Why Treat Insomnia?

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Objective: To make the case that insomnia is better conceptualized, not as a symptom, but as a primary disorder.

Data Sources: PubMed was searched from 1975–2009 using the search terms *insomnia*, *insomnia* and *treatment*, *insomnia* and *cost*, and *insomnia* and *treatment* and *safety*.

Study Selection: English-language articles and other materials were selected to address the following claims: insomnia is unremitting, insomnia is disabling, insomnia is costly, insomnia is pervasive, insomnia is pernicious, and insomnia treatment is safe and effective.

Data Extraction/Synthesis: Insomnia, at least when chronic, should be conceptualized as a comorbid condition, one for which effective interventions are available.

Conclusions: It is speculated that treatment for insomnia will only become the norm when it has been demonstrated that treatment not only addresses the problem of insomnia but also serves to reduce medical and psychiatric morbidity. At that time, the question will no longer be "Why treat insomnia?" but instead "When isn't insomnia treatment indicated?"

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- Consider chronic insomnia to be a treatment target

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For several decades beginning in the 1970s, insomnia was considered a "symptom" not a "disorder." To the extent that insomnia was considered just a symptom of medical or psychiatric disease, it was believed that treatment of the parent disorder was sufficient and would result in the resolution of the insomnia. More recently, this perspective has given way to the position that, when chronic, insomnia should be characterized as a primary disorder, which, when it co-occurs with other medical and psychiatric illness, should be designated a comorbid condition (as opposed to a secondary symptom). These nosologic designations carry with them the clear implication that chronic insomnia merits targeted treatment. This perspective, however, has yet to influence the standard of practice. More often than not, insomnia continues to be undiagnosed and/or untreated.

In the present article, we attempt to answer the question: Why treat insomnia? PubMed was searched for English-language articles from 1975–2009 using the search terms *insomnia*, *insomnia* and *treatment*, *insomnia* and *cost*, and *insomnia* and *treatment* and *safety*.

Insomnia, when chronic, tends to be unremitting, disabling, costly, pervasive, and pernicious. These factors, in combination with the existence of effective treatments, provide more than sufficient justification for the perspective that insomnia should be a primary focus for treatment.

INSOMNIA IS UNREMITTING

There are very few studies on the natural history of insomnia. To our knowledge, there are a handful of such investigations.[1–5] In general, these studies

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Clinical Points

- Insomnia is best conceptualized as a disorder (as opposed to a symptom)
- When insomnia occurs along with other disorders, it is best conceptualized as a comorbid disorder
- Benzodiazepine receptor agonists and cognitive-behavioral therapy for insomnia (CBT-I) are effective to treat insomnia in the short term, and CBT-I has effects that persist beyond treatment discontinuation
- Targeted treatment of insomnia may serve to diminish the severity of disorders that are comorbid with the insomnia
- The primary barrier to successful treatment of insomnia is the relative unavailability of CBT-I providers

find that chronic insomnia does not spontaneously resolve,[1,3,5] and the presenting form of insomnia (ie, initial, middle, or late) tends to be unstable or variable over time. With respect to spontaneous remission, Mendelson[1] found that subjects who reported difficulty sleeping at their initial assessment (average chronicity of 10 years) continued to report insomnia at 2 follow-up intervals (70% at 40 months and 88% at 64 months) (Figure 1).

INSOMNIA IS DISABLING

To date, there are a number of investigations that suggest that individuals with chronic insomnia, as opposed to no or occasional insomnia, have more difficulty with intellectual, social, and/or vocational functioning (Figure 2).

With respect to intellectual functioning, there are numerous studies[6–8] documenting that patients with chronic insomnia report impaired cognitive performance. In fact, this type of daytime complaint constitutes one of the defining attributes of insomnia as it is delineated in *The International Classification of Sleep Disorders*, Second Edition.[9] This said, neuropsychological evaluations of patients with chronic insomnia have not yielded reliable data regarding specific cognitive deficits.[10] This discrepancy between perceived and measured impairment may be reflective of several things.

First, there may be an attentional bias toward negative performance, which nevertheless occurs at a normal rate.[11,12] Second, a neurotic preoccupation with poor performance irrespective of whether or not it occurs may be present. Third, and finally, the perception of performance deficits may not be related to actual poor performance, or altered self-monitoring, but rather to the patient's real appreciation of the fact that extra effort is required to maintain normal or near-normal performance.[10]

With respect to social functioning, patients with chronic insomnia reliably report decreased interest in, facility with, and satisfaction from interpersonal relationships and social interactions. For example, in patients being seen in a primary care practice, chronic insomnia is associated with decreased ability to handle minor irritations, decreased ability to enjoy family/social life, and poorer interpersonal relationships with spouses.[8]

With respect to vocational performance, several studies have found that sleep disturbance and/or chronic insomnia are associated with less job satisfaction, lower performance scores, less productivity, and higher rates of absenteeism.[13,14] A study by Leger et al[15] found that those with insomnia had more absenteeism compared to good sleepers (31% vs 19%) and made more errors at work in the previous month (15% vs 6%) and that 18% of those with insomnia, versus 8% of good sleepers, reported poor work efficiency in the past month.

INSOMNIA IS COSTLY

In the United States alone, the direct and indirect costs attributable to insomnia exceed $100 billion annually.[16] Direct costs, including physician visits, prescriptions, and procedures, equal or exceed $13 billion per annum.[17] These costs are, in part, related to the increased tendency of patients with insomnia to use health care resources and to the costs of pharmacotherapy.[15] The estimated cost of physician visits is over $600 million per year, and the cost of prescription medications is estimated to be over $800 million per year.[17]

Indirect costs associated with motor vehicle and workplace accidents, reduced productivity, and absenteeism are thought to account for the majority of the economic consequences of insomnia with cost estimates between $77 and $92 billion per annum. Individuals with a variety of sleep disorders are thought to be at increased risk for motor vehicle accidents.[18] Patients with insomnia in particular have been found to be 2½ times more likely to report car crashes because of feeling tired as compared to those who do not report insomnia.[19]

One study in an Australian cohort estimated the cost of sleep-related motor vehicle accidents to be in excess of $180 million per year (Australian $).[20] Patients with insomnia are also thought to be at

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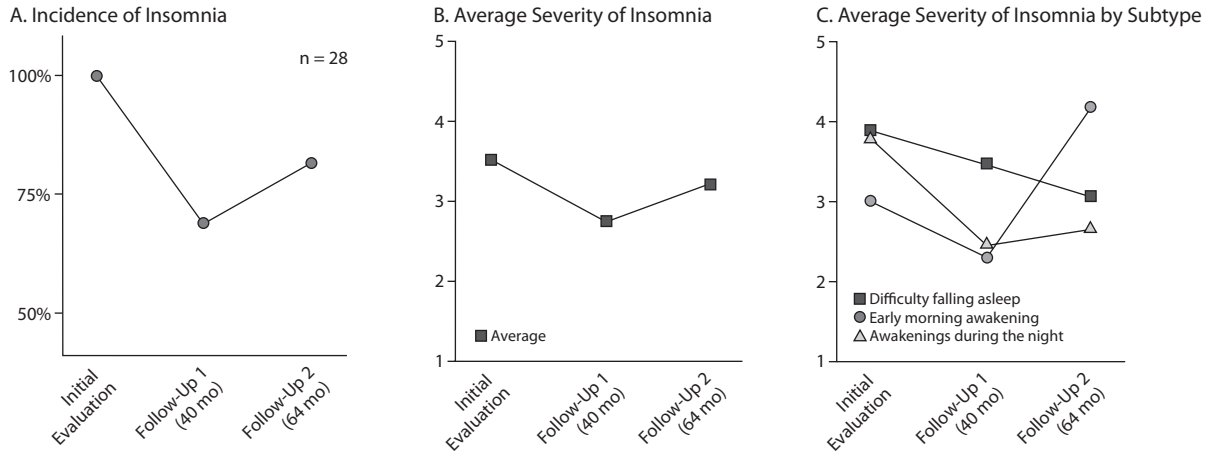
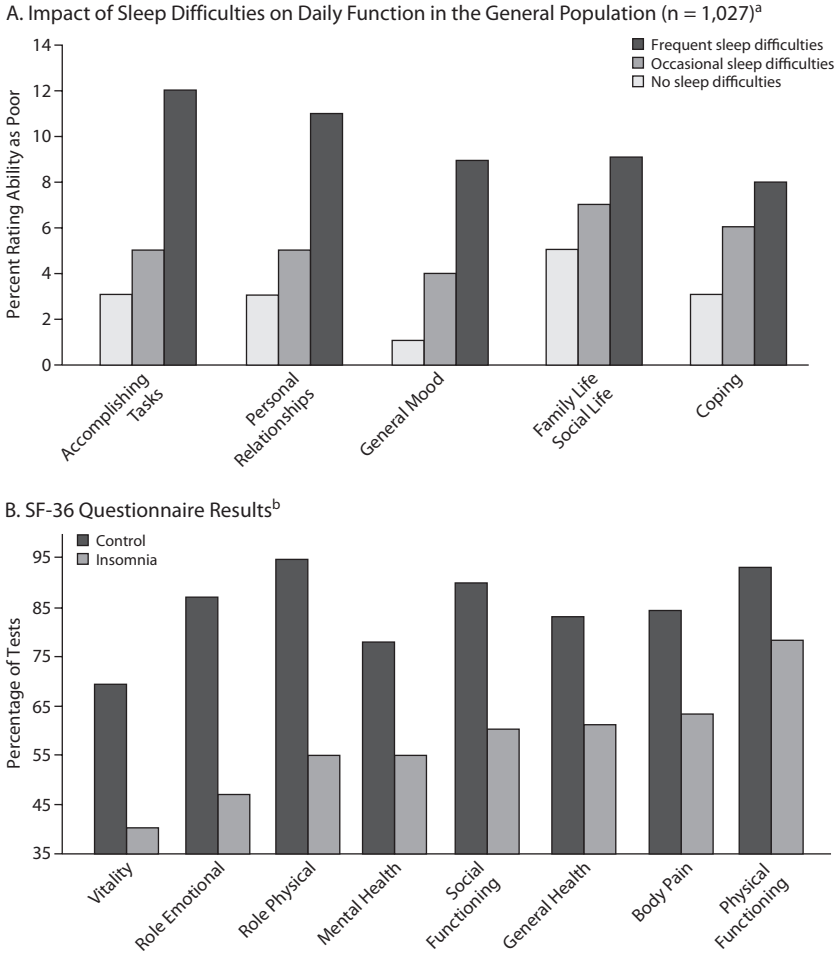
Figure 1. Insomnia Incidence and Severity Over Time (n = 28)[a]



[a]Based on data from Mendelson.[1]

Figure 2. Sleep and Function



[a]Based on data from Roth and Ancoli-Israel.[102]
[b]Based on data from Zammit et al.[103]Abbreviation: SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

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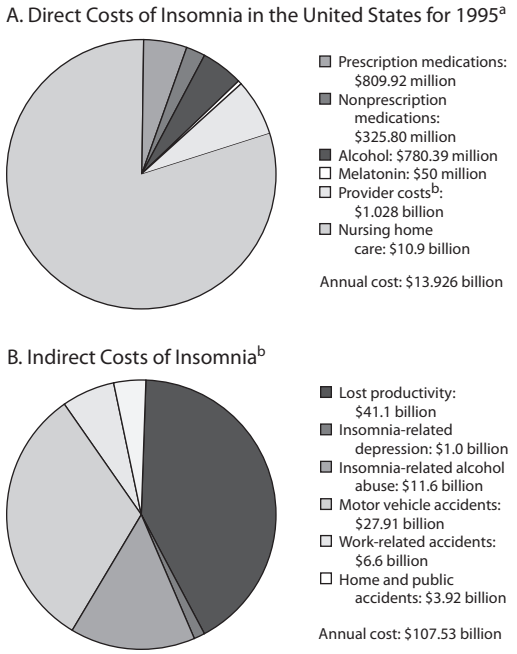
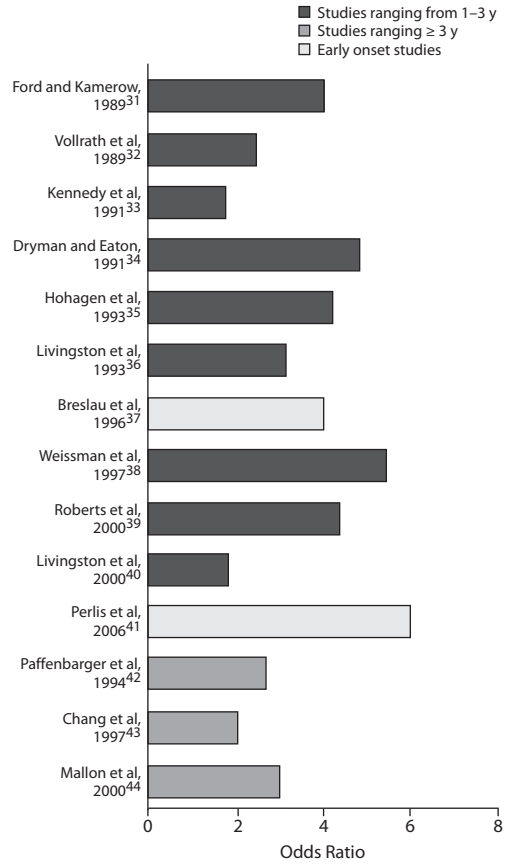
Figure 3. The Economic Burden of Insomnia



[a]Based on data from Walsh et al.[56] Provider costs include outpatient physician visits, psychologist visits, social worker visits, sleep specialist visits, mental health organizations, and inpatient hospital care.
[b]Based on data from Stoller MK.[104]

Figure 4. Odds Ratios From Longitudinal Studies Showing the Elevated Risk for the Development or Presence of Depression When There Are Symptoms of Sleep Disturbance Consistent With Persistent Insomnia



increased risk for workplace accidents (industrial accidents). In the Australian cohort, it was found that patients with insomnia were approximately 8 times more likely to have such accidents as compared to good sleepers. In this instance, the annual cost of work place accidents was estimated to be in excess of $1.9 billion (Australian $).[20] Finally, as noted above, insomnia is associated with reduced productivity and absenteeism. These costs have been estimated to exceed 1.3 billion per annum (Australian $).[20]

The aforementioned direct and indirect costs were assessed at the societal level. Recent work by Ozminkowski et al[21] suggests that the individual cost per annum among patients with insomnia is $1,253 in younger adults and $1,143 in older adults more than the direct health care expenses of the same groups of patients without insomnia. Figure 3 provides further cost data.

INSOMNIA IS PERVASIVE

As stated in the 2005 National Institutes of Health (NIH) State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults:[22]

> . . . chronic insomnia is known to be common. Population-based studies suggest that about 30% of the general population complains of sleep disruption, while approximately 10% has associated symptoms of daytime functional impairment consistent with the diagnosis of insomnia, although it is unclear what proportion of that 10% suffers from chronic insomnia. Not surprisingly, higher prevalence rates are found in clinical practices, wherein about half of respondents report symptoms of sleep disruption.

INSOMNIA IS PERNICIOUS

While it may seem an overstatement to say "insomnia is pernicious," there are a variety of studies suggesting that chronic insomnia is a significant risk factor for both new-onset and recurrent medical and psychiatric illness.

With respect to medical disease, the data suggesting that insomnia confers risk are preliminary. Only a few epidemiologic studies have been conducted, and even fewer studies have assessed the association prospectively. This said, the data that exist suggest that patients with

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insomnia are more likely to suffer from pain conditions and gastrointestinal distress[13] and that untreated insomnia puts sufferers at risk for hypertension[23,24] and heart disease.[23,25] It has also been suggested that insomnia may be a risk factor for the development of diabetes. Experimental data in good sleeper subjects have shown that sleep loss is associated with reduced insulin sensitivity.[26] Observational data in patients with type II diabetes have shown that poor sleep quality is associated with poor glycemic regulation.[27] Finally, there are data indicating that insomnia and/or short sleep duration are associated with increased mortality.[28,29] Whether these associations are causal remains to be determined as does what factors related to insomnia in specific confer and moderate/mediate risk.

With respect to psychiatric disease, there is a preponderance of data to suggest that insomnia confers increased risk for new-onset and recurrent illness and that this is particularly true for depression/major depressive disorder (MDD).[30] There are now at least 14 longitudinal studies showing that subjects with chronic insomnia are between 2 and 6 times more likely to have a new-onset or recurrent episode of depression (within 6 months to 3 years) as compared to subjects without chronic insomnia (Figure 4).[31–44]

In addition to the risk for new-onset and recurrent illness, there are 2 studies that suggest that insomnia is associated with the clinical course of MDD. In the first study,[45] subjects with recurrent MDD were assessed to determine whether insomnia severity increases prior to recurrence of MDD (ie, whether insomnia exists as a prodromal or precipitating factor for MDD). The time series data from this study showed that the nonrecurrent group exhibited an elevated, but stable, level of insomnia, while the recurrent group exhibited an increased level of sleep disturbance that began 5 weeks prior to, and was of highest severity at, the week of recurrence.[45]

In the second study,[46] the association of insomnia to treatment response was assessed in a large interventional study of late-life depression. Subjects were assessed for their clinical status at baseline and at 3, 6, and 12 months to determine whether insomnia at baseline and 3 months (classified as no insomnia, insomnia, and persistent insomnia) was associated with clinical improvement and/or the occurrence of remission at 6 and 12 months.[46] The groups were found to be significantly different in terms of the percentage of subjects who remained ill at 6 months according to 2 measures of depression (remission and < 50% improvement). Overall, patients with persistent insomnia were 2–4 times less likely to achieve remission or an improvement ≥ 50% in depressive symptoms as compared with patients with no insomnia.[46]

Taken together, these data suggest that insomnia may serve as a predisposing, precipitating, and/or perpetuating factor for depression. This said, as with medical disorders, it remains to be (1) shown that these associations are causal and (2) determined as to what factors related to insomnia confer and mediate risk. For additional information on the association between insomnia and depression, the reader is referred to Pigeon and Perlis[30] and Perlis et al.[47]

INSOMNIA TREATMENT IS SAFE AND EFFECTIVE

There are a number of meta-analyses that summarize the literature for both benzodiazepines and benzodiazepine receptor agonists (BZRAs; ie, zolpidem, eszopiclone, and zaleplon) and for cognitive-behavioral therapy for insomnia (CBT-I).[48–51] There is also 1 comparative meta-analysis that evaluates the relative efficacy of benzodiazepines and BZRAs as compared to CBT-I.[52] The data from these studies suggest, consistent with the conclusions of the NIH State-of-the-Science Conference Statement,[22] that (1) BZRAs and CBT-I are effective to treat insomnia in the short term, and CBT-I appears to have more durable effects when active treatment is discontinued, and (2) there is limited evidence that BZRAs retain their efficacy during long-term treatment.

As for safety, most agree that the first-line treatment modalities have very benign safety profiles. To date, only a few studies have been conducted on the relative safety of benzodiazepines and BZRAs, and no studies have been conducted comparing the efficacy and safety of medications with an indication for insomnia and/or CBT-I to medications that are used off label.

ARE THESE REASONS ENOUGH TO JUSTIFY TREATMENT?

The central proposition for this review is because chronic insomnia tends to be unremitting, disabling, costly, pervasive, and pernicious, and because there are effective treatments, there is more than sufficient justification for the perspective that insomnia should be a primary focus for treatment. While reasonable, this proposition does not address the issue that would eliminate any and all doubt about the appropriateness of aggressive treatment of insomnia: the possibility that insomnia is a modifiable risk factor for medical and psychiatric illness.

To date, all that can be definitively said is that insomnia treatment diminishes the severity of insomnia and/or the psychological distress that accompanies this disorder. While a laudable outcome, there is little information available regarding the daytime consequences of improved sleep. This is the case because treatment outcome has almost exclusively focused on the sleep continuity variables,[53] and there is not yet a consensus regarding the criteria to determine what constitutes successful

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outcomes.[54] What is needed are clear demonstrations that insomnia treatment reduces the incidence and severity of insomnia and that such outcomes serve to improve daytime function and/or reduce the incidence and severity of other forms of medical and psychiatric symptomatology and/or morbidity. To date, there are only a handful of such studies.

Within the daytime function arena, there are 3 studies that show that treatment positively impacts this domain. Leger and colleagues[55] have shown that medical treatment of insomnia results in significant improvements with respect to quality of life. Krystal[53] has shown that pharmacologic treatment results in improved self-reported health, mood, concentration/alertness, daytime functioning, and quality of life. Walsh and colleagues[56] have shown similar gains with pharmacotherapy on quality of life measures and extend these findings to include positive outcomes with respect to work limitations.

Within the medical and psychiatric domain, there are 2 studies with medical outcomes and 3 investigations with psychiatric outcomes. With respect to medical outcomes, Edinger and colleagues[57] found that CBT-I leads to improvements in medical and psychological functioning in patients with fibromyalgia. Preliminary data from Pigeon et al[58] show that CBT-I in chronic pain patients with comorbid insomnia leads to significant reductions in insomnia, depression, and perceived pain (as measured by the Pain Disability Index and the Multidimensional Pain Inventory) as compared to patients who received nondirective-supportive therapy or were randomized to a wait-list condition.

With respect to psychiatric outcomes, Fava and colleagues[59] have shown that concomitant treatment of insomnia in the context of acute depression (fluoxetine ± eszopiclone) yields (1) effects on insomnia that are comparable with those seen in primary insomnia and (2) effects on the clinical course of the comorbid disorder. That is, a larger proportion of patients treated with dual therapy experienced treatment response and/or remission and did so at an accelerated rate. Similar preliminary data with CBT-I were recently reported by Manber et al.[60] Finally, there is a study by Taylor and colleagues[61] suggesting that CBT-I, when administered as a monotherapy, is associated with a significant decrease in depression severity in acutely ill patients with mild depression. Taken together, these data provide the first examples that insomnia treatment may improve quality of life and have larger effects on at least mental health.

CONCLUSION

Ultimately, the question "Why treat insomnia?" is derived from the broader question "Why bother treating insomnia?" The latter concept is rooted in the belief that insomnia is primarily only a symptom, is occasionally a primary disorder, and more often than not occurs secondary to other medical and psychiatric conditions. Implicit in this point of view is that (1) it is possible to, for the purposes of diagnosis, distinguish between primary and secondary insomnia; (2) when the primary condition is properly treated, the insomnia will (as a symptom of that primary disorder) abate; and (3) targeted treatments for primary insomnia will be relatively, or completely, ineffective for secondary insomnia (chronic insomnia that occurs in the context of, for example, depression, posttraumatic stress disorder, chronic pain, cancer, etc).

In recent years, there has been a growing interest in the veracity of the concept of secondary insomnia. This challenge has largely occurred at the theoretical level. Lichstein and colleagues[62–65] have argued that it is nearly impossible to substantiate that insomnia is truly secondary (ie, that the onset of the insomnia co-occurred with the onset of, and temporally covaries with the severity of, the primary disorder), and, thus, the distinction has little nosological value and should not be used to dictate when targeted treatment is warranted. This point of view is further buttressed by the Spielman Model of Insomnia,[66,67] which clearly suggests that chronic insomnia is maintained by a set of factors that function independently of what may have predisposed the individual to, or precipitated the acute episode of, insomnia. If this is true, the concept of secondary insomnia has little value beyond designating the factor that may have served to precipitate the insomnia.

Apart from the above theoretical considerations are the more practical tests of the concept that are related to treatment outcome. That is, "Is it really the case that, when the primary condition is properly treated, the insomnia abates?" Conversely, "Is it really the case that targeted treatments for primary insomnia are relatively, or completely, ineffective for secondary insomnia?"

In the case of the former question, there are few studies that evaluate the effects of treatment of primary conditions on the incidence and severity of insomnia. Of the investigations that exist, most (if not all) have been conducted in subjects with major depression. Reynolds et al,[68] for example, found in subjects who were treated with nortriptyline and designated as "recovered" from depression, that their insomnia severity (as measured with the Pittsburgh Sleep Quality Index) was reduced but not normalized. In a similar study, Nierenberg et al[69] found that 45% of the subjects successfully treated with fluoxetine continued to experience insomnia and that this "symptom" was more persistent than any of the other 9 symptoms of depression in this sample.

Comparable observations have come from CBT treatments of depression.[70,71] In 2 separate randomized trials comparing CBT for depression to antidepressant medication, approximately 50% of those who remitted

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from depression had residual insomnia.[72,73] This was also the case for a trial of CBT for posttraumatic stress disorder, in which approximately half of treatment responders had residual insomnia.[74] While further studies are needed, these investigations serve to illustrate that insomnia (1) should not simply be understood as a symptom of other disorders and (2) when it occurs in the context of medical and/or psychiatric illness, may be better understood as (and treated as) a comorbid condition.

In the case of the latter question, there are now a variety of studies evaluating the efficacy of targeted insomnia treatment in patient populations with secondary insomnia. The majority of these studies have been undertaken with CBT-I. To date, there are at least 23 such investigations in both heterogeneous samples of medical or psychiatric illness and the context of specific disorders like major depression, posttraumatic stress disorder, chronic pain, fibromyalgia, and cancer.[57,75–96] In general, the findings with CBT-I (assessed prospectively with sleep diaries) clearly indicate that the treatment outcomes are comparable, and in some cases superior, to those found in patients with primary insomnia. In general, the findings with CBT-I (assessed prospectively with sleep diaries) clearly indicate that the treatment outcomes are comparable, and in some cases superior, to those found in patients with primary insomnia. These findings serve as a further challenge to the relevance of the concept of secondary insomnia.

The findings with pharmacotherapy, while far fewer in number, are nicely captured by a mega-analysis recently conducted by Schaefer and colleagues.[97] In this analysis, it was found that a BZRA (eszopiclone) was associated with moderate to large effects on all sleep outcomes analyzed for each of the secondary insomnias, including insomnia comorbid with MDD, generalized anxiety disorder, perimenopausal transition, and rheumatoid arthritis. The largest effects, however, were generally observed in subjects with primary insomnia. This, unlike the findings with CBT-I, serves to support the notion that the concept of secondary insomnia is relevant for treatment.

In summary, Why treat insomnia? At present, the answer is simply because insomnia can be effectively treated, and treatment can be expected to reduce insomnia-related distress and suffering in the tens of millions of patients who live with this disorder. In the future, the answer to this query is likely to be more compelling. If it can be shown that insomnia is a modifiable risk factor for medical and/or psychiatric illness and/or that targeted treatment of comorbid insomnia reliably reduces illness severity and/or promotes remission, then the answer to the question will be "because treatment for insomnia promotes better medical and/or psychiatric health." In fact, the question "Why treat insomnia?" will, at that time, be moot, and the new questions to answer will be "When isn't insomnia treatment indicated?" and "Which treatment works best?" The latter of these 2 questions has been the topic of some research in the last 10 years. Unfortunately, the question has been narrowly construed as "Which treatment is better: CBT-I or pharmacotherapy with BZRAs?" On the basis of the existing studies, the simple answer to this question is that the 2 approaches yield comparable outcomes in the short term but only CBT-I has effects that persist beyond treatment discontinuation.[52,98–101]

The more comprehensive answer is not, at this time, possible because the more complex questions have not been addressed. For example, is it possible to produce durable effects with standard BZRAs by using alternative treatment regimens? If not, is the best use of hypnotics to promote prophylaxis in the context of acute insomnia? Is it possible that some of the types of insomnia (eg, psychophysiologic, paradoxical, idiopathic, or the pediatric insomnias) are more or less responsive to either of the current therapeutic approaches? Is it possible that some of the subtypes of insomnia (initial, middle, late, or mixed insomnia) are more or less responsive to CBT-I or pharmacotherapy? When these questions are addressed, the issues regarding the proper treatment of insomnia will have been fully explicated, and the indications for insomnia treatment will be entirely clear.

Drug names: fluoxetine (Prozac, Sarafem, and others), nortriptyline (Pamelor), zaleplon (Sonata and others), zolpidem (Ambien, Zolpimist, and others).

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REFERENCES

1. Mendelson WB. Long-term follow-up of chronic insomnia. *Sleep.* 1995;18(8):698–701.
2. Morin CM, Belanger L, LeBlanc M, et al. The natural history of insomnia: a population-based, 3-year, longitudinal study. *Arch Intern Med.* 2009;169(5):447–453.
3. Young TB. Natural history of chronic insomnia. *J Clin Sleep Med.* 2005;1:e466–e467.
4. Hohagen F, Kappler C, Schramm E, et al. Sleep onset insomnia, sleep maintaining insomnia and insomnia with early morning awakening: temporal stability of subtypes in a longitudinal study

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on general practice attenders. *Sleep.* 1994;17(6):551–554.
5. LeBlanc M, Mérette C, Savard J, et al. Incidence and risk factors of insomnia in a population-based sample. *Sleep.* 2009;32(8):1027–1037.
6. Roth T, Roehrs T. Insomnia: epidemiology, characteristics, and consequences. *Clin Cornerstone.* 2003;5(3):5–15.
7. Carey TJ, Moul DE, Pilkonis P, et al. Focusing on the experience of insomnia. *Behav Sleep Med.* 2005;3(2):73–86.
8. Shochat T, Umphress J, Israel AG, et al. Insomnia in primary care patients. *Sleep.* 1999;22(suppl 2):S359–S365.
9. American Academy of Sleep Medicine. *The International Classification of Sleep Disorders*. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
10. Orff HJ, Drummond SPA, Nowakowski S, et al. Discrepancy between subjective symptomatology and objective neuropsychological performance in insomnia. *Sleep.* 2007;30(9):1205–1211.
11. Harvey AG. A cognitive model of insomnia. *Behav Res Ther.* 2002;40(8):869–893.
12. Espie CA, Broomfield NM, MacMahon KMA, et al. The attention-intention-effort pathway in the development of psychophysiologic insomnia: an invited theoretical review. *Sleep Med Rev.* 2006;10(4):215–245.
13. Kuppermann M, Lubeck DP, Mazonson PD. Sleep problems and their correlates in a working population. *J Gen Intern Med.* 1995;10(1):25–32.
14. Johnson L, Spinweber C. Quality of sleep and performance in the navy: a longitudinal study of good and poor sleepers. In: Guilleminault C, Lugaresi E, eds. *Sleep/Wake Disorders: Natural History, Epidemiology, and Long-Term Evaluation*. New York, NY: Raven Press; 1983:13–28.
15. Leger D, Guilleminault C, Bader G, et al. Medical and socio-professional impact of insomnia. *Sleep.* 2002;25(6):625–629.
16. Fullerton DS. The economic impact of insomnia in managed care: a clearer picture emerges. *Am J Manag Care.* 2006;12(suppl 8):S246–S252.
17. Walsh JK, Engelhardt CL. The direct economic costs of insomnia in the United States for 1995. *Sleep.* 1999;22(suppl 2):S386–S393.
18. Aldrich MS. Automobile accidents in patients with sleep disorders. *Sleep.* 1989;12(6):487–494.
19. Roth T, Ancoli-Israel S. Daytime consequences and correlates of insomnia in the United States: results of the 1991 National Sleep Foundation Survey II. *Sleep.* 1999;22(suppl 2):S354–S358.
20. Hillman DR, Murphy AS, Pezzullo L. The economic cost of sleep disorders. *Sleep.* 2006;29(3):299–305.
21. Ozminkowski RJ, Wang SH, Walsh JK. The direct and indirect costs of untreated insomnia in adults in the United States. *Sleep.* 2007;30(3):263–273.
22. NIH State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults: 2005. National Institutes of Health; June 13–15, 2005. http://consensus.nih.gov/2005/2005InsomniaSOS026html.htm.
23. Phillips B, Mannino D. Do insomnia complaints cause hypertension or cardiovascular disease? *J Clin Sleep Med.* 2007;3(5):489–494.
24. Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. *J Occup Health.* 2003;45(6):344–350.
25. Schwartz S, McDowell AW, Cole SR, et al. Insomnia and heart disease: a review of epidemiologic studies. *J Psychosom Res.* 1999;47(4):313–333.
26. Mander B, Colecchia E, Spiegel K, et al. Short sleep: a risk factor for insulin resistance and obesity. *Diabetes.* 2001;50(suppl 2):A45.
27. Knutson KL, Ryden AM, Mander BA, et al. Role of sleep duration and quality in the risk and severity of type 2 diabetes mellitus. *Arch Intern Med.* 2006;166(16):1768–1774.
28. Kripke DF, Simons RN, Garfinkel L, et al. Short and long sleep and sleeping pills: is increased mortality associated? *Arch Gen Psychiatry.* 1979;36(1):103–116.
29. Dew MA, Hoch CC, Buysse DJ, et al. Healthy older adults' sleep predicts all-cause mortality at 4 to 19 years of follow-up. *Psychosom Med.* 2003;65(1):63–73.
30. Pigeon W, Perlis ML. Insomnia and depression: birds of a feather? *Int J Sleep Disord.* 2007;1:82–91.
31. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders: an opportunity for prevention? *JAMA.* 1989;262(11):1479–1484.
32. Vollrath M, Wicki W, Angst J. The Zurich study. VIII. Insomnia: association with depression, anxiety, somatic syndromes, and course of insomnia. *Eur Arch Psychiatry Neurol Sci.* 1989;239(2):113–124.
33. Kennedy GJ, Kelman HR, Thomas C. Persistence and remission of depressive symptoms in late life. *Am J Psychiatry.* 1991;148(2)174–178.
34. Dryman A, Eaton WW. Affective symptoms associated with the onset of major depression in the community: findings from the US National Institute of Mental Health Epidemiologic Catchment Area Program. *Acta Psychiatr Scand.* 1991;84(1):1–5.
35. Hohagen F, Rink K, Kappler C, et al. Prevalence and treatment of insomnia in general practice: a longitudinal study. *Eur Arch Psychiatry Clin Neurosci.* 1993;242(6):329–336.
36. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? a study in inner London. *Br J Gen Pract.* 1993;43(376):445–448.
37. Breslau N, Roth T, Rosenthal L, et al. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry.* 1996;39(6):411–418.
38. Weissman MM, Greenwald S, Nino-Murcia G, et al. The morbidity of insomnia uncomplicated by psychiatric disorders. *Gen Hosp Psychiatry.* 1997;19(4):245–250.
39. Roberts RE, Shema SJ, Kaplan GA, et al. Sleep complaints and depression in an aging cohort: a prospective perspective. *Am J Psychiatry.* 2000;157(1):81–88.
40. Livingston G, Watkin V, Milne B, et al. Who becomes depressed? The Islington community study of older people. *J Affect Disord.* 2000;58(2):125–133.
41. Perlis ML, Smith LJ, Lyness JM, et al. Insomnia as a risk factor for onset of depression in the elderly. *Behav Sleep Med.* 2006;4(2):104–113.
42. Paffenbarger RS, Lee IM, Leung R. Physical activity and personal characteristics associated with depression and suicide in American college men. *Acta Psychiatr Scand.* 1994;89(suppl 377):16–22.
43. Chang PP, Ford DE, Mead LA, et al. Insomnia in young men and subsequent depression: The Johns Hopkins Precursors Study. *Am J Epidemiol.* 1997;146(2):105–114.
44. Mallon L, Broman JE, Hetta J. Relationship between insomnia, depression, and mortality: a 12-year follow-up of older adults in the community. *Int Psychogeriatr.* 2000;12(3):295–306.
45. Perlis ML, Giles DE, Buysse DJ, et al. Self-reported sleep disturbance as a prodromal symptom in recurrent depression. *J Affect Disord.* 1997;42(2-3):209–212.
46. Pigeon WR, Hegel MT, Unutzer J, et al. Is insomnia a perpetuating factor for late-life depression in the IMPACT cohort? *Sleep.* 2008;31(4):481–488.
47. Perlis M, Smith M, Orff H. Commentary on neurobiological basis for the relation between sleep and depression. *Sleep Med Rev.* 2002;6(5):353–357.
48. Nowell PD, Mazumdar S, Buysse DJ, et al. Benzodiazepines and zolpidem for chronic insomnia: a meta-analysis of treatment efficacy. *JAMA.* 1997;278(24):2170–2177.
49. Glass J, Lanctot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ.* 2005;331(7526):1169.
50. Morin CM, Culbert JP, Schwartz SM. Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *Am J Psychiatry.* 1994;151(8):1172–1180.
51. Murtagh DR, Greenwood KM. Identifying effective psychological treatments for insomnia: a meta-analysis. *J Consult Clin Psychol.* 1995;63(1):79–89.
52. Smith MT, Perlis ML, Park A, et al. Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *Am J Psychiatry.* 2002;159(1):5–11.
53. Krystal AD. Treating the health, quality of life, and functional impairments in insomnia. *J Clin Sleep Med.* 2007;3(1):63–72.
54. Morin CM. Measuring outcomes in randomized clinical trials of insomnia treatments. *Sleep Med Rev.* 2003;7(3):263–279.
55. Leger D, QueraSalva MA, Philip P. Health-related quality of life in patients with insomnia treated with zopiclone. *Pharmacoeconomics.* 1996;10(suppl 1): 39–44.
56. Walsh JK, Krystal AD, Amato DA, et al. Nightly treatment of primary insomnia with eszopiclone for six months: effect on sleep, quality of life, and work limitations. *Sleep.* 2007;30(8):959–968.
57. Edinger JD, Wohlgemuth WK, Krystal AD, et al. Behavioral insomnia therapy for fibromyalgia patients: a randomized clinical trial. *Arch Intern Med.* 2005;165(21):2527–2535.
58. Pigeon W, Jungquist C, Matteson S, et al. Pain, sleep and

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mood outcomes in chronic pain patients following cognitive behavioral therapy for insomnia. *Sleep.* 2007;30:A255–A256.
59. Fava M, McCall WV, Krystal A, et al. Eszopiclone co-administered with fluoxetine in patients with insomnia coexisting with major depressive disorder. *Biol Psychiatry*. 2006 59(11):1052–1060.
60. Manber R, Edinger JD, Gress JL, et al. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep.* 2008;31(4):489–495.
61. Taylor DJ, Lichstein KL, Weinstock J, et al. A pilot study of cognitive-behavioral therapy of insomnia in people with mild depression. *Behav Ther.* 2007;38(1):49–57.
62. Lichstein KL. Secondary insomnia: a myth dismissed. *Sleep Med Rev.* 2006;10:3–5.
63. Lichstein KL, McCrae CS, Wilson NM. Secondary insomnia: Diagnostic issues, cognitive-behavioral treatment and future directions. In: Perlis M, Lichstein KL, eds. *Treating Sleep Disorders: Principles and Practice of Behavioral Sleep Medicine*. New York, NY: John Wiley & Sons, Inc; 2003:286–304.
64. McCrae CS, Lichstein KL. Secondary insomnia: diagnostic challenges and intervention opportunities. *Sleep Med Rev.* 2001;5(1):47–61.
65. McCrae CS, Lichstein KL. Secondary insomnia: a heuristic model and behavioral approaches to assessment, treatment, and prevention. *Appl Prev Psychol.* 2001;10:107–123.
66. Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. *Psychiatr Clin North Am.* 1987;10(4):541–553.
67. Spielman AJ, Saskin P, Thorpy MJ. Treatment of chronic insomnia by restriction of time in bed. *Sleep.* 1987;10(1):45–56.
68. Reynolds CF III, Hoch CC, Buysse DJ, et al. Sleep in late-life recurrent depression: changes during early continuation therapy with nortriptyline. *Neuropsychopharmacology.* 1991;5(2):85–96.
69. Nierenberg AA, Keefe BR, Leslie VC, et al. Residual symptoms in depressed patients who respond acutely to fluoxetine. *J Clin Psychiatry.* 1999;60(4):221–225.
70. Simons AD, Murphy GE, Levine JL, et al. Cognitive therapy and pharmacotherapy for depression: sustained improvement over one year. *Arch Gen Psychiatry.* 1986;43(1):43–48.
71. Thase ME, Simons AD, Cahalane JF, et al. Cognitive behavior therapy of endogenous depression, pt 1: an outpatient clinical replication series. *Behav Ther.* 1991;22(4):457–467.
72. Manber R, Rush J, Thase ME, et al. The effects of psychotherapy, nefazodone, and their combination on subjective assessment of disturbed sleep in chronic depression. *Sleep.* 2003;26(2):130–136.
73. Carney CE, Segal ZV, Edinger JD, et al. A comparison of rates of residual insomnia symptoms following pharmacotherapy or cognitive-behavioral therapy for major depressive disorder. *J Clin Psychiatry.* 2007;68(2):254–260.
74. Deviva JC, Zayfert C, Pigeon WR, et al. Treatment of residual insomnia after CBT for PTSD: case studies. *J Trauma Stress.* 2005;18(2):155–159.
75. Germain A, Shear MK, Hall M, et al. Effects of a brief behavioral treatment for PTSD-related sleep disturbances: a pilot study. *Behav Res Ther.* 2007;45(3):627–632.
76. Germain A, Moul DE, Franzen PL, et al. Effects of a brief behavioral treatment for late-life insomnia: preliminary findings. *J Clin Sleep Med.* 2006;2(4):403–406.
77. Jungquist C, O'Brien C, Matteson-Rusby S, et al. The efficacy of cognitive behavioral therapy for insomnia in patients with chronic pain. *Sleep Medicine*. In press.
78. Cannici J, Malcolm R, Peek LA. Treatment of insomnia in cancer patients using muscle relaxation training. *J Behav Ther Exp Psychiatry.* 1983;14(3):251–256.
79. Currie SR, Wilson KG, Pontefract AJ, et al. Cognitive-behavioral treatment of insomnia secondary to chronic pain. *J Consult Clin Psychol.* 2000;68(3):407–416.
80. Currie SR, Clark S, Hodgins DC, et al. Randomized controlled trial of brief cognitive-behavioural interventions for insomnia in recovering alcoholics. *Addiction.* 2004;99(9):1121–1132.
81. Dashevsky BA, Kramer M. Behavioral treatment of chronic insomnia in psychiatrically ill patients. *J Clin Psychiatry.* 1998;59(12):693–699.
82. Davidson JR, Waisberg JL, Brundage MD, et al. Nonpharmacologic group treatment of insomnia: a preliminary study with cancer survivors. *Psychooncology.* 2001;10(5):389–397.
83. De Berry S. An evaluation of progressive muscle relaxation on stress related symptoms in a geriatric population. *Int J Aging Hum Dev.* 1981;14(4):255–269.
84. Dopke CA, Lehner RK, Wells AM. Cognitive-behavioral group therapy for insomnia in individuals with serious mental illnesses: a preliminary evaluation. *Psychiatr Rehabil J.* 2004;27(3):235–242.
85. French AP, Tupin JP. Therapeutic application of a simple relaxation method. *Am J Psychother.* 1974;28(2):282–287.
86. Kolko DJ. Behavioral treatment of excessive daytime sleepiness in an elderly woman with multiple medical problems. *J Behav Ther Exp Psychiatry.* 1984;15(4):341–345.
87. Krakow B, Hollifield M, Johnston L, et al. Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: a randomized controlled trial. *JAMA.* 2001;286(5):537–545.
88. Lichstein KL, Wilson NM, Johnson CT. Psychological treatment of secondary insomnia. *Psychol Aging.* 2000;15(2):232–240.
89. Morawetz D. Depression and insomnia. *Aust Fam Physician.* 2000;29(11):1016.
90. Morin CM, Kowatch RA, Wade JB. Behavioral management of sleep disturbances secondary to chronic pain. *J Behav Ther Exp Psychiatry.* 1989;20(4):295–302.
91. Quesnel C, Savard J, Simard S, et al. Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. *J Consult Clin Psychol.* 2003;71(1):189–200.
92. Savard J, Simard S, Ivers H, et al. A randomized study of on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, pt 1: sleep and psychological effects. *J Clin Oncol.* 2005;23(25):6083–6096.
93. Rybarczyk B, Lopez M, Benson R, et al. Efficacy of two behavioral treatment programs for comorbid geriatric insomnia. *Psychol Aging.* 2002;17(2):288–298.
94. Perlis ML, Sharpe M, Smith MT, et al. Behavioral treatment of insomnia: treatment outcome and the relevance of medical and psychiatric morbidity. *J Behav Med.* 2001;24(3):281–296.
95. Stam HJ, Bultz BD. The treatment of severe insomnia in a cancer patient. *J Behav Ther Exp Psychiatry.* 1986;17(1):33–37.
96. Tan TL, Kales JD, Kales A, et al. Inpatient multidimensional management of treatment-resistant insomnia. *Psychosomatics.* 1987;28(5):266–272.
97. Schaefer K, McCall W, Krystal A, et al. Relative effect sizes of eszopiclone treatment for insomnia in patients with primary insomnia and insomnia comorbid with major depressive disorder, generalized anxiety disorder, perimenopausal transition or rheumatoid arthritis. *Sleep.* 2007;30:A243–A244.
98. Varni JW. Behavioral treatment of disease-related chronic insomnia in a hemophiliac. *J Behav Ther Exp Psychiatry.* 1980;11(2):143–145.
99. Perlis M, Gehrman P, Riemann D. Intermittent and long-term use of sedative hypnotics. *Curr Pharm Des.* 2008;14(32):3456–3465.
100. Riemann D, Perlis ML. The treatments of chronic insomnia: a review of benzodiazepine receptor agonists and psychological and behavioral therapies. *Sleep Med Rev*. 2009;13(3):205–214.
101. Roscoe JA, Kaufman ME, Matteson-Rusby SE, et al. Cancer-related fatigue and sleep disorders. *Oncologist.* 2007;12(suppl 1):35–42.
102. Roth T, Ancoli-Israel S. Daytime consequences and correlates of insomnia in the United States: results of the 1991 National Sleep Foundation Survey. II. *Sleep.* 1999;22(suppl 2):S354–S358.
103. Zammit GK, Weiner J, Damato N, et al. Quality of life in people with insomnia. *Sleep.* 1999;22(suppl 2):S379–S385.
104. Stoller MK. Economic effects of insomnia. *Clin Ther.* 1994;16(5):873–897.

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