Qualitative Assessment of Women's Experiences of Sleep Disturbances Associated with Menopause to Evaluate the Content Validity of Patient-Reported Outcomes

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OBJECTIVES

- Sleep disturbances are one of the most bothersome menopausal symptoms, significantly impacting women's health-related quality of life (HRQoL);[1-3] yet no treatments are specifically approved for this indication.
- The experience of menopause-associated sleep disturbances from the perspective of women is not well-defined, and to be considered fit-for-purpose, patient-reported outcome (PRO) measures require evidence that they measure the concept of interest in the intended context of use.[4-7]
- This study aimed to obtain in-depth insights into these experiences and assess the content validity of the PROMIS Sleep Disturbance Short Form 8b (PROMIS SD SF 8b),[8] Insomnia Severity Index (ISI),[9] and a de novo Sleep Diary (SD).

METHODS

- **Twenty women experiencing sleep disturbances associated with menopause were recruited** from four geographically diverse US states (MO, IL, PA, and CA).
- Semi-structured, qualitative concept elicitation and cognitive debriefing interviews (~60 min) were conducted per regulatory and industry standards to elicit symptoms and impacts, and to assess understanding and suitability of selected PRO measures.[5-7]
- Interview transcripts were analysed using qualitative thematic and framework analytical methods in line with best practices,[10-12] and findings refined the draft conceptual model derived from a qualitative literature review.
- **Three individual discussion sessions were also conducted with clinical experts (N=3)** from the US (n=2) and Canada (n=1) who were experienced in the treatment of sleep disturbances associated with menopause.

Table 1. Descriptions of PRO measures

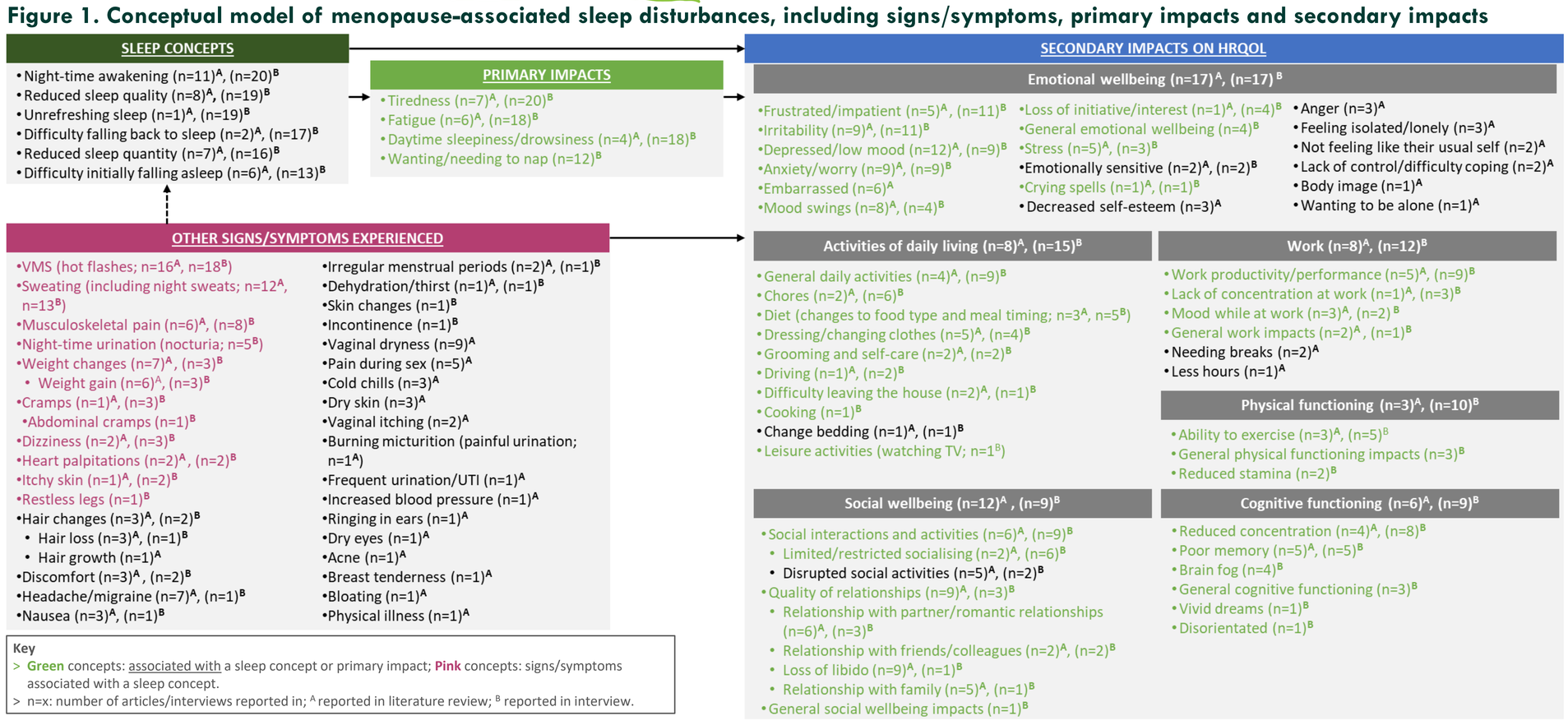
PRO	Description
PROMIS SD SF 8b[8]	•8 items assessing sleep disturbances over the past 7 days.
ISI[9]	•7 items quantifying participants' perception of insomnia severity and the impact of insomnia on daytime functioning, over the past 2 weeks.
SD	•7-items assessing total sleep time duration via self-reported bedtime, sleep-onset time, wake time, time in bed, and number and duration of night-time awakenings.

RESULTS

KEY SAMPLE CHARACTERISTICS

Characteristic	N (%)
Age (years)	
Mean (range)	51.7 (40-64)
Race, n (%)	
White	12 (60.0)
Black/African American	4 (20.0)
Other	4 (20.0)
Menopausal stage, n (%)	
Perimenopausal: ≥3-11 months of amenorrhea	8 (40.0)
Postmenopausal: ≥12 months of amenorrhea	12 (60.0)
Most relevant description of hot flashes experienced over the past 7 days, n (%)	
No hot flashes	5 (25.0)
Mild hot flashes only: Feeling of heat without sweating	6 (30.0)
Moderate to severe hot flashes: Hot flashes that induce sweating	9 (45.0)

Figure 1. Conceptual model of menopause-associated sleep disturbances, including signs/symptoms, primary impacts and secondary impacts



Key
> Green concepts: associated with a sleep concept or primary impact; Pink concepts: signs/symptoms associated with a sleep concept.
> n=x: number of articles/interviews reported in; A reported in literature review; B reported in interview.

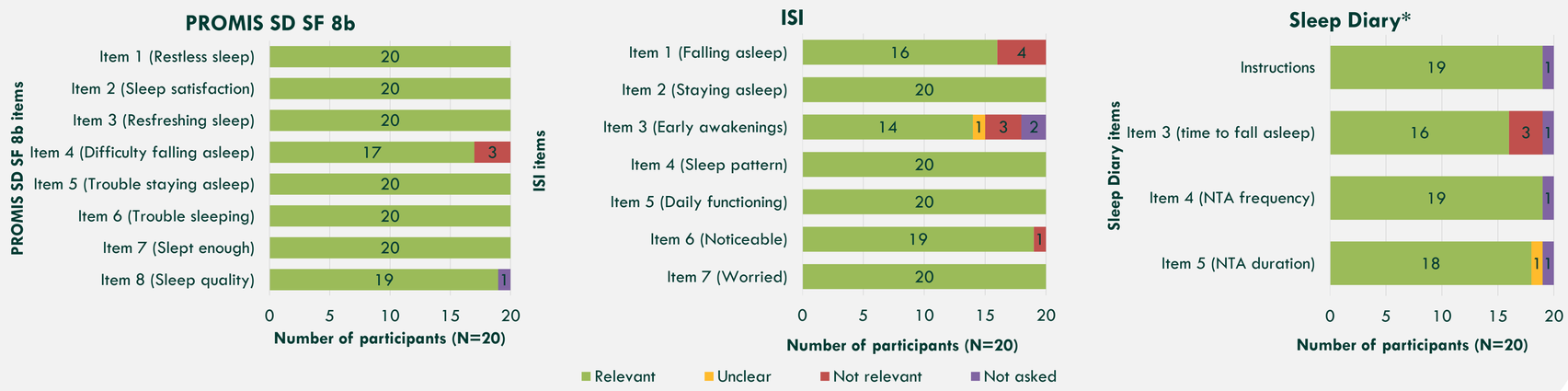
CONCEPT ELICITATION

- Six sleep disturbance concepts associated with menopause were identified, with all women reporting nighttime awakenings (**Figure 1**).
- Impacts on HRQoL were categorized as primary (proximal) or secondary (distal) according to their proximity to and association with sleep disturbances.
- Symptoms commonly associated with sleep disturbances included vasomotor symptoms (VMS; hot flashes), sweating (including night sweats) and musculoskeletal pain, though sleep disturbances were experienced irrespective of these symptoms.
- Saturation analysis indicated that the sample size was sufficient to elicit key signs/symptoms and impacts.
- **Clinical experts** confirmed the relevance of concepts included in the conceptual model (**Figure 1**). They also highlighted that sleep disturbance can occur independently of VMS (hot flashes) and can directly lead to secondary impacts, with primary impacts not always acting as a mediator.

COGNITIVE DEBRIEFING

- Most participants asked (n≥18, ≥84.2%) demonstrated a clear understanding of the PROMIS SD SF 8b, ISI, and SD items, including the recall period, response options and associated instructions.
- All PROMIS SD SF 8b and SD items were considered relevant to most participants' experience (n≥16, ≥84.2%), and most ISI items were considered relevant to most participants' experience (n≥14, 70%; **Figure 2**).
  - A slightly smaller proportion found ISI items 1 and 3 relevant, consistent with CE findings and prior research indicating that women with moderate to severe VMS typically do not report difficulties initially falling asleep.[13]
- Most participants considered the following as meaningful improvements in SD concepts:
  - Having one or two fewer night-time awakenings
  - Reducing night-time awakening duration by 5-30 minutes.
- **Clinical experts** reported familiarity and experience with the PRO measures and considered each to be relevant and appropriate to this population.

Figure 2. Relevance of PRO items



** Participants were not asked about the relevance of items 1 (time to bed), 6 (time woke up) and 7 (time got up) as each would be relevant to all individuals irrespective of sleep disturbances.*

CONCLUSIONS

Findings provide in-depth insights and rich qualitative confirming the relevance and importance of sleep disturbances associated with menopause, and the associated impacts on quality of life. In line with regulatory guidance,[4-7] results provide evidence to support the content validity and the appropriateness of the PROMIS SD SF 8b,[8] ISI[9] and SD for use within clinical studies assessing sleep disturbances associated with menopause.

DISCLOSURES

This study was funded by Bayer. AT is a Bayer plc employee. CS, FK, and HS are Bayer AG employees. HW is a Bayer Oy employee. KOS is a Bayer US LLC employee. MB, HB, RJ, AL, and MC are Adelphi Values employees.

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