

**The Natural History of Insomnia:
Does Sleep Extension Differentiate Between Those That Do and Do Not Develop Chronic Insomnia?**

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ABSTRACT (n=298)

According to the 3P model of insomnia, the variable that mediates the transition from acute-to-chronic insomnia is “sleep extension” (the behavioral tendency to expand sleep opportunity to compensate for sleep loss). In the present analysis, we sought to evaluate how Time in Bed (TIB) varies relative to the new onset of acute and chronic insomnia. 1,248 subjects were recruited as good sleepers (GS). Subjects were monitored over one year’s time with sleep diaries. State transitions were defined, a priori, for Acute Insomnia (AI), Recovered from Acute Insomnia (AI-REC), and Chronic Insomnia (AI-CI). Two additional groupings were added based on profiles that were unanticipated: subjects that exhibited persistent poor sleep following acute insomnia (AI-PPS [those that neither recovered or developed chronic insomnia]) and subjects that recovered from chronic insomnia (CI-REC). All Subject groups (GS, AI-REC, AI-CI, AI-PPS and CI-REC) were evaluated for TIB differences with longitudinal mixed effects models. Post Hoc analyses for percent of group that were typed as TIB “restrictors, maintainers, and expanders” were conducted using longitudinal mixed effects models and contingency analyses. Significant differences for pre-to-post acute insomnia TIB were not detected for the insomnia groups. Trends were apparent for the AI-CI group which suggested that minor increases in TIB occurred weeks before the declared onset of acute insomnia. Additionally, it was found that a significantly larger percentage of AI-CI subjects engaged in sleep extension (as compared to good sleepers). The present data suggest that transition from acute insomnia to chronic insomnia does not appear to be initiated by sleep extension and the transition may occur before the elapse of three months of three or more nights of sleep continuity disturbance. Given these findings, it may be that the mismatch between sleep ability and sleep opportunity is perpetuated over time given the failure to “naturally” engage in sleep restriction (as opposed to sleep extension).

Keywords: insomnia; aging; natural history; acute insomnia; sleep extension

STATEMENT OF SIGNIFICANCE

While there are several seminal studies on the natural history of insomnia, none to date have had high temporal resolution over an extended monitoring period. In the present study, using such methods, it was found that sleep extension does not occur after the onset of acute insomnia and that the average magnitude of sleep extension over time is minimal. While this calls into question the relevance of the “3rd P” as the etiologic factor for chronic insomnia, it does not change the established finding that subjects with chronic insomnia exhibit a mismatch between sleep opportunity and sleep ability and that alignment of these measures via sleep restriction has well established therapeutic value.

INTRODUCTION

In 1987, Spielman and colleagues introduced the behavioral perspective on insomnia (The “3P” model) (Spielman, Caruso, & Glovinsky, 1987). During the same year, they presented the results of a treatment based on the 3P model, referred to as sleep restriction therapy (SRT) (Spielman, Saskin, & Thorpy, 1987)^Ψ. For the next decade, no additional models were proffered, or at least gained traction, with respect to the etiology of insomnia. This may have been the case because of the high face validity of the theory and/or because the success of SRT was considered sufficient evidence for the behavioral perspective. Both the 3P model and SRT rest upon two foundational ideas: 1) acute sleeplessness is common and a natural response to stress and 2) the expected and understandable reaction to sleep loss is the attempt to recover lost sleep by increasing time in bed (e.g., going to bed early and/or “sleeping in” and/or napping). Spielman’s central concept was that stress may precipitate acute insomnia, but it is the behavioral compensatory response of sleep extension^Ψ that perpetuates insomnia over time, long after the initial stress has resolved. That is, sleep extension (excessive time in bed) mediates the transition from acute to chronic insomnia, and that the mismatch between sleep ability and opportunity should be the primary target for treatment (i.e., align sleep ability with opportunity). Please note sleep extension represents only one of 8 (or more) perpetuating factors for insomnia (Spielman, Saskin, & Thorpy, 1987). Sleep Extension (as measured by Time in Bed [TIB]) is the focus of the present study owing to its centrality to both the behavioral model and to sleep restriction therapy.

To our knowledge none of the natural history studies conducted on insomnia (Morin et al., 2009; Abiona, Gureje,⁴ Makanjuola, Oladeji, & Esan, 2011; Ellis, Perlis, Neale, Espie, & Bastien, 2012) have attempted, or had the resolution, to empirically define how Time in Bed (sleep opportunity) varies over time. That is, none of the prior studies have provided evidence that patients that develop chronic insomnia actually expand sleep opportunity following a bout of acute insomnia.

^Ψ The terms Sleep Restriction and Sleep Extension are in some ways misnomers. While it would be more accurate to say time in bed extension and time in bed restriction, we have opted to use the founders terminology so that the terms are held in common and there can be no confusion about whether we’re talking about the same behaviors as the 3P model and SRT.

Recently, we undertook a natural history study (from good sleep [GS] to acute insomnia [AI] to chronic insomnia [AI-CI] or recovery [AI-REC]) that had very high temporal resolution (daily diary data for a period of one year). This study (referred to as “NITES”) was undertaken to: 1) estimate the incident rate of AI per annum (Perlis et al., 2019); 2) evaluate whether those that develop chronic insomnia engage in a level of sleep extension that is not evident in temporally matched good sleepers or those that recover from acute insomnia; and 3) assess whether acute and/or chronic insomnia can be empirically defined. To date, we reported that the one-year incidence rate of AI was 27.0%, that 72.4% of those that develop AI recover good sleep, and that only 6.8% developed chronic insomnia. It was also found, contrary to expectation, that two other outcome conditions existed: one where 19.3% of subjects that experienced AI developed persistently poor sleep (but did not meet formal criteria for insomnia); and one where 1.5% of subjects that developed CI recovered good sleep. It was concluded that 1) the incidence rate of acute insomnia was remarkably high but that most incident cases resolve within days to weeks (Perlis et al., 2019), 2) the incidence rate of chronic insomnia was remarkably low; and 3) that up to 20% of subjects neither recover nor develop chronic insomnia as traditionally defined. In the present study, we address our second aim: Does sleep extension (increased TIB) differentiate between those that do and do not develop chronic insomnia?

METHODS

Subjects and Procedure. Adult good sleeper subjects (≥ 35 years of age) were recruited from two nationwide platforms over three recruitment intervals, separated by approximately one year’s time. Recruitment did not include individuals from 18-35 years of age because the study was focused on insomnia in middle-aged and older adults. Subjects were recruited from Zogby Analytics (Zogby Analytics, 2019) (an international polling agency) and ResearchMatch (Harris et al., 2012). The study was conducted in two phases, described as follows.

Phase-1. For subjects recruited by Zogby, age-appropriate self-reported good sleepers were identified and screened via a preliminary survey administered to panel members. Appropriate individuals were referred on to the NITES study website. For ResearchMatch, age-appropriate individuals were identified via an internal poll.

Interested subjects were then referred to a NITES study Redcap screening questionnaire. In both cases (Zogby and ResearchMatch) potential study candidates provided a yes response to the following statement: *“Are you a good sleeper? That is, do you reliably (5 or more nights per week) take less than 15 minutes to fall asleep and are awake during the night for less than 15 minutes? Has this been true for you for at least the last 6 months?”*. The screening criteria (i.e., 15 minutes or less) was rigorous to enhance the likelihood that those recruited were enduringly good sleepers. No other inclusion or exclusion criteria were applied. Eligible subjects who expressed an interest in participating in the study were then referred to the NITES study website where they 1) reviewed HIPAA forms and provided their informed consent, 2) completed an intake survey (profiling sleep, health, and mental health status and history), and 3) completed two weeks of online sleep diaries (baseline assessment) to corroborate their status as good sleepers.

Phase-2. Subjects that entered into Phase-2 of the study were those that 1) exhibited an average sleep profile that was consistent with their characterization as good sleepers and 2) completed > 70% of the 14 daily diaries and weekly questionnaires. During Phase-2, subjects were monitored for a year and completed daily sleep diaries and weekly, biweekly, monthly, and end of study retrospective questionnaires (e.g., weekly = a med symptom checklist; bi-weekly = PHQ-9 (Kroenke, Spitzer, & Williams, 2001); monthly = AUDIT/CAGE (Saunders, Aasland, Babor, De la Fuente, & Grant, 1993)). Subjects that transitioned to acute or chronic insomnia also completed an additional measure that was specific to insomnia (i.e., weekly administrations of the insomnia severity index [ISI] (Bastien, Vallières, & Morin, 2001)). For a complete list of instruments, please see the first paper in this series or contact one of the study investigators (Perlis et al., 2019).

Daily Sleep Diary. The prospective assessment of sleep continuity disturbance (i.e., difficulty initiating or maintaining sleep) was conducted via online daily sleep diaries through a dedicated web-portal (all questionnaires were completed on this study-specific site). The online sleep diary items were based on the Consensus Sleep Diary

(Carney et al., 2012). Primarily, the diary was used to quantify nightly variations in sleep latency (SL), number of nocturnal awakenings (NWAK), wake after sleep onset (WASO), early morning awakenings (EMA), and total sleep time (TST). Three additional variables were calculated based on the self-report data including 1) Time in Bed (TIB-C), calculated as the difference in minutes between Time to Sleep (TTS) and Time Out of Bed (TOB), $TIB-C = TTS - TOB$, 2) a second measure of total sleep time (TST-C), $TST-C = TIB-C - (SL + WASO + EMA)$, and 3) sleep efficiency (SE%) = $(TST-C / TIB-C) * 100$. Participants received daily email reminders to complete their entries. Participants were also emailed if they missed a diary entry and sent a “notice” email if their compliance dropped below 60% across 14 days at any point during the study.

Subject Compensation. In order to encourage high compliance rates (i.e., the completion of daily sleep diaries), a novel compensation strategy was used: a lottery. All study participants were automatically enrolled in the study lottery. The lottery was conducted once a month where each questionnaire that a subject completed was automatically counted as an 'entry' into the lottery. Each subject accumulated multiple entries over the course of each month. At the end of each month, a drawing was conducted where winners were randomly selected from all the submitted entries. Each subject was eligible to win one prize per month, and one prize of each dollar value over the year. The prizes were as follows: 2 of \$750, 4 of \$500, 10 of \$250, and 20 of \$100 (total of 36 awards /month). At the end of the year, a final lottery was conducted for all the participants that completed the study. In this case, 22 awards of \$1000 were randomly awarded.

Identification of Cohort. While the study recruited good sleepers by self-report (5 or more nights per week taking 15 minutes or less to fall asleep and awake during the night for 15 minutes or less [including early morning awakenings]), extra steps were taken to confirm stable good sleep continuity in the analysis stage. Using moving 7-day windows (successive, overlapping 7-day segments; i.e., first window consists of days 1-7, the second window consists of days 2-8, the third window consists of days 3-9, etc.) each week was determined to be a good sleeping

week or poor sleeping week. In order to be classified as a good sleeper, the subject was required to exhibit 10 of 12 weeks good sleep.

Identification of Transitions (Sleep Groups). Each subjects' sleep diary data was used to identify instances of sleep initiation and/or maintenance difficulties and to determine if such difficulties persisted. Acute insomnia (AI) was defined as two consecutive weeks with a frequency of ≥ 3 nights per week of sleep initiation and/or maintenance complaints (as defined by > 30 minutes' SL or WASO, or EMA)(Ellis, Gehrman, Espie, Riemann, & Perlis, 2012). For the definitions of recovery (AI-REC) and chronic insomnia (AI-CI), we chose 3 months since it is consistent with current diagnostic criteria for defining a new and enduring state. Because, however, the above rules were being applied to prospective, high frequency sampled data (i.e., daily sleep diaries), a more quantitatively precise definition was required. Accordingly, the definition of new onset chronic insomnia required that at least 10 of 12 weeks had to be scored as "insomnic" (3 or more days per week) and the definition of recovery required that at least 10 of 12 weeks had to be scored as "not-insomnic". In both cases, change-in-state cases were prospectively flagged at 1 month (4 consecutive weeks of good or bad sleep) for logistical reasons (i.e., to be able to recruit subjects for lab studies). See Table 1 for the various state definitions. Please note, in contrast to the DSM-5's criteria for Insomnia Disorder, qualitative assessments of distress and/or impairment in daytime functioning were not included in these definitions so that post hoc analyses could be conducted to empirically determine what levels of sleep continuity severity, frequency and chronicity are associated with daytime complaints and when such associations occur.

PLACE TABLE 1 HERE

Statistical Analyses. Demographic characteristics were compared between groups using analysis of variance (ANOVA) for continuous measures and an exact test for binary measures. A statistically significant omnibus test was followed with Bonferroni corrected pairwise comparisons. For the purposes of examining TIB over time, the

data were arrayed relative to the onset date for acute insomnia. Specifically, the day at the start of the transition to AI marks the anchor date. Good sleepers were given a pseudo AI transition date of 12 weeks from entry into the study. In preliminary descriptive analyses, TIB was aggregated and summarized with means and standard deviations by group over four time periods: +/- 2 weeks and +/- 12 weeks from the anchor date.

The primary analysis proceeded using linear mixed models to assess the change in TIB over time by group while adjusting for age, sex, BMI, and race. While age, sex and race represent a standard way to control for potential non-specific confounders, BMI was included to “control” for occult OSA. In addition to group indicators, fixed components of the model included: 1) time measured continuously as weeks since AI transition, modeled flexibly with splines; 2) time-group interactions; and 3) baseline covariates. A random intercept for subject and random slope for time, with unstructured covariance, was used to account for correlated longitudinal measurements. The model allows for missing data, assuming that data are missing completely at random. Model estimated mean TIB was obtained at the time points of interest by group, along with the change in TIB. A statistically significant time-group interaction indicated a difference in TIB over time by group.

Finally, in post hoc analyses, TIB was categorized in terms of three groups: restrictors (>30 min decrease in TIB); expanders (>30 minute increase in TIB); and maintainers (<= 30 minute change in TIB). Groups were compared across TIB categories using a multinomial logistic regression model while accounting for covariates.

Note: Due to a small group that recovered from CI, the group was excluded from hypothesis testing and models (and are not represented in Figures 1 & 2) All Statistical analyses were performed in SAS v9.4 (SAS; Institute Cary, NC) and Stata v15.1 (College Station, TX).

RESULTS

1,248 subjects were recruited as good sleepers (GS) and were retained in the start sample for the present analysis. As previously published (Perlis et al., 2019), the one-year incidence rate of acute insomnia (AI) was 27.0% ($n=337$). Of these, 72.4% of subjects recovered good sleep (AI-REC, $n=244$), and 6.8% ($n = 23$) developed new onset chronic insomnia (AI-CI). As noted previously, 19.3% neither recovered nor went on to develop chronic insomnia (AI-PPS, $n = 65$). Of those that developed AI-CI ($n=23$), 5 subjects recovered good sleep (CI-REC [1.5% of the AI sample]). Note: As indicated above, the definition of new onset insomnia was based solely on quantitative criteria for severity, frequency and chronicity. Daytime impairment was not included as a criterion but rather was a priori specified as a dependent variable.

Group Characteristics (GS, AI-REC, AI-PPS, AI-CI & CI-REC)

The five groups were assessed for differences with respect to age, sex, race, income, and BMI. The groups were only found to significantly differ with respect to sex and BMI. In the case of the former, more subjects were female in the AI-REC group as compared to GS group (76% AI-REC vs. GS 65%, Bonferroni adjusted exact $p=0.005$). In the case of the latter, AI-PPS subjects had higher BMIs than GS subjects (PPS 29.2 vs. GS 28.5, Bonferroni adjusted ANOVA $p=0.003$). In both cases the differences were small. For additional information see Table 2.

INSERT TABLE 2 ABOUT HERE

Mean TIB by Group for 2 & 12 Weeks Prior To and Following the Onset of Acute Insomnia.

The five groups were assessed for differences with respect to mean TIB for 2 and 12 weeks prior to and following the onset of acute insomnia. The shorter time frame was to capture new onset sleep continuity disturbance (normal variations in good and poor sleep) and the longer time frame was to capture the onset of sub-chronic insomnia (Ellis, Gehrman, et al., 2012). When evaluating these two time frames, clinically significant differences were not detected (see Table 3). This said, at two weeks prior to, and following, incident AI, all four AI groups (AI-

REC, AI-CI, AI-PPS and CI-REC) exhibited mean increases in TIB. The magnitude of these increases were small to moderate (means 6-25 min) and highly variable (e.g., standard deviations 37-79 minutes). The increase in TIB for the AI-CI group was 11.0 min increase +/- 37.4 minutes. At twelve weeks, three groups exhibited mean increases in TIB (AI-REC, AI-CI, and CI-REC). Here again the magnitudes were small (means 3-12 min) and the variability was large (e.g., standard deviations 36-57 minutes). The CI group exhibited a 10.8 min increase +/- 36.0 minutes). These values, were not within the expected range (i.e., at least a 30 min difference between TST and TIB [and more likely an hour or more] to reach sleep efficiencies of $\leq 85\%$).

INSERT TABLE 3 ABOUT HERE

Modeled TIB by Group for 2 & 12 Weeks Prior to and Following the Onset of Acute Insomnia.

In order to better represent changes in TIB over time and to do so in a manner that does not require illness duration thresholds, the data were modeled to represent estimated TIB over time relative to the first day of the acute episodes (see Figure 1, note AI is demarcated as time zero)]. As can be seen in this graphic, only the AI-CI group showed a mean trend towards sleep extension; one that begins some 12 weeks prior to the declaration of the acute episode, peaks at approximately 3 weeks post AI onset, and begins to decline at about 6 weeks post AI onset. As shown with descriptive data in Table 3, the magnitude of this change was modest.

The statistical evaluation of the change in TIB, overall by time by group was found to be statistically significant (time-group interaction $p=0.032$). Pairwise comparisons revealed that the change in TIB over time for the AI-CI group significantly differed from those of the good sleeper group (Bonferroni adjusted $p=0.028$). This effect, however, was largely due to the small but reliable reduction in good sleeper TIB as compared to the more variable increase in AI-CI TIB (GS: -7 min vs. AI-CI: +12 min). Estimated slope values and 95% confidence intervals during the periods of 2 weeks prior to acute episode, 2 weeks after acute episode, and 24 weeks (+/- 12 weeks) around

the acute episode [demarcated at time zero]), can be found in Table 4. As would be expected from the prior representations of central tendency, the AI-CI group showed the largest within-group slope values (estimate values), but confidence intervals included zero indicating the increase in TIB over the 24 week period was not statistically different from zero.

PLACE FIGURE 1 AND TABLE 4 ABOUT HERE

% Subjects by Group characterized as “Restrictors, Maintainers, and Expanders” (+/- 2 & 12 Weeks Onset of AI).

Four of the groups (GS, AI-REC, AI-PPS, and AI-CI) were assessed for the percent of sample that were subtyped as “restrictors, maintainers, and expanders”. The multinomial logistic regression models adjusted for age, sex, and BMI, both 4x3 contingency analyses (+/- 2 & 12 weeks onset of AI) were found to be significant for the association between TIB subtype and group (2 week: Chi-square (df=6)=40.16, $p < 0.001$; 12 week: Chi-square (df=6)=18.3, $p = 0.006$). In the follow up assessments for each subtype, only the model assessing the +/- 2 week interval was found to differ with respect to the percentage of sample typed as expanders (Chi-square (df=3)=16.4, $p < 0.001$); AI-CI’s were found to have the highest percentage of subjects designated as expanders (39.1%), see Figure 2.

PLACE FIGURE 2 ABOUT HERE

DISCUSSION

The data from our prior NITES study suggested that acute insomnia is common (affects about 27% of the population per annum) and that for most people, sleep continuity disturbance is self-limiting (about 72% of those with incident insomnia recover) (Perlis et al., 2019). Of those that develop AI, only about 7% developed chronic insomnia (AI-CI). In the present study, we evaluated whether sleep extension (increased TIB) differentiated between those that do and do not develop chronic insomnia. Specifically, we compared the groups that developed AI (AI-REC, AI-CI, and AI-PPS) for differences with respect to change in TIB (as compared to GS) and for percent of

groups that were typed as TIB “restrictors, maintainers, and expanders”. Significant differences for pre-post-AI TIB were not detected for the insomnia groups. Model estimated trends were apparent for the AI-CI group which suggested that minor increases in TIB occur weeks before the declared onset of acute insomnia. Consistent with this observation, it was found that (while not a majority of AI-CI subjects) a larger percentage of AI-CI subjects were typed as expanders. . Taken together, these data do not provide clear evidence that the transition from acute to chronic insomnia is largely driven by increases in sleep extension. Instead, the sleep extension that occurs, occurs prior to AI (as it is currently defined), is (on average) of small magnitude, and occurs in less than 40% of AI-CI subjects.

Given the present findings, is it the case that the 3P model is wrong (i.e., that sleep extension [as assessed with nocturnal TIB] does not mediate the transition from AI to CI or that engaging in sleep extension does not preclude recovery from AI)? As a rule, it does not appear that the majority of subjects that develop chronic insomnia increase TIB following acute insomnia (as it is now defined). While this does seem at odds with the 3P model, part of the issue may be the arbitrary but precise definition of acute (and chronic) insomnia. For example, it may be the case that even one week of ≥ 3 days of insomnia followed by sleep extension may be enough to initiate the transition to chronic insomnia. Alternatively, or additionally, one week of insomnia, while failing to sleep restrict, may be enough to initiate the transition (AI to AI-CI). Further, it is possible that the use of means over weeks and months may serve to obscure the phenomenon of interest. It may be that sleep extension is a variable phenomenon that occurs following “bad nights” and that average nights don’t prompt a sleep extension response and that “good nights” are followed by either no increases and/or possibly reductions in TIB. If this is the case, the net (mean over weeks) would be small and/or statistically non-significant (as was the case). Please note, there is evidence that sleep continuity disturbance, at least in chronic insomnia, varies night to night such that 2-3 bad nights are followed by either better than average sleep, or definitive good sleep (Perlis et al., 2010, 2014). Whether TIB in the context of acute insomnia is similarly variable is unknown. This possibility is currently under

investigation. Finally, while sleep extension and/or the failure to sleep restrict may contribute to the development of chronic insomnia, it may also be the case that these things may variably apply to the various at risk groups (e.g., women and/or older adults) and/or interacts with other factors like cumulative morbidity of insomnia (e.g., number of “insomnic” incidents per unit time and the severity of the given incidents), and/or the subjects overall health status and/or basal sleep need. For example, those that experience more frequent incidents of insomnia and/or more severe bouts and/or who are in poorer mental or medical health and/or have higher basal sleep need may be 1) less likely to engage in “natural” sleep restriction (can’t sleep, don’t: do something else) and more likely to engage in sleep extension (attempt to recover lost sleep) and 2) more likely set into motion the homeostatic dysregulation and/or to experience the conditioned wakefulness that may perpetuate sleep continuity disturbance ad infinitum.

Study Limitations and Strengths. The current study had both important limitations and strengths. One significant limitation (apart from using standardized but arbitrary temporal definitions of AI and CI), was the high exclusion rate (i.e., loss of subjects owing to ineligibility, non-compliance, subject withdrawal, and disenrollment). This said, the results are likely generalizable to the population at large, as our sample was only moderately different than the general population (based on 2018 U.S. Census data). Our sample had a greater proportion of persons that identified as female (67% as compared to 51%) and white (82.5% as compared to 76.5%). Perhaps a larger concern related to attrition was the loss of statistical power to 1) detect rare events (new-onset chronic insomnia) and/or 2) resolve small and/or highly variable (within and between subjects) TIB effects. Another limitation is that the present study did not include adults between the ages of 18-35 years of age. While this was done to focus on insomnia as it presents in middle aged and older adults, unconfounded by developmental forms of delayed sleep phase disorder, the findings of the present study simply may not be true for younger adults. Future studies may be advised to evaluate age issues, not by focusing on the age group of interest, but by studying the whole of the adult population and evaluating age as a moderating factor. Another limitation is that, for the purposes of the present analyses, TIB was narrowly construed as an expansion of the nocturnal sleep period (i.e., phase advance

in time to bed and/or phase delay in time out of bed). Napping was not assessed. Analyses taking into account napping (alone and in combination with nocturnal sleep extension) are currently underway. Finally, future studies that incorporate the use of smart phone technologies (use of apps and texting) may find it easier to retain subjects and to obtain the large-scale samples needed to determine what factors apply to whom and when with respect to the etiology of chronic insomnia.

The present study also had a number of important strengths. This study is, to our knowledge, the first study to prospectively assess the incidence of acute and chronic insomnia using a dense-sampling approach (i.e., daily sleep diaries) in a large sample of good sleepers. This assessment strategy was particularly advantageous because it offered (1) the opportunity to more accurately determine whether a transition occurred and (2) the temporal resolution to identify when the transition(s) occurred.

Concluding Comment. The present paper is the 2nd publication in what is expected to be a series of six papers. The next analyses in this series will evaluate (while accounting for age and sex interactions): 1) day-to-day fluctuations in TIB as predictive of the transition from AI to CI; 2) napping as it relates to sleep extension; 3) the empirical definition of normal sleep and acute, sub-chronic, and chronic insomnia; and 4) what, if any, factors, predict the transition from incident to persistent insomnia. .

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DISCLOSURE STATEMENT

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Non-financial Disclosure: None

FIGURE CAPTIONS

Figure 1. TIB by groups from -12 to 12 weeks AI.

Figure 2. Percent of groups subtyped by TIB +/- 2 weeks AI.

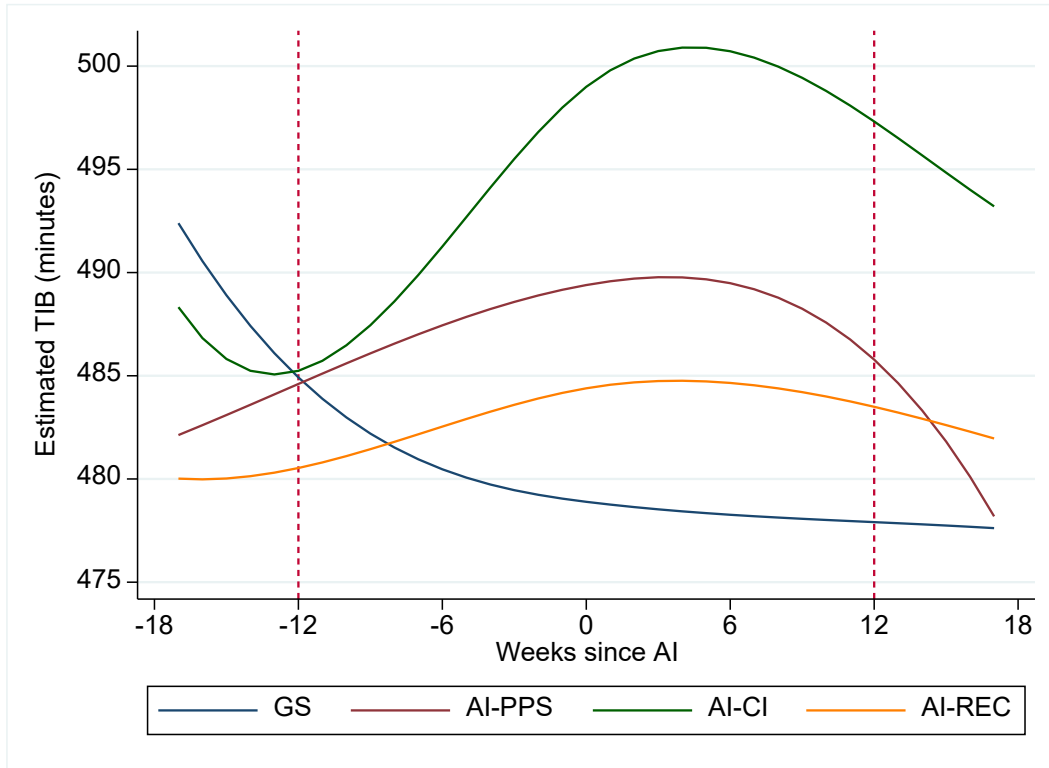
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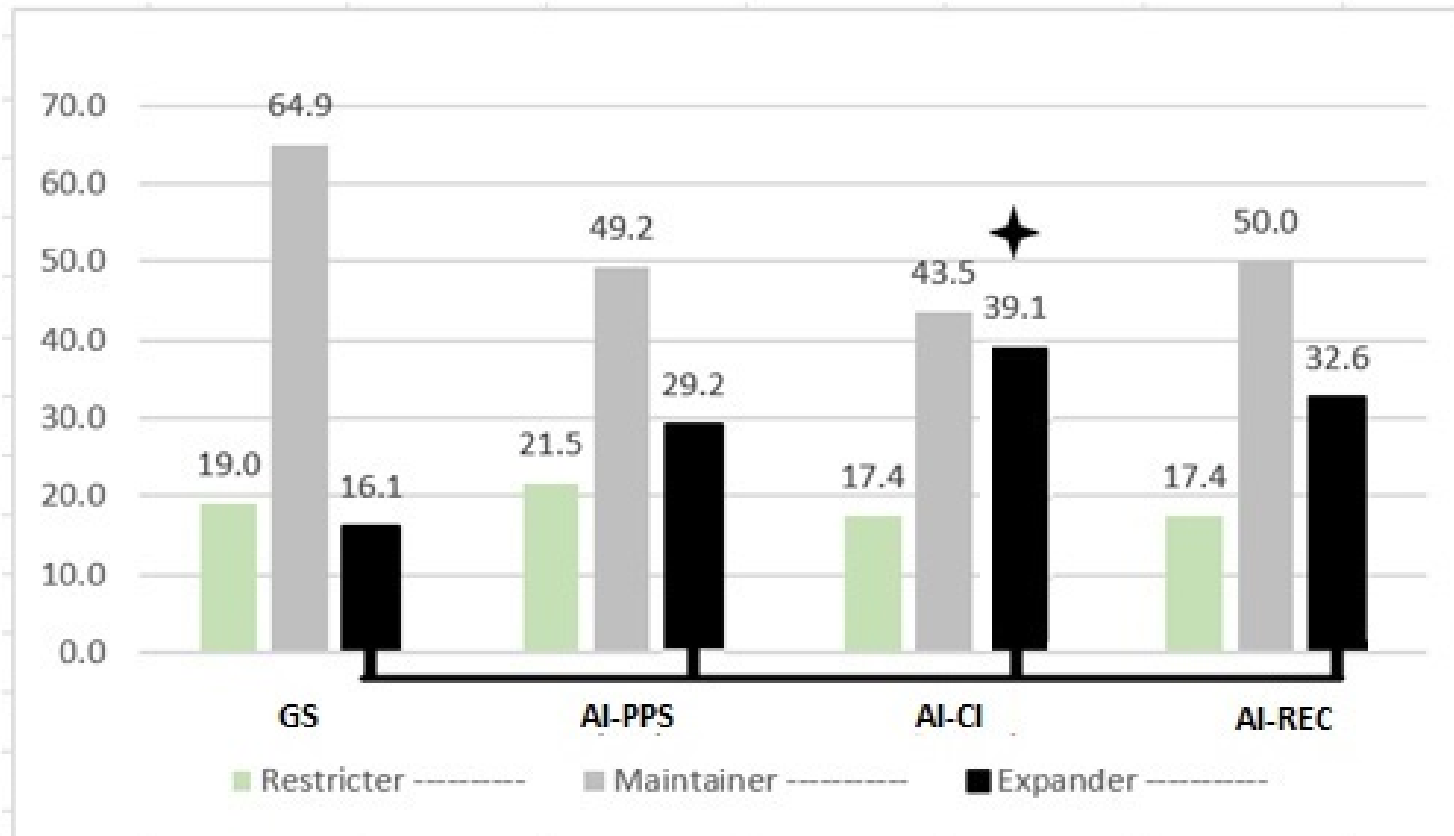
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Figure 1. Model estimated TIB Prior to and Following the Onset of AI



Note: CI-REC (given the small sample size) is not represented here

Figure 2. Percent of Groups Subtyped by TIB at +/- 2 Weeks AI



Note: CI-REC (given the small sample size) is not represented here

Table 1. Definitions for state transitions

<u>A Priori</u>	Acute Insomnia (AI)	Two or more consecutive weeks with a frequency of ≥ 3 nights/week of sleep latency and/or wake after sleep onset (WASO) severity ≥ 30 min
	Recovery (AI-REC)	Within a 12-week period, 7 or more weeks of good sleep after AI episodes where the final 4 weeks in the period were designated as good sleep.
	Chronic Insomnia (AI-CI)	10 or more weeks in a 12-week period with same frequency and severity criteria as AI
<u>Post Hoc</u>	Persistent Poor Sleep (AI- PPS)	Recurring bouts of AI without transition to CI or REC
	Recovery from CI (CI-REC)	Within a 12-week period, 7 or more weeks of good sleep after CI episodes where the final 4 weeks in the period were designated as good sleep

* Participants that did not meet the transition criteria for AI were considered continuous good sleepers.

Table 2. Group means and percentages with respect to age, sex, race, income, and BMI

	GS			AI-PPS			AI-CI			AI-REC			CI-REC			ANOVA or exact p-value
Variable	N	Mean or %	Std Dev	N	Mean or %	Std Dev	N	Mean or %	Std Dev	N	Mean or %	Std Dev	N	Mean or %	Std Dev	
Age (years)	904	53.02	10.84	65	51.83	10.8	23	54.96	14.61	244	53.95	11.28	5	49.6	9.07	0.479
BMI (kg/m ²)	904	28.54	6.98	65	31.97	10.76	23	29.17	7.59	244	29.28	7.69	5	26.78	7.41	0.006
Female	904	64.6		65	73.85		23	60.87		244	75.93		5	100		0.003
Income(>=\$30,000)	904	78.98		65	76.92		23	65.22		244	75.1		5	60		0.24
Ethnic minority	904	16.81		65	16.92		23	13.04		244	18.67		5	20		0.923

Table 3. Descriptive Statistics for Mean TIB by Final Group Status (2 and 12 Weeks Prior to and Following the Onset of AI)

	GS			AI-PPS			AI-CI			AI-REC			CI-REC		
TIB-C	N	Mean	Std Dev	N	Mean	Std Dev	N	Mean	Std Dev	N	Mean	Std Dev	N	Mean	Std Dev
<u>2 WEEK +/- AI</u>															
Pre AI (2w)	900	478.30	72.44	65	494.02	83.75	23	498.69	74.25	242	484.92	69.22	5	511.20	34.17
Post AI (2w)	857	476.39	78.12	65	500.79	62.82	23	509.78	80.88	244	498.09	70.71	5	536.63	79.88
Post-Pre	855	-2.41	50.02	65	6.77	66.17	23	11.09	37.44	242	10.85	57.67	5	25.43	79.53
<u>12 WEEK +/- AI</u>															
Pre AI (12w)	911	481.32	63.17	65	492.04	83.31	23	489.88	64.99	243	482.57	61.73	5	498.94	48.13
Post AI (12w)	860	477.74	71.78	65	491.26	60.75	23	500.69	53.92	244	486.85	58.25	5	511.10	37.71
Post-Pre	860	-2.62	42.93	65	-0.78	57.95	23	10.81	36.04	243	3.74	41.53	5	12.16	33.82

Table 4. Model estimated TIB at 2 and 12 Weeks Prior to and Following the Onset of AI

	GS			AI-PPS			AI-CI			AI-REC		
	Estimate	SE	95% CI	Estimate	SE	95% CI	Estimate	SE	95% CI	Estimate	SE	95% CI
2 WEEK +/- AI												
Pre AI (2w)	479.20	2.20	(474.88, 483.66)	488.92	8.03	(472.61, 504.67)	496.41	12.74	(474.78, 523.91)	483.93	3.51	(477.02, 490.91)
Post AI (2w)	478.63	2.16	(474.69, 483.12)	489.83	8.14	(474.53, 506.02)	500.18	12.39	(477.38, 525.93)	484.73	3.56	(477.73, 491.58)
Post-Pre	-0.60	0.56	(-1.68, 0.55)	0.82	2.69	(-3.57, 6.75)	3.56	3.15	(-2.79, 9.76)	0.78	0.81	(-0.73, 2.46)
12 WEEK +/- AI												
Pre AI (12w)	485.00	2.39	(480.13, 489.85)	484.42	9.76	(463.25, 503.46)	484.22	14.84	(460.43, 516.83)	480.54	4.28	(472.50, 489.11)
Post AI (12w)	477.99	2.28	(473.92, 482.65)	486.51	11.13	(463.23, 507.83)	497.42	9.56	(479.04, 516.80)	483.58	3.56	(476.64, 490.72)
Post-Pre	-7.01	2.17	(-10.90, -2.26)	1.18	10.49	(-18.00, 23.59)	12.08	14.12	(-18.75, 38.18)	2.97	3.89	(-4.56, 10.82)

Note: If the confidence interval does not contain the null hypothesis value (cross zero), the results are statistically significant.

CI-REC (given the small sample size) is not represented here