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Psychometric Evaluation of a Treatment Acceptance Measure for Use in Patients Receiving Treatment via Subcutaneous Injection

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ABSTRACT

Background: Alirocumab, a proprotein convertase subtilisin/kexin type 9 inhibitor, significantly reduces low-density lipoprotein cholesterol, but requires subcutaneous injections rather than oral pills. To measure patients' acceptance of this treatment modality, a new patient-reported outcome, the Injection-Treatment Acceptance Questionnaire (I-TAQ), was developed. **Objectives:** To psychometrically evaluate the I-TAQ with patients at high risk of cardiovascular events receiving alirocumab. **Methods:** The 22-item, 5-domain I-TAQ was administered cross-sectionally to 151 patients enrolled in alirocumab clinical trials. Item response distributions, factor and multitrait analyses, interitem correlations, correlations with an existing measure of acceptance (convergent validity), and comparison of known-groups were performed to assess the I-TAQ's psychometric properties. **Results:** Completion rates were high, with no patients missing more than two items and 91.4% missing no data. All items displayed high ceiling effects (>30%) because of high treatment acceptance. Factor analysis supported the *a priori* hypothesized item-domain structure with good fit indices (root mean square error approximation = 0.070; comparative fit index = 0.988) and high factor loadings. All items demonstrated item convergent validity (item-scale correlation ≥0.40), except for the side effects domain, which was limited by small numbers (n = 46). Almost all items correlated most highly with the domain to which they were assigned (item discriminant validity). Internal reliability was acceptable for all domains (Cronbach α range 0.72–0.88) and convergent validity was supported by a logical pattern of correlations with the Chronic Treatment Acceptance Questionnaire. **Conclusions:** These findings provide initial evidence of validity and reliability for the I-TAQ in patients treated with subcutaneous alirocumab. The I-TAQ could prove to be a valuable patient-reported outcome for therapies requiring subcutaneous injection.

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

Introduction

Elevated low-density lipoprotein cholesterol (LDL-C) levels are associated with an increased risk of cardiovascular (CV) events [1], occurring in more than 2 million Americans each year and accounting for approximately one-quarter of total inpatient costs [2]. Lowering LDL-C levels with statin and nonstatin lipid-modifying therapies [3] reduces the risk of CV events [4]. Alirocumab is a fully human monoclonal antibody against proprotein convertase subtilisin/kexin type 9 that is administered via subcutaneous injection for the treatment of elevated LDL-C levels. Alirocumab has demonstrated significant incremental reduction in LDL-C levels with or without background statin therapy [5–9].

Given the requirement for subcutaneous, as opposed to oral, administration, there is a need to assess patients' acceptance of the subcutaneous treatment approach. Accordingly, a novel patient-reported outcome (PRO) instrument, the Injection-Treatment Acceptance Questionnaire (I-TAQ), was developed to measure treatment acceptance. The concepts generated from a literature and instrument review informed the initial drafting of a 17-item version of the I-TAQ. Content validity, as outlined in the Food and Drug Administration PRO guidance [10], was then assessed through three successive rounds of qualitative interviews conducted with 29 US-English–speaking patients who were participating in the phase III program for alirocumab. Each round of interviews included both concept elicitation (to ensure no

Conflicts of interest: Laura Grant, Sophi Tatlock, and Rob Arbuckle were employees of Adelphi Values Ltd., a consultancy paid by Regeneron Pharmaceuticals and Sanofi to perform the study and develop the manuscript. John Spertus received payment as a consultant for engagement in the research as a clinical expert, but not for involvement in the writing of the article.

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important or relevant concepts were missing) and cognitive debriefing activities (to provide further evidence of relevance and ensure the items were well understood), the results of which informed revisions to the measure, resulting in a 22-item I-TAQ with established content validity [11].

Once the content validity of the I-TAQ was established, an evaluation of the instrument's psychometric properties was required to evaluate reliability and validity in measuring patients' acceptance of subcutaneous treatments. The primary objective of this study, therefore, was to evaluate the psychometric properties of the I-TAQ to finalize the conceptual framework, evaluate the appropriateness of the *a priori* hypothesized scoring algorithm, and establish its validity and reliability.

Methods

Study Design

This was a multicenter, non-interventional, cross-sectional study to psychometrically validate the I-TAQ. The 22-item I-TAQ as well as two other PROs used for convergent validity, the Chronic Treatment Acceptance Questionnaire (ACCEPT) and a patient global impression of acceptance (PGI-A) measure, were all administered at one time point to each participant. The analyses are presented in Figure 1. The appropriateness of the *a priori* conceptual framework and the scoring algorithm were evaluated through the examination of item-level statistics and dimensionality analyses. Then, the resulting measure and the scoring algorithm were subject to psychometric validation to evaluate the validity and reliability of the established scores.

The study was conducted in accordance with the Declaration of Helsinki and was overseen by a centralized independent review board in the United States (ethical approval reference: ADE1-14-383). Written informed consent was obtained from all participants before the collection of any data and before any study-related activities.

Patient Recruitment

All 151 patients were enrolled in alirocumab phase III trials and were recruited for participation in this observational study through 11 clinical sites in the United States. All patients were diagnosed with elevated LDL-C levels and were 18 years or older. The inclusion criteria required all patients to have experience of self-administering alirocumab (or placebo) via prefilled pen or prefilled syringe. Patients self-injecting alirocumab (or placebo), either as a single 1-ml dose every 2 weeks or two 1-ml doses every 4 weeks, were considered eligible for the study.

Data Collection

PRO measures

Injection-Treatment Acceptance Questionnaire. The I-TAQ is a 22-item, self-administered questionnaire, developed as a measure of treatment acceptance in patients who inject their medications via subcutaneous injections (Appendix A). The I-TAQ assesses five domains of treatment acceptance: perceived

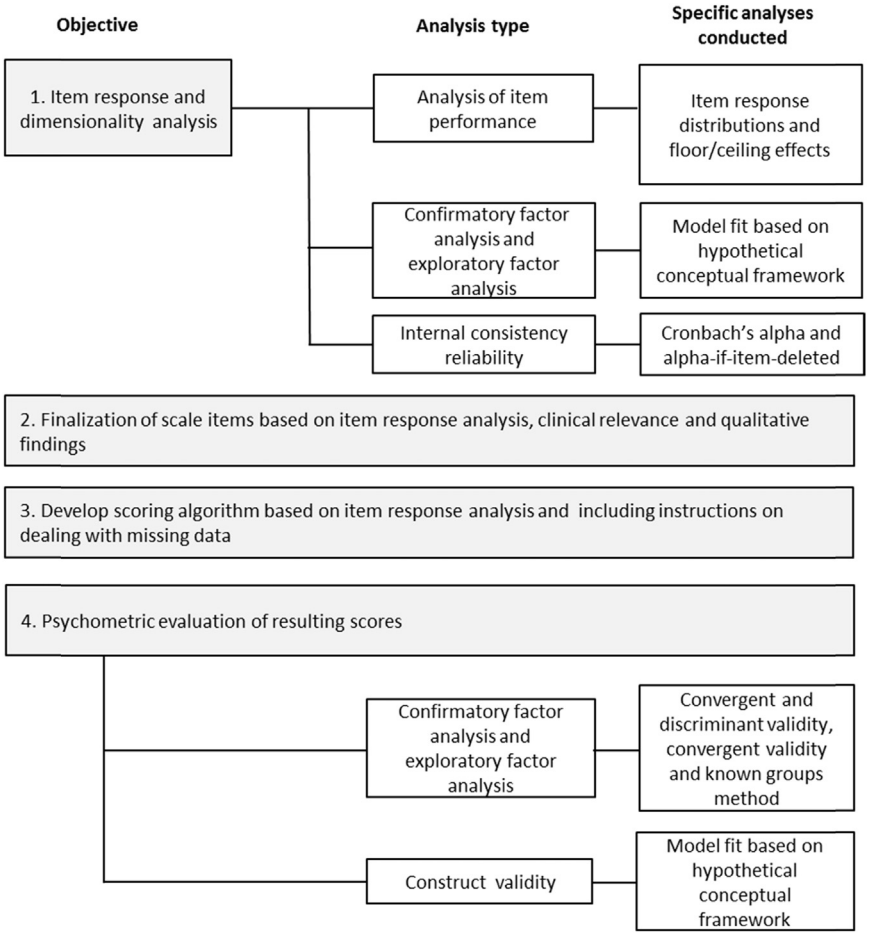

Fig. 1 – Overview of study analyses.