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The Link between Suicide and Insomnia: Theoretical Mechanisms

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Abstract

Insomnia has been established as a risk factor for depression and mental illness for decades, but a growing body of evidence has recently exposed insomnia to be an independent risk factor for suicide that encompasses all age ranges. This discovery has invigorated investigation to elucidate the relationship between insomnia and suicide, and over 20 studies reinforcing this association in adults have been published since 2010 alone. This article analyzes relevant research and emphasizes studies published within the last three years with the intent of proposing theoretical mechanisms explaining the link between suicide and insomnia. These mechanisms may then be used as targets for future investigation of treatment.

Keywords

Sleep; Depression; Suicide; Risk factors; Insomnia; Hopelessness; Nightmares; Mechanisms; Dysfunctional belief about sleep; Decision making; Serotonin; Hyperarousal; Circadian rhythm of suicide; Psychiatry

Introduction

Millions of Americans suffer from sleep related disorders such as obstructive sleep apnea, insomnia, and parasomnias, yet the study of sleep disorders and their long-term consequences is still relatively in its infancy. The recognition of Sleep Medicine as a legitimate subspecialty of medicine came upon the wings of a series of developments that include the establishment of a defined body of specialty-based knowledge, recognition by the American Medical Association, the creation of fellowship training programs approved by the Accreditation Council for Graduate Medical Education (ACGME), and the creation of board exams sponsored by the American Board of Medical Specialties (ABMS). In the course of these developments, the discovery that one sleep disorder, obstructive sleep apnea

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(OSA), is associated with excess mortality [1] elevated sleep problems from the status of trivial to urgent. In contrast to OSA, the realization that insomnia is a risk factor for suicide has come only recently.

Solid evidence has shown that insomnia is a risk factor for the development of mental illness, with the strongest risk ratios for depressive illness [2]. The causal mechanism of this association is not clear. For example, it is unknown whether insomnia is an independent phenomenon that if interrupted could forestall the emergence of a mental disorder, or whether insomnia is simply the leading edge of an illness that is already on the way. Investigators are already examining the former possibility, by way of focusing on preventing recurrent depressive illness. Success in this line of investigation would be of immense importance as there are presently limited numbers of means to prevent or minimize the recurrence of mental disorders of any type.

The importance of these findings has been paralleled by an accumulating body of evidence that insomnia is a risk factor for suicidal ideation, suicidal behavior, and suicide death (which we will collectively refer to here as “suicide”). Suicidal ideation is defined as a desire to die, or at least an indifference towards living, that may be accompanied by specific plans to kill oneself [3, 4]. By extension, suicidal behavior is a self-harm behavior, or a behavior that is preparatory to self-harm, and it is intended to lead to the possibility of death or increase the risk of death. Death by intentional self-harm would seem to be straightforward, yet sometimes death is the result of a self-harm act that was originally intended only to generate a response from others in the environment. This example would hence not be considered as suicidal. Suicidal behavior may be attended by simultaneous rescue behaviors, i.e., a person cuts their wrists with the idea of dying yet then goes to lie down in a public place to see if someone will rescue him/her. This example, however, would be coded as suicidal behavior [4]. Suicide is complex and is driven by different motivations in different individuals; several competing and potentially conflicting motivations may operate simultaneously in a given individual.

The evidence base linking insomnia and suicide is both wide and deep. There are more than 60 separate research reports that encompass children, adolescents, young adults, and older persons, and these reports come from the Americas, Europe, and Asia. A summary of the studies in adults can be found in Table 1. The reports include population studies, clinical samples, chart reviews, prospective case-control cohorts, and clinical trials. The methods of assessing insomnia vary widely across these studies, with some studies using validated and standardized measures of insomnia and other studies only using one-off indicators of insomnia. Furthermore, some studies reported insomnia as either present versus absent while other studies used dimensional measures of insomnia intensity. The measurement of suicide was similarly varied across these studies. Despite the variability in assessment, the basic findings remain remarkably consistent with relative risks in the range of 2.0 (Table 1).

Multiple investigations have simultaneously assessed both “insomnia” and “nightmares”, and these studies typically found that the presence of nightmares was as potent, or more potent, than insomnia in predicting suicide [5•, 6]. The term “nightmares” connotes the experience of a dysphoric dream during rapid eye movement (REM) sleep, characterized by a narrative (albeit a disjointed narrative), high visual impact, and good recall upon awakening. Indeed, frequent nightmares are reported to increase the risk of suicidal thoughts by a factor of 1.5 – 3 and increase the risk for suicide attempts by a factor of 3 – 4 [7•]. Nightmares are a common feature of post-traumatic stress disorder (PTSD), and perhaps play a role in explaining the rising rates of suicide in US servicemen returning from the Global War on Terror [8]. When nightmares as well as dysfunctional beliefs and attitudes about sleep (DBAS) are simultaneously considered as mediators between insomnia and

suicide, then the association between insomnia and suicide disappears [9•]. It is of note, however, that the correlation between nightmares and suicide may not hold true in older adults [10], and this may possibly be due in part because of the sleep changes that occur with increased age such as altered REM sleep patterns and decreased number of reported nightmares [10].

Recent Reports on the Sleep-Suicide Link

The sheer variety of the sources of data and the convergence of the findings make a compelling case that the association between insomnia and suicide is real. Healthy skepticism, nonetheless, would note that insomnia is a frequent symptom of depression, and depression is a known risk for suicide. It could therefore be argued that it is the depression syndrome rather than the insomnia symptom itself that conveys the risk. However, meta-analysis shows that the association between insomnia and suicide still holds even after controlling for the presence or absence of depressive disorder [11•] and after controlling for the intensity of specific symptoms such as depressed mood and hopelessness [12]. In fact, persistent insomnia among individuals who lacked depression at baseline increases the risk of both depression and suicidal thoughts prospectively across the span of six years [13•].

Nightmares are an additional independent predictor of suicide [7•]. Nightmares, especially when persistent over time, can foreshadow suicidal behavior in the form of repeated suicide attempts among those who had attempted suicide within the preceding two years [6]. The temporal duration of insomnia and nightmares, like the intensity of insomnia and nightmares, is also predictive of suicide. Indeed, unresolved insomnia and nightmare symptoms were significantly correlated with suicidal ideation among depressed patients who remitted across a span of four years. Residual nightmares, in particular, were associated with suicidal ideation with a large odds ratio of 8.4 [5]. Furthermore, the overall duration of insomnia and nightmares increased suicide risk independently of the current severity of sleep disturbance and depression [14]. Not only is the duration of the insomnia complaint relevant as a predictor of suicide, but insomnia is also often temporally proximal to suicide. In one sample of veteran suicide deaths, insomnia was documented in nearly half of the last doctor's visits preceding suicide death [15].

The associations among insomnia and nightmares and suicide may or may not be uniform across all ages of patients. For example, the mechanism explaining the linkage in children might be different from the linkage in adults. For this reason, the remainder of this paper will focus on these relationships in adults.

Insomnia, Hopelessness, and Nightmares—Modifiable Risk Factors for Suicide

Insomnia, hopelessness, and nightmares can be viewed as part of the collection of modifiable risk factors for suicide. Some of the strongest risk factors for suicide cannot be (easily) modified, and these include age, gender, and race/ethnicity. On the other hand, there are a larger number of risk factors that are potentially modifiable which include active symptoms of depression, active alcohol or substance abuse, social isolation, and some chronic diseases in addition to the aforementioned processes of hopelessness, insomnia, and nightmares [16].

Hopelessness is among the strongest psychological risk factors for suicide, and specific psychological treatments have been devised in order to address hopeless ideation [17]. It has been shown to an independent factor that distinguishes depressed individuals with suicidal ideation from depressed individuals without suicidal ideation [18•], and it has recently been

implicated as a unique contributor in the contemplative phase of impulsive suicide attempts [19]. There are also cognitive aspects of chronic insomnia that have a hopeless “flavor”, such as “I have little ability to manage the negative consequences of disturbed sleep” or “When I sleep poorly on one night, I know it will disturb my sleep schedule for the whole week”. These sorts of pessimistic cognitions are captured in the Dysfunctional Beliefs and Attitudes about Sleep (DBAS) scale [20, 21]. Of note, the word “hopeless” never appears in any item of the scale, although the feeling of hopelessness is certainly reflected by some of the items.

Psychological Mechanisms

Hopelessness versus Dysfunctional Beliefs and Attitudes about Sleep

Based upon the well-described association between hopelessness and suicide, it might be expected that some of the relationship between insomnia and suicide was mediated via hopelessness. To this end, we examined whether hopelessness was correlated with dysfunctional beliefs and attitudes about sleep and with the intensity of suicidal ideation in a sample of 50 persons with depressive disorders of various types, degrees of severity, and treatment settings. We found that the DBAS was related to the intensity of suicidal ideation, and insomnia and hopelessness were correlated with suicide as expected. To our surprise, however, we found that hopelessness as measured in the Beck Hopelessness Scale (BHS) was unrelated to the DBAS [9]. In other words, the pessimistic cognitions measured by the DBAS represent a separate cognitive process from the conventional understanding of hopelessness. Moreover, both the DBAS score and the BHS score separately and independently predicted suicidal ideation. Consistent with cross-sectional evidence, neither depression nor hopelessness were found to mediate the link between insomnia and prospective suicidal ideation and behavior in a study of young adults in the military [12]. These discoveries potentially offer a new target for mitigating suicide: dysfunctional beliefs and attitudes about sleep.

Sleep, Executive Decision Making, and Suicide

Apart from self-defeating cognitions, insomnia may also adversely impact cognitive function through impaired decision making. The role of sleep in memory consolidation has been well described, as sleep loss is associated with decrements in verbal and visual memory [22]. We recognize that insomnia and sleep deprivation are different problems. Insomnia and sleep deprivation, nonetheless, share the common feature of reduced total sleep time, and reduced sleep time has been associated with impaired decision making [22]. In particular, insomnia is associated with deficient problem-solving capacity, especially when involving complex tasks [23•].

Suicide attempters demonstrate problem-solving abnormalities that parallel those described in insomniacs. Multiple studies have shown past suicide attempters exhibit reduced attention and working memory performance as compared with depressed non-attempters and non-depressed controls [24•, 25, 26]. Prior attempters of suicide produced a fewer number of solutions when faced with an experimental problem, and those solutions were more passive and less effective than those created by controls [27]. Moreover, suicide attempters may perceive their problem solving skills as inadequate, even without any actual problem-solving impairment upon testing [28]. Deficits in problem solving are seen regardless of the current severity of suicidal thoughts or the severity of prior suicide attempt [24•, 27], suggesting that this is a stable trait. Together these findings raise the possibility that insomnia leads to perceived or documentable deficiencies in decision making that may lead psychiatrically ill patients to consider a poorer quality and diminished number of solutions to their problems. Suicide may perhaps be left as the only remaining possibility. Under this scenario, treatment

of insomnia might lead to improvements in decision-making and hence reduced risk of suicide.

Possible Biological and Physiological Mechanisms between Insomnia, Nightmares, and Suicide

Serotonin

The insomnia-suicide link may be mediated by serotonergic mechanisms. The first collection of evidence stems from the knowledge that serotonin (5-HT) has an important and complex role in the induction and maintenance of sleep [29•], and the complexity of the 5-HT/sleep relationship is exemplified by a wide variety of 5-HT receptors with different regional brain distributions [29•]. For this reason, it is impossible to distill the 5-HT/sleep relationship down to a simple statement such as “5-HT helps you sleep”. For example, administration of the 5-HT precursor, L-tryptophan, is helpful for sleep [30], and yet facilitation of 5-HT with a serotonin re-uptake inhibitor can lead to deterioration of sleep [31]. The possibility that manipulation of sleep could alter the dynamics of 5-HT has been recently reported. In humans, one *in vivo* study of cerebral serotonin receptors showed a 9.6% increase in receptor binding potential after as little as 24 hours of total sleep deprivation [32•]. Furthermore, sleep deprivation of rodents led to a loss of sensitivity of post-synaptic 5-HT receptors [33, 34], and this serotonin desensitization was paralleled by a blunted hypothalamic-pituitary-adrenal (HPA) axis stress reaction in the form of decreased pituitary cortisol response [33].

Abnormalities in 5-HT function are also seen in suicide attempters. One of the most replicable biological findings in suicide is reduced CNS serotonergic (5-HT) function, as reflected by low levels of serotonin's main metabolite, 5-Hydroxyindoleacetic acid (5-HIAA), in the cerebrospinal fluid (CSF) of suicide victims and perpetrators of violence upon others [35••]. In addition, pre-synaptic serotonin midbrain transporters were diminished in binding potential distinctively among those who attempted suicide and/or suffered suicide death as contrasted to individuals with major depression who lacked a past history of suicide [36, 37]. These findings are consistent with evidence that chronic alterations of pre-synaptic serotonin availability is intercorrelated with changes in the sensitivity and density of both pre-synaptic transporters and post-synaptic receptors [38, 39]. Under this scenario, insomnia, and the associated reduction in total sleep time, could lead to a loss of 5-HT function, and in turn, increased risk of suicide.

The prefrontal cortex and its control over executive function are under the influence of the serotonergic system as well. Inadequate serotonin input to the prefrontal cortex is known to foster impoverished decision making [40•] and its ensuing array of aforementioned consequences. Together these raise the possibility that low 5-HT function is not just a marker of suicide, but is more so a marker of violent impulsivity and diminished decision-making skills that lower the threshold to suicide.

Hyperarousal

Converging lines of evidence have led to the view that primary insomnia is a condition of hyperarousal, and its 24-hour span of symptoms is paralleled by a variety of biological and physiological abnormalities [41]. HPA dysfunction was previously mentioned to be a consequence of sleep deprivation [33], and cortisol is also a potent biological marker of suicide risk, particularly in the setting of stress-related suicide. Stress activates the HPA system and thus releases a cascade of hormones including but not limited to corticotrophin-releasing hormone (CRH), adrenocorticotrophic hormone (ACTH), and cortisol; these hormones then augment susceptibility to hyperarousal, REM alterations, and subsequently

suicidal behavior [42••]. Hyperarousal is typified by inhibition of night time sleep, elevated core body temperature (especially at night), accelerated electroencephalogram (EEG) rhythms both awake and asleep, and elevated brain metabolism both awake and asleep [43]. The view of insomnia as a disorder of physiologic hyperarousal parallels the view that nightmare symptoms in PTSD are related to adrenergic overdrive [44]. Thus the link between insomnia and suicide as well as the link between nightmares and suicide may share a common feature in hyperarousal and HPA dysfunction.

Unpleasant mental experiences, however, can presumably occur outside of REM sleep. These dysphoric non-REM sleep experiences may be characterized by depressive cognitions occurring during sleep, but without the complex narratives and high visual impact of a nightmare. Persons with depression are more likely to report depressive mental content during sleep [45]. Prior reports linking nightmares to suicide have not clarified whether the link exists for classic REM sleep-nightmares, or for non-REM sleep depressive cognition, or both. Clarity is needed as there are treatments available for PTSD-REM sleep-nightmares that may or may not have effect in non-REM sleep dysphoric sleep experiences. Specific treatments for PTSD-nightmares include blocking adrenergic receptors with prazosin [46], suggesting that adrenergic overdrive is a mechanism behind nightmares and perhaps other PTSD symptoms such as hypervigilance [47].

Circadian Rhythm of Suicide

The preceding discussion on insomnia, nightmares, and suicide raises the question of whether a preponderance of suicides occurs at night. To the contrary, suicide between midnight and 8 AM is relatively uncommon, but rises abruptly between 8 AM and noon [48 – 51]. How then might sleep problems contribute to excess suicide during the morning hours? Much may revolve around what time of the day an individual naturally feels better. In colloquial terms, some individuals are naturally “larks” or morning chronotypes, and others are better described as “night owls” or evening chronotypes. Neural imaging has even reinforced these concepts by showing diurnal variations in positive-affect related structures that are in accordance with an individual's reported chronotype [52]. Chronotype has not been found to be casual of suicide, per se. However, morningness is associated with less aggression, is protective against the incidence of major depression, and provides relief of symptoms among those who already suffer from major depression regardless of subjective sleep quality [53••, 54•]. Eveningness, on the other hand, raises the likelihood of experiencing nightmares, difficulty falling asleep, poor sleep quality, fewer hours spent asleep, feeling worse in the morning, and has a well-established correlation with depression [54•, 55, 56]. The eveningness chronotype even correlated with a higher degree of impulsivity and lethality of suicide method in contrast to morning-type individuals [57]. It is also of interest to note that new research indicates eveningness to be associated with a higher cardiovascular disease rate [58, 59], and one does indeed find that other serious medical crises, such as myocardial infarction [60] and stroke [61], tend to peak during the same 8am – 12pm time frame.

The Way Forward

The understanding of the insomnia-suicide link is in the earliest stages of development, and therefore most of what has been presented in this paper is conjectural and intended only to provide ideas for hypothesis testing. Still, we have presented a broad array of targets for attack on suicide risk ranging from distorted cognitions about sleep, to deficient decision making, to under-performing 5-HT systems, to hyperarousal. A visual schematic of proposed mechanisms is presented in Figure 1. Potential interventions could include medications, brain stimulation, or psychotherapy depending upon the model being tested.

There are a series of intermediate steps that could precede clinical trials of these targets in depressed, suicidal insomniacs. In the case of dysfunctional beliefs and attitudes about sleep (DBAS), it would be useful to establish whether DBAS can be modified by pharmacology or only through cognitive behavior therapy for insomnia. The finding of deficient decision-making begs the question as to whether any form of insomnia treatment, either pharmacologic or psychotherapeutic, leads to improvements in decision-making. Finally, the possibility of a link between hyperarousal-insomnia or hypervigilance-nightmares and suicide suggests that treatments that dampen hyperarousal may lower suicide risk. To this end there is preliminary evidence that standard benzodiazepine agonist hypnotics reduce hypermetabolism in relevant brain regions of non-depressed insomniacs [62]. It is not known whether a similar effect can be reproduced in depressed insomniacs or with cognitive behavior therapy for insomnia, and it remains unknown whether these effects would lead to diminished suicidality.

Conclusion

Global death rates from dysentery and tuberculosis have fallen in the last 20 years as medicine continues to advance in the fight against infectious causes of illness, yet suicide is rising in its importance as a global killer, increasing from 14th to 13th place of all causes of mortality [63]. As once was the case for infection, strategies are lacking for the prevention of suicide. Recent research has raised the possibility that the treatment of insomnia and nightmares, or addressing the mechanisms that drive insomnia and nightmares, may be an avenue for prevention tactics against the rising threat of suicide.

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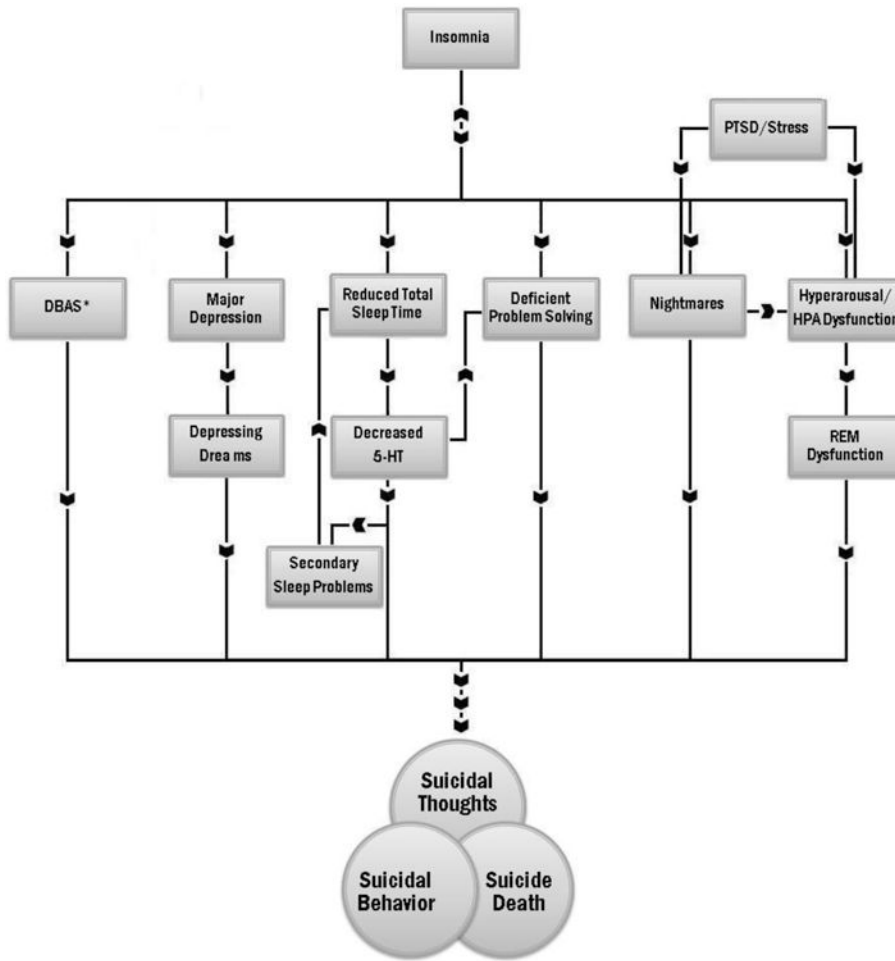


Figure 1. The Link between Insomnia and Suicide: Theoretical Mechanisms Schematic
*Dysfunctional Beliefs and Attitudes about Sleep

Table 1
The Relationship between Sleep and Suicide in Adults, by Year of Publication

Author/year	Source of sample	Design, N=	Sleep disturbance	Specified outcome
Barracough 1975 [64]	Suicidal/depressed outpatients	Cross-sectional, N=192	Insomnia	Suicide death
Fawcett 1990 [65]	Depressed patients	Prospective, N=954	Insomnia	Suicide death
Agargun 1997 [66]	Depressed patients	Cross-sectional, N=41	Insomnia	Suicidal thoughts
Agargun 1997 [67]	Depressed patients	Cross-sectional, N=113	Insomnia	Suicidal thoughts
Agargun 1998 [68]	Depressed patients	Cross-sectional, N=63	Nightmares	Suicidal thoughts
Krakow 2000 [69]	Female sexual assault survivors	Cross-sectional, N=153	Sleep breathing & sleep movement disorders	Suicidal thoughts
Tanskanen 2001 [70]	Population survey	Prospective, N=36,211	Nightmares	Suicide death
Turvey 2002 [71]	Population survey	Prospective, N=14,456	Insomnia	Suicide death
Agargun 2003 [72]	Depressed patients	Cross-sectional, N=26	REM disturbances	Suicidal thoughts
Smith 2004 [73]	Chronic pain patients	Cross-sectional, N=51	Insomnia	Suicidal thoughts
Bernert 2005 [74]	Psychiatric outpatients	Cross-sectional, N=176	Insomnia & nightmares	Suicidal thoughts
Fujino 2005 [75]	Population survey	Prospective, N=15,597	Insomnia	Suicide death
Agargun 2007 [76]	Depressed inpatients	Cross-sectional, N=149	Insomnia & nightmares	Prior suicide attempt
Chellappa 2007 [77]	Depressed outpatients	Cross-sectional, N=70	Insomnia	Suicidal thoughts
Sjostrom 2007 [78]	Suicide attempters	Cross-sectional, N=165	Insomnia & nightmares	Prior suicide attempt
Goodwin 2008 [79]	Population survey	Cross-sectional, N=8,098	Short sleep	Suicidal thoughts & attempts
Bernert 2009 [80]	Depressed outpatients	Cross-sectional, N=82	Insomnia & nightmares	Suicidal thoughts
Sjostrom 2009 [6]	Suicide attempters	Prospective, N=165	Insomnia & nightmares	Repeat suicide attempt
Lee 2010 [81]	Population survey	Cross-sectional, N=2,054	Insomnia	Suicidal thoughts
Li 2010 [82]	Outpatient psychiatric clinic	Prospective, N=1,231	Insomnia & nightmares	Suicide attempts
McCall 2010 [83]	Depressed insomniacs	Longitudinal, N=60	Insomnia	Suicidal thoughts
Nadorff 2010 [84]	College survey	Cross-sectional, N=583	Insomnia & nightmares	Suicidal thoughts
Selvi 2010 [76]	Depressed patients	Cross-sectional, N=160	Sleep quality, chronotype	Suicidal thoughts
Benute 2011 [85]	High-risk pregnancy patients	Cross-sectional, N=268	Insomnia	Suicidal thoughts
Bjerkset 2011 [86]	Population survey	Prospective, N=74,977	Sleep problems	Suicide death
Brower 2011 [87]	Population survey	Cross-sectional, N=5,692	Insomnia	Suicidal thoughts
Carli 2011 [88]	Prisoners	Cross-sectional, N=1,420	Insomnia	Suicidal thoughts
Krakow 2011 [89]	Sleep patients	Cross-sectional, N=1,584	Insomnia & nightmares	Suicidal thoughts
Susanszky 2011 [7]	Community survey	Cross-sectional, N=4,642	Insomnia & nightmares	Gender differences & suicidal thoughts & attempts
Klimkiewicz 2012 [90]	Substance abusers	Cross-sectional, N=304	Insomnia	Suicidal thoughts
Li 2012 [5]	Depressed outpatients	Prospective, N=371	Insomnia & nightmares	Suicidal thoughts
Pigeon 2012 [15]	Veteran suicides	Chart review, N=381	Insomnia	Latency to suicide death
Ribeiro 2012 [12]	Suicidal active duty military	Cross-sectional and longitudinal, N=311	Insomnia	Suicidal thoughts & attempts

Author/year	Source of sample	Design, N=	Sleep disturbance	Specified outcome
Suh 2012 [13]	Non-depressed population survey	Longitudinal, N=1,282	Insomnia	Depression & suicide thoughts or attempts
Bae 2013 [91]	General population	Cross-sectional, N=1,000	Insomnia	Suicidal thoughts
Gunnell 2013 [92]	Outpatients	Prospective, N=393,983	Insomnia	Suicide death
McCall 2013 [9]	Depressed insomniacs	Cross-sectional, N=50	Insomnia, nightmares, & dysfunctional beliefs and attitudes about sleep	Suicidal thoughts
Nadorff 2013 [10]	Elderly population	Cross-sectional, N=81	Insomnia, nightmares	Suicidal thoughts
Nadorff 2013 [14]	Population survey	Cross-sectional, N=972	Insomnia, nightmares	Suicidal thoughts & attempts
Suh 2013 [13]	Non-depressed population survey	Longitudinal, N=1,282	Insomnia	Suicidal thoughts & attempts

Adapted from McCall et al. [83] and Norra et al. [93].