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Measuring priority symptoms in advanced bladder cancer: development and initial validation of a brief symptom index

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Abstract

Background—Improved measurement of clinically meaningful symptoms is needed in advanced bladder cancer.

Objective—This study developed and examined the initial reliability and validity of a new measure of advanced bladder cancer-specific symptoms, the NCCN-FACT Bladder Symptom Index-18 (NFBISI-18), which assesses the symptoms perceived as most important by patients and oncology clinical experts.

Methods—A total of 31 individuals with advanced bladder cancer rated the importance of 28 symptoms. In addition, 10 oncology clinical experts rated symptoms as treatment- or disease-related. Patient-rated symptoms were reconciled with published clinicians' symptom priorities,

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producing the NFBISI-18. Participants completed measures of quality of life (QOL) and performance status to examine initial validity.

Results—An 18-item symptom index for advanced bladder cancer included 3 subscales: disease-related symptoms, treatment side effects, and general function/well-being. Lower scores indicate greater symptom burden. Preliminary reliability reveals good internal consistency for the full NFBISI-18 ($\alpha = 0.83$). The NFBISI-18 was significantly associated with QOL criteria and performance status, in the expected direction.

Limitations—Limitations include the cross-sectional design and the relatively low reliability of the disease-related symptoms subscale.

Conclusion—The NFBISI-18 demonstrates preliminary evidence as a valid brief measure of the most important symptoms of advanced bladder cancer, as rated by both patients and oncology clinical experts. The NFBISI-18 should have greater acceptability to regulatory authorities than previously developed questionnaires.

Urinary bladder cancers are estimated to account for 73,510 new diagnoses and 14,880 deaths in the United States in 2012.¹ Approximately 25% of individuals with bladder cancer are initially diagnosed with metastatic disease and 50% of those diagnosed with early-stage cancer will eventually progress to metastatic disease.² The curative benefits of therapy for advanced bladder cancer remain limited, as evidenced by a 5-year survival rate of 35% for individuals diagnosed with regional staged disease and 5% for individuals with distant staged disease.¹ Given that it is also the costliest of all cancers in terms of lifetime treatment costs per patient,³ there is renewed attention to bladder cancer research. Patient-reported quality of life (QOL) represents an important outcome. Symptoms such as bleeding, pain, dysuria, constipation, fatigue, emotional distress, and urinary obstruction adversely impact QOL in advanced bladder cancer.^{4–5} Thus, there is a need for well-constructed and validated patient-reported outcome measures to ensure future patient-centered research in advanced bladder cancer.

Symptom management and QOL preservation are important outcomes in advanced cancer treatment and research. However, oncology experts and regulatory agencies have expressed concerns about multidimensional QOL measures for use in clinical practice and trials.⁶ A new initiative to enhance regulatory fitness for purpose has emerged in response to the Food and Drug Administration Oncologic Drug Advisory Committee Quality of Life Subcommittee's recent statement that pharmaceutical company claims of improved QOL outcomes should be specific to the QOL domain measured and should reflect the patient's perspective.⁷

Several valid and reliable bladder cancer-specific QOL measures, including the Functional Assessment of Cancer Therapy-Bladder Cancer (FACT-BI),⁸ the Functional Assessment of Cancer Therapy-Vanderbilt Cystectomy Index (FACT-VCI),⁹ and the Bladder Cancer Index (BCI),¹⁰ are currently available. The items on these instruments were developed through input from patients and clinicians; however, patients had no direct input in the selection of items included on the scales. Although the symptoms rated the highest priority by oncology experts are likely to reflect symptoms amenable to improvement by chemotherapy,¹¹ they may not reflect the same symptoms prioritized by patients,¹² especially when considering

psychosocial symptoms.¹² As a result, although experts selected items from a pool generated from patient input, the FACT-BL, FACT-VCI, and BCI may not fully reflect symptoms prioritized by patients. In order to meet the FDA regulatory standard, we therefore need a psychometrically sound measure of advanced bladder cancer–specific symptoms that not only includes input from patients and oncology clinical experts, but also incorporates both patient and expert priorities in the selection of items. Although the European Organisation for Research and Treatment of Cancer (EORTC) has developed 2 bladder cancer–specific modules that incorporate patients’ ratings of symptom importance, the EORTC superficial bladder cancer module (EORTC QLQ-BLS24) and the EORTC muscle invasive bladder cancer module (EORTC QLQ-BLM30), validity data have not yet been published.¹³

Recent findings reveal less clinical trials activity in the area of bladder cancer than other types of cancer when corrected for their relative incidences and mortalities, thus highlighting the need for increased bladder cancer clinical trials research [Hirsch et al; manuscript submitted]. Consequently, patient-reported measures that meet FDA regulatory standards are critical to ensuring that patient-centered endpoints are incorporated. Research utilizing a multi-step process has begun to improve the clinical utility of QOL measurement, as well as improve adherence to FDA guidance on patient-reported outcomes. A measure of bladder cancer-specific QOL was developed from interviews with patients and providers, followed by the assessment of oncology clinical experts’ ratings of the highest priority symptoms in advanced bladder cancer.¹¹ In the present study, we sought to develop a new symptom index specific to advanced bladder cancer, including the symptoms that were rated highest priority by oncology clinicians and individuals with advanced bladder cancer.¹⁴ Specifically, we sought to create a measure that reflects the relevant concerns across the spectrum of advanced bladder cancer disease and treatment. We also examined the preliminary validity and reliability of the new symptom index for advanced bladder cancer.

Material and methods

Design

The development of the index was a multi-step process. Prior to this study, semi-structured interviews were conducted with patients and oncology clinicians regarding patient symptoms which lead to the development of the FACT-BL.⁸ Next, oncology physicians and nurses from 17 National Comprehensive Cancer Network (NCCN) member institutions were surveyed about symptom priorities using the items from the FACT-BL.¹¹ These oncology clinical experts rated the 5 most important advanced bladder cancer symptoms, resulting in a subscale of 7 items: pain, fatigue, weight loss, nausea, feel ill, worry that condition will get worse, and urinary incontinence.¹¹

This study was part of a larger study conducted from 2003–2004 that sought to develop 11 symptom indexes for different types of advanced cancer.¹⁴ Individuals with advanced bladder cancer were recruited from a subset of NCCN member institutions (Northwestern University, NorthShore University HealthSystem [Formerly Evanston Northwestern Healthcare. At the time of this study, this institution was affiliated with the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.], Moffitt Cancer Center, Fred Hutchinson Cancer Research Center, and Duke University Medical Center) and a private,

non-profit social service organization (Cancer Wellness Center, Northbrook, IL). Individuals with advanced bladder cancer first completed an open-ended (ie, without any preconceived reference to what might be expected by the study investigators) questionnaire to express their symptom experiences. This was followed by a more targeted survey of candidate items from the FACT-G and FACT-BI. Responses from participants in this study were combined with results from previous surveys of oncology clinicians¹¹ to derive a symptom index comprised of the most important patient- and oncology clinician-rated symptoms specific to advanced bladder cancer. All symptoms endorsed as among the very most important, at a rate exceeding chance by either patients or oncology physicians, were retained in the final measure. Then, 10 expert oncology physicians rated whether the identified priority symptoms were predominantly disease or treatment-related. Participants also completed the FACT-BI to provide initial validation of the new symptom index. Initial validation was completed through the extraction of symptom index items from the FACT-BI and subsequent analysis of the reliability and validity.

Participants

A total of 31 individuals with advanced bladder cancer were enrolled in the study, which is comparable to previous studies examining QOL in advanced bladder cancer.⁵ Previous research suggests that saturation can typically be achieved with 12 to 15 participants; therefore, the number of cases here (n = 31) exceeds the number of cases typically required for saturation in qualitative research.^{15–17} Inclusion criteria for the patient sample included: (1) diagnosis of Stage III or IV bladder cancer, (2) prior experience with chemotherapy for at least 2 cycles (1 month for non-cyclical chemotherapy), (3) no other primary malignancy diagnosed and/or treated within previous 5 years except non-melanoma skin cancer, (4) ability to understand and provide signed informed consent, (5) sufficient cognitive ability to complete questionnaires without assistance, (6) fluency (reading and speaking) in English, and (7) at least 18 years of age. Personnel at each participating site determined participant eligibility. Participants' cognitive ability to complete the questionnaires without assistance was determined by personnel at each participating NCCN member institution. Typically, the patient's treating physician, who had an established clinical relationship with the patient, made the determination about whether the patient possessed sufficient cognitive ability to complete the questionnaire without assistance. This was further evaluated by the impression of the interviewer. All participants provided informed consent in accordance with Institutional Review Board guidelines prior to participating and completed all self-report questionnaires at one time point. Participants received \$50 for their participation.

In all, 10 oncology physicians with expertise in either medical oncology or urologic oncology recruited from 8 NCCN member institutions participated in the present study. Potentially eligible expert oncology physicians were identified through review of NCCN panel participants and NCCN databases. Expert oncology physicians were eligible to participate if they could attest to at least 3 years' experience treating at least 100 patients with advanced bladder cancer. All participating expert oncology physicians provided informed consent in accordance with Institutional Review Board guidelines prior to participating. Expert oncology physicians received \$100 for their participation.

Patient measures

The participants' sociodemographic and clinical information was collected from their patient record; and if further information was needed, it was supplemented by direct query of the patient. Participants first completed a qualitative written survey asking them to generate up to 10 symptoms perceived as most important to monitor when evaluating treatment. Participants were then asked to rate the importance of each symptom they generated using a scale from 0 ("not important") to 10 ("extremely important").

The participants then completed a checklist containing the list of 28 symptoms derived from the FACT-BI.⁸ Participants selected the 10 symptoms they perceived as most important in evaluating treatment for bladder cancer from the checklist. After selecting the 10 most important symptoms, participants identified the 5 symptoms perceived as the *very* most important symptoms/concerns to monitor when assessing the value of treatment. In order to control for potential response bias, 4 versions of the checklist presenting symptoms, each in a different order, were administered.

Participants next completed the FACT-BI, a self-report measure of general QOL related to cancer, as well as specific symptoms and concerns related to bladder cancer. The 27 items that assess general QOL related to cancer are derived from the Functional Assessment of Cancer Therapy-General (FACT-G).⁸ The FACT-G is a well-established, multidimensional patient-reported QOL instrument comprised of 4 subscales: (1) physical well-being, (2) social/family well-being, (3) emotional well-being, and (4) functional well-being. The 13 additional items measuring symptoms/concerns specific to bladder cancer resulted from prior input from 15 bladder cancer patients and 5 clinical experts to develop the original FACT-BI. Higher scores on the FACT-BI indicate better QOL.

Finally, participants rated themselves into one of the following categories on the Eastern Cooperative Oncology Group Performance Status (ECOG):¹⁸ 0, fully ambulatory without symptoms; 1, fully ambulatory with some symptoms; 2, requiring less than 50% of awake time to rest; 3, requiring more than 50% of awake time to rest; and 4, bedridden.

Expert oncology clinician measures

Oncology physicians with expertise in advanced bladder cancer completed an online survey which assessed the degree to which oncology experts believed the 36 bladder cancer-related symptoms or concerns, generated from patient interviews and source items, were disease or treatment-related. Oncology experts used a five-point scale that ranged from "Exclusively disease-related" to "Exclusively treatment-related."

Data analysis

Frequency distributions were evaluated for all items appearing in the checklist of bladder cancer symptoms. The frequency of chance endorsement as one of the top 5 symptoms was calculated by dividing 5 (the allowable number of "very most important symptoms") by 28 (the total number of items in the bladder cancer-specific checklist) and multiplying this number by 31 (number of participants). Items which exceeded this a priori cut-off were included in the NCCN-FACT Bladder Symptom Index-18 (NFBISI-18) index.

Items generated from the qualitative written survey were reviewed to identify potential new concepts not covered in the symptom checklist. If more than 10% of patients reported a particular new symptom that was not rated to be treatment related by the Principal Investigator, or more than 20% of patients if the new symptom was judged to be treatment related, it was included. The lower threshold for disease symptoms was established because the primary goal of the project was to develop a concise questionnaire focused principally upon disease-related symptoms.

Frequency distributions were also evaluated for the expert oncology physician symptom attribution ratings. An item was categorized in the Treatment Side-Effects subscale if greater than 50% of experts rated the symptom as treatment related. Items that were rated as predominately disease related were categorized in the Disease-Related Symptoms subscale and items rated as predominately related to general functioning and well being were categorized in the General Function and Well-being subscale.

Of the 18 items selected for the new NFBISI index, 2 were newly identified by participants, and had not been previously included on the FACT-BI, nor were they added to this study based on previous clinician reports. Because these items were not administered to participants in the present study, they were treated as missing and scores on the NFBISI-18 were prorated according to the standard Functional Assessment of Chronic Illness Therapy system scoring protocol.¹⁹ Cronbach's alpha assessed the internal consistency reliability of each subscale and also the total scale of the NFBISI-18. Convergent validity was assessed using Spearman correlations among the NFBISI-18 total scale and subscales as well as the FACT-BI total scale and subscales, with adjustment for overlapping items that would artificially inflate the correlation. A one-way analysis of variance examined the relationship between performance status and NFBISI-18 in an effort to assess criterion validity.

Results

Participant characteristics

The average age of the 31 participants was 62.5 years (SD = 8.8 years). Participants were predominantly male (71.0%), White (93.6%), educated (67.7% with greater than high school education) and not working outside of the home (80.6%). Table 1 presents the sociodemographic characteristics of the participants.

Patient ratings of symptom importance

Of the 28 symptoms on the Bladder Cancer Symptom Checklist, 9 were endorsed as important at a probability greater than chance. The frequencies of symptoms endorsed as very important are presented in Table 2. Table 2 also displays a comparison of the symptoms endorsed as important at a probability greater than chance by participants in the present study and those endorsed as important by oncology clinicians in Cella et al.¹¹ Only 3 of the symptoms rated as high priority by individuals with advanced bladder cancer in the present study were also rated as high priority by oncology clinical experts.¹¹ Participants generated a mean of 4.5 symptoms (SD = 3.0). Table 3 identifies the most commonly listed symptoms generated by participants with bladder cancer and their importance.

Reliability and validity of the NFBISI-18

Items from the Functional Assessment of Chronic Illness Therapy system were identified for those priority symptoms that were patient-generated. The 18 items were classified into the disease-related symptoms, treatment side effects, and general function/well-being subscales based on oncologist ratings. Table 4 displays the 18 NFBISI items and their subscales. The internal consistency reliability for the full NFBISI-18 was good (15 items with data after excluding one item for men only, $\alpha = 0.83$). The disease-related symptoms subscale (8 items with data after excluding one item for men only, $\alpha = 0.57$) demonstrated less adequate internal consistency reliability. However, the treatment side-effects sub-scale (5 items, $\alpha = 0.75$) and the general function/well-being subscale (2 items, $\alpha = 0.85$) demonstrated adequate to good internal consistency reliability. The NFBISI-18 was associated with the bladder cancer-specific subscale of the FACT-BI in the expected direction ($r = .41$, $P < .05$, adjusted for overlap). The bladder cancer-specific scale of the FACT-BI was also associated with the treatment side-effects subscale ($r = .41$, $P < .05$, adjusted for overlap) and the general function/well-being ($r = .49$, $P < .01$). The disease-related symptoms subscale was not significantly associated with the bladder cancer-specific scale of the FACT-BI after adjustment for overlapping items ($r = .21$, $P = .27$). Participants' scores on the NFBISI-18 differed significantly by performance status, $F(2, 28) = 4.47$, $P < .05$, such that participants with worse performance status reported worse scores on the NFBISI-18.

Discussion

Patient-reported symptoms and QOL constitute important treatment outcomes in advanced urologic cancer. The NFBISI-18, a new index comprised of the symptoms rated as highest priority by oncology clinicians and individuals with advanced bladder cancer, addresses a need for improved clinical utility in symptom and QOL measurement.¹⁴ The use of a multi-step qualitative and quantitative methodology has produced a more comprehensive assessment of response to interventions in advanced cancer. The incorporation of patient symptom priorities addresses previous findings suggesting differences between patients and clinicians in the rating of priority symptoms,¹² and is consistent with recent FDA guidance regarding the assessment of drug efficacy with respect to symptomatology. Thus, this new measure of QOL containing symptoms rated as important by both clinical experts and patients is of critical importance, from both a clinical and regulatory perspective.

As the first symptom index developed to assess the highest priority symptoms in advanced bladder cancer as perceived by clinicians *and* patients, the full NFBISI-18 demonstrated good internal consistency and was associated with validity criteria such as bladder cancer-specific QOL and performance status, in the expected direction. The inclusion of 2 items on the NFBISI-18 which were not originally included in the FACT-BI ("I feel weak all over," and "I feel light-headed (dizzy)") limits the ability to directly calculate NFBISI-18 scores from the FACT-BI. However, if more than 50% of the 18 items are completed, it is possible to calculate comparable scores using the FACT-BI data by pro-rating scores to make them comparable to the NFBISI-18 according to the following formula: $18 \times [(\text{sum of NFBISI item responses}) / (\text{number of NFBISI items completed})]$.¹⁹

There was a lack of concordance between patients and clinicians with regard to high-priority physical symptoms, with nausea and fatigue constituting the only physical symptoms rated as high priority by both patients and clinicians.¹¹ Interestingly, the clinical experts' most frequently rated high-priority symptom was pain, which was absent among the patients' list of highest-priority symptoms. This may reflect increased attention to pain as a treatable symptom among clinicians. Similar differences between patient and clinician ratings of high-priority symptoms emerged with respect to psychosocial symptoms. Although patients rated a number of psychosocial symptoms as high-priority, "worry that my condition will get worse" was the only psychosocial symptom rated as high-priority by clinical experts.¹¹ This finding may reflect a tendency on the part of oncology clinicians to focus on treatment-related symptoms. Variability in perceived importance of symptoms between clinicians and patients highlights the need for a measure that encompasses both perspectives, in accordance with regulatory guidance from agencies such as the FDA.

Implications

As the measurement of patient outcomes in advanced cancer has evolved, QOL and patient-reported disease-specific symptoms have received greater emphasis. As a result, the development of disease-specific symptom measures has become essential to the comprehensive assessment of QOL in clinical trials and the clinical setting, especially when curative options are limited. The present study extends previous findings in urologic oncology through the development and initial validation of a measure of symptoms specific to advanced bladder (NFBISI-18). This measure is the first to assess the advanced bladder cancer-specific symptoms perceived as important by both patients and oncology clinical experts, allowing for more accurate and comprehensive measurement of disease-specific QOL and better adherence to regulatory requirements for patient-reported outcomes. From a clinical standpoint, improved measurement of disease-specific QOL has the potential to improve symptom monitoring and intervention, patient satisfaction with treatment, medical decision-making, and health policy. From a regulatory perspective, inclusion of symptoms prioritized by patients also provides a foundation for better assessment of the QOL effects of emerging treatments in urologic oncology.

The NFBISI-18 shows promise as a new option for clinical researchers and clinicians who wish to assess patient response to treatment in accordance with regulatory requirements. However, it should be noted that the NFBISI-18 is not an appropriate measure of patient-reported outcomes in non-invasive bladder cancer, given that it was developed specifically to reflect priority symptoms in advanced disease. Although there are similarities between the NFBISI-18 and the FACT-BL, the methodological considerations of the NFBISI-18 result in a measure with enhanced adherence to regulatory guidance. Questions may arise concerning when it is appropriate to use the NFBISI-18 versus the FACT-BL. We recommend the use of the NFBISI-18 when the goal is focused assessment of symptoms identified as most important when treating advanced disease. When the goal is the assessment of more multidimensional aspects of QOL, or assessment of QOL and/or symptoms in individuals with early-stage disease, the FACT-BL would be an appropriate choice.

Further research and development plans for the NFBISI-18

Although the NFBISI-18 demonstrates preliminary promise as a measure of patient-reported symptoms specific to advanced bladder cancer, it will benefit from additional refinement in future research. Several future steps are planned to further develop and establish the psychometric properties of this measure. First, the less adequate reliability and validity of the disease-related symptoms subscale compared to the full NFBISI-18 and the other subscales highlight an important area for further research. Research employing cognitive interviewing will enhance understanding of how to use this subscale and may lead to revisions to improve reliability and validity. Second, research with longitudinal administration of the NFBISI-18 will play an important next step in the assessment of the reliability over time and sensitivity to change as individuals' clinical status changes. Third, enhancing the generalizability through the use of more diverse samples also constitutes an important step in further validating the NFBISI-18. This is of particular importance given the evidence suggesting high rates of sexual dysfunction among women with bladder cancer,²⁰ which may have been under-represented as a patient-rated high-priority symptom in the present study. Future research should over-sample women with advanced bladder cancer to ensure their perspective is appropriately reflected in bladder cancer-specific QOL measures. Future research should also examine the validity of the measure in specific subgroups of individuals with advanced bladder cancer, such as those with locally advanced disease, to ensure that the symptoms on the measure represent these patients' perspectives as well.

In addition to these areas of further research, the need for patient-reported outcome measures to keep pace with changes in treatment and supportive care constitutes an important ongoing future direction. Although there has been little change in chemotherapy regimens for advanced bladder cancer since the early 2000's, as reflected by the NCCN guidelines for the treatment of bladder cancer,²¹ the current interest in bladder cancer research may yield future treatment advances that change which symptoms are perceived as high-priority. The present study utilized a relatively broad definition of "advanced bladder cancer" in order to develop a measure that was reflective of a representative range of patient experiences across the spectrum of advanced bladder cancer. Future efforts should identify practical solutions to update symptom scales to reflect the current priority symptoms, as well as relate older versions of symptom scales to updated scales. We recommend re-examining the reliability and validity of the NFBISI-18 every 5 to 10 years to ensure that it can be revised as needed to reflect substantive changes to the treatment guidelines.

Although additional future research is warranted, this is the first study to present on the development and initial validation of an index of the symptoms in advanced bladder cancer perceived as most important by both patients and clinicians. As such, it improves upon existing bladder cancer-specific QOL measures through better satisfaction of regulatory requirements.

Conclusion

The initial findings demonstrate good internal consistency reliability and validity for the total NFBISI-18. Thus, this index offers promise as a brief measure of the most important symptoms in advanced bladder for use in clinical research and practice. Future research will

address questions regarding reliability and validity that were beyond the scope of this initial report.

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TABLE 1Sociodemographic characteristics of study participants^a

Characteristics	
Mean Age (SD)	62.5 (8.8)
Gender (%)	
Female	9/31 (29.0)
Male	22/31 (71.0)
Race/Ethnicity (%)	
African-American	2/31 (6.4)
White	29/31 (93.6)
Non-Hispanic (%)	31/31 (100.0)
Highest Education (%)	
Some high school or less	3/31 (9.7)
High school graduate or GED	7/31 (22.6)
Vocational college or some college	8/31 (25.8)
College degree	6/31 (19.4)
Professional or graduate degree	7/31 (22.6)
Current Occupational Status (%)	
Homemaker	2/31 (6.4)
Unemployed	0/31 (0.0)
Retired	16/31 (51.6)
On disability	6/31 (19.4)
On leave of absence	1/31 (3.2)
Part-time employed	0/31 (0.0)
Full-time employed	6/31 (19.4)
ECOG Performance Status (%)	
0	7/31 (22.6)
1	13/31 (41.9)
2	11/31 (35.5)
3	0/31 (0.0)

^aN = 31 individuals with advanced bladder cancer.

TABLE 2

Comparison of advanced bladder cancer patient and oncology clinician symptom rankings

Symptom	Patient overall rank	Patients who endorsed top 5 (%)	Oncology clinician overall rank [11]
Lack of energy (Fatigue)	1	15/31 (48.4)	2
Worry that my condition will get worse	2	14/31 (45.2)	5
Because of my physical condition, having trouble meeting the needs of my family	3	10/31 (32.3)	—
Being able to enjoy life	4	8/31 (25.8)	—
Control of my bowels	4	8/31 (25.8)	—
(For men only) Having and maintaining an erection	6	7/31 (22.6)	—
Being content with the quality of my life right now	6	7/31 (22.6)	—
Nausea	6	7/31 (22.6)	4
Being able to sleep well	9	6/31 (19.4)	—
Pain	—	3/31 (9.7)	1
Weight loss	—	—	3
Feel ill	—	5/31 (16.1)	5
Urinary incontinence	—	5/31 (16.1)	7

TABLE 3Patient-generated symptoms^a and their perceived importance

Symptom	Rank	Proportion of responses (%)	Mean importance rating (0–10)	Symptom currently in checklist
Tired/Fatigue	1	13/30 (43.3)	8.2	Yes
Effectiveness of treatment	2	12/30 (40.0)	8.7	Yes
Nausea	2	12/30 (40.0)	6.6	Yes
Pain	4	6/30 (20.0)	7.2	Yes
Mental well-being	5	5/30 (16.7)	8.0	Yes
Loss of taste	5	5/30 (16.7)	7.4	No
Diarrhea	5	5/30 (16.7)	7.2	Yes
Hair loss	5	5/30 (16.7)	6.8	No
Blood count	5	5/30 (16.7)	6.0	No
Anxiety	10	4/30 (13.3)	9.3	Yes
Communication with medical staff	10	4/30 (13.3)	9.3	No
Dizziness	10	4/30 (13.3)	7.8	No
Effect of chemotherapy	10	4/30 (13.3)	7.3	No
Constipation	10	4/30 (13.3)	7.0	No

^aData is based on a subset of 30/31 participants.

TABLE 4

NFBISI-18 items and subscales

Subscale	Item	Included in FACT-BI?
Disease-related symptoms	I have pain	Yes
	I am losing weight	Yes
	I have trouble controlling my urine	Yes
	I feel weak all over	No
	I feel light-headed (dizzy)	No
	Because of my physical condition, I have trouble meeting the needs of my family	Yes
	I worry that my condition will get worse	Yes
	I feel sad	Yes
	I have a good appetite	Yes
	(For men only) I am able to have and maintain an erection	Yes
	I am sleeping well	Yes
Treatment side effects	I have nausea	Yes
	I have a lack of energy	Yes
	I feel ill	Yes
	I have control of my bowels	Yes
	I am bothered by side effects of treatment	Yes
General function/ well-being	I am able to enjoy life	Yes
	I am content with the quality of my life right now	Yes