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Development of the Hypogonadism Impact of Symptoms Questionnaire Short Form: Qualitative Research

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ABSTRACT

Introduction: Hypogonadism in men is often associated with poor libido, erectile dysfunction, irritability, fatigue, and psychological and relationship problems. Many of these symptoms can be best assessed through patient report. The 28-item Hypogonadism Impact of Symptoms Questionnaire (HIS-Q) was developed to evaluate hypogonadism symptoms in men with low testosterone in the context of clinical trials.

Aim: To develop a briefer version of the HIS-Q that could be practical for use in treatment settings.

Methods: Participants with low testosterone levels and symptoms consistent with hypogonadism were recruited through clinical sites. Focus groups and interviews were conducted to elicit symptom concepts and identify those that were most relevant to patients, including changes as a consequence of treatment.

Main Outcome Measures: Systematic analysis of the qualitative data and expert clinician input were used to develop the HIS-Q short form (HIS-Q-SF). One-on-one cognitive interviews were conducted to confirm the content validity of the HIS-Q-SF.

Results: Thirty-five men participated in this qualitative research. Concept elicitation was conducted through focus group discussions (n = 18) and telephone interviews (n = 2); then, the draft HIS-Q-SF was evaluated through cognitive interviews (n = 15). The mean age of total sample was 53.2 ± 6.8 years, and the mean serum total testosterone level was 184.9 ± 55.2 ng/dL. Results suggest that the HIS-Q-SF has demonstrated content validity, including the content coverage, comprehensibility, and the appropriateness of the response options and recall period. The final version of the HIS-Q-SF includes 17 items and is aligned with the original longer version of the instrument.

Conclusion: The HIS-Q-SF is a comprehensive measurement of hypogonadism symptom severity in men. Content coverage and content validity were confirmed. The instrument will be evaluated further to establish the psychometric characteristics and to assess the utility of the measurement in clinical treatment settings.

Key Words: Hypogonadism Impact of Symptoms Questionnaire; Hypogonadism; Low Testosterone; Patient-Reported Outcome; Instrument Development; Symptoms; Qualitative Research; Interviews; Content Validity

INTRODUCTION

Hypogonadal (low testosterone or testosterone deficiency) symptoms and their subsequent effects have substantial negative effects on the functioning and quality of life of affected men.[1,2] Findings from the Massachusetts Male Aging Study suggested that approximately 2.4 million men 40 to 69 years old have some degree of hypogonadism.[3] Once believed to affect primarily sexual functioning, androgens are now known to have a much broader impact on target organ systems such as bone, muscle, and cardiovascular and brain functioning, with lower levels being

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associated with poor libido, erectile dysfunction, irritability, fatigue, and psychological and relationship problems.[4–6]

Clinical trials evaluating treatments for hypogonadism often incorporate self-reported outcomes from patients, commonly referred to as patient-reported outcomes (PROs). PROs are useful because many of the signs and symptoms of hypogonadism (eg, low libido, fatigue) are known only to patients and cannot be evaluated through clinical assessments or tests.[7] Although existing instruments have been used to assess the symptoms of low testosterone in men, none have been specifically designed to comprehensively measure symptoms and effects in this patient population. In addition, many measurements currently being used were developed without any input directly from patients. To address this gap, the Hypogonadism Impact of Symptoms Questionnaire (HIS-Q) was developed to assess changes in symptom frequency and severity in the context of clinical trials.[4,8] The HIS-Q is comprised of 28 items and was developed according to Food and Drug Administration guidance[9] for the development of PRO measurements. This guidance emphasizes the importance of soliciting input directly from patients during the development of PRO instruments to ensure that the measurements are meaningful and relevant to patients.

The objective of the present study was to develop and establish the content validity of a shorter version of the HIS-Q (the HIS-Q Short Form [HIS-Q-SF]) that would be more suitable for use in clinical practice. The developmental work for the original HIS-Q included focus groups and interviews with 65 participants of diverse clinical and demographic characteristics,[4] and the present work builds on this previous body of evidence by focusing more specifically on patients' experiences with changes in hypogonadism symptoms after testosterone replacement therapy (TRT). Qualitative work with patients is often helpful when developing or adapting a new PRO instrument to ensure that the measurement's content and format are consistent with patients' experiences. In particular, the study team wanted direct patient input on the relevance of individual symptoms and the importance of changes in these symptoms after TRT. This was achieved by conducting a qualitative study to identify the most important symptoms, to understand changes in symptoms as a result of treatment, and to establish the content validity of the draft HIS-Q-SF in patients with low testosterone. This initial qualitative work is the first step in developing a PRO instrument; once a draft version of the instrument is available, the psychometric properties can be established and then the instrument can be used to track changes in symptom severity throughout treatment.

METHODS

Study Design and Procedures

A two-part cross-sectional qualitative study involving (i) semistructured focus groups and one-on-one interviews and (ii) cognitive interviews through similar methods with a total of 35 adult male patients with hypogonadism was conducted. Part 1 included concept elicitation focus groups and discussions to solicit spontaneous input on patients' hypogonadism experiences, including sorting hypogonadism symptoms in order of importance. Part 2 involved cognitive interviews on the newly created draft version of the HIS-Q-SF that focused on participants' understanding of the items, decision processes about the responses, interpretation of response options, and understanding and evaluating recall period appropriateness (ie, whether the suggested recall time for the questions was deemed reasonable and appropriate by the participants). The study included in-person and telephone discussions. Participants took part in only one stage of the research process (part 1 or 2).

Participants were recruited through three clinical sites located in New Jersey, New York, and Washington State from November 2013 through November 2014. The study was reviewed and approved by an institutional review board and all participants provided informed consent. Inclusion criteria were the same for the two parts of the study and included men 18 to 65 years of age; a history of signs and symptoms consistent with a diagnosis of hypogonadism; serum total testosterone concentration lower than 300 ng/dL; able to read, speak, and understand English; willing and able to attend and participate in a discussion on the topic; willing to provide informed consent; and were currently receiving or had previously received TRT within the past 2 years. Participants were remunerated a modest amount at completion of the study.

Part 1: Concept Elicitation

A discussion guide was developed for the concept elicitation portion of the interview based on a review of the literature, prior research by the investigators in the development of the original HIS-Q, and input from clinical experts. The discussion guide was designed to elicit patients' symptom experiences and changes in these symptoms in response to treatment. Focus group and interview sessions were audio-recorded with the participants' permission.

The sessions began with emergent discussion of hypogonadism symptoms followed by symptom ranking exercises. These ranking exercises were designed to identify (i) which symptoms were of greatest importance or relevance to the patients overall and (ii) which symptoms were important for improvement as a result of treatment. To complete the symptom ranking exercise, participants were asked to prioritize three mood symptom concepts that were most relevant to them from a list of 16 mood concepts identified through prior qualitative research. Then, participants were given 18 cards, each of which displayed a common symptom of hypogonadism (including the three mood concepts they had just selected as most relevant). These symptoms represented the major concepts that were identified during the qualitative development of the original HIS-Q and were selected based on prior qualitative research and input from expert clinicians. Participants were asked to select the five symptom