

A thorough psychometric comparison between Athens Insomnia Scale and Insomnia Severity Index among patients with advanced cancer, *Journal of Sleep Research*, in press.

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Summary

For patients with cancer, sleep disturbance is commonplace. Using classical test theory and Rasch analyses, the present study compared two commonly used psychometric instruments for insomnia – Athens Insomnia Scale (AIS) and Insomnia Severity Index (ISI) – among patients with advanced cancer. Through convenience sampling, patients with cancer at stage III or IV ($n=573$; 326 males; mean age=61.3 years; $SD=10.7$) from eight oncology units of university hospitals in Iran participated in the study. All the participants completed the AIS, ISI, Edmonton Symptom Assessment Scale (ESAS), Hospital Anxiety and Depression Scale (HADS), General Health Questionnaire-12 (GHQ-12), Epworth Sleepiness Scale (ESS), and Pittsburgh Sleep Quality Index (PSQI). Additionally, 433 participants wore an Actigraph device for two continuous weekdays. Classical test theory and Rasch analysis both supported the construct validity for AIS (factor loadings from confirmatory factor analysis [CFA] = 0.61 to 0.87; test-retest reliability = 0.72 to 0.82; infit mean square [MnSq] = 0.81 to 1.17; outfit MnSq = 0.79 to 1.14) and for ISI (factor loadings from CFA = 0.61 to 0.81; test-retest reliability = 0.72 to 0.82; infit MnSq = 0.72 to 1.14; outfit MnSq = 0.76 to 1.11). Both AIS and ISI had significant associations with ESAS, HADS, GHQ-12, ESS, and PSQI, as well as having good sensitivity and specificity. Significant differences in the actigraphy measure were found between insomniacs and non-insomniacs based on AIS or ISI score. With promising results, healthcare providers can use either AIS or ISI to understand the insomnia of patients with advanced cancer.

Keywords: confirmatory factor analysis; insomnia; sleep disorders; oncology; psychometrics; Rasch

Introduction

For patients with cancer, sleep disturbance is a common occurrence particularly among those with breast cancer, lung cancer, head and neck cancer, and gynecologic cancer (Langford et al., 2012). In previous studies, the prevalence of disturbed sleep in patients with cancer has varied between 30% (Miaskowski et al., 2011) to 93.1% (Lin et al., 2013), which is higher than the 9% (Bastien et al., 2001) to 33% (Ohayon & Roth, 2003) found in the general population.

Sleep disturbances appear to be even more common in patients with advanced cancer (Mercadante et al., 2017). Approximately half to three-quarters of outpatients attending cancer or palliative care clinics complain of some sleep disturbances (George et al., 2016; Yennurajalingam et al., 2015). These complaints were heterogeneous in nature and involved difficulties in falling asleep, trouble staying asleep, early morning awaking, or a complaint of nonrestorative sleep with a poor corresponding sleep efficiency (Savard & Morin, 2001). These complaints are all related to unsatisfactory sleep quantity and quality or insomnia. According to the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5), criteria for insomnia include a series of complaints of difficulty initiating/maintaining sleep, nonrestorative sleep for at least one month, and impairment of daily functioning (American Psychiatric Association, 2013). Sleep disturbance has been proven to be associated with poor clinical outcomes in terms of lower overall survival, more rapid disease progress, and poorer treatment response (Innominato et al., 2015). As a result, insomnia problems in patients with advanced cancer should not be neglected.

Patients with advanced cancer usually have numerous physical and psychosocial needs, including sleep problems. Unfortunately, oncologists and healthcare providers may pay too little attention or not have sufficient time to evaluate the cause for the sleep disturbance among patients with advanced cancer (Mercadante et al., 2017). Therefore, healthcare

providers need brief and robust instruments for assessing insomnia with sound psychometric properties. The Athens Insomnia Scale (AIS) and the Insomnia Severity Index (ISI) were developed according to standard diagnostic criteria for insomnia (Chiu et al., 2016). More specifically, the AIS uses the sleep difficulty described in the tenth International Statistical Classification of Diseases and Related Health Problems (ICD-10) (Soldatos et al., 2000). The ISI adopts the diagnostic criteria for insomnia outlined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), and the International Classification of Sleep Disorders (ICSD) (Bastien et al., 2001).

Moreover, the AIS contains two items assessing sleep duration and sleepiness which are not shared by the ISI. Additionally, the ISI emphasizes individuals' worry about their sleep and noticeability of their sleep problems to others. Therefore, the AIS and ISI feature some dissimilarities in assessing insomnia. Nevertheless, both AIS and ISI have been found to be valid and reliable instruments for patients with cancer (Savard et al., 2005; Sun et al., 2011). Therefore, using either the AIS or ISI may assist healthcare providers to quickly assess insomnia for patients with advanced cancer. More importantly, among the well-established instruments on insomnia (e.g., the Sleep Condition Indicator) (Espie et al., 2014), the AIS and ISI are the most commonly used tools in both research and clinical practice.

However, it is unclear whether the two instruments (AIS and ISI) are *equally good* in assessing insomnia for patients with advanced cancer. Given that the AIS and ISI are both brief instruments (eight items in the AIS, and seven in the ISI) which increase the likelihood that all items will be completed, the major concern in defining whether the AIS and ISI are equally good is their psychometric properties (including factorial structure, reliability, and different types of validity). Unfortunately, psychometric properties of the AIS and ISI are lacking. To the best of the present authors' knowledge, only two previous studies have simultaneously compared the psychometric properties of the AIS and ISI. One was on

adolescents (Chung et al., 2011), and the other was a meta-analysis (Chiu et al., 2016).

Although both studies shared similar conclusions on the promising properties of both the AIS and ISI, their conclusions may not be generalized to patients with advanced cancer because most of the samples used in the psychometric testing were not patients with cancer. More specifically, in the meta-analysis (Chiu et al., 2016), there were only two studies separately assessing the psychometric properties of AIS and ISI: the AIS testing 195 patients with cancer (Sun et al., 2011) and the ISI testing 210 patients with cancer (Savard et al., 2005). As a result, the current literature lacks direct comparisons of the psychometric properties between the AIS and ISI among patients with advanced cancer.

Another consideration in the AIS and ISI is whether such subjective measures can accurately assess and quantify the insomnia. However, to the best of the present authors' knowledge, most previous studies have used clinical insomnia diagnosis or subjective measures (e.g., self-reported depression) as the external criteria to examine the criterion-related validity for the AIS and ISI (Enomoto et al., 2018; Gómez-Benito et al., 2011; Jeong et al., 2015; Morin et al., 2011). Therefore, empirical data on an objective sleep measure (i.e., actigraphy) is needed to verify the psychometric properties of such subjective measures (Lin et al., 2018).

The present study examined the psychometric properties of the AIS and ISI among Iranian patients with advanced cancer. More specifically, two different approaches in psychometric testing were applied (i.e., classical test theory and Rasch models in the modern test theory). Additionally, sensitivity and specificity of AIS and ISI were performed to obtain the optimal cutoff for indicating insomnia. Finally, a series of external criteria, including objectively measured sleep, were used to further understand AIS and ISI properties. It was anticipated that both the AIS and ISI would have satisfactory properties (including good internal consistency, acceptable test-retest reliability, verified unidimensional structures, and

supported measurement invariance or differential item functioning [DIF] across sex and insomnia condition) in both classical test theory and Rasch analyses. It was also expected that both the AIS and ISI would have good sensitivity and specificity to detect diagnosed insomnia. Finally, it was hypothesized that the AIS and ISI would have comparable associations with all the external criteria.

Methods

Participants and procedure

The present methodological study was conducted among eight oncology units of university hospitals in Tehran (n=5), Karaj (n=2), and Qazvin (n=1) from June 2015 to October 2018. Patients who met the following criteria were recruited using convenience sampling: (i) histologically verified malignant disease with cancer stage III or IV, (ii) were 18 years of age or older, (iii) understood and communicated in the Persian language, and (iv) provided signed informed consent. Patients were excluded if they (i) were pregnant or lactating, (ii) had scheduled surgery within the next week, (iii) had cognitive problems as assessed by the Mini-Mental State Exam (≤ 23 ; Folstein et al., 1975), and (iv) had substance abuse problems. The study was approved by the ethics committee of the Qazvin University of Medical Sciences. All patients provided written informed consent.

Patients were recruited by three research nurses prior to their follow-up appointment. These nurses rated the level of functional impairment for each patient. The patients were trained to wear an Actigraph device in the hospitals (Ambulatory Monitoring, Inc. USA). Afterward, the patients wore the Actigraph on their wrists in two continuous weekdays of their own choice. Given that Iran has working days on Saturday and Sunday (resting days on Thursday and Friday), the participants selected two continuous days from Saturday to Wednesday.

Measures

Clinical and demographic characteristics. Clinical information was collected from patient's medical records. In addition, three trained psychiatrists, all were unaware of the patients' insomnia conditions prior to the psychiatric interview, assessed the patients to determine whether the patients had insomnia. The interviews were held face-to-face in clinic rooms and the diagnosis was determined using the revised text DSM-IV. Interrater reliability scores between the psychiatrists were acceptable (intraclass correlation coefficient [ICC]=0.88) in pilot testing (n= 36).

Athens Insomnia Scale (AIS). The AIS comprises eight items that assess the severity and effects of insomnia, and all items are rated using a 4-point Likert scale (0=no problem or equivalent meaning; 3=very severe problem or equivalent meaning). A total score is obtained after summing up all responses, and the total score ranges between 0 and 24, where the commonly accepted cutoff is 6 (Jeong et al., 2015). Additionally, a higher AIS score indicates a higher level of insomnia. The psychometric properties of the AIS have been supported in different language versions, including Spanish ($\alpha=0.86$; test-retest reliability using ICC=0.75) (Gómez-Benito et al., 2011), Korean ($\alpha=0.88$; test-retest reliability using ICC=0.94) (Jeong et al., 2015), and Chinese ($\alpha=0.83$; test-retest reliability using Pearson correlation coefficient [r]=0.94) (Sun et al., 2011). However, to the best of our knowledge, there is no Persian version of the AIS. Thus, the authors used the standard translation procedure described below to translate the English AIS into Persian and ensure the linguistic validity.

The linguistic adaptation of AIS was performed through a standard procedure (Beaton et al., 2000) comprising several steps: (i) two bilingual translators who were native Persian speakers translated the English AIS into Persian independently. The translated versions were then synthesized into an interim Persian version via a discussion between both translators and a project manager. The interim Persian version was then translated back into English by two bilingual translators who were fluent in English. Also, the two back-translators were blinded

to the original English AIS. The back-translated English AIS was then assessed by an expert committee (comprising all translators, a methodologist, a health psychologist, a nurse, an oncologist, and a psychometrician). The committee evaluated the wordings and cultural equivalency of the back-translated English and original English AIS. The confirmed Persian AIS was then piloted on 35 patients with advanced cancer to ensure readability and cultural relevance. The final version of AIS was then administered to 573 patients with advanced cancer.

Insomnia Severity Index (ISI). The ISI comprises seven items that assess the severity and effects of insomnia, and all items are rated using a five-point Likert scale (0=no problem; 4=very severe problem). A total score is obtained after summing up all responses, and the total score ranges between 0 and 28, where 0-7 indicates absence of insomnia, 8-14 indicates sub-threshold insomnia, 15-21 indicates moderate insomnia, and 22-28 indicates severe insomnia (Morin et al., 2011). The ISI has been translated into Persian with good internal consistency ($\alpha=0.82$ and 0.87), good test-retest reliability ($ICC=0.84$), and supported convergent validity ($r=0.58$ with Pittsburg Sleep Quality Index) (Yazdi et al., 2012).

Edmonton Symptom Assessment Scale (ESAS). The ESAS comprises 10 items that assess the objective and subjective symptoms of patients with cancer across all stages. All items are rated on a 0-10 scale, where a higher score indicates a worse condition of symptoms. A total score is obtained after summing up all responses and the total score ranges between 0 and 100 (Carvajal et al., 2011). The ESAS has been translated Persian with good internal consistency ($\alpha=0.88$) and good test-retest reliability ($r=0.86$) (Khalili-Parapary et al., 2017).

Hospital Anxiety and Depression Scale (HADS). The HADS comprises 14 items that assess two types of emotional distress: anxiety (seven items) and depression (seven items). All items are rated on a four-point Likert scale (from 0 to 3), where a higher score indicates the greater level of emotional distress. Two subscale scores are obtained after summing up related

responses (score ranges between 0 and 21 for each subscale) with each higher HADS subscale scores indicating higher level of anxiety or depression. The HADS has been translated Persian with good internal consistency ($\alpha=0.82$ in the Anxiety subscale and 0.79 in the Depression subscale) (Lin & Pakpour, 2017).

General Health Questionnaire-12 (GHQ-12). The GHQ-12 comprises 12 items that assess health, especially in psychiatric wellbeing. All items are rated on a four-point Likert scale (from 0 to 3), where a higher score indicates poor health. A total score is obtained after summing up all responses and the total score ranges between 0 and 36. The GHQ-12 has been translated into Persian with good internal consistency ($\alpha=0.87$) and acceptable convergent validity ($r=0.56$ with quality of life measure) (Montazeri et al., 2003).

Epworth Sleepiness Scale (ESS). The ESS comprises eight items that assess severity of daytime sleepiness. All items are rated on a four-point Likert scale (0=would never doze or sleep; 3=high chance of dozing or sleeping). A total score is obtained after summing up all responses and the total score ranges between 0 and 24, where a higher ESS score indicates greater sleepiness. The ESS has been translated into Persian with adequate internal consistency ($\alpha=0.79$) and good test-retest reliability (ICC=0.84) (Imani et al., 2018).

Pittsburgh Sleep Quality Index (PSQI). The PSQI comprises 19 self-rated items that assess sleep quality and disturbances. All items are rated on a four-point Likert scale (from 0 to 3), where a higher score indicated poor sleep quality. A total score is obtained after summing up all responses and the total score ranges between 0 and 57. The PSQI has been translated into Persian with adequate internal consistency ($\alpha=0.77$) (Moghaddam et al., 2012).

Actigraphy. Participants were invited to wear home-based wrist actigraphy (Ambulatory Monitoring, Inc. USA) to provide a measure of objective sleep (e.g., sleep and wake pattern; activity cycle). The sleep pattern was recorded in one-minute epochs and was digitized using the zero-crossing mode to a computer using Action-W software, version 2.6.9905. Following

this, sleep parameters were estimated using a Sadeh algorithm (Lin et al., 2018; Sadeh et al., 1994).

Statistical analysis

Participants' characteristics, including demographics and clinical characteristics, were analyzed using mean and SD (for continuous variables) or frequency and percentage (for categorical variables). Regarding the psychometric properties using classical test theory on the AIS and ISI, McDonald's ω was used to test the internal consistency (a value > 0.7 is preferred); corrected item-total correlation (a value > 0.4 is preferred), average variance extracted (a value > 0.5 is preferred), and composite reliability (a value > 0.6 is preferred) to assess the item coherence; and ICC to examine the test-retest reliability across two weeks (a value > 0.4 is preferred). Additionally, ceiling and floor effects for the AIS and ISI total scores were computed, where a value $< 20\%$ is desirable. Finally, two confirmatory factor analyses (CFAs) – assuming that the AIS and ISI have unidimensional structures (one CFA for AIS and another CFA for ISI) – were conducted to investigate the construct validity. The CFAs were performed using mean- and variance-adjusted weighted least squares (WLSMV) estimator. Comparative fit index (CFI) > 0.9 , Tucker-Lewis index (TLI) > 0.9 , root mean square error of approximation (RMSEA) < 0.08 , and standardized root mean square residual (SRMR) < 0.08 were used to determine a supported CFA.

Regarding the psychometric properties using Rasch on AIS and ISI, the partial credit model was used. Additionally, a separation person and item reliability was adopted (a value > 0.7 is preferred) to assess the reproducibility of respondents and items in responding AIS and ISI items, separation person and item index (a value > 2 is preferred) to examine how the respondents and items spread, infit mean square (MnSq) and outfit MnSq to investigate the item fit (a value between 0.5 and 1.5 is preferred), and differential item functioning (DIF) to

detect whether any AIS or ISI item has substantial DIF across sex or insomnia condition (a DIF contrast < 0.5 is preferred).

Apart from the formal psychometric testing mentioned above, a Receiver Operating Characteristic (ROC) curve and Youden's index were used to examine the best cutoffs for AIS and ISI. Additionally, sensitivity and specificity were computed together with the area under curve (AUC), and an AUC > 0.7 was anticipated. After obtaining the cutoffs, McNemar's test was used to understand whether the cutoffs are consistent with the psychiatric diagnosis and a nonsignificant p -value was expected. Afterward, several Pearson correlations were conducted to understand the associations between the AIS and ISI, and external criteria (anxiety, depression, function status, psychiatric wellbeing, daytime sleepiness, and sleep quality). Finally, different types of pain medications and Actigraph data were used to evaluate whether AIS and ISI cutoffs can effectively differentiate the insomnia severities among patients with advanced cancer.

Results

Participants' characteristics

The 573 patients with advanced cancer had a mean age of 61.3 years (SD=10.7) years, and slightly more than half of them were males (n=326; 56.9%). Additionally, 304 of the participants had cancer stage IV (53.1%), and the remainder had stage III. The patients, on average, had received 8.7 years of education (SD=3.2), had Mini-Mental State Exam score of 24.3 (SD=2.8), a Karnofsky Performance Scale Score at 51.8 (SD=11.6), and were 32.8 months after diagnosis (SD=25.7). The highest three cancer diagnoses were gastrointestinal cancer (n=183; 31.9%), lung cancer (n=108; 18.8%), and breast cancer (n=91; 15.9%; Table 1). Among the 573 participants, 458 agreed to wear the Actigraph and 25 had missing data in the Actigraph reports.

(Insert Table 1 here)

Psychometric properties of the AIS

The AIS demonstrated promising psychometric properties (Table 2). At the item level, acceptances were high (88% to 100%); CFA-derived factor loadings were strong (0.61 to 0.87); corrected item-total correlations were high (0.56 to 0.76); test-retest reliability was satisfactory (0.72 to 0.82); Rasch-derived infit (0.81 to 1.17) and outfit MnSq (0.79 to 1.14) fitted the underlying construct; and no substantial DIF was found across sex (DIF contrast=-0.43 to 0.43) or insomnia condition (DIF contrast=-0.23 to 0.19).

At the scale level using classical test theory (Table 3), the AIS had low ceiling (4.5%) and floor effects (3.9%); satisfactory internal consistency ($\omega=0.88$); acceptable fitness, except for significant χ^2 test, in the CFA (CFI=0.987, TLI=0.980, RMSEA=0.049, and SRMR=0.033); adequate average variance extracted (0.56) and high composite reliability (0.91); low standard error of measurement (2.57); and acceptable test-retest reliability (ICC=0.82). The Rasch analysis also supported the contention that the AIS has promising psychometric properties at scale level: separation reliability (0.88 and 0.84) and separation indices (2.75 and 2.30) were acceptable.

(Insert Tables 2 and 3 here)

Psychometric properties of the ISI

The ISI also demonstrated promising psychometric properties (Table 2). At the item level, acceptances were high (88% to 96%); CFA-derived factor loadings were strong (0.61 to 0.81); corrected item-total correlations were high (0.43 to 0.67); test-retest reliability was satisfactory (0.72 to 0.82); Rasch-derived infit (0.72 to 1.14) and outfit MnSq (0.76 to 1.11) fitted the underlying construct; and no substantial DIF was found across sex (DIF contrast=-0.12 to 0.48) or insomnia condition (DIF contrast=-0.19 to 0.33).

At the scale level using classical test theory (Table 3), the AIS had low ceiling (7.4%) and floor effects (6.1%); satisfactory internal consistency ($\omega=0.79$); acceptable fitness,

including nonsignificant χ^2 test, in the CFA (CFI=0.995, TLI=0.990, RMSEA=0.029, and SRMR=0.023); adequate average variance extracted (0.54) and high composite reliability (0.89); low standard error of measurement (2.00); and acceptable test-retest reliability (ICC=0.79; Table 3). The Rasch analysis also supported the contention that the AIS has promising psychometric properties at scale level: separation reliability (0.98 and 0.78) and separation indices (7.20 and 2.71) were acceptable.

Sensitivity and specificity values for AIS and ISI

The best cutoff score for AIS in distinguishing a patient with advanced cancer having insomnia was 7 with 86% sensitivity and 81% specificity. Also, the AUC for the AIS was 0.86 (95% CI=0.82 to 0.90). The best cutoff score for ISI in distinguishing a patient with advanced cancer having insomnia was 9 with 86% sensitivity and 83% specificity. Also, the AUC for the ISI was 0.82 (95% CI=0.78 to 0.87; Table 4). Additionally, McNemar's test showed that both the AIS and ISI cutoffs were consistent with psychiatric diagnosis ($p=0.54$ for AIS and $p=0.61$ for ISI; Table 5).

(Insert Tables 4 and 5 here)

Relationships between AIS, ISI, and external criteria

AIS and ISI were mutually correlated ($r=0.64$). Additionally, the AIS and ISI shared similar magnitudes of correlations with all the external criteria: $r=0.38$ (AIS) and 0.41 (ISI) with ESAS score; 0.58 (AIS) and 0.53 (ISI) with the anxiety subscale from the HADS; 0.56 (AIS) and 0.62 (ISI) with the depression subscale from the HADS; -0.50 (AIS) and -0.41 (ISI) with the Karnofsky Performance Scale Score; 0.61 (AIS) and 0.54 (ISI) with the GHQ-12 score; 0.62 (AIS) and 0.64 (ISI) with the ESS score; and 0.55 (AIS) and 0.58 (ISI) with the PSQI score.

Relationships between the AIS, ISI, types of pain medication, and objectively measured sleep

Analysis of variance showed that patients who took opioids had the highest AIS scores

($M \pm SD = 9.48 \pm 3.57$) and ISI scores ($M \pm SD = 10.33 \pm 4.61$), followed by those taking non-opioid analgesics ($M \pm SD = 7.13 \pm 3.22$ for AIS and 7.60 ± 4.27 for ISI) and those taking other medications ($M \pm SD = 7.29 \pm 4.75$ for AIS and 6.41 ± 3.80 for ISI; $F = 7.28$ [$p < 0.001$] for AIS and $F = 13.45$ for ISI [$p < 0.001$]). Finally, Actigraph data (total sleep time, sleep efficiency, bedtime, wake time, sleep onset latency, and wake after sleep onset) were significantly different between insomniacs and non-insomniacs using the cutoffs found in the ROC findings (i.e., scoring 7 for the AIS and 9 for the ISI) (Table 6).

(Insert Table 6 here)

Discussion

To the best of the present authors' knowledge, this is the first study to examine the psychometric properties of two commonly used instruments assessing insomnia (AIS and ISI) among patients with advanced cancer. Additionally, empirical evidence was provided to support the use of AIS and ISI for healthcare providers in caring for patients with an advanced cancer diagnosis. More specifically, the CFA and Rasch analysis findings supported the unidimensional structure for both the AIS and ISI. Previous studies have reported different factorial structures for AIS (one or two factors) (Enomoto et al., 2018; Gómez-Benito et al., 2011) and ISI (one to three factors) (Chung et al., 2011; Fernandez-Mendoza et al., 2012; Gerber et al., 2016) across different populations (e.g., adolescents and people with chronic pain). However, the different findings in the factorial structures could be contributing to the different sample characteristics. Indeed, psychometric properties of an instrument are usually sample-dependent and are likely to be varied in different populations (Lin et al., 2019). Given that the two previous studies comparing AIS and ISI properties did not examine the factorial structure (Savard et al., 2005; Sun et al., 2011), future studies are therefore warranted in investigating the AIS and ISI structures in

patients with cancer to corroborate the findings presented here. Nevertheless, the unidimensional findings in the present study justify the use of cutoffs for both AIS and ISI. The item scores can be summed because all the items are embedded in the same construct (i.e., insomnia).

Although the present study's results indicated that both the AIS and ISI shared robust and promising psychometric properties in the sample with advanced cancer, the AIS appeared to be slightly less inferior to the ISI regarding several psychometric characteristics. For example, the AIS as compared with the ISI had poorer CFA indices, higher standard error of measurement, and lower item separation reliability and index. One possible reason for this is that AIS includes some objective questions (e.g., sleep duration), which are likely to introduce bias due to recall error. On the other hand, the ISI emphasizes psychological aspects and may be biased by the recall error less than the AIS. Indeed, the present study also showed that the AIS had smaller effect sizes than the ISI in objectively measured data. The ISI also had its effect sizes of sleep efficacy and sleep onset latency that were twice the effect sizes of sleep efficacy and sleep onset latency in the AIS.

With the use of unidimensional AIS and ISI, healthcare providers can quickly assess insomnia among patients with advanced cancer. Healthcare providers may have some notion as to whether patients with advanced cancer have sleep disorders because insomnia is usually comorbid with other diagnostic issues. Use of these insomnia scales may also help healthcare providers to gain insight into the patients' sleep problems, pain levels, and possible psychological health. Specifically, with the high accuracy (~90%) in classifying the diagnosis of insomnia, oncologists or related healthcare providers can use either AIS or ISI to quickly identify (or screen) whether an individual with advanced cancer has sleep problems. Additionally, as the present study's results showed the relationships between AIS/ISI and other external criteria (e.g., pain and psychological health problems), healthcare providers

may use the AIS/ISI to further identify whether a detailed investigation on psychosocial health of the patient with advanced cancer is needed. Treatment directed to the causes for insomnia or the sleep problem per se could also more easily be initiated when the problem is detected.

Apart from the factorial structures, other psychometric findings in the present study were comparable with previous studies, especially the two studies on patients with cancer (Savard et al., 2005; Sun et al., 2011). More specifically, both Sun et al. (2011) and the present study found that the AIS had good internal consistency ($\alpha=0.83$ vs. 0.871), good test-retest reliability ($r=0.94$ in a three-day interval vs. $ICC=0.82$ in a two-week interval), supported criterion-related validity, and satisfactory ROC findings ($AUC=0.91$ vs. 0.86). Moreover, both Savard et al. (2005) and the present study found that the ISI has acceptable internal consistency ($\alpha=0.90$ vs. 0.776), good test-retest reliability ($r=0.83$ in a one-month interval vs. $ICC=0.79$ in a two-week interval), supported criterion-related validity, and satisfactory ROC findings ($AUC=0.86$ vs. 0.82). However, unlike prior research, which indicates a strong correlation between the ISI and PSQI ($r=0.8$) among a community sample of the general population (Morin et al., 2011), the present study found only moderate correlation between ISI and PSQI ($r=0.58$). A likely explanation for the different correlations is the different characteristics of the studied samples (elder people with advanced cancer [in this present study vs. middle-age adults in the general population [Morin et al., 2011]). Because people with cancer may have other reasons affecting their sleep quality (e.g., routine vital checks), the correlation between their insomnia and sleep quality may be lower. The aforementioned postulation is somewhat evidenced by the moderate correlation between the AIS and PSQI ($r=0.55$) in the present study. The study had several strengths. First, both AIS and ISI were tested using classical test theory and modern test theory (i.e., the Rasch models). Using different approaches to assess the psychometric properties of an instrument can

provide comprehensive information for potential users. Thus, different potential users can use the information if they are familiar or interested in such data. For example, use of classical test theory can ensure most healthcare providers are capable of interpreting the results because they are familiar with this method (Chang et al., 2015). On the other hand, the Rasch model conveys psychometric information with several well-known advantages, including the conversion from ordinal scale (e.g., Likert type scale) to an interval scale (i.e., using the unit of logit), reliability estimations separately for item and respondents, and measurement invariance (i.e., DIF) at the item level. Hence, DIF findings in the Rasch as compared with the measurement invariance findings from CFA are easier to identify which item is not invariant across subgroups.

The second strength of this study is that it used a series of external criteria to demonstrate the validity of AIS and ISI. Moreover, the external criteria included both subjective and objective measures. The use of objectively measured sleep is somewhat important because the use of actigraphy for assessing sleep outcomes has been well established and validated recently (Kapella et al., 2017; Weiss et al., 2010). Moreover, the major benefit of using actigraphy is to eliminate recall and social desirability biases. Although the AIS and ISI assess insomnia differently from actigraphy data (i.e., insomnia-related complains vs. activity level), the relationship between actigraphy data and the AIS/ISI cutoffs suggested some overlap. Future studies assessing insomnia among patients with cancer may adopt the proposed cutoffs presented here.

There are some limitations to the present study. First, all the patients with advanced cancer were recruited in Iran using a convenience sampling method. Although patients were recruited in different oncology units, the results are not necessarily generalizable to other ethnicities, other disease groups, or early stage of cancer, especially since different AIS and ISI structures have been reported across different populations in previous studies (Chung et

al., 2011; Enomoto et al., 2018; Fernandez-Mendoza et al., 2012; Gerber et al., 2016; Gómez-Benito et al., 2011). Second, the different early treatments may also contribute to different sleep performance among the patients with advanced cancer. However, the present study did not collect such information and cannot exclude such potential influences. Third, the cancer diagnoses varied among the participants (see Table 1) with some diagnoses having small sample sizes (e.g., 15 patients with skin cancer). Therefore, the findings might have little representativeness to some cancer types, including myeloma and skin cancer. Future studies using a large sample size for different cancer types are therefore needed.

Fourth, those with cognitive problems were excluded from the study. Therefore, using AIS or ISI to assess insomnia for a specific proportion of patients with cancer might be questionable because cognitive impairment (e.g., chemo brain) is commonly observed among patients with cancer (Pendergrass et al., 2018).

Fifth, the present study did not control for a potential confounder (i.e., sleep-breathing disorders), which might have affected the CFA results for both the AIS and ISI. Future studies are therefore warranted in considering sleep-breathing disorders and to verify the CFA findings in the present study. Sixth, insomnia was diagnosed using the DSM-IV rather than the DSM-5 in this present study because the current psychiatric and medical practice in Iran is to use the DSM-IV (although the use of DSM-5 appears to be increasing among newer disorders that were not in DSM-IV such as internet gaming disorder [e.g., Wu et al., 2017]). Finally, the objective sleep measure using actigraphy may have limited validity because only two days for each participant was recorded. The recommendation of retrieving accurate sleep information using an actigraphy is 10 hours a day for at least four days (Lin et al., 2018). Unfortunately, the patients with advanced cancer in the present study found it difficult to tolerate wearing such a device for long periods. Therefore, this was an unavoidable limitation. Following the limitation of using actigraphy, the lack of using sleep diaries is another

potentially important limitation. Without sleep diaries, the collected data from actigraphy could not be supported. Therefore, the present study only used actigraphy to calculate the estimations of bedtime and waking time using the Sadeh algorithm (Sadeh et al., 1994).

Conclusion

In conclusion, the AIS was translated into Persian and the study demonstrated that both Persian AIS and ISI have satisfactory psychometric properties among an advanced cancer sample in Iran. The unidimensional constructs of the AIS and ISI were supported by both CFA and Rasch models. Both AIS and ISI demonstrated promising concurrent validity as associations were found between the AIS, ISI, psychological factors, and cancer symptoms. Additionally, objective sleep measured using actigraphy was significantly related to the cutoffs of the AIS and ISI, where the cutoffs suggested by the ROC findings had strong sensitivity and specificity with satisfactory AUC. Consequently, the Persian AIS and ISI are appropriate instruments for healthcare providers to assess insomnia of patients with advanced cancer.

AUTHOR CONTRIBUTIONS

Study concept and design: AHP and CYL. Data collection: VI, BN and AHP.

Drafting the manuscript: CYL, AHP, ASC, MDG, MU and MB. Statistical analysis: AHP, CYL, and AB. Preparation and final approval of the manuscript: all authors.

REFERENCES

- American Psychiatric Association. *The diagnostic and statistical manual of mental disorders, 5th ed.* American Psychiatric Association, Washington, DC, 2013.
- Bastien, C. H., Vallières, A., and Morin, C. M. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med.*, 2001, 2: 297-307.
- Beaton, D. E., Bombardier, C., Guillemin, F., and Ferraz, M. B. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine*, 2000, 25: 3186-3191.
- Carvajal, A., Centeno, C., Watson, R., and Bruera, E. A comprehensive study of psychometric properties of the Edmonton Symptom Assessment System (ESAS) in Spanish advanced cancer patients. *Eur J Cancer*, 2011, 47: 1863-1872.
- Chang, C.-C., Su, J.-A., Tsai, C.-S., Yen, C.-F., Liu, J.-H., and Lin, C.-Y. Rasch analysis suggested three unidimensional domains for Affiliate Stigma Scale: Additional psychometric evaluation. *J Clin Epidemiol*, 2015, 68: 674-683.
- Chiu, H.-Y., Chang, L.-Y., Hsieh, Y.-J., and Tsai, P.-S. A meta-analysis of diagnostic accuracy of three screening tools for insomnia. *J Psychosom Res*, 2016, 87: 85-92.
- Chung, K.-F., Kan, K.-K., and Yeung, W.-F. Assessing insomnia in adolescents: Comparison of Insomnia Severity Index, Athens Insomnia Scale and Sleep Quality Index. *Sleep Med.*, 2011, 12: 463-70.
- Enomoto, K., Adachi, T., Yamada, K., et al. Reliability and validity of the Athens Insomnia Scale in chronic pain patients. *J Pain Res*, 2018, 11: 793-801.
- Espie, C. A., Kyle, S. D., Hames, P., et al. Sleep Condition Indicator: A clinical screening tool to evaluate insomnia disorder. *BMJ Open*, 2014, 4, e004183.
- Fernandez-Mendoza, J., Rodriguez-Muñoz, A., Vela-Bueno, A., et al. The Spanish version of the Insomnia Severity Index: A confirmatory factor analysis. *Sleep Med.*, 2012, 13: 207-210.

- Folstein, M. F., Folstein, S. E., and McHugh, P. R. "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*, 1975, 12: 189-198.
- George, G. C., Iwuanyanwu, E. C., Anderson, K. O., et al. Sleep quality and its association with fatigue, symptom burden, and mood in patients with advanced cancer in a clinic for early-phase oncology clinical trials. *Cancer*, 2016, 122: 3401-3409.
- Gerber, M., Lang, C., Lemola, S., et al. Validation of the German version of the Insomnia Severity Index in adolescents, young adults and adult workers: Results from three cross-sectional studies. *BMC Psychiatry*, 2016, 16: 174.
- Gómez-Benito, J., Ruiz, C., and Guilera, G. A Spanish version of the Athens Insomnia Scale. *Qual Life Res*, 2011, 20: 931-937.
- Imani, V., Lin, C.-Y., Jalilolqadr, S., and Pakpour, A. H. Factor structure and psychometric properties of a Persian translation of the Epworth Sleepiness Scale for Children and Adolescents. *Health Promot Perspect*, 2018, 8: 200-207.
- Innominato, P. F., Spiegel, D., Ulusakarya, A., et al. Subjective sleep and overall survival in chemotherapy-naïve patients with metastatic colorectal cancer. *Sleep Med.*, 2015, 16: 391-398.
- Jeong, H. S., Jeon, Y., Ma, J., et al. Validation of the Athens Insomnia Scale for screening insomnia in South Korean firefighters and rescue workers. *Qual Life Res*, 2015, 24: 2391-2395.
- Kapella, M. C., Vispute, S., Zhu, B., and Herdegen, J. J. Actigraphy scoring for sleep outcome measures in chronic obstructive pulmonary disease. *Sleep Med.*, 2017; 37: 124-129.
- Khalili-Parapary, Y., Heidarzadeh, M., Mozaffari, N., and Naseri, P. The psychometric properties and factor structure of Persian version of Edmonton Symptom Assessment

- Scale in cancer patients. *Indian J Palliat Care*, 2017, 23: 419-424.
- Langford, D. J., Lee, K., and Miaskowski, C. Sleep disturbance interventions in oncology patients and family caregivers: A comprehensive review and meta-analysis. *Sleep Med Rev*, 2012, 16: 397-414.
- Lin, C.-Y., and Pakpour, A, H. Using Hospital Anxiety and Depression Scale (HADS) on patients with epilepsy: Confirmatory factor analysis and Rasch models. *Seizure*, 2017, 45: 42-46.
- Lin, C.-Y., Hwang, J.-S., Wang, W.-C., et al. Psychometric evaluation of the WHOQOL-BREF, Taiwan version, across five kinds of Taiwanese cancer survivors: Rasch analysis and confirmatory factor analysis. *J Formos Med Assoc*, 2019, 118: 215-222.
- Lin, C.-Y., Strong, C., Siu, A. M. H., et al. Validating the Persian Adolescent Sleep Hygiene Scale-Revised (ASHSr) using comprehensive psychometric testing methods. *Sleep Med.*, 2018, 50, 63-71.
- Lin, S., Chen, Y., Yang, L., and Zhou, J. Pain, fatigue, disturbed sleep and distress comprised a symptom cluster that related to quality of life and functional status of lung cancer surgery patients. *J Clin Nurs*, 2013, 22: 1281-1290.
- Mercadante, S., Adile, C., Ferrera, P., Masedu, F., Valenti, M., and Aielli, F. Sleep disturbances in advanced cancer patients admitted to a supportive/palliative care unit. *Support Care Cancer*, 2017, 25, 1301-1306.
- Miaskowski, C., Lee, K., Dunn, L., et al. Sleep-wake circadian activity rhythm parameters and fatigue in oncology patients before the initiation of radiation therapy. *Cancer Nurs*, 2011, 34: 255-268.
- Moghaddam, J. F., Nakhaee, N., Sheibani, V., Garrusi, B., and Amirkafi, A. Reliability and validity of the Persian version of the Pittsburgh Sleep Quality Index (PSQI-P). *Sleep*

Breath, 2012, 16: 79-82.

Montazeri, A., Harirchi, A. M., Shariati, M., Garmaroudi, G., Ebadi, M., and Fateh, A. The 12-item General Health Questionnaire (GHQ-12): Translation and validation study of the Iranian version. *Health Qual Life Outcomes*, 2003, 1: 66.

Morin, C. M., Belleville, G., Bélanger, L., and Ivers, H. The Insomnia Severity Index: Psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*, 2011, 34: 601-608.

Ohayon, M. M., and Roth, T. Place of chronic insomnia in the course of depressive and anxiety disorders. *J Psychiatr Res*, 2003, 37: 9-15.

Pendergrass, J. C., Targum, S. D., and Harrison, J. E. Cognitive impairment associated with cancer: A brief review. *Innov Clin Neurosci*, 2018, 15: 36-44.

Sadeh, A., Sharkey, K. M., and Carskadon, M. A. Activity-based sleep-wake identification: An empirical test of methodological issues. *Sleep*, 1994, 17: 201-207.

Savard, J., and Morin, C. M. Insomnia in the context of cancer: A review of a neglected problem. *J Clin Oncol*, 2001, 19: 895-908.

Savard, M. H., Savard, J., Simard, S., and Ivers, H. Empirical validation of the Insomnia Severity Index in cancer patients. *Psychooncology*, 2005, 14: 429-441.

Soldatos, C. R., Dikeos, D. G., and Paparrigopoulos, T. J. Athens Insomnia Scale: Validation of an instrument based on ICD-10 criteria. *J Psychosom Res*, 2000, 48: 555-560.

Sun, J.-L., Chiou, J.-F., and Lin, C.-C. Validation of the Taiwanese version of the Athens Insomnia Scale and assessment of insomnia in Taiwanese cancer patients. *J Pain Symptom Manage*, 2011, 41: 904-914.

Weiss, A. R., Johnson, N. L., Berger, N. A., and Redline, S. Validity of activity-based devices to estimate sleep. *J Clin Sleep Med*, 2010, 6: 336-342.

Wu, T-Y., Lin, C-Y., Årestedt, K., Griffiths, M.D., Broström, A., Pakpour, A.H. (2017).

Psychometric validation of the Persian Internet Gaming Disorder Scale-Short Form:

Does gender and hours spent gaming online affect the interpretations of item

descriptions? *J Behav Addict*, 2016, 6; 256-263.

Yazdi, Z., Sadeghniaat-Haghighi, K., Zohal, M. A., and Elmizadeh, K. Validity and reliability

of the Iranian version of the Insomnia Severity Index. *Malays J Med Sci*, 2012, 19:

31-36.

Yennurajalingam, S., Chisholm, G., Palla, S. L., Holmes, H., Reuben, J. M., and Bruera, E.

Self-reported sleep disturbance in patients with advanced cancer: Frequency, intensity,

and factors associated with response to outpatient supportive care consultation – A

preliminary report. *Palliat Support Care*, 2015, 13, 135-143.