

## Brief communication (Original)

# Development of a Thai version of the neutropenia subscale for the Functional Assessment of Cancer Therapy–Neutropenia questionnaire

Nongluck Ananta-ard, Sureeporn Thanasilp, Chanokporn Jitpanya

Faculty of Nursing, Chulalongkorn University, Bangkok 10330, Thailand

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**Background:** There is a need for a validated translation of the neutropenia subscale (NS) of the Functional Assessment of Cancer Therapy–Neutropenia (FACT-N) questionnaire used to assess neutropenia-specific concerns and health-related quality of life for Thai patients receiving cancer chemotherapy.

**Objectives:** To translate the NS of the FACT-N questionnaire into Thai and examine the psychometric properties of the Thai version.

**Methods:** The 19 item NS was translated into Thai in accordance with the guidelines of the Functional Assessment of Chronic Illness Therapy (FACIT) translation methodology. The psychometric properties of the translated version were then tested. We randomly selected 260 patient participants with hematological malignancies from four hospitals in Thailand. All participants completed the Thai version of FACT-N at the time of expected neutropenia (7–14 days after receiving chemotherapy). The Thai NS content validity was evaluated by a panel of 5 experts. The construct validity of the Thai NS was tested by confirmatory factor analysis (CFA). The internal consistency of the Thai NS was tested with Cronbach's  $\alpha$  coefficients.

**Results:** The Thai version of the NS was semantically equivalent to the English version. The content validity index was good at 0.95. The CFA of the Thai NS indicated acceptable construct validity. All 19 items on the Thai NS had significant estimated factor loadings ( $P < 0.05$ ). Cronbach's  $\alpha$  coefficient was 0.82.

**Conclusions:** The Thai NS, as part of FACT-N, is appropriate in terms of translation and psychometric properties for assessing specific neutropenia-related concerns in Thai patients undergoing cancer chemotherapy.

**Keywords:** FACT-N, health-related quality of life, hematological malignancies, neutropenia subscale, scale translation, scale validation

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Chemotherapy induced neutropenia is the most common toxicity experienced by cancer patients receiving chemotherapy [1]. In hematological malignancies, myelosuppressive chemotherapy, which forms the mainstay of treatment, interferes with hematopoiesis and immunity, placing patients at a high risk of infections and other manifestations because of neutropenia [2]. This poses a burden on the patients during the neutropenia risk period and could adversely affect their health-related quality of life (HRQOL) [3-5]. In a qualitative study, patients with grade 4 neutropenia have been found to have symptoms of fatigue, impairment of physical and social functions, and low coping ability [6]. A significant correlation between increasing grades of neutropenia with

symptom burden and HRQOL was reported after a prospective study [7].

The Functional Assessment of Cancer Therapy–Neutropenia (FACT-N) questionnaire assesses self-reported symptoms and impact on HRQOL associated with neutropenia. The FACT-N questionnaire consists of the 27-item Functional Assessment of Cancer Therapy–General (FACT-G), which assesses core HRQOL, and a neutropenia subscale (NS; 19 items), which specifically assesses neutropenia-related manifestations [8]. The FACT-G was developed and validated by Cella [9]. It was designed for measuring general HRQOL specifically in cancer patients and consists of four dimensions. These include physical well-being (PWB; 7 items), functional well-being (FWB; 7 items), social/family well-being (SWB; 7 items), and emotional well-being (EWB; 6 items). The original FACT-G has been validated in various types of cancer and shown to have good psychometric properties [10].

The initial testing of psychometric properties of the NS on the FACT-N was performed by Wagner and colleagues [8]. It was tested in 852 cancer patients on chemotherapy, aged 65 years and above. The validity of the NS was tested using exploratory factor analysis, concurrent validity testing, and construct validity testing using known groups. The results of factor analysis indicated that the 19-item NS comprised three subscales: malaise, worry, and flu-like symptoms. Three items (N6: I have mouth sores, N8: My low blood counts interfere with my intimate relationship, MS3: I have night sweats) did not correlate with these factors; however, the experts agreed to retain them in the NS. Item loading was reported to be acceptable to high, ranging from 0.39 to 0.87. In the concurrent validity testing, the 19-item NS had significant correlations with the FACT-G total score, and the depression and anxiety subscales of Hospital Anxiety and Depression Scale. Known group validation showed the FACT-N and NS differentiated between participants who had grade 3/4 neutropenia and those who were not at risk of neutropenia from the first cycle of chemotherapy at the time of testing. The reliability was measured by using a test-retest analysis and internal consistency with Cronbach's  $\alpha$  coefficient; the test-retest correlation coefficient ranged from 0.43 to 0.96, and Cronbach's  $\alpha$  coefficient ranged from 0.92 to 0.94 respectively.

FACT-G version 4 was translated into Thai and its psychometric properties tested in 364 patients with various types of cancer [11]. It was also validated in a sample of 252 patients with cholangiocarcinoma and lung cancer who had only completed a primary school education [12]. The results of both studies indicate that Thai version of FACT-G has appropriate psychometric properties and even persons with low literacy levels can use it for self-reporting.

Despite the appropriate psychometric properties of the NS in patients with various types of cancer were reported, a culturally relevant Thai equivalent of the NS is needed. Hence, this study aimed to translate and validate the NS of FACT-N, to measure neutropenia-specific concerns and HRQOL in Thai patients undergoing cancer chemotherapy.

## Materials and methods

Data used in this study were collected as part of the cross-sectional study, "Predicting factors of health-related quality of life among hematological malignancy patients receiving chemotherapy". The study was

approved by the institutional ethics committee of each hospital (Faculty of Medicine, Chulalongkorn University 005/56/119/2013; Narasual Hospital 008/56/001/2013; Siriraj Hospital 061/2556/Si125/2013; Sapphasitthiprasong Hospital 116/2556). This study was carried out in two phases: (I) translation phase and (II) Psychometric phase.

### *Phase I: Translation*

Our team translation consisted of two oncology nurses (the first and the second investigators), one hematologist, four English instructors from the Language Institute and the Faculty of Mass Communication, Chulalongkorn University (one of the instructors is a native English speaker who can read and write Thai fluently), and one professional translator.

The 19-item NS was translated according to the FACIT translation methodology guidelines [13]. The translation process ensured equivalence with the English version and cultural appropriateness. A rigorous multistep translation/back-translation process was employed. First, two independent forward translations from English to Thai were prepared by two native Thai speakers (a senior English instructor and a professional translator). Then, a hematologist formulated a single translated version by combining the two forward translations. A back-translation of the combined version into English was performed by the English instructor, who is a native English speaker. The back-translation was reviewed by people from the FACIT organization and our team (one English instructor and two oncology nurses), and following this, two English instructors proofread the final Thai version. The FACIT staff then formatted the test versions into Word documents. We performed a pilot testing with ten patients having hematological malignancies and receiving chemotherapy. The ten participants were asked to read and answer the Thai version of the questionnaire and were questioned on its conceptual clarity. We also solicited feedback and comments to refine the translation further.

Once this 19-item Thai version of the NS was approved, we obtained a copyright for it from FACIT.org for use in the main study.

### *Phase II: Psychometric analysis*

To exam psychometric properties of the Thai version NS, 260 patient participants were randomly selected from four hospitals in Thailand: King Chulalongkorn Memorial Hospital, Siriraj Hospital,

Narasual Hospital, and Sapphasitthiprasong Hospital. The participants were aged 18 years or older, diagnosed with lymphoma, acute myeloid leukemia, or multiple myeloma, and physically and mentally capable of completing the self-administered questionnaire in Thai. Those with active infection or progressive disease were excluded. All participants provided written informed consent and completed the questionnaires at the time of expected neutropenia (7–14 days after receiving chemotherapy). This happened either at the hospital, while awaiting follow up with the hematologist, or at home, while awaiting the subsequent cycle of chemotherapy. For those who completed the questionnaires at home the participants returned them by post.

### **Instruments**

The instruments used in this study were the personal data form, medical record form, and FACT-N. The personal data form recorded age, sex, marital status, and education, while the medical record form recorded details of the disease type, performance status, and types of chemotherapy received. FACT-N consists of the 27 items of the FACT-G questionnaire and 19 items of the NS. The details of FACT-N have already been described.

### **Data analysis**

Demographic characteristics of the participants were analyzed by descriptive statistics. Content and construct validity and reliability were used to confirm the psychometric properties of the Thai NS.

Content validity was evaluated by a panel of 5 experts. The purpose of this method is to examine the relevancy of items for measuring a concept or construct [14]. The panel of experts was composed of one hematologist, and 4 nurses. All of the nurses have a PhD in nursing, and have more than 10 years of experience in work related to cancer patients. The experts were asked to rate the relevancy between the original and the Thai version of each item using three point rating scale: 1 (irrelevant), 2 (questionably relevant), and 3 (relevant). The content validity index (CVI) was computed as the proportion of either 2 or 3 on the scale by all rates. A CVI of 0.78 to 1.0 was considered acceptable to justify relevance between the original English and Thai versions of the NS [15].

Construct validity was examined by confirmatory factor analysis (CFA) using the LISREL statistical

software package (version 8.72). Nineteen items that were identified in the analyses of the English version were used in the model [8]. Multiple criteria were employed for evaluating absolute fit indices of the model. These included non-significant *P*-values on a  $\chi^2$  test, a goodness-of-fit index (GFI) greater than 0.95, a comparative fit index (CFI) > 0.95, and a root mean square error of approximation (RMSEA) of less than 0.08 [16].

The reliability of the Thai NS and its three dimensions (as per the original English version) were examined for internal consistency using Cronbach's  $\alpha$  coefficients. Coefficient values  $\geq 0.70$  were considered acceptable reliability coefficients [17].

## **Results**

### **Translation and pilot testing**

The patients during pilot testing reported that they understood the translation and that the items in the translated version were easy to score. Among the 19 items, three had feedback comments. Single unmarried participants found it difficult to answer items N7 and N8 (which refer to a spouse or partner); however, they answered these items with a score of 0, which is the correct response. Some participants preferred that the more specific term of "white blood cells" be used instead of "blood cells" in item N1 (which referred to white blood cells); however, they were able to understand the translation. In consensus with the team, the term "blood cells" was retained in order to maintain accuracy of translation from the English to the Thai version. Thus, the newly formulated Thai version of the 19-item NS was approved without further changes following the pilot study.

### **Sample characteristics**

Among the 260 patients who participated in this study, 57.7% were male, their mean age of all participants was 45.7 years (SD = 16.54). Over half (56.5%) were married, and a major portion (31.2%) had only elementary school education. The majority of the patients had a diagnosis of non-Hodgkin lymphoma (56.5%), a performance status of "some symptoms, but did not require bed rest during awake hours" (60.8%). Cyclophosphamide, hydroxydaunorubicin, Oncovin (vincristine), prednisone or prednisolone (CHOP) or rituximab and CHOP (R-CHOP) was the treatment regimen (38.8%) most commonly encountered (**Tables 1 and 2**).

**Table 1.** Demographic characteristics of participants

Data	n	Percent
<b>Sex</b>		
Male	150	57.7
Female	110	42.3
<b>Age (years) (mean = 45.72, SD = 16.54)</b>		
18–30	60	23.1
31–40	42	16.2
41–50	43	16.5
51–60	63	24.2
>60	52	20.0
<b>Status</b>		
Married	147	56.5
Single	81	31.2
Widowed	14	5.4
Divorced	18	6.9
<b>Education</b>		
Elementary school	81	31.2
Secondary school	67	25.8
Diploma	26	10.0
Graduate	60	23.1
Postgraduate	26	10.0

**Table 2.** Clinical characteristics

Data	n	Percent
<b>Performance Status (PS)</b>		
1. Normal activity, without symptoms	82	31.5
2. Some symptoms, but does not require bed rest during awake hours	158	60.8
3. Require bed rest for less than 50% of awake hours	16	6.2
4. Require bed rest for more than 50% of awake hours	4	1.5
<b>Type of disease</b>		
Non-Hodgkin's lymphoma	147	56.5
Acute myeloid leukemia	64	24.6
Hodgkin's lymphoma	32	12.3
Multiple myeloma	17	6.5
<b>Chemotherapy regimen</b>		
Non-Hodgkin's lymphoma		
CHOP/R-CHOP	101	38.8
EPOCH	15	5.8
ICE/R-ICE	13	5.0
CVP/R-CVP	7	2.7
ESHAP	4	1.5
Hyper-CVAD	6	2.3
R-FC	1	0.4
Hodgkin's lymphoma		
ABV/ABVD	32	12.3
Acute myeloid leukemia		
HIDAC	64	24.6
Multiple myeloma		
Bortezomib	11	4.2
VCD	6	2.3

CHOP = Cyclophosphamide, doxorubicin, vincristine, prednisolone, R = Rituximab  
 EPOCH = Etoposide, vincristine, doxorubicin, cyclophosphamide, prednisolone  
 ICE = Ifosfamide, carboplatin, etoposide  
 CVP = Cyclophosphamide, vincristine, prednisolone  
 ESHAP = Etoposide, methylprednisolone, cytarabine, cisplatin  
 Hyper-CVAD = Cyclophosphamide, mesna, vincristine, doxorubicin, dexamethasone, methotrexate  
 FC = Fludarabine, cyclophosphamide  
 ABV = Adriamycin, bleomycin, vinblastine  
 ABVD = Adriamycin, bleomycin, vinblastine, dacarbazine  
 HDAC = High dose cyclophosphamide  
 VCD = Vincristine, doxorubicin, dexamethasone

### Psychometric properties

#### Validity

##### Content validity

The average degree of agreement of the panel experts of the questionnaire items used in this study was 95% (CVI = 0.95), which indicates a good content validity for the Thai NS.

##### Construct validity

CFA for the Thai NS indicated an acceptable fit as per absolute fit indices:  $\chi^2 = 125.50$  ( $P = 0.148$ ),

degree of freedom = 110, goodness of fit index (GFI) = 0.952, comparative fit index (CFI) = 0.991, and root mean squared error of approximation (RMSEA) = 0.023. All 19 items on the Thai NS had significant ( $P < 0.05$ ) estimated factor loadings. The individual standardized factor loadings of the 19-items in the model ranged from poor to very good (0.16–0.85), while the loading of the three subscales ranged from moderate to good (0.67–0.74) (**Table 3**).

**Table 3.** The results of the confirmatory factor analysis of the neutropenia subscale

Item number	Item content	Item loading ( $\beta$ )
Malaise subscale (8 items)		
An1	I feel listless (“washed out”)	0.6
An5	I have energy	0.2
MS10	I need to rest during the day	0.5
An3	I have trouble starting things because I am tired	0.7
An14	I need help doing my usual activities	0.6
An16	I have to limit my social activity because I am tired	0.2
An13	I am motivated to do my usual activities	0.2
P1	I get aches and pains that bother me	0.6
Worry subscale (5 items)		
N3	I worry about getting infections	0.9
N1	I worry about getting sick due to low blood counts	0.8
N2	I avoid public places for fear of getting an infection	0.4
N4	I worry my condition will not improve if my treatment is delayed	0.6
N7	My partner worries about me when my blood counts are low	0.4
Flu-like symptoms subscale (3 items)		
BRM3	I am bothered by fevers (episodes of high body temperature)	0.7
BRM2	I am bothered by the chills	0.8
ES3	I have night sweats	0.4
Items that did not load on a factor		
N6	I have mouth sores	0.4
N8	My low blood counts interfere with my intimate relationship	0.5
MS3	I am bothered by headaches	0.6
Subscales		
Malaise		0.7
Worry		0.7
Flu-like symptoms		0.7

$\beta$ : Standardized factor item loading



**Table 4.** Mean subscale

Subscale	Mean	SD	Cronbach's $\alpha$
Neutropenia Subscale (NS) (19 items)	47.33	10.15	0.82
Malaise	19.66	4.88	0.71
Worry	10.47	3.94	0.72
Flu-like symptoms	8.17	2.58	0.64

Scores and Cronbach's  $\alpha$  values

*Reliability*

Cronbach's  $\alpha$  coefficients for the Thai NS and its three dimensions were in the adequate to good (0.71–0.82) range, with the exception of the flu-like symptoms subscale (0.64) (**Table 4**).

**Discussion**

Translation of the NS was appropriate with semantic equivalence between the English and Thai versions. The result of content validity testing provides evidence that the NS Thai version truly reflects the concept or construct of neutropenia-related concern of the original NS English version. In addition, the NS on the FACT-N was validated and found to be reliable.

The CFA confirmed that three factors (malaise, worry, and flu-like symptoms) and the three items accurately measure specific neutropenia-related concerns on FACT-N in Thai people. Especially, the finding supported the three items should be retained in the Thai NS. The results are consistent with the findings reported by Wagner and colleagues [8]. However, seven items: An 5, An13, An16, N2, N6, N7, and, ES3 had individual standardized factor loadings less than 0.5 (standardized loading estimates should be  $\geq 0.5$ ) [18]. Among those the factor loading are different from the first published psychometric properties of the FACT-N in malaise subscale [8]. This finding may have resulted from cultural differences, variations in clinical characteristics, and symptom experiences.

In Thai people, cancer patients who experience fatigue usually use coping strategies such as taking on less activity or doing nothing [19]. All of participants were outpatients and among those the majority had performance status level of “some symptoms, but does not require bed rest during awake hours” (60.8%) and “normal activity, without symptoms of disease” (31.5%) respectively. Some participants may have received colony-stimulating factor to prevent the occurrence of neutropenia. They may not have had

experiences related to neutropenia and infection. This may have affected the participants' responses to those items for which the analysis showed low factor loadings.

The reliability scores of the Thai NS and most of its subscales showed adequate to very good range (0.71–0.82). The reliability of the Flu-like symptoms subscale was weak (0.64). This finding is consistent with the initial psychometric testing, the reliability of flu-like subscale was lower than the other subscales, 0.6 at cycle 1, day 1, of chemotherapy, and 0.73 at nadir period of cycle 1. Although the generally agreed lower limit for Cronbach's  $\alpha$  is 0.7, lower criteria are sometimes used in the literature [15]. However, this study has limited generalizability, because only a specific group of patients—those with hematological malignancies—was included.

The NS Thai version met the standards of translation methodology, and demonstrated adequate construct validity and reliability for assessing specific neutropenia-related concerns in Thai patients undergoing cancer chemotherapy.

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**Conflict of interest statement**

The authors have no conflicts of interest to declare.

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