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Development and Content Validity Testing of a Patient-Reported Treatment Acceptance Measure for Use in Patients Receiving Treatment via Subcutaneous Injection

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ABSTRACT

Background: New therapies in development for lowering low-density lipoprotein cholesterol, such as alirocumab, require administration by subcutaneous injections. There is a need to assess the acceptance of such treatments and their mode of administration. **Objectives:** To develop a novel patient-reported outcome measure, the Injection-Treatment Acceptance Questionnaire (I-TAQ), and assess its content validity using qualitative methods. **Methods:** Concepts generated from a literature and instrument review informed the initial drafting of 17 items in the I-TAQ, with item wording adapted from three existing instruments. Three rounds of qualitative interviews were conducted with 29 US-English speaking patients at high cardiovascular risk. Concept elicitation questioning was used to explore patients' treatment experiences followed by cognitive debriefing of the I-TAQ using "think-aloud" methods. Verbatim transcripts were analyzed using thematic analysis. **Results:** Qualitative analysis of concept elicitation data identified the following relevant concepts: perceived efficacy, side effects, self-efficacy, convenience, and overall acceptance. Seven (24%) patients discussed an initial fear of needles, but described this as subsiding with no impact on adherence. Five items were added after round one interviews, three of which were retained after round two testing in which two further items were added, forming the conceptually comprehensive 22-item I-TAQ. Patients demonstrated good understanding of item wording, instructions, response scales, and recall period. **Conclusions:** Successive rounds of in-depth interviews resulted in a treatment acceptance measure with strong content validity. Pending demonstration of its psychometric properties, the I-TAQ may prove to be a valuable measure of patients' perspectives toward being treated with low-density lipoprotein cholesterol–lowering therapies requiring subcutaneous injections.

Keywords: acceptance, instrument development, patient-reported outcome, qualitative research.

Introduction

Elevated low-density lipoprotein cholesterol (LDL-C) levels are associated with an increase in the risk of cardiovascular (CV) events, including myocardial infarction, unstable angina, need for coronary revascularization procedures, ischemic stroke, and death. Evidence from numerous randomized clinical trials have demonstrated that LDL-C reduction, via statin- and non–statin-based therapies, leads to a reduction in CV events [1–5]. Recently, treatment with monoclonal antibodies to proprotein convertase subtilisin–kexin type 9, such as alirocumab, has been shown to reduce LDL-C levels in phase 3 studies with populations at moderate to very high levels of baseline CV risk who are being treated with statins or are unable to tolerate statins [6,7]. These therapies are being further tested for their impact on reducing CV outcomes [8]. These agents, however, require patients to self-administer the medication with subcutaneous injections, a treatment strategy that has seldom been used in the management of CV disease. Given the novelty of this treatment strategy, understanding patients' perspectives about using injection treatments, as opposed to oral medications, is important, but difficult to quantify with existing measures.

The aim of this work was to develop a patient-reported outcome (PRO) to assess patients' acceptance of a subcutaneous injection treatment for lowering LDL-C in a high CV risk population, following the Food and Drug Administration patient-reported outcome guidance as a framework [9]. A literature review, followed by three rounds of patient interviews, was

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conducted to develop and assess the content validity of a newly drafted measure, the Injection-Treatment Acceptance Questionnaire (I-TAQ).

Methods

Drafting of the I-TAQ

The first conceptual step was to consider whether it would be more appropriate to assess patient "satisfaction" or "acceptance" toward an injection treatment for an asymptomatic condition as both concepts have been used in previous studies of populations receiving injectable treatments [10,11]. Given the asymptomatic nature of hypercholesterolemia, it was felt to be more appropriate and relevant to assess whether patients are willing to "accept" taking their injection treatment, as opposed to asking patients how "satisfied" they are with having to inject a treatment.

After defining the overall measurement concept the conceptual domains of the Health Belief Model were used as a framework for developing the I-TAQ, including perceived severity, perceived susceptibility, perceived benefits, perceived barriers, modifying variables, cues to action, and self-efficacy [12]. In addition, five existing PRO instruments of greatest relevance were identified from the literature and reviewed in detail: the Treatment Satisfaction Questionnaire for Medication (TSQM) [13], the Treatment Satisfaction with Medication Questionnaire (SATMED-Q) [14], the Preference and Satisfaction Questionnaire (PSQ) [15], the Self-Injection Assessment Questionnaire (SIAQ) [16], and the Acceptance by the Patients of their Chronic Treatment Acceptance Questionnaire (ACCEPT) [17]. The instruments, however, were not deemed to have appropriate content validity for this population as none was adequately focused on assessing treatment acceptance *specifically in relation to injection treatments*. Therefore, it was felt that patients' concerns or experiences related to this treatment modality might not be adequately captured. In addition, the unique nature of elevated LDL-C level as a "silent" condition warranted a renewed effort to understand patients' perspectives of using subcutaneous injection therapies. Initial items were therefore drafted to capture relevant concepts identified from the literature and existing instruments and within the constructs articulated in the Health Belief Model.

Qualitative Study Design

A non-interventional qualitative study was conducted with 29 US-English speaking patients at high CV risk who had experience of self-administering their treatment for lowering LDL-C every 2 weeks via subcutaneous injection. Qualitative face-to-face interviews were conducted in three rounds (n = 9, n = 10, and n = 10 patients in each round, respectively) by trained interviewers and were audio recorded. The first two rounds involved patients who had self-administered their treatment with pre-filled pens (PFPs; n = 19), and the last round involved patients who had self-administered their treatment with pre-filled syringes (PFSs; n = 10). Interim analysis was performed after each round of interviews to enable consideration of additional items and subsequent testing of revisions. The first part of each interview, conducted before the patient had been shown the questionnaire, focused on concept elicitation. The second part focused on cognitive debriefing of the I-TAQ.

Patient recruitment

All participants were recruited through purposeful sampling from either a randomized double-blind, placebo-controlled clinical trial or an open-label extension trial for alirocumab. Inclusion criteria for the interview study required all patients to have been diagnosed with elevated LDL-C, be 18 years of age or older, and have experience of self-administering alirocumab or placebo via PFP or PFS. Quotas relating to diagnosis (heterozygous familial hypercholesterolemia, high or very high CV risk), treatment, ethnicity, and education were used to recruit a sample with a broad range of clinical and demographic characteristics. Categorization of high and very high CV risk was based on the National Cholesterol Education Program Adult Treatment Panel III guidelines [18].

Concept elicitation

To support the capture of a broad range of concepts articulated in the Health Belief Model, an interview guide was constructed containing a number of broad, open-ended, and non-leading questions to guide the interviewer (see Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2015.09.2937). The questions were designed to encourage patients to describe their experiences using their own language and to prohibit any possible bias. The discussions were exploratory and focused on eliciting spontaneous comments from patients regarding their treatment experience and the factors that (positively or negatively) affected their treatment acceptance and adherence. If the patients did not spontaneously mention a concept of interest identified from the literature in response to the broad questioning, more direct questions were used to explore that concept toward the end of the interview. In addition, the relevance of the concepts 'satisfaction' and 'acceptance' was explored with patients in terms of how they described their treatment experience.

Cognitive debriefing

After the concept elicitation (CE) section of the interview, cognitive debriefing (CD) was performed. Patients were asked to complete the I-TAQ using a "think-aloud" approach, requiring the patients to read each instruction, question, response option, and recall period out loud while verbally sharing their reasoning for selecting each response [19,20]. Patients were also asked detailed debriefing questions about their understanding of terms and response scale wording, relevance of concepts, and appropriateness of the response options and the recall period. More time was spent on the CE part of the interview in round one to ensure all relevant and important concepts were captured. As saturation was achieved, more time was spent on thoroughly debriefing the I-TAQ, and revisions made following interim analysis, in the subsequent interviews.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved and overseen by a centralized independent review board in the United States (reference: ADEL-13-347). Written informed consent was obtained from all participants before the collection of any data and before any study-related activities.

Qualitative Analysis

All interviews were transcribed verbatim with all identifiable information removed to protect anonymity of the patients. Thematic analysis of the verbatim transcripts was performed using computer-assisted qualitative data analysis software, ATLAS.Ti [21], and each transcript was quality assessed, coded, and analyzed by the researchers. Using an inductive approach, a code list was created and adapted as new codes were added [22]. Patient quotes were grouped by code/theme to enable findings to be summarized and conclusions drawn. Saturation of concepts was evaluated for the CE results, defined as the point at which no

new concept-relevant information emerged from analysis of further interviews [23]. The CD transcripts were analyzed to evaluate patients' comprehension, interpretation, and perceived relevance of items as well as the appropriateness of response options and recall period of the I-TAQ.

Results

Demographic and Clinical Characteristics

Key demographic and clinical information for the qualitative sample is presented in Table 1. In total, 29 patients with high CV risk (n = 10), very high CV risk (n = 9), and heterozygous familial hypercholesterolemia (n = 10) participated in the study, 19 of whom self-administered their treatment using a PFP and 10 of whom self-administered using a PFS. A broad age range of participants was achieved (50–77 years), two-thirds of whom were men (n = 20 [69%]). Patients had a range of highest education levels, from some high school (n = 4 [14%]) to graduate degree (n = 3 [10%]). There was minimal diversity in ethnicity or race as all but one of the patients were white (n = 28 [97%]). All patients (with the exception of one (n=28 [97%])), regardless of their specific diagnosis, had been self-administering alirocumab for at least 7 months. A large proportion of the sample had comorbid conditions, with hypertension being the most common, experienced by more than half of the sample (n = 15 [51.7%]). In addition, more than half of the sample were also taking a high-potency statin (n = 15 [51.7%]). All patients were recruited from sites based in the United States.

Table 1 – Key clinical and demographic information for the qualitative sample (N = 29).

Summary characteristic	Value
Age (y)	
Mean	60.9
Range	50–77
Sex, n (%)	
Female	9 (31.0)
Male	20 (69.0)
Mode of administration, n (%)	
PFP	19 (66.5)
PFS	10 (34.5)
CV risk categorization, n (%)*	
Heterozygous familial hypercholesterolemia	10 (34.5)
Very high risk of cardiovascular events	9 (31.0)
High risk of cardiovascular events	10 (34.5)
Duration of the diagnosis of CV risk condition, n (%)	
4–7 years ago (2010–2006)	10 (34.5)
8+ years ago (≤2005)	19 (65.5)
Duration of treatment with alirocumab, n (%)	
1–6 months	1 (3.5)
7–11 months	15 (51.7)
12+ months	13 (44.8)
Background lipid-lowering medications n (%)	
High-potency statin	15 (51.7)
Other statins	4 (13.8)
Ezetimibe	2 (10.4)
Niacin, fibrate, bile acid sequestrant	4 (13.8)
Comorbid condition, n (%)	
Hypertension	15 (51.7)
Type II diabetes	4 (13.8)
Coronary artery disease	4 (13.8)
Rheumatoid arthritis	1 (3.4)
Prior myocardial infarction	2 (6.9)
Peripheral vascular disease	1 (3.4)

CV, cardiovascular; PFP, prefilled pen; PFS, prefilled syringe.
* As reported by the referring clinicians. Categorization of very high and high risk was based on the National Cholesterol Education Program Adult Treatment Panel III guidelines [18].

CE Findings

Concepts of treatment acceptance

Key themes that emerged from the CE interviews included perceived efficacy of the treatment, acceptance of side effects, injection self-efficacy, injection convenience, and overall acceptance. Table 2 summarizes the number of patients who reported each concept (either spontaneously, in response to an open-ended question, or in response to a direct probe) with example quotes.

Self-Efficacy in administering the Injection. When probed, patients described self-efficacy in terms of confidence in their ability to administer the injection treatment. All patients (n = 29 [100%]) described high levels of confidence and reported feeling "100% confident" (02-02), describing administering the injection as "second nature" (03-09). Although most patients when asked (n = 15 of 20 [75%]) recalled experiencing apprehension when administering their first injection (seven of whom had a previous fear of needles), all reported feeling confident in administering their most recent injection. Similarly, seven patients (24%) reported an initial fear of needles that subsided as experience in administering the treatment was gained.

> Nervous – and once I did it, uh, I realized that it's not that hard. It was very simple. (03-04)

Most patients (n = 23 [79%]) did not report the injection to have any impact on their psychological/emotional well-being. Feeling scared of the needle (n = 1 [3%]) and stress associated with remembering when to take the injection were both mentioned as negative effects (n = 1 [3%]). Four patients (13%) reported a positive change in their psychological well-being after the treatment due to the improvements in test results.

Perceived efficacy of the treatment. Perceived efficacy of the treatment was defined as the patient's belief that the treatment was effectively treating their condition. Most of the patients interviewed (n = 19 [66%]) did not know whether the treatment was working because they had not seen their LDL-C levels; such patients, therefore, relied on a belief as to whether or not their treatment was effective. Patients recruited from the open-label study had access to their results and therefore had knowledge of their LDL-C levels as an indicator of efficacy. Perceived efficacy of the treatment was reported to substantially influence patients' acceptance and attitudes toward long-term use and adherence.

Injection convenience. The patients discussed how convenient they found administering the injection, specifically by discussing practical aspects such as the scheduling and frequency of doses, remembering doses, managing missed doses, storage of the treatment, and the time taken to prepare and administer the treatment.

Almost all patients (n = 27 [93%]) found it easy to fit the injection into their schedule, comparing it to other routine activities of daily living such as "brushing my teeth" (01-07). All patients (n = 29 [100%]) took the injection at home and reported this to be the most convenient place to administer the treatment, the majority of whom (n = 21 [72%]) spontaneously reported using a reminder to help them take their injection at the correct time (e.g., setting a timer). In addition, 13 patients (45%) had

Table 2 – Counts of concepts and example quotes elicited through CE in qualitative interviews (N = 29).

Concept	Subconcept	Spontaneous	Probed	Example quote
Self-efficacy	Self-efficacy in administering the treatment	0	29	"Confident. You know, done it enough times now. It's…second nature now." (03-09)
Perceived efficacy of the treatment	Perceived efficacy of the treatment	8	21	"I feel it's helping my cholesterol." (02-04)
Injection convenience	Use of reminder	21	0	"I've got a calendar thing. And it's written on there when I do it." (01-04)
	Overall convenience	19	10	"It was convenient. Um, bec – again, because it fit into my… day without any big, uh – big issues." (01-06)
	Ease of use	17	12	"It's real easy. Once you place it against your skin and that, you press down on a little lever. And it stays in until the injector's empty. It pops back up, you know, you're done." (01-03)
	Injection site	20	9	"You can do your arm or your leg or whatever, but I always do abdomen." (03-11)
	Preparation	9	1	"Use an alcohol swab – on the injection site. And then I inject myself." (03-10)
	Storage	9	20	"The drug needs to be stored in a refrigerator. And so, if you're on vacation or something you need to stay somewhere where there's a refrigerator." (01-02)
	Frequency	6	23	"Once every two weeks, it's easy." (03-10)
	Scheduling	6	22	"it's easy. It's like flossing my teeth and brushing my teeth in the morning, you kind of just fit it in." (01-07)
	Missed dose	6	14	"I travel a lot – and so I missed one of the windows one time. I took it when I got back. I think I was two or three days late or something… they said if I missed the date, to go ahead and take it when – when I could." (01-06)
	Time to administer	0	10	"Probably less than 15 minutes because I – after I take it out of the refrigerator, I let it, you know, warm up to room temperature." (03-07)
	Impact on daily life	0	29	"Well,…it doesn't take any time (laughter) It doesn't affect anything I do." (01-01)
Side effects	Presence of side effects	12	13	"Sometimes just like a little…raised area in the skin, but, you know, that goes away." (01-05)
	Impact on psychological/ emotional well-being	0	29	"Well, I would say positive…because it makes me feel like maybe it's given me a few more years on to my life." (03-02)
	Pain	4	1	"The pain portion of it is when you're positioning the needle on your skin and then working it through and poking it through. It's just a bit of a pinprick sensation, you know." (03-10)
Overall acceptance	Overall acceptance	0	29	"Very acceptable for me. It's…painless and it's quick." (01-01)
	Acceptance of treatment in addition to existing treatments	0	27	"It's easier because I only have to do it every two weeks. So there's less pills laying around and less to remember." (01-02)
Other	Previous fear of needles	3	4	"Most of my life, I've kind of had a problem with, you know, getting shots or needles or injections or whatever. And I was really – had a lot of reservations about this. It ended up not being a problem whatsoever." (03-11)

CE, concept elicitation.

missed or forgotten to take an injection, at least once, on the correct day. One patient felt neutral about the scheduling, "It wasn't easy or difficult" (02-02), and one patient reported difficulty remembering the injection due to a busy schedule, "Uh, one time I was two days late because I forgot" (01-03).

All patients reported storing the injection treatment in the refrigerator, as instructed. Most patients (n = 21 [72%]) found it easy to store the injection, whereas five (17%) reported some elements of bother with storage, specifically while on vacation.

Side effects. Side effects were described in terms of general side effects and side effects specific to the injection site (e.g., bruising and swelling). Approximately half of the patients (n = 15 [52%]) reported experiencing some kind of injection site–specific side effect, such as a "prick," "sting," or "drop of blood," but no effects or bother was reported. The patients using the PFS reported more site-specific side effects, such as bruising, stinging, and swelling, than did patients using the PFP, but were not bothersome. Notably, no side effects were reported to affect adherence, persistence, or discontinuation.

Only five patients reported pain associated with injecting (three spontaneously, two when probed); all five described pain as minimal, brief, and of no burden. One of the five patients reported a little pain at first followed by saying that it was painless:

> Little bit painful from the point of view of, uh, when you position the needle – on the outside of your skin – there's a little bit of like a – a pinprick type feeling, you know. After I pop the, uh, needle through the skin, it's painless. (03-10)

Similar to the lack of bother associated with side effects, patients did not report any negative impact of the injection on their daily activities or physical functioning.

Overall acceptance. All patients (100%) described the injection to be an acceptable form of treatment overall, describing it as "100% acceptable" and "no big deal." Because of the high proportion of patients with comorbidities, it was important to explore patients' experience of administering the injection in addition to their existing treatments/medications. All patients who administered their injection in conjunction with other regular treatments (n = 27 [93%]) found the injection treatment to be an acceptable addition to their treatment regime.

Treatment satisfaction and treatment acceptance

As part of CE, approximately half of the patients (n = 14 [48%]) were asked to discuss the relevance of the terms "treatment acceptance" and "treatment satisfaction" in describing their injection-treatment experience. Five patients (36%) preferred the term treatment acceptance, two (14%) preferred treatment satisfaction, five (36%) did not have a preference, and two (14%) felt that it was inappropriate to compare the two concepts. Findings indicated patients interpreted acceptance as a concept associated with willingness due to necessity.

> Accepting means that you – you're willing to work with it. You're willing to take it on and do what has to be done. (02-04)

Given the asymptomatic nature of the condition and the fact that the benefit of treatment is in terms of reducing long-term risk of CV events, rather than alleviating symptoms, it was concluded that acceptance would be a more appropriate and relevant concept to measure in assessing the patient experience of self-administering a subcutaneous injection treatment.

Item Generation

The I-TAQ was developed as a paper-based PRO designed to assess patient acceptance of an injectable treatment. All items used a five-point response scale, with response options ranging from "not at all confident" to "very confident," "very unacceptable" to "very acceptable," "not at all effective" to "very effective," "very difficult" to "very easy," "very inconvenient" to "very convenient," "definitely not" to "yes definitely," and "not at all" to "yes, very much." The initial I-TAQ had 17 items grouped into four domains: acceptance of perceived efficacy (n = 2 items), acceptance of side effects (n = 5 items), acceptance of administration (n = 7 items), and overall acceptance (n = 3 items). The conceptual framework was revised after each round of interviews and the domain of injection self-efficacy was added, resulting in a final five-domain framework (Fig. 1). All revisions to items and detailed rationales for each decision are presented in Appendix 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2015.09.2937.

Cognitive Debriefing Findings

Overall, all items in the I-TAQ were well understood and reported to be relevant to patients. Minor revisions to items were incorporated, however, after each round of patient interviews on the basis of patient feedback to enhance relevance and content validity. Figure 2 provides an overview of the changes made to the I-TAQ in each round.

Cognitive debriefing of instructions and recall period

The instructions provided at the top of the I-TAQ ask patients to think specifically about the injection treatment when selecting a response and were well understood by most of the patients (n = 25 [86%]). Most of the patients across all rounds (n = 27 [93%]) understood the recall period, but only 28% (n = 8) of the patients reported actually using the 4-week recall period when completing the questionnaire. To aid consistent reporting, "over the past four weeks" was included in every item to encourage patients to use the correct recall period.

Revisions after round 1 interviews with patients using the PFP (n = 9)

After the first round of patient interviews (n = 9), 5 items were added to the original 17-item I-TAQ to further explore understanding, relevance, and, in some cases, alternative item wording for the assessment of a given concept. Specifically, items capturing injection site reactions, self-efficacy, time to administer the injection, and overall acceptance were added for testing in round 2.

Despite patients describing injection site reactions during CE, only one patient completed side effects items during CD. Therefore, an item asking specifically about injection site reactions was added in addition to a general side effects item to ensure the experience was fully captured. Because of being reported in CE, a self-efficacy item measuring the level of self-belief/confidence in ability to self-administer the injection treatment was added for testing in round 2.

When discussing the time taken to administer the injection, several patients talked about the time taken to prepare the injection (e.g., treatment rested at room temperature). Therefore, a new item asking about acceptance of time taken to prepare the injection was added. In addition, CE findings from round 1 indicated that most of the patients (n = 8 [89%]) associated the frequency of dosing with the need to "remember" to take their dose. Therefore, an additional item assessing how easy or difficult it was for patients to remember to take the injection treatment was added for testing in round 2.

Some patients felt that the final "overall acceptance" item was repetitious. Therefore, an alternative version of the item was included for testing in round 2, which used revised wording to enhance clarity.

Revisions after round 2 interviews with patients using the PFP (n = 10)

Overall, the updated version of the 22-item I-TAQ was well understood by patients and reported to be relevant in round 2 interviews (n = 10). Low relevance was reported for perceived efficacy of the treatment because most of the patients did not

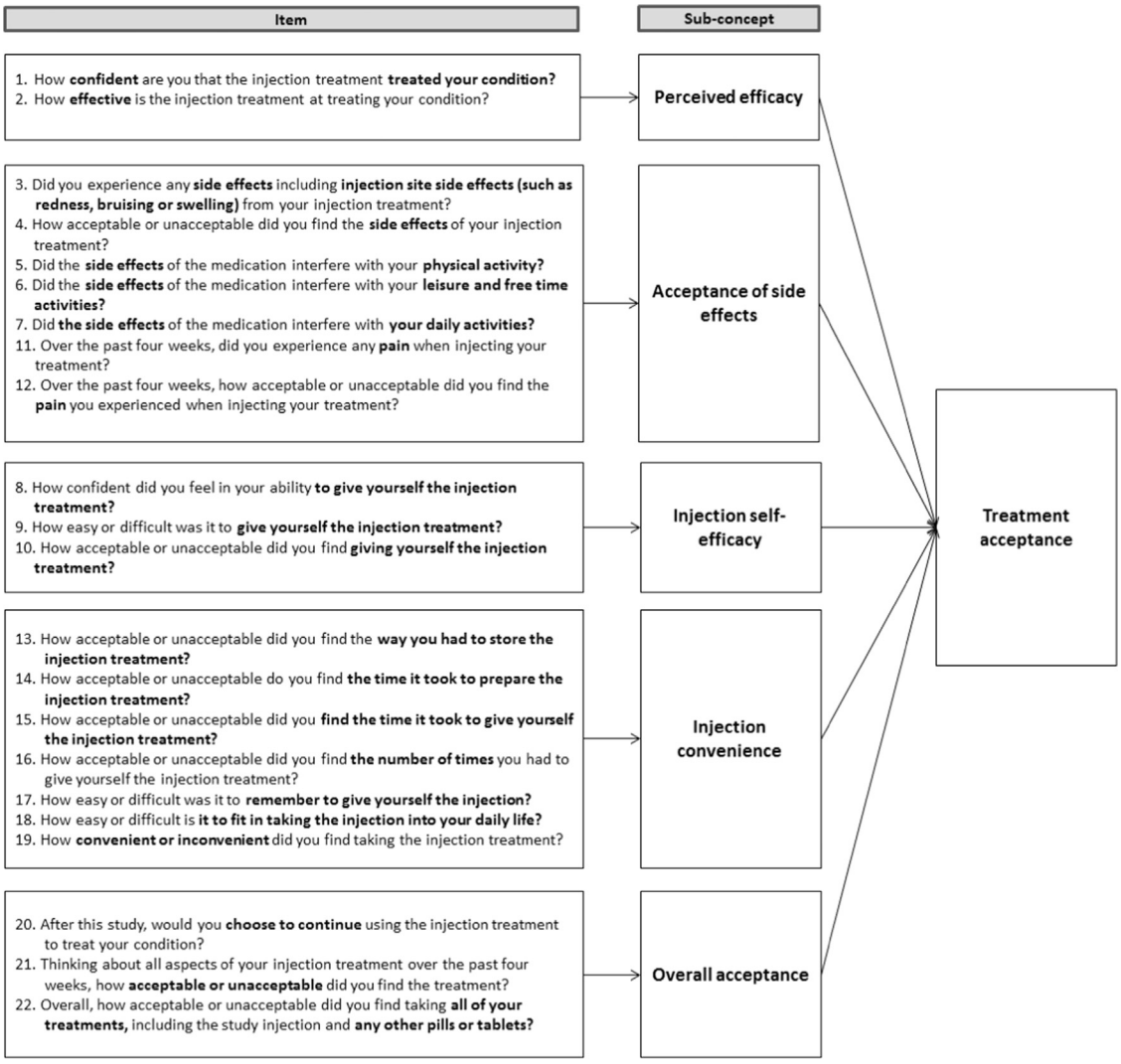

Fig. 1. – Final conceptual framework for the Injection-Treatment Acceptance Questionnaire (I-TAQ).

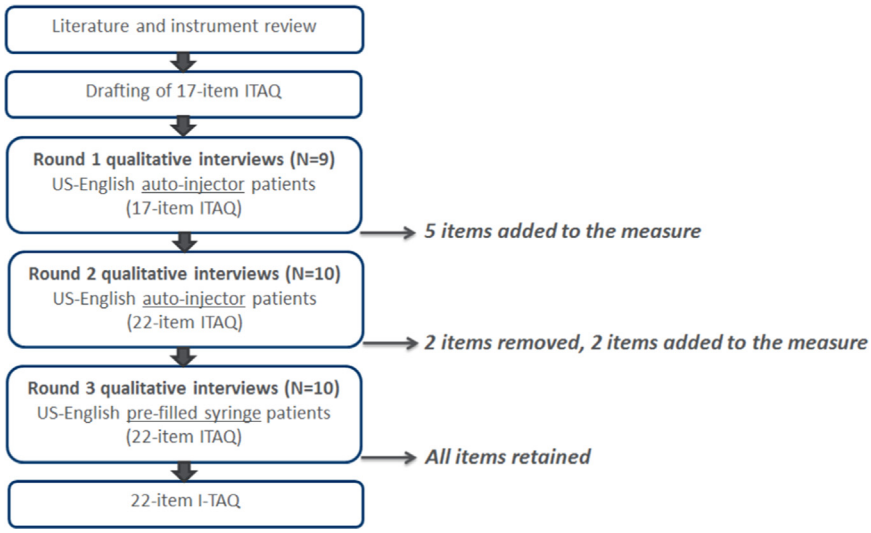

Fig. 2. – Overview of changes made to the I-TAQ after each round of interviews. I-TAQ, Injection-Treatment Acceptance Questionnaire. (Color version of figure available online).

know their LDL-C levels. Because the concept was described to substantially influence treatment acceptance, however, both items were retained.

Furthermore, the new items capturing self-efficacy, preparation time, and remembering to take the treatment were understood and relevant to all 10 patients and were therefore retained. The item asking specifically about injection site reactions was merged with the general side effects item because patients did not appear to interpret a conceptual distinction between the two concepts.

Both the original and revised overall acceptance items were well understood in round 2, although patients preferred the newly added item wording overall. Therefore, the new item was retained and the original overall acceptance item deleted.

Although not frequently experienced, pain was reported by two patients in CE and was acknowledged to be a concept that may significantly affect treatment acceptance. Therefore, two items assessing pain were added to form the 22-item I-TAQ and were tested in round 3. The first pain item asked about the presence of pain when injecting, using a dichotomous "yes or no" response option, whereas the second item captured acceptance of pain. A skip pattern was used so that only those patients who experienced pain reported acceptance.

Revisions after round 3 interviews with patients using the PFS ($n = 10$)

Overall, the 22-item I-TAQ tested in round 3 was well understood and all concepts were reported to be relevant to the 10 patients using the PFS, with no new concepts reported to be missing. Therefore, all items were retained and no new items added, forming the final 22-item I-TAQ ready for psychometric evaluation (Fig. 2).

Discussion

As new therapies requiring injections are introduced for CV disease management, it is important to understand the patients' perspectives of the treatment [6–8]. Because new treatments in development, such as alirocumab [6–8], require subcutaneous injection rather than orally consumed pills, it is important to assess how acceptable patients find this mode of administration and their willingness to self-inject. To measure acceptance of the subcutaneous treatment, a new PRO was needed, the initial development and content validity testing of which is presented in this article. Three rounds of successive qualitative interviews with interim analysis informed revisions to the I-TAQ, resulting in the development of a treatment acceptance measure with strong content validity, appropriate for use with both patients administering the treatment via a PFP and/or a PFS (Fig. 2). Performing combined CE and CD in the same interview facilitated an iterative approach to the refinement of the instrument content. Although less commonly used than an approach whereby pure CE interviews are followed by pure CD interviews [24–26], this approach facilitates early testing of items and more rapid instrument revision without sacrificing the opportunity to introduce new items and concepts into the tool.

The constructs of the Health Belief Model [12] provided a useful framework for the development of the I-TAQ. Perceived efficacy of the treatment, self-efficacy, side effects, injection convenience, and overall acceptance were identified as domains of importance in relation to treatment acceptance, with pain being a less commonly relevant concept. Nevertheless, because it is important to capture the presence or absence of pain in a self-injected population, a question was added to the I-TAQ to understand the pain associated with the injection [15,16]. Notably, where the impact of treatment satisfaction/acceptance on adherence has been reported in the literature [27,28] (supported by the Health Belief Model [12]), the presence of pain was deemed a concept that may negatively affect acceptance and therefore adherence and so was deemed a key concept to capture in an injection population. Although no bothersome side effects or effects on physical functioning/daily activities were reported in this population, it was deemed important to capture the absence of these effects. In addition, it is known from the literature that such effects are relevant concepts of treatment satisfaction/acceptance to capture and may well be relevant in other patient populations receiving treatment via subcutaneous injection.

The TSQM and the SATMED-Q are widely used measures of treatment satisfaction in the literature [29–32]. Although there is overlap in the concepts assessed by these measures and those captured in the I-TAQ (e.g., perceived efficacy, side effects, and convenience), these generic measures are not conceptually comprehensive for injection-treatment populations. In addition, although the SIAQ is specific to satisfaction with injection treatments, the questions are phrased to ask about satisfaction with injections in general, rather than asking specifically about a particular treatment the patient is currently taking. Furthermore, the SIAQ uses a "pre" and "post" injection recall period, whereas an instrument with the option of being administered only once in a study would provide greater flexibility of use as it could be included in both cross-sectional and longitudinal studies. Moreover, although the ACCEPT is a measure of treatment acceptance, it is not specific to injectable treatments and includes items measuring acceptance of oral medications. Therefore, the I-TAQ is a new instrument with appropriate content validity for use with patients who self-administer injection treatments that overcomes the limitations of these other measures.

In addition, the study explored the relevance of treatment acceptance in patients who self-administer their treatment via subcutaneous injection. Findings from this qualitative study support treatment acceptance as a more relevant concept for this population, with more patients voicing a preference for the term acceptance as opposed to satisfaction when describing their treatment experience.

Study Limitations

All patients were recruited from a randomized controlled trial and as a result had experience of using the injection treatment. Although this can be of substantial value in terms of gaining insight into relevant concepts relating to long-term use, transient concerns before patients initiated therapy may have not been accurately recalled and captured during interviews. In addition, because of the lack of diversity in ethnicity, there is a lack of evidence to support the generalizability of the I-TAQ in a non-Caucasian population. Therefore, there could be value in assessing the content validity of the measure in other cultures to confirm cross-cultural validity.

Although saturation was achieved for the whole sample, only 10 patients using the PFS were interviewed. Therefore, there may be value in interviewing a larger sample of patients who use the PFS to confirm that no additional concepts are missing from the questionnaire. Finally, the content validity of the I-TAQ has been documented for use in high CV risk populations, therefore, assessment of conceptual comprehensiveness in other self-administered injection populations (e.g., diabetes) would be required for wider use.

Future Research

A PRO was successfully developed to measure patients' perspectives of using self-administered, subcutaneous injections as a

therapeutic strategy. The next step is to psychometrically validate the I-TAQ to establish its reliability and validity, as well as the appropriateness of the hypothesized conceptual framework and inform development of scoring, with possible item reduction. Ideally, the responsiveness and predictive validity for long-term adherence would also be established. Following psychometric validation, the expectation is that the I-TAQ might form a reliable and valid instrument with which to quantify the acceptability of injection treatments in different disease populations.

Conclusions

The I-TAQ is a treatment acceptance measure designed for use with patients who self-administer their treatment via subcutaneous injection. Drafted by drawing on insights from existing validated instruments, the I-TAQ has demonstrated strong content validity in injection-treatment samples through successive rounds of qualitative interviews, with interim results informing revisions iteratively. The next step is to psychometrically validate the I-TAQ in a larger injection population to develop a scoring algorithm and evaluate psychometric properties.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2015.09.2937. or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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