Brief Methodological Report

Validation of the Dutch Version of the Breakthrough Pain Assessment Tool in Patients With Cancer

Wendy H. Oldenmenger, PhD, RN, Anne Lucas, MD, PhD, Gertruud F.H. van der Werff, MANP, Katherine Webber, MD, PhD, Dick Visser, MANP, Annette W.G. van der Velden, MD, and Carin C.D. van der Rijt, MD, PhD

Department of Medical Oncology (W.H.O., C.C.D.v.d.R.), Erasmus MC Cancer Institute, University Medical Center, Rotterdam; Department of Anesthesiology (A.L., D.V.), Intensive Care and Pain Medicine, The Netherlands Cancer Institute, Amsterdam; Department of Internal Medicine and Palliative Care (G.F.H.v.d.W., A.W.G.v.d.V.), Martini Hospital, Groningen, The Netherlands; Department of Supportive and Palliative Care (K.W.), Royal Surrey County Hospital, Guidford, United Kingdom; and Netherlands Comprehensive Cancer Organization (C.C.D.v.d.R.), Utrecht, The Netherlands

Abstract

Context. Essential for adequate management of breakthrough cancer pain is a combination of accurate (re-)assessment and a personalized treatment plan. The Breakthrough Pain Assessment Tool (BAT) has been proven to be a brief, multidimensional, reliable, and valid questionnaire for the assessment of breakthrough cancer pain.

Objectives. The aim of this study was to examine the validity and reliability of the Dutch Language version of the BAT (BAT-DL) in patients with cancer.

Methods. The BAT was forward-backward translated into the Dutch language. Thereafter, the psychometric properties of the BAT-DL were tested, that is factor structure, reliability (internal consistency and test-retest reliability), validity (content validity and construct validity), and the responsiveness to change.

Results. The BAT-DL confirmed the two-factor structure in 170 patients with cancer: pain severity/impact factor and pain duration/medication efficacy factor. The Cronbach's alpha coefficient was 0.72, and the intraclass correlation for the test-retest reliability was 0.81. The BAT-DL showed to be able to differentiate between different group of patients and correlated significantly with the Brief Pain Inventory. In addition, the BAT-DL was capable to detect clinically important changes over time.

Conclusion. The BAT-DL is a valid and reliable questionnaire to assess breakthrough pain in Dutch patients with cancer and is a relevant questionnaire for daily practice. J Pain Symptom Manage 2020;■:■−■.

Key Words

Breakthrough pain, cancer, pain assessment, validation studies, pain measurement, psychometrics

Key Message

This article describes a prospective study that tested the psychometric factors of the Dutch language version of the Breakthrough Pain Assessment Tool (BAT-DL) in 170 patients with cancer-related pain. The results indicate that the BAT-DL is a valid and reliable questionnaire. Therefore, the BAT-DL seems to be a relevant questionnaire for daily practice.

Introduction

Pain is one of the most common symptoms in patients with cancer. Depending on the cancer type, stage of the disease, and setting, 33%−64% of the

Address correspondence to: Wendy H. Oldenmenger, PhD, RN, Department of Medical Oncology, Erasmus MC Cancer Institute, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands. E-mail: w.h.oldenmenger@erasmusmc.nl

Accepted for publication: December 2, 2019.

0885-3924/$ - see front matter
https://doi.org/10.1016/j.jpainsymman.2019.12.009

patients with cancer experience pain.[1] Moreover, half of the patients with cancer-related pain experience breakthrough cancer pain (BTcP).[2] Breakthrough pain has been defined as a transient exacerbation of pain that occurs either spontaneously or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain.[3] Characteristics of BTcP are the rapid onset of the pain, short duration, frequent occurrence, and moderate-to-severe intensity.[4–6] BTcP interferes with daily activities. Patients with BTcP report loss of control, changes in lifestyle, and diminished quality of life.[4–7]

Because the intensity, impact, and consequences of BTcP varies per patient, a thorough (re-)assessment of patients' pain and a personalized treatment plan is required to successfully manage the pain.[8,9] Patients' pain assessment exists of a thorough examination and a detailed history, inclusive of detailed information about the different aspects of the exacerbations of the pain.[8,9]

The Breakthrough Pain Assessment Tool (BAT) has been developed for the assessment and monitoring of BTcP in daily practice, based on published guidelines, and a Delphi process with pain experts in codesign with 10 patients with BTcP.[4,10] Thereafter, the psychometric factors of the questionnaire were tested in 100 patients with cancer: it was proven to be a multidimensional, reliable, and valid questionnaire for the assessment of BTcP.[10] The aim of this study was to examine the validity and reliability of the Dutch Language version of the BAT (BAT-DL).

Methods

In this study, the BAT was first translated into the Dutch language, after which the psychometric properties of the BAT-DL were tested.

Translation

We translated the BAT into the Dutch language according the European Organisation for Research and Treatment of Cancer guidelines.[11] The forward translation was performed by two Dutch physician-nurse couples, experts in palliative care. The project manager merged the translated questionnaires into one questionnaire. Subsequently, four native-English health care professionals translated the questionnaire back into English, after which the four versions were synthesized. The final backward-translated questionnaire was confirmed by the authors of the original BAT. The BAT-DL was tested by 15 patients with BTcP. Every patient self-completed the questionnaire, and afterward, the project manager interviewed these patients to determine if the questions were difficult to answer, difficult to understand, confusing, shocking or offensive, and finally what other suggestions they would have to reformulate the question. As a result, we reformulated the Dutch language of two questions after agreement with all eight translators. The final version of the BAT-DL was approved by the pain consultation team of the Erasmus University Medical Center (MC), the translators and involved patients.

Psychometric Properties

The psychometric properties of the BAT-DL were tested in a prospective multicenter observational study conducted at the Erasmus MC, Netherlands Cancer Institute, Martini Hospital, University Medical Center Utrecht, Rijnstate Hospital, Spaarne Hospital, and Hospice Kuria. The ethic committee of each of the participating centers approved the study. The study was conducted in accordance with the Declaration of Helsinki and the local governance procedures. All patients provided written informed consent.

Patients. The psychometric properties of the BAT-DL were assessed in 170 patients with cancer. Each institute had a study coordinator who was responsible for the inclusion. All patients were recruited from the inpatient and outpatient populations. The inclusion criteria were histologically confirmed diagnosis of cancer; pain because of cancer or its treatment; regular scheduled analgesia taken in the previous week; breakthrough pain according to a pain specialist;[3,12] use of at least one dose of rescue medication for an episode of BTcP in the previous week; cognitive status sufficient for accurate completion of the study; and age older than 18 years, Dutch speaking, and able to provide written informed consent. Exclusion criteria were patients whose performance status[13] was too poor to allow them to complete the study as judged by a pain specialist.

Measurements. Patients completed a questionnaire containing the BAT-DL and Brief Pain Inventory (BPI) at baseline and after a week. In addition, patients were asked to provide demographic information and complete questions about the adequacy of BTcP and the need for changes in their analgesics. At the same time, pain specialists assessed all patients at baseline and were asked to provide clinical information, for example, performance status, using the Eastern Cooperative Oncology Group (ECOG) performance status,[13] and to complete questions about the adequacy of breakthrough pain control, the need for changes in the patients' analgesics, and to report the current analgesic regimen. During the assessment after a week, both patients and clinicians were asked to comment on any change in the breakthrough pain compared with the week before (i.e.,

better, same, worse). This was used to assess the responsiveness to change of the BAT-DL. In addition, an extra assessment took place, 24 hours after baseline, when patients were asked to complete the BAT-DL to assess the test-retest reliability of the questionnaire.[10,14]

The BAT-DL contains 14 questions evaluating current pain management: nine questions related to pain and five questions related to the pain treatment. In six questions, 0−10 Numerical Rating Scales are used; in three questions, categorical scales are used; in four questions, free text; and in one question, a body shape outline to mark the site of the pain is used.[10]

The BPI measures pain intensity and daily interference on a 0−10 Numerical Rating Scale. Pain intensity is measured as current pain, worst pain, average pain, and least pain. Interference by pain in daily life (daily interference) is assessed by seven items: general activity, mood, walking ability, normal work, sleep, relations with other people, and enjoyment of life. A mean interference score is computed by taking the average of the seven items. In addition, there is one question on the benefit of the treatment rated as the percentage of pain relief (0% = no relief and 100% = complete relief).[15,16]

Data Analysis. The data of this study were analyzed using IBM SPSS, Version 25 (IBM Corporation, Armonk, NY). Descriptive statistics (percentages, means, and SD) were used to present the study sample's demographics and disease-related characteristics.

Different aspects of validity and reliability were analyzed (Appendix Table 1). Structural validity was determined by confirmatory factor analysis. We hypothesized a two-factor structure for the BAT-DL, based on the structure of the original BAT.[10] Construct validity was measured by a known-group analysis; the between-group differences were calculated using an independent t-test. Convergent validity was determined by correlating BAT item scores and related measurements, using a Pearson correlation analysis for continuous variables and the Spearman rank-order correlation analysis for ranked or ordered variables. Responsiveness to change was calculated to determine whether the BAT can detect clinically significant changes in breakthrough pain. For this analysis, we used both patients' and clinicians' assessment of the BTcP after one week. Internal consistency reliability was estimated by Cronbach's alpha coefficients. Test-retest reliability was analyzed by calculation of the intraclass correlation coefficients between the baseline data and after 24 hours to measure whether the BAT was stable under similar conditions (Appendix Table 1).

Table 1
Patient Characteristics

Characteristics	Number of Patients ($N = 170$), n (%)
Age; median (range)	61 (30−89)
Gender	
Male	95 (56)
Female	75 (44)
Cancer diagnosis, n (%)	
Gastrointestinal	37 (22)
Urological	34 (20)
Breast	33 (19)
Lung	23 (14)
Head and neck	18 (11)
Sarcoma	9 (5)
Multiple myeloma	6 (4)
Melanoma	5 (3)
Others	5 (3)
Disease stage, n (%)	
Locally advanced	34 (20)
Metastatic	130 (77)
Unknown	6 (4)
Subject type, n (%)	
Outpatient	40 (24)
Inpatient	130 (76)
Anticancer treatment, n (%)	
None	55 (32)
Chemotherapy	55 (32)
Hormonal therapy	14 (8)
Radiotherapy	42 (25)
Other	33 (20)
Pain etiology, n (%)	
Cancer-related	132 (78)
Cancer treatment-related	13 (8)
Mixed	24 (14)
Unknown	2 (1)
Type of pain, n (%)	
Nociceptive	84 (49)
Neuropathic	2 (1)
Mixed	81 (48)
Missing	3 (2)
Pain intensity, mean (SD)	
Current pain	3.4 (2.1)
Average pain	4.8 (1.9)
Worst pain	8.1 (1.5)

Results

Between August 2015 and August 2018, we included 170 patients with BTcP. The median age was 61 years (range 30−89); 56% were males; the most common cancer sites were gastrointestinal (22%), urological (20%), and breast (19%); and 77% of the patients had metastatic disease (Table 1). Twelve patients (7%) did not complete the assessment after 24 hours, and 17 patients (10%) did not complete the assessment after a week. The main reasons for this were patients who felt too unwell to complete the questionnaire ($n = 10$), problems getting in contact with the patient ($n = 5$), or the reason was unknown ($n = 2$).

According to the pain specialist, 49% of the patients had incident BTcP, 10% spontaneous BTcP, and 41% had a combination. The most prevalent frequency of BTcP was greater than four times a day (45%), and

Table 2
Factor Loading of BAT Items

	Factor	
BAT Items	1	2
How often do you get breakthrough pain?	0.474	
How long does a typical episode of breakthrough pain last?		0.592
How severe is your worst breakthrough pain?	0.598	
How severe is a typical breakthrough pain?	0.662	
How much does the breakthrough pain distress you?	0.854	
How much does the breakthrough pain stop you from living a normal life?	0.797	
How effective is the painkiller for your breakthrough pain (reversed)?		0.319
How long does the painkiller take to have meaningful effect?		0.794
How much do the side effects from your breakthrough painkiller bother you?	0.450	

BAT = Breakthrough Pain Assessment Tool.

the duration of a BTcP episode varied from less than five minutes (19%) to >60 minutes (15%) (Appendix Table 2). Most patients reported that their pain significantly interfered with their daily life (Appendix Table 3). Most patients had cancer-related pain, used long-acting opioids for their background pain (median morphine equivalent daily dose 120 mg [interquartile range 60,240 mg]), and immediate-release opioids (80%) and/or rapid-onset opioids (20%) for their BTcP (Appendix Table 4; Table 1).

Reliability

The questions of the BAT-DL loaded onto two factors, a *pain severity and impact factor* and a *pain duration and medication efficacy factor* (Table 2). The Cronbach's alpha coefficient for the BAT-DL was 0.72. The values for the separate factors were 0.76 (pain severity and impact factor) and 0.27 (pain duration and medication efficacy factor). To determine the test-retest reliability, we calculated the intraclass correlation coefficient for the BAT-DL (0.81; 95% CI 0.74−0.87), pain severity and impact factor (0.88; 95% CI 0.83−0.92), and pain duration and medication efficacy factor (0.60; 95% CI 0.43−0.73).

Validity

In the group with patient-determined adequately controlled BTcP, the mean scores for all BAT-DL questions were statistically significantly lower compared with the group with patient-determined inadequately controlled BTcP, except for two questions (*How long does the painkiller take to have a meaningful effect* and *How much do the side effects for the breakthrough painkiller bother you*). This was confirmed with the clinicians' global impression of BTcP, except for the question *How long does a typical episode of BTcP last?*, which was not significant (Table 3).

Patients with an ECOG performance status of 3−4 scored statistically significantly higher on BAT-DL questions about pain severity, distress, and interference compared with patients with an ECOG status of 0−2.

The correlations between the BAT-DL and the BPI are presented in Table 4. There was a strong correlation between the item *How severe is your worst BTcP?* and the BPI worst pain item ($r = 0.65$). The BAT-DL item *How severe is a typical BTcP?* has a strong correlation with the BPI items' worst pain ($r = 0.55$) and average pain ($r = 0.54$). In addition, the BAT-DL item *How much does the BTcP stop you from living a normal life?* was strongly correlated with the BPI item general activity ($r = 0.59$), work ($r = 0.57$), and the BPI total item ($r = 0.55$). The BAT-DL item *How effective is the painkiller for your BTcP* was strongly correlated to the BPI item pain relief ($r = 0.65$; Table 4).

The BAT-DL was able to detect clinically significant changes in BTcP (Table 5). When patients assessed their BTcP after a week as better, six of the nine BAT-DL items were also statistically significantly lower compared with the baseline measurements. When the clinician assessed patients' pain as better after a week, patients scored five of the nine BAT-DL items statistically significantly lower compared with the baseline measurements (Table 5).

Discussion

In this study, we translated the BAT into the Dutch language. The BAT-DL showed to be a valid and reliable instrument for the assessment and evaluation of breakthrough pain in Dutch patients with cancer, and it is a relevant questionnaire for daily practice.

The factor analysis showed that the BAT-DL loaded onto two factors, pain severity and impact factor and pain duration and medication efficacy factor, similar to the other validation studies in the U.K. and South Korea.[10,14] However, the last question, *How much do the side effects from the breakthrough painkiller bother you?*, loaded in the Korean version onto the second factor. Our present study confirmed the factors and factor loading of the original study.[10]

An important feature of the BAT-DL is that this questionnaire is able to distinguish various groups of patients, such as between groups with adequately vs. inadequately controlled BTcP. As expected, patients with inadequately controlled BTcP had significantly

Table 3
Comparison of BAT by Global Impression of Breakthrough Pain Control

	Patient's Global Impression of BTcP			Clinician's Global Impression of BTcP		
BAT Items	Adequately Controlled ($N = 97$)	Inadequately Controlled ($N = 50$)	*P*	Adequately Controlled ($N = 105$)	Inadequately Controlled ($N = 43$)	*P*
How often do you get breakthrough pain?	5.2 (2.0)	6.6 (1.5)	**0.000**	5.4 (1.9)	6.4 (1.8)	**0.006**
How long does a typical episode of breakthrough pain last?	5.5 (2.4)	6.4 (2.4)	**0.041**	5.8 (2.4)	5.9 (2.5)	0.816
How severe is your worst breakthrough pain?	6.9 (2.2)	7.7 (1.5)	**0.009**	6.8 (2.1)	8.1 (1.4)	**0.000**
How severe is a typical breakthrough pain?	4.99 (2.1)	5.98 (1.6)	**0.002**	4.9 (2.0)	6.4 (1.3)	**0.000**
How much does the breakthrough pain distress you?	5.95 (2.5)	7.4 (1.8)	**0.000**	5.97 (2.5)	7.5 (1.6)	**0.000**
How much does the breakthrough pain stop you from living a normal life?	6.2 (2.9)	7.9 (2.0)	**0.000**	6.2 (2.9)	8.2 (1.5)	**0.000**
How effective is the painkiller for your breakthrough pain (reversed)?	2.6 (1.7)	4.4 (2.1)	**0.000**	3.0 (2.0)	3.9 (1.9)	**0.011**
How long does the painkiller take to have meaningful effect?	6.5 (1.8)	6.6 (2.1)	0.604	6.4 (1.9)	6.6 (1.9)	0.709
How much do the side effects from your breakthrough painkiller bother you?	2.9 (2.8)	3.7 (3.1)	0.127	3.0 (2.9)	3.5 (3.0)	0.308

BAT = Breakthrough Pain Assessment Tool; BTcP = breakthrough cancer pain.
Significance of bold values is as follows: *P*-value ≤ 0.5.

higher BAT item scores than patients whose BTcP was adequately controlled. In contrast to the original study, our study also showed a statistically significant improvement of pain intensity and distress in patients in whom BTcP became adequately controlled according to the clinicians.[10] However, the differences between these groups at two other questions (about time to a meaningful effect and side effects) were not significant in our study in contrast to the U.K. study.[10] The Korean study did not describe such an analysis.[14] Another comparison was based on the performance status. As expected, patients with a bad performance also scored worse at the BAT, especially on items about pain intensity, pain interference, and distress, as in the original study.[10]

The BAT-DL correlated well with the BPI (convergent validity). The BAT-DL pain severity items, interference items, as well as the distress items were moderately good correlated with the BPI total interference item, the same as in the original study.[10] The Korean study did not report on the BPI total interference item.[14] In addition, the items about the worst and typical BTcP episode correlated well with all BPI pain intensity items in the present study, comparable to the Korean study.[14] However, in the U.K. study, these two items showed no correlation with BPI least pain intensity and current pain intensity.[10] Moreover, the BAT-DL items about distress and disruption of normal life correlated well to most BPI questions, comparable to the earlier studies.[10,14] This confirmed that there is an easier way to ask for interference of pain. Based on the known-group analyses and the convergent validity, we conclude that the BAT-DL demonstrated acceptable levels of construct validity.

Another important factor for daily practice is the ability to demonstrate clinically relevant changes over time. The BAT-DL confirmed the responsiveness to change of the BAT[10] to detect clinically significant changes in BTcP. When the BTcP was scored as better after a week (Table 5), especially the pain severity and interference items scored statistically significantly lower at the questionnaire one week later. The only item that did not show a difference was about the side effects; however, patients scored the influence of side effects already as mild at baseline.

Finally, the BAT-DL demonstrated acceptable levels of reliability: test-retest reliability (>0.8) and internal consistency (>0.7), both above the recommended cut-off,[17] comparable to the two earlier studies.[10,14] Therefore, the BAT-DL seems to be a reliable questionnaire for breakthrough pain assessment in patients with cancer.

As all studies, this study has some limitations. An advantage is that this is a multicenter study; however, the consequence is a possible variation in clinical experiences in BTcP. In every hospital, a pain specialist included the patients, which might have caused variation in patients' pain management. However, this is also a reflection of daily practice. Some of the hospitals had problems to include patients as most of the patients had uncontrolled background pain, and therefore, these patients did not adhere to the definition of BTcP we used in this study.[3] The included patients had BTcP as assessed by a pain specialist,[3] although some patients independently scored their pain intensity >4 on the research questionnaire. The definition of BTcP does not use any description related to pain intensity. In this study, the clinical examination was used as the gold standard.[3] An

Table 4
Convergent Validity Between BAT and BPI

	BPI Pain Intensity Items					BPI Interference Items							
BAT Items	Worst Pain	Least Pain	Average Pain	Pain Now	% of Pain Relief	General Activity	Mood	Walking	Work	Relations With Others	Sleep	Enjoyment of Life	Total
How often do you get breakthrough pain?	0.217	0.190	**0.364**	**0.321**	**−0.355**	**0.477**	**0.307**	0.206	**0.389**	0.122	0.252	0.236	**0.367**
How long does a typical episode of BTcP last?	0.202	**0.308**	0.237	**0.326**	−0.158	0.031	0.172	0.17	0.057	0.182	0.064	0.168	0.165
How severe is your worst breakthrough pain?	**0.646**	**0.358**	**0.468**	**0.361**	−0.239	**0.340**	0.262	0.227	**0.317**	0.203	0.209	0.214	**0.318**
How severe is a typical breakthrough pain?	**0.551**	**0.334**	**0.540**	**0.468**	−0.209	**0.400**	**0.423**	0.176	0.285	**0.329**	**0.428**	0.293	**0.410**
How much does the BTcP distress you?	**0.447**	0.287	**0.375**	**0.323**	−0.277	**0.466**	**0.324**	0.188	**0.391**	0.277	**0.354**	**0.300**	**0.436**
How much does the BTcP stop you from living a normal life?	**0.441**	0.184	**0.346**	0.250	−0.239	**0.594**	**0.397**	**0.385**	**0.569**	0.237	0.266	**0.417**	**0.549**
How effective is the painkiller for your BTcP?	−0.05	−0.159	−0.211	−0.276	**0.652**	−0.288	−0.157	−0.153	−0.228	−0.084	−0.027	−0.066	−0.200
How long does the painkiller for your BTcP take to have a meaningful effect?	0.119	0.169	0.100	0.097	0.036	−0.056	−0.017	0.144	0.121	0.051	0.054	−0.011	0.066
How much do side effects from your BTcP painkiller bother you?	0.165	0.260	0.287	0.166	−0.040	0.193	**0.395**	0.131	0.171	0.097	0.225	0.222	0.257

BAT = Breakthrough Pain Assessment Tool; BPI = Brief Pain Inventory; BTcP = breakthrough cancer pain.
Correlation coefficient values >0.1 represent a small correlation, >0.3 medium, and >0.5 large.
Significance of bold values is as follows: *P*-value ≤ 0.5.

Table 5
Responsiveness to Change Based on Assessment of BTcP Baseline Compared With One Week Later

	Patient's Assessment of BTcP Better ($N = 71$)			Clinician's Assessment of BTcP Better ($N = 75$)		
	Baseline	After One Week		Baseline	After One Week	
BAT Items	Mean (SD)		*P*	Mean (SD)		*P*
How often do you get breakthrough pain?	7.8 (1.6)	5.5 (2.0)	**0.000**	6.8 (1.7)	5.5 (1.9)	**0.000**
How long does a typical episode of breakthrough pain last?	5.8 (2.5)	5.4 (2.3)	0.167	5.6 (2.5)	5.6 (2.5)	0.925
How severe is your worst breakthrough pain?	8.2 (1.4)	6.8 (2.3)	**0.000**	8.0 (1.6)	6.6 (2.1)	**0.000**
How severe is a typical breakthrough pain?	6.2 (1.7)	4.7 (1.9)	**0.000**	6.0 (1.8)	4.8 (2.0)	**0.000**
How much does the breakthrough pain distress you?	7.6 (2.1)	5.9 (2.7)	**0.000**	7.4 (2.2)	6.1 (2.6)	**0.000**
How much does the breakthrough pain stop you from living a normal life?	7.6 (2.2)	5.9 (2.7)	**0.000**	7.5 (2.2)	6.6 (2.8)	**0.004**
How effective is the painkiller for your breakthrough pain (reversed)?	3.5 (2.3)	2.6 (1.6)	**0.005**	3.3 (2.1)	3.1 (2.1)	0.696
How long does the painkiller take to have meaningful effect?	6.8 (2.3)	6.5 (1.8)	0.313	6.4 (2.2)	6.4 (1.9)	1.0
How much do the side effects from your breakthrough painkiller bother you?	3.4 (3.1)	2.8 (2.7)	0.228	3.7 (2.9)	2.9 (2.8)	0.233

BTcP = breakthrough cancer pain.
Significance of bold values is as follows: *P*-value ≤ 0.5.

advantage of the present study was the number of included patients ($n = 170$), which ensured that there were enough patients for the subgroup analyses.

In conclusion, this study confirmed that the BAT-DL is a valid and reliable questionnaire to assess breakthrough pain in patients with cancer.

Disclosures and Acknowledgments

The authors acknowledge the assistance of the staff at the research institutions: Erasmus University Medical Center, Netherlands Cancer Institute, Martini Hospital, University Medical Center Utrecht, Rijnstate Hospital, Spaarne Hospital, VU University Medical Center, and Hospice Kuria, The Netherlands. In addition, they thank Dr. Andrew Davies for his contribution during the translation of the questionnaire.

This work was financially supported by a grant from the Innovation Fund of the Dutch Health Insurers, The Netherlands, without any influence on study design, analysis, interpretation, or presentation.

Ethical approval: The study protocol was approved by the Institutional Review Board of the Erasmus MC (MEC-2013-056).

The authors declare no conflicts of interest.

References

1. van den Beuken-van Everdingen MH, Hochstenbach LM, Joosten EA, Tjan-Heijnen VC, Janssen DJ. Update on prevalence of pain in patients with cancer: systematic review and meta-analysis. J Pain Symptom Manage 2016;51:1070–1090.e9.

2. Deandrea S, Corli O, Consonni D, Villani W, Greco MT, Apolone G. Prevalence of breakthrough cancer pain: a systematic review and a pooled analysis of published literature. J Pain Symptom Manage 2014;47:57–76.

3. Davies AN, Dickman A, Reid C, Stevens AM, Zeppetella G. The management of cancer-related breakthrough pain: recommendations of a Task Group of the Science Committee of the Association for Palliative Medicine of Great Britain and Ireland. Eur J Pain 2009;13:331–338.

4. Webber K, Davies AN, Cowie MR. Breakthrough pain: a qualitative study involving patients with advanced cancer. Support Care Cancer 2011;19:2041–2046.

5. Davies A, Zeppetella G, Andersen S, et al. Multi-centre European study of breakthrough cancer pain: pain characteristics and patient perceptions of current and potential management strategies. Eur J Pain 2011;15:756–763.

6. Bedard G, Hawley P, Zhang L, et al. A survey of Canadian cancer patients' perspectives on the characteristics and treatment of breakthrough pain. Support Care Cancer 2013;21:2557–2563.

7. Hjermstad MJ, Kaasa S, Caraceni A, et al. Characteristics of breakthrough cancer pain and its influence on quality of life in an international cohort of patients with cancer. BMJ Support Palliat Care 2016;6:344–352.

8. Vissers KCP, Van den Beuken-van Everdingen MHJ, Dijstra D, et al. Dutch guideline: Diagnostics and treatment of pain in patients with cancer. 2016, Nederlandse Vereniging voor Anesthesiologie, Utrecht, The Netherlands.

9. Davies AN, Elsner F, Filbet MJ, et al. Breakthrough cancer pain (BTcP) management: a review of international and

national guidelines. BMJ Support Palliat Care 2018;8:241–249.

10. Webber K, Davies AN, Zeppetella G, Cowie MR. Development and validation of the breakthrough pain assessment tool (BAT) in cancer patients. J Pain Symptom Manage 2014;48:619–631.

11. Dewolf L, Koller M, Velikova G, et al. EORTC quality of life group, translation procedure, 3rd ed. Brussels: EORTC, 2009.

12. Webber K. Development of the Breakthrough Pain Assessment Tool (BAT) in cancer patients. Int J Palliat Nurs 2014;20:424.

13. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5:649–655.

14. Shin J, Cho SJ, Lee J, Choi YS. Validation of the Korean version of the Breakthrough Pain Assessment Tool in cancer patients. J Pain Symptom Manage 2017;54:361–367.

15. Enting RH, Oldenmenger WH, Van Gool AR, van der Rijt CC, Sillevis Smitt PA. The effects of analgesic prescription and patient adherence on pain in a Dutch outpatient cancer population. J Pain Symptom Manage 2007;34:523–531.

16. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 1994;23:129–138.

17. Cronbach L, Warrington W. Coefficient alpha and internal structure of tests. Psychometrika 1951;16:297–334.

Appendix

Appendix Table 1
Validity and Reliability Testing of the BAT-DL

Psychometric Property	Description
Reliability	The purpose of this analysis was to ensure that the items correlate with the remainder of the questionnaire
Internal consistency	• Cronbach's alpha coefficients were calculated for the six questions with a 0−10 Numeric Rating Scale • Cronbach's alpha coefficient >0.7 indicate good internal consistency[17]
Test-retest reliability	The purpose was to ensure that the underlying construct is stable, and that similar results are reached over two distinct periods in unchanged conditions
	• In patients who scored their BTcP as stable after 24 hours, the intraclass correlation coefficient was calculated for the BAT-DL and the two factors
Validity	The purpose of this analysis is to determine whether the instrument is an adequate reflection of the dimensionality of the construct to be measured
Structural validity	*Hypothesis:* The BAT-DL will confirm the two-factor structure of the original BAT • Confirmatory factor analysis
Content validity	During the translation of the BAT, the project group, a group of clinical experts, assessed the BAT-DL and gave their opinion on its relevance, appropriateness, and to what extent the BAT is a sufficient assessment tool for breakthrough pain
Construct validity	The purpose of this analysis was to determine the ability of the BAT to differentiate between different group of patients
Known group analysis/hypothesis testing	*Hypothesis*: BAT scores should be significantly higher in patients defined as having inadequately controlled BTcP • Patient-determined adequately controlled BTcP vs. inadequately controlled BTcP • Clinician-determined adequately controlled BTcP vs. inadequately controlled BTcP (*Table 3*)
	Hypothesis: BAT scores should be significantly higher in patients with a lower performance status • Patients with ECOG performance status 3−4 vs. ECOG performance status 0−2
Construct validity	The purpose of these analysis was to determine correlations between the BAT item scores and related measures:
Convergent validity	• BPI item scores and total interference score (*Table 4*)
Responsiveness to change	The purpose of this analysis was to determine whether the BAT can detect clinically important changes over time that are related to BTcP
	• BAT item scores at baseline vs. BAT item scores after a week in patients who assessed their BTcP as better after a week • BAT item scores at baseline vs. BAT item scores after a week in patients whose clinician assessed their BTcP as better after a week (*Table 5*)

BAT-DL = the Dutch Language version of the Breakthrough Pain Assessment Tool; BTcP = breakthrough cancer pain; ECOG = Eastern Cooperative Oncology Group.

Appendix Table 2
Breakthrough Pain Assessment Tool

	Baseline ($N = 170$)	After One Day ($N = 153$)	After One Week ($N = 153$)
BAT Items	Mean (SD)		
How often do you get breakthrough pain?	6.5 (1.7)	6.1 (1.9)	5.7 (1.9)
How long does a typical episode of breakthrough pain last?	5.6 (2.6)	5.9 (2.6)	5.8 (2.4)
How severe is your worst breakthrough pain?	8.2 (1.5)	7.5 (1.7)	7.2 (2.0)
How severe is a typical breakthrough pain?	6.2 (1.7)	5.5 (1.7)	5.3 (2.0)
How much does the breakthrough pain distress you?	7.2 (2.1)	6.7 (2.2)	6.5 (2.4)
How much does the breakthrough pain stop you from living a normal life?	7.3 (2.3)	7.0 (2.4)	6.8 (2.7)
How effective is the painkiller for your breakthrough pain? (reversed)	3.3 (2.1)	3.3 (2.0)	3.2 (2.0)
How long does the painkiller take to have meaningful effect?	6.7 (2.2)	6.7 (2.1)	6.5 (1.9)
How much do the side effects from your breakthrough painkiller bother you?	3.4 (3.0)	3.4 (2.8)	3.1 (2.9)

Appendix Table 3
Brief Pain Inventory

	Baseline ($N = 170$)	After One Week ($N = 150$)
BPI Items	Mean (SD)	
Worst pain intensity	8.1 (1.5)	7.1 (2.1)
Least pain intensity	2.4 (1.7)	2.4 (1.7)
Average pain intensity	4.8 (1.9)	4.4 (1.9)
Current pain intensity	3.4 (2.1)	3.4 (2.2)
Pain relief (%)	69.9 (20.4)	66.2 (22.1)
Pain interference: general activity	6.4 (2.7)	5.7 (2.7)
Pain interference: mood	4.4 (2.8)	4.4 (2.7)
Pain interference: walking ability	5.6 (3.4)	5.3 (3.1)
Pain interference: normal work	7.1 (3.0)	6.6 (3.0)
Pain interference: sleep	4.2 (3.1)	3.5 (2.8)
Pain interference: relations with other people	3.5 (3.0)	3.4 (2.8)
Pain interference: enjoyment of life	4.6 (2.9)	4.8 (2.9)
Brief Pain Inventory total (interference)	5.1 (2.1)	4.8 (2.1)

Appendix Table 4
Prescribed Analgesics

Analgesics	Baseline ($N = 170$), n (%)	After One Week ($N = 152$), n (%)
MEDD (mg/day); median (IQR)	120 (60, 240)	120 (60, 270)
Analgesics, Step 1		
Paracetamol	157 (92)	138 (91)
NSAID	47 (28)	42 (28)
Analgesics, Step 2		
Tramadol	1	0
Analgesics, Step 3 (background pain)		
Morphine	32 (19)	25 (16)
Fentanyl	72 (42)	63 (41)
Oxycodone	50 (29)	43 (28)
Hydromorphone	15 (9)	19 (13)
Buprenorphine	2 (1)	1 (1)
Methadone	4 (2)	4 (3)
Adjuvant analgesics		
Antidepressants	18 (11)	18 (12)
Anticonvulsants	42 (25)	41 (27)
Steroids	7 (4)	5 (3)
Rescue analgesics		
Morphine (IR)	48 (28)	36 (24)
Oxycodone (IR)	71 (42)	65 (43)
Hydromorphone (IR)	15 (9)	19 (13)
Fentanyl (IV)	1	1 (1)
Buprenorphine (IR)	2 (1)	1 (1)
Intranasal fentanyl spray	4 (2)	2 (1)
Sublingual fentanyl	30 (18)	31 (20)

MEDD = morphine equivalent daily dose; IQR = interquartile range; NSAID = nonsteroidal anti-inflammatory drug; IR = immediate release; IV = intravenous.