

Development of a clinical trials version of the Impact of Weight on Quality of Life-Lite questionnaire (IWQOL-Lite Clinical Trials Version): results from two qualitative studies

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What is already known about this subject

- Obesity is widely studied in clinical trials, perhaps due to its extremely high prevalence worldwide.
- Health-related quality of life (HRQOL) and patient functioning are important secondary end points in clinical trials.
- Existing measures of HRQOL and patient functioning, such as the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire, lack the developmental rigour required by the Food and Drug Administration (FDA) to support product labelling.

What this study adds

- An alternative version of the IWQOL-Lite questionnaire has been developed and refined through two qualitative studies involving 71 patients.
- The IWQOL-Lite Clinical Trials Version consists of a comprehensive set of items optimized for use in a patient population typically targeted for obesity clinical trials.
- Ultimately, it is anticipated that the final measure will be qualified by the FDA for use in clinical trials of new weight-loss medications to support product approval and labelling claims.

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Summary

Existing measures of health-related quality of life and patient functioning in obesity, such as the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire, lack the developmental rigour required by the Food and Drug Administration (FDA) to support product labelling. Two iterative qualitative studies informed development of a version of the IWQOL-Lite questionnaire optimized for use in obesity clinical trials: the IWQOL-Lite Clinical Trials Version. Study 1 included 42 patients with body mass index (BMI) ≥ 30 kg m⁻² (obesity); and Study 2 included 29 patients with type 2 diabetes and BMI ≥ 27 kg m⁻² (overweight). Candidate items were selected and/or modified from the IWQOL-Lite or developed *de novo* based on concept elicitation and cognitive debriefing interviews, as well as input from clinical experts and the FDA. Participants consistently reported that excess weight limited physical activity and comfort, energy/stamina and self-confidence/self-esteem. Impacts on emotional, social and sexual functioning, as well as productivity and overall health, were also reported. Each concept addressed in the 22-item pilot IWQOL-Lite Clinical Trials Version was consistently reported as salient and likely to change with 10% weight loss. Data from ongoing and planned clinical trials will be used to finalize and conduct psychometric evaluations of the pilot measure in several patient populations.

Keywords: Health-related quality of life, Impact of Weight on Quality of Life-Lite (IWQOL-Lite), qualitative research, questionnaire development.

Introduction

There is growing support for the assessment of patient impact (beyond symptom severity) in clinical trials to inform the decisions of drug licencing agencies and healthcare payers (1,2). Because obesity has been associated with decrements in health-related quality of life (HRQOL) (3,4) and weight loss has been associated with improvements in patient functioning (5,6), measurement of these impacts in clinical trials of new products for weight loss is crucial.

Generic measures, such as the Medical Outcomes Study-Short Form 36 (SF-36) (7), assess broad aspects of functioning and are suitable for any population or disease, whereas disease-specific measures assess concerns/challenges commonly experienced by individuals with a specific disease or condition. Several obesity-specific measures of HRQOL and patient functioning have been developed (8–12), including the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire (13), which is the focus of this study.

The IWQOL-Lite, developed using rigorous methods, has demonstrated strong psychometric properties and been linguistically validated for ≥ 80 languages. Many pharmacological trials for obesity have used the IWQOL-Lite as a supportive end point (14–16). Because the IWQOL-Lite was developed with patients enrolled in a residential/day-treatment programme, including some patients with extreme obesity, it is possible that the IWQOL-Lite may be missing important concepts and/or include concepts that are not relevant to clinical trial populations. In addition, the IWQOL-Lite was developed prior to the publication of the Food and Drug Administration's (FDA) guidance pertaining to claims in medical product labelling based on patient-reported outcome measures (17).

The purpose of this research was to develop and test, using qualitative methods, a comprehensive set of concepts and items appropriate for use in clinical trials of medications for the treatment of obesity (i.e. body mass index [BMI] ≥ 27 kg m⁻² with one or more obesity-related comorbid conditions or BMI ≥ 30 kg m⁻²) with the rigour required by the FDA for product labelling (17).

Materials and methods

Study 1: participants with obesity but no obesity-related comorbid conditions

Participants

Participants were recruited for concept elicitation (CE) and cognitive debriefing (CD) interviews by qualitative research facilities in four US cities. Inclusion criteria are as follows:

- Male and female participants ≥ 18 years of age;

- Stable body weight (no more than a 10-pound change within the 90 d before screening);
- History of having tried to lose weight by dieting in the past;
- Able to read and understand English.

CE participants were restricted to those with BMI ≥ 30 and ≤ 45 kg m⁻² (based on self-report). CD participants had no upper BMI limit to include a broader sample of participants.

Exclusion criteria were as follows: diagnosis of type 1 or type 2 diabetes, history of endocrine disorders, previous surgical treatment for obesity (excluding liposuction if performed >1 year pre-screening), or history of any severe psychiatric disorder. Recruitment targets were imposed to yield a diverse sample in terms of sex, race, ethnicity, age, BMI and educational levels. Approval was obtained by RTI International's institutional review board (IRB) prior to participant recruitment.

Concept elicitation interviews

Nineteen interviews were conducted by study authors (RLK, SEF and CME) in Raleigh, NC, and Tampa, FL. Input from 1-h teleconferences with two clinical experts at the beginning of the study informed the development of the CE interview guide and the patient screening questionnaire. Interviews used a semi-structured guide with three components:

- Spontaneous CE: General open-ended questions designed to identify all weight-related impacts and challenges, e.g. 'What specific areas or aspects of your life, if any, are affected most by your weight?' 'Is there anything you'd like to do and can't because of your weight?'
- Probed CE: If not mentioned spontaneously, participants were asked about other impacts considered relevant by clinical experts and described in obesity literature. Participants were also asked to discuss any improvements expected with a 10% weight loss and the most important improvements desired.
- Review of IWQOL-Lite concepts: Participants were asked to review the concepts in the IWQOL-Lite to identify relevant and irrelevant items, missing concepts and items unlikely to change within the context of a 6–12-month clinical trial.

Item selection, modification and development

Using the principles outlined in the FDA guidance (17), items were selected and/or modified from the IWQOL-Lite or developed *de novo* based on thematic analysis of CE and CD interviews, as well as input from both clinical experts and the FDA. The primary objective for the adapted measure was to ensure that the final item set addressed those aspects of functioning that were most relevant and generalizable across the target patient population

and had the potential to change with 10% weight loss. A 10% reduction in body weight was chosen as an estimate of the average amount of weight loss expected in 6–12-month clinical trials for obesity.

IWQOL-Lite items begin with the phrase ‘because of my weight’, requiring respondents to attribute any reported impacts/limitations to their weight. In previous feedback to the first author, the FDA indicated that such attributions may be difficult to make, particularly in items assessing physical functioning, given that comorbid conditions, age or other factors might contribute to physical limitations. The IWQOL-Lite Clinical Trials Version minimizes the need for respondents to isolate weight-related impairments. However, elimination of this attribution for some self-image and emotional concepts would have caused items to become unnecessarily vague and compromise the questionnaire’s ability to measure the impact of weight on patient functioning. For example, feeling self-conscious is a very general concept, whereas feeling self-conscious about one’s weight is more specific regarding the impact of weight. Consequently, items with and without mention of weight were tested across concepts in CD interviews to ensure that the final item set was easily understood, could be answered reliably and measured the concepts of interest.

The 5-point response scale used in the IWQOL-Lite uses response options ranging from ‘Always True’ to ‘Never True’. In response to FDA feedback suggesting the use of a frequency scale as a potential alternative, each item in the initial IWQOL-Lite Clinical Trials Version offered these response options: ‘Never’, ‘Rarely’, ‘Sometimes’, ‘Usually’ and ‘Always’. The recall period of ‘in the past week’ (IWQOL-Lite) was also modified to ‘currently’ to more objectively assess respondents’ current status.

Cognitive debriefing interviews

Three iterative rounds of CD interviews were conducted with 23 adults in Raleigh, NC; San Antonio, TX; and Baltimore, MD. Each interview was conducted by two members of the research team (RK, SEF, and CE), using a semistructured interview guide that began with open-ended questions designed to identify the impacts of being overweight and changes anticipated with weight loss that were most important to each individual. Participants were then asked to describe their thought processes as they responded to each IWQOL-Lite Clinical Trials Version pilot item. Interviewers posed additional questions to further elucidate the response process and assess the potential for change following a 10% weight loss. While the same methodology was employed across all 23 CD interviews, the third round of interviews provided the opportunity to test items electronically via tablet. Draft items were revised following each round of interviews.

Study 2: participants with obesity and type 2 diabetes

Participants

Similar inclusion/exclusion criteria and recruitment procedures were used for Study 2, with the following exceptions: a diagnosis of type 2 diabetes was required and the lower bound on the BMI range was reduced to 27 kg m⁻². At FDA request the population with type 2 diabetes was included in Study 2 to support a broader context of use.

Recruitment targets were again imposed to yield a diverse sample in terms of BMI, sex, race, ethnicity, age, and educational levels. This study was approved by RTI International’s IRB prior to recruitment.

Concept elicitation interviews

Nineteen interviews were conducted by study authors (RK, SEF, and CE) in Raleigh, NC, and San Antonio, TX, using the same format as in Study 1. In Study 2, participants were asked to provide feedback on the concepts addressed in the pilot IWQOL-Lite Clinical Trials Version (i.e. to identify any concepts that might be missing, irrelevant or unlikely to change over 6–12 months).

Item selection, modification and development

Results of the 19 CE interviews were analysed to determine if any items in the pilot questionnaire needed modification prior to CD interviews.

Cognitive debriefing interviews

To further refine the revised version of the IWQOL-Lite Clinical Trials Version, CD interviews were conducted (RLK and SEF) with 10 participants in Tampa, FL, following the same format as in Study 1.

Results

Study 1: participants with obesity but no obesity-related comorbid conditions

Participants

Forty-two participants (22 females and 20 males) were included in the CE and CD interviews. The average BMI was 38 (range: 30.4–51.6). Table 1 illustrates that participants were diverse in age, race/ethnicity and education.

Concept elicitation interviews

As expected, participants with lower BMIs generally reported fewer and less extreme impacts than participants with higher BMIs. For example, only participants with BMIs at the upper end of the range were likely to report discomfort or inability to fit into small spaces; these participants were also more likely to report feeling self-conscious in social situations and public places.

Table 1 Participant demographics: obesity only (no obesity-related comorbid conditions)

	Concept elicitation		Cognitive debriefing			
	Round 1 (n = 10)	Round 2 (n = 9)	Round 1 (n = 8)	Round 2 (n = 7)	Round 3 (n = 8)	Total (N = 42)
Sex, n (%)						
Female	5 (50.0)	4 (44.4)	4 (50.0)	4 (57.1)	5 (62.5)	22 (52.4)
Male	5 (50.0)	5 (55.7)	4 (50.0)	3 (42.9)	3 (37.5)	20 (47.6)
Age, average (range)	41.4 (26–59)	45.0 (22–70)	44.3 (23–68)	34.1 (19–55)	47.5 (30–65)	42.7 (19–70)
Race/ethnicity, n (%)						
White	7 (70.0)	7 (77.8)	4 (50.0)	4 (57.0)	4 (50.0)	26 (61.9)
African American	3 (30.0)	2 (22.2)	2 (25.0)	0 (0.0)	4 (50.0)	11 (26.2)
Hispanic	1 (10.0)	2 (22.2)	1 (12.5)	3 (42.9)	0 (0.0)	7 (16.7)
Asian	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	1 (2.4)
Mixed race	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	2 (4.8)
Other	0 (0.0)	0 (0.0)	1 (12.5)	1 (14.3)	0 (0.0)	2 (4.8)
Education						
High school	2 (20.0)	2 (22.2)	0 (0.0)	1 (14.3)	1 (12.5)	6 (14.3)
Some college	2 (20.0)	3 (33.3)	4 (50.0)	5 (71.4)	3 (37.5)	17 (40.5)
College graduate	4 (40.0)	3 (33.3)	4 (50.0)	1 (14.3)	3 (37.5)	15 (35.7)
Some grad school	2 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.8)
Graduate degree	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	1 (12.5)	2 (4.8)
Body mass index, average (range)	35.7 (32.0–40.2)	37.5 (30.5–43.5)	39.2 (30.5–51.5)	40.1 (30.4–51.6)	38.4 (30.7–47.1)	38.0 (30.4–51.6)

Concepts reported during CE interviews were organized into the following categories: physical impacts (general physical activity, specific physical activities and physical discomfort), energy/stamina, self-confidence/self-esteem, emotions, sexual life, social life and productivity. While each area is presented separately, there was a great deal of overlap. For example, many participants reported that their participation in physical activities was limited both by reductions in energy and increases in bodily pain that were either caused by or exacerbated by weight. Similarly, avoidance of social activities could be due to low energy/stamina, heightened self-consciousness and/or strong emotions, such as sadness or shame. Saturation was demonstrated by the lack of additional concepts being identified in later interviews within Study 1.

Physical impacts

Of 19 participants, 15 wanted to be more physically active, citing a wide variety of activities such as exercising, participating in sports/recreational activities, playing with or keeping up with children, walking, climbing stairs and doing work around the house. Physical limitations included pain, inflexibility, shortness of breath and insufficient energy/stamina. All but one participant reported that physical activity was limited by weight, citing low energy/stamina (n = 11) and shortness of breath (n = 11) as well as self-consciousness in some contexts, such as recreational activities at the beach or activities with co-workers. Fourteen participants reported limitations in mobility or flexibility, with the most commonly reported limitation being trouble bending over (n = 10). Seventeen participants

reported that excess weight either caused or exacerbated body pain.

Energy/Stamina

Eleven participants reported that weight limited energy or stamina for engaging in physical activities (e.g. exercise, recreational activities, housework and sexual activities). Nine participants reported a more general lack of energy or feeling of sluggishness that was not necessarily related to physical activity.

Self-confidence/Self-esteem

Seventeen participants – 10 females and 7 males – reported that their weight affected how they felt about themselves. Self-esteem was generally described as an internal perception about oneself that is not subject to situational fluctuations, whereas impacts of weight on self-esteem were typically described across the long term, focused on an inability to lose and maintain weight (e.g. frustration that controlling their weight was something that they had never been able to master, despite success in many other areas of their life). Sixteen participants reported that weight lowered their self-esteem/self-confidence and/or led to their feeling self-conscious across a variety of situations (n = 14), such as eating in restaurants or when in social situations.

Emotions

Thirteen participants expressed negative emotions associated with their appearance and/or inability to maintain a healthy weight, especially frustration, self-criticism, anger,

shame and embarrassment. Some of these emotions were related to specific triggers, such as shopping for clothing, seeing themselves in pictures or receiving comments from others about their weight. In addition, current BMI, weight history, gender, age and marital status appeared to contribute to the variability in the source and severity of negative emotions across participants. For example, older, married men generally expressed fewer emotional and social impacts compared to younger, single women.

Sexual life

Seven participants reported limitations or concerns related to sexual activity. These concerns were attributed to insufficient energy/stamina, shortness of breath, self-consciousness or decreased libido.

Social life

Ten participants reported reluctance to attend and/or avoidance of social events depending on factors such as who would be in attendance and how they would need to dress. Women ($n = 8$) were more likely than men ($n = 2$) to describe this reluctance. In general, participants were less comfortable when meeting or socializing with new people, people they had not seen in a long time (if thin previously), or people much smaller than they. Avoidance and/or discomfort in social situations was also reported when in the 'spotlight', such as giving a speech, when eating or buying food in public (e.g. restaurants, grocery stores) and/or when less covered by clothing, such as at the beach or pool.

Productivity

Twelve participants reported that productivity was limited by weight, due to insufficient energy/stamina, and/or physical limitations.

Participants' feedback on IWQOL-Lite concepts

Among the items in the IWQOL-Lite physical function subscale, those endorsed as both 'relevant and important' by at least half of participants pertained to painful/stiff joints, worry about health, trouble using stairs and shortness of breath with mild exertion. For the self-esteem subscale, the most 'relevant and important' items addressed being self-conscious and having reduced self-esteem. For the sexual life subscale, the majority of participants found the items to be 'not relevant'. Only one item on the public distress subscale (worrying about fitting into seats) and no item on the work subscale was endorsed as 'relevant and important' by $\geq 50\%$ of participants.

Item selection, modification and development

Participants in all three rounds of interviews reported that the instructions were clear and easy to understand. In addition, participants consistently and accurately interpreted

the reference period in the instructions as meaning 'currently' or at their 'current weight'.

In Round 1, approximately half of the participants indicated that the frequency response scale was not appropriate for certain concepts, such as overall physical activity or self-confidence/self-esteem. As a result, an alternative response scale addressing the degree to which each item is true was included in Rounds 2 and 3 (a 5-point scale ranging from 'not at all true' to 'completely true'). When both response scales were administered, participants reported that the frequency scale was more appropriate for situational items in which one could think of distinct events, whereas the truth scale was more appropriate for more general or stable concepts.

Thirty items, four of which used alternative wordings for the same concept, were tested in Round 1. At the completion of Round 3, seven items had been deleted and 12 were modified, resulting in a 23-item questionnaire. The breakdown of item content was as follows: general physical activity (1 item), specific physical activity (4 items), physical discomfort (2 items), energy/stamina (1 item), self-confidence/self-esteem (6 items), emotions (6 items), sexual life (1 item), social life (1 item) and productivity (1 item). Seventeen items used a frequency response scale, and six used a truth scale.

No participant spontaneously indicated that any concepts were missing from the IWQOL-Lite Clinical Trials Version. While 9 of 20 participants offered additions when asked directly if any concepts were missing, no concepts were mentioned by more than one participant.

No differences were noted between participants' interpretations of the items when presented in an electronic format compared to the paper-and-pencil format. Similarly, no difficulties were observed in participants' ability to understand or respond to items administered electronically.

Study 2: participants with obesity and type 2 diabetes

Participants

Twenty-nine participants (16 females and 13 males) who were, on average, slightly older than Study 1 participants (average age, 52.5 years; range, 21–75) were included in the CE and CD interviews. As shown in Table 2, all other participant characteristics, including average BMI (37.4; range: 27.1–45.7), were similar to Study 1 participant characteristics.

Concept elicitation interviews

Consistent with Study 1, participants with lower BMIs generally reported fewer and less extreme impacts than participants with higher BMIs. Importantly, participants' responses during CE were closely aligned with those later

Table 2 Participant demographics: obesity and type 2 diabetes

	Concept elicitation		Cognitive debriefing Round 1 (n = 10)	Total (N = 29)
	Round 1 (n = 10)	Round 2 (n = 9)		
Sex, n (%)				
Female	5 (50.0)	6 (66.7)	5 (50.0)	16
Male	5 (50.0)	3 (33.3)	5 (50.0)	13
Age, average (range)	58.5 (46–67)	42.6 (21–69)	55.5 (30–75)	52.5 (21–75)
Race/ethnicity, n (%)				
White	6 (60.0)	3 (33.3)	4 (40.0)	13 (44.8)
African American	4 (40.0)	3 (33.3)	2 (20.0)	9 (31.0)
Hispanic	0 (0.0)	4 (44.4)	4 (40.0)	8 (27.6)
Other	0 (0.0)	3 (33.3)	0 (0.0)	3 (10.3)
Education				
Less than high school	0 (0.0)	1 (11.1)	0 (0.0)	1 (3.4)
High school	0 (0.0)	1 (11.1)	1 (10.0)	2 (6.9)
Some college	2 (20.0)	6 (66.7)	3 (30.0)	11 (37.9)
College graduate	6 (60.0)	0 (0.0)	5 (50.0)	11 (37.9)
Graduate degree	2 (20.0)	1 (11.1)	1 (10.0)	4 (13.8)
Body mass index, average (range)	37.3 (30.3–45.7)	38.9 (30.2–45.4)	36.2 (27.1–45.3)	37.4 (27.1–45.7)

addressed in the pilot IWQOL-Lite Clinical Trials Version (Table 3).

When asked to identify the most important improvements expected with a 10% weight reduction, participants said they would ‘feel better’ mentally and physically, look better, have more energy, move with greater ease and potentially experience health benefits such as improvements in diabetes and/or blood pressure. While participants in the highest BMI group did not anticipate comparable benefits,

they reported that it would motivate them to lose more weight.

Item categories remained unchanged in Study 2. Saturation was demonstrated by the consistency between results of Study 1 and Study 2.

Table 3 Concepts addressed in the pilot Impact of Weight on Quality of Life-Lite (IWQOL-Lite) Clinical Trials Version

Pilot IWQOL-Lite Clinical Trials Version concept	
Physical impacts	Trouble bending over
	Tired or winded
	Unable to stand comfortably
	Uncomfortable in small seats
	Not physically active
Energy/stamina	Lack energy
Emotions	Frustrated shopping for clothes
	Feel bad or upset about pictures of self
	Down or depressed about weight
	Worried about health
	Frustrated or upset about weight
Self-confidence/ self-esteem	Self-conscious eating in social settings
	Less confident
	Feel judged by others
	Viewed as less important or less worthy
	Decreased self-esteem
Sexual life	Self-conscious
Social life	Less interest in sexual activity
Productivity	Avoid social gatherings
	Less productive

Physical impacts

Seventeen participants (15 during CE discussion and 2 upon reviewing the pilot questionnaire) indicated that they were not as physically active as they wanted to be due to their weight, citing physical factors such as a lack of energy/stamina (n = 16) and shortness of breath (n = 9). This included the ability to exercise and engage in recreational activities, such as sports or playing with children. Many participants also reported (during CE) or endorsed (upon questionnaire review) issues with everyday physical activities, such as shortness of breath while walking up a flight of stairs (n = 13) and/or an inability to walk as far or as quickly as they would like (n = 15).

In general, the extent of activity limitations increased with BMI and with age and the presence of conditions such as back problems, knee problems and previous injuries. Advancing age and comorbid conditions (e.g. fibromyalgia) made it difficult for some participants to tease out the specific limitations attributable to their weight from limitations due to these other factors.

While not as salient as activity limitations, 16 participants reported or acknowledged at least one limitation in mobility or flexibility during CE interviews, including 10 during the discussion and 6 upon review of the pilot questionnaire. The only concept in this category reported or endorsed by more than half of participants was trouble

bending over ($n = 12$), specifically in the context of picking things up from the floor, cutting toenails and tying shoelaces or trying on shoes.

All participants reported that excess weight either caused or exacerbated bodily pain (15 during CE and 4 during questionnaire review). Although the majority of participants, particularly those at lower BMIs, were able to stand for short periods of time, many, especially those at higher BMIs, were uncomfortable doing so. In addition, 15 of 29 participants reported physical discomfort when sitting in small seats in public places.

Energy/Stamina

Sixteen of 19 participants (14 during CE and 2 during questionnaire review) reported that weight had a negative impact on energy level and/or stamina.

Self-confidence/Self-esteem

Eighteen participants reported or endorsed feeling self-conscious about their weight. Fifteen participants reported reduced self-esteem related to weight, either during CE ($n = 9$) or pilot questionnaire review ($n = 6$). Similarly, 17 participants reported a lack of confidence due to their weight (15 during CE and 2 during questionnaire review). Furthermore, eight participants reported feeling self-conscious while eating in social situations, such as at restaurants or parties, or while buying groceries. An additional relevant concern was the belief that others were judging them negatively because of their weight (13 reported this during CE, and 4 endorsed this during review of the pilot questionnaire).

Emotions

All participants reported or endorsed at least one negative emotion (e.g. frustration, shame, sadness, depression) related to weight. A particular concern among 18 participants was frustration associated with shopping for clothing. Another highly reported concern was the experience of negative emotions (e.g. frustration, self-criticism, anger, shame, sadness and embarrassment) associated with appearance and/or ability to maintain a healthy weight (reported by 10 participants during CE and endorsed by six additional participants during questionnaire review). In addition, 17 of 19 participants expressed concern or worry about health (13 during CE and 4 upon questionnaire review), with the majority of concerns associated with diabetes. While only one participant specifically mentioned negative feelings associated with seeing oneself in pictures, 13 participants endorsed this concept upon review of the pilot questionnaire.

Sexual life

Only three participants reported that weight had an impact on their sexual life; however, five additional participants

endorsed the item related to interest in sexual activity while reviewing the pilot questionnaire.

Social life

Avoidance of social activities due to weight was reported ($n = 8$) or endorsed ($n = 1$) by nine participants. Feeling self-conscious or lacking confidence in social settings because of their appearance, participants reported reluctance to attend or avoidance of certain social events. Women were more likely than men to report such reluctance.

Productivity

Thirteen participants reported during the discussion that they were less productive than they would like to be because of their weight. One additional participant endorsed this concept while reviewing the pilot questionnaire.

Item selection, modification and development

The majority of participants found 19 of the 23 items on the pilot IWQOL-Lite Clinical Trials Version to be relevant to their experiences. Based on results of CE interviews, two items in the initial pilot IWQOL-Lite Clinical Trials Version were modified prior to CD; these items pertained to difficulty standing and self-consciousness when eating in public. Another item pertaining to frustration choosing clothing to wear was deleted (as it was deemed similar to and less relevant than the item addressing frustration shopping for clothing), resulting in a 22-item questionnaire.

Cognitive debriefing interviews

Participants indicated that the instructions and items were easy to understand, and they correctly interpreted the reference period of 'currently' as 'now' or at their 'current weight'. Most participants indicated that both sets of response options (i.e. frequency scale and truth scale) were easily understood, distinct from each other, and covered the full range of impacts. No participant reported difficulty using either response scale.

One item (pertaining to difficulty standing) was interpreted differently by the first five CD participants. Consequently, another version of this item was tested on the remaining five participants. These participants interpreted the revised item as intended and responded with ease. Based on these results, this item was reworded in the final pilot IWQOL-Lite Clinical Trials Version.

The pilot questionnaire was viewed as comprehensive by study participants; no participant spontaneously indicated that any additional concept should be considered for inclusion. When specifically asked if any important concept was missing, five participants reported that no concept of importance was missing. Two participants suggested the addition of an item about the type of job they were able to

get and work they were able to do. Other concepts were noted as missing by only one participant each (e.g. impact on family members; ability to drive a car). Based on this feedback, no items were added to the final pilot IWQOL-Lite Clinical Trials Version, and the 22-item version is ready for quantitative evaluation.

Discussion

These two qualitative studies indicate that the 22-item pilot IWQOL-Lite Clinical Trials Version is comprehensive and easily understood by individuals with obesity, both with and without type 2 diabetes. Development of this instrument was in accordance with the FDA's guidance on patient-reported outcomes (17). Items and concepts contained in the pilot IWQOL-Lite Clinical Trials Version represent the most important concerns of this population, including those likely to change with a 10% reduction in body weight. Although the hurdle for regulatory approval is 5% and meaningful changes in health parameters may be seen with 5% reduction, participants expected to see positive changes in functioning and quality of life with a 10% reduction.

Among the many measures used to assess the impact of obesity on patients' functioning and HRQOL (8–12), none has been rigorously developed for use in clinical trials for obesity. The original IWQOL-Lite continues to be extensively used to further elucidate the impact of obesity and the potential benefits of obesity interventions. In addition, the breadth of knowledge gained in its use since 2001 can continue to be of value and applicable in clinical research and clinical practice.

Similar to the IWQOL-Lite, the pilot IWQOL-Lite Clinical Trials Version contains items pertaining to physical functioning, mobility, bodily discomfort and pain, self-confidence/self-esteem, productivity and sexual life. In addition, both instruments place a strong emphasis on physical functioning and self-confidence/self-esteem. The new 22-item pilot instrument contains seven items that pertain broadly to physical functioning and six items that relate to self-confidence/self-esteem.

Only four items on the pilot IWQOL-Lite Clinical Trials Version include the phrase 'because of my weight', whereas all but four items used this attribution on the IWQOL-Lite. This modification was made to facilitate ease of responding and minimize measurement error for concepts for which the specific impact of weight would be difficult to discern. Whereas the IWQOL-Lite uses a 5-point response scale of 'always true' to 'never true', the pilot IWQOL-Lite Clinical Trials Version uses a 5-point frequency scale ('never' to 'always') for 16 of the 22 items and a 5-point truth scale ('not at all true' to 'completely true') for the remaining six items. This change was made in response to FDA feedback to the first author about the original IWQOL-Lite. The

recall period was also changed from 'in the past week' to 'currently' to accurately assess respondents' current status. Another difference between the two instruments is that the pilot IWQOL-Lite Clinical Trials Version includes several items pertaining to emotions (such as feeling down about one's weight, feeling frustrated about shopping for clothing), as well as one item that specifically addresses energy/stamina.

While it was anticipated that sleep would be a concern for the study population (based on expert opinion and feedback from FDA), we did not develop items to address this concept because a minority of participants reported sleeping difficulties, and there were multiple causes for these difficulties.

Although impacts on sexual life were reported by a minority of participants, we decided to include one item that addresses this concept. A literature review on the topic of sexual functioning and obesity (18) concluded that there are robust relationships between obesity and reduced sexual functioning as well as between weight loss and improved sexual functioning. The item we selected is potentially relevant to all participants regardless of relationship status. However, if this item is not responsive in the trials, it will be a candidate for removal.

Similar to the IWQOL-Lite, we found gender and age differences on some of the concepts. This is not unexpected but also not of major concern given that patients will be randomized to different treatment arms in clinical trials.

Exclusive use of US participants is a potential limitation of our study in that several studies have reported differences between IWQOL-Lite scores obtained in non-US samples compared to US samples (e.g. (19–23)). It is anticipated that the IWQOL-Lite Clinical Trials Version will be used in international clinical trials, providing the opportunity to explore the potential for cultural/regional differences. We have plans to obtain rigorous translation and cultural adaptation of the measure prior to its use in upcoming clinical trials, including harmonization of forward and back translations and CD with the target patient population in each country of interest.

The IWQOL-Lite Clinical Trials Version is designed to measure the impact of weight loss on HRQOL and patient functioning regardless of treatment intervention. It is unknown whether results would be influenced by the type of weight loss intervention (e.g. bariatric surgery).

The pilot IWQOL-Lite Clinical Trials Version is currently being used in clinical trials for obesity, both in individuals with and without type 2 diabetes. Once quantitative data become available, tests of reliability, validity and responsiveness will be conducted and a scoring algorithm will be developed. Scoring will be based on analyses of quantitative data that are currently being collected in clinical trials; however, computations of composite or summary scores addressing concepts that may be

important for product labelling (e.g. physical function) are likely. Ultimately, it is anticipated that the final measure will be qualified by FDA for use in clinical trials of new weight-loss medications to support product approval and labelling claims.

Conflict of Interest Statement

RLK served as a consultant to RTI Health Solutions for this project. She is also a consultant for Novo Nordisk, the sponsor of this project, as well as Eisai and Janssen. RLK receives royalties from Duke University for the IWQOL-Lite. CME and SEF are employees of RTI Health Solutions. RTI Health Solutions received consulting fees, travel support and payment from Novo Nordisk for this project. SEF and CME are consultants for Novo Nordisk and other pharmaceutical companies. HHM and LH are employees of Novo Nordisk.

Author contributions

All authors were involved in writing the manuscript and had final approval of the submitted version. RLK, CME and SEF conducted CE and CD interviews, as well as qualitative data analysis.

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