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**Title**: Predictors of daytime consequences of insomnia: the roles of quantitative criteria and nonrestorative sleep

**Running title:** Daytime Consequences of Insomnia

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**Abstract**

Background: The implications of removing nonrestorative sleep (NRS) and adding quantitative criteria in the most recent diagnostic criteria of insomnia disorder remain unresolved. The study was aimed to investigate how nighttime quantitative measures of sleep quality and NRS relate to daytime functioning in a general population sample.

Sampling and methods: Data of 905 subjects (mean age = 47.0 years; 64.5% females) in a population-based survey who had insomnia symptoms or NRS at least 1 night in a typical week were analyzed to evaluate their relationship with "functional impairment", "concerns/distress", and "interference with daily activities" over the past 30 days. Receiver operating characteristic curve analysis was performed, while controlling for age and gender.

Results: Moderate to severe NRS was the first-level predictor of all 3 daytime variables. Insomnia frequency ≥ 3 times per week and sleep onset latency ≥ 10-20 minutes were second-level predictors.

Conclusions: We found that NRS was more important than insomnia symptoms in determining daytime consequences of insomnia. On the basis of our findings we express concerns whether the removal of NRS from the most recent diagnostic criteria may lead to its under-recognition, but support the quantitative criteria on insomnia frequency of at least 3 nights per week.

**Keywords**: insomnia, DSM-5, ICSD-3, nonrestorative sleep, daytime consequences, functional impairment, quantitative criteria

Predictors of daytime consequences of insomnia: the roles of quantitative criteria and nonrestorative sleep

Current diagnostic systems define insomnia disorder by the presence of sleep difficulties and the associated daytime consequences such as fatigue, sleepiness, cognitive deficit, mood disturbance, reduced motivation, proneness for accidents, distress, and impaired functioning [1, 2]. Studies have shown that daytime symptoms in patients with insomnia play more important roles in determining help-seeking and quality of life than nighttime symptoms [3-5]. A review article supported that self-reported daytime difficulties are more common in people with insomnia, compared to people not complaining of insomnia [6], while greater frequency and severity of insomnia symptoms are associated with greater distress and functional impairment [7-9]. Among 235 individuals with insomnia and 499 individuals with no sleep problems, Ustinov et al. (2010) showed that self-report of insomnia, sleep onset latency, and wake after sleep onset were the main predictors of anxiety and depressive symptoms, sleepiness, fatigue, and functional impairment [9]. By hierarchical tree analysis, Ohayon et al. (2012) found that the first-level predictor of daytime symptoms was global sleep dissatisfaction, followed by nonrestorative sleep (NRS), difficulty initiating sleep, and difficulty resuming sleep after awakening [8]. Using receiver operating characteristic (ROC) curve analyses, Drake et al. (2015) found that insomnia frequency of 3-4 nights per week and sleep onset latency of 36-40 minutes were the optimal cutoffs for predicting daytime impairment [7].

In the newly published Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) [1] and International Classification of Sleep Disorders, 3rd Edition (ICSD-3) [2], NRS has been removed as one of the symptoms of insomnia disorder; in addition, the frequency of insomnia for at least 3 nights per week and for a duration of at least 3 months are required. The implications of the revised diagnostic criteria in terms of the diagnosis and treatment of insomnia remain unclear.

NRS, a subjective experience of unrefreshing sleep, began to interest practitioners and researchers in the 1970s as it is frequently observed in patients with chronic fatigue syndrome and fibromyalgia. NRS is also common in subjects with specific sleep disorders (e.g., sleep apnea and periodic limb movement disorder), psychiatric disorders (e.g., anxiety and depressive disorders), and insomnia [10, 11]. Recent studies support the notion NRS is a distinct phenomenon [10, 12]. For instance, Sarsour et al. (2010) showed that NRS was associated with physical, cognitive and emotional functioning independent of insomnia severity and depression [13]. Another study showed that a complaint of NRS every night belonged to one distinct subtype of insomnia, which was characterized by frequent and severe insomnia symptoms, functional impairment, medical and psychiatric comorbidities, significant healthcare cost, and frequent use of hypnotics [14]. In view of the limited literature on the roles of NRS and quantitative criteria in the diagnosis of insomnia, the current study aimed to investigate how nighttime quantitative measures of sleep quality and NRS relate to daytime functioning in a general population sample. The hypothesis was that insomnia frequency and severity and NRS would be positively associated with daytime consequences of insomnia, but the relative importance of each parameter was unclear.

## Method

### Participants

Data of the present study were obtained from a population-based telephone survey on the prevalence of insomnia in Hong Kong. The randomization procedure and telephone interview, conducted by the Public Opinion Programme, University of Hong Kong, have been presented in our original paper [15]. At the time of the study, the fixed telephone line density in Hong Kong was 102 lines per 100 households, which was among the highest in the world. We selected telephone numbers randomly from a computerized residential telephone directory, and then generated some unlisted numbers by adding and subtracting 1 and 2 from the selected numbers, while duplicated numbers were screened out. Within households, we selected participants who were going to celebrate their birthday next, aged ≥ 18 years, and could communicate in Chinese. We were able to complete interviews in 2,011 of 3,127 eligible subjects (response rate = 64.3%). Of the 2,011 subjects, 1,204 (59.9%) reported having at least 1 night out of 7 in a typical week with insomnia symptoms or NRS, defined as feeling tired and unrested in the morning. Among the 1,204 subjects with self-report of insomnia symptoms or NRS, 905 (75.2%) had full datasets; hence were included in the final analysis.

**Procedure**

A fully-structured, lay-administered telephone interview was conducted. The first section included an introduction and verbal consent, followed by the Brief Insomnia Questionnaire (BIQ), and lastly the sociodemographic characteristics, including age, gender, occupation, and level of education. The Chinese version of BIQ, which has satisfactory test-retest reliability and is valid in establishing insomnia disorder diagnoses according to the DSM-5 criteria [16, 17], was used to measure the frequency, severity, and duration of insomnia symptoms and NRS and the associated distress and daytime impairment. All procedures used in the study were reviewed and approved by the local institutional review board.

**Variables**

**Nighttime sleep and NRS.** Participants were asked how many nights out of 7 in a typical week they had problem falling asleep, staying asleep, waking too early, or NRS. The number of nights with any one of the symptoms was then asked. Participants were also asked to estimate how long they usually took to fall asleep, spent awake in bed, took to get back to sleep, and woke up earlier than they wanted, the number of awakenings, and the severity of NRS using a 5-point scale (0 = none, 4 = very severe). Other questions include insomnia duration and the amount of sleep on a typical weekday night. The full version of the BIQ can be obtained from its validation paper [18]. The following sleep variables were analyzed: insomnia duration and frequency, total sleep time, sleep onset latency, wake after sleep onset, number of awakenings, sleep latency after awakening, earliness of waking in the morning, and the severity of NRS.

**Daytime consequences.** Three aspects of daytime consequences of insomnia are covered by the BIQ, including (1) impairment in daytime functioning, (2) concerns or distress, and (3) interference with daily activities, over the past 30 days. There are 8 items on impairment in daytime functioning, including reduced motivation, reduced performance at work, school, or social activities, errors or accidents, irritability, nerves, or mood disturbance, daytime attention, concentration, or memory problems, daytime fatigue, daytime sleepiness, and tension headache or digestive problems. Participants rated each item using a 4-point scale (none, mild, moderate, or severe). There are 2 items on concerns or distress. Participants rated how severe the concerns or worries they had about their sleep and how worried or distressed they were about their sleep problems using a 4-point scale (none, mild, moderate, or severe). The BIQ includes 4 items on interference with daily activities. Subjects rated how their sleep problems interfered with their home management, ability to work, their social life, and their close personal relationship using a 10-point Likert scale (0 = no interference, 10 = very severe interference). In line with the BIQ scoring algorithms [18], impairment in daytime functioning was present when at least 2 of the 8 items were rated as moderate or severe, concerns or distress was present when any 1 question was rated as moderate or severe, and interference with daily activities was present when any 1 of the 4 items was rated as 7 or above.

**Data analysis**

We used ROC analyses to identify the set of cutoffs based on nighttime quantitative measures of sleep quality and NRS that could predict daytime consequences (ROC5.02 revised version: available at www.stanford.edu/~yesavage/ROC.html). ROC analysis is a nonparametric technique that is used to evaluate the interaction among multiple predictors without making restrictive assumptions required by linear models, in which a priori entry of interaction is necessary, and to identify subgroups of individuals who have a higher or lower probability of resulting in a particular binary outcome based on cutoff scores. The best cutoff value is determined based on an optimal balance between sensitivity and specificity. Once the best predictor and cutoff are identified, the group with the success criterion is tested against a stopping rule. The analyses are then restarted for each of the 2 subgroups in an iterative process until the stopping rule is not met. Sleep variables which had significant univariate relationships with daytime variables were included while controlling for age and gender. The sensitivity cutoff value was set at 0.5 to balance the risk of false positives and false negatives and the stopping rule was set at $p < .01$.

## Results

The mean age of the sample was 47.0 years; 64.5% were females, and 65.3% were married (Table 1). Participants reported a mean insomnia duration of almost 4 years and an average insomnia frequency of 3.5 times per week. The mean sleep onset latency and wake after sleep onset was roughly 60 and 45 minutes, respectively, while 387 of 905 participants (42.8%) reported having moderate, severe, or very severe NRS. Univariate logistic regression analysis revealed that all sleep variables, except insomnia duration, were significantly associated with impairment in daytime functioning, concerns or distress, and interference with daily activities (Table 2).

**Impairment in daytime functioning**

Significant predictors of functional impairment included NRS, sleep onset latency, insomnia frequency, and age (Figure 1). Participants with moderate, severe, or very severe NRS had greater chance of having functional impairment (68.2%) compared to those with no or mild NRS (20.3%). The second-order predictors were sleep onset latency and insomnia frequency. For subjects with moderate, severe, or very severe NRS, sleep onset latency greater or equal to 10 minutes was associated with a higher risk of functional impairment (Figure 1 right side). For subjects with no or mild NRS, insomnia occurring 3 or more times per week was associated with a higher risk of functional impairment (Figure 1 left side). The third-order predictor was age and insomnia frequency. Younger age groups were more likely to report functional impairment than older age groups. For subjects with moderate, severe, or very severe NRS, the cutoff level was 64 years of age; for those with no or mild NRS, the cutoff level was 26 years of age.

**Distress or concerns**

In the prediction model of distress or concern about sleep disturbance, the significant predictors included NRS, sleep onset latency, and age (Figure 2). Participants with moderate, severe, or very severe NRS had a greater chance of having distress or concern (58.7%) compared to those with no or mild NRS (15.1%). The second-level predictor was sleep onset latency. For those with moderate, severe, or very severe NRS, sleep onset latency 15 minutes or longer was associated with a higher risk of distress or concerns; for those with no or mild NRS, sleep onset latency 20 minutes or longer was associated with a higher risk. The third-order predictors were age and NRS.

**Interference in daily activities**

Significant predictors of interference with daily activities include NRS, back-to-sleep latency, and insomnia frequency (Figure 3). Subjects with severe or very severe NRS had a greater chance of reporting interference (48.1%) compared with those with no, mild or moderate NRS (10.8%). There was no second-order predictor for subjects with severe or very severe NRS; for those with no, mild or moderate NRS, the second-order predictor was NRS again and the third-order predictor was back-to-sleep latency and insomnia frequency.

## Discussion

The current study aimed to investigate how nighttime quantitative measures of sleep quality and NRS relate to daytime functioning in a general population sample. We found that moderate to severe level of NRS was the most important determinant of functional impairment, distress or concerns, and interference with daily activities in subjects with insomnia. Insomnia frequency and sleep onset latency were second-order predictors. Age and back-to-sleep latency were third-level predictors. As a second-order predictor, the cutoff for insomnia frequency was ≥ 3 times per week, while the cutoff for sleep onset latency varied from 10-20 minutes. The findings suggest that NRS is an important symptom in subjects with insomnia. We express concerns whether the removal of NRS from the recent diagnostic criteria for insomnia disorder may lead to its under-recognition, but support the quantitative criteria on insomnia frequency of at least 3 nights per week.

Our finding that NRS was more important than insomnia symptoms in determining daytime consequences of insomnia is in line with the literature [8, 9]. Previous studies have reported a wide range in the point prevalence of NRS, from 1.4% to 35% [10], probably due to variation in the definition of NRS and whether a minimum sleep duration is required. Our study took into account total sleep time and other sleep variables in analysis and showed that the first-level predictor of daytime consequences of insomnia was moderate to severe NRS.

Recent studies suggest that NRS has a close relationship with cognitive function, inflammatory markers, and physical and mental health [19-21]. Although only a small proportion of subjects with insomnia present with NRS alone, while a majority complain of NRS and insomnia symptoms [22], our findings support that the assessment of insomnia should include an evaluation of NRS. With the help of standardized rating scales on NRS [23, 24], further studies are needed to determine the health risks of NRS and its relationship with insomnia symptoms.

We found that the quantitative cutoff for determining daytime consequences of insomnia was an episode frequency of 3 times per week, which is in line with the most recent diagnostic criteria. The sleep onset latency cutoff for daytime consequences was 10-20 minutes in our study, which is shorter than the 36-40 minutes cutoff in a previous study [7]. Recent studies found that the quantitative cutoff for sleep onset latency to distinguish subjects with insomnia from good sleepers was in the range of 16-20 minutes [25, 26], which is also shorter than the 30-minute cutoff in an early study [27]. It seems that the quantitative cutoff of sleep onset latency for distinguishing case from non-case of insomnia and determining daytime consequences of insomnia is variable. The different sample characteristics (e.g., community or clinic samples), research instruments (e.g., questionnaires or sleep diary), and statistical analyses (e.g., decision tree or ROC curve) may be explanations for the inconsistency. Another finding is that younger age groups seem to be more severely affected in their daytime functioning by poor sleep than older age groups. However, age was only a third-level predictor, meaning that it was relatively less important than NRS and insomnia symptoms as a predictor in our study. We found that insomnia duration was unrelated to daytime consequences of insomnia, suggesting that acute insomnia and chronic insomnia likely experience similar levels of impairment.

The current study has several limitations. All assessments were retrospective and subject to recall bias. The possibility that subjects mistakenly attributed their daytime symptoms to unrefreshing sleep could not be ruled out, but the possibility was low as NRS and daytime symptoms were asked in separate questions. Our assessment of NRS was based on a single question and failed to cover all aspects of NRS. The newly developed Restorative

Sleep Questionnaire [23] or Nonrestorative Sleep Scale [24] may be used in future studies. Lastly, we did not exclude potential causes of NRS, such as chronic fatigue syndrome, sleep apnea, and psychiatric disorders, which may partly explain the association between NRS and daytime symptoms of insomnia.

In conclusion, our study provided important data on the roles of NRS and quantitative criteria in determining daytime consequences of insomnia. We replicated the literature on the importance of NRS in the nosology of insomnia. On the basis of our findings we express concerns whether the removal of NRS may lead to its under-recognition, but support the quantitative criteria on insomnia frequency of at least 3 nights per week. A recent study showed that the inherent circadian preference for evening activity, known as evening chronotype, was associated with NRS on weekdays, but not weekends, in a college undergraduate sample [28]. Further studies are needed to examine the etiological models and treatment of NRS and the epidemiology of NRS by means of standardized questionnaires.

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Table 1. Sociodemographic and insomnia characteristics

| Variables [a] | Participants |
|---|---|
| Age, yr | 47.0 (17.5) |
| Male/female | 321/584 (1/1.82) |
| Education [b] | |
| Primary | 167 (8.5) |
| Secondary | 457 (50.6) |
| Tertiary | 280 (31.0) |
| Marital status [b] | |
| Never married | 248 (27.5) |
| Married | 591 (65.5) |
| Others | 63 (7.0) |
| Occupation [b] | |
| Professional and associate professional | 169 (18.9) |
| Skilled and semi-skilled worker | 190 (21.2) |
| Unskilled worker | 60 (6.7) |
| Retired | 163 (18.2) |
| Students | 83 (9.3) |
| Homemakers/others | 211 (23.5) |
| Unemployed | 20 (2.2) |
| Insomnia duration, mo | 46.6 ± 76.8 |
| Insomnia frequency, times/wk | 3.5 ± 2.2 |
| Sleep onset latency, min | 61.0 ± 94.4 |
| Wake after sleep onset, min | 44.9 ± 68.9 |
| Number of awakenings | 1.6 ± 1.6 |
| Sleep latency after awakening, min | 29.1 ± 50.8 |
| Earliness of waking in morning, min | 28.0 ± 38.1 |
| Non-restorative sleep | |
| None | 172 (19.0) |
| Mild | 346 (38.2) |
| Moderate | 279 (30.8) |
| Severe | 86 (9.5) |
| Very severe | 22 (2.4) |
| Impairment in daytime functioning (≥2 out of 8 items rated as moderate or severe) | 369 (40.8) |
| Concerns or distress (≥1 out of 2 items rated as moderate or severe) | 305 (33.7) |
| Interference with daily activities (≥1 out of 4 items rated as ≥7 on a 10-point scale) | 138 (15.2) |

[a] Data are presented as mean ± SD or number (%). [b] Number of missing data: education (n = 1), marital status (n = 3), occupation (n = 9).

Table 2. Factors associated with daytime consequences by univariate logistic regression analysis

| Variables | Univariate OR (95% CI) | *P* value | Univariate OR (95% CI) | *P* value | Univariate OR (95% CI) | *P* value |
|---|---|---|---|---|---|---|
| | Impairment in daytime functioning | | Concerns or distress | | Interference with daily activities | |
| Insomnia duration | 1.001 (0.999, 1.003) | 0.17 | 1.002 (1.000, 1.004) | 0.04 | 1.002 (1.000, 1.004) | 0.13 |
| Insomnia frequency | 1.26 (1.19, 1.34) | <0.001 | 1.21 (1.14, 1.29) | <0.001 | 1.28 ( 1.18, 1.39) | <0.001 |
| Total sleep time | 0.996 (0.994, 0.997) | <0.001 | 0.996 (0.994, 0.997) | <0.001 | 0.996 (0.994, 0.997) | <0.001 |
| Sleep onset latency | 1.005 (1.003, 1.006) | <0.001 | 1.005 (1.003, 1.007) | <0.001 | 1.004 (1.002, 1.005) | <0.001 |
| Wake after sleep onset | 1.006 (1.004, 1.008) | <0.001 | 1.005 (1.003, 1.007) | <0.001 | 1.005 (1.003, 1.007) | <0.001 |
| Number of awakenings | 1.27 (1.16, 1.39) | <0.001 | 1.22 (1.12, 1.34) | <0.001 | 1.30 (1.17, 1.44) | <0.001 |
| Sleep latency after awakening | 1.006 (1.003, 1.009) | <0.001 | 1.006 (1.003, 1.008) | <0.001 | 1.006 (1.003, 1.009) | <0.001 |
| Earliness of waking in the morning | 1.008 (1.004, 1.011) | <0.001 | 1.005 (1.001, 1.008) | 0.01 | 1.007 (1.003, 1.011) | 0.001 |
| Severity of nonrestorative sleep | 3.28 (2.72, 3.95) | <0.001 | 3.26 (2.70, 3.94) | <0.001 | 2.57 (2.09, 3.15) | <0.001 |

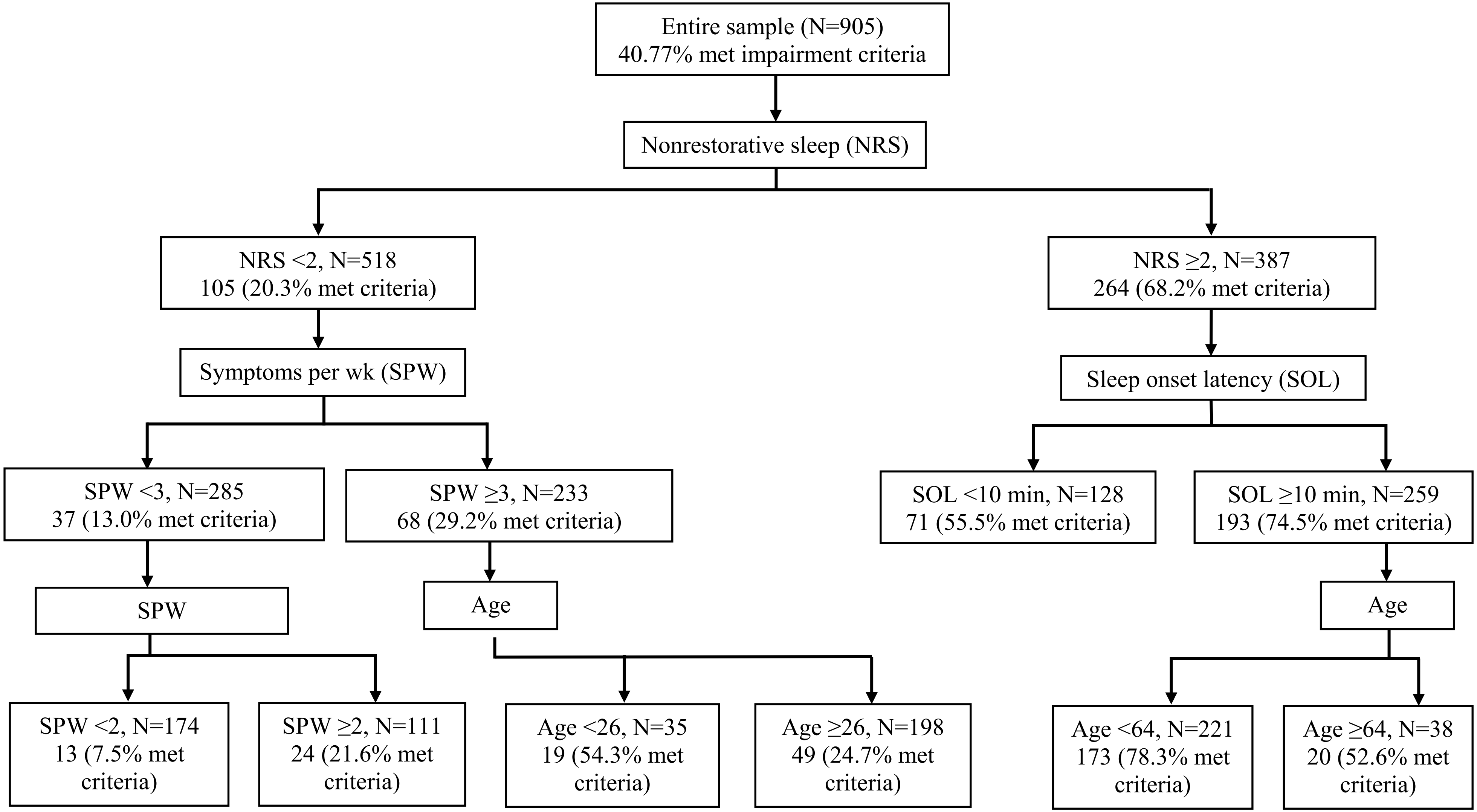


Figure 1. Hierarchy of predictors of functional impairment.

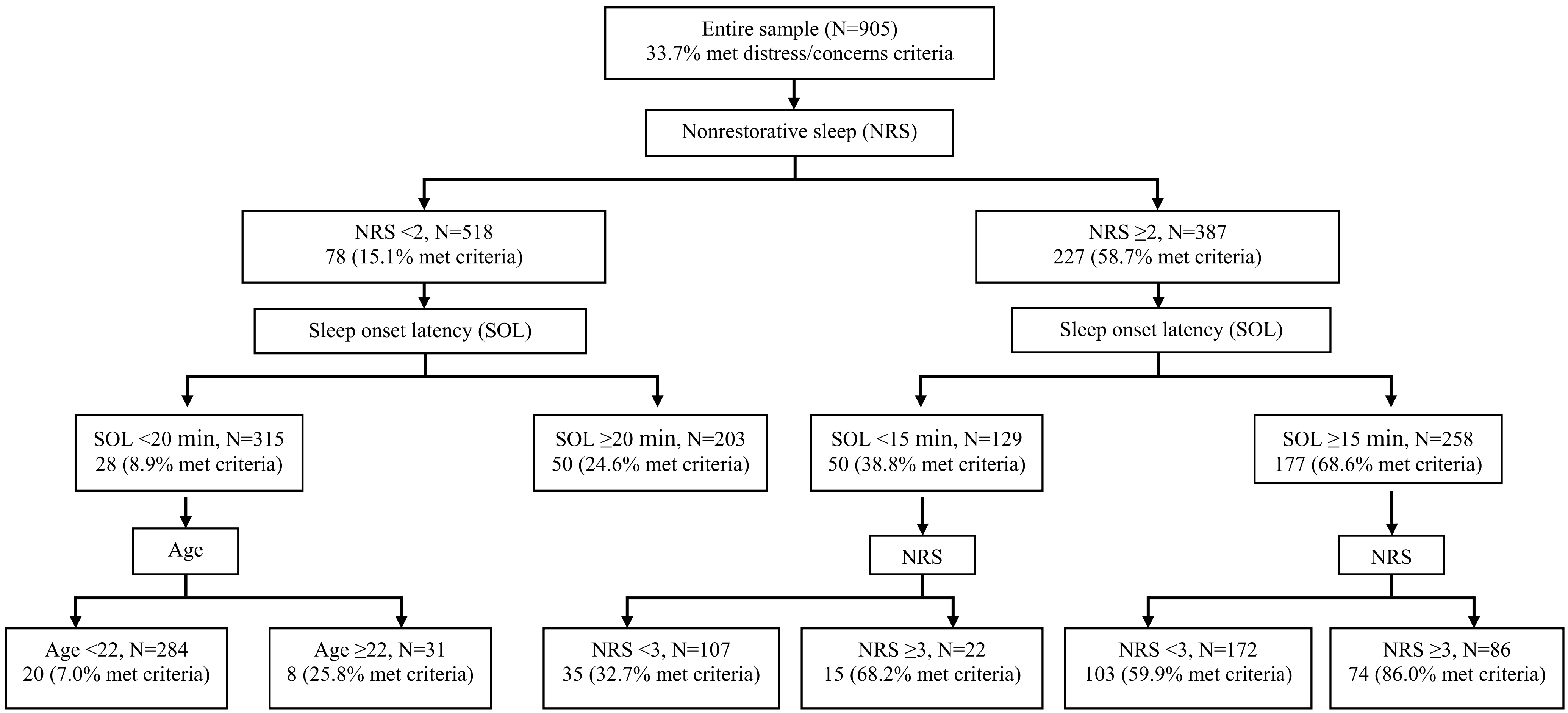


Figure 2. Hierarchy of predictors of distress or concerns.

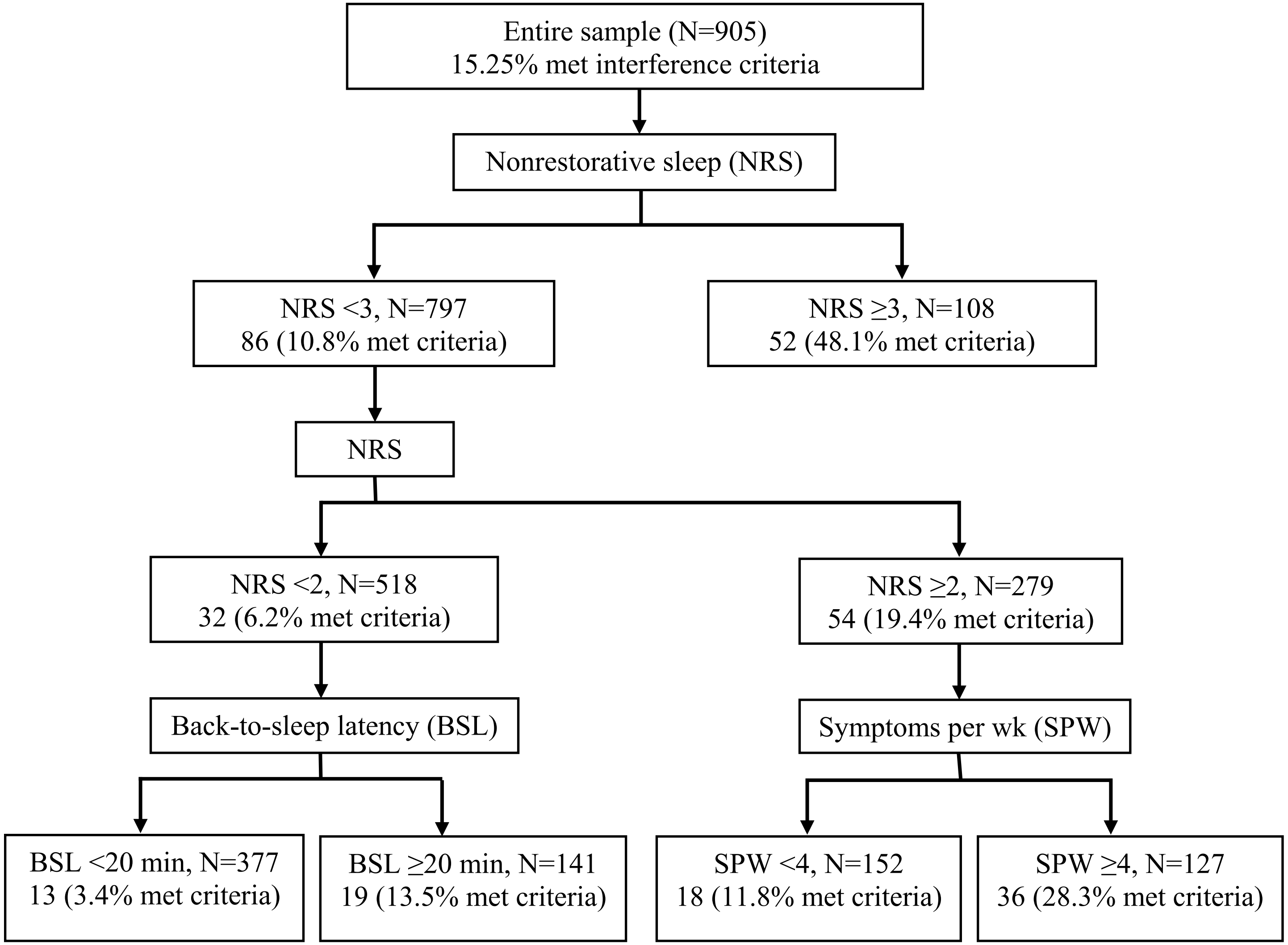


Figure 3. Hierarchy of predictors of interference of daily activities.