



## CLINICAL REVIEW

## Measurement of non-restorative sleep in insomnia: A review of the literature

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## S U M M A R Y

*Keywords:*Patient-reported outcomes  
Non-restorative sleep  
Literature review

*Objective:* Non-restorative sleep (NRS) is a core symptom of insomnia, typically defined as a subjective feeling of being unrefreshed upon awakening. NRS symptoms have been less consistently studied than other symptoms of insomnia, and there is no consensus regarding measurement of NRS. Given its subjective nature, patient-reported outcome (PRO) instruments are important for evaluating NRS symptom severity and treatment-related changes. The objective of this literature review was to identify PROs used in insomnia populations that purport to measure NRS, and to evaluate their psychometric characteristics.

*Methods:* A comprehensive review of PRO instruments used in insomnia was conducted; instruments were reviewed for NRS content by two independent reviewers; a total of 26 instruments identified to contain NRS content were retained for further review.

*Results:* Of the 26 instruments reviewed, 23 contained at least one item evaluating subjective nighttime aspects of NRS; 17 contained at least one item evaluating daytime aspects of NRS. Only the Sleep Assessment Questionnaire contained a specific NRS domain score. However, little published evidence was available regarding measurement properties of the NRS domain in insomnia populations.

*Conclusions:* There is currently no reliable and well-validated PRO instrument available for specifically evaluating NRS symptom severity and response to interventions in insomnia populations. Reliable and valid measurement tools are needed to measure the symptom of NRS in insomnia.

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## Introduction

Non-restorative sleep (NRS) is one of the core symptoms of primary insomnia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition<sup>1</sup> and the International Classification of Sleep Disorders 2nd Edition.<sup>2</sup> Despite NRS/sleep quality being part of the defining features of insomnia, NRS has been less consistently defined and less well-studied than other symptoms of primary insomnia such as sleep latency and total sleep time which are standard measures included in studies of insomnia. The comorbidities, antecedents, and consequences of NRS are poorly understood.<sup>3</sup> NRS is often defined as a subjective

feeling of being unrefreshed upon awakening, which may be the result of poor quality or unrefreshed sleep.<sup>4,5</sup>

In addition to being one of the core symptoms of insomnia, recent epidemiological studies have suggested that there may be a population of insomnia patients who do not report difficulty initiating or maintaining sleep, but who do report NRS.<sup>6</sup> Ohayon and Roth<sup>7</sup> suggest that NRS may or may not be accompanied by other insomnia symptoms and that NRS may occur even when individuals have normal sleep duration. They propose that NRS in the absence of other insomnia symptoms be defined by the following criteria: 1) report of NRS at least 3 times per week; 2) normal sleep duration; and 3) report of feeling unrefreshed upon awakening or difficulty getting started in the morning almost daily.<sup>7</sup>

NRS has also been associated with other chronic diseases such as chronic fatigue syndrome, fibromyalgia syndrome, and Obstructive Sleep Apnea.<sup>2,8,9</sup> Given that NRS in insomnia has not been carefully studied or well understood, and given that we do not know whether NRS in insomnia is experienced similarly to NRS in other diseases/disorders, this review focused on measurement of NRS in insomnia populations. NRS has been receiving increasing attention

*Abbreviations:* HRQL, health-related quality of life; NIH, National Institutes of Health; NLM, National Library of Medicine; NRS, Non-restorative sleep; PIRS, Pittsburgh Insomnia Rating Scale; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcome Measurement Information System; SAQ, Sleep Assessment Questionnaire.

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in the literature and as a potential target of treatment interventions. The German Society of Sleep Research and Sleep Medicine has proposed specific guidelines for identification and treatment of NRS, defined as feeling unrefreshed upon awakening and throughout the day.<sup>10</sup> As such, it is essential that measurement tools be available to evaluate NRS symptoms if they are to be targeted for treatment intervention.

Since NRS is defined as a *subjective* feeling of unrestful sleep or feeling unrefreshed upon awakening, patient-reported outcome (PRO) instruments are important measurement tools for evaluating NRS severity and treatment-related changes. The objective of this literature review is to identify published PROs that measure NRS suitable for use in insomnia populations, and to evaluate their psychometric properties. We were interested in reviewing scales that either purport to evaluate NRS through a domain score or scales that contain item content that appears as if it would measure NRS. In keeping with the typical definition of NRS in the literature, we included only PROs that contained NRS domain scores and/or items related to subjective aspects of sleep experience (often discussed as quality of sleep) or feelings of being unrefreshed, unrested, or tired upon awakening, or throughout the day. Many PRO instruments evaluate some aspect of daytime sleepiness or fatigue. However, if the instruments did not contain items that subjectively evaluated aspects of nighttime sleep experience or feelings of morning/daytime refreshment, the instruments were not considered to evaluate NRS. The rationale for this decision is that daytime symptoms of sleepiness or fatigue are different measurement constructs from NRS, and can occur for a variety of reasons other than NRS.

The measurement properties of potential PROs for evaluating NRS in insomnia populations were evaluated against standard criteria for development and validation of PRO instruments presented by the Scientific Advisory Committee of the Medical Outcomes Trust<sup>11</sup> and summarized in the Food and Drug Administration (FDA) draft guidance on use of PROs.<sup>12</sup> In particular, we considered whether the development of a PRO included both qualitative and quantitative research. Qualitative research in the form of interviews or focus groups is necessary in order to ensure that the content of the instrument is consistent with patients' experiences, and that the concepts measured by the instrument include the elements that patients consider most important (thus ensuring content validity).<sup>12,13</sup> Quantitative research is also essential to ensure adequate reliability, validity, and treatment responsiveness.<sup>12,14</sup> PROs uncovered in the review were evaluated to determine whether they include content relevant to NRS symptoms, including subjective evaluation of sleep experience and/or feelings of being unrefreshed upon awakening or throughout the day. Thus, as a first step, instruments were selected that had items with NRS face validity, or content that appeared as if it would measure NRS. Next, instruments judged to have NRS content were evaluated for evidence of psychometric properties, including evidence of both qualitative work to support content validity and assessment of quantitative measurement properties. Relative strengths and weaknesses of available instruments are summarized.

## Methods

In order to conduct a broad, comprehensive review of all PROs that are used in insomnia studies with adults and that evaluate some aspect of NRS, two initial search strategies were employed. The first involved a formal literature search, and the second involved a search of recent (2007, 2008, 2009) APSS/SLEEP conference abstracts for PROs used in insomnia studies. The second strategy was employed in order to make sure that newly-developed

PROs were considered for review even if development and/or validation manuscripts on those PROs have not been published. All abstracts identified through the literature and conference searches were reviewed, and a comprehensive list of all PROs used in insomnia studies that included adult patients was developed. Instruments that are not available in the public domain (i.e., published or available for public distribution) were not reviewed. Copies of all PRO instruments on the initial comprehensive list that were publicly available were reviewed independently by one of the authors (M.V.) and a research assistant (S.K.; see Acknowledgements) to determine whether the instrument contained NRS content, which was operationalized as items that assess either the individual's sleep experience (often, but not always, appearing in the PRO instrument as "sleep quality") or some aspect of morning or daytime refreshment. The two raters' assessments were compared, and inter-rater reliability was determined with percent agreement. When a discrepancy occurred, the two raters reviewed the instrument together, discussed the discrepancy, and jointly made a determination about whether the instrument contains NRS content. Instruments that were determined to contain NRS content were retained for further review. After identifying all PROs used in insomnia studies that contained NRS content, we conducted literature searches to identify publications regarding the development and validation of each identified instrument.

### Literature search strategy

Three literature databases (PUBMED<sup>a</sup>, EMBASE<sup>b</sup>, and PsycInfo<sup>c</sup>) were searched as part of the initial literature search (see Table 1). Search strategies were initially broad to ensure that no relevant instruments were missed; instruments were reviewed and retained or eliminated based on study objectives (methods used for elimination are described below). The three database searches had similar search terms and search sequence logic; however, slight modifications were made between searches in order to fit within search format and parameters of the individual databases (See Table 1, column 2 for search terms and strategy for each database). The searches were designed to identify studies that 1) contained a PRO measure; 2) included content related to sleep, insomnia, or sleep quality; and 3) included content related to NRS, as defined above. Searches were limited to studies published in English, studies in humans, and studies published in the past 11 years (1998–2009). Given advancement in standards for instrument development and advancement of sleep medicine in the past decade, instruments that did not appear in the scientific literature and that were not used within a scientific study within the past 11 years were excluded. However, instruments that appeared in the literature but that were initially developed and published more than 11 years ago were included. We compared our PRO list to two recent sleep instrument reviews to increase confidence that our review did not omit any important instruments; we did not find gaps between the instruments that we evaluated and instruments reviewed in other studies.<sup>15,16</sup> Column 3 of Table 2 presents the number of unique abstracts each database search yielded. Abstracts identified in more than one search were only counted once. All

<sup>a</sup> MEDLINE (Medical Literature Analysis and Retrieval System Online) is the U.S. National Library of Medicine's (NLM) premier bibliographic database that contains approximately 13 million references to journal articles in life sciences with a concentration on biomedicine. PubMed is a platform used to access bibliographic information that includes MEDLINE and OLDMEDLINE as well as other databases.

<sup>b</sup> Comprehensive index of world literature on human medicine and related disciplines. Contains 15 million records drawn from the international literature.

<sup>c</sup> PsycInfo contains abstracts of articles from about 1200 journals on psychology topics.



**Table 2**  
Conference search results.

Conference	Search terms	Number of abstracts identified and reviewed
APSS/Sleep 2007	"questionnaire," "subjective," "patient reported"	58
APSS/Sleep 2008	"questionnaire," "subjective," "patient reported"	84
APSS/Sleep 2009	"questionnaire," "subjective," "patient reported"	70

instrument measures the concept it is intended to measure (often assessed through content validity, construct validity, and known groups validity).<sup>11</sup> Interpretation guidelines generally refer to information regarding interpretation of an instrument's scoring.<sup>11</sup> Psychometric properties presented in the Appendix for each instrument typically include properties of total scores or domain scores but not NRS items on their own. Analyses conducted and statistics presented for instruments reviewed vary from study to study. Therefore, measurement properties presented for each instrument represent available information as presented in the literature and are not consistent. The Appendix can be used to understand the level of information available for each instrument as a whole rather than for individual items.

## Results

Based on the literature and conference abstract search strategies, a list of 97 PROs used in published sleep/insomnia research was identified. Of these, 12 were excluded from further review because they were more general HRQL measures, and not specific to sleep. Of the remaining 85 PROs, 26 were excluded from further review because the instrument or item(s) was not publicly available. A copy of the instrument or instrument items was located for 59 PROs. Two researchers independently reviewed each of the 59 PROs to determine whether or not the instrument contained NRS content. Inter-rater reliability for the review of the 59 PROs was 90.5%. After review, 33 were deemed not to contain NRS content according to the definition provided above, and a total of 26 instruments were determined to contain NRS content and were retained for detailed review. Instruments retained for review as well as their NRS concepts of measurement are presented in Table 3. Available measurement properties for instruments reviewed are presented in the Appendix.

Only one of the 26 PROs identified to contain NRS content (The Sleep Assessment Questionnaire)<sup>9,17,18</sup> specifically evaluates the measurement concept of non-restorative sleep with a domain score. This instrument has evidence of content validity through qualitative work with patients.<sup>17</sup> The instrument has been demonstrated to have excellent test-retest reliability and construct validity.<sup>17,18</sup> Further, the NRS domain score has been demonstrated to be sensitive in evaluating unrefreshing sleep in a population of fibromyalgia and chronic fatigue syndrome patients.<sup>9</sup> However, in reviewing the instrument, only one item specifically met our criteria for NRS content (waking up not feeling refreshed or rested). Furthermore, psychometric work has included sleep disorder patients of varying etiologies, and little is known about the instrument's performance for evaluating NRS in an insomnia population.

As summarized in Table 3, many of the remaining PROs measured more general aspects of sleep patterns and disturbance, and often contained 1–2 items evaluating aspects of nighttime sleep experiences or morning or daytime restoration and refreshment.

Of the PROs reviewed, the Pittsburgh Insomnia Rating Scale (PIRS)<sup>19</sup> contained the largest number of items (4 items) evaluating both nighttime and daytime aspects of NRS. Three of the four NRS items evaluated quality of nighttime sleep, and the additional NRS item evaluated being unrefreshed due to poor quality of sleep.<sup>19</sup> This instrument was not designed for NRS specifically, and the standard scoring of this instrument does not produce an NRS domain score that could be used to evaluate NRS alone. Further, limited psychometric evaluation has been conducted for this measure as a whole. The only published psychometric evaluation study for the PIRS is an abstract, rather than a full manuscript (see Moul et al., 2002<sup>19</sup>). The information provided in this abstract does not indicate whether content validity work to increase sensitivity and precision of this instrument has been conducted.

The remaining 24 PROs typically contained 1 or 2 items evaluating some aspect of subjective sleep quality and/or morning or daytime restoration and refreshment. None had standard scoring which included an NRS domain score. Thus, the psychometric work that is available for these instruments does not provide insights into their suitability for evaluating the concept of NRS specifically.

Nine PROs contained a single item evaluating overall subjective sleep experience. The exact wording, recall periods, and response options varied between instruments (see Table 3 for NRS content). For example, some instruments asked a global sleep quality item, while other instruments evaluated more specific aspects of sleep experience, including: whether sleep was good or poor, calm or restless (e.g., Karolinska Sleep Diary);<sup>20</sup> quiet sleep (Medical Outcomes Study Sleep Scale);<sup>21</sup> depth of sleep/deep sleep (St. Mary's Hospital Questionnaire);<sup>22</sup> soundness of sleep (Post-Sleep Evaluation Questionnaire)<sup>23</sup>; and restorative function of sleep (Sleep-EVAL system).<sup>24</sup> Further, recall periods ranged from 1 to 3 months (e.g., Pittsburgh Sleep Quality Index),<sup>25</sup> to the previous night's sleep (e.g., Lack's Sleep Diary).<sup>26</sup> Response scales varied from 3, 4, or 5 point Likert-type Scales (e.g., Post-Sleep Questionnaire)<sup>27</sup> to 100 mm visual-analog scale (VAS)-type scales (e.g., Leeds Sleep Evaluation Questionnaire).<sup>28</sup> Thus, there was no consistency in how nighttime sleep quality was evaluated among instruments. This lack of standardization does not indicate that measures are invalid. However, there was no content validity work in the form of qualitative patient research conducted in the development of any of these instruments, making it difficult to determine which instrument's item(s) and format might be optimal for evaluating subjective sleep experience. Further, this lack of standardization in the operationalization and definition of NRS as evidenced by variability in measurement of this construct makes it difficult to compare results across studies when instruments with different item concepts are used.

In addition to instruments that contained items evaluating only nighttime sleep experience, 14 instruments contained 2–3 items evaluating both nighttime sleep experience and some aspect of morning or daytime refreshment/restoration. Items evaluating morning/daytime refreshment again varied in specific concept measured, recall periods, and response formats. For example, measurement concepts included: difficulty getting up, not feeling rested in the morning (e.g., Angst's Questions,<sup>29</sup> Leeds Sleep Evaluation Questionnaire,<sup>28</sup> Medical Outcomes Study Sleep Scale<sup>21</sup>); feeling excessively sleepy after awakening (e.g., Basic Nordic Sleep Questionnaire,<sup>30</sup> Patient Morning Questionnaire<sup>31</sup>); feeling refreshed after awakening (e.g., Karolinska Sleepiness Diary<sup>20</sup>); and waking up tired versus rested (Post-Sleep Inventory,<sup>32</sup> Subjective Evaluation of Sleep<sup>33</sup>). With the various item concepts, response options and recall periods also varied. While some instruments did have some evidence of reliability and validity for the various domain or total scores which contained the daytime NRS item(s),

**Table 3**  
NRS content.

Measure name	Measurement
Angst's questions Angst et al., 1989 <sup>29</sup>	NRS Content (2 items): Quality of sleep (good, moderate, poor). Difficulty getting up, not feeling rested in the morning.
Athens Insomnia Scale (AIS-8) and short version (AIS-5) Soldatos et al., 2000 <sup>36</sup> Soldatos et al., 2003 <sup>37</sup>	NRS Content (1 item): Overall quality of sleep.
Basic Nordic Sleep Questionnaire Partinen et al., 1995 <sup>30</sup>	NRS Content (2 items): "How well" sleeping. Excessive sleepiness in the morning.
General Sleep Disturbance Scale Lee, 1992 <sup>38</sup> Lee, 2007 <sup>39</sup>	NRS Content (1 item): Sleeping Poorly.
Jenkins Sleep Problem Scale Jenkins et al., 1988 <sup>40</sup>	NRS Content (1 item): Wake up feeling tired/worn out.
John's Instrument Johns et al., 1971 <sup>41</sup>	NRS Content (1 item): Usual sleep (Good – Bad).
Karolinska Sleepiness Diary Akerstedt et al., 1994 <sup>20</sup> Keklund et al., 1997 <sup>42</sup>	NRS Content (3 items): How sleep (poor – good). Calm sleep (restless – calm). Feeling refreshed after awakening (completely – not at all).
Lacks' Daily Sleep Diary Lacks, 1987 <sup>26</sup>	NRS Content (2 items): Quality of last night's sleep (Excellent – Very poor). How rested this morning? (Very rested – Poorly rested).
Leeds Sleep Evaluation Questionnaire (LSEQ) Parrott and Hindmarch, 1980 <sup>28</sup> Tarrasch et al., 2003 <sup>43</sup> PROQOLID	NRS Content (2 items): Compare the quality of sleep using the medication with non-medicated sleep. (More restless than usual – More restful than usual). Feel on waking? (Tired – alert).
Medical Outcomes Study Sleep Scale (MOS-SS) Hays and Stewart, 1992 <sup>21</sup> Rejaset al., 2007 <sup>44</sup> Lau et al., 2006 <sup>45</sup> Hays et al. 2005 <sup>46</sup> Spritzer & Hays 2003 <sup>47</sup>	NRS Content (2 items): Feel that your sleep was not quiet (All of the time – None of the time) Get enough sleep to feel rested upon waking (All of the time – None of the time).
Patient Morning Questionnaire (PMQ) Krystal et al., 2008 <sup>31</sup> Buchanan et al., 2005 <sup>48</sup>	NRS Content (2 items): Quality of Sleep measured using 4 point categorical scale. Level of sleepiness in the morning.
Pittsburgh Insomnia Rating Scale (PIRS) Moul et al., 2002 <sup>19</sup>	NRS Content (4 items): Overall sleep quality (100 mm VAS) Sleep that doesn't fully refresh you (Not bothered at all – Severely bothered). Your sleep quality, compared to most people (Excellent – Poor). The soundness of sleep (Excellent – Poor).
Pittsburgh Sleep Diary Monk et al., 1994 <sup>49</sup>	NRS Content (1 item): Sleep Quality VAS scale (Very bad – Very good).

**Table 3** (continued)

Measure name	Measurement
Pittsburgh Sleep Quality Index (PSQI) Buysse et al., 1989 <sup>25</sup> PROQOLID	NRS Content (1 item): Sleep quality overall (Very good – Very bad).
Post-Sleep Evaluation Questionnaire Hoch et al., 1987 <sup>23</sup>	NRS Content (2 items): How restless was your sleep? How soundly did you sleep?
Post-sleep inventory Webb et al., 1976 <sup>32</sup> Webb et al., 1978 <sup>50</sup>	NRS Content (2 items): Lightest sleep possible – deepest sleep possible. Woke up extremely tired – woke up as rested as possible.
Post-Sleep Questionnaire Porter and Horne, 1981 <sup>27</sup>	NRS Content (1 item): Quality of your sleep last night (Much better than normal – Much worse than normal).
Quality of Life in Insomniacs Rombaut et al., 1990 <sup>51</sup> Mayers et al., 2003 <sup>52</sup>	NRS Content (2 items): Quality of sleep. Quality of waking.
Sleep Assessment Questionnaire (SAQ) Cesta et al., 1996 <sup>17</sup> Cesta et al., 1997 <sup>18</sup> Cesta et al., 1999 <sup>9</sup>	NRS Content (1 item): Waking up not refreshed or rested.
Sleep-EVAL System Ohayon et al., 1997 <sup>24</sup> Ohayon et al., 1999 <sup>53</sup>	NRS Content (2 items): Restorative function of sleep. Depth of sleep.
Spielman Insomnia Symptom Questionnaire (SISQ) Spielman et al., 1987 <sup>54</sup>	NRS Content (1 item): Sleep quality.
St. Mary's Hospital Sleep Questionnaire (SMHSQ) Ellis et al., 1981 <sup>22</sup>	NRS Content (3 items): Light vs. Deep Sleep. How well sleep (Very badly – Very well). How clear-headed feel in the morning (Still very drowsy indeed – Very alert).
Subjective Evaluation of Sleep (Post-Sleep Inventory) Schneider-Helmert and Kumar, 1995 <sup>33</sup>	NRS Content (2 items): Sleep quality (100 mm VAS). Not rested after sleep.
Verran and Snyder-Halpern Sleep Scale (VSH) Synder-Halpern and Verran, 1987 <sup>55</sup>	NRS Content (3 items): Subjective quality of sleep. Soundness of sleep. Rested upon awakening (VAS: awoke exhausted – Awoke refreshed).
WHO Composite International Diagnostic Interview Wittchen, 1994 <sup>34</sup>	NRS Content (3 items): Feel fatigued during the day because of poor sleep (Never–Often). Feel refreshed after sleeping (Never – Often). Wake up feeling rested (Never – Often)
Woman's Health Initiative Insomnia Rating Scale Levine et al., 2003 <sup>56</sup> Levine et al., 2005 <sup>57</sup>	NRS Content (1 item): Typical night's sleep (Very sound or restful – Very restless).

NRS, Non-restorative sleep, VAS, visual-analog scale, WHO, World Health Organization.

none had any evidence of content validity work in the form of qualitative patient research, making it difficult to determine which instrument's item(s) and format might be optimal for evaluating daytime aspects of NRS.

Finally, the World Health Organization (WHO) Composite International Diagnostic Interview contained 3 items evaluating daytime aspects of NRS (wake up feeling rested; feeling fatigued because of poor sleep quality; feeling refreshed after sleeping<sup>34</sup>). No items were identified in the WHO instrument which evaluated subjective aspects of nighttime sleep quality.

## Discussion and conclusions

The objective of this literature and instrument review was to identify and evaluate the suitability of available PRO instruments for measuring non-restorative sleep symptoms in insomnia populations. Consistent with definitions in the literature, identified sleep measures were reviewed for NRS domain scores and/or item content, which was operationalized in this research as items that were related to subjective assessment of sleep experience (including quality of sleep) and/or refreshment in the morning or throughout the day. Thus, instruments were selected for further review that had face validity of NRS content. Despite the attention NRS has recently received in the literature and in the clinical community,<sup>3,10</sup> and despite the large number of patient-reported sleep-related measures available in the public domain, we did not identify in the literature any NRS-specific instruments, and only one instrument identified included a specific NRS domain score (e.g., the Sleep Assessment Questionnaire<sup>17,18</sup>). Further, the instruments which contained NRS items had variable item concepts, response scales, and recall periods.

Among the instruments which evaluated non-restorative nighttime sleep experience, there was no standardized way of defining or evaluating this concept; item stems, recall periods, and response options all differed between instruments. Among instruments that evaluated morning or daytime experiences of NRS, item stems, recall period, and response options differed between the instruments evaluating this concept. Given differing item concepts included in different instruments, operationalization and therefore definitions of NRS continue to be variable across studies.

The Sleep Assessment Questionnaire was the only instrument identified which includes an NRS domain score. However, only one item in the instrument seems to evaluate daytime aspects of NRS. The instrument also does not contain any items evaluating nighttime aspects of NRS, which according to the definition of NRS presented in the literature (e.g., Morlock et al.<sup>4</sup>, Ohayon and Hong<sup>5</sup>) suggests that this instrument may not comprehensively capture all relevant NRS symptom experiences.

The results from this review suggest that while a number of measures exist that evaluate some aspect of NRS, the majority of measures identified do not adequately evaluate both nighttime and daytime aspects of NRS as a distinct entity or set of symptoms. The lack of available instruments to evaluate NRS as a measurement concept on its own may not be entirely surprising given that as one of the core symptoms of insomnia, NRS symptom items may likely be included in sleep measures that evaluate all symptoms of insomnia (for example, with items evaluating sleep latency and maintenance). Given that NRS is a subjective concept that may be multi-dimensional (e.g., have nighttime and daytime aspects) and given that NRS symptoms may be a target of treatment intervention, its specific measurement should be further studied and standardized. This literature review made clear that operationalization of NRS is variable and that little qualitative research with patients has been conducted to develop a measure consistent with

patients' experiences and that comprehensively evaluates this concept. Since a variety of items across diverse measures were identified in the literature, one option would be to further validate items and potentially use them together in a scale that evaluates the various dimensions of NRS. However, very little evidence of content validity was found for any of the instruments. In the absence of a standard definition of NRS and without qualitative work with patients, it is not possible to determine whether using items from the identified instruments to form a single scale would comprehensively evaluate all relevant aspects of NRS from patients' perspectives. Thus, before a patient-reported instrument is developed to evaluate NRS specifically, it is essential that patients experiencing NRS symptoms provide input into various aspects of measurement including item concepts, recall period, and response format, in order to ensure that a new measure is precise and sensitive to optimally evaluate NRS symptom experience and changes in NRS symptoms with a treatment intervention.

We would recommend as a first step in understanding the symptom of NRS in insomnia patient populations that qualitative work with patients with different insomnia severity levels, as well as patients with NRS only (i.e., patients without difficulty initiating and/or maintaining sleep), be conducted. Information from the literature, sleep experts, and patients can be used to develop a measurement tool that would sensitively evaluate NRS for this patient population. We suggest that an instrument which evaluates NRS should take into account both nighttime experiences and daytime experiences.

Once information is available regarding the NRS experience in insomnia populations, additional qualitative work could be conducted with patients who suffer from NRS as a result of other conditions (for example, Obstructive Sleep Apnea) to determine whether NRS is similar or different across conditions. If the experience of NRS is similar across conditions, a measure that is used in insomnia may also be suitable for measuring NRS in other populations.

This literature review revealed discrepancies in the definition of NRS and gaps that exist in understanding and characterizing NRS and the causes and consequences of NRS. It does appear, however, that NRS may occur as part of primary insomnia, as part of other chronic diseases, and it may sometimes occur even in the absence of difficulty initiating and maintaining sleep.<sup>6,8,9</sup> Conducting qualitative work with patients with NRS of varying etiologies will also help to refine the definition of NRS. More consistent and clear definitions of NRS should aid in standardization of diagnosis and management of NRS symptoms, regardless of etiology.

One limitation of this review was that of the 85 Sleep PROs identified, we could not locate copies of 26 of the PROs. Often this occurred when a PRO was developed for a specific study, and was therefore mentioned in the methods section but no other information was found in the literature about this PRO. It is possible that some of these study-specific or privately-used PROs do contain NRS content. However, since these PROs are not available in the public domain, nor was further information surrounding their psychometric properties found in the literature, it is unlikely that they would be suitable for evaluating NRS in a clinical trial setting.

Currently, the Patient-Reported Outcome Measurement Information System (PROMIS) network is developing item banks to cover sleep disturbance and wake disturbance domains. The sleep disturbance scale focuses on perceived sleep quality, sleep depth and restoration, and perceived adequacy of and satisfaction with sleep. The wake disturbance scale covers the level of waking alertness, sleepiness, and function related to overall sleep-wake function.<sup>35</sup> While complete psychometric data are not yet published in the scientific literature, these item banks may provide

a potential pool of items that may be useful for developing an NRS-specific assessment instrument.

Based on these results, we conclude that there is no reliable and valid instrument available in the public domain that is suitable for comprehensively and specifically evaluating NRS symptom severity and treatment response with confidence in research or clinical settings. Further, while diagnostic criteria, treatment guidelines, and epidemiological studies provide varying clinical definitions of NRS, little is known about how patients describe their symptoms and what they view as the most relevant aspects of NRS and its daytime consequences. A psychometrically sound measurement tool to quantify NRS severity and response to interventions is critical to advance our understanding of NRS. Further, the development of a standardized measurement tool for NRS will allow for consistent measurement of this important concept in clinical studies, allowing for comparisons of treatment efficacy results across studies. Whether instruments are developed based on

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### Appendix. Supplementary information

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.smrv.2009.10.002.

### References

- \*1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th ed. Washington, DC: American Psychiatric Association; 2000.
- \*2. American Academy of Sleep Medicine. *International classification of sleep disorders, revised: diagnostic and coding manual*. Chicago, Illinois: American Academy of Sleep Medicine; 2001.
- \*3. Stone KC, Taylor DJ, McCrae CS, Kalsekar A, Lichstein KL. Nonrestorative sleep. *Sleep Med Rev* 2008 Aug;12(4):275–88.
- \*4. Morlock R, Tan M, Mitchell D. Prevalence and correlates of nonrestorative sleep in those 65 years and older. *Sleep Med* 2006;6(s2):s123.
5. Ohayon MM, Hong SC. Prevalence of insomnia and associated factors in South Korea. *J Psychosom Res* 2002 Jul;53(1):593–600.
- \*6. Ohayon MM. Prevalence and correlates of nonrestorative sleep complaints. *Arch Intern Med* 2005 Jan 10;165(1):35–41.
7. Ohayon MM, Roth T. What are the contributing factors for insomnia in the general population? *J Psychosom Res* 2001 Dec;51(6):745–55.
8. Moldofsky H. Nonrestorative sleep, musculoskeletal pain, fatigue, and psychological distress in chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, temporal mandibular joint dysfunction disorders. In: Yehuda S, editor. *Chronic fatigue syndrome*. New York, NY: Plenum Press; 1997. p. 95–117.
9. Cesta A, Moldofsky H, Sammut C. The sensitivity and specificity of the Sleep Assessment Questionnaire<sup>®</sup> (SAQ<sup>®</sup>) as a measure of non-restorative sleep. *Sleep* 1999;22(1 Suppl.):14.
- \*10. Deutsche Gesellschaft fuer Schlafforschung und Schlafmedizin. Leitlinie S2: Nicht erholsamer Schlaf. AWMF-Leitlinien-Register Nr. 063/001. [Guideline S2: Non-restorative sleep. AWMF registry number 063/001.]. Available from: [http://www.charite.de/dgsm/dgsm/akkreditierung\\_leitlinie.php](http://www.charite.de/dgsm/dgsm/akkreditierung_leitlinie.php) [accessed 06.03.09].
- \*11. Scientific Advisory Committee of the Medical Outcomes Trust. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res* 2002 May;11(3):193–205.
- \*12. Food and Drug Administration. Draft guidance for industry on patient-reported outcome measures: use in medical product development to support labeling claims. *Federal Register* 2006;71(23):5862–3.
- \*13. Leidy NK, Vernon M. Perspectives on patient-reported outcomes: content validity and qualitative research in a changing clinical trial environment. *Pharmacoeconomics* 2008;26(5):363–70.
- \*14. Revicki DA, Gnanasakthy A, Weinfurt K. Documenting the rationale and psychometric characteristics of patient reported outcomes for labeling and promotional claims: the PRO Evidence Dossier. *Qual Life Res* 2007 May;16(4):717–23.
15. Devine EB, Hakim Z, Green J. A systematic review of patient-reported outcome instruments measuring sleep dysfunction in adults. *Pharmacoeconomics* 2005;23(9):889–912.
16. Moul DE, Hall M, Pilkonis PA, Buysse DJ. Self-report measures of insomnia in adults: rationales, choices, and needs. *Sleep Med Rev* 2004 Jun;8(3):177–98.
17. Cesta A, Moldofsky H, Sammut C. The University of Toronto Sleep Assessment Questionnaire<sup>®</sup> (SAQ<sup>®</sup>). *Sleep Res* 1996;25:486.
18. Cesta A, Moldofsky H, Sammut C. The University of Toronto Sleep Assessment Questionnaire<sup>®</sup> (SAQ<sup>®</sup>). *Sleep Res* 1997;26:646.
19. Moul DE, Pilkonis PA, Miewald JM, Carey TJ, Buysse DJ. Preliminary study of the test-retest reliability and concurrent validities of the Pittsburgh Insomnia Rating Scale (PIRS). *Sleep* 2002;25(Abstr. Suppl.):A246–7.
20. Akerstedt T, Hume K, Minors D, Waterhouse J. The subjective meaning of good sleep, an intraindividual approach using the Karolinska Sleep Diary. *Percept Mot Skills* 1994 Aug;79(1 Pt 1):287–96.

\* The most important references are denoted by an asterisk.

### Practice points

Non-restorative sleep (NRS) is one of the core symptoms of primary insomnia according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition;<sup>1</sup> however, NRS has been less consistently defined and less well-studied than other symptoms of primary insomnia.

NRS has been receiving increasing attention in the literature and as a potential target of treatment interventions.

Despite attention given to NRS symptoms, little has been published about how patients experience or define NRS, and this literature review demonstrated that there is no reliable and valid instrument available in the public domain that is suitable for comprehensively and specifically evaluating NRS symptom severity and treatment response with confidence in research or clinical settings.

### Research agenda

In the future, we need to conduct qualitative research with patients in order to understand how patients experience and define NRS. Further, we need to develop standardized measurement tools which take patients' perspectives into account for evaluating NRS symptoms. Reliable and valid measurement tools are needed for use in research or clinical settings to evaluate NRS symptom severity and treatment-related changes.

existing items, or if a new instrument is developed or adapted to evaluate NRS, it will be essential to conduct both qualitative work with patients in order to inform measurement concepts and format of an NRS patient-reported outcome measure, and quantitative work to establish reliability and validity.

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21. Hays RD, Stewart AL. Sleep measures. In: Stewart AL, Ware JE, editors. *Measuring functioning and well-being: the medical outcomes study approach*. Durham, NC: Duke University Press; 1992. p. 235–59.
22. Ellis BW, Johns MW, Lancaster R, Raptopoulos P, Angelopoulos N, Priest RG. The St. Mary's Hospital sleep questionnaire: a study of reliability. *Sleep* 1981;**4**(1):93–7.
23. Hoch CC, Reynolds 3rd CF, Kupfer DJ, Berman SR, Houck PR, Stack JA. Empirical note: self-report versus recorded sleep in healthy seniors. *Psychophysiology* 1987;**24**(3):293–9.
24. Ohayon MM, Guilleminault C, Paiva T, Priest RG, Rapoport DM, Sagales T, et al. An international study on sleep disorders in the general population: methodological aspects of the use of the Sleep-EVAL system. *Sleep* 1997 Dec;**20**(12):1086–92.
25. Buysse DJ, Reynolds 3rd CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989 May;**28**(2):193–213.
26. Lacks P. *Behavioral treatment for persistent insomnia*. 1st ed. New York: Pergamon Press; 1987.
27. Porter JM, Horne JA. Exercise and sleep behaviour. A questionnaire approach. *Ergonomics* 1981 Jul;**24**(7):511–21.
28. Parrott AC, Hindmarch I. The Leeds Sleep Evaluation Questionnaire in psychopharmacological investigations – a review. *Psychopharmacology (Berl)* 1980;**71**(2):173–9.
29. Angst J, Vollrath M, Koch R, Dobler-Mikola A. The Zurich study. VII. Insomnia: symptoms, classification and prevalence. *Eur Arch Psychiatry Neurol Sci* 1989;**238**(5–6):285–93.
30. Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995 Jun;**4**(S1):150–5.
31. Krystal AD, Erman M, Zammit GK, Soubrane C, Roth T. Long-term efficacy and safety of zolpidem extended-release 12.5 mg, administered 3 to 7 nights per week for 24 weeks, in patients with chronic primary insomnia: a 6-month, randomized, double-blind, placebo-controlled, parallel-group, multicenter study. *Sleep* 2008 Jan 1;**31**(1):79–90.
32. Webb WB, Bonnet M, Blume G. A post-sleep inventory. *Percept Mot Skills* 1976;**43**:987–93.
33. Schneider-Helmert D, Kumar A. Sleep, its subjective perception, and daytime performance in insomniacs with a pattern of alpha sleep. *Biol Psychiatry* 1995;**37**(2):99–105.
34. Wittchen HU. Reliability and validity studies of the WHO – Composite International Diagnostic Interview (CIDI): a critical review. *J Psychiatr Res* 1994 Jan–Feb;**28**(1):57–84.
- \*35. PROMIS. Available from: [www.nihpromis.org](http://www.nihpromis.org).
36. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. *J Psychosom Res* 2000 Jun;**48**(6):555–60.
37. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. The diagnostic validity of the Athens Insomnia Scale. *J Psychosom Res* 2003 Sep;**55**(3):263–7.
38. Lee KA. Self-reported sleep disturbances in employed women. *Sleep* 1992;**15**(6):493–8.
39. Lee SY. Validating the General Sleep Disturbance Scale among Chinese American parents with hospitalized infants. *J Transcult Nurs* 2007 Apr;**18**(2):111–7.
40. Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol* 1988;**41**(4):313–21.
41. Johns MW, Gay TJ, Goodyear MD, Masterton JP. Sleep habits of healthy young adults: use of a sleep questionnaire. *Br J Prev Soc Med* 1971 Nov;**25**(4):236–41.
42. Keklund G, Akerstedt T. Objective components of individual differences in subjective sleep quality. *J Sleep Res* 1997 Dec;**6**(4):217–20.
43. Tarrasch R, Laudon M, Zisapel N. Cross-cultural validation of the Leeds sleep evaluation questionnaire (LSEQ) in insomnia patients. *Hum Psychopharmacol* 2003 Dec;**18**(8):603–10.
44. Rejas J, Ribera MV, Ruiz M, Masramon X. Psychometric properties of the MOS (Medical Outcomes Study) Sleep Scale in patients with neuropathic pain. *Eur J Pain* 2007 Apr;**11**(3):329–40.
45. Lau DT, Morlock RJ, Hill CD. Psychometric evaluation of the medical outcomes study-sleep scale in persons with overactive bladder. *Clin Ther* 2006 Dec;**28**(12):2119–32.
46. Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. *Sleep Med* 2005 Jan;**6**(1):41–4.
47. Spritzer KL, Hays RD. MOS sleep scale: a manual for use and scoring, version 1.0. Los Angeles, CA; 2003.
48. Buchanan T, Ali T, Heffernan TM, Ling J, Parrott AC, Rodgers J, et al. Nonequivalence of on-line and paper-and-pencil psychological tests: the case of the prospective memory questionnaire. *Behav Res Methods* 2005 Feb;**37**(1):148–54.
49. Monk TH, Reynolds 3rd CF, Kupfer DJ, Buysse DJ, Coble PA, Hayes AJ, et al. The Pittsburgh sleep diary. *J Sleep Res* 1994;**3**:111–20.
50. Webb WB, Bonnet MH. The sleep of 'morning' and 'evening' types. *Biol Psychol* 1978 Sep;**7**(1–2):29–35.
51. Rombaut N, Maillard F, Kelly F, Hindmarch I. The quality of life of insomniacs questionnaire (QOLI). *Med Sci Res* 1990;**18**:845–7.
52. Mayers AG, van Hooff JC, Baldwin DS. Quantifying subjective assessment of sleep and life-quality in antidepressant-treated depressed patients. *Hum Psychopharmacol* 2003;**18**(1):21–7.
53. Ohayon MM, Caulet M, Arbus L, Billard M, Coquerel A, Guieu JD, et al. Are prescribed medications effective in the treatment of insomnia complaints? *J Psychosom Res* 1999;**47**(4):359–68.
54. Spielman AJ, Saskin P, Thorpy MJ. Treatment of chronic insomnia by restriction of time in bed. *Sleep* 1987 Feb;**10**(1):45–56.
55. Snyder-Halpern R, Verran JA. Instrumentation to describe subjective sleep characteristics in healthy subjects. *Res Nurs Health* 1987 Jun;**10**(3):155–63.
56. Levine DW, Kaplan RM, Kripke DF, Bowen DJ, Naughton MJ, Shumaker SA. Factor structure and measurement invariance of the Women's Health Initiative Insomnia Rating Scale. *Psychol Assess* 2003 Jun;**15**(2):123–36.
57. Levine DW, Dailey ME, Rockhill B, Tipping D, Naughton MJ, Shumaker SA. Validation of the Women's Health Initiative Insomnia Rating Scale in a multicenter controlled clinical trial. *Psychosom Med* 2005 Jan–Feb;**67**(1):98–104.