CLINICAL REVIEW

Contribution of sleep deprivation to suicidal behaviour: A systematic review

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SUMMARY

Sleep disturbances and suicidal behaviour are highly prevalent phenomena, representing with a significant burden to society. Sleep has been acknowledged as a potential biomarker for suicidal behaviour. Over the past decade several studies have explored the association between sleep problems and suicidal behaviour. This area has attracted a growing research interest, hence updated information is needed. We therefore present a wide-scope review of the literature summarizing the most relevant studies on epidemiological and theoretical issues underlying this association. Implications of these findings for clinical practice and future research are discussed.

We performed a systematic search of PubMed and Embase databases up to October 2018 to identify studies exploring the association between sleep and suicide. Sixty-five articles met the selection criteria, thus they were included in the review.

There was a significant and independent association between sleep disturbances and suicide risk. Psychiatric disorders, sleep deprivation-induced neurocognitive deficits, emotional dysregulation, alterations in circadian rhythms, and negative feelings, among other factors, contributed to this relationship. Sleep loss may lead to higher levels of impulsivity, thus increasing unplanned suicidal behaviour. Sleep disturbances may therefore predict suicidal behaviour, hence becoming a potential therapeutic target.

Introduction

Sleep disturbances are highly prevalent both in psychiatric and non–psychiatric populations. Insomnia alone affects between six and 18% of the general population [1]. Reduced quality or quantity of sleep, and abnormal sleep phenomena have a significant impact on functioning. High rates of comorbidity, poor quality of life and increased mortality have been associated with sleep disturbances [2,3]. However, Sleep Medicine has been neglected by research in comparison to other medical disciplines [4], even though sleep problems have been linked with an increased risk of suicidal behaviour [5].

Up to a million people die from suicide every year worldwide, making it a leading cause of unnatural death [6]. Unlike other (preventable) public health issues, suicide prevention has been largely unsuccessful [7], which may have been due to suicidal behaviour being a complex multifactorial phenomenon that also remains poorly understood. .

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Abbreviations	
AASM	American academy of sleep medicine
BD	bipolar disorder
CBT	cognitive behavioural therapy
EEG	electroencephalography
EMA	ecological momentary assessment
MINI	mini international neuropsychiatric interview
NREM	non–rapid eye movement
PRISMA	preferred reporting items for systematic reviews and meta-analyses
PTSD	post-traumatic stress disorder
REM	rapid eye movement
SA	suicide attempt
SB	suicidal behaviour
SI	suicidal behaviour
SMS	short messaging service
SP	suicide plan
SR	suicide risk

One of the long–standing goals of suicide research has been to identify valid biomarkers of those at risk in order to focus prevention strategies on these high–risk individuals. This approach has yielded poor results so far [8].

Nevertheless, sleep, which can be easily assessed, may become a promising biomarker for suicidal behaviour, and has attracted research interest over the last few decades given its potential role in prevention as a therapeutics target [9,10]. The relationship between sleep disturbances and suicidal behaviour has been supported by a growing body of evidence. However, there are issues around the conceptualization of both phenomena, since they cannot be easily separated from other mental disorders, which has hampered research in this area [11,12].

Several studies over the past few decades have examined the association between sleep disturbances and suicide risk, some of which have focused on the epidemiological basis of this association. Thus, in 2012, Pigeon et al. carried out an extensive meta–analysis on this topic [5], while two years later Malik et al. restricted the search to psychiatric populations [13]. However, only a few risk factors reviews focused on the mechanisms underlying this association, investigating certain explanatory factors, such as staying awake at night [14] or psychological factors [15].

The present review aims to explore the epidemiological evidence of the association between sleep disturbances and suicidality and to focus on the explanatory putative mechanisms underlying this association, including neurocognition, mental disorders, serotonin dysregulation, circadian rhythms and psychological factors. In particular, we hypothesised that the potential neurocognitive alterations caused by disordered sleep may lead to impulsive decisions and increase the risk of a suicide attempt. Finally, we will discuss the implications of these findings for suicidal behaviour prevention.

Methods

The Preferred Reporting Items for Systematic reviews and Meta–Analyses (PRISMA) guidelines were complied with as applicable [16].

Terminology and definitions

Sleep and sleep disturbances: Sleep is considered as a dimension of mental health according to the research domain criteria (RDoC) for mental illnesses classification [17]. The diagnostic and statistical manual of mental disorders (DSM−5) criteria defined sleep−wake disorders as alterations in the quality, timing, and amount of sleep, resulting in daytime distress and impairment [18]. In our review any type of sleep disturbance, particularly sleep disorders, was included. We also used 'insomnia' and 'nightmares' as search terms, along with the broader terms 'sleep' and 'circadian', given their high prevalence.

Suicide−related constructs: The suicide terminology was based on the standardized definitions given by O'Carroll et al. in 1996 [19] and redefined by Silverman in 2007 [20]. 'Suicidal behaviour' referred to any type of suicidality, including suicidal ideation, suicidal plans, non−fatal suicide attempts and death by suicide. 'Suicidal ideation' was defined as 'unelaborated thoughts related to the wish and/or intention of taking one's life'. 'Suicidal plan' was defined as 'an elaborated and structured suicidal ideation, with decisions made as to how to perform the suicide attempt. 'Suicide attempt(s)' included any act of self−harm performed with the intention of taking one's life. A suicide attempt with a fatal outcome was referred to as 'death by suicide'. The search terms 'suicide' and 'suicidal' were used in the search strategy.

Inclusion/exclusion criteria

In order to be included in the review, articles had to fulfil the following criteria:

1) Only peer−reviewed publications were included.
2) There was a search limitation by English or Spanish languages.
3) Information on the association between sleep and suicide had to be available, that is, either epidemiological data and/or the mechanisms underlying this association.
4) The studies had to use objective measures, clinical evaluation or standardized questionnaires for the sleep assessment.
5) The definition of suicidal behaviour was consistent with standard terminology [19,20].

Those studies included in previous meta−analyses were excluded to report on an up−to−date literature review.

Search strategy

We performed a PubMed and EMBASE databases review by using the text words ("suicide" OR "suicidal") AND ("sleep" OR "circadian" OR "insomnia" OR "nightmares") in the title or abstract. Last search date was October 2018 and the only limitation was language: English or Spanish. No specific date restrictions were used, although most recent studies were given priority. We included both original research and reviews. The articles were selected on the basis on relevance to the topic and methodological quality. Critical appraisal checklists were used to assess the quality of the studies [21].

Studies selection process

Two researchers (APS and EBG) independently assessed the articles for inclusion. Agreement between reviewers, measured by intraclass correlation coefficient (ICC), was 0.84 (95% CI 0.80−0.88). After discussion, consensus was reached by the two researchers.

Results

The initial search yielded 2586 results. Following initial screening of abstracts, full−text revision and selection process as

appropriate, 65 articles were finally included in the review (see Fig. 1).

Epidemiological evidence for the relationship between sleep and suicide

Outcome assessment methods

Most studies used standardized questionnaires to measure sleep. The most commonly used questionnaire was the Pittsburgh sleep quality index [13,27,43,49,50,52]. Two studies relied on clinical diagnosis of sleep disorders, namely sleep apnea and insomnia [22,23]. Only four selected studies provided an objective measure of sleep, particularly one study used polysomnography (PSG) [24], and three papers reported actigraphy data [10,25,26]. A further study, included in two of the reviewed meta–analyses [5,13], also used PSG for sleep assessment [27].

Suicidal behaviour measures varied according to the outcome. Suicidal ideation and planification were assessed through standardized questionnaires in all the selected studies that explored this variable. Suicide attempts were measured by questionnaires in ten papers [28–37], while two articles relied on clinical data [23,38]. Death by suicide was only reported by four studies and recorded through clinical sources [22,39–41].

Meta–analyses

A meta–analysis carried out in 2012 concluded that there was a significant association between sleep disturbances and suicidal behaviour, with HRs ranging from 1.95 (95% CI, 1.45–2.69) to 2.95 (95% CI, 2.48–3.50). This association remained significant (at $p < 0.05$) after adjusting for the presence of psychiatric diagnoses [5].

A later meta–analysis of observational studies focused on psychiatric populations found sleep disturbances to be associated with suicidal behaviour in a range of mental disorders with an overall

ORs of 2.69 (95% CI, 1.62–4.48) for suicidal ideation, 4.36 (95% CI 2.2–8.33) for suicide attempt, and 1.59 (95% CI 1.17–2.17) for death by suicide [13].

Sleep duration acted as a dose–response protective factor in a 2018 meta–analysis, which explored the effects of sleep on suicidal behaviour in adolescents. Suicide plans were linearly and inversely associated with sleep duration, with an OR of 0.89 (95%CI 0.88–0.90) for every hour of increase in sleep duration. For suicide ideation and suicide attempts, dose of sleep showed a U–shaped curve, in which the smaller risks were linked with a sleep duration of 8–9 h. Depressive symptoms did not mediate these associations [42].

Insomnia and other sleep deficits

Insomnia and other reductions in sleep quantity/quality were the most frequently explored sleep–related variables across studies. Insomnia was consistently associated with suicidal behaviour in all the reviewed studies, although one of the studies included in the meta–analyses by Pigeon et al. [5] did not replicate this association [43]. In a 21–day follow–up study, actigraphy–defined sleep variability was a significant predictor of suicidal ideation [26], while suicidal ideation at 24 h was related to insomnia in another investigation [10]. In a retrospective cohort study of 479,967 patients under mental healthcare, insomnia tripled the risk for a suicide attempt over the 13-year follow–up [23].

Parasomnias

Nightmares were also strongly associated with suicidal behaviour. In a two–year follow–up study included in the Pigeon et al.'s meta–analysis [5], frequent nightmares, but not other sleep disturbances, were associated with higher risk of re–attempting suicide in a sample of past suicide attempters [43]. Nightmares and suicidal behaviour showed stronger associations than those between suicidality and other sleep disturbances in two studies
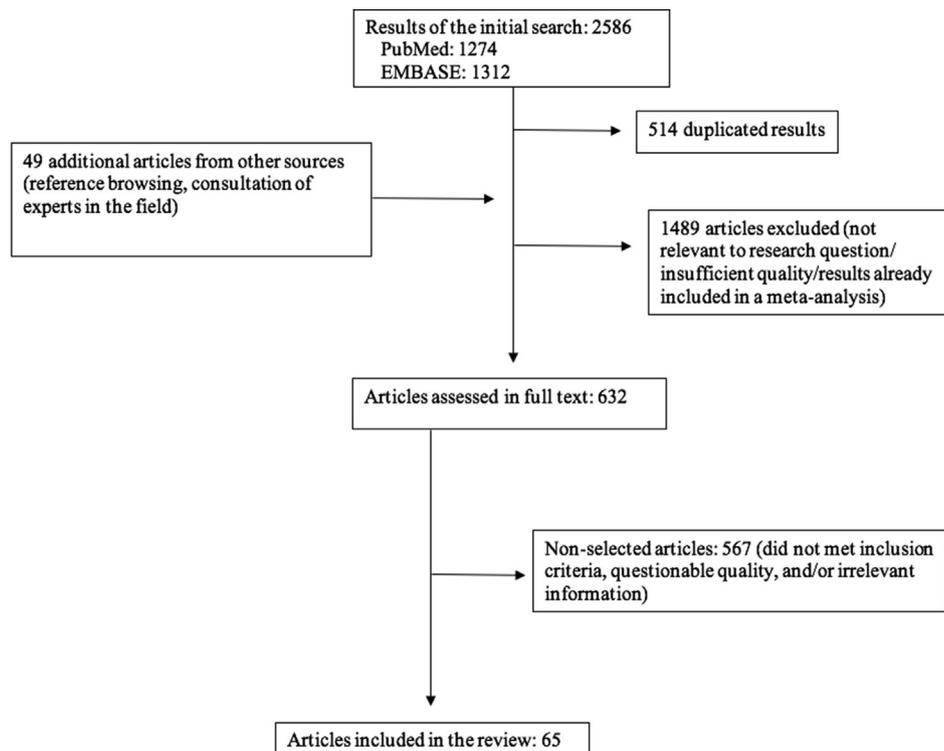

Fig. 1. Studies flow chart.

[35,44]. Nightmares also increased the risk of suicide in PTSD patients independently of insomnia [32].

Other sleep disturbances

Other sleep disorders, such as hypersomnia, have been hardly explored in relation to suicidal behaviour. In the meta−analyses by Malik et al., hypersomnia was the only sleep disorder that was not significantly associated with suicidal behaviour (OR = 1.90; 95% CI, 0.60−6.06) [13].

In a prospective study performed with a cohort of 394,000 community−dwelling adults, sleeping over eight hours per night increased the risk of dying by suicide (HR = 1.5; 95% CI, 1.1−2.0). However, in this study a reduction of sleep time increased the risk too [39].

In another study, a longer total sleep time was associated with greater risk of suicidal behaviour. Sleep time squared was also directly associated with suicidal behaviour, suggesting a U−shaped curve for the relationship between sleep time and suicide [34].

Sleep-related breathing disorders were also associated with suicidal behaviour [13,22,36]. A 2018 cross-sectional study of 40,149 community−dwelling adults found that sleep apnea was associated with suicidal ideation (OR = 1.56; 95% CI, 1.08−2.26) and suicidal plans (OR = 1.50; 95% CI, 1.18−1.91), but not with suicide attempts. In a case-control study, sleep apnea significantly increased the risk of dying by suicide (HR in men = 1.76, 95% CI, 1.19−2.60; HR in women = 4.33, 95% CI, 1.96−9.56) [22]. Another study, included in the meta-analysis by Malik et al. [13], reported an association between sleep-related breathing disorder and suicidal behaviour (OR = 2.56; 95% CI, 1.91−3.43) [45].

Tables 1, 2 and 3 summarize these results.

Mechanisms involved in the relationship between sleep and suicide

Neurobiological factors

Neurocognitive impairments leading to impulsivity and risk−taking have been associated with suicidal behaviour, especially with unplanned suicide attempts [55−57].

Insufficient sleep has also been associated with impairments in decision−making, as well as emotional dysregulation, including difficulties in discriminating the importance of different emotional stimuli [58−60].

Despite this shared association, few studies have specifically explored the role of neurobiological factors as mediators between sleep and suicide. In a 2016 systematic review, Perlis et al. suggested that the effect of impaired sleep on suicidal behaviour may be the result of executive dysfunction caused by being awake at night−time [14].

Ballard et al. (2016) also pointed out to the potential role of executive function and emotional regulation in mediating this relationship, linking sleep loss with risky decision−making and negative affect [24]. Thus, sleep loss was associated with risky decision-making and negative affect [24].

Another study with 972 community−dwelling adults found that emotion dysregulation, particularly downregulation of negative affect, mediated the association between nightmares and suicidal behaviour [61]. Additionally, increased functional connectivities between certain brain areas, including the lateral orbitofrontal cortex and anterior cingulate cortex, were identified as mediators in the relationship between sleep quality and depressive symptoms [62].

Fig. 2 illustrates the neurocognitive consequences of sleep loss on suicidal behaviour.

Comorbidity with mental disorders

Although in most of the selected studies the association between sleep disturbances and suicidal behaviour remained significant after adjusting for mental disorders, effect sizes were frequently reduced [5,28,31,32,34,35].

Also, the effect of sleep on suicidal behaviour was increased, as demonstrated by the meta−analysis by Malik et al. (2014), in which the strength of the association between sleep disturbances and suicidal behaviour varied across psychiatric diagnoses. Depression (OR = 3.05; 95%, CI 2.07−4.48), PTSD (OR = 2.56; 95% CI, 1.91−3.43), panic disorder (OR = 3.22; 95% CI, 1.09−9.45), and schizophrenia (OR = 12.66, 95% CI, 1.40−114.44) showed the highest OR [13].

Sleep disturbances were associated with higher recurrence and treatment resistance in depression, while antidepressants affected sleep patterns [63,64]. In a recent study, the relationship between sleep disturbances and suicide ideation was mediated by depressive symptoms [65]. Another study showed that depressive symptoms mediated the relationship between insomnia and suicidal ideation, with no effect on the relationship between insomnia and suicide attempts [66].

Sleep disturbances are also a common feature of PTSD. Disturbed sleep and recurrent distressing dreams are DSM−5 criteria for the diagnosis of PTSD and it is estimated that 85% of PTSD patients suffer from insomnia, while over 65% of them report nightmares [18,67]. A recent study carried out in a large sample of Korean firefighters showed that insomnia, along with alcohol use, largely mediated the association between PTSD and suicide risk [68].

Circadian rhythms

With regard to circadian rhythm abnormalities, a polymorphism in the clock gene rs1801260, which is one of the genes involved in the regulation of circadian rhythms, was associated with insomnia, depressive symptoms and suicidal behaviour in patients with bipolar affective disorder in two studies [69,70]. 'Violent' suicide attempts were also associated with polymorphisms in the genes CLOCK rs3805148, CLOCK rs534654, TIMELESS rs11171856, and

Table 1
Epidemiological association between sleep and suicide: Meta−analyses.

Study	Sleep outcome	Suicide outcome	N	Population	Association (95% CI)
Pigeon et al., 2012 [5]	Any sleep disturbance	Any SB	31 samples	Mixed samples	RR = 1.91 (1.64−2.23)
		SI			RR = 1.86 (1.52−2.28)
		SA			RR = 2.01 (1.47−2.74)
		Death by suicide			RR = 1.96 (1.32−2.91)
Malik et al., 2014 [13]	Any sleep disturbance	SI	19 samples	Psychiatric patients	OR = 2.69 (1.62−4.48)
		SA			OR = 4.36 (2.2−8.33)
		Death by suicide			OR = 1.59 (1.17−2.17)
Chiu et al., 2018 [42]	Sleep duration	SI	12 samples	Community−dwelling adolescents	U−shaped dose−response curve; lowest risk at 9 h
		SP			OR = 0.89 (0.88−0.90)
		SA			U−shaped dose−response curve; lowest risk at 8−9 h

BD: bipolar disorder; OR: odds ratio; NS: non−significant; SA: suicide attempt; SB: suicidal behaviour; SI: suicidal behaviour; SP: suicide plan; SR: suicide risk.

Table 2
Epidemiological association between sleep and suicide: Longitudinal studies.

Study	Sleep outcome	Suicide outcome	Follow–up period	N	Population	Association (95% CI)
Gunnel et al., 2013 [39]	<4 h sleep (vs. 6–8) 4–6 h sleep (vs. 6–8) >8 h sleep (vs. 6–8)	Death by suicide	7.4 y	393,983	Community–dwelling adults	OR = 3.5 (2.0–6.1) OR = 1.5 (1.1–1.9) OR = 1.5 (1.1–2.0)
Bernert et al., 2014 [40]	Poor sleep quality Difficulty falling asleep Non–restorative sleep	Death by suicide		420	Suicide decedents vs. community–dwelling adults	OR = 1.39 (1.14–1.69) OR = 2.24 (1.27–3.93) OR = 2.17 (1.28–3.67)
Kodaka et al., 2014 [41]	Any sleep disturbance	Death by suicide		49	Suicide decedents	OR = 12.7
Koyawala et al., 2015 [28]	Increased wakefulness Trouble getting back to sleep	SA		80	Adolescent with a history of SA and healthy controls	OR = 4.2 (1.55–11.55) OR = 3.4 (1.27–9.13)
Ballard et al., 2016 [24]	Nocturnal wakefulness	SI	24 h	65	MDD and BD patients	β = 0.31
Li et al., 2016 [38]	Insomnia	SA	8 y	388	Schizophrenic patients	HR = 4.63 (1.40–15.63)
Bernert et al., 2017 [26]	Sleep variability Nightmares Insomnia Other sleep parameters	SI	21 d	4847	College students	β = 0.27 (0.06–0.66) β = 0.22 (0.03–0.33) β = 0.18 (0.0–0.40) NS
Rod et al., 2017 [22]	Sleep apnea Earlier onset of daily activity Other sleep parameters	Death by suicide	5.1 y	446,135	Sleep apnea cases and patient controls	Men: HR = 1.76 (1.19–2.60) Women: HR = 4.33 (1.96–9.56) OR = 1.27 (1.05–1.54) NS
Rössler et al., 2018 [29]	Mild sleep problems Moderate sleep problems Severe sleep problems	SB		591	Community–dwelling adults	OR = 1.9 (1.4–2.5) OR = 3.3 (2.5–4.4) OR = 1.9 (1.3–2.8)
Eikelenboom et al., 2018 [46]	Insomnia	SA	6 y	1713	MDD patients	1.51 (1.13–2.02)
Lin et al., 2018 [23]	Insomnia	SA	13 y	479,967	Insomnia cases and patient controls	HR = 3.53 (3.06–4.08)
Littlewood et al., 2018 [10]	Objective short sleep duration Subjective short sleep duration Subjective poor sleep quality Sleep efficiency; Sleep onset latency	SI severity	24 h	51	Patients with a history of SB	−0.0876−0.1387 to −0.0133 −0.0801−0.0984 to −0.0071 −0.1093−0.2508 to −0.0532 NS

BD: bipolar disorder; OR: odds ratio; NS: non–significant; SA: suicide attempt; SB: suicidal behaviour; SI: suicidal behaviour; SP: suicide plan; SR: suicide risk.

TIMELESS rs2291739, which was also linked to multiple suicide attempts and a family history of suicide attempts along with the TIMELESS rs11171856 [70].

Another study found that suicidal behaviour was associated with life–time alterations in circadian rhythms in PTSD patients [71].

A 2016 study found a higher–than–expected rate of suicide attempts during night–time, with the maximum rate occurring between 2 am and 3 am [72]. Another study found that the highest risk for suicide attempts occurred from 5 pm to 11 pm, while 4 am–7 am was the lowest risk period [73].

The evening chronotype —a greater performance in terms of functioning in the evening and a preference for remaining awake at night–time—, may also be related to suicidality. Benard et al. (2018) found an association between rigidity in the circadian type inventory and suicidal behaviour, although this association did not survive the final model multivariable models [25].

Psychological and related factors

In a study with a sample of adolescents, feelings of defeat and entrapment mediated the relationship between suicidal ideation and insomnia, while the effects of nightmares on this association were moderated by these feelings [44]. Defeat, entrapment and hopelessness were also mediators in the relationship between nightmares and suicide in a PTSD study [32]. In an another study exploring the role of thwarted belongingness in the relationship between insomnia and suicidal ideation, this feeling was found to

moderate this association, although the direct effect of insomnia on suicidal ideation survived after adjusting for confounders [74].

Three studies explored the subjective views of sleep role in suicidal behaviour. Feelings of loneliness during sleepless nights and the detrimental effects of sleep disturbances on daytime functioning were reported to contribute to this association [15,75–77]. These studies also commented on the link between sleep as escape from reality and suicidality, hence reducing the risk [15,75–77].

Two more studies suggested that disruption in sleep may also lead to suicidal behaviour through circumstantial factors, such as being awake at night, which may represent a time window during which rescue is less likely, although still possible [78,79].

Discussion

We conducted a systematic review aimed to examine the relationship between sleep disturbances and suicidal behaviour with a focus on the mechanisms and contributory factors underlying such as association, from which several findings emerged, which may have relevant implications on clinical practice and future research, as detailed below.

Sleep and the motivational–volitional model of suicide

The motivational–volitional model of suicide describes three steps in the pathway leading to a suicide attempt. First,

Table 3
Epidemiological association between sleep and suicide: Cross–sectional studies.

Study	Sleep outcome	Suicide outcome	N	Population	Association (95% CI)
Jang et al., 2013 [30]	< 4 h sleep (vs. 6—7)	SI	75,066	Community–dwelling adolescents	Men: OR=1.64 (1.29—2.08)
					Women: OR=2.50 (1.69—3.69)
	< 4 h sleep (vs. 6—7)	SA			Men: OR=2.06 (1.34—2.17)
					Women: OR=3.89 (1.74—8.66)
McCall et al., 2013 [47]	Insomnia	SI severity	50	Depressed patients	β=0.64 (0.14—1.15)
An et al., 2015 [48]	Short sleep duration	SI	4,674	Community–dwelling adults	OR=75 (1.17—2.62)
Blank et al., 2015 [31]	Insomnia	SI/SP/SA	6,483	Community–dwelling adolescents	OR=2.63 (1.34—5.16)
Gelaye et al., 2016 [49]	Poor sleep quality	SI	1054	Community–dwelling adults	OR=3.46 (2.27—5.26)
Littlewood et al., 2016 [32]	Nightmares	SB	91	PTSD patients	OR=1.71 (1.05—2.45)
Lopes et al., 2016 [31]	Early awakening	SB	214	Depressed children and adolescents	OR=2.3 (1.1—4.9)
		SI			OR=2.5 (1.3—5.0)
		SA			OR=4.4 (1.9—10.4)
	Night awakening	SB			OR=4.4 (2.4—8.0)
		SP			OR=4.9 (2.5—9.5)
		SA			OR=4.8 (2.1—10.9)
	Initial insomnia	SB			OR=4.9 (2.8—8.8)
		SI			OR=6.0 (3.2—11.2)
		SA			OR=10.8 (4.7—25.2)
	Daytime sleepiness	SI			OR=9.5 (9.1—10.0)
		SA			OR=5.5 (2.2—13.2)
Supartini et al., 2016 [50]	Poor sleep quality	SI	1,992	Community–dwelling young adults	OR=2.65 (1.81—3.89)
	Increased sleep–onset latency; Short sleep duration; Late bedtime; Late waketime				NS
Wong et al., 2016 [51]	Difficulty falling sleep	SI	10,123	Community–dwelling adolescents	OR=3.51 (2.51—4.90)
	Difficulty maintaining sleep				OR=4.44 (3.42—5.75)
	Early morning awakening				OR=2.47 (1.77—3.43)
	Difficulty falling sleep	SP			OR=5.56 (3.03—10.20)
	Difficulty maintaining sleep				OR=5.44 (3.08—9.60)
	Early morning awakening				OR=3.52 (2.07—6.01)
	Difficulty falling sleep	SA			OR=5.37 2.48—11.64
	Difficulty maintaining sleep				OR=5.95 (2.61—13.56)
	Early morning awakening				OR=2.64 (1.64—4.26)
Gelaye et al., 2017 [52]	Poor subjective sleep quality	SI	1298	Pregnant women	OR=1.28 (1.15—1.41)
Michaels et al., 2017 [34]	(Total sleep time)²	SB	789	Community–dwelling adults	β =0.02
Richardson et al., 2017 [53]	Insomnia	SI	6700	Military personnel	OR=1.34 (1.18—1.52)
Stanley et al., 2017 [35]	Nightmares	SR	379	Children and adolescents with BD	OR=1.83
	Sleep terrors; Sleepwalking				NS
Bishop et al., 2018 [36]	Sleep apnea	SP	40,149	Community–dwelling adults	OR=1.56 (1.08—2.26)
		SI			OR=1.50 (1.18—1.91)
		SA			NS
Russel et al., 2018 [44]	Insomnia	SI	1,045	Community–dwelling adolescents	OR=3.19 (2.05—4.99)
	Nightmares				OR=3.38 (2.35—4.85)
Verkooijen et al., 2018 [37]	Any sleep disturbance	SI/SP/SA	16,781	Community–dwelling adolescents	OR=3.90—4.14
Whitmore, 2018 [54]	Short sleep duration: 4—5 hours	SI	12,974	Community–dwelling adolescents	OR=1.81 (1.62—2.02)
	Short sleep duration: 6—7 hours				OR=1.17 (1.06—1.29)

BD: bipolar disorder; OR: odds ratio; NS: non–significant; SA: suicide attempt; SB: suicidal behaviour; SI: suicidal behaviour; SP: suicide plan; SR: suicide risk.

predisposing factors can concur at the pre–motivational stage, which is followed by motivational stage, during which suicidal ideation/plans are developed further. . Finally, at the volitional stage precipitating factors lead this subject to make a (suicidal) act [80].

Sleep disturbances may play a crucial role in the last steps towards suicide, hence acting as proximal predictors of a suicide attempt and distinguishing those will go on to make a suicidal behaviour from those who will not.

Sleep disturbances as a precipitating factor for suicidal attempt: The role of neurocognition

The impact of sleep loss on neurocognitive performance may affect decision–making processes. Sleep disturbances, which have a relevant impact on neurocognition may pave the pathway linking cognitive impairment with an increased risk of suicide attempts [55—57]. Thus, disturbed sleep–induced cognitive impairments may lead to more impulsive decisions, which tend to more underestimate the potential consequences of actions.

If in addition to such a predisposing mental state the individual suffers from significant life events and/or there is a genetic vulnerability, the risk increases. This may explain the association of sleep disturbances with an increased suicide risk at night–time [78,79].

Acute vs. chronic presentations

The course of sleep disturbances over time may increase/decrease its impact on the association between sleep and suicide. Thus, acute sleep disturbances may have a stronger impact on neurocognition since there is no time for adaptation and compensation, which is linked with decision–making issues potentially leading to suicidal behaviour. One sleepless night tends to have detrimental effect on the risk/reward discrimination system and the decision–making process. In this acute presentation, disturbance of sleep is more likely to act as a precipitating factor for suicidal behaviour. This acute presentation should therefore warn clinicians (and family members as appropriate) about the need for caution in management, which has been consistently demonstrated by previous research [10,24,26].
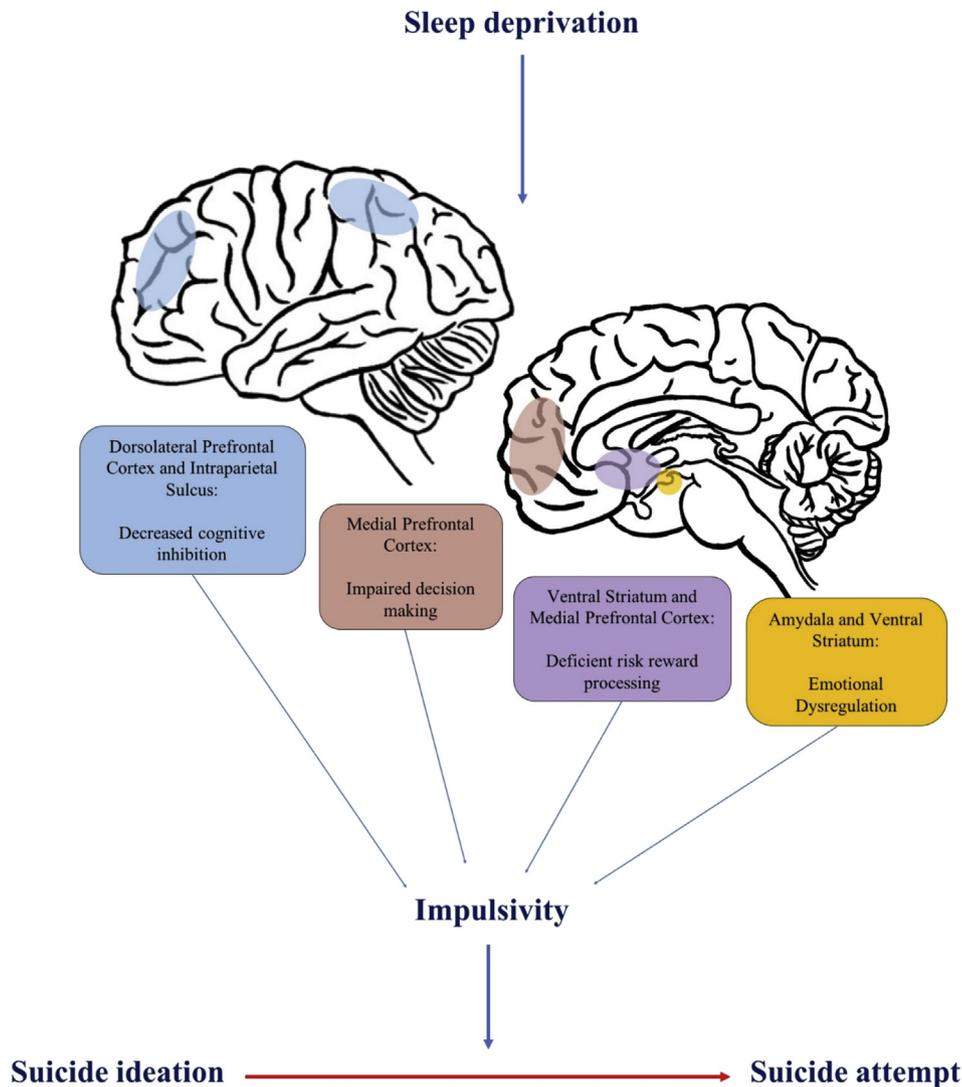
Fig. 2. Neurocognitive consequences of sleep loss on suicidal behaviour.

Although subacute and chronic presentations are characterized by a less abrupt onset of the condition over time which also tends to last for longer, they may increase the risk for other mediating factors, such as mental disorders, which have an impact on sleep. Hence, in this chronic presentation sleep disturbances may become useful markers of suicide risk. In addition, we found evidence of the long−lasting after−effects of early−onset sleep disturbances on suicide risk. Thus, sustained sleep problems at young ages were reported to have a negative impact on the neuropsychological development, which may result in cognitive and behavioural issues in the adulthood, which was mainly related to hypoactivity of the 5−HT system in the prefrontal cortex [80].

Implications for prevention and treatment

Sleep disturbances as a predictor for suicide

Based on our systematic review findings, it seems that early detection of sleep problems in primary care settings may help to reduce suicide rates. Interestingly, unlike other mental health issues, sleep disturbances lack the stigma associated with 'psychiatric' conditions that comes with other mental health symptoms, which may increase engagement rates. In keeping with this, up to 46% of suicide victims were reported to have contacted their general practitioner in the month prior to death [81]. Likewise, 90% of young suicide victims had also received primary care in the year leading to death [82]. However, a specific comment on suicidal behaviour risk was documented in less than 3% of suicide decedents who had been seen in primary care. Suicide risk tend to go unnoticed in primary care unless directly self−reported by patients since risk assessment is not routinely performed [83,84]. Insomnia, nightmares and other sleep disturbances could be warning signs of suicidal behaviour, especially when combined with other known risk factors for suicide. Therefore, a proper screening of sleep disturbances should become part of routine suicide risk assessment, both in primary care and mental healthcare. In particular, the use of mobile phone−based applications may represent a helpful tool to objectively monitor symptoms severity, including sleep disturbances, thus assessing risk of suicidal behaviour, particularly to follow−up suicide attempters; for instance through short messaging service (SMS) [85−87].

Sleep as a therapeutic target

Sleep disturbances are therefore modifiable risk factors for suicide. Specifically, tackling sleep problems is an underutilized therapeutic strategy to reduce suicidal behaviour risk [88]. The

management of sleep disturbances is, however, very challenging in the clinical setting, with a need for more evidence–based treatments and guidelines.

Insomnia has been reported to be the most frequent sleep disorder. The first line treatment for insomnia is cognitive–behavioural therapy (CBT) [89], which has also been shown to reduce suicidal ideation among psychiatric patients [90,91]. Of note, CBT and other psychotherapeutic interventions, unlike medications, have not been associated with side–effects, although they may take longer to respond.

Although pharmacological interventions are associated with faster responses, they are usually recommended only as short–term measures due to the high risk of addiction and potential side effects, including insomnia [92]. Specifically, concerns have been raised about the use of hypnotics and sedative drugs, which might increase suicidal risk, particularly when misused [92,93], including non–benzodiazepine hypnotic drugs, such as Zolpidem, which has been associated with a dose–response increase in the risk of suicide attempt and death by suicide [94].

Antidepressants are also first–line treatments of insomnia, especially when there is comorbid depression. Although serotonin–selective reuptake inhibitors (SSRI) antidepressants initially increase total sleep time at the expense of NREM sleep, recent evidence suggests that they may have a detrimental effect in the long–term, thus increasing sleep latency and reducing the number of REM periods [95,96]. However, SSRI antidepressants have also been shown to improve subjective sleep quality in the long term. In a 2016 prospective population–based study, continued use of SSRI was associated with better subjective sleep quality (PSQI questionnaire) even after controlling for depressive symptoms [97].

In addition to insomnia, nightmares are the second sleep problem more frequently investigated in relation to suicide. Image rehearsal therapy (IRT) is the first–line treatment recommended by the American academy of sleep medicine (AASM) for the management of PTSD–related nightmares and nightmare disorder [98]. The use of IRT for the treatment of nightmares has reduced suicidal ideation in psychiatric inpatients [99].

Regarding psychopharmacological interventions for nightmares, prazosin has lost some support over the last few years. A 2015 meta–analysis of clinical trials comparing prazosin with IRTs in nightmares showed no differences between both PTSD groups and its effectiveness was also supported by a previous meta–analysis [100,101]. However, two clinical trials in 2018 revealed no reduction in suicidal ideation in PTSD patients on prazosin [102,103].

New technologies may become a potential valuable tool for the management of sleep disturbances, such as the mobile–based application Sleepcare app, which delivers specific CBT techniques for insomnia, which was trialled in a sample of community–dwelling adults with promising results [104].

With regard to the management of suicidal behaviour, ketamine has recently received much research interest. For instance, ketamine has been found to have a quick antidepressant effect, which lasts for up to one week [105]. As a result, ongoing studies are testing longer–acting ketamine–related drugs and formulations. . Of relevance, the anti–suicidal and antidepressant properties of ketamine are thought to be related to its effect on sleep, including reduction of wakefulness and induction of changes in the circadian system [106,107].

Challenges for future research

Suicide research faces significant issues around the conceptualization of suicide, particularly regarding the extent to which suicide is the result of a mental disorder. Specifically, rather than a symptom of an underlying mental illness, suicide may represent a cross–sectional phenomenon or a separated diagnosis, which was proposed in an editorial [108]. This proposal may have contributed to increasing its external validity and specificity, thus facilitating future research.

Additionally, many authors have voiced that suicide is a heterogeneous phenomenon encompassing several types of suicidal behaviour, with different neurobiological underpinnings and pathways towards suicide [109,110]. Hence, these mixed groups of patients under the same umbrella may have contributed to the relatively unsuccessful suicide research over the past few decades, particularly suicide neurobiological research [110].

Sleep disturbances share with suicidal behaviour this ambiguity, that is, whether they should be considered a symptom or a disorder. Despite the high prevalence of sleep disturbances in the general population and the evidence of their independent pathophysiological mechanisms, they are frequently considered as mere symptoms of other mental disorders.

Sleep assessment poses an additional challenge. Many aspects of sleep, such as quality or dream content, are highly subjective constructs. Even more straight–forward components, such as total sleep time, are difficult to be measured in research settings since there are few objective measurement tools for these variables. Sleep questionnaires represent the most common sleep assessment instruments; however, they are subjective and prone to recall bias [111]. Polysomnography (PSG) provides the most objective measure of sleep, which should be therefore taken as the gold standard, although there are some issues around its practicality in real–world research/clinical settings [111].

Finally, sleep trackers, which are wearable devices equipped with an actigraph and synced to a mobile phone application may represent valid alternatives to assess sleep. They provide an objective measure of sleep in an ecological setting, but the validation of these devices is still in progress and their use in clinical settings has not been recommended yet [111,112].

Practice points

- Sleep disturbances are relevant contributors to suicidal behaviour, particularly in the final pathways to suicidal behaviour.
- The relationship between sleep disturbances and suicidal behaviour is likely to be multifactorial. However, some mechanisms have received particular attention regarding their potential role as mediators in this relationship. Some of the most relevant factors underlying this association are neurobiological alterations, comorbidity with mental disorders, abnormalities in the circadian rhythms, and a range of circumstantial and psychological factors.
- The neurocognitive impairment associated with insufficient sleep and suicidal behaviour, particularly through its role in affecting decision–making and reduced cognitive inhibition underlies, to some extent, this association. Insufficient sleep may lead to rushed decisions, hastening the progression to action even in the absence of previous suicidal ideation.
- Sleep disturbances may be specifically associated with suicide outcomes, which could help to identify subgroups of at–high–risk patients.
- Sleep problems may be a cause of consultation less prone to stigma, allowing for early detection, thus becoming a promising therapeutic target to decrease suicide risk.

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Research agenda

- One of the most promising directions for future research is the development and implementation of mobile phone —based applications to objectively monitor sleep in at —risk populations, hence predicting suicidal behaviour.
- In line with this, monitoring of sleep using wearable devices has received much attention from research recently.
- Finally, ketamine—like agents with long—lasting therapeutic effects may improve the acute management of suicidal behaviour since ketamine has both anti—suicidal and antidepressant properties, which could be due to its effect on sleep problems.

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Conflicts of interest

The authors declare they have no potential conflicts of interest.

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References

[1] Ohayon M. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6(2):97–111.

[2] Ferrie J, Shipley M, Cappuccio F, Brunner E, Miller M, Kumari M, et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. Sleep 2007;30(12):1659–66.

[3] Rosekind MR, Gregory KB. Insomnia risks and costs: health, safety, and quality of life. Am J Manag Care 2010;16:617–26.

[4] Avidan A, Zee P, Avidan A. Handbook of sleep medicine. Philadelphia: Wolters Kluwer; 2015.

*[5] Pigeon WR, Pinquart M, Conner K. Meta—analysis of sleep disturbance and suicidal thoughts and behaviors. J Clin Psychiatry 2012;73(9): e1160–7.

[6] World Health Organization. Suicide data [internet]. 2018. Available from: http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/.

[7] Baca—Garcia E, Perez—Rodriguez M, Keyes K, Oquendo M, Hasin D, Grant B, et al. Suicidal ideation and suicide attempts in the United States: 1991–1992 and 2001–2002. Mol Psychiatry 2008;15(3):250–9.

[8] De Leon J, Baca—García E, Blasco—Fontecilla H. From the serotonin model of suicide to a mental pain model of suicide. Psychother Psychosom 2015;84(6):323–9.

[9] Bernert RA, Kim JS, Iwata NG, Perlis ML. Sleep disturbances as an evidence—based suicide risk factor. Curr Psychiatry Rep 2015;17(3):554.

*[10] Littlewood D, Kyle S, Carter L, Peters S, Pratt D, Gooding P. Short sleep duration and poor sleep quality predict next—day suicidal ideation: an ecological momentary assessment study. Psychol Med 2018:1–9.

[11] Lutz P, Mechawar N, Turecki G. Neuropathology of suicide: recent findings and future directions. Mol Psychiatry 2017;22(10):1395–412.

[12] Harvey A, Murray G, Chandler R, Soehner A. Sleep disturbance as transdiagnostic: consideration of neurobiological mechanisms. Clin Psychol Rev 2011;31(2):225–35.

*[13] Malik S, Kanwar A, Sim L, Prokop L, Wang Z, Benkhadra K, et al. The association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses: a systematic review and meta—analysis. Syst Rev 2014;3(1).

[14] Perlis M, Grandner M, Chakravorty S, Bernert R, Brown G, Thase M. Suicide and sleep: is it a bad thing to be awake when reason sleeps? Sleep Med Rev 2016;29:101–7.

[15] Littlewood D, Kyle S, Pratt D, Peters S, Gooding P. Examining the role of psychological factors in the relationship between sleep problems and suicide. Clin Psychol Rev 2017;54:1–16.

[16] Moher D, Altman D, Liberati A, Tetzlaff J. PRISMA statement. Epidemiology 2011;22(1):128.

[17] National Institute of Mental Health (NIMH). Construct: sleep—wakefulness. 2018. Retrieved from: https://www.nimh.nih.gov/research—priorities/rdoc/constructs/sleep—wakefulness.shtml.

[18] American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders: DSM—5. Washington, DC: American Psychiatric Association; 2013.

[19] O'Carroll PW, Berman AL, Maris RW, Moscicki EK, Tanney BL, Silverman MM. Beyond the Tower of Babel: a nomenclature for suicidology. Suicide Life Threat Behav 1996;26:237–52.

[20] Silverman MM, Berman AL, Sanddal ND, O'Carroll PW, Joiner TE. Rebuilding the Tower of Babel: a revised nomenclature for the study of suicide and suicidal behaviors. Part 2: suicide—related ideations, communications, and behaviors. Suicide Life Threat Behav 2007;37:264–77.

[21] Cardiff University. Cardiff University. 2018. Published, https://www.cardiff.ac.uk/specialist—unit—for—review—evidence/resources/critical—appraisal—checklists.

[22] Rod N, Kjeldgård L, Åkerstedt T, Ferrie JE, Salo P, Vahtera J, et al. Sleep apnea, disability pensions, and cause-specific mortality: a Swedish nationwide register linkage study. Am J Epidemiol 2017;186(6). https://doi.org/10.1093/aje/kwx138. 709 g–18.

*[23] Lin H, Lai C, Perng H, Chung CH, Wang CC, Chen WL, et al. Insomnia as an independent predictor of suicide attempts: a nationwide populationebased retrospective cohort study. BMC Psychiatry 2018;18(1). https://doi.org/10.1186/s12888—018—1702—2.

*[24] Ballard E, Vande Voort J, Bernert R, Luckenbaugh D, Richards E, Niciu M, et al. Nocturnal wakefulness is associated with next—day suicidal ideation in major depressive disorder and bipolar disorder. J Clin Psychiatr 2016: 825–31. https://doi.org/10.4088/jcp.15m09943.

*[25] Benard V, Etain B, Vaiva G, Boudebesse C, Yeim S, Benizri C, et al. Sleep and circadian rhythms as possible trait markers of suicide attempt in bipolar disorders: an actigraphy study. J Affect Disord 2018;244:1–8. https://doi.org/10.1016/j.jad.2018.09.054.

*[26] Bernert R, Hom M, Iwata N, Joiner T. Objectively assessed sleep variability as an acute warning sign of suicidal ideation in a longitudinal evaluation of young adults at high suicide risk. J Clin Psychiatry 2017;78(06): e678–87.

[27] Agargun M, Cartwright R. REM sleep, dream variables and suicidality in depressed patients. Psychiatry Res 2003;119(1–2):33–9. https://doi.org/10.1016/s0165—1781(03)00111—2.

[28] Koyawala N, Stevens J, McBee—Strayer S, Cannon E, Bridge J. Sleep problems and suicide attempts among adolescents: a case—control study. Behav Sleep Med 2014;13(4):285–95.

*[29] Rössler W, Angst J, Ajdacic—Gross V, Haker H, Berrouiguet S, Ujeyl M, et al. Sleep disturbances and suicidality—A longitudinal analysis from a representative community study over 30 y. Front Psychiatry 2018;9.

[30] Jang S, Lee K, Park E. Relationship between current sleep duration and past suicidal ideation or attempt among Korean adolescents. J Prev Med Public Health 2013;46(6):329–35.

[31] Blank M, Zhang J, Lamers F, Taylor A, Hickie I, Merikangas K. Health correlates of insomnia symptoms and comorbid mental disorders in a nationally representative sample of US adolescents. Sleep 2015;38(2): 197–204.

[32] Littlewood D, Gooding P, Panagioti M, Kyle S. Nightmares and suicide in posttraumatic stress disorder: the mediating role of defeat, entrapment, and hopelessness. J Clin Sleep Med 2016;12(03):393–9.

[33] Lopes M, Boronat A, Wang Y, Fu—I L. Sleep complaints as risk factor for suicidal behavior in severely depressed children and adolescents. CNS Neurosci Ther 2016;22(11):915–20.

*[34] Michaels M, Balthrop T, Nadorff M, Joiner T. Total sleep time as a predictor of suicidal behaviour. J Sleep Res 2017;26(6):732–8. https://doi.org/10.1111/jsr.12563.

[35] Stanley I, Hom M, Luby J, Joshic PT, Wagnerd KD, Emsliee GJ, et al. Co-morbid sleep disorders and suicide risk among children and adolescents with bipolar disorder. J Psychiatr Res 2017;95:54–9. https://doi.org/10.1016/j.jpsychires.2017.07.027.

[36] Bishop T, Ashrafioun L, Pigeon W. The association between sleep apnea and suicidal thought and behavior. J Clin Psychiatry 2018;79(1): 17m11480. https://doi.org/10.4088/jcp.17m11480.

[37] Verkooijen S, de Vos N, Bakker-Camu B, Branje S, Kahn R, Ophoff R, et al. Sleep disturbances, psychosocial difficulties, and health risk behavior in 16,781 Dutch adolescents. Acad Pediatr 2018;18(6):655–61.

[38] Li S, Lam S, Zhang J, Yu M, Chan J, Chan C, et al. Sleep disturbances and suicide risk in an 8—year longitudinal study of schizophrenia—spectrum disorders. Sleep 2016;39(6):1275–82. https://doi.org/10.5665/sleep.5852.

[39] Gunnell D, Chang S, Tsai M, Tsao C, Wen C. Sleep and suicide: an analysis of a cohort of 394,000 Taiwanese adults. Soc Psychiatry Psychiatr Epidemiol 2013;48(9):1457–65.

[40] Bernert R, Turvey C, Conwell Y, Joiner T. Association of poor subjective sleep quality with risk for death by suicide during a 10—year period. JAMA Psychiatry 2014;71(10):1129.

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* The most important references are denoted by an asterisk.

[41] Kodaka M, Matsumoto T, Katsumata Y, Akazawa M, Tachimori H, Kawakami N, et al. Suicide risk among individuals with sleep disturbances in Japan: a case—control psychological autopsy study. Sleep Med 2014;15(4):430—5.

*[42] Chiu H, Lee H, Chen P, Lai Y, Tu Y. Associations between sleep duration and suicidality in adolescents: a systematic review and dose—response meta—analysis. Sleep Med Rev 2018;42:119—26. https://doi.org/10.1016/j.smrv.2018.07.003.

[43] Sjöström N, Hetta J, Waern M. Persistent nightmares are associated with repeat suicide attempt. Psychiatry Res 2009;170(2—3):208—11. https://doi.org/10.1016/j.psychres.2008.09.006.

[44] Russell K, Rasmussen S, Hunter S. Insomnia and nightmares as markers of risk for suicidal ideation in young people: investigating the role of defeat and entrapment. J Clin Sleep Med 2018;14(05):775—84.

[45] Krakow B, Artar A, Warner T, Melendrez D, Johnston L, Hollifield M, et al. Sleep disorder, depression, and suicidality in female sexual assault survivors. Crisis 2000;21(4):163—70. https://doi.org/10.1027//0227-5910.21.4.163.

[46] Eikelenboom M, Beekman A, Penninx B, Smit J. A 6—year longitudinal study of predictors for suicide attempts in major depressive disorder. Psychol Med 2018:1—11. https://doi.org/10.1017/s0033291718001423.

[47] McCall W, Batson N, Webster M, Case L, Joshi I, Derreberry T, et al. Nightmares and dysfunctional beliefs about sleep mediate the effect of insomnia symptoms on suicidal ideation. J Clin Sleep Med 2013. https://doi.org/10.5664/jcsm.2408.

[48] An K, Jang J, Kim J. Sedentary behavior and sleep duration are associated with both stress symptoms and suicidal thoughts in Korean adults. Tohoku J Exp Med 2015;237(4):279—86.

[49] Gelaye B, Okeiga J, Ayantoye I, Berhane H, Berhane Y, Williams M. Association of suicidal ideation with poor sleep quality among Ethiopian adults. Sleep Breath 2016;20(4):1319—26.

[50] Supartini A, Honda T, Basri N, Haeuchi Y, Chen S, Ichimiya A, et al. The impact of sleep timing, sleep duration, and sleep quality on depressive symptoms and suicidal ideation amongst Japanese freshmen: the EQUSITE study. Sleep Dis 2016;2016:1—10.

[51] Wong M, Brower K, Craun E. Insomnia symptoms and suicidality in the national comorbidity survey — adolescent supplement. J Psychiatr Res 2016;81:1—8.

[52] Gelaye B, Addae G, Neway B, Larrabure—Torrealva G, Qiu C, Stoner L, et al. Poor sleep quality, antepartum depression and suicidal ideation among pregnant women. J Affect Disord 2017;209:195—200.

[53] Richardson J, Thompson A, King L, Corbett B, Shnaider P, Cyr K, et al. Insomnia, psychiatric disorders and suicidal ideation in a national representative sample of active Canadian Forces members. BMC Psychiatry 2017;17(1). https://doi.org/10.1186/s12888—017—1372—5.

[54] Whitmore L, Smith T. Isolating the association of sleep, depressive state, and other independent indicators for suicide ideation in United States teenagers. Arch Suicide Res 2018:1—27.

[55] Jollant F, Bellivier F, Leboyer M, Astruc B, Torres S, Verdier R, et al. Impaired decision making in suicide attempters. Am J Psychiatry 2005;162(2):304—10.

[56] Nock MK, Park JM, Finn CT, Deliberto TL, Dour HJ, Banaji MR. Measuring the suicidal mind: implicit cognition predicts suicidal behavior. Psychol Sci 2010;21(4):511—7.

[57] Dombrovski A, Siegle G, Szanto K, Clark L, Reynolds C, Aizenstein H. The temptation of suicide: striatal gray matter, discounting of delayed rewards, and suicide attempts in late—life depression. Psychol Med 2011;42(06):1203—15. https://doi.org/10.1017/s0033291711002133.

[58] Franzen PL, Buysse DJ, Dahl RE, Thompson W, Siegle GJ. Sleep deprivation alters pupillary reactivity to emotional stimuli in healthy young adults. Biol Psychol 2009; Mar;80(3):300—5.

[59] Fortier—Brochu É, Beaulieu—Bonneau S, Ivers H, Morin C. Insomnia and daytime cognitive performance: a meta—analysis. Sleep Med Rev 2012;16(1):83—94.

[60] Krause AJ, Simon EB, Mander BA, Greer SM, Saletin JM, Goldstein-Piekarski J, et al. The sleep—deprived human brain. Nat Rev Neurosci 2017;18(7):404—18.

[61] Ward—Ciesielski E, Winer E, Drapeau C, Nadorff M. Examining components of emotion regulation in relation to sleep problems and suicide risk. J Affect Disord 2018;241:41—8. https://doi.org/10.1016/j.jad.2018.07.065.

[62] Cheng W, Rolls E, Ruan H, Feng J. Functional connectivities in the brain that mediate the association between depressive problems and sleep quality. JAMA Psychiatry 2018;75(10):1052. https://doi.org/10.1001/jamapsychiatry.2018.1941.

[63] Emslie G, Kennard B, Mayes T, Nakonezny PA, Zhu L, Tao R, et al. Insomnia moderates outcome of serotonineselective reuptake inhibitor treatment in depressed youth. J Child Adolesc Psychopharmacol 2012;22(1):21—8. https://doi.org/10.1089/cap.2011.0096.

[64] Lee E, Cho H, Olmstead R, Levin M, Oxman M, Irwin M. Persistent sleep disturbance: a risk factor for recurrent depression in community—dwelling older adults. Sleep 2013. https://doi.org/10.5665/sleep.3128.

[65] Richardson J, King L, Cyr K, Shnaider P, Roth M, Ketcheson F, et al. Depression and the relationship between sleep disturbances, nightmares, and suicidal ideation in treatmenteseeking Canadian Armed Forces

members and veterans. BMC Psychiatry 2018;18(1). https://doi.org/10.1186/s12888—018e1782—z.

[66] Allan N, Conner K, Pigeon W, Gros D, Salami T, Stecker T. Insomnia and suicidal ideation and behaviors in former and current U.S. service members: does depression mediate the relations? Psychiatry Res 2017;252:296—302. https://doi.org/10.1016/j.psychres.2017.03.009.

[67] Maher MJ, Rego SA, Asnis GM. Sleep disturbances in patients with post—traumatic stress disorder: epidemiology, impact and approaches to management. CNS Drugs 2006;20(7):567—90.

[68] Kim J, Park H, Kim J. Alcohol use disorders and insomnia mediate the association between PTSD symptoms and suicidal ideation in Korean firefighters. Depress Anxiety 2018. https://doi.org/10.1002/da.22803.

[69] Benedetti F, Riccaboni R, Dallaspezia S, Locatelli C, Smeraldi E, Colombo C. Effects of CLOCK gene variants and early stress on hopelessness and suicide in bipolar depression. Chronobiol Int 2015;32(8):1156—61.

[70] Pawlak J, Dmitrzak—Weglarz M, Maciukiewicz M, Wilkosc M, Leszczynska—Rodziewicz A, Zaremba D, et al. Suicidal behavior in the context of disrupted rhythmicity in bipolar disorder—data from an association study of suicide attempts with clock genes. Psychiatry Res 2015;226(2—3):517—20.

[71] Dell'Osso L, Massimetti G, Conversano C, Bertelloni CA, Carta MG, Ricca V, et al. Alterations in circadian/seasonal rhythms and vegetative functions are related to suicidality in DSM—5 PTSD. BMC Psychiatry 2014;14(1). https://doi.org/10.1186/s12888—014—0352—2.

[72] Perlis M, Grandner M, Brown G, Basner M, Chakravorty S, Morales KH, et al. Nocturnal wakefulness as a previously unrecognized risk factor for suicide. J Clin Psychiatry 2016:e726—33. https://doi.org/10.4088/jcp.15m10131.

[73] Akkaya—Kalayci T, Kapusta N, Waldhör T, Blüml V, Poustka L, Özlü—Erkilic Z. The association of monthly, diurnal and circadian variations with suicide attempts by young people. Child Adolesc Psychiatry Ment Health 2017;11(1). https://doi.org/10.1186/s13034—017—0171—6.

[74] Chu C, Hom M, Rogers M, Ringer F, Hames J, Suh S, et al. Is insomnia lonely? Exploring thwarted belongingness as an explanatory link between insomnia and suicidal ideation in a sample of South Korean University students. J Clin Sleep Med 2016;12(05):647—52.

[75] Littlewood D, Gooding P, Kyle S, Pratt D, Peters S. Understanding the role of sleep in suicide risk: qualitative interview study. BMJ Open 2016;6(8), e012113.

[76] Woosley J, Lichstein K, Taylor D, Riedel B, Bush A. Hopelessness mediates the relation between insomnia and suicidal ideation. J Clin Sleep Med 2014;10(11):1223—30.

[77] Ribeiro J, Yen S, Joiner T, Siegler I. Capability for suicide interacts with states of heightened arousal to predict death by suicide beyond the effects of depression and hopelessness. J Affect Dis 2015;188:53—9.

[78] Hochard K, Heym N, Townsend E. Investigating the interaction between sleep symptoms of arousal and acquired capability in predicting suicidality. Suicide Life Threat Behav 2017;47(3):370—81.

[79] O'Connor R, Kirtley O. The integrated motivational—volitional model of suicidal behaviour. Phil Trans R Soc B: Biol Sci 2018;373(1754):20170268. https://doi.org/10.1098/rstb.2017.0268.

[80] Kohyama J. Neural basis of brain dysfunction produced by early sleep problems. Brain Sci 2016;6(1):5.

[81] Hauge L, Stene—Larsen K, Grimholt T, Øien-Ødegaard C, Reneflot A. Use of primary health care services prior to suicide in the Norwegian population 2006—2015. BMC Health Serv Res 2018;18(1).

[82] McCarty C, Russo J, Grossman D, Katon W, Rockhill C, McCauley E, et al. Adolescents with suicidal ideation: health care use and functioning. Acad Pediatr 2011;11(5):422—6.

[83] Schulberg H, Bruce M, Lee P, Williams J, Dietrich A. Preventing suicide in primary care patients: the primary care physician's role. Gen Hosp Psychiatry 2004;26(5):337—45.

[84] Feldman M, Franks P, Duberstein P, Vannoy S, Epstein R, Kravitz R. Let's not talk about it: suicide inquiry in primary care. Ann Fam Med 2007;5(5):412—8.

[85] Berrouiguet S, Alavi Z, Vaiva G, Courtet P, Baca-García E, Vidailhet P, et al. SIAM (Suicide intervention assisted by messages): the development of a post-acute crisis text messaging outreach for suicide prevention. BMC Psychiatry 2014;14(1):294. https://doi.org/10.1186/s12888-014-0294-8.

[86] Larsen M, Shand F, Morley K, Batterham P, Petrie K, Reda B, et al. A mobile text message intervention to reduce repeat suicidal episodes: design and development of reconnecting after a suicide attempt (RAFT). JMIR Ment Health 2017;4(4):e56. https://doi.org/10.2196/mental.7500.

[87] Nuij C, van Ballegooijen W, Ruwaard J, de Beurs D, Mokkenstorm J, van Duijn E, et al. Smartphone—based safety planning and self—monitoring for suicidal patients: rationale and study protocol of the CASPAR (Continuous Assessment for Suicide Prevention and Research) study. Internet Interv 2018;13:16—23. https://doi.org/10.1016/j.invent.2018.04.005.

[88] DeVylder J. Sleep as an underused target for rapid response in the treatment of depression and suicidal ideation. Health Soc Work 2016;41(3). 211—211.

[89] Riemann D, Baglioni C, Bassetti C, Bjorvatn B, Dolenc Groselj L, Ellis J, et al. European guideline for the diagnosis and treatment of insomnia. J Sleep Res 2017;26(6):675—700.

[90] Manber R, Bernert R, Suh S, Nowakowski S, Siebern A, Ong J. CBT for insomnia in patients with high and low depressive symptom severity:

adherence and clinical outcomes. J Clin Sleep Med 2011. https://doi.org/10.5664/jcsm.1472.

[91] Trockel M, Karlin BE, Taylor CB, Brown GK, Manber R. Effects of cognitive behavioral therapy for insomnia on suicidal ideation in veterans. Sleep 2015;38(2):259–65.

[92] Belleville G. Mortality hazard associated with anxiolytic and hypnotic drug use in the National Population Health Survey. Can J Psychiatry 2010;55:558–67.

[93] Brower K, McCammon R, Wojnar M, Ilgen M, Wojnar J, Valenstein M. Prescription sleeping pills, insomnia, and suicidality in the national co-morbidity survey replication. J Clin Psychiatry 2011;72(04):515–21.

[94] Sun Y, Lin C, Lu C, Hsu C, Kao C. Association between Zolpidem and sui-cide: a nationwide population–based case–control study. Mayo Clin Proc 2016;91(3):308–15. https://doi.org/10.1016/j.mayocp.2015.10.022.

[95] Holshoe J. Antidepressants and sleep: a review. Perspect Psychiatr Care 2009;45(3):191–7.

[96] Kierlin L, Littner M. Parasomnias and antidepressant therapy: a review of the literature. Front Psychiatry 2011;2.

[97] Aarts N, Zuurbier L, Noordam R, Hofman A, Tiemeier H, Stricker BH, et al. Use of selective serotonin reuptake inhibitors and sleep quality: a pop-ulationebased study. J Clin Sleep Med 2016;12(07):989–95. https://doi.org/10.5664/jcsm.5932.

[98] Morgenthaler T, Auerbach S, Casey K, Kristo D, Maganti R, Ramar K, et al. Position paper for the treatment of nightmare disorder in adults: an American Academy of Sleep Medicine position paper. J Clin Sleep Med 2018;14(06):1041–55.

[99] Ellis T, Rufino K, Nadorff M. Treatment of nightmares in psychiatric in-patients with imagery rehearsal therapy: an open trial and case series. Behav Sleep Med 2017:1–14. https://doi.org/10.1080/15402002.2017.1299738.

[100] Augedal A, Hansen K, Kronhaug C, Harvey A, Pallesen S. Randomized controlled trials of psychological and pharmacological treatments for nightmares: a meta–analysis. Sleep Med Rev 2013;17(2):143–52. https://doi.org/10.1016/j.smrv.2012.06.001.

[101] Seda G, Sanchez–Ortuno M, Welsh C, Halbower A, Edinger J. Comparative meta–analysis of prazosin and imagery rehearsal therapy for nightmare frequency, sleep quality, and posttraumatic stress. J Clin Sleep Med 2015. https://doi.org/10.5664/jcsm.4354.

[102] McCall W, Pillai A, Case D, McCloud L, Nolla T, Branch F, et al. A pilot, randomized clinical trial of bedtime doses of prazosin versus placebo in suicidal posttraumatic stress disorder patients with nightmares. J Clin Psychopharmacol 2018;1. https://doi.org/10.1097/jcp.0000000000000968.

[103] Raskind M, Peskind E, Chow B, Harris C, Davis-Karim A, Holmes HA, et al. Trial of prazosin for posttraumatic stress disorder in military veterans. N Engl J Med 2018;378(6):507–17. https://doi.org/10.1056/nejmoa1507598.

[104] Horsch C, Lancee J, Griffioen–Both F, Spruit S, Fitrianie S, Neerincx M, et al. Mobile phone–delivered cognitive behavioral therapy for insomnia: a randomized waitlist controlled trial. J Med Internet Res 2017;19(4):e70. https://doi.org/10.2196/jmir.6524.

[105] Duman R. Ketamine and rapid–acting antidepressants: a new era in the battle against depression and suicide. F1000Research 2018;7:659.

[106] Vande Voort J, Ballard E, Luckenbaugh D, Bernert R, Richards E, Niciu M, et al. Antisuicidal response following ketamine infusion is associated with decreased nighttime wakefulness in major depressive disorder and bi-polar disorder. J Clin Psychiatry 2017;78(8):1068–74.

[107] Duncan W, Slonena E, Hejazi N, Brutsche N, Yu K, Park L, et al. Motor–activity markers of circadian timekeeping are related to ket-amine's rapid antidepressant properties. Biol Psychiatry 2017;82(5):361–9.

[108] Oquendo M, Baca-Garcia E. Suicidal behavior disorder as a diagnostic entity in the DSM-5 classification system: advantages outweigh limita-tions. World Psychiatry 2014;13(2):128–30. https://doi.org/10.1002/wps.20116.

[109] Courtet P, Gottesman I, Jollant F, Gould T. The neuroscience of suicidal behaviors: what can we expect from endophenotype strategies? Transl Psychiatry 2011;1(5). e7–e7.

[110] Saffer B, Klonsky E. Do neurocognitive abilities distinguish suicide attempters from suicide ideators? A systematic review of an emerging research area. Clin Psychol Sci Pract 2018;25(1), e12227.

[111] Ibáñez V, Silva J, Cauli O. A survey on sleep questionnaires and diaries. Sleep Med 2018;42:90–6. https://doi.org/10.1016/j.sleep.2017.08.026.

[112] De Zambotti M, Claudatos S, Inkelis S, Colrain IM, Baker FC. Evaluation of a consumer fitness–tracking device to assess sleep in adults. Chronobiol Int 2015;32(7):1024–8. https://doi.org/10.3109/07420528.2015.1054395.