiatric diagnosis.<sup>39</sup>

Given this background, the objective of the current study was to examine the characteristics of the BSI and its shorter version (the BSI-18) compared with a structured psychiatric interview, as a gold standard, among patients with cancer in Italy and within a wider European study.<sup>40-42</sup>

## MATERIALS AND METHODS

### *Patients*

A convenience sample of newly diagnosed outpatients and day-hospital patients with cancer from 4 hospitals in the same catchment area (University S. Anna Hospital, Ferrara, Northern-East Italy, and 3 other Community Health Authorities hospitals in the province of Ferrara) were contacted individually by psychosocial research assistants from the psychooncology service and by workers in the cancer wards during 1 of their visits. Criteria for recruitment were: 1) a diagnosis of cancer within 6 months; 2) a Karnofsky performance status score  $>80$ <sup>43</sup>; 3) no clinically significant cognitive deficits (as assessed through the 10-question abbreviated mental test to explore orientation in time, space, and person; attention and concentration; capacity to read and write; and memory),<sup>44</sup> or central nervous system involvement by disease (eg, brain tumors, brain metastases, psychoorganic side effects of therapy); and 4) age between 18 and 70 years. Patients who had mood or anxiety disorders clearly related to their medical condition (organic mental disorders) or who had substance use disorders (dependence and abuse of alcohol and nicotine), schizophrenia, psychotic disorders, or personality disorders (eg, borderline or antisocial personality disorder) were excluded from the analysis.

This study was approved by the ethical committee or related boards of the participating hospitals. Each patient was informed by the researcher performing the interview about the objective of the study. After each patient provided his or her written consent to participate, an individual appointment was planned in the outpatient cancer service.

The WHO CIDI, as used previously in its Italian version in other studies,<sup>45,46</sup> was administered by trained interviewers according to the methodology we applied in

a previous investigation of patients with cancer<sup>47</sup> to make a psychiatric diagnosis according to the ICD-10th Revision (ICD-10). For the specific purpose of this study, of the several areas explored by the CIDI, the interview was concentrated mainly on mood disorders (unipolar and bipolar depression), anxiety disorders (including stress-related disorders), adjustment disorders, and somatoform disorders.

After the interview, the BSI was administered to assess psychosocial morbidity. The BSI<sup>48</sup> is a 53-item questionnaire that evaluates psychological stress symptoms during the past 7 days. Each item is rated on Likert scale from 0 (not at all) to 4 (extremely), and responses are summed to provide the following symptom scales: depression, somatization, obsessive-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. Together, these scales yield a global score (the global severity index [GSI]), which reflects both the number and severity of all items endorsed. Three other scores also can be computed, the grand total (GT) (the sum of raw scores from the 53 items), the positive symptom total (PST) (the number of all *nonzero* responses made by the patient), and the positive symptom distress index (PSDI) (obtained by dividing the GT by the PST).

The BSI-18,<sup>49</sup> as a short-form scale, consists of 18 items extrapolated from the BSI but, unlike the BSI, it has only 3 symptom scales: somatization (6 of the 7 items from the original BSI somatization subscale), depression (6 items, corresponding to the BSI depression subscale), and anxiety (6 items, corresponding to the BSI anxiety subscale).<sup>49</sup> For the BSI, each item is rated on the same 0 to 4 Likert scale in the last 7 days, and the sum of responses to the items yields a global severity index (GSI). Sociodemographic and clinical data also were gathered from the patient and the patient's records.

### Scoring Procedure

Participants completed the BSI, and their responses were analyzed according to the scoring system provided in the manual. BSI scores were converted to standardized T-scores, as recommended,<sup>48</sup> with *cases* (estimated psychological morbidity) identified by a cutoff T-score of  $\geq 63$  points on the GSI or on 2 primary subscales. This case rule exhibited good levels of sensitivity and specificity for the identification of caseness in previous Italian studies of patients both with<sup>50,51</sup> and without<sup>52,53</sup> cancer.

According to the procedure described by Recklitis and Rodriguez,<sup>37</sup> the 18 items constituting the BSI-18 were taken from the completed BSI forms to generate the

BSI-18 scores, which were re-scored in the respective subscales. The case rule specified by the BSI-18 manual<sup>49</sup> for identifying respondents who have clinically significant symptom elevations is similar to the rule used with the BSI, with a respondent considered positive on the BSI-18 if the GSI T-score or any 2 subscale T-scores are 63 or greater. However, as noted by Recklitis and Rodriguez,<sup>37</sup> with only 3 subscales, this case rule would be likely to operate somewhat differently in the BSI-18. Indeed, when validating the BSI-18 compared with the BSI in a sample of adult patients who had cancer, Zabora et al<sup>28</sup> suggested using a case rule based only on a GSI score corresponding to the 75th percentile (ie, a GSI T-score  $\geq 57$ ) as an alternative and more effective method for identifying individuals with elevated levels of psychological distress (*cases*). On the same basis, Recklitis and Rodriguez<sup>37</sup> reevaluated the BSI-18 and observed that a less conservative case rule based on a GSI T-score  $\geq 50$  maximized the possibility of classifying a respondent as a clinical case. Unlike other authors, Zabora et al<sup>28</sup> also carried out an analysis of the BSI-18 by sex and suggested using the raw total GSI score (range, 0-72), with cutoff scores of  $\geq 10$  for men and  $\geq 13$  for women, to maximize specificity and sensitivity for identifying caseness.

Therefore, in the current study, we evaluated BSI-18 responses by using all of the above-mentioned scoring systems; namely, the original standard system (a GSI T-score or any 2 subscale T-scores  $\geq 63$ ), the Zabora case-rule system (a GSI T-score  $\geq 57$ ), the Recklitis case-rule system (a GSI T-score  $\geq 50$ ), and the Zabora case-rule system by sex (raw GSI scores of  $\geq 10$  for men and  $\geq 13$  for women). We also explored other possible cutoff scores for detecting caseness in our sample.

### Statistical Analysis

Distribution and frequency analyses were used to describe the sample. Cronbach  $\alpha$  values were used to examine the reliability and internal consistency of the instruments. Student *t* tests, analyses of variance, and chi-square tests were used to analyze differences between samples. The sensitivity (ie, the probability that the test result will be positive when the disease is present [the true-positive rate]), specificity (ie, the probability that the test result will be negative when the disease is not present [the true-negative rate]), positive predictive value (PPV) (ie, the probability that the disease is present when the test is positive), and negative predictive value (NPV) (ie, the probability that the disease is not present when the test is negative) of different scores on the psychometric instruments were examined for their ability to discriminate

**TABLE 1.** Sociodemographic and Clinical Characteristics of the Patients

Characteristic	No. of Patients (%)	Characteristic	No. of Patients (%)
Age: Mean $\pm$ SD [range], y	54.8 $\pm$ 10.6 [22-70]	Education: Mean $\pm$ SD [range], y	9.3 $\pm$ SD [5-18]
Sex		Cancer site	
Men	176 (35.4)	Gastrointestinal	
Women	322 (64.6)	Breast	214 (43)
KPS: Mean $\pm$ SD	96.2 $\pm$ 7.9	Genitourinary	104 (21)
Marital status		Respiratory	72 (14.4)
Never married	39 (7.8)	Other	18 (3.6)
Separated/divorced	25 (5.1)	Stage	
Married	327 (65.7)	Local	225 (45.2)
Widowed	107 (21.5)	Locoregional	140 (28.1)
Occupation		Metastatic	119 (23.9)
Employed	152 (30.5)	Free	14 (2.9)
Unemployed	78 (56.6)	Treatment	
Housewife	122 (24.5)	Chemotherapy	254 (51)
Retired	27 (25.5)	Chemotherapy + radiotherapy	60 (12)
Other	12 (2.4)	Hormone therapy	184 (37)
Unknown	7 (1.4)	Surgery	
		Yes	220 (74)
		No	82 (26)

Abbreviations: KPS, Karnofsky performance status; SD, standard deviation.

between ICD-10 cases and noncases. The area under the receiver operating characteristic (ROC) curve (the AUC) was used to summarize the diagnostic utility of the BSI and the BSI-18, and ROC analysis was used to explore the optimal cutoff for detecting cases in our sample.<sup>54</sup> In these analyses, an AUC value  $\geq 0.80$  indicated good discrimination, and an AUC value  $\geq 0.90$  indicated excellent discrimination.<sup>38,55,56</sup>

Also, in agreement with Mitchell,<sup>57</sup> we conducted further analyses by computing the clinical utility index (CUI), which estimates the clinical value of a diagnostic test, taking into account both the accuracy of the test and its occurrence (ie, a proxy for the applied value of a test with a qualitative as well as quantitative interpretation). More specifically, positive CUI (CUI-positive = sensitivity  $\times$  PPV) and negative CUI (CUI-negative = specificity  $\times$  NPV) were computed as reflecting rule-in accuracy (case finding) and rule-out accuracy (screening), respectively. The CUI can be graded qualitatively using revised thresholds<sup>58</sup> of  $>0.81$  (excellent),  $>0.64$  (good),  $>0.49$  (fair/adequate),  $>0.36$  (poor), and  $<0.36$  (very poor; for further explanation see [www.clinicalutility.co.uk](http://www.clinicalutility.co.uk), Accessed January 23, 2018).

## RESULTS

### **Clinical and Sociodemographic Characteristics**

Of 590 patients who met the recruitment criteria and were approached for the study, and after excluding those who received a diagnosis of a severe psychiatric disorder ( $n = 5$ ; 0.8%), 503 patients (85.9%) agreed to participate, and 82 declined (30 felt tired and not well enough to

wait, 11 had transportation problems, 42 did not have an interest in taking part in the study). No difference was observed between those who agreed and those who declined participation. Of those who agreed to participate, complete data were available for 498 patients (99%). These included 322 women (64.6%) and 176 men (35.4%). The mean  $\pm$  standard deviation age was  $54.8 \pm 10.6$  years. Most patients were diagnosed with breast cancer ( $n = 214$ ; 43%). The disease stage was local in 225 patients (45.2%), locoregional in 140 (28.1%), and metastatic in 119 (23.9%); and 14 patients (2.9%) were free from disease and were not receiving treatment at the time of the interview. The complete sociodemographic and clinical characteristics are reported in Table 1.

### **ICD-10 Prevalence of Psychiatric Morbidity**

One hundred ninety-eight patients (39.75%), including 36.8% of men and 40.3% of women, met the criteria for an ICD-10 psychiatric diagnosis; specifically, adjustment disorders (code F43.2;  $n = 107$ ; 21.5%), mood disorders ( $n = 56$ ; 11.2% including codes F32-F33 [depressive episode and recurrent depressive disorder;  $n = 37$ ; 7.4%] and code F34.1 [persistent mood disorder;  $n = 19$ ; 3.8%]), anxiety disorders (codes F40-42; F43-43.1;  $n = 31$ ; 6.2%), and other disorders (mood or anxiety disorders Not Otherwise Specified (NOS);  $n = 4$ ; 0.8%). No difference was observed in psychiatric morbidity according to sex (chi-square test, 1.03 [with 1 degree of freedom];  $P$  value, nonsignificant), whereas patients with metastatic cancer had a slightly higher prevalence of ICD-10 morbidity (47%) than patient with local disease (42%) or locoregional disease

**TABLE 2.** Differences Between Brief Symptom Inventory (BSI) and BSI-18 Mean  $\pm$  Standard Deviation T-Scores Among International Classification of Diseases-10th Revision (ICD-10) Cases and Noncases and Between Individual ICD-10 Diagnoses

Subscale	ICD-10				ICD Psychiatric Diagnosis				
	Noncases, n = 300	Cases, n = 198	T	P	Adjustment Disorders, n = 107	Depressive Disorders, n = 56	Anxiety Disorders, n = 31	F	P
<b>BSI</b>									
SOM	46.8 $\pm$ 6.4	54.7 $\pm$ 11.5	9.3	.001	53.8 $\pm$ 10.7	57.8 $\pm$ 13.6	55.4 $\pm$ 10.3	12.7	.05
ANX	46.1 $\pm$ 6.8	55.8 $\pm$ 11.1	12.1	.001	53.1 $\pm$ 10.3	60.9 $\pm$ 12.1	60.8 $\pm$ 10.9	38.9	.001
OC	46.6 $\pm$ 6.3	55.5 $\pm$ 11.6	11.2	.001	53.7 $\pm$ 11.2	60.6 $\pm$ 12.5	57.6 $\pm$ 10.9	29.9	.001
DEP	45.5 $\pm$ 5.4	56.7 $\pm$ 11.4	14.5	.001	53.4 $\pm$ 9.7	66.7 $\pm$ 12.9	57.8 $\pm$ 8.6	67.6	.001
INTSEN	46.1 $\pm$ 5.1	55.9 $\pm$ 12.3	12.4	.001	53.0 $\pm$ 10.3	62.2 $\pm$ 14.1	60.3 $\pm$ 14.4	42.9	.001
PHOB	46.1 $\pm$ 6.4	55.1 $\pm$ 12.1	10.1	.001	52.2 $\pm$ 8.7	60.9 $\pm$ 14.9	60.1 $\pm$ 15.1	30.7	.001
HOS	47.1 $\pm$ 6.4	54.3 $\pm$ 12.4	8.4	.001	52.0 $\pm$ 10.5	56.9 $\pm$ 14.8	60.5 $\pm$ 15.6	19.7	.001
PAR	46.8 $\pm$ 6.1	54.7 $\pm$ 12.7	9.2	.001	51.6 $\pm$ 11.6	60.7 $\pm$ 11.2	57.5 $\pm$ 13.8	24.9	.001
PSY	46.5 $\pm$ 4.7	55.3 $\pm$ 13.1	10.1	.001	52.0 $\pm$ 11.3	64.3 $\pm$ 16.3	56.6 $\pm$ 12.1	37.2	.001
GSI	45.2 $\pm$ 4.9	57.3 $\pm$ 11.2	16.4	.001	53.7 $\pm$ 9.6	65.5 $\pm$ 11.9	61.3 $\pm$ 10.6	77.8	.001
GT	45.2 $\pm$ 5.1	57.3 $\pm$ 11.1	12.1	.001	53.9 $\pm$ 9.7	65.3 $\pm$ 11.9	61.1 $\pm$ 10.4	76.7	.001
PSDI	46.3 $\pm$ 7.9	55.5 $\pm$ 10.2	11.17	.001	53.1 $\pm$ 9.7	62.5 $\pm$ 10.7	56.7 $\pm$ 9.3	33.3	.001
PST	45.3 $\pm$ 6.7	57.1 $\pm$ 9.95	15.8	.001	54.2 $\pm$ 9.5	62.4 $\pm$ 9.1	61.4 $\pm$ 9.1	62.1	.001
<b>BSI-18</b>									
SOM	46.9 $\pm$ 7.2	54.6 $\pm$ 11.7	9.0	.001	53.4 $\pm$ 10.7	58.1 $\pm$ 13.8	54.9 $\pm$ 10.8	18.6	.05
ANX	46.6 $\pm$ 6.8	55.8 $\pm$ 11.1	12.1	.001	53.1 $\pm$ 10.3	60.9 $\pm$ 12.1	60.8 $\pm$ 10.9	38.9	.001
DEP	45.5 $\pm$ 5.4	56.7 $\pm$ 11.4	14.5	.001	53.4 $\pm$ 9.7	66.7 $\pm$ 12.9	57.8 $\pm$ 8.6	67.6	.001
GSI	45.3 $\pm$ 5.8	57.1 $\pm$ 10.8	15.6	.001	54.1 $\pm$ 9.6	65.1 $\pm$ 11.5	59.7 $\pm$ 9.4	67.2	.001

Abbreviations: ANX, anxiety; BSI, 53-item version of the Brief Symptom Inventory; BSI-18, 18-item version of the Brief Symptom Inventory; GSI, global severity index; GT, grand total; HOST, hostility; INTSEN, interpersonal sensitivity; OC, obsessive-compulsiveness; PAR, paranoia; PHOB, phobia; PSDI, positive symptom distress index; PST, positive symptom total; PSY, psychoticism; SD, standard deviation; SOM, somatization.

(45.8%; chi-square test 6.28 [with 2 degrees of freedom];  $P < .04$ ).

### The BSI and BSI-18

On the BSI, high levels of internal consistency (Cronbach  $\alpha$ ) were observed for all scales (range, .82-.94). Cronbach  $\alpha$  coefficients for the BSI-18, with the exception of the somatization subscale ( $\alpha = .76$ ), were similar to those for the original BSI-18 (anxiety,  $\alpha = .81$ ; depression,  $\alpha = .81$ ; GSI,  $\alpha = .87$ ).

Higher scores were observed on both the BSI and the BSI-18 for patients who had a psychiatric diagnosis versus those without such a diagnosis (Table 2). When the former sample was analyzed according to their type of psychiatric diagnosis, patients with ICD-10 major depression had higher scores on all BSI and BSI-18 subscales ( $P < .01$ ), except for the somatization subscale, on which scores were higher only among patients who had an ICD-10 diagnosis of anxiety disorder ( $P < .01$ ) (Table 2).

BSI and BSI-18 GSI scores were not related to age (correlation coefficient [ $r$ ] =  $-0.05$  and  $r = -0.06$ , respectively). Women reported higher GSI scores on both the BSI and the BSI-18 ( $t = 11.25$  [ $P < .001$ ] and  $t = 11.32$  [ $P < .001$ ], respectively) compared with men. Patients who had metastatic cancer reported higher scores

for somatization ( $F = 6.43$ ;  $P < .01$ ) and depression ( $F = 4.02$ ;  $P < .01$ ) and marginally higher GSI scores ( $F = 3.06$ ;  $P = .05$ ) than those who had local and locoregional disease.

### Accuracy of the BSI in Detecting ICD Cases

On the BSI, when the standard case-rule scoring (cutoff point,  $\geq 63$  T-score on the GSI or on 2 primary dimensions) was used to identify cases (those with estimated psychological morbidity),<sup>48</sup> 178 patients were identified as cases (35.7%), 144 of 198 who had an ICD-10 diagnosis were correctly identified as cases (sensitivity, 72.7%; 95% confidence interval [CI], 66.5%-77.9%), and 266 of 300 who had no current psychiatric diagnosis were correctly identified as noncases (specificity, 88.7%; 95% CI, 85.1%-92.3%; chi-square statistic, 195.3;  $P = .001$ ). The PPV was 80.9% (95% CI, 75.1%-86.7%; 144 true ICD cases of 178 BSI cases), and the NPV was 83.1% (95% CI, 79.0%-87.2%; 266 non-ICD cases of 320 BSI noncases), with a misclassification rate of 17.7% ( $n = 88$  patients). From these results, the clinical utility of the BSI was qualitatively rated as adequate for case finding (CUI-positive = 0.58) and good for screening purposes (CUI-negative = 0.73).

Because the sensitivity of the BSI using the case-rule scoring from the original manual<sup>48</sup> was lower than the

**TABLE 3.** Classification Agreement Between International Classification of Diseases-10th Revision Caseness and the 18-Item Brief Symptom Inventory (BSI-18) Using Standard and Alternative BSI-18 Case Rules

Raw Numbers	Criterion: ICD-10 vs BSI-18															
	Standard BSI-18 Case Rule (GSI or Any Subscale T-Score $\geq 63$ )				Zabora Case Rule (GSI T-Score $\geq 57$ )				Recklitis Case Rule (GSI T-Score $\geq 50$ )				Current Study Case Rule (GSI T-Score $\geq 48$ )			
	Cases	Noncases	Total		Cases	Noncases	Total		Cases	Noncases	Total		Cases	Noncases	Total	
No. of cases	58	3	61	89	19	108		153	70	223		163	84	247		
No. of noncases	140	297	437	109	281	390		45	230	275		35	216	251		
Total no.	198	300	498	198	300	498		198	300	498		198	300	498		

Measure	Criterion: ICD-10 vs BSI-18															
	Standard BSI-18 Case Rule (GSI or Any Subscale T-Score $\geq 63$ )				Zabora Case Rule (GSI T-Score $\geq 57$ )				Recklitis Case Rule (GSI T-Score $\geq 50$ )				Current Study Case Rule (GSI T-Score $\geq 48$ )			
	Overall	Lower CI	Upper CI		Overall	Lower CI	Upper CI		Overall	Lower CI	Upper CI		Overall	Lower CI	Upper CI	
Accuracy, %	29.3	23.0	35.6	44.9	38.0	51.9		77.3	71.4	83.1		82.3	76.3	87.4		
Sensitivity	99.0	97.9	100.0	93.7	90.9	96.4		76.7	71.9	81.5		72.0	66.5	77.0		
Specificity	95.1	89.7	100.0	82.4	75.2	89.6		68.6	62.5	74.7		66.0	61.5	70.2		
PPV	68.0	63.6	72.3	72.1	67.6	76.5		83.6	79.3	88.0		86.1	81.9	89.4		
NPV	29.29	9.31	92.19	7.10	4.47	11.26		3.31	2.66	4.12		2.94	2.43	3.56		
Likelihood ratio Positive	0.71	0.65	0.78	0.59	0.52	0.67		0.30	0.23	0.39		0.25	0.18	0.33		
Likelihood ratio Negative	0.28 (Very poor)	0.176	0.381	0.37 (Poor)	0.277	0.46		0.53 (Adequate)	0.46	0.6		0.54 (Adequate)	0.47	0.61		
CUJ	0.67 (Good)	0.64	0.7	0.67 (Good)	0.64	0.71		0.64 (Good)	0.6	0.68		0.63 (Good)	0.57	0.66		

Abbreviations: CI, confidence interval; CUJ, clinical utility index; GSI, global severity index; ICD-10, International Classification of Diseases-10th Revision; NPV, negative predictive value; PPV, positive predictive value.

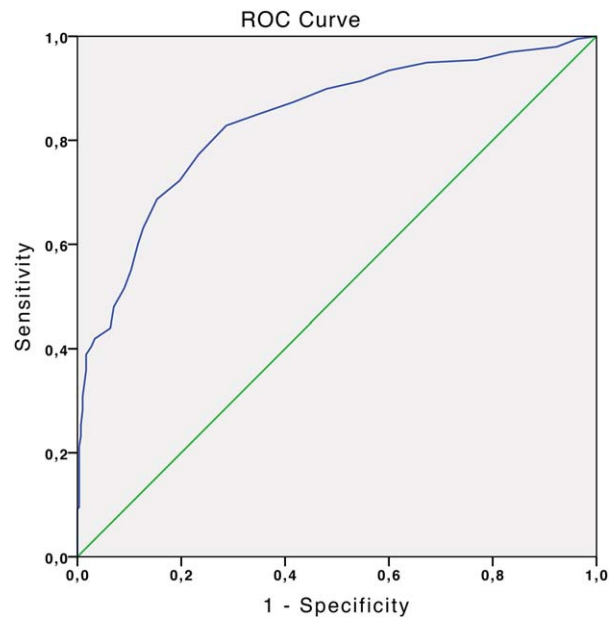
specificity, and because clinical screening programs often give more weight to increasing sensitivity to accurately ensure that most patients who have the condition are identified by the screening instrument,<sup>37,59-61</sup> we investigated further possible cutoff scores, increasing sensitivity and maintaining acceptable levels of specificity, by using only the GSI T-scores (as proposed for the BSI-18). In this way, we demonstrated that the less conservative GSI T-score ( $\geq 48$ ) produced a 49.5% prevalence of cases ( $n = 247$ ) with 84.3% sensitivity (95% CI, 79.3%-89.4%), 75% specificity (95% CI, 70%-80%), a PPV of 69% (95% CI, 63.2%-74.8%), and an NPV of 87.9% (95% CI, 83.9%-91.9%; chi-square test 168.78 [ $P = .001$ ]; AUC, 0.84 [95% CI, 0.8-0.87]) (Supporting Table 1). In terms of clinical utility, there was no change with respect to the original scoring system (CUI-positive [adequate for case finding] = 0.58; CUI-negative [good for screening purposes] = 0.66).

#### Accuracy of the BSI-18 in Detecting ICD Cases

Table 3 provides details about the accuracy of the BSI-18 in identifying ICD-10 cases. When we used the standard case-rule system (any 2 subscale scores or a GSI T-score  $\geq 63$ ),<sup>49</sup> only 61 patients (12.2%) were identified as cases, with 29.3% sensitivity (95% CI, 23.0%-35.6%; 58 of 198 patients) and 99% specificity (95% CI, 97.9%-100.0%; 297 of 300 patients; chi-square test 88.3;  $P = .001$ ). The PPV was 95% (58 of 61 patients), the NPV was 68% (297 of 437 patients), and the misclassification rate was 28.7% ( $n = 143$ ). The clinical utility of the BSI-18 standard case rule was qualitatively rated as very poor for case finding (CUI-positive = 0.27), even if it was adequate for screening purposes (CUI-negative = 0.60).

When using the Zabora case-rule system (GSI T-score  $\geq 57$ ), 108 patients (21.7%) were identified as cases, with 45% sensitivity (95% CI, 38.0%-51.9%; 89 of 198 patients) and 93.6% specificity (95% CI, 90.9%-96.4%; 281 of 300 patients; chi-square test 104.7;  $P = .001$ ). The PPV was 82.4% (89 of 108 patients), the NPV was 72.1% (109 of 390 patients), and the misclassification rate was 25.7% ( $n = 128$ ). The clinical utility of the BSI-18 Zabora case rule was qualitatively rated as poor (CUI-positive = 0.36) for case finding and good for screening purposes (CUI-negative = 0.67).

When using the Recklitis case-rule system (GSI T-score  $\geq 50$ ), 223 patients (44.8%) were identified as cases, with 77.3% sensitivity (95% CI, 71.4%-83.1%; 153 of 198 patients) and 76.6% specificity (95% CI, 71.9%-81.5%; 230 of 300 patients; chi-square test 140.34;  $P = .001$ ). The PPV was 68.6% (153 of 223 patients), the



**Figure 1.** This chart illustrates a receiver operating characteristic (ROC) curve analysis (blue line) of Brief Symptom Inventory-18 (BSI-18) scores versus psychiatric caseness according to the World Health Organization Composite International Diagnostic Interview for the International Classification of Diseases-10th Revision. (the green line represents a non-discriminatory test)

NPV was 83.6% (230 of 275), and the misclassification rate was 23% ( $n = 115$ ). The clinical utility of the BSI-18 Recklitis case rule was qualitatively rated as adequate for case finding (CUI-positive = 0.52) and adequate/good for screening purposes (CUI-negative = 0.63).

In addition to using the BSI-18 algorithms proposed by the cited authors, we also used ROC analysis to explore the optimal cutoff for the BSI-18 in our sample. A less conservative T-score ( $\geq 48$ ) on the GSI identified 247 patients (49.6%) as cases (AUC, 0.85; 95% CI, 0.8-0.89), with an improvement in sensitivity (82.3%; 95% CI, 76.3%-87.4%; 163 of 198 patients) but a decrease in specificity (72.%; 95% CI, 66.5%-77.5%; 216 of 300 patients; chi-square test 140.8;  $P = .001$ ) (Fig. 1, Table 3, Supporting Table 2). The PPV was 66% (163 of 247 patients), the NPV was 86% (216 of 251 patients), and the misclassification rate was 23.9% ( $n = 119$ ). The clinical utility of this case rule was qualitatively rated as adequate for case finding (CUI-positive = 0.54) and adequate/good for screening purposes (CUI-negative = 0.63).

We also added another analysis according to sex in which we used the Zabora suggested cutoff scores for caseness (GSI raw scores of  $\geq 10$  for men and  $\geq 13$  for women). The cumulative prevalence of caseness was

41.8% (n = 208), with 145 of 198 patients who had an ICD-10 diagnosis correctly identified as cases (sensitivity, 73.2%) and 237 of 300 those who had no current ICD diagnosis correctly identified as noncases (specificity, 79%; chi-square test 113.8;  $P = .001$ ). The PPV was 69.7% (145 of 208 BSI cases), the NPV was 81.7% (237 of 290 BSI noncases), and the misclassification rate was 23.3% (n = 116). The clinical utility of this approach was qualitatively rated as adequate for case finding (CUI-positive = 0.50) and good for screening purposes (CUI-negative = 0.64). In ROC analysis of our sample separated by sex, however, different cutoff GSI raw scores ( $\geq 11$  for men and  $\geq 12$  for women) optimized sensitivity (77.3%; 95% CI, 71.4%-83.1%) and specificity (76.7%; 95% CI, 71.9%-81.5%) in detecting ICD cases (AUC, 0.83; 95% CI, 0.80-0.847; PPV, 68.6%; NPV, 83.6%), with CUIs similar to those obtained using the Zabora method (CUI-positive [adequate] = 0.53; CUI-negative [good] = 0.64) (Supporting Table 3).

A separate series of ROC analyses also were performed according to the ICD-10 psychiatric diagnosis using the GSI T-score from the BSI-18 on the subgroups of patients who had diagnoses of adjustment disorder (code F43.2; n = 107; group 1), mood disorder (F32-F34; n = 46; group 2), and anxiety disorder (F40-F43.1; n = 31; group 3). For group 1, the AUC was 0.79 (95% CI, 0.73-0.84), with a GSI T-score cutoff  $\geq 48$  maximizing sensitivity (76%) and specificity (72%) for identifying ICD-10 cases of adjustment disorder. For group 2, the AUC was 0.90 (95% CI, 0.86-0.95), and a GSI T-score cutoff  $\geq 51$  was associated with 83% sensitivity and 77% specificity. For group 3, the AUC was 0.90 (95% CI, 0.84-0.95), and a GSI T-score cutoff  $\geq 49$  indicated 85% sensitivity and 85% specificity.

## DISCUSSION

In this report, we describe the diagnostic validity of the BSI and the BSI-18 for the detection of psychiatric morbidity, as assessed according to the CIDI (the WHO ICD-10 system), among patients with cancer. In general, the prevalence of psychiatric morbidity was similar to that reported previously in oncology research that used structured or standardized psychiatric interviews as a gold standard.<sup>1-9</sup> Almost 40% of patients had an ICD-10 psychiatric diagnosis, underlining the importance of taking mental health into consideration for whole-patient cancer care.<sup>62,63</sup>

Our current results confirm that the BSI may be a reliable tool for assessing psychiatric morbidity in cancer settings. Compared with the gold standard of a clinical

psychiatric interview (CIDI), the standard case-rule scoring (a GSI T-score or any 2 subscale T-scores  $\geq 63$ )<sup>48</sup> allowed us to identify 35.7% of patients as BSI cases, with a misclassification rate of 17.7%, although specificity (88.7%) was higher than sensitivity (72.7%). These results are generally in agreement with our previous data from both cancer and noncancer settings, confirming that the BSI is useful as an instrument for screening purposes and is adequate for case finding among patients who have clinically significant psychological disorders, mainly in the area of anxiety, depressive, and adjustment disorders. An improvement of sensitivity (84.3%) was obtained by using a less conservative cutoff GSI T-score of  $\geq 48$ ; however, that did not improve the CUI, which remained adequate for case finding and good for screening purposes.

Regarding the shorter BSI-18 version, the results of our study in a cancer setting did not confirm the validity of the scoring system as based on the original standardized BSI-18 manual (a GSI T-score or any 2 subscale T-scores  $\geq 63$ ).<sup>49</sup> Indeed, the prevalence of BSI caseness was low (12.2%), with poor accuracy in the identification of ICD-10 cases, low sensitivity (29%), and a high misclassification rate (28.7%). In terms of clinical utility, this scoring system indicated that the tool was very poor for case finding, even if it was adequate for screening purposes. These findings confirm previous studies<sup>34,36</sup> demonstrating that the BSI-18 standard case-rule method performs poorly, because more than one-half of patients with cancer who have psychological distress (cases) are not identified by the tool. One possible explanation is that the standard scoring system is too conservative to identify less severe disorders, such as adjustment disorders, which were the most prevalent ICD-10 psychiatric diagnoses in our sample (21.5%). In line with this finding, the hypothesis raised by Recklitis et al<sup>31</sup> that, with only 3 subscales, this case rule operates somewhat differently in the BSI-18 compared with the BSI, seems to be confirmed. When using the less conservative case-rule scoring system proposed by Zabora et al<sup>27</sup> (GSI T-score  $\geq 57$ ), there was an improvement in accuracy, although the overall capacity of the BSI-18 to identify cases remained low. With this scoring system, the BSI-18 was classifiable as poor in terms of case finding and good for screening purposes. A more significant improvement in sensitivity (77.3%) was obtained by following the case-rule scoring system proposed by Recklitis et al<sup>31</sup> (GSI T-score  $> 50$ ). With this scoring system, the BSI-18 was qualitatively rated as adequate for case finding and good for screening purposes.

In our ROC analysis, we demonstrated that a better threshold for the BSI-18 was a GSI T-score  $\geq 48$ , which



improved the identification of cases, increased sensitivity of the tool (82.3%), and had a good level of discrimination (AUC, 0.85). However, the clinical utility of this case rule was qualitatively comparable to that of the scoring system reported by Recklitis et al,<sup>31</sup> because it was rated as adequate for case finding and adequate/good for screening purposes.

It is noteworthy that different cutoff scores had to be used to detect specific individual ICD-10 psychiatric diagnoses. A GSI T-score cutoff  $\geq 48$  maximized sensitivity (76%) and specificity (72%) when identifying patients who had an ICD-10 diagnosis of adjustment disorder, but with an AUC of 0.79, which is at the low limits of good discrimination. This may be because of poor delineation of the diagnosis of the adjustment disorder itself, as repeatedly reported,<sup>64-66</sup> or an inherent problem with the BSI-18. A GSI T-score cutoff  $\geq 51$  was associated with good levels of sensitivity (83%) and specificity (77%) and with excellent discrimination (AUC, 0.90) in patients diagnosed with depressive disorders; whereas, for those diagnosed with anxiety disorders, the optimal cutoff was  $>49$ , with good levels of sensitivity (85%) and specificity (85%) and, again, excellent discrimination (AUC, 0.90). The possibility that different cutoff scores on the BSI-18 may be needed for specific psychiatric disorders associated with cancer may be relevant for services that use the BSI-18 at a single, fixed cutoff. Previous studies have indicated that other scales, such as the Hospital Anxiety and Depression Scale, also may need an adjusted cutoff score for cancer patients, depending on the setting, prevalence, and screening objective.<sup>67,68</sup>

Some interesting results also were observed using the BSI-18 raw GSI score (instead of the T-score) according to sex, considering the need to adjust the scoring procedure because of a possible tendency for men to underreport psychological symptoms (and, thus, to apparently experience a lower prevalence of mental disorders).<sup>27</sup> This hypothesis seems to be supported by findings from a large epidemiologic study indicating that men are more vulnerable than women to mixed anxiety/depression symptoms and pure depression, whereas women are more vulnerable to pure anxiety symptoms.<sup>69,70</sup> Our findings confirmed the observations reported by Zabora et al,<sup>27</sup> who used GSI cutoff scores of 10 for men and 13 for women. The clinical utility of that approach was qualitatively rated as adequate for case finding and good for screening purposes. When we tried to examine other possible GSI raw cutoff scores in our sample, we observed marginal differences by sex, with a cutoff GSI score (for caseness) of 11 for men and 12 for women, and no differences in the CUI with

respect to the Zabora method. Further research is necessary to properly understand the possible differences by sex in cancer settings, including the possible role of cultural differences among patients with cancer in influencing the psychological response to disease and psychiatric morbidity.<sup>71,72</sup>

Taken together, our current results confirm the usefulness of the BSI in its original 53-item form for screening and case finding in patients with cancer who have a definite psychiatric diagnosis, as assessed by a standardized clinical interview instead of other nondiagnostic psychometric tools used in other studies. Regarding the BSI-18, we confirmed the caveats for the use of case-rule cutoff scores recently raised by Recklitis et al<sup>39</sup> in young adult survivors of cancer, indicating that, compared with using psychiatric interviews to make psychiatric diagnoses according to the DSM, general concordance between the BSI-18 GSI scale and psychiatric diagnosis was good; however, the 2 most widely used BSI-18 case rules failed to identify the majority of survivors who had a DSM psychiatric diagnosis. In our study, we indeed confirmed that the Recklitis et al GSI T-score cutoff of  $\geq 50$  maximized sensitivity and specificity for case detection; however, we also identified another cutoff score ( $\geq 48$ ) that supported the clinical value of the BSI-18. Also, raw GSI scores can be used, but more research will be needed to understand possible differences in cutoff scores for men and women. The advantage of the BSI-18 is that it remains significantly shorter and easier to complete than the BSI. However, as we have repeatedly indicated, the advantages should be balanced with costs.<sup>22-25</sup> One disadvantage, for example, is that the profile of the BSI-18 is less complete than that of the BSI, because some dimensions (eg, irritability, interpersonal sensitivity, obsessive-compulsive) are not evaluated and yet may be of relevance in patients who have cancer in terms of interference with quality of life and referral for psychosocial intervention.

The strength of this study is that, unlike previous research examining the validity of the BSI and BSI-18 compared only with other self-report psychometric tools (mostly the SCL-90-R), we used a standardized clinical psychiatric interview (WHO CIDI, ICD-10) as a gold standard to identify cases and noncases, and we examined possible different cutoff scores according to the ICD psychiatric diagnosis (depressive, anxiety, and adjustment disorders).

There are also limitations in this study. First, the nature of the sample (a convenience sample of outpatients with good performance status) prevented us from

generalizing our results and drawing conclusions in other contexts, such as patients admitted to the hospital and those with more advanced disease, in whom psychological disorders are not easy to detect.<sup>73</sup> A second limitation is the large number of patients who had breast cancer versus other types of cancer and the low number of men with cancer. Also, we cannot generalize the results to patients with cognitive difficulties or central nervous system involvement by disease, who merit special attention in terms of psychosocial concomitants and consequences.<sup>74</sup> A specific, related aspect is that this study did not involve patients with severe mental illness (eg, schizophrenia, bipolar disorders, severe personality disorders), for whom the possible use of screening tools for distress should be part of more specific studies. Indeed, the problem of cancer among patients who have severe mental illness and the needs for integrated assessment and intervention deserve to be urgently examined.<sup>75,76</sup> Third, because of the cross-sectional nature of the study, conclusions regarding the reliability of the instruments over time, across the illness trajectory, are not possible. The importance of prospective evaluation was underlined in a recent, large, prospective German study,<sup>77</sup> which reported a 31.8% prevalence of mental disorders 4 weeks after diagnosis and a 39.8% prevalence at 12 months using the same instrument we used (CIDI). Finally, although we used a formal, semistructured psychiatric interview as a current gold standard to make diagnoses according to the ICD-10, it is possible that subthreshold disturbances or other clinical expressions of significantly maladaptive responses to cancer (eg, demoralization, abnormal illness behavior)<sup>78,79</sup> may have gone unrecognized. These psychological reactions often are not picked up by classic psychiatric nosological systems but could affect from 15% to 20% of patients with cancer.<sup>80</sup>

In summary, the current study confirms the usefulness of the BSI for the screening and detection of psychiatric morbidity in cancer settings. It could be used as an add-on to an ultrashort visual analog scale, like the DT or emotion thermometers. Also, the abbreviated version, the BSI-18, can give physicians useful information about psychiatric disorders secondary to cancer. However, attention should be paid to the scoring procedure, because only the alternative case-rule systems, rather than the case rule specified by the BSI-18 manual, appears to have acceptable levels of accuracy for identifying patients with cancer who have an ICD psychiatric diagnosis.

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## CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

## AUTHOR CONTRIBUTIONS

**Luigi Grassi:** Conceptualization, funding acquisition, methodology, validation, visualization, writing—original draft, and writing—review and editing. **Rosangela Caruso:** Data curation, formal analysis, and visualization. **Alex J Mitchell:** Methodology, visualization, writing—original draft, and writing—review and editing. **Silvana Sabato:** Formal analysis, investigation, resources, software, and visualization. **Maria Giulia Nanni:** Data curation, methodology, project administration, supervision, and visualization.

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