Understanding changes in quality of life in cancer patients: a cognitive interview approach

Bloem, E.F.

Citation for published version (APA):
Opening the black box of cancer patients’ quality-of-life change assessments: a qualitative study examining the cognitive processes underlying responses to transition items

Taminiau-Bloem EF, van Zuuren FJ, Visser MRM, Tishelman C, Schwartz CE, Koeneman MA, Koning CCE, Sprangers MAG

Submitted
Abstract

Objective
The use of transition items has become a popular anchor-based approach to determine the clinical significance of patient-reported change. These items assume that patients (1) arrive at a change assessment by comparing posttest and pretest functioning, and (2) accurately recall their pretest functioning. Although results from quantitative studies have raised questions about these assumptions, this is the first study to qualitatively examine them.

Methods
We conducted think-aloud interviews with 25 cancer patients prior to and following radiotherapy at the Academic Medical Center in Amsterdam to elicit the cognitive processes they used in answering seven transition items. Content analysis of their responses to pretest and transition items was independently carried out by two researchers using a qualitative analysis scheme based on cognitive process models of Tourangeau et al. and Rapkin & Schwartz.

Results
In 112 of the 164 responses to transition items, patients verbalized a comparison between current and prior functioning. However, in 104 of these responses, patients did not refer to their functioning at pretest and/or posttest according to the transition design's first assumption, but rather used a variety of time frames as point of reference. Additionally, in 79 transition responses, the time frame employed and/or description of prior functioning provided differed from those verbalized when responding to the corresponding pretest items. Transition design's second assumption of accurate recall of pretest functioning therefore appears not to be in line with patients' cognitive processes used in the majority of their change assessments.

Conclusions
Our findings demonstrate that patients provide change assessments based on personally meaningful time frames and content, which might deviate from the time frames considered relevant by researchers. Retrospective recall is a useful method to assess change experienced by the subjects. However, in interpreting transition assessments in the context of treatment evaluation, one needs to be aware of the fact that patients provide change assessments, which, in general, are not based on the cognitive processes assumed by researchers.
Introduction

Patient-reported ratings of quality of life (QoL) are increasingly included in treatment evaluations to demonstrate treatment effects beyond clinical efficacy and safety [1-3]. The use of transition items has become a popular anchor-based approach to determine the clinical significance of patient-reported change in QoL [4, 5]. Transition items extend the conventional pretest-posttest design by asking patients at posttest to rate the extent to which they have experienced change in their functioning since pretest (e.g., Is your current QoL better or worse since you started treatment?).

In arriving at such a change assessment, patients are assumed to (1) compare posttest and pretest functioning, and (2) accurately recall their pretest functioning. However, results from quantitative studies have raised questions about these assumptions. First, there is correlational evidence indicating that patients do not make a change assessment by comparing posttest and pretest functioning, but rather base their responses to transition questions on their current posttest functioning—a “present-state bias” [6, 7]. Second, there is ample evidence that retrospective appraisal is subject to recall bias [8-11]. These quantitative findings imply that patients’ self-reported ratings of change are not based on the processes intended, possibly resulting in an erroneous understanding of time and treatment effects.

Despite these suggestive findings, insight into the way patients actually arrive at their responses to transition questions is lacking. In their review on the clinical significance of health status measures, Guyatt et al. [12] indicated that qualitative studies are needed to investigate the cognitive processes that individuals use to retrospectively assess change over time. To the best of our knowledge, only Wyrwich & Tardino [13] have conducted a qualitative investigation of cognitive processes underlying health-related quality of life (HRQoL) transition questions. In their study, 41 chronically ill patients were interviewed to identify cognitive processes used in answering questions about change in HRQoL, although these transition questions had been completed at an earlier occasion. These data indicated that patients generally based their answers solely on their current or recent functioning, without comparison to their prior functioning. This study thus confirmed earlier quantitative findings [6, 7].

As Wyrwich & Tardino [13] pointed out, one limitation of their study is that it might have been difficult for their respondents to report change as they had not experienced a salient health-related intervention. A second limitation is that the HRQoL transition questions were answered between one week and two months prior to the qualitative interview. Therefore, it is unclear whether respondents recalled, or rather reconstructed the cognitive processes they used to answer the transition questions. Further, patients’ ability to recall their prior functioning was not studied.

In the present study, we are specifically interested in qualitatively studying the assumptions underlying transition questions. Therefore, our objectives are to examine whether patients (1) arrive at a change assessment by comparing posttest and pretest functioning, and (2) accurately recall their pretest functioning. In accordance with the design used in treatment evaluation, pretest assessments were administered prior to, and posttest and transition assessments at the end of a salient health-related intervention, in this case radiotherapeutic treatment.
In contrast to Wyrwich & Tardino’s study [13], we administered think-aloud interviews to elicit underlying cognitive processes at pretest and at posttest. Moreover, we conducted the think-aloud interviews immediately after patients’ response to each pretest and transition item. This study will provide insight into how patients’ self-reported change can be interpreted.

Methods

Participants
The study sample comprised cancer patients undergoing radiotherapy at the Department of Radiation Oncology at the Academic Medical Center (AMC) in Amsterdam. Inclusion criteria were a minimum age of 18 years, fluent command of Dutch, absence of cognitive impairments, not diagnosed with a brain tumor and/or treated with brain irradiation, expected survival of ≥ 3 months, and undergoing ≥ 3 weeks of radiation treatment. Two researchers (ETB, MK) purposefully identified patients who varied by factors conceptualized as affecting their treatment experience, i.e., gender, age, tumor site, and length of radiation treatment (i.e., length of interval between patients’ pretest, and posttest and transition assessments). Radiotherapists recruited these identified participants and provided them with an information letter describing the study background and interview procedure. Patients who expressed interest in participating were contacted by telephone by a researcher (ETB, MK) to schedule the pretest interview. Since this study was not intrusive and based solely on self-reports, the Medical Ethics Committee (MEC) of the AMC provided exemption from seeking formal approval, as is standard practice for such studies.

Procedure
We administered a pretest assessment on the same day the patient had a simulator appointment to plan treatment or received their first radiation treatment. The posttest and the transition assessments took place on patients’ last day of radiotherapy. Items were derived from the 30-item EORTC QLQ-C30 [14], a HRQoL instrument widely used in European cancer clinical trials [15]. To limit patient burden, we selected the following seven items to cover both global and specific content, including physical, psychological and social dimensions: 1) Do you have any trouble taking a short walk outside of the house? 2) Have you had pain? 3) Were you tired? 4) Did you worry? 5) Has your physical condition or medical treatment interfered with your social activities? 6) How would you rate your overall health during the past week? 7) How would you rate your overall quality of life during the past week? All items employ a one week time frame. The transition questions were adapted versions of these items, formulated as e.g., Do you have more or less pain since the first interview? Patients answered the transition questions on a 7-point Likert scale ranging from ‘a great deal worse’ to ‘a great deal better’, with the middle point labeled ‘the same’.

We used the Three-Step Test Interview [16], combining cognitive think aloud interviewing and verbal probing techniques [17] at the pretest, posttest and transition assessments to enable an unequivocal interview procedure and comparisons of patients’ cognitive processes. As suggested in Willis’ manual for cognitive interviewing [18], we began each interview with
an exercise to acquaint participants with the think-aloud procedure. In this exercise, patients were asked to visualise their home and think out loud what they were seeing and thinking while counting all the windows. When patients immediately provided a response without thinking aloud (for example “8 windows”), the interviewer again explained the think aloud procedure and repeated the exercise. All patients were able to perform this exercise, after which we commenced with the actual think-aloud interview. In this interview, patients were asked to read each question out loud and subsequently think out loud as they assigned a score to the question. Immediately after the think-aloud response to each item, we probed to elicit more information about participants’ cognitive processes using non-leading questions like “Could you tell me more about that?” At posttest patients were first asked to assess their posttest functioning, with the administration of transition items following. Non-leading probes for the transition items included e.g. “You just referred to your functioning prior to the start of radiotherapy, could you explain to me how you tried to recall this period?”

The interviews were conducted by two researchers (ETB, MK) not involved in the patient’s clinical care. The same interviewer conducted both interviews for a patient whenever possible (22 of the 25 patients), to increase consistency of the interview procedure and to stimulate patients to recall their pretest functioning. All interviews were audio-recorded and transcribed verbatim.

Analysis
Qualitative analysis was independently carried out by two researchers (ETB, MK) using MAXqda software [19]. All interviews were coded using a previously established qualitative analysis scheme [20] based on the frameworks of Tourangeau et al. [21] and Rapkin & Schwartz [22], and developed to capture the cognitive processes underlying QoL assessment. Combined, these frameworks encompass five cognitive processes underlying QoL appraisal. We previously documented the usefulness of this analysis scheme for qualitative analysis of patients’ cognitive processes [20].

To study the first assumption underlying the transition design, we initially examined whether patients’ responses to transition items were based on a comparison of posttest and pretest functioning. If not, we analyzed how patients described their reasoning when responding to transition items. When responses were based on a comparison of current and prior functioning, we further studied transition design’s second assumption of accurate recall. We operationalized accurate recall by examining whether the time frame employed and the description of prior functioning provided in answering each transition item were similar to those of the corresponding pretest item. The two researchers continually discussed their findings and achieved agreement through negotiated consensus [23]. Throughout the period of data collection and analysis, all codes and subsequent analyses were discussed with FvZ and MS.

In our prior study, we had found that the content of the cognitive processes used by a respondent to assess HRQoL over time was not constant across questionnaire items, but instead, varied by item [20]. Again, in analyzing patients’ think aloud response to each transition item, we found that the content of the cognitive processes differed within the same patient across items (see Appendix 1 for an illustration). Moreover, the cognitive processes underlying the response to a transition item were not found to result in the use of the same processes
for the subsequent item. These previous findings underlay our decision, to examine each response to all HRQoL transition items separately in the present study.

Results

Participants
Of 53 eligible patients approached, 19 refused to participate explaining they considered it too burdensome to be interviewed prior to and after radiation treatment. Thirty-four patients gave written informed consent. Twenty-five patients completed all interviews, while nine patients were unable to complete the posttest and transition interviews due to severe health deterioration. The median number of days between the pretest assessment and the posttest and transition assessment was 49 days (Mean 50 days, SD 13.7, range 30-82). Table 1 depicts the characteristics of the 25 participants (median age 59 years, range 35-85). Fifteen patients completed all seven transition items, with an additional nine patients providing interpretable data for six items, and another patient for five items. We therefore could analyze 164 responses to transition items.

Table 1 – Patient characteristics

<table>
<thead>
<tr>
<th>No. of patient</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender:</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>12</td>
</tr>
<tr>
<td>Women</td>
<td>13</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>2</td>
</tr>
<tr>
<td>40-49</td>
<td>3</td>
</tr>
<tr>
<td>50-59</td>
<td>8</td>
</tr>
<tr>
<td>60-69</td>
<td>6</td>
</tr>
<tr>
<td>70-79</td>
<td>4</td>
</tr>
<tr>
<td>≥ 80</td>
<td>2</td>
</tr>
<tr>
<td>Tumor site:</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>2</td>
</tr>
<tr>
<td>Breast</td>
<td>6</td>
</tr>
<tr>
<td>Esophageal</td>
<td>5</td>
</tr>
<tr>
<td>Gynecological</td>
<td>3</td>
</tr>
<tr>
<td>Lung</td>
<td>4</td>
</tr>
<tr>
<td>Prostate</td>
<td>5</td>
</tr>
<tr>
<td>Length of interval between pretest and posttest transition interview (median)</td>
<td></td>
</tr>
<tr>
<td>&lt; 49 days</td>
<td>12</td>
</tr>
<tr>
<td>≥ 49 days</td>
<td>13</td>
</tr>
</tbody>
</table>
Assumption 1: Comparison of posttest and pretest functioning

Results on patients’ cognitive processes underlying transition items are graphically presented in Figure 1.

Box 1.1. Eight of the 164 responses to transition items indicated that patients compared posttest and pretest functioning according to the time frames as instructed (see Figure 1; box 1.1.). The following interview excerpt illustrates one of the responses that was in line with this first assumption. In answering the question “Do you have more or less pain since the first interview?” this patient explained: “I didn’t have pain at that time, I wasn’t even coughing. And now I suffer these discomforts. I feel nauseous, and my esophagus... So I have ‘somewhat more’ pain now compared to the first interview.” (Answer: Somewhat more; score 3) [Female, 65 years, lung cancer]

Box 1.2. In an additional 104 responses to transition items, patients verbalized a comparison between current and prior functioning, but they employed a time frame other than that instructed when explaining their assessment of current and/or prior functioning. Instead of explicitly comparing pretest and posttest functioning, a variety of different time periods were used as point of reference (see Figure 1; box 1.2.). For example, prior functioning was referred to as prior to cancer diagnosis and treatment (N=37 responses); following other cancer treatment, but prior to radiotherapy (N=25); or as the first weeks of radiotherapy (N=13). Examples of periods referred to as current functioning included: since diagnosis (N=5); the entire period of radiotherapy (N=23); or the final weeks of radiotherapy (N=8).

Box 1.3. In 52 responses to transition items, patients’ change assessments did not include any explicit verbalization of a comparison between current and prior functioning (see Figure 1; box 1.3.). In the majority of these responses, patients primarily assessed their posttest functioning (N=34) without comparing it to another time point. The following excerpt exemplifies one such typical response. In response to the question “Do you worry more or less since the first interview?” this patient explains her answer ‘less’ (score 6) as follows: “I don’t want to worry, it’s not good for your body and soul. I try to remain happy, so I need to choose the answer ‘less’.” [Female, 57 years, esophageal cancer]
Figure 1 – Flow chart of participants’ responses to transition items according to the underlying assumptions

Assumption 1
Comparison of posttest and pretest functioning

Box 1.1.
Comparison of posttest and pretest functioning according to the time frames as instructed:

- Dissimilarity in time frame
- Similarity in description of pretest functioning

8 responses

Assumption 2
Accurate recall of pretest functioning

Box 2.1.1.
- Dissimilarity in time frame
- Similarity in description of pretest functioning

3 responses

Box 2.1.2.
- Dissimilarity in time frame
- Dissimilarity in description of pretest functioning

5 responses
164 responses to transition items

Box 1.2.
Comparison of current and/or prior functioning not according to the time frames as instructed:
104 responses

Prior functioning:
- Prior to cancer diagnosis and treatment (N=37)
- Receiving cancer diagnosis (N=6)
- Between cancer diagnosis and start of treatment (N=17)
- Following other cancer treatment, prior to radiotherapy (N=25)
- Pretest functioning (N=3)
- First weeks of radiotherapy (N=13)
- Other (N=3)

Current functioning:
- Since diagnosis (N=5)
- Following other cancer treatment, prior to radiotherapy (N=7)
- Posttest functioning (N=57)
- Entire radiotherapeutic treatment (N=23)
- Final weeks of radiotherapy (N=8)
- Other (N=4)

Box 1.3.
No comparison of current and prior functioning:
52 responses

- Posttest functioning (N=34)
- Overall functioning during cancer treatment (including cancer treatment other than radiotherapy) (N=5)
- Overall functioning during radiotherapy (N=6)
- Other (N=7)

Box 2.2.1.
- Similarity in time frame
- Similarity in description of pretest functioning
33 responses

Box 2.2.2.
- Similarity in time frame
- Dissimilarity in description of pretest functioning
15 responses

Box 2.2.3.
- Similarity in time frame
- Dissimilarity in description of pretest functioning
16 responses

Box 2.2.4.
- Dissimilarity in time frame
- Dissimilarity in description of pretest functioning
40 responses
Assumption 2: Accurate recall of pretest functioning
In studying transition design’s second assumption of accurate recall, we first compared the eight responses to transition items that matched the first assumption (see Figure 1; box 1.1.) with the corresponding eight pretest responses. However, we found that when answering these eight pretest items, patients had not employed the instructed one week time frame.

Box 2.1.1. Despite the different time frames employed in answering the transition items and the corresponding pretest items, the descriptions of pretest functioning in three responses to transition items were similar to the descriptions provided at pretest (see Figure 1; box 2.1.1.).

Box 2.1.2. In the other five responses to transition items, both the employed time frames and the descriptions of pretest functioning differed from those provided for the same items at pretest (see Figure 1; box 2.1.2.). The following interview excerpts illustrate one of these latter five responses. The patient cited below refers to the time frame following surgery in responding to the pretest item, describing the pain he suffered as a consequence of this previous cancer treatment: “I have had an operation on my lymph nodes, and afterwards I experienced some pain because of a sore spot at my abdomen.” (Answer: A little). However, in responding to the transition item, the patient referred to the time of the first interview, describing an absence of pain at that time: “I haven’t had any pain in the time of the first interview. Not at all, and I don’t suffer from any pain now either. So ‘less’ pain isn’t a response option, since that implies you have suffered pain once.” (Answer: The same; score 4) [Male, 66 years, prostatic cancer].

Box 2.2.1. In 33 responses to transition items, patients employed a time frame different than that instructed to assess pretest functioning. Although not following researcher instructions, the time frames the patients employed and the descriptions of prior functioning were in line with those of the corresponding pretest items (see Figure 1; box 2.2.1.). Thus, apart from not employing the time frames as instructed at both the pretest and transition assessments, these responses were in line with both assumptions underlying the transition design. For example, the patient cited below employs the time frame ‘prior to cancer diagnosis and treatment’ in answering the transition and the pretest item. Additionally, in answering the transition item the patient provides a description of prior functioning, which is similar to the description provided at pretest, i.e. not having trouble taking a short walk outside of the house (item 1). At pretest, the patient responded “A short walk is around 20 minutes. It’s routine, I do it every day. Taking a walk to the station or doing groceries. I don’t have any trouble with that.” (Answer: Not at all). In answering the transition item, the patient answered “I always take a walk to the station, that’s a walk of 15 to 20 minutes. When I compare the way I normally have experienced taking this walk, with the way I experience it now, I notice that it tires me somewhat more.” (Answer: Somewhat more; score 3) [Male, 59 years, prostatic cancer].
Box 2.2.2. In 15 responses to transition items, the time frames employed were in line with the time frames employed in the corresponding pretest items, although these time frames were not in line with the researcher’s instructions at either time point. However, patients’ descriptions of prior functioning provided in response to these transition items differed from those provided when responding to the corresponding items at pretest (see Figure 1; box 2.2.2.). In these responses, patients defined the target construct of the item differently at the transition assessment and/or retrieved different information about their functioning than was the case at pretest. In the following example, the patient referred to the same period in both assessments, i.e. the period between cancer diagnosis and start of treatment, but provides a different description of pretest functioning in both interviews. At pretest the patient responded “a little” to the question “Did you worry?”, indicating that he worried about his health, although he also expressed confidence in the health care staff: “I worry a little about my health, but I am confident that the people here in the hospital can help me. So, I would say ‘a little’, I’ll just wait and see.” When answering the transition item at posttest, the patient explained: “I worry less because I expect a promising result. Prior to radiotherapy, I greatly dreaded the treatment. At that time, I didn’t know what the future would bring. But now it’s over, I worry less.” (Answer: Less; score 6). [Male, 79 years, lung cancer].

This transition response reflects an understandable way of coping; however the description of prior functioning is not consistent with the description provided in the corresponding pretest item and thus not in line with the underlying assumption.

Box 2.2.3. In 16 responses to transition items, the time frames employed by the patients differed from the time frames employed when responding to the corresponding pretest items. However, the patients’ descriptions of prior functioning provided in response to these transition items were similar to those provided in the corresponding pretest items (see Figure 1; box 2.2.3.). To illustrate, the patient cited below refers to her functioning following previous surgery when answering the pretest item “Have you had pain?”, whereas she refers to the first weeks of radiotherapy in assessing prior level of pain when answering the transition item. However, in both responses the patient assesses the same pain as a result of a cut nerve. In response to the pretest question the patient responded: “I have a little pain in my left upper arm. That’s because a nerve has been cut during surgery.” (Answer: A little). In answering the transition item, the patient indicated: “I think that in the first period of radiotherapy, I still suffered from that nerve that had been cut. But at this stage, it isn’t sensitive anymore.”(Answer: Less; score 6) [Female, 51 years, breast cancer].

Although consistency in time frame might not have altered the response to the transition item in this case, the assumptions underlying the transition design differ from this patient’s cognitive processes of assessment.
Table 2 – Responses per transition item according to the underlying assumptions

<table>
<thead>
<tr>
<th>Assumption 1: Comparison of posttest and pretest functioning</th>
<th>Comparison of current and prior functioning*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumption 2: Accurate recall of pretest functioning</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Similarity in time frame</td>
</tr>
<tr>
<td></td>
<td>Similarity in description of pretest functioning</td>
</tr>
<tr>
<td></td>
<td>(Figure 1; Box 2.2.1.)</td>
</tr>
<tr>
<td></td>
<td>Similarity in time frame</td>
</tr>
<tr>
<td></td>
<td>Dissimilarity in description of pretest functioning</td>
</tr>
<tr>
<td></td>
<td>(Figure 1; Box 2.2.3.)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assumption 1: Comparison of posttest and pretest functioning</th>
<th>Comparison of current and prior functioning*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you have more or less trouble taking a short walk outside of the house since the first interview?</td>
<td>9</td>
</tr>
<tr>
<td>2. Do you have more or less pain since the first interview?</td>
<td>7</td>
</tr>
<tr>
<td>3. Are you more or less tired since the first interview?</td>
<td>4</td>
</tr>
<tr>
<td>4. Do you worry more or less since the first interview?</td>
<td>4</td>
</tr>
<tr>
<td>5. Does your physical condition or medical treatment interfere more or less with your social activities since the first interview?</td>
<td>3</td>
</tr>
<tr>
<td>6. Would you rate your overall health worse or better since the first interview?</td>
<td>4</td>
</tr>
<tr>
<td>7. Would you rate your overall quality of life worse or better since the first interview?</td>
<td>2</td>
</tr>
<tr>
<td>Total responses</td>
<td>33</td>
</tr>
</tbody>
</table>

*These columns encompass comparison of posttest and pretest functioning\(^1\), as well as comparison of current and prior functioning\(^2\).
### Cognitive processes underlying transition items

<table>
<thead>
<tr>
<th>Dissimilarity in time frame</th>
<th>Similarity in description of pretest functioning</th>
<th>No comparison of current and prior functioning</th>
<th>Total responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Figure 1; Box 2.1.1. &amp; Box 2.2.3.)</td>
<td>(Figure 1; Box 2.1.2. &amp; Box 2.2.4.)</td>
<td>(Figure 1; Box 1.3.)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>0</td>
<td>5</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>$4^1 + 16^2$</td>
<td>$4^1 + 40^2$</td>
<td>52</td>
<td>164</td>
</tr>
</tbody>
</table>
Box 2.2.4. There were 40 responses to transition items, which indicated that the time frames employed by the patients differed from those provided for the same items at pretest. In addition, these responses also differed in the descriptions of prior functioning due to differences in definition of the target construct and/or the retrieval of different information at the transition assessment (see Figure 1; box 2.2.4.). In the following example, the patient assesses her functioning at pretest by referring to the week prior to the start of radiotherapy, whereas in the transition assessment she assesses prior functioning by referring to the first weeks of radiotherapy. Additionally, at pretest she defines tiredness as a result of physical activity, whereas in answering the transition item she defines tiredness as a mental state due to feeling tense. In response to the pretest question “Were you tired?”, the patient explained: “In the past week I had to go to the hospital for all kinds of tests, a blood test, and a bone scan. Well, that really tires you, all that walking back and forth to the hospital.” (Answer: Quite a bit). Whereas, in response to the transition item, she indicated: “In the beginning of treatment, you’re constantly thinking about the radiotherapy, and whether it will be effective. All that thinking tires you. The tension really made me tired. But now I feel good about going home.” (Answer; Less; score 6) [Female, 54 years, breast cancer].

Length of the interval between pretest and transition assessments
The length of the interval between patients’ pretest assessment on the one hand, and posttest and transition assessments on the other hand (range 30-82 days) was not found to influence the cognitive processes used in answering the transition items. That is, patients with a shorter recall period did not provide responses to transition items according to its underlying assumptions more often, than patients with a shorter recall period.

Results on the item level
When looking at the item level (see Table 2), the assessment of change in trouble taking a short walk outside of the house (item 1) was most often based on a comparison of current and prior functioning. Moreover, the transition responses to this item were most often in line with the corresponding pretest items in employed time frame and description of prior functioning. Conversely, assessing change in pain (item 2) was most often expressed with different time frames and descriptions of prior pain when compared to those of the corresponding pretest item. The questions least often based on an explicit comparison of current and prior functioning were those enquiring about change in fatigue (item 3), worry (item 4), overall health (item 6), and overall QoL (item 7).
Discussion

In 112 of these 164 responses to transition items, patients verbalized a comparison between current and prior functioning. However, in 104 of these 112 responses, patients did not refer to their functioning at pretest and/or posttest according to the transition design’s first assumption, but rather used a variety of other time frames as point of reference. Additionally, in 79 of these 112 responses to transition items, the time frame employed and/or description of prior functioning provided differed from those verbalized in the corresponding pretest items. Transition design’s second assumption of accurate recall of pretest functioning therefore appears not to be in line with patients’ cognitive processes used in the majority of their change assessments.

In 52 responses to transition items no explicit change assessment was made between patient’s current and prior functioning. In the majority of these responses, patients solely assessed their posttest functioning, thereby confirming the occurrence of present-state bias [6, 7]. However, in contrast to Wyrwich and Tardino’s qualitative study [13] in which patients primarily or even solely based their answers to transition items on their current state, patients in this study did verbalize a comparison between current and prior functioning in most responses to transition items, although they employed other time frames than those instructed.

Responses to transition items, in which the time frames employed and descriptions of prior functioning differed from those provided in the corresponding pretest items, are presented here as deviating from transition design’s second assumption of accurate recall of pretest functioning. However, our data demonstrate that this dissimilarity cannot be attributed unequivocally to possible recall bias, but appears to also reflect patients’ response strategies, motivated by mechanisms such as impression management, coping, social desirability and response shift [24].

In treatment evaluation, transition items usually focus on change in QoL domains instead of change in single QoL items. In this study, we selected seven single items of the EORTC QLQ-C30 for the pretest and posttest assessments covering global domains as well as specific items. To maximize the comparability of pretest and transition assessments, the transition questions were adapted versions of these items. Whereas this choice may have limited the generalizability of our results, they may also be viewed as an upper limit of the extent to which transition assessments may meet the underlying assumptions. In other words, the cognitive processes used for answering transition items based on domains are expected to deviate even more from those used when responding to single pretest items.

We would like to highlight that our selection of items provided us with the opportunity to obtain information about the cognitive processes patients use in answering transition items with a varying level of specificity. Interestingly, the responses to the specific transition item “Do you have more or less trouble taking a short walk outside of the house since the first interview?” were most often in line with the assumptions underlying the transition design, whereas the global transition item “Would you rate your overall quality of life worse or better since the first interview?” was least often in line with the underlying assumptions.
This finding confirms results of previous studies in which specific questions were answered more reliably and with greater validity than global health status measures [8]. As indicated by Norman [25], answering transition questions is a complex cognitive task. Patients need to arrive at an assessment of their posttest functioning, remember their pretest state, contrast their posttest functioning with their recalled pretest functioning, and finally mentally subtract these two states to arrive at a change assessment. Adjustments to the wording of transition items and the accompanying instructions might facilitate this cognitive task [17, 26]. For example, the instructions to the transition assessment should provide cues to elicit patient's memory about the time they completed the pretest assessment, as is common in administering the thentest [27]. For example, “These questions ask you to recall your health status in the week prior to the start of radiation treatment. Take a moment to think back to this period. At that time, you might have undergone a different treatment such as surgery or chemotherapy. You might have felt sad, or nervous, or maybe you haven’t felt sad or nervous at all. You might have suffered from physical complaints, or maybe you haven’t had physical complaints at all.” Additionally, rephrasing transition items by including words explicitly referring to comparison might help patients to actually compare posttest and pretest functioning, e.g., “Compared to the week prior to the start of radiotherapy, are you currently experiencing more, less or the same level of pain?” The limitations of this study should be noted. Nineteen patients refused participation because they considered it too burdensome, and severe health deterioration prevented nine patients from completing the posttest and transition assessments. This might indicate that the most severely ill patients were not included in our sample. We cannot exclude the possibility that these patients might have used different cognitive processes in answering the transition items, which limits the interpretation of our findings to the less severely ill patients. However, to ensure a heterogeneous sample, we purposively selected participants based on characteristics which might affect their treatment experience in different ways. Second, the extent to which think-aloud interviews adequately reflect patients' cognitive processes can be questioned. Patients who did not compare current and prior functioning might have made this comparison implicitly, without mentioning their prior functioning in the interview. Therefore, we not only asked patients to think aloud while answering the transition items, but also probed them for clarification to capture patients' cognitive processes as comprehensively as possible. In addition, we probed our participants immediately after their think-aloud response to each item instead of retrospectively after administering all questionnaire items, to diminish the chance of participants reconstructing their response process instead of recalling it [20]. While one disadvantage of this approach might be that participants' cognitive processes are influenced by the probing of the preceding item, we found no sign of this since the cognitive processes underlying the response to a transition item differed from those used in responding to subsequent items. Our results demonstrate that patients employ a variety of time frames besides those instructed. This finding demonstrates that patients select personally meaningful time frames and content when assessing the extent to which they have experienced change in their functioning, which might deviate from the (more standardized) time frames considered...
relevant by researchers. For example, a patient might assess experienced change in functioning prior to and following cancer diagnosis, whereas the transition items are intended to measure patient-reported change as a result of radiotherapy. Interestingly, the finding that each patient could vary the time frames used in assessing prior functioning by item, indicates that the time frame perceived to be meaningful to the patient differs by QoL domain. As argued previously [28], retrospective recall is a useful method when the measurement goal is to assess the patient's perspective of change. However, in interpreting transition assessments in the context of treatment evaluation, one needs to be aware of the fact that patients provide change assessments that are not necessarily based on the cognitive processes as intended by researchers. Rather, patients arrive at change assessments which are meaningful to them, based on personal experiences and complex cognitive processes. With this study we have further opened the black box to shed light onto these cognitive processes.
References

8. Hermann D. Reporting current, past and changed health status. What we know about distortion. Medical Care 1995; 33: AS77-88
Cognitive processes underlying transition items

27. Schwartz CE, Sprangers MAG. Guidelines for improving the stringency of response shift research using the thentest. Quality of Life Research 2010; 19: 455-464
Appendix 1 - Illustration of a patient's cognitive processes underlying the responses to 7 pretest and transition items
[Male, 79 years, lung cancer]

Item 1
Pretest: Do you have any trouble taking a short walk outside of the house? Answer: Very much
1. “I can immediately respond to that question in saying that I have a lot of trouble with that.
2. (…) For 10 years now, my right hip and right knee no longer function as they did before.
3. (…) A short walk for me is a movement of necessity, for example running an errand or walking to the mailbox.
4. (…) I am able to go for a walk, but I cannot walk energetically.”

Transition: Do you have more or less trouble taking a short walk outside of the house since the first interview?
Answer: Somewhat less
A. “During my first weeks of radiotherapy, I regularly used a wheelchair for my transportation within the hospital.
B. (…) However, during treatment I decided to walk, taking it slowly, at my own pace.
C. (…) I feel that I experience somewhat less trouble. I showed more guts, and less laziness.”

Assumption 1. Comparison of posttest and pretest functioning
Box Prior functioning: First weeks of radiotherapy
A. “During my first weeks of radiotherapy (…)”
Current functioning: Final weeks of radiotherapy
B. “(…) However, during treatment I decided to walk (…)”

Assumption 2. Accurate recall of pretest functioning
Box Dissimilarity in time frame
Figure 1; Box 1.2. Prior test functioning:
Prior to cancer diagnosis and treatment
2. “(…) For 10 years now, my right hip and right knee no longer function as they did before.
Dissimilarity in description of pretest functioning
Pretest description of functioning:
4. (…) I am able to go for a walk, but I cannot walk energetically.”
Transition - description of prior functioning
A. “During my first weeks of radiotherapy, I regularly used a wheelchair for my transportation within the hospital.”

1 We have only provided a selection of the most relevant text fragments of each interview
**Item 2**
Pretest: Have you had pain?
Answer: A little
1. “(…) It [pain in the knee] is annoying.
2. For example, I always need to bring my knee in a particular position when I get into bed.
3. Just to make sure it doesn’t cause me pain.
4. (…) I manage to bear the pain, I rather see it as a discomfort.

Transition: Do you have more or less pain since the first interview?
Answer: The same
A. “I haven’t had pain actually.
B. To me pain is the need to scream ‘ouch’, but I haven’t experienced that at all.
C. (…) At the moment I am free of pain, and I cannot recall that I suffered pain when I started this treatment.”

**Assumption 1. Comparison of posttest and pretest functioning**

<table>
<thead>
<tr>
<th>Box</th>
<th>Prior functioning:</th>
<th>Current functioning:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1; Box 1.2</td>
<td>First weeks of radiotherapy</td>
<td>Posttest functioning</td>
</tr>
<tr>
<td></td>
<td>C. “(…) I cannot recall that I suffered pain when I started this treatment.”</td>
<td>C. “(…) At the moment I am free of pain (…)”</td>
</tr>
</tbody>
</table>

**Assumption 2. Accurate recall of pretest functioning**

<table>
<thead>
<tr>
<th>Box</th>
<th>Dissimilarity in time frame</th>
<th>Transition - prior functioning:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1; Box 2.2.4</td>
<td>Pretest functioning: Prior to cancer diagnosis and treatment</td>
<td>First weeks of radiotherapy</td>
</tr>
<tr>
<td></td>
<td>2. “(…) I always need to bring my knee in a particular position when I get to bed.”</td>
<td>C. “(…) I cannot recall that I suffered pain when I started with this treatment.”</td>
</tr>
</tbody>
</table>

**Dissimilarity in description of pretest functioning**

| Pretest description of functioning: I-3. “(…) It [pain in the knee] is annoying. For example, I always need to bring my knee in a particular position when I get into bed. Just to make sure it doesn’t cause me pain.” | Transition - description of prior functioning: C. “(…) I cannot recall that I suffered pain when I started this treatment.” |
Item 3
Pretest: Were you tired?
Answer: Not at all
1. “(...) No, I wasn’t tired. I am energetic by nature. However, certain things can limit your possibilities.
2. (...) For example, if you’re not feeling too well, or due to a certain [medical] treatment.
3. (...) However, that happens seldomly.”

Transition: Are you more or less tired since the first interview?
Answer: Somewhat more
A. “I feel tired somewhat more. I think that’s because all these influences, like the radiation treatment, are physically tiring for your body.
B. Thus, you feel somewhat more tired than you would feel normally.
C. (...) I got tired gradually”

Assumption 1. Comparison of posttest and pretest functioning
Box Prior functioning: Current functioning:
Figure 1; Box 1.2. Prior to cancer diagnosis and treatment Entire radiotherapeutic treatment B. “Thus, you feel somewhat more tired than you would feel normally.”
C. “(...) I got tired gradually.”

Assumption 2. Accurate recall of pretest functioning
Box Similarity in time frame
Figure 1; Box 2.2.1. Pretest functioning: Transition - prior functioning:
Prior to cancer diagnosis and treatment Prior to cancer diagnosis and treatment
1. “(...) No, I wasn’t tired. I am energetic by nature.” B. “Thus, you feel somewhat more tired than you would feel normally.”

Similarity in description of pretest functioning
Pretest description of functioning: Transition - description of prior functioning
1. “(...) No, I wasn’t tired. I am energetic by nature.” B. “Thus, you feel somewhat more tired than you would feel normally.”
Item 4
Pretest: Did you worry?
Answer: A little
1. “(...) I worry a little about my health, but I am confident that the people here in the hospital can help me.
2. So, I would say ‘a little’, I’ll just wait and see.”

Transition: Do you worry more or less since the first interview?
A. “I worry less because I expect a promising result.
B. Prior to radiotherapy, I greatly dreaded the treatment.
C. At that time, I didn’t know what the future would bring.
D. But now it’s over, I worry less.”

Assumption 1. Comparison of posttest and pretest functioning
Box
Figure 1; Box 1.2. Prior functioning: Between cancer diagnosis and start of treatment
B. “Prior to radiotherapy (…)”
D. “But now it’s over (…)”

Box
Figure 1; Box 2.2.2. Current functioning: Posttest functioning

Assumption 2. Accurate recall of pretest functioning
Box
Figure 1; Box 2.2.2. Transition - prior functioning: Between cancer diagnosis and start of treatment
B. “Prior to radiotherapy (…)”

Similarity in description of pretest functioning
Pretest description of functioning:
1. “(...) I worry a little about my health, but I am confident that the people here in the hospital can help me.”
Transition - description of prior functioning
B. “Prior to radiotherapy, I greatly dreaded the treatment.”
**Item 5**

Pretest: Has your physical condition or medical treatment interfered with your social activities

Answer: A little

1. “(...) I am editor of a local journal, that’s an activity with a social purpose.
2. (...) And I am member of the gardencommite of our tennis club.
3. Although I am no longer able to help remove the excess green.
4. (...) Thus, I carry out social activities, but with moderation.”

Transition: Does your physical condition or medical treatment interfere more or less with your social activities since the first interview?

Answer: The same

A. “I didn’t carry out any social activities actually.
B. (...) So at the moment I am not limited in my social activities.
C. Thus, I should answer ‘the same’ probably.”

**Assumption 1. Comparison of posttest and pretest functioning**

Box 1.3. Posttest functioning

B-C. “(...) So at the moment I am not limited in my social activities.
Thus, I should answer ‘the same’ probably.”
Item 6
Pretest: How would you rate your overall health during the past week?
Answer: 4
1. “(...) I have more trouble taking a walk, and I experience a bit more difficulty doing household chores.
2. I am no longer able to clean the windows or sponge down the doors for my wife.
3. But I am still able to vacuum the house.
4. I definitely got a lot older.”

Transition: Would you rate your overall health worse or better since the first interview?
Answer: Somewhat better.
A. “Thanks to the medication I’ve had, my health has improved a little in comparison to the first interview.”
B. “So my current health is somewhat better.”

Assumption 1. Comparison of posttest and pretest functioning
Box 1.1
Prior functioning:
Pretest functioning:
A. “(...) in comparison to the first interview”
Current functioning:
Posttest functioning
B. “(...) my current health (...)”

Assumption 2. Accurate recall of pretest functioning
Box 2.1.2
Dissimilarity in time frame
Prior to cancer diagnosis and treatment
Pretest functioning:
4. “I definitely got a lot older.”
Transition - prior functioning:
A. “(...) in comparison to the first interview.”

Dissimilarity in description of pretest functioning
Pretest description of functioning:
1-4. “(...) I have more trouble taking a walk, and I experience a bit more difficulty doing household chores.
I am no longer able to clean the windows or sponge down the doors for my wife. But I am still able to vacuum the house. I definitely got a lot older.”
Transition - description of prior functioning
B. “Thanks to the medication I’ve had, my health has improved a little in comparison to the first interview.”
**Item 7**

Pretest: How would you rate your overall quality of life during the past week?

Answer: 6

1. “First of all, quality of life is having little physical complaints.
2. (…) Having the feeling that you count in life, that they appreciate your participation.
3. (…) Sure, my physical shape isn’t excellent, but I would rate my quality of life a ‘6’ anyway.”

Transition: Would you rate your overall quality of life worse or better since the first interview?

Answer: The same

A. “My condition remained the same.
B. The only thing is that you notice that the radiation treatment is affecting your health.
C. (…) It’s the same, I don’t feel more or less of a person than I used to feel.”

### Assumption 1. Comparison of posttest and pretest functioning

<table>
<thead>
<tr>
<th>Box</th>
<th>Prior functioning:</th>
<th>Current functioning:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to cancer diagnosis and treatment</td>
<td>Entire radiotherapeutic treatment</td>
<td></td>
</tr>
<tr>
<td>C. “(…) It’s the same, I don’t feel more or less of a person than I used to feel.”</td>
<td>B. “The only thing is that you notice that the radiation treatment is affecting your health.”</td>
<td></td>
</tr>
</tbody>
</table>

### Assumption 2. Accurate recall of pretest functioning

<table>
<thead>
<tr>
<th>Box</th>
<th>Similarity in time frame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to cancer diagnosis and treatment</td>
<td>Transition - prior functioning:</td>
</tr>
<tr>
<td>2. “(…) Having the feeling that you count in life, that they appreciate your participation.”</td>
<td>Prior to cancer diagnosis and treatment</td>
</tr>
<tr>
<td>C. “(…) It’s the same, I don’t feel more or less of a person than I used to feel.”</td>
<td>Transition - description of prior functioning</td>
</tr>
</tbody>
</table>

2. “(…) Having the feeling that you count in life, that they appreciate your participation.”

2. “(…) It’s the same, I don’t feel more or less of a person than I used to feel.”