The Patient Care Monitor–Neutropenia Index: Development, Reliability, and Validity of a Measure for Chemotherapy-Induced Neutropenia

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Chemotherapy-induced neutropenia is a treatment side effect with several notable consequences for patients with cancer. The most important is increased likelihood of infection, particularly when the absolute neutrophil count falls below 500/mm³. More than 60,000 patients with cancer were hospitalized for neutropenia in 1999, with a corresponding 7% inpatient mortality rate (Caggiano, Weiss, Rickert, & Linde-Zwirble, 2005). In addition, neutropenia is a dose-limiting factor for many regimens and may compromise optimal cancer treatment by requiring dose reduction or delay (Chang, 2000; Crawford et al., 1991; Elting, 1998; Pettengell et al., 1992), both of which can impact disease progression and long-term survival (Bonadonna & Valagussa, 1981; Glaspy, Hackett, Flyer, Dunford, & Liang, 2001).

Neutropenia complications can adversely affect health-related quality of life (HRQOL) (Nirenberg et al., 2006a, 2006b; Padilla & Ropka, 2005). For example, patients with febrile neutropenia had worse symptom profiles than patients without neutropenia for abdominal pain, anorexia, asthenia, dehydration, fatigue, rigors, and vomiting (Glaspy et al., 2001). Similar patterns have been shown in patients with severe afebrile neutropenia, although those results were nonsignificant trends (Glaspy et al., 2001). Another investigation showed greater symptom burden for patients with neutropenia grades 3–4 compared to those with grades 0–2; symptoms included depression, physical symptom distress, social limitations and isolation, and limitations on normal physical activities (Fortner, Houts, & Schwartzberg, 2006).

To date, few self-report instruments are sensitive to changes in HRQOL specific to neutropenia. One measure, the Functional Assessment of Cancer Therapy–Neutropenia Subscale (FACT-NS) (Calhoun, Chih-Hung, Welshman, & Cella, 2002; Wagner et al., 2008), was designed to assess HRQOL specific to neutropenia and has demonstrated good psychometric properties. However, the FACT-NS has been unable to use a single time point score to differentiate patients who had grades 3–4 neutropenia from those who did not, and the tool has not been validated on a broad demographic sample (Wagner et al., 2008). In addition, whether the FACT-NS will be useful as an outcome measure or a clinical symptom screener is unclear.

Purpose/Objectives: To provide an initial evaluation of the psychometric properties of the Patient Care Monitor 1.0 Revised–Neutropenia Index (PCM-N), a symptom-based assessment tool designed to measure health-related quality-of-life (HRQOL) changes associated with chemotherapy-induced neutropenia.

Design: Known-groups methodology and self-report instrument validation.

Setting: A large community oncology practice in Memphis, TN.

Sample: 424 patients with cancer in four samples.

Methods: All patients in the first three samples were assessed at baseline of chemotherapy administration and at a point analogous to midcycle. The fourth sample underwent a cross-sectional evaluation of the ability of the PCM-N to distinguish patients with febrile neutropenia, severe afebrile neutropenia, and no neutropenia.

Main Research Variables: PCM-N score, grade of neutropenia, and febrile status.

Findings: Internal consistency reliability and factor analysis supported the single additive scale structure of the 13 items of the PCM-N. The PCM-N demonstrated good known-groups validity and was able to distinguish patients with grades 3–4 neutropenia from those with grades 0–2. The tool also was able to distinguish patients with febrile neutropenia, severe afebrile neutropenia, and no neutropenia. Receiver operating characteristic analyses provided a psychometrically based threshold score.

Conclusions: The PCM-N is a reliable and valid instrument sensitive to changes in HRQOL associated with moderate-to-severe chemotherapy-induced neutropenia.

Implications for Nursing: Nurses can use the PCM-N as a rapid and cost-effective tool for monitoring symptoms of neutropenia in patients with cancer.
because some items do not convey information useful to clinicians and researchers, such as, “My partner worries about me when my blood counts are low.” The usefulness of the FACT-NS as a clinical measure also is limited by the absence of any previously determined threshold scores.

To maximize clinical utility, HRQOL measures must demonstrate excellent psychometric qualities and convey clinically useful information such as symptom severity. A measure designed with an emphasis on symptom severity can increase the efficiency of frontline oncologists who frequently assess symptoms during treatment and routine care. Ropka and Padilla (2007) explored the need for the development of a neutropenia-specific HRQOL measure with clinical utility. They outlined the rationale for such a measure to include monitoring QOL to ensure patient willingness and ability to complete treatment, screening for potential treatment problems, facilitating patient dialogue with clinicians and caregivers, and integrating QOL considerations into decisions regarding the course of treatment. Ropka and Padilla (2007) also highlighted several necessary qualities of such an instrument, including simplicity of use for patients and clinical staff, sensitivity and specificity to neutropenia-specific HRQOL changes, and threshold scores to aid intervention decisions.

The current study describes the development and psychometric properties of the Patient Care Monitor 1.0 Revised–Neutropenia Index (PCM-N) (formerly referred to as the Cancer Care Monitor–Neutropenia), an assessment tool designed to assess HRQOL specific to neutropenia. The PCM-N was designed to maximize clinical utility, and items were created to emphasize clinically useful information. The current study reports the internal consistency and factor structure of the PCM-N and explores its ability to distinguish grades of neutropenia. The authors also used known-groups methodology to report the ability of the PCM-N to discriminate among patients with febrile neutropenia, severe afebrile neutropenia, and no neutropenia. Finally, an optimal threshold score for the PCM-N is determined using area under the curve and Youden’s index scores.

### Methods

#### Design and Procedures

The current study combined information from four samples of patients with cancer (N = 424) from West Clinic, a large community oncology practice in Memphis, TN. Inclusion criteria were being aged 18 years or older, having a primary diagnosis of cancer, and being able to complete questionnaires. All patients agreed to anonymous use of their medical records and completed informed consents for study participation. The University of Memphis Institutional Review Board approved all study procedures.

**Sample 1:** The first sample (n = 212) was from a database of patients with cancer who received myelosuppressive chemotherapy and completed the PCM-N as part of routine care (Fortner, Durrence, Mao, Schwartzberg, & Houts, 2002). Inclusion criteria were having a normal absolute neutrophil count (ANC) at baseline, having completed the PCM-N at baseline and 3–14 days after chemotherapy, and having ANC data taken at both time points. The assessment 3–14 days after chemotherapy was a midcycle check when patients were most likely to have neutropenia. This was a convenience sample from the extant database and was not constrained to disease or treatment type. In the current study, sample 1 was used to examine psychometric properties of the PCM-N and to predict neutropenia grade from the total score of the PCM-N.

**Sample 2:** The second sample (n = 51) of patients who received myelosuppressive chemotherapy was previously studied in a retrospective chart review investigation of neutropenia symptom burden (Fortner & Houts, 2006). Inclusion criteria were having completed the PCM-N both at baseline and 6–14 days after chemotherapy (midcycle check) and having ANC data taken at both time points. Patients treated with granulocyte–colony-stimulating factor were excluded. This sample was used in the current study to examine psychometric properties of the PCM-N and to predict neutropenia grade from the total score of the PCM-N.

**Sample 3:** The third sample (n = 71) was from a prospective HRQOL study of neutropenia with patients receiving myelosuppressive chemotherapy (Fortner, Schwartzberg, et al., 2005). Patients completed the PCM-N on days 0, 7, 10, 14, 21, and 28 (if necessary), and ANC data were taken at each time point. The lowest ANC point was the observed nadir. Patients were excluded if they were scheduled to receive granulocyte–colony-stimulating factor, were enrolled in another clinical trial, or had a life expectancy shorter than three months. As with the aforementioned samples, sample 3 was used to assess psychometric properties of the PCM-N and to predict neutropenia grade.

**Sample 4:** The fourth sample (n = 90) was recruited to evaluate known-groups validity in a set of patients with febrile neutropenia, severe afebrile neutropenia, and no neutropenia. Patients on myelosuppressive therapy were recruited in the order in which they arrived for appointments for regularly scheduled midcycle blood count checks. Participants received $15 as compensation. Inclusion criteria were having an ANC either higher than 2,000/mm³ (no neutropenia) or lower than 500/mm³ (grade 4 neutropenia). Patients were excluded if they had received granulocyte–colony-stimulating factor during the previous two weeks. Patients without...
fever completed the PCM-N before they were informed about blood tests. All patients with fevers completed measures in the hospital.

**Measures**

The data were collected during a period when common toxicity criteria were being revised, but the two versions did not change definitions of neutropenia (National Cancer Institute Cancer Therapy Evaluation Program, 2003a, 2003b). Patients in samples 1–3 were classified into five groups based on ANC: grade 0 (2,000/mm³ or higher), grade 1 (1,500–1,999/mm³), grade 2 (1,000–1,499/mm³), grade 3 (500–999/mm³), and grade 4 (lower than 500/mm³). Patients in sample 4 were classified into three groups: febrile neutropenia (ANC lower than 500/mm³ and a temperature of 101.3°F or higher), severe febrile neutropenia (ANC lower than 500/mm³ and a temperature lower than 101.3°F), and no neutropenia (ANC = 2,000/mm³ or higher).

The PCM-N was developed from the 61 items of the Patient Care Monitor 1.0 Revised (PCM) (formerly called the Cancer Care Monitor), a symptom-based scale administered on tablet computers (Fortner & Houts, 2006). The PCM was revised and redeveloped to include symptoms unique to patients treated for cancer. The PCM-N was developed using a priori and empirical methods. The a priori method for content validity included reviewing neutropenia literature and interviewing oncologists and oncology nurses to identify symptoms that rationally should be associated with neutropenia in patients treated for cancer. This process was aided by a previous empirical examination of patient-nominated symptoms following grade-4 episodes of chemotherapy-induced neutropenia (Fortner, Tauer, Okon, Houts, & Schwartzberg, 2005). To reduce interview data, the empirical approach consisted of examining the PCM item pool to determine which items best predicted neutropenia status in a large archival database (about 10,000 observations at time of PCM-N development). Correlations of items by grade of neutropenia were examined, and a series of discriminant function analyses were performed to identify items that best classified the extreme groups (grade 4 versus grade 0). Concurrent validity for the items was reported previously (Fortner, Baldwin, Schwartzberg, & Houts, 2006).

By satisfying a priori and empirical methods, the authors identified the 13 items of the PCM-N. Patient-reported responses of symptom severity from the 13 items, ranging from 0 (not a problem) to 10 (as bad as possible), were summed to create the PCM-N index score. Scores range from 0–130, with higher scores indicating increased symptom burden related to neutropenia. The items of the PCM-N were presented individually on tablet computers in identical order as they appear in Table 1.

### Table 1. Items on the Patient Care Monitor 1.0 Revised—Neutropenia Index

<table>
<thead>
<tr>
<th>Item</th>
<th>Item-Total Correlation</th>
<th>Alpha if Item Was Deleted</th>
<th>Factor Loading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue, tiredness, or weakness</td>
<td>0.61</td>
<td>0.81</td>
<td>0.663</td>
</tr>
<tr>
<td>Trouble with bowel movements (e.g., diarrhea, constipation)</td>
<td>0.49</td>
<td>0.83</td>
<td>0.503</td>
</tr>
<tr>
<td>Sore throat or trouble swallowing</td>
<td>0.53</td>
<td>0.82</td>
<td>0.645</td>
</tr>
<tr>
<td>Reduced sexual enjoyment, interest, or performance</td>
<td>0.38</td>
<td>0.84</td>
<td>0.424</td>
</tr>
<tr>
<td>Trouble sleeping</td>
<td>0.53</td>
<td>0.82</td>
<td>0.576</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>0.54</td>
<td>0.82</td>
<td>0.621</td>
</tr>
<tr>
<td>Numbness or tingling</td>
<td>0.47</td>
<td>0.83</td>
<td>0.479</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>0.61</td>
<td>0.82</td>
<td>0.695</td>
</tr>
<tr>
<td>Patient losing interest in people he or she used to want to be around</td>
<td>0.47</td>
<td>0.83</td>
<td>0.482</td>
</tr>
<tr>
<td>Fever or chills</td>
<td>0.54</td>
<td>0.82</td>
<td>0.653</td>
</tr>
<tr>
<td>Swollen glands</td>
<td>0.4</td>
<td>0.83</td>
<td>0.493</td>
</tr>
<tr>
<td>Headache</td>
<td>0.46</td>
<td>0.83</td>
<td>0.705</td>
</tr>
<tr>
<td>Mouth sores</td>
<td>0.39</td>
<td>0.83</td>
<td>0.529</td>
</tr>
</tbody>
</table>

Results

**Sample**

Most participants were married Caucasian women aged 50 years and older with at least a high school education (see Table 2). Although each sample was selected based on different criteria, chi-square analyses confirmed that none of the demographic data differed significantly between the samples. In addition, samples 1–3 demonstrated no marked differences across neutropenia grade with respect to age, level of education, marital status, and ethnicity. The most frequent diagnoses were breast cancer and lung cancer. No patients in any of the samples received colony-stimulating factors at baseline.

**Internal Consistency Reliability and Factor Structure**

The 13 items of the PCM-N showed strong internal consistency in samples 1 (Cronbach alpha = 0.88), 2 (Cronbach alpha = 0.81), 3 (Cronbach alpha = 0.91), and
4 (Cronbach alpha = 0.85), suggesting the items measure a common factor. The authors aggregated samples 1–3 to increase the sample size (n = 334) for the factor analysis. A varimax rotated factor analysis of the combined data set supported a single factor interpretation that accounted for 62% of the variance with an Eigen value of 4.4. Using the aggregated sample, the authors computed item-total correlations and Cronbach alpha if the item was deleted. The analyses suggested that the PCM-N is an internally consistent measure.

### Table 2. Patient and Clinical Characteristics Across the Four Samples

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Sample 1 (N = 212)</th>
<th>Sample 2 (N = 51)</th>
<th>Sample 3 (N = 71)</th>
<th>Sample 4 (N = 90)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>𝒙̅</td>
<td>Range</td>
<td>𝒙̅</td>
<td>Range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.46</td>
<td>25–94</td>
<td>58.01</td>
<td>27–78</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>128</td>
<td>60%</td>
<td>39</td>
<td>76%</td>
</tr>
<tr>
<td>Male</td>
<td>84</td>
<td>40%</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>143</td>
<td>67%</td>
<td>30</td>
<td>59%</td>
</tr>
<tr>
<td>Widowed</td>
<td>20</td>
<td>9%</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Divorced</td>
<td>26</td>
<td>12%</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>Single</td>
<td>11</td>
<td>5%</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Not stated</td>
<td>12</td>
<td>6%</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>32</td>
<td>15%</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>High school to associate degree</td>
<td>118</td>
<td>56%</td>
<td>19</td>
<td>37%</td>
</tr>
<tr>
<td>Bachelor’s degree or higher</td>
<td>60</td>
<td>28%</td>
<td>14</td>
<td>27%</td>
</tr>
<tr>
<td>Not stated</td>
<td>2</td>
<td>1%</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Ethnic background</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian, not Hispanic</td>
<td>179</td>
<td>84%</td>
<td>40</td>
<td>78%</td>
</tr>
<tr>
<td>African American</td>
<td>27</td>
<td>13%</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>Asian or Hispanic</td>
<td>6</td>
<td>3%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cancer type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>45</td>
<td>21%</td>
<td>13</td>
<td>25%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>50</td>
<td>24%</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>17</td>
<td>8%</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>9</td>
<td>4%</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>Leukemia, lymphoma, or myeloma</td>
<td>18</td>
<td>8%</td>
<td>13</td>
<td>25%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>47</td>
<td>22%</td>
<td>14</td>
<td>27%</td>
</tr>
<tr>
<td>Skin</td>
<td>5</td>
<td>2%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
<td>10%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Metastatic disease</td>
<td>77</td>
<td>36%</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>Chemotherapy regimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin and paclitaxel</td>
<td>NA</td>
<td>NA</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>Carboplatin and docetaxel</td>
<td>NA</td>
<td>NA</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>Doxorubicin, cyclophosphamide, and fluorouracil</td>
<td>NA</td>
<td>NA</td>
<td>16</td>
<td>31%</td>
</tr>
<tr>
<td>Single-agent docetaxel</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CHOP</td>
<td>NA</td>
<td>NA</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>Carboplatin and gemcitabine</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Other</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Grade of neutropenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>79</td>
<td>37%</td>
<td>21</td>
<td>41%</td>
</tr>
<tr>
<td>1</td>
<td>39</td>
<td>18%</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>12%</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>14%</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>18%</td>
<td>16</td>
<td>31%</td>
</tr>
</tbody>
</table>

CHOP—cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone; NA—not applicable

Note. Because of rounding, not all percentages total 100.
**Known-Groups Validity**

To examine whether the PCM-N can distinguish among neutropenia grades, the authors compared PCM-N scores across neutropenia grades at midcycle in the first two samples and at ANC nadir in the third sample. ANC nadir was defined as the lowest measured ANC across the cycle, occurring at about midcycle for all patients. To control for baseline differences in HRQOL, the authors used analysis of covariance (ANCOVA) with baseline PCM-N scores and time interval from baseline to midcycle as covariates. Midcycle or ANC nadir PCM-N scores served as the dependent variable, and neutropenia grade was the independent variable.

Table 3 presents covariance adjusted means of the PCM-N scores for samples 1–3 by neutropenia grade. In sample 1, ANCOVA was significant (F[4, 205] = 4.15, p = 0.003). Bryant Paulson post hoc analyses showed that patients with grade 4 neutropenia had significantly higher PCM-N scores than those with either grade 0 or grade 1 (p < 0.05). A trend toward higher scores existed in grade 3 compared to grade 1 (p = 0.1). All other comparisons were not statistically significant.

In sample 2, patients with grades 0–2 neutropenia were grouped together because of small sample size and because their respective means and standard deviations were similar. The ANCOVA was significant (F[2, 46] = 5.22, p = 0.009). Bryant Paulson post hoc analyses indicated that patients with neutropenia grades 3 and 4 had significantly worse PCM-N scores than those with grades 0–2 (p < 0.05).

In sample 3, patients with grades 0–2 neutropenia were again grouped together because of small sample size and because their respective means and standard deviations were similar. The ANCOVA was significant (F[1, 63] = 7.7, p = 0.007). Bryant Paulson post hoc analyses indicated that patients with neutropenia grades 3 and 4 had significantly worse PCM-N scores than those with grades 0–2 (p < 0.05).

Sample 4 included 13 patients with febrile neutropenia, 30 patients with severe afebrile neutropenia, and 47 patients without neutropenia. Table 4 presents the means and standard deviations for the PCM-N. A one-way ANOVA was used to compare the three neutropenia status groups on the PCM-N (F[2, 87] = 44.67, p < 0.001). Tukey post hoc comparisons showed that both neutropenia groups had worse scores than the non-neutropenia group. In addition, patients in the febrile group had worse scores than patients with afebrile neutropenia. Therefore, the PCM-N was sensitive to HRQOL differences between febrile and severe afebrile neutropenia and between severe neutropenia and no neutropenia (regardless of presence of fever). Taken together, the results from the known-groups validity analyses suggest that the PCM-N correctly differentiates patients with no neutropenia or mild neutropenia from those with moderate to severe neutropenia. In addition, the PCM-N differentiates among febrile neutropenia, severe afebrile neutropenia, and no neutropenia.

### Table 3. Means and Standard Errors (SEs) of the Patient Care Monitor 1.0 Revised—Neutropenia Index by Neutropenia Grade for Samples 1–3

<table>
<thead>
<tr>
<th>Grade</th>
<th>n</th>
<th>Baseline</th>
<th>Midcycle</th>
<th>Adjusted Midcycle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>X</td>
<td>SE</td>
<td>X</td>
</tr>
<tr>
<td>Sample 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>79</td>
<td>20.36</td>
<td>2.11</td>
<td>21.74</td>
</tr>
<tr>
<td>1</td>
<td>39</td>
<td>24.24</td>
<td>2.49</td>
<td>21.72</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>26.24</td>
<td>3.99</td>
<td>28.05</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>23.09</td>
<td>3.3</td>
<td>28.03</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>22.69</td>
<td>2.98</td>
<td>30.19</td>
</tr>
<tr>
<td>Sample 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>27</td>
<td>15.03</td>
<td>2.86</td>
<td>15.5</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>6.4</td>
<td>3.12</td>
<td>25.21</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>8.94</td>
<td>2.3</td>
<td>18.07</td>
</tr>
<tr>
<td>Sample 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>24</td>
<td>22.38</td>
<td>3.57</td>
<td>24.34</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>16.18</td>
<td>3.53</td>
<td>21.7</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>20.39</td>
<td>2.37</td>
<td>30.49</td>
</tr>
</tbody>
</table>

a Significantly worse than grade 0 and grade 1 (p < 0.05)
b Significantly worse than grades 0–2 (p < 0.05)

Receiver Operating Characteristics Analysis and Cutoff Score Generation

To further evaluate the ability of the PCM-N to discriminate neutropenia, an area under the receiver operating characteristics (ROC) curve was computed using sample 4. ROC analysis produces a range of cutoff scores from the minimum to the maximum observed test values. For each cutoff value, the ROC curves plot true positive rate (sensitivity) on the y-axis against the false positive rate (1 – specificity) on the x-axis to produce a plot showing how well the test separates the participants into those with or without a diagnosis. To assess the accuracy of the measure, the ROC analysis produces a statistic called area under the curve (AUC), which ranges from 0–1. An AUC of 0.5 represents diagnostic performance equal to chance; an AUC of 1 represents perfect diagnostic performance.

To simplify classification, the authors collapsed the two neutropenic groups from sample 4 into one group with grade 4 neutropenia (febrile nonspecific), which was compared to the non-neutropenic group. The area under the ROC curve was significant for the PCM-N (0.8; standard error ± 0.05), indicating that the PCM-N

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*Note: The table and text are meant to be self-contained and provide all necessary information. Further details and context can be inferred from the provided text.*
is a good discriminative measure at midcycle. The 95% confidence interval for the PCM-N indicated that the area under the ROC curve was from 0.71–0.9. Figure 1 shows the ROC curve for the PCM-N. The results provide further indication that the PCM-N can serve as a discriminative instrument for neutropenia.

Several potential scores were evaluated to determine threshold scores. From these data, the authors computed five statistics: sensitivity, specificity, positive predictive value, negative predictive value, and Youden’s index. Sensitivity was the proportion of individuals with neutropenia who were classified accurately with the cutoff score. Specificity was the proportion of individuals without neutropenia who were classified accurately. Positive predictive value was the probability that neutropenia was present when indicated by the cutoff score. Negative predictive value is the probability that neutropenia is not present when indicated by the cutoff score. Finally, Youden’s index is a summary score incorporating both sensitivity and specificity into a single numeric value, with values closer to 1 representing a more valuable discriminative cutoff score. Table 5 shows the variables for each potential cutoff score.

The data supported an optimal cutoff score of 20. The score corresponded to the maximum Youden’s index value and showed good positive and negative predictive values. The score encapsulated about 81% of all patients with grade 4 neutropenia in this sample and correctly identified 78% of patients without neutropenia. The results suggest that patients who score higher than 20 on the PCM-N are likely to have current grade 4 neutropenia and should be evaluated further to determine their ANC status.

Discussion

The current study was conducted to develop and validate an index designed to assess HRQOL related to neutropenia. Results indicate that the PCM-N is an internally consistent, single-factor measure sensitive to HRQOL changes associated with neutropenia. Consistent with previous research, a negative relationship between neutropenia and HRQOL was observed (Fortner, Stolshek, Durrence, et al., 2002; Fortner, Stolshek, Tauer, et al., 2002; Glaspy et al., 2001). Specifically, the PCM-N detected statistically significant HRQOL differences between patients with neutropenia grades 0–2 and those with grades 3–4. In addition, the results showed evidence for a nonlinear relationship between HRQOL and neutropenia, with patients experiencing a marked decrease in HRQOL only as they become moderately to severely neutropenic. As a result, patients with mild neutropenia may not notice the effects of neutropenia. Wagner et al. (2008) made a similar conclusion in their validation of the FACT-NS. This nonlinear relationship also may result from the possibility that the PCM-N is not sensitive enough to detect important HRQOL changes among mildly neutropenic patients. Further refinement and study of the PCM-N should help address this issue.

The current study offered several advantages for use of the PCM-N versus the FACT-NS. The FACT-NS has failed to differentiate patients with grade 3 or 4 neutropenia from those who did not when using cross-sectional data (Wagner et al., 2008). The current study demonstrated that the PCM-N can differentiate patients with grade 4 neutropenia from those without neutropenia, as well as the ability to discriminate among patients with febrile neutropenia, severe afebrile neutropenia, and no neutropenia. Consistent with previous research (Glaspy et al., 2001), patients with febrile neutropenia showed the worst HRQOL
scores as indicated by the PCM-N. The scores were significantly higher than those of patients with afebrile neutropenia who, in turn, had significantly higher scores than patients without neutropenia. Therefore, the results demonstrated that the PCM-N can be used to assess HRQOL changes among patients with severe neutropenia, regardless of febrile status. This ability has not been demonstrated for the FACT-NS. Nonetheless, the current samples were composed primarily of Caucasian women aged older than 50 years. Cultural and sexual differences may affect the way individuals report neutropenia-related symptoms; as a result, future inquiry will be needed to replicate the current findings with differing demographic groups.

Using the PCM-N has several other advantages. First, the PCM-N and its parent scale, the PCM, were designed and validated for use on tablet computers. Consequently, the PCM-N provides a means for regular and thorough assessment of HRQOL related to neutropenia in an efficient, reliable, and cost-effective manner. The individual items on the PCM-N were designed to maximize clinical utility and have been shown to correspond with oncology nurse evaluations (Fortner, Baldwin, et al., 2006). In addition to providing a total HRQOL score, the individual items on the PCM-N provide information that is useful to clinicians as well as researchers. In particular, item responses indicate the presence or absence of neutropenia-specific symptoms and the severity of those symptoms at the point of care.

Another advantage in using the PCM-N is the presence of an empirically generated threshold score. A score of 20 or higher was determined to offer a maximum balance of sensitivity and specificity when differentiating patients with grade 4 neutropenia from those without neutropenia. This achievement represents the first time that a neutropenia-specific threshold score has been generated successfully for a self-report HRQOL measure and may prove useful for clinicians and patients in neutropenia symptom monitoring. However, as mentioned previously, the current samples were composed from a narrow demographic, which may limit the generalizability of this score for use with individuals of differing demographics. Until a larger investigation of optimal threshold scores for a broad range of demographic groups is conducted, caution should be exercised when attempting to use a threshold score for the PCM-N.

Future research should address three important issues. First, researchers should study the clinical significance of the observed nonlinear relation of PCM-N scores across grades of neutropenia because HRQOL differences likely are not realized by patients until they have already developed grade 3 or 4 neutropenia. Second, researchers should evaluate the performance of the PCM-N longitudinally to examine how neutropenia-related HRQOL symptoms evolve over time based on factors such as length of chemotherapy. Additional comparisons should be made with respect to changes in patients’ HRQOL before and after the development of neutropenia. This would provide more precise information about HRQOL changes associated with neutropenia. Finally, research has suggested that change scores may be better at differentiating neutropenia status than a single score (Wagner et al., 2008). Accordingly, threshold scores for change in PCM-N scores could be developed to allow patients with available pretreatment scores to be evaluated for neutropenia with their own baseline scores acting as a reference point. This approach may allow for even greater sensitivity and specificity than the current study was able to generate.

### Implications for Nursing Practice

The validation of the PCM-N is an important development for the field of oncology nursing for several reasons. First, the PCM is well suited for nurses to use in routine practice as a time- and cost-efficient tool for monitoring symptoms of neutropenia in patients with cancer. When the instrument is administered via tablet computer, staff workload is reduced because of automated scoring and report generation. Therefore, the PCM-N can be delivered efficiently in concert with a broad assessment of chemotherapy-related HRQOL. Second, the PCM-N may be used as a tool in nursing research. When used in this capacity, the index can help advance the understanding of key questions concerning HRQOL in patients with cancer. Finally, implementation of the PCM-N can help nurses identify patients with cancer who are at risk for neutropenia. This information can be used to help guide interventions in an effort to decrease the probability of severe neutropenia, associated treatment delays, and morbidity. Overall, the PCM-N is a much-needed tool that will aid oncology nurses in improving the HRQOL of patients with cancer.

### Table 5. Sensitivity-Specific Analyses of the Patient Care Monitor 1.0 Revised–Neutropenia Index

<table>
<thead>
<tr>
<th>Cut Point</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Youden’s Index</th>
<th>Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher than 10</td>
<td>0.86</td>
<td>0.43</td>
<td>0.29</td>
<td>0.55 0.77</td>
</tr>
<tr>
<td>Higher than 20</td>
<td>0.81</td>
<td>0.78</td>
<td>0.59*</td>
<td>0.78 0.82</td>
</tr>
<tr>
<td>Higher than 30</td>
<td>0.65</td>
<td>0.85</td>
<td>0.5</td>
<td>0.8 0.73</td>
</tr>
<tr>
<td>Higher than 40</td>
<td>0.35</td>
<td>0.94</td>
<td>0.29</td>
<td>0.83 0.61</td>
</tr>
</tbody>
</table>

* Optimal t-score cut point was indicated by maximum value on Youden’s index.
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References


