The Vulvovaginal Atrophy Questionnaire (VVAQ): A Novel Patient-Reported Outcome (PRO) for Assessing Symptoms of Vulvovaginal Atrophy in Menopausal Women

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Background

- Symptoms of vulvovaginal atrophy (VVA), a principal component of the genitourinary syndrome of menopause (GSM), are prevalent and bothersome in studies of menopausal women.[1-3]
- Validated, self-report measures are needed to better characterize and to quantify the prevalence and degree of unmet medical need associated with this symptom complex.
- Given the prevalence of VVA symptoms and potential impact on women's health, there is an urgent clinical and research need for a patient-based, culturally-sensitive, validated instrument for assessing VVA symptoms and their impact on women's lives.
- We present results from the first four phases of development of a novel PRO measure for assessing VVA symptoms in menopausal women.

Methods

- The broad objective of the VVAQ program of research is to design, develop and validate a new PRO measure for assessing symptomatic VVA in both research and clinical settings.
- Following established guidelines, this new PRO measure was developed in 5 distinct phases (Figure 1).
  - Phase 1 – Based on literature review and clinical expert input, an initial conceptual model was proposed
  - Phase 2 – Concept elicitation interviews were performed to assess domains and generate items in (N=36) post-menopausal women with clinically confirmed, symptomatic VVA (Figure 2).
  - Phase 3 – Based on qualitative interview findings, a draft questionnaire was developed.
  - Phase 4 – Cognitive debriefing interviews were conducted to assess comprehension and content validity in open-ended focus groups of women with and without symptomatic VVA (N=26 with VVA, N=15 without VVA) Participants were recruited from 3 geographically diverse sites. All interviews were performed by a trained qualitative interviewer and coded for content analysis according to standard coding procedures and analysis methods.
  - Phase 5 – The final stage of psychometric validation is planned for 2018.

Figure 1. Stages of PRO Development

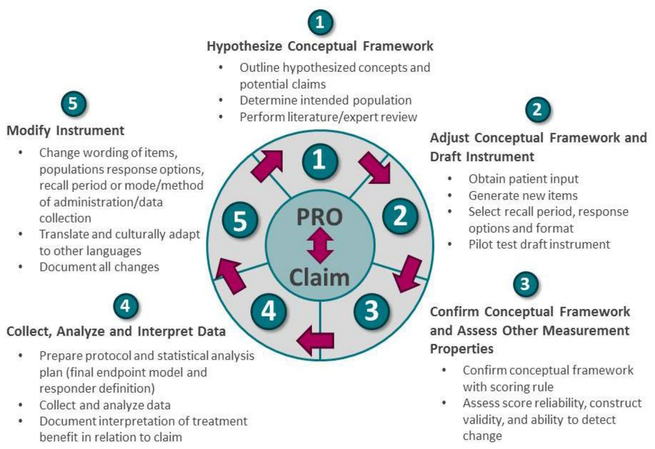
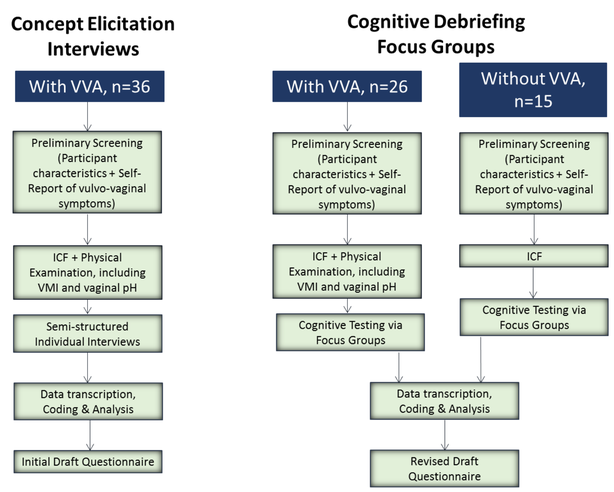


Figure 2. Study Design



References:
1. Levine KB, Williams RE, Hartmann KE. Vulvovaginal atrophy is strongly associated with female sexual dysfunction among sexually active postmenopausal women. *Menopause*. Jul-Aug 2008;15(4 Pt 1):661-666.
2. Williams RE, Levine KB, Kalilani L, Lewis J, Clark RV. Menopause-specific questionnaire assessment in US population-based study shows negative impact on health-related quality of life. *Maturitas*. Feb 20 2009;62(2):153-159.
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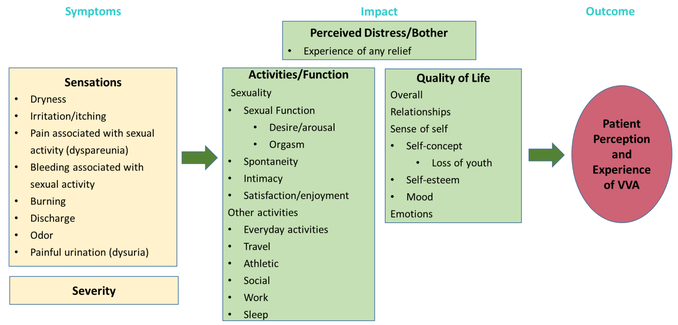
Results

- Based on findings from the concept elicitation interviews and cognitive debriefing focus groups, a draft PRO was developed consisting of 14 individual items to asses vaginal and urinary health, impact on sexual function, and associated distress.
- A high degree of inter-rater reliability (r=0.93) was observed for the coding of interview transcripts.
- The PRO includes specific terminology women use to describe their VVA symptoms not previously included in questionnaires, e.g. "sand paper" and "choice of looser clothing."
- The PRO assesses degree of bother associated with symptoms, as symptoms must be bothersome to make a diagnosis of GSM and for treatment to be indicated.
- Revised conceptual model proposed with four major domains to fully assess all components of GSM (Figure 3).
- Unique properties of the GSM PRO/VVAQ are:
  - Identifies GSM/symptomatic VVA in women who are not sexually active
  - Includes symptoms involving both vagina and vulva ('inside/outside')
  - Includes urinary symptoms
  - Sexual activity questions are designed to cover a range of activities (penetrative and non-penetrative, with and without a partner, male and/or female partners)
  - Reason(s) for sexual inactivity elicited, as often due to VVA symptoms
  - Effect of symptoms on partner relationship ascertained
  - Questions assessing treatment effects available for use in trials of of therapeutic interventions (e.g., OTC product, physical therapy, device, drug)

Figure 3. Revised Conceptual Model



Interview Quotes

"I dread having sex. It's not fun. I don't think I even can get aroused anymore because I fear that it's going to hurt when I have intercourse."

"I didn't know there was a name for it. I just felt like, oh well, this is a part of me getting older."

"Well, I would like to quit thinking about it every day when it happens and not have to worry about what I'm wearing or that my pants are too tight or my underwear is too tight."

"You go through the worthlessness and not feeling that you're a real woman anymore."

Conclusions

- In response to the urgent need for a patient-based, validated questionnaire of symptomatic VVA, a novel PRO measure has been developed based on qualitative responses of post-menopausal women with and without exam-confirmed VVA.
- This new PRO measure was developed in close accordance with FDA's Guidance for PRO development and validation, based on expert advice from clinicians and researchers.
- Further clinical validation is planned, along with broader use of the measure in epidemiologic research; clinical trials; drug, device, and OTC product development; and as a screening questionnaire in clinical practice.
- It is hoped that FDA will endorse the use of this validated PRO in place of the current limited endpoint measure of "most bothersome symptom".

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