Climate change and sleep: A systematic review of the literature and conceptual framework

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S U M M A R Y

From disaster related stress causing insomnia, to poor air quality causing sleep related breathing problems, climate change poses a potentially serious threat to human sleep. We conducted a systematic review evaluating the relationship between climate change and human sleep in the PubMed, Scopus, and Cochrane databases from 1980 through 2017 following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Inclusion criteria included epidemiologic studies published in English that reported observational population data on human sleep and its relationship to climate change, temperature, extreme weather events and climate related disasters (e.g. hurricanes, floods, and wildfires). We excluded non-human studies, laboratory or experimental physiology studies, commentaries or letters, review articles, and articles on wind turbines. Using a systematic search strategy, 16 studies met the inclusion criteria. Six studies related to the effects of rising temperature, seven studies related to extreme weather events, and three studies related to floods or wildfires. Diminished total sleep times and sleep disruption were most commonly reported, especially among the most vulnerable populations including the elderly and low-income; however, the body of evidence was limited and further well-designed human studies are clearly needed. We present a conceptual framework for identifying the emerging threats of climate change and understanding their respective effects on human sleep.

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Background

Climate change is posing a substantial threat to human health [1], U.S. average temperatures have increased by 1.3 °F–1.9 °F since 1895, most of which has occurred since 1970 [1]. Temperatures are projected to rise another 2 °F–4 °F in most areas of the United States and around the world over the next few decades [1]. Rising temperatures related to climate change cause extreme heat events, which are the leading cause of weather-related deaths in the United States [12]. Food and water borne diseases, including salmonella and campylobacteriosis are more prevalent at higher temperatures [3]. Dengue fever and Lyme disease are vector borne illnesses in North America that have been spreading northward in recent years as a result of climate change [4,5]. Hurricanes, tornados, and other extreme weather events are leading to fatalities, displacing vulnerable populations, and affecting mental health [1]. Independent of exposure to extreme weather events, some members of the population experience anxiety from the impending threat of climate change itself [6,7]. While many of the health consequences of climate change are well documented, the effect of climate change on sleep has not been a topic of investigation among sleep medicine or climate change experts.

In 2015, the Centers for Disease Control and Prevention declared sleep disorders, and insufficient sleep in particular, to be a public health epidemic [8]. Recent data suggest that human adults require approximately 7–8 h of sleep per night to feel fully rested [9,10]. Yet despite this specific recommendation, only 47% of working Americans achieve it [11]. Japanese adults report even less sleep with 34% sleeping more than 7 h on work nights [11]. Inadequate sleep results in profound consequences, including increasing the risk of hypertension, diabetes, heart disease, dementia, and stroke [12]. Inadequate sleep, whether self-imposed or due to an undiagnosed or untreated sleep disorder, also has profound psychological and economic impacts. In the US alone, more than 100,000 automobile crashes, 1550 deaths, 71,000 injuries, and $12.5 billion...
in monetary losses are attributable to drowsy driving accidents each year [13].

In the US, 50–70 million people are affected by a sleep disorder [14]. In addition to self-induced sleep deprivation, numerous sleep disorders lead to inadequate sleep. Obstructive sleep apnea (OSA), for example, is a highly prevalent, yet under-diagnosed sleep disorder [15]. If left untreated, OSA increases the risk of chronic diseases such as hypertension, heart disease, diabetes and stroke [12]. Through disrupted sleep, OSA also leads to sleepiness and grogginess throughout the day and diminishes productivity and quality of life [16]. Insomnia, another common sleep disorder affecting between 4% and 50% of adults, can lead to inadequate sleep and subsequent sequelae [17,18]. Insomnia is also co-morbid with numerous mental health illnesses including depression and post-traumatic stress disorder. The consequences of sleep deprivation also affect school age children and adolescents [19]. Sleep problems in the developing world are fast approaching those in developed nations. According to the first ever pan-African and Asian sleep analysis, an estimated 150 million adults are suffering from sleep-related problems across the developing world [20].

Many effects of climate change are likely to have an impact of the prevalence of inadequate sleep and sleep disorders. Extreme weather events caused by the rise in global temperatures can lead to stress and trauma—both physical and psychological [21]. They also lead to population displacement, an increase in food scarcity, and other stressors that directly affect sleep. Higher temperatures during the day (especially in urban areas) are leading to persistently higher temperatures at night [1,22,23]. As evidenced by numerous physiologic studies, the thermal environment is an extremely important determinant of sleep quality. Even moderate increases in temperature can disrupt the tightly coupled thermoregulation of sleep as sleep preferably occurs during the circadian phase of decreased heat production and increased heat loss. Key review articles by Okamoto-Mizuno and Mizuno, and Lack et al. highlight these physiologic effects and others in greater detail [24–28]. A recent study using US survey data found that higher temperatures were associated with diminished sleep quality among 765,000 US residents [29].

We conducted a systematic review of the literature, to evaluate the scientific evidence on how climate change impacts human sleep. Informed by this review, we present a new conceptual framework to elucidate the mechanisms by which climate change may negatively impact sleep. We use the framework to highlight current gaps in the scientific literature and identify strategies for further research on how the myriad changes in our atmosphere and environment may be impacting healthy sleep in the population.

Methods

Using PRISMA (Preferred reporting items for systematic reviews and meta-analyses) guidelines, we systematically examined the literature to identify empirical studies published to date on the association between changes in temperature and climate with any aspects of human sleep [30]. Prior to search, details of the protocol for this systematic review were registered on PROSPERO and can be accessed at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017080868 [31]. From September through November 2017, we searched the PubMed, Scopus, and Cochrane databases from 1980 through 2017. Search terms and specific search strategies for each database are included in the Supplementary material section Appendix A. We included studies if they were published in English and reported observational, population data on human sleep and its relationship to climate change, temperature, extreme weather events and climate related disasters (e.g. hurricanes, floods, droughts, wildfires). We excluded studies reporting on climate impacts on plants or non-human animals, laboratory or experimental physiology studies, commentaries or letters, review articles, and articles on wind turbines. Due to a recent systematic review on air pollution and sleep related breathing disorders, key words including “air pollution” or “ozone” were excluded from the search, and studies reporting similar effects were not included [32]. Studies were independently reviewed and required consensus by two reviewers (DR and ML) for inclusion.

Data and background information were extracted from each paper and characteristics were recorded according to the focus of each article. A quality assessment of each article was not undertaken due to diverse nature of the reviewed material and generalized lack of scientific framework in most studies. Table 1 below identifies these same characteristics and a brief description of focus of the included articles.

Results

A total of 1719 studies were retrieved for screening by title and possible inclusion. After exclusion of duplicates and non-pertinent titles, 68 were screened for inclusion by abstract. Of these studies, 24 studies were screened for inclusion by full text and 16 met final inclusion criteria (Fig. 1). Most studies were excluded due to their irrelevance (i.e. physiology or sleep deprivation study, occupational assessment, device efficacy).

Temperature and sleep

The systematic review yielded six studies on the effects of rising temperature on sleep. All six studies reported negative effects of higher temperatures on sleep time and sleep quality. In a study using objective measurements of sleep quality, Weinreich et al. found that higher ambient temperature was associated with increased severity of obstructive sleep apnea [33]. Over all seasons, an interquartile range increase in temperature (8.6 °C) was associated with a 10.1% (95% CI 2.0–18.9%) increase in the Apnea—Hypopnea Index [33]. Fukuda et al. established a set of disability weights for sleep problems, other than sleep apnea, to quantify the burden of symptoms and concluded the rising burden of symptoms could be attributable to rising temperatures [34]. In the largest study identified, Obradovich et al. analyzed data on self-reported sleep and objectively measured temperature geolocated to the city level—with station-level daily temperature from the National Centers for Environmental Information Global Historical Climatology Network—Daily (GHCN-D) from 765,000 participants in a repeated cross-sectional telephone survey conducted annually from 2002 to 2011 in the United States [29]. The authors estimated that a 1 °C deviation in monthly nighttime temperatures was associated with an increase of three nights with insufficient sleep per 100 people [29]. In stratified analyses, the authors found that the negative effect of temperature was stronger among elderly and lower income respondents. The study included a projection of the number of nights of insufficient sleep by US geographic location in 2050 and 2099 using existing climate change models.

Extreme weather events and sleep

A total of seven studies, all related to hurricanes, were identified. A small study conducted after Hurricane Andrew in the early 1990s included 54 individuals, and was the first study to show an increase in subjective sleep complaints following a natural disaster [35]. The Pittsburgh Sleep Quality Index (PSQI), a previously validated measure of subjective sleep quality, was administered 6–12 mo after the hurricane. A modified version was used to assess sleep one month prior to the hurricane. The complaints appeared to be most
Table 1
Documents included in systematic review.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Period of study</th>
<th>Sample size</th>
<th>Geographic focus</th>
<th>Age</th>
<th>Biases and Limitations</th>
<th>Summary findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Temperature and Sleep</strong></td>
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<tr>
<td>Obradovich N et al., 2017</td>
<td>2002 to 2011</td>
<td>n – 765k</td>
<td>United States</td>
<td>Under and over 65</td>
<td>Self-reported data; No objective measures on sleep</td>
<td>Increases in night time temperatures amplify self-reported nights of insufficient sleep; however, coefficient estimates remain mostly unchanged by the inclusion of common demographic variables like age, ethnicity, education, and income, Increase in temp and ozone was associated with an increase in AHI</td>
</tr>
<tr>
<td>Weinreich G et al., 2015</td>
<td>2006 to 2008</td>
<td>n – 1773</td>
<td>Germany</td>
<td>Mean 63.8</td>
<td>OSA not via gold standard PSG; Possible Type II error</td>
<td>Participants who considered themselves more sensitive to heat reported significantly more sleep disturbance (p &lt; .001) and excessive sweating (p = .004) compared to participants who did not consider themselves sensitive to heat.</td>
</tr>
<tr>
<td>van Loenhout JA et al., 2016</td>
<td>2012</td>
<td>n – 113</td>
<td>Netherland</td>
<td>Mean 73.8</td>
<td>Self-reported data; Selection bias (self-selected)</td>
<td>Approximately 80% of the subjects reported signs or symptoms of heat strain in warm weather, mostly thirst (68%), drying of mouth (43%), impaired endurance (43%) and sleep disturbances (32%). Higher temperature and longer day length both were associated with small reductions of nightly sleep duration. Adolescents were less physically active during winter and on rainy and short sunlight days. There was an inverse U-shaped relationship between PA and mean temperature.</td>
</tr>
<tr>
<td>Nayha S et al., 2014</td>
<td>2007</td>
<td>n – 4007</td>
<td>Finland</td>
<td>Range 25–74</td>
<td>Self-reported; Selection bias as symptomatic people are more likely to answer</td>
<td>Based on the valuation protocol establishing varying disability weights, the authors determined the burden of symptoms as attributable to increasing temperatures.</td>
</tr>
<tr>
<td>Quante M et al., 2017</td>
<td>2011–2014</td>
<td>n – 669</td>
<td>United States</td>
<td>Mean 12.9</td>
<td>Cross-sectional analysis</td>
<td></td>
</tr>
<tr>
<td>Fukuda S et al., 2013</td>
<td>2002</td>
<td>Japan</td>
<td>NA</td>
<td>NA</td>
<td>Relied on expertise of reporting primary physician and specialist to assess disability weights</td>
<td></td>
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<tr>
<td><strong>Extreme Weather Events and Sleep</strong></td>
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<tr>
<td>McKibben JB et al., 2010</td>
<td>2005</td>
<td>n – 2249</td>
<td>United States</td>
<td>Range 20-78 Median 49</td>
<td>Self-referral bias (selection)</td>
<td>Sleep disturbance and elevated arousal were strongly associated with impaired work performance (odds ratios [ORs] 3.33 and 3.34, respectively), &quot;bad&quot; mental health (ORs 3.01 and 3.64), &quot;bad&quot; physical health (ORs 3.21 and 2.01), and limited day-to-day function (ORs 4.71 and 2.32).</td>
</tr>
<tr>
<td>Anastario MP et al., 2008</td>
<td>2006</td>
<td>n-194</td>
<td>United States</td>
<td>Mean 43.3</td>
<td>Selection bias; self-report (thus risk of under reporting in GBV studies); Cultural biases</td>
<td>Of the nine symptoms assessed with the Patient Health Questionnaire-9 (PHQ-9), four were associated with PDGBV. Among women with sleep dysregulation, the odds of PDGBV were 2.5 times higher in comparison with women without sleep.</td>
</tr>
<tr>
<td>Brown TH et al., 2011</td>
<td>2007 and 2008</td>
<td>n – 191</td>
<td>United States</td>
<td>Range 8-15 Mean 11.5</td>
<td>Subjective sleep data; small sample size; absence on sleep data prior to Katrina</td>
<td>Found cross-sectional relationships of sleep disturbance and fear of sleeping alone with PTSD symptom severity. Subjective sleep complaints are common after a natural disaster and are most prominent among those with psychiatric morbidity. Women with abuse reported 4.3 times odds of poor sleep compared without reported abuse.</td>
</tr>
<tr>
<td>Mellman TA et al., 1995</td>
<td>1992–1993</td>
<td>n – 54</td>
<td>United States</td>
<td>Mean 40.4</td>
<td>Recall bias; selection bias; small sleep study sample size</td>
<td></td>
</tr>
<tr>
<td>Hoag JR et al., 2015</td>
<td>2006 to 2012</td>
<td>n – 375</td>
<td>United States</td>
<td>Range 18-31</td>
<td>Low income population i.e. external validity</td>
<td>A significant association was detected between the post-like PSQI and overall sleep quality from the baseline pre-Ike. Random telephone survey 6 months after storm; persons with sleep problems worthy of surveillance given increased predictor of PTSD (OR 4.18).</td>
</tr>
<tr>
<td>Wu ZH et al., 2015</td>
<td>2006 to 2012</td>
<td>n – 296</td>
<td>United States</td>
<td>Range 18-31</td>
<td>PSQI subjective data;</td>
<td></td>
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<tr>
<td>Boscarno JA et al., 2014</td>
<td>2013</td>
<td>n – 200</td>
<td>United States</td>
<td>Mean 59.3</td>
<td>Self-reported data; Selection bias (self-selected)</td>
<td>Random telephone survey 6 months after storm; persons with sleep problems worthy of surveillance given increased predictor of PTSD (OR 4.18). Those experiencing post disaster sleep disorders may be good candidates for cognitive behavioral interventions following traumatic exposures.</td>
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<td><strong>Floods, Wildfires, and Sleep</strong></td>
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<tr>
<td>Zhen R et al., 2017</td>
<td>2016</td>
<td>n – 187</td>
<td>China</td>
<td>Range 13-80 Mean 41.9</td>
<td>Information bias; self-reported or documented by personnel</td>
<td>Traumatic exposure had a direct and positive association with sleep problems and could also be indirectly associated with sleep problems through fear, depression, but not negative cognitions. Residents whose households were directly affected by flooding were more likely to report poor sleep quality (OR 2.3; 95% CI, 1.2–4.4). The diagnosis of insomnia, as well as certain specific insomnia complaints, were more frequent in female victims of wildfires who have experienced “fear of imminent death” and have developed PTSD.</td>
</tr>
<tr>
<td>Alderman K et al., 2013</td>
<td>2011</td>
<td>n – 960</td>
<td>Australia</td>
<td>Mean 51</td>
<td>Selection bias if only individuals who felt affected by flood responded</td>
<td></td>
</tr>
<tr>
<td>Psarras C et al., 2016</td>
<td>N/A</td>
<td>n – 92</td>
<td>Greece</td>
<td>N/A</td>
<td>Self-reported data; cross-sectional study</td>
<td></td>
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</tbody>
</table>

prominent in those individuals with underlying psychiatric morbidity, and were highest for global severity, sleep quality, daytime dysfunction, and sleep disturbances (particularly frequent awakenings and “bad dreams”). Polysomnographic data were obtained in a subgroup of 10 hurricane victims with underlying psychiatric morbidity (six meeting full criteria for PTSD) and compared with nine non-hurricane victims. The results revealed significantly more awakenings and entries into stage 1 sleep in the hurricane victim subgroup.

In a cohort of low income women, pre-hurricane PSQI was available to compare with post-hurricane PSQI following Hurricane Ike. Similarly, a significant association was detected between the post-like PSQI and overall decline in sleep quality from the baseline pre-like questionnaire (P < .01). Another study included in the analysis examined a subgroup with childhood abuse from this same cohort of low-income women, and those women with abuse reported 4.3 times higher odds of poor sleep compared to those without reported abuse. Rather than using abuse as a predictor, investigators used poor sleep as a predictor of abuse following the event. Anastasio and colleagues used mental health indicators to identify post-disaster gender-based violence (PDGBV) among women displaced by Hurricane Katrina and found that among women with poor sleep, the odds of PDGBV were 2.5 times higher compared to women without poor sleep (95% CI 1.2–5.1).

Among the seven studies identified, the largest study (n = 2249) examined a cohort of public health workers involved with the 2004 hurricane season. Based on online data collected following contact via email recruitment, sleep disturbance and elevated arousal were associated with impaired work performance (ORs 3.33 and 3.34, respectively), “bad” mental health (ORs 3.01 and 3.64), “bad” physical health (ORs 3.21 and 2.01), and limited day-to-day functioning (ORs 4.71 and 2.32), and these associations persisted after adjusting for age, race, sex, education, and marital status.

Floods, wildfires, and sleep

Of the three studies meeting criteria for analysis, two related to floods and one to wildfires. All three studies, utilizing self-reported information, found higher rates of disrupted sleep after exposure to these events. In a study of more than 900 subjects affected by the 2011 summer floods in Brisbane, Australia, residents whose households were directly affected by flooding were more likely to report poor sleep quality (OR 2.3; 95% CI, 1.2–4.4). In a study of flood victims in China, traumatic exposure had not only a direct and positive association with sleep problems, but this association was mediated by fear and depression and not negative cognitions. In a study examining the role of “fear of imminent death” among female victims of wildfires in Greece, researchers found more insomnia, as well as certain specific insomnia complaints.

Discussion

This review identified a limited body of research examining the relationship between the effects of climate change and human
sleep. Altogether, only 16 studies were identified. Included studies reported a consistent link between temperature and weather events associated with climate change and impaired sleep. More specifically, total sleep time is diminished due to sleep disruption as opposed to specific new-onset sleep disorders or self-induced insufficient sleep. Sleep maintenance difficulty, in contrast to sleep-onset difficulty, is more widely characterized. Patients report impaired sleep quality. As is true for many of the negative effects of climate change, sleep in those most vulnerable, including the elderly and impoverished, is highly affected.

Our review identified significant gaps in the literature. We were unable to identify a single study on the effects of droughts and sleep, nor on the effects of extreme weather events other than hurricanes. Studies evaluating the impact of hurricanes were limited to specific highly vulnerable cohorts, which limits their generalizability. The lack of evaluation of a broader set of weather events associated with climate change limits our ability to recommend targeted prevention strategies. Loss of power during blizzards, for example, may cause very different effects on sleep than the loss of power in the warmth of hurricanes. Despite reliance on artificial cooling and heating in higher income countries, there were no studies that evaluated the loss of power due to an extreme weather event and its effect on sleep. Of particular importance to sleep medicine specialists, no study addressed the emerging threats of climate change on sleep health services. Sleep laboratories and sleep centers play an integral role in the sleep health of populations, and the loss of these services due to climatic events could be devastating to the ongoing care of individuals with sleep disorders.

That most studies relied on self-reported data raises methodological problems because subjective sleep quality often differs from objective measurements, especially in the elderly and in those with comorbid insomnia [43]. For example, female trauma survivors with posttraumatic stress disorders demonstrate a discrepancy between subjective and objective measurements of sleep with an overestimation of sleep disruption when measured concurrently [44]. In our review, only a handful of studies objectively measured sleep, and even fewer used polysomnographic measures as the gold standard measure of sleep.

Air pollution is expected to increase as a result of climate change which can have significant effects on sleep via sleep-related breathing disorders in adults and children. However, this review did not include air pollution due to a recent systematic review by Tenero and colleagues [32]. Their results suggest an involvement of environmental pollution in the worsening of sleep-disordered breathing in children; however, the review identified only eight studies of mixed quality which is likely insufficient given the variability and complexity of sleep-related breathing disorders in general [32].

To support greater understanding, interest, and to guide future study, Fig. 2 highlights a conceptual framework with the known consequences of climate change as they relate to prominent non-communicable diseases via a “sleep” pathway. The schematic emphasizes some of the findings in this review, in addition to other

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**Fig. 2.** Consequences of climate change on human health via sleep disruption—a systems framework.
climate change sequelae, including food insecurity and vector-borne illnesses among others, and their respective effects on sleep. Novel concerns, such as the possible effects of air pollution on circadian rhythms through loss of light entrainment, might also be considered. Further, one must not only consider the direct impact of the consequence of climate change on sleep, but also consider the effects of potential adaptation and mitigation strategies.

Perhaps the most striking feature in Fig. 2 is the recognition of strong scientific evidence supporting the emerging threats of climate change, as well as the strong scientific evidence identifying sleep loss as strong contributor to non-communicable disease burden. What appears to be lacking, and confirmed by our systematic review, is the scientific evidence identifying a clear link between the effects of climate change on sleep itself. Despite evidence that one should emphasize sufficient and adequate sleep as a critical component of health and well-being, its virtual absence in climate change and health literature is an important gap that needs attention.

Even more surprising is the virtual absence of attention to sleep health from the humanitarian response literature. Extreme weather events, floods, and wildfires are demanding rapid, and more frequent, humanitarian responses from governmental aid agencies and NGOs. Yet, even with clear recommendations from expert panels on sleep requirements from birth through adulthood, adequate sleep is rarely, if ever, mentioned. For example, adequate living space, bedding, and room climates highlight certain minimum standards in the Sphere Project (a comprehensive international guideline for humanitarian response); however, total sleep hours as a “core standard” are missing [45–47]. Just as one requires a certain amount of water each day, so too does one require sleep for ongoing health. Prolonged exposure to sleepless nights have profound consequences on one’s health. Of course, as evidenced by this systematic review, greater study is necessary to link climate change to sleeplessness, but a vast array of scientific evidence systematically links inadequate sleep to poor health.

The retrospective study by Obradovich et al. perhaps the most relevant study in our review, should inform further epidemiologic study on climate change and sleep given its scientific rigor. In regions highly susceptible to the threats of climate change, large prospective cohort studies comparing the sleep and subsequent health sequelae of those exposed to those not-exposed to the threats of climate change might also be highly informative. Because the objective measurement of sleep parameters in a laboratory environment (e.g. polysomnography) may be unsuitable in population-based studies, data from technology wearables (e.g. actigraphy) is a more practical and adopted strategy [48,49]. Large epidemiological studies like the Obradovich study, as well as exposure assessments and risk analyses, are lacking in this realm and would add greater depth to the literature. Further, studies identified were predominantly descriptive in nature. There was not standardization in measurement across studies, nor were there enough studies to perform a meta-analysis. This review was limited by including only papers published in English.

Sleep health should be included as an integral part of any climate resilient system. The World Health Organization defines a climate resilient health system as one that is capable to anticipate, respond to, cope with, recover from and adapt to climate-related shocks and stress, so as to bring sustained improvements in population health, despite an unstable climate [50]. Partnering with national organizations such as the American Academy of Sleep Medicine along with experts in sleep and public health will help raise both national and international awareness around incorporating sleep health into climate resilient health systems that are prepared to protect the health of future generations [51].

### Practice Points
- Clinicians should be aware of the different ways that climate change affects human health.
- To date, limited studies have evaluated how climate change affects sleep. Of the few that have been conducted, they illustrate sleep disruption from climate related temperature changes as well as stress responses.
- Sufficient and adequate sleep is critical for good health and should be emphasized as part of climate adaptation, including in the context of humanitarian response.

### Research Agenda
- Improving study methods to include large sample sizes while moving beyond self-reported sleep parameters and cross-sectional studies.
- Standardization of exposure measurements, in regions highly susceptible to climate change, to allow for sleep-related exposure assessment study, a key scientific framework in climate change research. For example, large prospective cohort studies comparing the sleep and subsequent health sequelae of those exposed to those not-exposed to the threats of climate change will be highly informative.
- Identifying adaptation and mitigation strategies to improve sleep in relevant climate change settings, especially among “climate change refugees”.

### Conflicts of interest
The authors do not have any conflicts of interest to disclose.

### Acknowledgements
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### Appendix A. Supplementary data
Supplementary data related to this article can be found at [https://doi.org/10.1016/j.smrv.2018.07.007](https://doi.org/10.1016/j.smrv.2018.07.007).

### References


* The most important references are denoted by an asterisk.


