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Running title: PORTUGUESE BREAKTHROUGH PAIN ASSESSMENT TOOL

Cultural Adaptation and Psychometric Validation of the Portuguese Breakthrough Pain Assessment Tool with Cancer Patients.

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Cultural Adaptation and Psychometric Validation of the Portuguese Breakthrough Pain Assessment Tool with Cancer Patients.

Abstract

Background and aims: Breakthrough cancer pain (BTcP) is a transient exacerbation of pain that occurs over persistent, stable, and adequately controlled cancer background pain. It is prevalent and bears severe consequences to patients' quality-of-life. The effective management of BTcP depends on fast and reliable (re)assessment. The Breakthrough pain Assessment Tool (BAT) is one of the most concise and reliable self-report instruments adapted to clinical contexts so far, showing good psychometric qualities in the United Kingdom, the Netherlands, and South Korea. As to promote the effective management of BTcP in Portuguese-speaking communities this study, first aimed to culturally adapt and validate the Portuguese version of the BAT (BAT-Pt). Second, and most importantly, it sought to provide novel evidence on its criterion validity by investigating its association with measures of psychological distress, which has not been yet investigated.

Methods: The BAT was translated into European Portuguese, using the back-translation method, and culturally adapted. Its psychometric properties (factor structure, internal consistency, construct and criterion validity) were analyzed in a cross-sectional multicenter study, with a sample of 65 cancer patients (49.2% women) recruited from eight hospitals in mainland Portugal (*a priori* power analysis determined a minimum sample of 50). Health professionals collected patients' clinical information, assessed their functional disability (*ECOG Performance Status*) and the adequacy of pain control. In addition to the Portuguese version of the BAT (BAT_Pt), patients completed the Portuguese versions of the *Brief Pain*

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Inventory, the *Hospital Anxiety and Depression Scale*, a *Distress Thermometer* and answered questions about the adequacy of pain control.

Results: The BAT-Pt was very well accepted by experts and patients. As hypothesized, a Principal Axis Factor Analysis revealed two underlying factors accounting for 55.2% of the variance: (1) *Pain Severity and Impact* of BTcP and (2) *Duration of BTcP and Medication Inefficacy*. Two items (on episode frequency and medication efficacy) were analyzed separately given their lower/cross loadings. The BAT-Pt showed good internal consistency overall (α=0,79) and for each sub-scale, namely, *Pain Severity and Impact* of BTcP (n=5 items; α=0,86) and *Duration of BTcP and Medication Inefficacy (n=2 items; r_{sb}=0,62)*. The BAT-Pt showed good convergent validity, being moderately to strongly associated with overall pain severity and interference (.46<*r*<.77, *p*<.001). It also showed good concurrent validity by being associated not only with physical outcomes - such as functional disability (r=.40, p<.001) and patient- and physician-determined adequacy of BTcP control (|.25<r_{pb}<.63|, p_s<.05). – but also, with distress (.33<r<.46, p_s<.001), anxiety (.28<r<.44, p_s<.05) and depression (r=.47, p<.001).

Conclusions: The BAT-Pt is a reliable and valid measure of breakthrough pain in Portuguese cancer patients and it is strongly associated to physical and psychological outcomes.

Implications: This study confirms and extends the psychometric validation of the BAT to a new cultural context, promoting its diffusion and use by researchers and clinicians in Portuguese-speaking communities. The BAT-Pt may be an invaluable tool for daily clinical practice by tapping multiple aspects of BTcP experiences that are associated to patients' physical and psychological outcomes.

Keywords

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Breakthrough pain, Neoplasms, Pain Measurement, Validity and Reliability, Psychological Distress

Background and aims

Pain is one of the most common and feared experiences of cancer patients [1]. Breakthrough cancer pain (BTcP) is a transient exacerbation of pain that occurs over persistent, stable, and adequately controlled cancer background pain [2-3]. BTcP is often characterized by relatively frequent pain spikes (1 to 4 per day) [4], of short duration (1 to 240 min) [3] and of moderate to severe intensity [5]. The prevalence of BTcP can reach 59% of cancer patients [5] and it is often associated with low pain control satisfaction, physical disabilities, sleep disturbances, stress, anxiety, depression, social isolation, and low quality of life [6-10].

An effective pharmacological treatment of BTcP often depends on reliable (re)assessment procedures [2]. The Breakthrough pain Assessment Tool (BAT) [11] seems to be one of the most useful, concise, and reliable self-report instruments adapted to clinical contexts so far. It taps into multiple specific dimensions of BTcP, namely, its severity and impact on daily life (dimension 1) and duration and medication efficacy (dimension 2). Its original psychometric study conducted in the United Kingdom [11] and the adaptation and validation studies for the Korean [12] and Dutch [13] populations have shown that the BAT has good psychometric qualities across these different cultures. In all three studies the BAT presented the expected two-factor structure, showed good levels of internal consistency and temporal stability for the total scale and its severity and impact subscale and fair levels of reliability for its duration and medication efficacy subscale [11-13]. The BAT has also shown good validity by differentiating patients based on their clinical characteristics, mostly physical outcomes such as levels of overall pain, medication dosage, disease progression and physical functioning [11-

13]. However, the extent to which the BAT is related to patients' psychological outcomes, such as distress, anxiety or depression is yet unknown. Given previous evidence suggesting a strong association between BTcP and psychological comorbidities [6-10], bridging this gap seems paramount.

Therefore, the aims of this study were: (1) to culturally adapt and validate the Portuguese version of the BAT (BAT-Pt) with cancer patients, hence, promoting the (re)assessment and effective management of BTcP in Portuguese-speaking communities, and (2) to provide and expand evidence on its criterion validity by investigating its association with psychological outcomes, such as distress, anxiety, and depression.

To do so, we started by translating and culturally adapting the BAT to Portuguese-speaking communities. Then, drawing upon international guidelines for psychometric testing of self-report measures [14], a validation plan was implemented. First, we sought to investigate BAT-Pt's factorial structure by conducting a Principal Axis Factor Analysis. We expected to find the two dimensions reported in previous studies (Hypothesis 1) [11-13]. Second, we aimed to test BAT-Pt's internal consistency. Drawing upon previous data [11-13], we expected good levels of internal consistency for the total scale and its severity and impact subscale but fair levels for the duration and medication efficacy subscale (Hypothesis 2). Third, to assess the instrument's convergent validity, we tested the hypothesis that more severe and incapacitating BTcP episodes would be associated with more severe and incapacitating overall pain (Hypothesis 3), an association found in previous studies [4,11-13]. Finally, as for BAT-Pt's criterion (concurrent) validity, we expected that BAT-Pt scores would be associated with physical but also psychological outcomes. More specifically, more severe and incapacitating BTcP episodes would be associated with higher levels of functional disability [11-13]

(Hypothesis 4) and worse BAT-Pt scores would be associated with patient- and physician-determined adequacy of BTcP control [11-13] (Hypothesis 5), and increased distress, anxiety and depression [6-10, 15] (Hypothesis 6).

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Methods

Translation and Cultural Adaptation

The BAT was translated following Beaton et al.'s recommendations for the cross-cultural adaptation of health status measures [16]: (1) translation from English to European Portuguese by three bilingual translators, (2) backtranslation by two independent bilingual translators, (3) resolving discrepancies in the (back-)translations with the translators, (4) resolving discrepancies between the translated and back-translated versions with the translators, (5) approval of the back-translated version by the developers of the BAT, (6) revision with the input of an external expert commission of four doctors (specialized in pain, oncology and palliative care), who were Portuguese native speakers, and (7) pre-test and refinement of the instrument with the help of 13 Portuguese cancer patients with BcTP using a think-aloud interviewing technique [17,18]; all interviews were conducted by the third author (SM).

Validation Study

Participants and Settings

Cancer patients were recruited by healthcare professionals from eight hospitals in mainland Portugal on the basis of the following criteria [11]: (1) being over 18 years of age, (2) presence of background pain for a period equal or greater than 12 hours/day during the previous week, which would be present if there was no analgesia; (3) controlled background pain, rated as absent or mild (vs. moderate or severe) for 12 hours/day or more during the previous week, (4) presence of BTcP pain; and (5) ability to understand the questionnaire. Patients who had undergone surgery or had not yet been discharged were not included in the study.

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Design and Validation Plan

This multicenter cross-sectional study analyzed the psychometric properties of the BAT-Pt drawing upon international guidelines for psychometric testing [14,19]. More specifically, it analyzed the BAT-Pt underlying factor structure, reliability by internal consistency and construct (convergent) and criteria (concurrent) validity by determining BAT-Pt association with measures of several related constructs and criteria as described below. Socio-demographic (sex, age, nationality, educational level, civil and work status) and clinical information (cancer diagnosis, presence/location of metastasis, pain pathophysiology, in/outpatient) was also requested to participants and their attending physicians, upon participants informed consent. Participants took on average 30 minutes to fill out the protocol. The study was approved by the Ethical Review Boards of Iscte (Final Approval 12/2018) and of the eight participating hospital units.

Measures

Like the original version developed by Webber et al. [11], the BAT-Pt is composed of 14 questions/items, with nine assessing BTcP and five assessing pain treatment (see Annex 1). Patients were instructed to provide answers to four open-ended questions (causes of BTcP, relief factors, painkillers and side-effects), mark the site of the pain on a body-shape outline and use numeric response scales in nine questions regarding pain-related duration, severity, distress and life interference, painkiller efficacy and medication-related discomfort (see items in Table 2). As in the previous studies [11-13], the latter items were used for BAT-Pt psychometric validation.

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Two sub-scales of the Portuguese version of the Brief Pain Inventory (BPI) [20] were used to assess convergent validity. The pain severity subscale included four items requesting patients to rate overall pain felt in the previous week at its worst, least, average and present moment, with 11-point rating scales ranging from 0 = ”no pain” to 10 = ”pain as bad as you can imagine ” (α=0.77). Pain interference with general activity, mood, walking ability, normal work, relationships with other people, sleep and with enjoyment of life (7 items) was evaluated with a 11-point rating scales ranging from 0 = ”does not interfere” to 10 = ”completely interferes” (α =0.92). Both indicators were obtained by averaging the respective items. The higher the scores the higher the overall pain severity and interference. It should be noted that, the BPI item “pain at its worst” of the overall pain severity subscale has shown the strongest and more consistent associations with the BAT items tapping BTcP severity and impact [11-13]. As these findings suggest that this BPI item may be partially reflecting BTcP, it was also used independently to assess the BAT-Pt’s convergent validity.

To assess the BAT-Pt’s ability to differentiate patients’ clinical characteristics (concurrent validity), physicians were asked to fill out the ECOG Performance Status [21], which measured how the disease affected patients’ ability to perform activities of daily living, *i.e.*, their functional disability, through the following rating scale: 0 = "Fully active, able to carry on all pre-disease performance without restriction"; 1 = “Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work”; 2 = “Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours”; 3 = " Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours "; 4 = “Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair”. Thus,

higher values in the ECOG Performance Status corresponded to higher values of functional disability.

As in Webber et al. [11], physicians and patients also assessed the perceived adequacy of BTcP control by answering to two yes-or-no questions about (1) treatment being effective in reducing BTcP - “Do you consider (your) breakthrough pain is under control, *i.e.*, if the treatment is being effective in reducing (your) breakthrough pain?” and (2) the need to change treatment -“Do you consider that there is a need to change the treatment of (your) breakthrough pain?".

Finally, to expand BAT-Pt concurrent validity, its association with the Hospital Anxiety and Depression Scale (HADS) and a Distress Thermometer was assessed. The Portuguese version of the HADS [22] assessed Anxiety (7 items, e.g., “I feel restless as I have to be on the move”, $\alpha = 0.76$) and Depression (7 items; “I still enjoy the things I used to enjoy”, $\alpha = 0.75$) on 4-point Likert scales ranging from 0 to 3. Both indicators were obtained by summing the respective items and varied between 0 and 21, with higher values indicating higher levels of anxiety and depression. The Distress Thermometer, adapted from Benze et al. [23], consisted of a visual scale (Thermometer) to measure the level of affective distress associated to BTcP in the previous week, on a response scale ranging from 0 = "no emotional disturbance" to 10 = "extreme emotional disturbance".

Statistical analyses

Descriptive statistics were used to describe the sociodemographic and clinical characteristics of the sample. A Principal Axis Factoring (PAF) with direct *oblimin* rotation was conducted to examine BAT-Pt underlying factor structure. Chronbach alphas and, in case of two-item

scales, the Spearman-Brown formula (r_{sb}), were used for assessing the internal consistency. Pearson and Spearman-rank correlations examined the association between the BAT-Pt and the BPI, ECOG performance status, HADS and Distress Thermometer. To assess if BAT-Pt could differentiate between perceived adequacy of BTcP control, patients' and physicians' yes-or-no answers to BTcP treatment efficacy and need to change the treatment were dummy coded (0=no;1=yes) and correlated with BAT-Pt scores (Point-biserial correlations). *A priori* power analysis determined a minimum sample size of 50 patients for correlations with a medium effect size (ρ=0.4), a power of 0.80 and 0.05 error probability (G*Power 3.1.9.4).

Results

Translations and Cultural Adaptation

The revision of the back-translated version of the BAT by the external expert commission resulted in minor changes aiming at: (1) clarifying the wording to be easier to understand by patients from different socioeconomic backgrounds (e.g., using 'pain medication' instead of 'analgesics'; write in full the anchors of the rating scales); (2) adjusting the wording to the most common terms used by Portuguese clinicians (e.g., using 'oncological disease' instead of 'cancer'; 'peaks' instead of 'short-lived increases'); (3) clarifying formatting (e.g., numbering the questions; increasing the figure size).

Afterwards, the resulting back-translated version was once more refined through think-aloud interviews with 13 cancer patients (61.5% men) with breakthrough pain, aged between 55 and 86 years (*M*=69.2, *SD*=9.8). This sample was very heterogenous in terms of patients' years of education (Min=2, Max=17, *M*=6.9, *SD*=4.5) and most of them were outpatients (n=11). The interviews resulted in very few changes, which once more consisted in wording and

formatting clarifications (e.g., using 'usual' instead of 'typical'; adding 'left/right' in the figure). All changes were introduced with the approval of the original author (K. Webber). Overall, the final Portuguese version of the BAT (BAT-Pt, Annex 1) was very well accepted by experts and patients, who deemed it as clear, relevant and with high face validity.

Validation Study

Sample Characteristics

A detailed description of patients' characteristics can be seen in Table 1. The study included 65 cancer patients (around half women), aged between 22 and 85 years (*M*=59.81; *SD*=12.03). Most patients had basic or secondary education, were married, or divorced/separated and retired or unemployed. More than three quarters were outpatients recruited in pain units (76.9%), palliative medicine (13.8%) and oncology services (4.6%). Gastrointestinal, breast and lung cancers were the most frequent diagnoses and only two patients had more than one diagnosis. More than 40% of the patients had bone metastases, mostly located in their spine, rib cage and pelvis. Pain pathophysiology was mostly mixed, and most patients were medicated with opioids.

Table 1 – Cancer Patients' Characteristics

Characteristics		Number of patients (n= 65) *n* (%)
Sex		
	Male	32 (50.8)
	Female	31 (49.2)
Education		
	Basic Education	29 (46.0)
	Secondary Education	29 (46.0)
	Higher Education	5 (7.9)
Marital Status		
	Married	40 (65.6)
	Divorced/Separated	10 (16.4)
	Single	8 (13.1)

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	Widowed	3 (4.9)
Work Activity		
	Retired	36 (57.1)
	Employed	16 (25.4)
	Unemployed	10 (15.9)
	Student	1 (1.6)
Type of Patient		
	Outpatient	51 (78.5)
	Inpatient	14 (21.5)
Cancer Diagnosis		
	Gastrointestinal	23 (35.4)
	Breast	15 (23.1)
	Lung	10 (15.4)
	Urological	9 (13.9)
	Head/Neck	8 (12.3)
	Gynecological	4 (6.2)
	Hematological	3 (4.6)
	Bone	2 (3.1)
	Thyroid	1 (1.5)
	Retroperitoneal sarcoma	1 (1.5)
Bone Metastases		
	No	37 (56.9)
	Yes	28 (43.1)
Location of Bone Metastases		
	Costal grid and spine	24 (36.9)
	Pelvis	13 (20.0)
	Long bones	4 (6.2)
	Mediastinum	1 (1.5)
Pain Physiopathology		
	Mixed	56 (86.2)
	Nociceptive	8 (12.3)
	Neuropathic	1 (1.5)
Pain Medication		
	Major opioids	50 (82.0)
	Minor opioids	7 (11.5)
	Non-opioids	4 (6.2)
	No medication	4 (6.2)

Note: Some categories' absolute frequency might not match the total number of participants due to a few missing values.

BAT-Pt Factor Structure and Reliability

Table 2 shows the descriptive characteristics, factor structure and internal consistency of the BAT-Pt. Regarding Hypothesis 1, the PAF revealed two factors accounting for 55.20% of the variance (KMO = 0.677; Bartlett's $\chi 2$ (36) = 88.090, $p < 0.001$): *Severity and Impact* (Factor 1)

and *Duration and Medication Inefficacy* (Factor 2). Noteworthy, Factor 2 label was changed from the original "Duration and medication efficacy" [11] to "Duration and medication inefficacy" to facilitate the interpretation of its scores. However, item 2 (*How often do you get breakthrough pain?)* clearly cross-loaded on both factors and item 11 (*How effective is the painkiller for your breakthrough pain?*) presented a weak loading on Factor 2. The internal consistency of the factors (Hypothesis 2) increased when these items were not included in the respective scores, showing good reliability for both factors. The BAT-Pt also showed good levels of overall internal consistency with ($\alpha = 0.82$) and without Items 2 and 11 ($\alpha = 0.79$). To investigate the validity of the BAT-Pt, factor scores were computed by averaging the respective items, but excluding items 2 and 11. The excluded items, given their high face validity, were henceforth analyzed separately.

Both factor scores approximated the normal distribution, and the factors were not intercorrelated ($r = 0.08$, $p = 0.52$). On average, patients reported high *Severity and Impact of BTcP* and moderate levels of *Duration and Medication Inefficacy*. Regarding BTcP frequency (Item 2), most patients reported episodes '1-2 times a day' (34.4%), 29.7% 'more than 4 times a day', 21.9% '3-4 times a day' and 14.1% 'less than once a day'. Item 2 showed a low positive correlation with *Severity and Impact of BTcP* ($r_s=.32$, $p=.05$) but no significant associations with Factor 2 or Item 11. As for painkiller effectiveness (Item 11), although patients' responses ranged between 0 and 10, most perceived their painkiller to have moderate to high effectiveness (Q1=6, Q2=7, Q3=9). Item 11 showed no significant associations with any of the factor scores.

Table 2 – Descriptive statistics of BAT-Pt items and scores, factor loadings and internal consistency.

Item/Factor [range]	Me	M	SD	Factor 1 Severity and Impact of BTcP	Factor 2 Duration and Medication Inefficacy
6. How severe is your worst episode of breakthrough pain? [0-10]	9	8.63	1.80	.93	--
9. How much does the breakthrough pain stop you from living a normal life? [0-10]	8	7.35	2.86	.88	--
7. How severe is a typical episode of breakthrough pain? [0-10]	7	6.83	2.09	.76	--
8. How much does the breakthrough pain distress you? [0-10]	8	6.94	2.88	.68	--
14. How much do the side-effects from the painkillers (…) bother you? [0-10] [1]	3	4.73	3.45	.60	--
2. How often do you get breakthrough pain? [1-4][2]	3	2.67	1.06	**.43**	.33
12. How long does the breakthrough painkiller take to have a meaningful effect? [1-5][3]	3	-	-	--	.97
5. How long does a typical episode last? [1-5][4]	3	-	-	--	.59
11. How effective is the painkiller for your breakthrough pain? [0-10]	7	6.95	2.36	--	**.34**
Factor 1 - Severity and Impact of Breakthrough Pain [0-10]	7.5	7.18	1.97	-	-
Factor 2 - Duration of Breakthrough Pain and Medication Ineffectiveness [1-5]	3	3.20	0.92	-	-
Chronbach alphas (α) with all items included				.81	.47
Internal consistency indices with item in bold deleted (α /$r_{Spearman-Brown}$)				.86	.62

Note. [1]n=26; [2]1=less than once a day; 2=1-2 times a day; 3= 3-4 times a day; 4= more than 4 times a day; [3] Item recoded for easier factor interpretation: 1=0-10 min, 2=10-20 min, 3=20-30 min e 4=more than 30 min, 5=no effect.; [4]1=less than 5 min; 2= 5-15 min; 3= 15-30 min; 4= 30-60 min; 5= more than 60 min; Factor 2 label was changed from the original "Duration and medication efficacy" [11] to "Duration and medication inefficacy" to facilitate the interpretation of its scores. Factor loadings lower than .300 are not presented.

BAT-Pt Validity

Table 3 presents the correlations between the BAT-Pt scores/items and the measures used to assess its validity. Concerning BAT-Pt's convergent validity (Hypothesis 3), overall pain severity and interference scores and the item "pain at its worst" (measured by the BPI) presented moderate to strong positive associations with *Severity and Impact of BTcP* (Factor 1) and *Frequency of BTcP episodes* (Item 2).

The associations between the BAT-Pt scores/items and functional disability (Hypothesis 4), patient- and physician-determined adequacy of BTcP control (Hypothesis 5), and psychological outcomes such as distress, anxiety and depression (Hypothesis 6) speak to the instrument's concurrent validity (Table 3). First, functional disability was positively and moderately associated with *Severity and Impact of BTcP* (Factor 1). Second, concerning patient- and physician-determined adequacy of BTcP control, Item 11 (*How effective is the painkiller?*) was positively associated with BTcP treatment efficacy (Patient: M_{yes}=8.03 vs. M_{no}=4.85; Physician: M_{yes}=7.41 vs. M_{no}=4.70) and negatively associated with perceived need to change treatment (Patient: M_{yes}=5.21 vs. M_{no}=7.78; Physician: M_{yes}=5.71 vs. M_{no}=7.49). These associations were stronger for patient-determined adequacy of BTcP control. Moreover, patient-determined BTcP treatment efficacy showed a negative low correlation with Frequency of BTcP episodes (Item 2) (M_{yes}=2.51 vs. M_{no}=3.05). Finally, regarding psychological outcomes, *Severity and Impact of BTcP* (Factor 1) was moderately and positively associated with distress, anxiety and depression and BTcP episode frequency (Item 2) presented low/moderate positive correlations with distress and anxiety.

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Table 3 – Descriptive statistics and correlations with BAT-Pt of patients' overall pain, functional disability, BTcP treatment efficacy and psychological outcomes.

Variable [range]	Me	*M*	*SD*	Factor 1 Severity and Impact of BTcP	Factor 2 Duration and Medication Inefficacy	Item 2 How often do you get BTcP?	Item 11 How effective is the painkiller for your BTcP?
Overall Pain Severity (BPI) [0-10]	3.87	4.39	1.70	.46**	-.01	.49**	-.21
Overall Pain Interference (BPI) [0-10]	5.42	5.24	2.72	.77**	.03	.50**	-.15
Pain at its worst (BPI) [0-10]	7.00	7.06	2.12	.43**	.04	.41**	-.14
Functional disability (ECOG) [0-4]	2.00	-	-	.40**	-.17	.21	-.19
Depression (HADS) [0-21]	3.00	3.84	3.59	.47**	-.04	.20	-.16
Anxiety (HADS) [0-21]	3.50	4.62	3.37	.44**	.12	.28*	-.14
Distress (Thermometer) [0-10]	5.00	4.77	2.92	.46**	.19	.33**	-.32
	No n (%)		Yes n (%)				
Treatment efficacy (patient)[a]	23 (35.9)		41 (64.1)	-.12	-.10	-.25*	.63**
Need to change treatment (patient) [a]	41 (64.1)		23 (35.9)	.10	.22	-.19	-.55**
Treatment efficacy (physician) [a]	11 (17.2)		53 (82.8)	-.05	.18	-.18	.36**
Need to change treatment (physician) [a]	45 (71.4)		18 (28.6)	.22	-.09	.18	-.32*

[a] Dummy coded variables (0=No vs. 1= Yes); ** p<.001, * p<.05; BPI- Brief Pain Inventory; ECOG – ECOG Performance Status; HADS- Hospital Anxiety and Depression Scale

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Discussion and conclusions

This study culturally adapted and validated the BAT-Pt and further extended knowledge on its criterion validity, by investigating its association with pain-related psychological outcomes. Overall, the BAT-Pt proved to be a practical, reliable, and valid measure of BTcP in Portuguese cancer patients.

Hypothesis 1 was confirmed, as the BAT-Pt presented the expected 2-factor structure [11-13]: (1) *Severity and Impact of BTcP* and (2) *Duration of BTcP and Medication Inefficacy*. Once again, Factor 1 encompassed multiple but strongly associated aspects of BTcP such as its intensity, interference, distress and medication-related discomfort [11-13]. However, whereas in previous studies this factor also included pain frequency (item 2) [11-13], in our sample this item poorly differentiated both factors. Our results regarding Factor 2 were consistent with the previous studies [11-13], showing the strong link between pharmacodynamics and pain episode duration. As in the Dutch study [13], overall appraisal of medication efficacy (Item 11) showed the lowest loading on this factor. Whether this was due to methodological issues (e.g., differences in rating scales) or patients' understanding of what "medication efficacy is" - which may be more associated to the ability of the medication to reduce pain intensity instead of its duration - is yet unclear.

The BAT-Pt also showed very good internal reliability for the total scale and its sub-scales, thus confirming (and exceeding) the expectations raised by the Hypothesis 2. Indeed, these indices were even stronger than the ones presented in the previous studies [11-13] (especially concerning Factor 2), which supported the exclusion of items 2/11 from Factors 1/2 scores and their use as single items with high face validity.

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Most of our findings also supported and extended the BAT-Pt´s validity. First, as in the previous studies [11-13], Hypothesis 3 was confirmed as overall pain severity (pain at its worst) and interference were positively and moderately associated to the *Severity and Impact of BTcP* and the pain episode frequency (convergent validity), but not associated with *Duration of BTcP and Medication Inefficacy* (nor item 11).

Second, regarding concurrent validity and in line with the U.K. and Dutch studies [11-13], increased functional disability was moderately associated with increased *Severity and Impact of BTcP* (confirming Hypothesis 4) but not with *Duration of BTcP and Medication Inefficacy*. Pain frequency, however, was also not associated with functional disability. Hence, BTcP temporal dimensions (frequency, duration) seem less associated with functional disability than BTcP severity and impact.

Third, and partly consistent with previous data [11], the BAT-Pt differentiated between those who reported treatment being effective vs. ineffective and those who needed vs. did not need treatment changes (both from patients´ and physicians´ perspectives) (Hypothesis 5). More specifically, it was Item 11 assessing patients´ overall perception of medication efficacy that more consistently differentiated these groups instead of the factor *Duration and Medication Inefficacy*. This again suggests that patient's conceptions of medication efficacy are not necessarily associated with duration of the episodes. Indeed, episode frequency (Item 2) was also able to differentiate patients who reported treatment being effective vs. ineffective. Contrary to what was expected and found in Webber et al.'s [11], BTcP *severity and impact* was not significantly different between patients with vs. without controlled pain. Differences in what patients and physicians from different samples consider to be an "effective treatment" may account for these inconsistencies.

Finally, although BTcP duration and medication inefficacy (Factor 2 and Item 11) were not associated to psychological outcomes, BTcP *Severity and Impact* and episode frequency (Item 2) were associated to higher levels of anxiety and emotional distress, and BTcP *Severity and Impact* was also associated to increased depression (confirming Hypothesis 6). These novel findings show that BTcP may seriously affect patients' mental health [6-9, 11, 15], while also differentiating which specific aspects of the BTcP experiences are better correlates of anxiety and depression.

Limitations and contributions

This study has some limitations related with its cross-sectional design, which does not allow to investigate BAT-Pt's temporal reliability nor its responsiveness to treatment changes. Moreover, a larger sample would have allowed to test BAT-Pt underlying structure with a Confirmatory Factor Analysis. These issues should be addressed in future studies. Nonetheless, this study bears important implications for research and clinical practice. Concerning research, it confirms and extends the psychometric validation of the BAT to a new cultural context, providing novel data on the association between the BAT-Pt scores and measures of frequent BTcP psychological comorbidities [6-10]. As for clinical practice, the BAT-Pt may contribute to more reliable BTcP (re)assessment procedures in Portuguese-speaking communities, which may facilitate tailoring treatments as to increase their efficacy. Of course, many challenges in cancer pain (re)assessment will persist, e.g., patient unwillingness or inability to report pain due to being critically ill, comatose, unconscious and/or cognitively impaired. In these situations, other more suitable BTcP assessment procedures should be developed and employed (e.g., based on physiological or behavioral

indicators). However, regarding patients who are willing and able to report their pain, this study shows that different BAT-Pt items/scores may be used to tap different aspects of their cancer-related breakthrough pain experiences. For example, frequency of pain episodes (Item 2) may be more indicative of distress, the score on BTcP *Severity and Impact* might be a better correlate of functional disability and depression and Item 11 might be particularly useful to differentiate patients with vs. without controlled BTcP. In conclusion, the BAT-Pt is a reliable and valid measure of BTcP, strongly associated with physical and psychological outcomes, hence, a valuable tool for daily clinical practice with Portuguese cancer patients.

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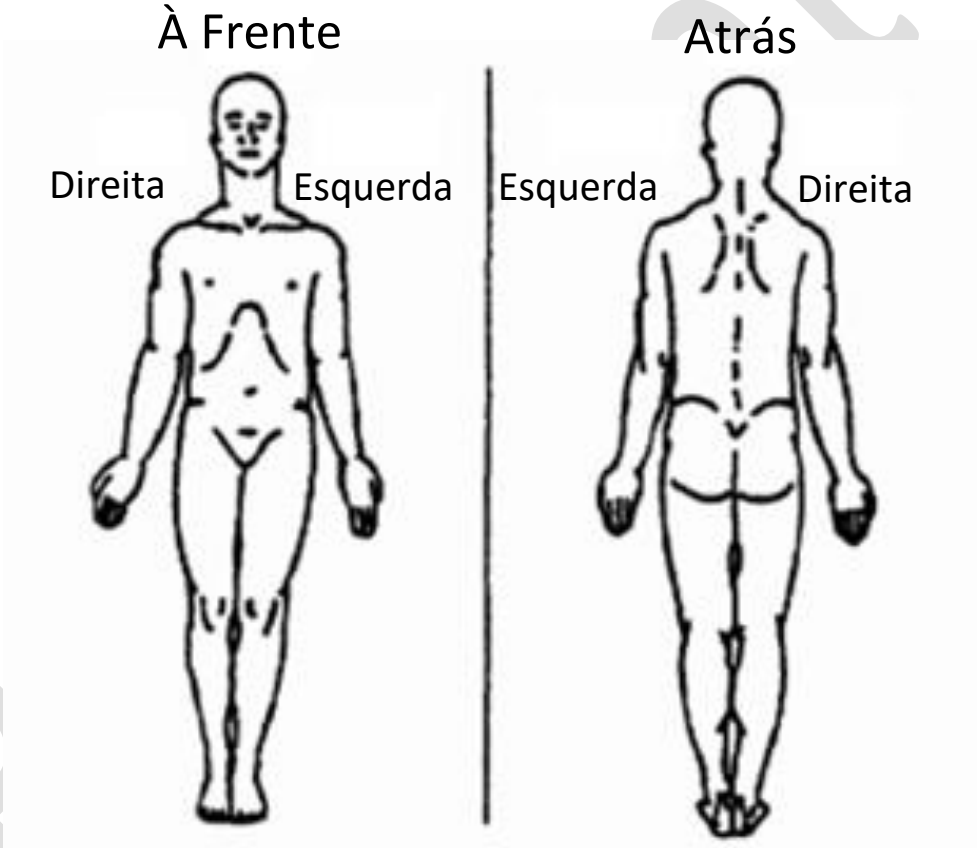
BAT_Pt

Instrumento para Avaliação da Dor Irruptiva

As perguntas que seguem relacionam-se com os episódios da dor irruptiva que sentiu durante a última semana. Dor irruptiva refere-se aos picos (aumentos passageiros) da dor relacionada com a sua doença oncológica.

1.Onde se localiza a sua dor irruptiva?

Por favor, indique na figura com uma cruz (x)



2. Com que frequência tem dor irruptiva?

Por favor, coloque um círculo à volta de uma resposta.

Menos do que uma vez por dia	1 a 2 vezes por dia	3 a 4 vezes por dia	Mais do que 4 vezes por dia

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3.Há alguma coisa que provoque a sua dor irruptiva?
Se sim, por favor, escreva o que a provoca.

4.Há alguma coisa que alivie a sua dor irruptiva? (medicamentos ou outras)
Se sim, por favor, escreva o que a alivia.

5.Qual a duração de um episódio ***habitual*** de dor irruptiva?
Por favor, coloque um círculo à volta de uma resposta.

Menor do que 5 minutos	5 a 15 minutos	15 a 30 minutos	30 a 60 minutos	Maior do que 60 minutos

6.Qual a intensidade do seu ***pior*** episódio de dor irruptiva?
Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que pode imaginar

7.Qual a intensidade de um episódio ***habitual*** de dor irruptiva?
Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que pode imaginar

8.Até que ponto é que a dor irruptiva o/a perturba emocionalmente?
Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Nada										Muitíssimo

9.Até que ponto é que a dor irruptiva o/a impede de viver uma vida normal?
Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Nada										Muitíssimo

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As perguntas que seguem relacionam-se com os episódios da dor irruptiva que sentiu durante a última semana. Dor irruptiva refere-se aos picos (aumentos passageiros) da dor relacionada com a sua doença oncológica.

10.Que medicamentos toma para aliviar a sua dor irruptiva (no caso de os tomar)?
Por favor, escreva o nome e a dose dos medicamentos.

11.Até que ponto o medicamento que habitualmente toma para aliviar a sua dor irruptiva é eficaz? Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Nada eficaz										Completamente eficaz

12.Quanto tempo demora o medicamento que habitualmente toma para aliviar a sua dor irruptiva a ter efeito significativo? Por favor, coloque um círculo à volta de uma resposta.

Não tem efeito.	0 a 10 minutos	10 a 20 minutos	20 a 30 minutos	Mais do que 30 minutos

13.Tem alguns efeitos secundários do medicamento que habitualmente toma para aliviar a sua dor irruptiva?
Se sim, por favor, escreva o tipo de efeitos secundários.

Se não tem efeitos secundários, por favor, não responda à questão que se segue.

14.Até que ponto é que o/a incomodam os efeitos secundários dos medicamentos que habitualmente toma para aliviar a sua dor irruptiva? Por favor, coloque um círculo à volta de um número.

0	1	2	3	4	5	6	7	8	9	10
Nada										Muitíssimo