Content validation of the EORTC QLQ-BN20+2 with patients and health care professionals to assess quality of life in brain metastases

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Abstract

Objective The validated EORTC quality of life (QOL) questionnaire QLQ-BN20 is a cancer subtype-specific supplement to the QLQ-C30 general QOL questionnaire for patients with primary brain neoplasms. The QLQ-C15-PAL core palliative questionnaire is an abbreviated version of the QLQ-C30 designed to decrease patient burden. We conducted content validation of the QLQ-BN20+2 for patients with brain metastases.

Methods and materials Patients undergoing treatment for brain metastases, along with health care professionals (HCPs) completed the QLQ-C15-PAL and QLQ-BN20+2 questionnaires. A structured interview followed to assess for any difficulties with the QLQ-BN20+2, irrelevant items, and whether additional pertinent items should be included.

Results Seventy-four patients and 71 HCPs participated. The majority of patients (84 %) were treated with whole-brain

radiotherapy only. Over 50 % of patients felt that seizures, hair loss and trouble controlling bladder were not related to brain metastases. Questions regarding uncertainty about the future were the most difficult, although still a small proportion (12–16 %). All items were endorsed by over 50 % of HCPs as ‘quite’ or ‘very’ relevant to brain metastases patients, with two exceptions: 15 and 12 % of HCPs rated pruritis and future uncertainty as irrelevant, respectively.

Conclusion We report the first content validation of the QLQ-BN20+2 and QLQ-C15-PAL QOL questionnaires for patients undergoing treatment for brain metastases, demonstrating feasibility and relevance. These questionnaires should be used together as universal QOL assessment tools in this setting.

Keywords Brain metastases · Palliative radiation · Quality of life · QLQ-BN20 · QLQ-C15-PAL

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Introduction

Brain metastases are a cause of significant morbidity [1] and are a frequent complication of primary neoplasms such as lung, with over 50 % of patients eventually developing spread to the central nervous system [2]. Improvements in the sensitivity of imaging modalities along with more frequent screening may result in the earlier diagnosis of smaller and/or fewer brain metastases. Overall, the incidence of brain metastases is increasing [3] leading to a greater number of patients undergoing various treatments.

Potential neurological symptoms arising from brain metastases include headache, focal weakness, mental disturbances and ataxia. Additionally, nearly 65 % of patients display some form of cognitive impairment [4, 5]. Symptoms may also arise from the treatment of brain metastases.

Whole-brain radiotherapy (WBRT) has long been the standard approach, with the aim of alleviating or reducing neurological symptoms and decreasing the need for long-term corticosteroids. Treatment options have evolved over the past few decades to include more aggressive approaches such as stereotactic radiosurgery or surgical resection and post-operative RT for certain subgroups of patients with favourable performance status [6]. Prognostic indices such as the Graded Prognostic Assessment identify patients who may benefit from more aggressive treatments [7]. However, even the most favourable prognosis group has a median survival of only 11 months versus 2.6 months in the group with worst prognosis [7]. Traditional endpoints such as survival should therefore not be the sole aim of treatment; quality of life (QOL) should also be evaluated [8].

Quality of life is a subjective, multidimensional construct that consists of physical and psychosocial factors [9]. To address the need for standardized assessment of QOL and symptoms in oncology, the European Organization for Research and Treatment of Cancer (EORTC) developed the quality of life core questionnaire (QLQ-C30) [10]. It is now one of the most frequently used measures of QOL in oncology clinical trials. Cancer subtype-specific QOL questionnaires have also been developed to supplement the general core questionnaire. One of these, the EORTC QLQ-BN20, was developed [11] and validated [12] in patients with primary brain tumours. The 15-question QLQ-C15-PAL core questionnaire was developed to decrease the burden of the longer QLQ-C30 on patients with advanced cancer [13].

Studies of patients with brain metastases continue to use the lengthy QLQ-C30 along with the QLQ-BN20 as there is no tool that has been validated specifically for use in this patient population [14–17]. A previous study

assessed QOL in patients with brain metastases prior to and after treatment by administering the QLQ-C15-PAL with the QLQ-BN20+2, a version of the QLQ-BN20 questionnaire with two additional questions to assess cognitive function [18].

The primary aim of this study was to conduct content validation of the EORTC QLQ-BN20+2 in patients with brain metastases and in health care professionals (HCPs) involved in the care of these patients.

Table 1 Patient and health care professional characteristics

Patient characteristics (N=74)	
Country	N (%)
Canada	39 (53 %)
Cyprus	20 (27 %)
Spain	15 (20 %)
Gender	
Female	43 (58 %)
Male	31 (42 %)
Age (years)	
Median (range)	61 (32–86)
KPS	
Median (range)	70 (30–100)
Primary cancer site	
Lung	36 (49 %)
Breast	16 (22 %)
Colorectal	10 (14 %)
Melanoma	2 (3 %)
Unknown	2 (3 %)
Other	8 (11 %)
Current treatment	
Whole-brain Radiation	62 (84 %)
Chemotherapy	6 (8 %)
Surgery + Radiation	2 (3 %)
None	4 (5 %)
Health care professional characteristics (N=71)	
Gender	
Female	39 (55 %)
Male	16 (23 %)
Not specified	16 (23 %)
Discipline	
Radiation Therapist	25 (35 %)
Nurse	15 (21 %)
Radiation Oncologist	18 (26 %)
Medical Oncologist	6 (8 %)
Social Worker	4 (6 %)
Palliative Care Physician	2 (3 %)
Neurosurgeon	1 (2 %)
Years of experience	
Median (range)	13 (1–32)

Patients and methods

Patients and health care professionals

All patients were accrued between 2009 and 2011 from six centres in three countries (Canada, Cyprus and Spain). All research was conducted following approval from each institution's research ethics board. Patients over the age of 18 years with histologically or radiographically documented single or multiple brain metastases were eligible. Demographics, primary cancer site, Karnofsky Performance Status (KPS) and current treatment were recorded. Patients who were not native speakers of the language of the questionnaires were excluded. All patients were administered the Mini Mental State Exam prior to enrolment, with a score greater than 23 indicating that the patient was cognitively competent to participate [19]. HCPs involved in the care of patients with brain metastases were accrued from Canada only. Gender, specialty and years of experience were recorded for HCPs.

Questionnaires

The QLQ-BN20+2 was developed by adding a two-item cognitive scale (concentration, memory) to the previously

validated QLQ-BN20. Although these items are included in the QLQ-C30, they are not on the QLQ-C15-PAL. The 20 main questions include: 7 single-item symptom scales (headaches, seizures, drowsiness, hair loss, itchy skin, leg weakness and bladder control), along with 4 multi-item scales (future uncertainty, visual disorder, motor dysfunction and communication deficit). The QLQ-C15-PAL consists of 15 questions: 2 multi-item functional scales (physical and emotional functioning), 2 multi-item symptom scales (fatigue and pain), 5 single-item symptoms (nausea/vomiting, dyspnea, insomnia, appetite loss and constipation) and one item regarding overall QOL.

Validation procedure

Patients completed the QLQ-BN20+2 and the QLQ-C15-PAL, which were followed by individual structured interviews. The interview invited further comments regarding: (1) the particular experience to which the item referred (e.g. was this experience related to brain metastases?); (2) the wording of each item (e.g. was the item difficult to respond to, annoying, confusing or upsetting? how would you have asked this question?); (3) items that patients found

Fig. 1 Patient scores for each QLQ-BN20+2 item

irrelevant; and (4) additional issues relevant for the patient, but not included in this questionnaire.

A similar procedure was followed by HCPs who were asked to indicate, for each item on the QLQ-BN20+2, its perceived relevance (1=not at all to 4=very much). Relevancy was defined as a combination of the frequency with which a specific complaint occurs, and the degree of difficulty it causes. HCPs were also asked to indicate whether there were irrelevant items, and any additional issues not included in either questionnaire.

Statistical methods

Results were expressed as medians (ranges) for continuous variables as well as proportions for categorical variables. The ranking of most to least important items by HCPs was obtained by the frequency of the top five to ten items that were rated to be included in the QLQ-BN20+2. Figures were created to illustrate both the levels of importance for each item of the QLQ-BN20+2 and whether it should be included in the final question, for patients and HCP's. All descriptive analyses were performed by Statistical Analysis Software (SAS version 9.2).

Results

A total of 74 patients and 71 health care professionals participated. Demographics are presented in Table 1. Nearly half of patients had a lung cancer primary (49 %). Median KPS was 70 (range 30–100). At the time of interview, 84 % of patients were undergoing WBRT. Healthcare professions were all from Canada and the majority were radiation therapists (35 %), followed by radiation oncologists (26 %) then nurses (21 %).

Patient responses

Most patients were not bothered at all by seizures (94 %), hair loss (85 %), double vision (84 %), difficulty speaking (82 %) or trouble controlling bladder (73 %; Fig. 1). Conversely, many patients were concerned about disruption in family life (80 %), felt unsteady on their feet (79 %) or felt that they had had setbacks in their condition (78 %). Items endorsed as potentially irrelevant (yes/no answer) were seizures (by 84 %), difficulty with bladder control (84 %) and hair loss (64 %; Fig. 2). All other items were assessed as being related to their brain metastases by the majority of respondents.

Fig. 2 Patient responses to whether they believe each QLQ-BN20+2 item is related to brain metastases

Although a small proportion of patients found each of the QLQ-BN20+2 items difficult to answer, there was no single question uniformly identified as upsetting, confusing, or annoying (Appendix I). The items presenting the most issues were: “Did you feel uncertain about the future?” (16 %); “Did you feel you had setbacks in your condition?” (12 %); and “Were you concerned about disruption of family life?” (16 %). However, nearly all stated that they would not change any of the 22 questions.

Only three patients stated that there were irrelevant items on the QLQ-BN20+2. Three sets of repetitive items were described by two patients (“Was your vision blurred?” and “Did you have difficulty reading because of your vision?”; “Did you have trouble with your coordination?” and “Did you feel unsteady on your feet?”; “Did you have trouble finding the right words to express yourself?” and “Did you have trouble communicating your thoughts?”). One patient felt that the question pertaining to hair loss was irrelevant to those not receiving WBRT. Ideas for additional issues not yet included in the questions included suggestions for additional questions regarding effects on family life; alternative

therapy options; and whether patients felt they had received enough information.

Health care professional responses

Over 50 % of HCPs described each QLQ-BN20+2 item as ‘quite’ or ‘very relevant’ except for ‘outlook on the future worsened’, and ‘bothered by itching of skin’ (Fig. 3). In terms of which items were least relevant, over 50 % suggested that ‘setbacks in condition’, ‘outlook on the future worsened’, and ‘bothered by itching of skin’ should be removed (Fig. 4).

HCPs’ detailed responses to each question are summarized in Appendix II. For the future uncertainty items mentioned above that were suggested to be removed, most comments were that HCPs were “not sure why these questions were specific to brain metastases versus any palliative patient” ($n=8$), and that these questions were “too subjective and situational dependent” ($n=3$). Many HCPs also stated that the item pertaining to itching of the skin is “of minimal importance and is easy to treat” ($n=11$). Additionally, there were questions deemed irrelevant because it had been

Fig. 3 Health care professional relevancy scores for QLQ-BN20+2 items

covered in other questions throughout the questionnaire. The most common similar items included: “Did you feel you had setbacks in your condition?” and “Did your outlook on the future worsen?” ($n=4$); “Did you have difficult reading because of your vision?” and “Did you have double visions?” or “Was your vision blurred?” ($n=4$); “Did you have trouble finding the right words to express yourself?” and “Did you have difficulty speaking?” ($n=3$); “Did you have trouble with your coordination?” and “Did you feel unsteady on your feet?” ($n=3$).

The overall ranking of the most to least important items is in Table 2. The main items to be definitely included in the final questionnaire pertained to physical symptoms such as seizures, headaches, weakness and difficulty speaking. Finally, 28 (40 %) HCPs described additional items that should be included. These nine common themes were: burden and impact on family and children; other physical and psychological side effects from treatment and disease; understanding prognosis; coping with stress/support system; financial hardship; language issues; independence/carrying out usual activities; intimacy/sex; and perception of whether their QOL is actually being impacted (Appendix III). Burden on family, coping with stress/support systems and inde-

pendence were the most commonly listed additional issues.

Discussion

To the best of our knowledge, this is the first study to conduct content validation of the EORTC QLQ-BN20+2 for use in brain metastases patients, for which there is currently no widely accepted tool. A review of 14 brain metastases RT trials which evaluated QOL demonstrated a total of 23 different instruments used [20].

While the QLQ-BN20 has become one of the most commonly used QOL tools in brain metastases studies, along with the Functional Assessment of Cancer Therapy Brain subscale [21], a recent review of 13 studies using the QLQ-BN20 and QLQ-C30 reveals challenges with compliance and attrition at follow-up assessments [22]. The QLQ-BN20 has been used to assess QOL in lung cancer patients undergoing prophylactic cranial irradiation [23]. Conducting content validation aims to demonstrate the subjective validity of the questionnaire, as primary brain tumour patients may present with slightly different issues than brain metastases patients.

Fig. 4 Health care professional responses to whether the QLQ-BN20+2 item should be included in the questionnaire

Table 2 Ranking of most to least important items by health care professionals

Rank ^a	Item
1	Seizures
2	Headaches
3	Weakness on one side of the body
4	Difficulty speaking
	Trouble communicating thoughts
	Difficulty remembering things
7	Concerned about disruption in family life
8	Trouble with coordination
9	Feel unsteady on feet
10	Difficulty concentrating
11	Feel uncertain about the future
12	Trouble finding the right words to express themselves
	Trouble controlling bladder
14	Bothered by hair loss
	Weakness of both legs
16	Double vision
	Difficulty reading because of vision
18	Outlook on the future worsened
	Feel drowsy during daytime
20	Feel had setbacks in condition
	Blurry vision
22	Bothered by itchy skin

^a Health care professionals were asked to rate the top 10 items that were most important to them; this table was created by calculating the frequency of each item

The use of the EORTC QLQ-BN20+2 with the QLQ-C15-PAL to assess QOL was first reported in 108 patients undergoing various treatments for brain metastases [19]. The questionnaires showed maintenance (no deterioration) of QOL and improvement in a few QOL scores, which was echoed by a study that used the QLQ-BN20 with the QLQ-C15-PAL to reduce patient burden [14]. It was suggested that these two questionnaires replace the use of the QLQ-BN20 and QLQ-C30 combination previously used in many brain metastases studies in order to decrease attrition rates. Future uncertainty was the most prominent symptom at baseline for these two studies. Our results also concurred with those results, with 77–79 % of patients reporting some level of future uncertainty. Validation of the QLQ-BN20+2 will facilitate comparison of QOL outcomes between trials using this tool.

For all 22 items on the QLQ-BN20+2, there were only three items (seizures, hair loss and incontinence) in which the majority of patients stated the issue was not related to their brain metastases. It is possible that

patients rated ‘seizure’ as unrelated because they had not experienced a seizure. This is in contrast with HCP responses, as seizures were ranked the most important item to be included on the final questionnaire.

As in any QOL questionnaire that assesses psychological and physical symptoms, it is expected that some questions may be difficult to answer, upsetting, confusing, or annoying depending on the patient. There were a small number of patients with such reactions to each of the 22 items. The three items that assessed future uncertainty were the most difficult; however, only two patients stated that these questions should be removed. Many HCPs also rated two future uncertainty items as not being specific to this patient population.

Patients and HCPs had similar opinions in items perceived as irrelevant because they had been addressed in another question. HCPs felt that pruritus was of low priority for inclusion because it is of minimal importance and easy to treat, which is in accordance with the overall ranking of all 22 items. Only three patients stated items should be included: family life, alternative therapy options and satisfaction with information received. More HCPs (40 %) stated that there were additional issues not covered.

The current study is limited in that the structured interview may have been cumbersome for patients to complete, and therefore patients may have been too tired to provide complete input on irrelevant items or additional important issues that may be missing. Furthermore, as cognitively impaired patients were ineligible for this study, our results may be more applicable to patients who have relatively better functioning. The therapeutic benefits of various treatment options for patients with brain metastases are beginning to be supplemented with more QOL research.

Conclusion

The limited consensus on the method of QOL endpoint measurement in clinical trials of patients with brain metastases is a significant barrier to the identification of the most effective treatment option. As we have demonstrated, content validation of the EORTC QLQ-BN20+2 when used concurrently with the EORTC QLQ-C15-PAL for patients with brain metastases, these two QOL tools should be used in future clinical trials involving these patients.

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Appendix I

Table 3 Summary of patient comments for each QLQ-BN20+2 Item

EORTC QLQ-BN20 Item	Comment(s)
During the past week,	
1 Did you feel uncertain about the future?	<ul style="list-style-type: none"> • Related to health and disease in general ($n=4$) • Confusing ($n=2$)—‘how do you feel about the future now?’ ($n=1$) • Difficult to answer ($n=4$)—‘define future’, ‘less direct’, • Annoying ($n=1$) • Upsetting ($n=5$)—wouldn’t have asked ($n=1$)
2 Did you feel you had setbacks in your condition?	<ul style="list-style-type: none"> • Difficult to answer ($n=2$) • Found the question annoying ($n=3$) • Upsetting ($n=3$)—patient said question should have been asked less directly • Confusing ($n=1$), did not understand the term “setbacks” ($n=1$) • Not related to brain metastases ($n=4$); the disease in general ($n=1$) • Difficult to answer ($n=5$) • Upsetting ($n=5$)—‘would not have asked’ ($n=2$) • Confusing ($n=2$) • Annoying ($n=2$) • Upsetting ($n=1$)
3 Were you concerned about disruption of family life?	<ul style="list-style-type: none"> • Difficult to answer ($n=2$) • Upsetting ($n=5$)—‘would not have asked’ ($n=2$) • Confusing ($n=2$) • Annoying ($n=2$) • Upsetting ($n=1$)
4 Did you have headaches?	<ul style="list-style-type: none"> • Difficult to answer ($n=2$) • Upsetting ($n=6$) • Confusing ($n=1$) • Related to health and disease in general ($n=4$), would not have asked question ($n=1$)
5 Did your outlook on the future worsen?	<ul style="list-style-type: none"> • Difficult to answer ($n=1$) • Confusing ($n=1$) • Annoying ($n=2$) • Not due to brain metastases ($n=2$), question repeated in others ($n=1$) • Upsetting ($n=3$) • Confusing ($n=1$) • Not due to brain metastases ($n=3$) • Thinks question 6 is similar ($n=1$) • Would not have asked the question ($n=1$) • Confusing ($n=2$) • Annoying ($n=1$) • Difficult to answer ($n=2$) • Annoying ($n=1$) • Confusing ($n=3$) • Uncertain whether related to disease itself or the treatment ($n=2$) • Difficult to answer ($n=2$) • Annoying ($n=2$) • Upsetting ($n=2$)
6 Did you have double vision?	<ul style="list-style-type: none"> • Related to my medications, my condition, the surgery ($n=1$) • Hard to describe what was happening to my body ($n=1$) • Upsetting ($n=1$) • Confusing ($n=1$)
7 Was your vision blurred?	<ul style="list-style-type: none"> • Did not know if this was related to brain metastases ($n=1$)
8 Did you have difficulty reading because of your vision?	
9 Did you have seizures?	
10 Did you have weakness on one side of your body?	
11 Did you have trouble finding the right words to express yourself?	
12 Did you have difficulty speaking?	

Table 3 (continued)

EORTC QLQ-BN20 Item	Comment(s)
13 Did you have trouble communicating your thoughts?	<ul style="list-style-type: none"> • Related to medications and condition ($n=1$) • Upsetting ($n=1$) • Confusing ($n=1$) • Trouble communicating because “I am not sure what I am going through” ($n=1$) • Confusing ($n=2$) • Annoying ($n=2$) • Would not have asked question, similar questions ($n=2$)
14 Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	<ul style="list-style-type: none"> • Difficult to answer ($n=1$), usually too weak or exhausted to concentrate ($n=2$) • Upsetting ($n=1$) • Annoying ($n=1$) • Confusing ($n=1$)
15 Have you had difficulty remembering things?	<ul style="list-style-type: none"> • Related to old age ($n=2$); “I don’t know whether it’s related to brain metastases” ($n=2$) • Not related to brain metastases ($n=1$) • Upsetting ($n=1$) • Confusing ($n=1$)
16 Did you feel drowsy during the daytime?	<ul style="list-style-type: none"> • Not related ($n=2$), Not likely related to brain metastases ($n=1$) • Due to dexamethasone ($n=1$), due to medications and condition ($n=2$) • Confusing ($n=2$)—confused about the term “drowsy” ($n=1$) • Would not have asked question ($n=1$)
17 Did you have trouble with your coordination?	<ul style="list-style-type: none"> • Difficult to answer ($n=2$) • Confusing ($n=2$)—confused about the term “coordination” ($n=1$) • Upsetting ($n=1$) • Due to chemotherapy ($n=1$)
18 Did hair loss bother you?	<ul style="list-style-type: none"> • Related to chemotherapy and brain metastases ($n=1$) • Due to chemotherapy ($n=1$) • Confusing ($n=2$) • Question did not apply to me because I did not have radiation ($n=1$) • Would not have asked question ($n=2$)
19 Did itching of the skin bother you?	<ul style="list-style-type: none"> • Related to chemotherapy ($n=1$) • Not related ($n=1$) • Would not have asked question ($n=1$)
20 Did you have weakness of both legs?	<ul style="list-style-type: none"> • Not related to brain metastases ($n=3$) • Upsetting ($n=2$) • Confusing ($n=2$)
21 Did you feel unsteady on your feet?	<ul style="list-style-type: none"> • Related to bone metastases as well ($n=1$) • Difficult to answer ($n=2$) • Upsetting ($n=1$) • Confusing ($n=2$)
22 Did you have trouble controlling your bladder?	<ul style="list-style-type: none"> • Not related ($n=3$) • Not sure if related to brain metastases ($n=1$) • Difficult to answer ($n=1$) • Upsetting ($n=2$)

Appendix II

Table 4 Detailed comments from health care professionals for each QLQ-BN20+2 item

QLQ-BN20+2 Questions		Inappropriate/ irrelevant (<i>n</i>)	Reasons for why stated question as inappropriate/irrelevant
<i>During the past week:</i>			
1	Did you feel uncertain about the future?	12	<ul style="list-style-type: none"> • Similar to Q5 (<i>n</i>=4) • Not too sure why these were specific to brain metastases vs. any palliative patient (<i>n</i>=8)
2	Did you feel you had setbacks in your condition?	15	<ul style="list-style-type: none"> • Too subjective/situational dependent (<i>n</i>=3) • Not too sure why these were specific to brain metastases vs. any palliative patient (<i>n</i>=8) • Overlaps with Q5, 1 or covered other questions (<i>n</i>=4)
3	Were you concerned about disruption of family life?	7	<ul style="list-style-type: none"> • Too subjective/situational dependent • Not too sure why these were specific to brain mets vs. any palliative patient (<i>n</i>=5) • This question is similar to and covered by Q1
4	Did you have headaches?	1	<ul style="list-style-type: none"> • This question should be part of a physical assessment and not on the QOL questionnaire
5	Did your outlook on the future worsen?	9	<ul style="list-style-type: none"> • Too subjective/situational dependent (<i>n</i>=2) • Virtually all patients with serious malignancy complicated by life threatening brain metastases will answer "yes" to this question—it is difficult to quantify, and as a result did not help to elucidate QOL. (<i>n</i>=4) • Unnecessarily negative • This question is similar to and covered by 1 (<i>n</i>=2)
6	Did you have double vision?	6	<ul style="list-style-type: none"> • Depended on location of brain metastases—might not be a common symptom for patients (<i>n</i>=2) • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • Question 8 sufficient (<i>n</i>=2)
7	Was your vision blurred?	6	<ul style="list-style-type: none"> • Depended on location- might not be common symptoms for patients (<i>n</i>=2) • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • Question 8 sufficient (<i>n</i>=2)
8	Did you have difficulty reading because of your vision?	8	<ul style="list-style-type: none"> • Depended on location of brain metastases—might not be common symptoms for patients (<i>n</i>=2) • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • Repetitive of 6 and 7 (<i>n</i>=4)—“is your vision different?”
9	Did you have seizures?	2	<ul style="list-style-type: none"> • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2)
10	Did you have weakness on one side of your body?	4	<ul style="list-style-type: none"> • Weakness was not generally on only one side of the body • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • Combine with Q20
11	Did you have trouble finding the right words to express yourself?	5	<ul style="list-style-type: none"> • Only relevant for patients who received WBRT • Q12 sufficient (<i>n</i>=3) • This is a symptom of the disease, “I’m not sure it is a QOL issue”
12	Did you have difficulty speaking?	3	<ul style="list-style-type: none"> • Covered in Q11 (<i>n</i>=2)

Table 4 (continued)

QLQ-BN20+2 Questions		Inappropriate/ irrelevant (<i>n</i>)	Reasons for why stated question as inappropriate/irrelevant
<i>During the past week:</i>			
13	Did you have trouble communicating your thoughts?	5	<ul style="list-style-type: none"> • This is a symptom of the disease, “I’m not sure it is a QOL issue” • Patients reported more difficulties with physical functioning than speech • Only relevant for patients who received WBRT • Q12 sufficient (<i>n</i>=2)
14	Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	3	<ul style="list-style-type: none"> • This is a symptom of the disease, “I’m not sure it is a QOL issue” • This symptom is more nonspecific and might relate to extra-cranial disease process (<i>n</i>=2) • This is not a main focus for patients
15	Have you had difficulty remembering things?	3	<ul style="list-style-type: none"> • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • This symptom is more nonspecific and might relate to extra-cranial disease process
16	Did you feel drowsy during the daytime?	9	<ul style="list-style-type: none"> • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=3) • Could be drowsy for so many reasons, not specific (<i>n</i>=2) • Usually at this point not a big deal in comparison to other QOL issues (<i>n</i>=4)
17	Did you have trouble with your coordination?	8	<ul style="list-style-type: none"> • This question should be part of a physical assessment as it is a symptom of disease and not on the QOL questionnaire (<i>n</i>=2) • They were not a main focus for patients (<i>n</i>=3) • Repetitive with Q19 and other questions (<i>n</i>=3)
18	Did hair loss bother you?	9	<ul style="list-style-type: none"> • This question should be part of a physical assessment and not on the QOL questionnaire • Treatments not disease related (<i>n</i>=2) • Patients usually chose treatment knowing about hair loss (Even if this was included—would we change management?) (<i>n</i>=2) • Not important (<i>n</i>=2) • Hair loss—most patients already had from chemo (<i>n</i>=2)
19	Did itching of the skin bother you?	16	<ul style="list-style-type: none"> • Only relevant for patients who received WBRT (<i>n</i>=3) • Minimal importance, easy to treat (<i>n</i>=11) • This question should be part of a physical assessment and not on the QOL questionnaire (<i>n</i>=2)
20	Did you have weakness of both legs?	6	<ul style="list-style-type: none"> • This question should be part of a physical assessment and not on the QOL questionnaire (<i>n</i>=2) • Other questions addressed this (i.e. Q15) (<i>n</i>=2) • Confusing: “Are you meaning fatigue or generalized weakness?” • Not clinically meaningful or reasonable; not related to brain mets.
21	Did you feel unsteady on your feet?	4	<ul style="list-style-type: none"> • This question should be part of a physical assessment and not on the QOL questionnaire (<i>n</i>=2) • This symptom is more nonspecific and may relate to extra-cranial disease process
22	Did you have trouble controlling your bladder?	14	<ul style="list-style-type: none"> • Having brain mets did not usually affect your bladder, nonspecific to brain mets (<i>n</i>=12) • This question should be part of a physical assessment and not on the QOL questionnaire (<i>n</i>=2)

WBRT whole-brain radiotherapy; QOL quality of life

Appendix III

Table 5 Additional issues listed by health care professionals that were not covered on the QLQ-BN20+2 or QLQ-C15-PAL

Additional issue not covered	Detailed comments from HCPs
Burden and impact on family/children	<ul style="list-style-type: none"> • Patients are worried about leaving children behind when they die; patients are concerned about high burden on family; they do not want to become a burden. They will often feel guilty about dependency • Patients with brain metastases are worried about being a burden, how their spouse and children are coping. They feel degraded having to ask for help with bathing, eating, toileting. Can get frustrated when they can't make themselves understood. • Feeling like a burden on loved ones can create guilt, stress, and negatively impact self-worth • Brain tumour patients are often concerned about their caregivers. Brain tumour patients must often stop employment.
Other side effects: hearing loss, skin sores, intellectual capacity, hopelessness, anxiety, loneliness	<ul style="list-style-type: none"> • Patients having cranial radiation that includes the ear canal often have hearing loss after treatment (temporary, but very disturbing for patient and family) • Temporary or permanent intellectual weakness from basic radiation • Depression and anxiety questions, focusing on patient's perception of future • Even a limited scope for hopefulness can positively impact patient's QOL • The need for a another person and for help at home
Understanding prognosis	<ul style="list-style-type: none"> • Patients are often confused and need clarity with respect to their future
Coping with stress/support systems	<ul style="list-style-type: none"> • To assess how patients are coping with stress, depending on less activities of daily living, little family/social support • To assess if patient feels supported by medical team, social supports • Need to ask if patients feel there is something else their health care team and/or family/social supports can do to help them either with symptoms or with their emotions. What do they find most helpful to get their day/week? • When patients don't have home support it can greatly affect their QOL and if needed we can intervene to make this situation improved for them • Insufficient help at home can result in increased levels of fear
Financial hardship	<ul style="list-style-type: none"> • Loss or reduction of financial health can negatively impact patient's QOL
Language issues	<ul style="list-style-type: none"> • More important if patient does not have family members or community help with translation when they have problems/worsening symptoms at home (i.e.: not getting help/care in a timely manner because they cannot communicate)
Independence/Ability to carry out usual activities	<ul style="list-style-type: none"> • To evaluate functional activity status and patient desired activity level • There are 4 questions dealing with fatigue, but none that deals with how much usual activity level is reduced and what impact this has on a sense of well-being. • Use of cane, walker or wheelchair • Activities of daily living are a common issue to patients with brain tumours • What about independence issues? Being able to function independently at home. • This is a bigger issue for brain metastases patients
Intimacy/Sex	<ul style="list-style-type: none"> • A fundamental aspect of QOL not addressed by any of the questionnaires
Perception	<ul style="list-style-type: none"> • All of the symptoms listed do not assess whether or not the patient perceives that their QOL is being impacted. I'm not sure we can say if they have pain or trouble sleeping etc., that they have a poor QOL. Expanding the questions to include "...so much so that it negatively impacts your QOL" would be much more meaningful

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