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TITLE: INFLUENCE OF SOCIOECONOMIC STATUS AND STRESS OVER QUALITY OF SLEEP: A SYSTEMATIC REVIEW

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SUMMARY

Sleep disorders (SD) have a complex aetiology, and socioeconomic status (SES) as determined by social class, household income, ethnicity and education plays an important role in their development. As SD are associated with cognitive impairment and mood disorders, they in turn impact SES. Socioeconomic status also influences allostatic load caused by chronic accumulation of stress throughout life. Environmental and psychological stressors have a direct effect on SD, and they are modulated by SES, in combination with comorbidities like obesity and cardiovascular disease. This review explores the recent theories about the influence of SES on the development of SD in the general population, whether or not occurring with comorbidities, and also focusses on the interplay between socioeconomic status, circadian rhythms, aging and clinical outcomes like metabolic diseases and cancer.

Keywords: sleep, socioeconomic status, stress, circadian rhythm, allostatic load, mood disorder, social class

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Abbreviations

SD: sleep disorders	CR: circadian rhythm	VLPO: ventrolateral preoptic area
SC: social class	CC: circadian cycle	REM: rapid eye movement
SES: socioeconomic status	BMI: body mass index	SCN: suprachiasmatic nuclei
MD: mood disorders	TTFL: transcription-translation feedback loop	

INTRODUCTION

Sleep is a physiological state that corresponds to one-third of a human life. Much more than just a passive state, sleep plays a major role in physical and psychological health [1]. Indeed, acute or chronic disruption of sleep can have major consequences on alertness, learning ability, mood, cardiovascular health, the immune system and weight regulation [2]. Sleep is a natural state of loss of consciousness of the external world that does not exclude the reception of sensory information but is accompanied by a progressive reduction of muscle tone and recurs in regular intervals.

The timing of the sleep-wake cycle is driven by two factors, the homeostatic build-up of sleep need and the circadian rhythm (CR) which defines the appropriate temporal niche for sleep [3,4]. Organization of the circadian cycle (CC) leads to alternation between the day before and sleep. Organization of ultradian cycles leads to alternation between slow sleep and paradoxical sleep [5,6]. The primary circadian pacemaker of the human brain is the suprachiasmatic nucleus of the hypothalamus, indirectly connected to the

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ventrolateral preoptic area (VLPO), a hypothalamic structure made up of GABAergic neurons which inhibit the arousal systems, therefore supporting sleep [7]. These processes are supported and maintained by various neurotransmitters like adenosine and histamine [8]. The CC, regulated by internal biological clocks, is aligned with the dawn-dusk cycle (the nychthemeral rhythm) by external synchronizing factors [8-10]. The nychthemeral rhythm leads to lower body temperature due to the action of melatonin, a cerebral hormone that is synthesized by the pineal body during the night. The scheduled secretion of this hormone partly depends upon genetic factors but is also modulated by epigenetic interactions through external stimuli such as luminosity, food supply, social relationships and the production of heat [9,10]. The molecular mechanisms at the origin of this homeostatic process are not fully understood. The result is a nightly sequence of three to five cycles of approximately 90-minutes of sleep, each one composed of several distinct phases, starting with the slow wave sleep and ending with the paradoxical sleep (when dreams start). It was recently shown that exposure to natural light improves symptoms related to disorders of the cycles of sleep, but research associating melatonin therapy with better sleep is continuously discussed as melatonin shows limited potency and is only applicable in some populations [9].

During sleep, many neuronal networks are rebuilt, and this mechanism could have explanations and implications for energy processing, metabolism and memory [9,11]. Consolidation of the information received during the wake phase of the day is carried out during sleep, due to inhibition of the cerebral activity supporting processes of homeostatic plasticity of the different neural networks [12,13]. The need for sleep (often termed sleep debt) varies from person to person, but also with cultural influences, geographical location and the practices of life. The ideal mean length of sleep for an adult would be eight hours per day, but it usually varies between six and ten hours per night, also affected by factors that may predispose to sleep disorders (such as age, the presence of a neurological disease and the exposure to intense psychological or environmental stress).

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Sleep disturbances or sleep disorders (SD) have many and varied causes, such as stress, mood disorders (MD), lifestyle habits, living conditions, diseases or aging [14,15]; and they are often associated with some clinical outcomes such as cognitive impairment and breathing abnormalities [8,16]. The spatial distribution of SD within a population is influenced by sociodemographic variables like age, sex, profession and comorbidities [17,18]. Socioeconomic status (SES), and thus living conditions, lifestyle habits, stress, physical and mental health and aging [14,16,19-22] can all influence the development and progression of SD. The variations in SES within the population correspond to variations in the level of access to different conditions and resources favorable to health [22-24]. While SES is an important determinant of health, its role in the development and maintenance of SD is not well studied. SES may induce some form of stress, often complex to figure out mainly because of the difficulty to evaluate the direction of this relationship [25,26]. This chronic accumulation of stress becomes a progressive burden (known as allostatic load); and correlation or association between the socioeconomic factors inducing psychological and environmental stress and the trajectory of SD remains unclear.

This review explains the recent theories about environmental and psychological stress in the context of different SD documented in current literature. Following that, the review gives a detailed synthesis of existing interactions among allostatic load, SD, SES and clinical outcomes like cancer, metabolic diseases, neurodegenerative diseases and circadian rhythm disturbances. Finally, the authors provide a theoretical model explaining how this interaction works, emerging from the current state of the knowledge and how researchers may improve current practice.

METHOD

Using PRISMA (Preferred reporting items for systematic reviews and meta-analyses) guidelines, a comprehensive literature search was performed on articles published in peer-reviewed journals from June 1974 until March 2018, according to the following

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types of studies: clinical, experimental, quasi-experimental and epidemiological. The databases used for this review were the following: PubMed, Web of Science, PsycINFO. We crossed the term “socioeconomic” with “social class” (55415 articles found). After that, the results were associated with the term “sleep” (623 articles found), then this syntax was crossed with the term “stress” (101 articles found). The final items were screened and reviewed in combination with Google Scholar, allowing us to identify the full-text manuscripts. Google Scholar was also useful to identify the most relevant references for our subject. The inclusion criteria upon which the studies were selected were: (i) the inclusion of empirically collected data (ii), an assessment of SD in some form (iii), the inclusion of human participants aged from 18 to 90 years old in the sample (iv), articles published in peer-reviewed journals (v), full-text availability (vi), an assessment of SES and SC in some form (vii), an assessment of stress, cortisol, anxiety and depression (vii) and (viii) written in either English or French. Methodological papers, editorials, opinion articles, policy and commentary papers were excluded. Papers focusing on one disease only (obesity, heart failure, etc.) in association or in correlation with sleep disturbances without assessing SES, or articles reporting only sleep disturbances without association or correlation with socioeconomic or sociodemographic factors were excluded. Research reporting stress or sleep problems related to natural disasters and stressful life events such as death of a close relative or moving from a location to another were also excluded. Articles on SES reporting associations, correlations or influence of psychological and social stressors on sleep problems were retained. Following this rigorous literature compilation, 23 empirical studies met the inclusion criteria. After reading and analyzing full texts and extracting data, 19 articles were considered interesting for the topic and selected for review.

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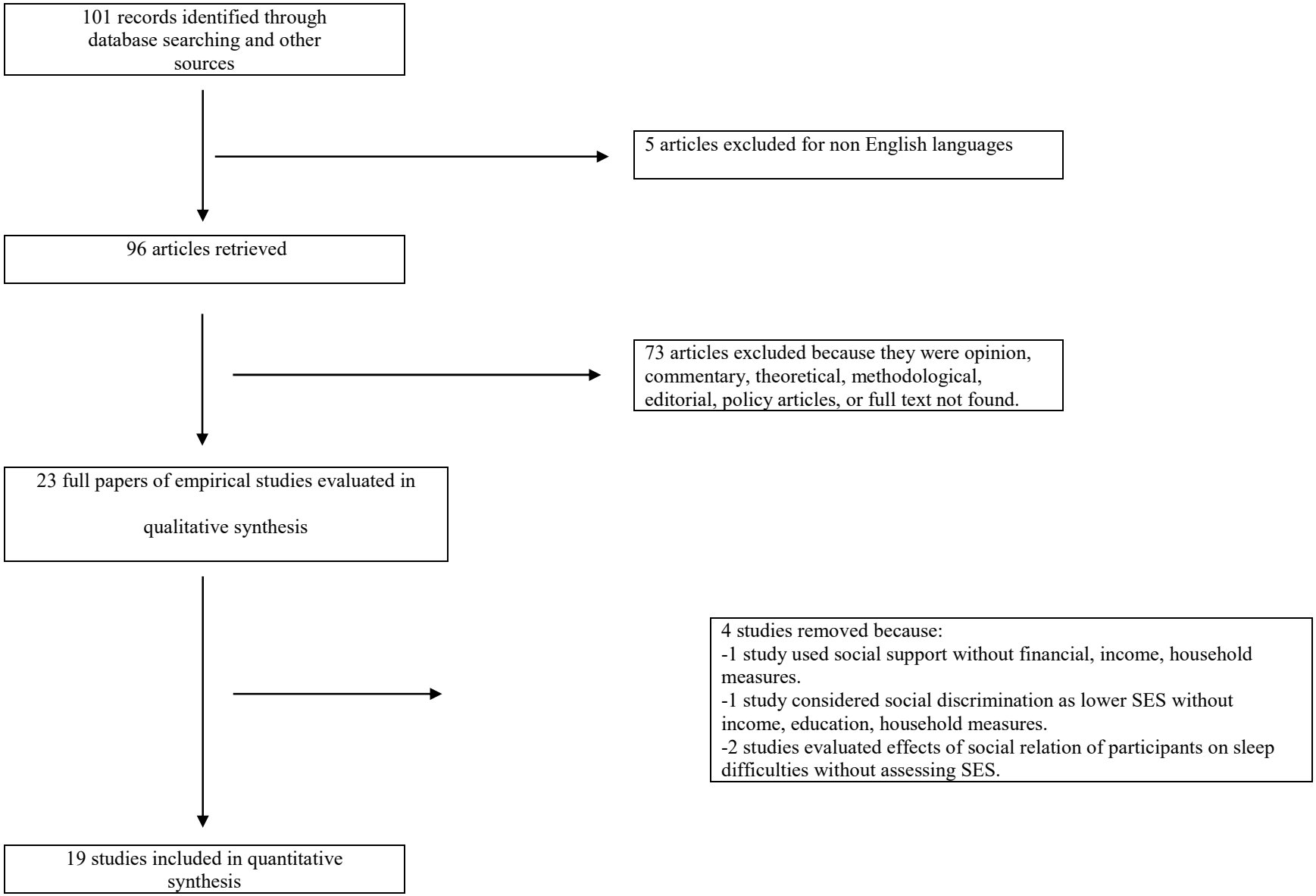

Fig 1: Flow chart for identifying eligible studies

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References	Aims	Population	Materials and Methods	Variables/Measures	Main Conclusions
Hoggard and Hill, 2016[27]	To examine the involvement of components of perseverative cognition in the association between ethnicity and subjective sleep quality.	68 self-identified African American college students (55.9% female; Mean age = 20.18, SD = 2.93) were recruited at a large predominantly white public university in the Midwest.	• recurrent patterns of reflexion were tested with the Ruminative Responses Scale. • socioeconomic and ethnic discrimination were measured with the Perceived Ethnic Discrimination Questionnaire • sleep was measured with the Pittsburgh Sleep Quality Index • socio-economic and pathological concerns were measured with the Penn State Worry Questionnaire	➢ negative thoughts ➢ SES ➢ racial discrimination ➢ quality and duration of sleep ➢ financial concern and pathological concern ➢ perseverative cognition	Ethnic discrimination and poor sleep quality are strongly associated with metabolic and cardiovascular diseases, as well as with mood disorders. Addressing those diseases in addition to coping strategies may reduce racial disparities in health.
Green et al, 2014[28]	This study investigated how the prospective patterning of distress over 20 years was associated with insomnia over that period.	999 respondents divided in three cohorts (born around 1932, 1952, and 1972) were followed for 20 years	• psychiatric distress was measured using the General Health Questionnaire at baseline and at 20-year follow-up. • gender and social class were assessed at baseline. • insomnia symptoms were assessed every five years.	➢ insomnia ➢ depression ➢ anxiety ➢ stress ➢ social class ➢ SES ➢ well being ➢ psychological health ➢ sleep habits	sex and socioeconomic disparities in psychiatric distress are strongly linked with disparities in insomnia symptoms.

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Okun et al, 2014[29]	To evaluate the effect of socioeconomic status on measures of sleep quality, continuity, and quantity in a large cohort of pregnant women.	One hundred and seventy pregnant women at 10-20 weeks gestation.	• sleep was assessed with the Pittsburgh Sleep Quality Index and actigraphy at 10-12, 14-16, and 18-20 weeks gestation. • SES was defined by self-reported annual household income. • mood disorders were assessed with the Inventory for Depressive Symptoms • perceived stress was measured with The Perceived Stress Scale	➢ sleep quality and sleep duration ➢ household income ➢ annual income ➢ marital status ➢ body mass index ➢ depression ➢ stress ➢ quality of life ➢ stressing events ➢ perceived stress ➢ race/ethnicity	Low SES was associated with poorer sleep quality and fragmented sleep. Perceived stress and financial support reduce the associations of SES with sleep.
Chen et al, 2013[30]	To assess the psychological and socioeconomic health status of community-dwelling older adults in Taiwan, and to compare the psychological and socioeconomic health inequalities among people of different age, gender, marital status, and exercise habits.	384 Taiwanese community-dwelling older adults aged 65 years old and more	• sleep measured with the Pittsburgh Sleep Quality Index • financial status • social support • emotional health measured with The Taiwanese Depression Questionnaire • the cognitive functioning measure with The Short Portable Mental Status Questionnaire • health promotion behaviors • social engagement	➢ sleep quality ➢ living expenses ➢ income ➢ level of satisfaction ➢ duration and frequency of physical activity ➢ cognition ➢ functional autonomy ➢ lifestyle ➢ social engagement	The major psychological and socio-economic health concerns were sleep disturbances and financial burden. Younger old adults had better psychological and sociological health.

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Karlamangla et al, 2013[31]	To identify disparities in the usual daytime cortisol rhythm by age, SES, and race/ethnicity	A final sample of 1693 participants (from 1409 families) recruited through MIDUS (Midlife in the United States Study) aged 25 to 74 years old.	• socio-demographic and socio-economic characteristics (age, race / ethnicity, gender, highest level of educational attainment, and annual household income) were self-reported with the MIDUS questionnaire • salivary collection kit to measure cortisol on waking, 30 min after waking, before lunch and before bed for seven days • average sleep time was assessed by way of the MIDUS questionnaire • physical and mental conditions were assessed by way of the MIDUS questionnaire	➢ SES (income, occupation, living area) ➢ the daily rate of cortisol ➢ quality and duration of sleep ➢ smoking ➢ depression ➢ anxiety ➢ body mass index ➢ age ➢ sex ➢ the ethnic group ➢ physical activity ➢ medications ➢ cardiovascular and metabolic diseases	Daytime cortisol levels are higher in older people and in men compared to women. Daytime cortisol rhythm is flatter in less privileged social classes, confirming that social stressors lead to poor health outcomes.
Stawski et al, 2013[32]	To assess the daily association between recurrent stressors and salivary cortisol levels.	1694 adults (mean age 57 years-old, range 33-84; 44% male)	• interviews by phone for eight successive days • The Daily Inventory of Stressful Events questionnaire assessed stressors • The negative mood scale used in	➢ elements causing stress in the living environment (work, family) ➢ daily cortisol levels ➢ negative daily effect of stressors	People with successive stressful days show a growing increase in cortisol levels and a decrease in the quality of their sleep.

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			MIDUS to measure the negative effects of stressors and the emotions associated with them. • a checklist of 25 physical symptoms to measure daily physical symptoms • salivary collection kit to measure cortisol on waking, 30 min after waking, before lunch and before bed for four days. • state of sleep	➢ physical symptoms ➢ emotions	
Tom and Berenson, 2013[33]	To investigate the associations between sleep quality and psychosocial stress with obesity in reproductive-age white, black, and Hispanic women of lower SES.	927 women aged 16-40 years	• Sleep was assessed with the Pittsburgh Sleep Quality Index • SES was measured by way of education, household income, profession • mood disorders were assessed with the Beck Depression Inventory • perceived stress was measured with The Perceived Stress Scale • lifestyle • health habits • obesity	➢ sleep quality ➢ sleep medications ➢ sleep latency ➢ sleep duration ➢ education ➢ income ➢ profession ➢ depression ➢ stress levels ➢ perceived stress ➢ body mass index ➢ weight ➢ alcohol consumption ➢ smoking status ➢ physical activity ➢ race/ethnicity	Even if they were common in reproductive-aged women of lower SES, poor sleep quality and psychosocial stressors were not linked with variation of weight.

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Green et al, 2012[34]	To describe longitudinal patterns of insomnia symptoms as people age and examines how they vary according to gender and profession.	One cohort approximately 36-57 years of age at baseline (n = 1,444), and another aging from 56-76 years (n = 1,551).	• sleep latency and the ability to stay asleep were measured with the Pittsburgh Sleep Quality Index • SES was measured with the household reference rank that takes into account the highest profession of the couple and material resources • three cohorts of different times of birth (1932, 1952 and 1972) were followed for 20 years with four interviews (1987/1988, 1990/1992, 1995/1997, 2000/2004, 2007/2008)	➢ quality of sleep ➢ SES ➢ sex ➢ age	Chronic symptoms expressed by difficulties in maintaining and initiating sleep are influenced by social factors.
Lo and Lee, 2012[35]	To explore sleep disorders among seniors by investigating the prevalence of poor sleep quality, the relationship between sleep quality and health-related quality of life, and associated factors of good sleepers in	Older community-dwelling individuals (n = 301) aged 60 years and more.	• a validated questionnaire collected socioeconomics and sociodemographic data • the state and quality of sleep are measured with the Pittsburgh Sleep Quality Index • Quality of life is measured with the	➢ sleep (quality, duration, number of awakenings, depth) ➢ demographic variables (age, gender, occupation, level of education, marital status, income, area and type of dwelling)	There is a strong negative association between poor quality and short-term sleep with a healthy quality of life, and it worsens with aging.

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	different age groups.		Medical Outcomes Study 36-item Short Form Health Survey.	➢ state of health related to quality of life	
Gureje et al, 2011[36]	To determine the incidence and risk factors for insomnia in a population of older people in sub-Saharan Africa.	A cohort of community-dwelling 1307 seniors, aged 65 years old and over, followed for 1 year	• insomnia and depression were measured with version 3 of the Composite International Diagnostic Interview • Dementia was measured with the 10-Word Delayed Recall Test, which is a memory test • Functional capacity was measured with the Clinician Home-based Interview, which is a 10-item questionnaire measuring the cognitive function of the senior and his knowledge of daily basic tasks to be performed. • the stressful events of the last 12 months that require social support and / or caregivers, were measured with the List of Threatening Experiences • SES was measured by evaluating the neighborhood /	➢ Insomnia ➢ SES ➢ autonomy and lifestyle ➢ anxious and depressive syndromes ➢ dementia ➢ the stressful events of the last 12 months ➢ the temporal evolution of the association between stressful events and symptoms of insomnia ➢ the general physical state (body mass index, cardiovascular diseases) ➢ comorbidities	Incidence and chronicity of insomnia are higher in older people. Individuals with chronic health conditions have higher risk of persistent insomnia.

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			type of house and its contents		
Hawkley et al, 2011[37]	To investigate implications of SES over physiological dysregulation.	A population-based study of 229 older adults (age range 51-69 years old)	• Allostatic Load was computed from 9 markers encompassing cardiovascular system functioning, sympathetic nervous and adrenomedullary system functioning • central obesity (waist circumference) • hypothalamic-pituitary-adrenal axis functioning (cortisol) • risk factors for development of atherosclerosis (high density lipoprotein and total cholesterol), and glucose metabolism (glycated hemoglobin) • chronic health conditions measured with validated questionnaires • psychosocial and personality variables • sleep • lifestyle	➢ sleep (quality and duration) ➢ allostatic load ➢ stress ➢ social network ➢ health behaviors ➢ coping style ➢ well-being ➢ depression ➢ emotional stability ➢ spirituality ➢ education ➢ household ➢ income ➢ neighborhood ➢ ethnicity ➢ social support ➢ alcoholism ➢ smoking ➢ nutritional habits	The effects of SES are specific to certain systems in a middle to early old-age population, creating and worsening the association between allostatic load and sleep disturbances.

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			• SES		
Goodin et al, 2010[38]	To investigate the relation between perceived social status and subjective sleep quality.	149 college students	• sociodemographic data collected with homemade questionnaire • Sleep • SES • ethnicity • health conditions	➢ sleep quality ➢ social class ➢ race ➢ quality of life ➢ perceived SES	A low perceived social status has a negative influence on sleep quality for African and Asian Americans.
Kumari et al, 2010[39]	To investigate if dysregulation of the hypothalamic-pituitary-adrenal axis associated with disadvantaged social position in working populations also occurs in retired old people.	3992 participants (mean age 61 years; range 50–74 years) from the Whitehall II Study	• salivary rate of cortisol measured six times per day (at waking, 30 minutes, 2.5 hours, 8 hours, 12 hours, and bedtime) with a commercial immunoassay with chemiluminescence detection • social position assessed by way of the MacArthur subjective social position scale • health behaviors • sleep habits • mood disorders assessed by way of The Center for Epidemiologic Studies Depression Scale • body mass index • stress	➢ cortisol ➢ awakening response ➢ sleep behaviors (waking up time, insomnia, sleep duration) ➢ smoking status ➢ diet/nutrition ➢ age ➢ sex ➢ SES (social position, education, income) ➢ depression ➢ blood pressure ➢ height ➢ weight ➢ daily level of stress	In men, poorer health, sleep behaviors and unstable income mediate the effect of occupational status and wealth on cortisol secretion
Phelan et al, 2010[40]	To review how social conditions and their determinants affect global	Population-based study.	• Narrative review of literature	➢ health status ➢ social class ➢ SES ➢ health policies	Without more programs of social management of resources or

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	health in the life course.			➢ consequences of social inequalities ➢ theory on correlations between social conditions and trajectory of health	evaluation of the development of socioeconomic disparities among sick people, many health issues will occur and be costly to citizens.
Tomfohr et al, 2010[41]	To measure the association between SES in childhood and adult sleep, to analyze adult sleep according to race, and whether associations between SES, race and sleep are influenced by factors such as health practices and current social status.	128 Black and White Adults	• sociodemographic data were collected during interviews • polysomnography in two successive nights from 9 pm to 6 am • SES of childhood was classified according to the levels of education of the parents (High SES with a post-high school diploma and Low SES without post-high school diploma) • SES of the adult was measured with the Hollingshead 2-Factor Index of Social Position (it measures the highest level of education + the profession) • the global SES (position in terms of money + diploma + job	➢ SES ➢ the low SES and the high SES ➢ clinical parameters of sleep ((slow-wave) ➢ the quality of sleep ➢ daytime sleepiness ➢ physical activity ➢ the social class ➢ the habits of life ➢ socio-demographic data (age, sex, years of education, skin color, income, occupation, body mass index)	Participants with lower childhood SES spent more time in Stage 2 sleep and less time in slow-wave sleep than those with higher childhood SES. Women from low childhood SES had more difficulties to fall asleep compared with women with high SES. Black participants spent less time in slow-wave sleep than White. An interaction Age X Race was identified in the prediction of subjective sleep quality.

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			respected in the USA) was measured with the MacArthur Scale • quality of sleep was measured by way of the Pittsburgh Sleep Quality Index • daytime sleepiness was measured by way of the Epworth Sleepiness Scale • health practices (alcoholism, smoking) were self-reported and physical activity was measured by way of the Leisure Time Exercise Questionnaire		
Friedman et al, 2007[42]	To test the hypothesis that SES would be associated with objectively measured sleep quality, even after controlling for related covariates (health status, psychosocial features).	94 women, 61 to 90 years of age	• SES is determined with pre-tax household income • sleep quality is measured with the Night Cap Sleep System + Pittsburgh Sleep Quality Index • the state of health is estimated with the objective measures of medical records • depression is measured with the Center for	➢ SES ➢ health ➢ quality of sleep ➢ depressive syndromes ➢ neuroticism ➢ lifestyle habits (smoking, alcoholism, caffeine)	There are behavioral and biological implications of social ladder and sleep quality in health processes, and a negative association exists among sleep disorders, low SES and chronic morbidities.

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			Epidemiology Disease Scale • Neuroticism is measured with a subscale of the NEO personality inventory		
Adler et al, 2000[43]	Associations between objective and subjective SES were compared with psychological and physical variables.	157 healthy white women	• social status measured by the subjective SES scale. • sleep measured with the Pittsburgh Sleep Quality Index • biological measures were performed in a laboratory • psychological variables were measured with the Perceived Stress Scale + the Negative Affect subscale of the Positive and Negative Affectivity Scale + the Life Orientation Test + the Coping Orientation to Problems Experienced	➢ subjective and objective SES ➢ self-rated health ➢ body mass index ➢ body fat distribution ➢ sleep ➢ resting physiological responses ➢ salivary cortisol ➢ negative affectivity ➢ pessimism ➢ coping style ➢ subjective stress	Psychological perceptions of lower social status contribute to the SES-health gradient and have significant relationships with stress, sleep disorders and metabolic diseases.
Bromberger and Matthews, 1999[44]	The authors focused on the first piece of the stress–sleep–health	a local cohort of 462 women from the multisite Study of Women's	• data were collected from SWAN study • SES was analyzed • sleep components were analyzed	➢ income ➢ education ➢ health conditions	poverty is associated with subjective sleep complaints in middle-aged

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	relationship, that is, the impact of the chronic stress of lower SES on subjective sleep complaints	Health Across the Nation (SWAN). Age range was 41-52 years, 35% were African-American and the remainder were Caucasian	• level of stress was computed • ethnicity	➢ sleep difficulties (insomnia, difficulty falling asleep) ➢ chronic stress ➢ ethnicity ➢ SES	women, irrespective of age, race and education. Chronic stress associated with lower SES mediate the association of poverty with poor sleep.
Van Cauter and Spiegel, 1999[45]	This article discusses the hypothesis that the adverse impact of low SES on health may be partly mediated by decrements in sleep duration and quality.	Young and healthy adults	• Division into two groups: strong SES and weak SES • Blood test of cortisol, glucose, insulin, markers of orthosympathetic and parasympathetic electrical activity • Sleep was measured with a mixed method of night-time sleep system + EEG + monitoring of brain waves + the Pittsburgh Sleep Quality Index + the Karolinska somnolence scale	➢ carbohydrates ➢ metabolism ➢ endocrine function ➢ sympatho-vagal balance ➢ cortisol ➢ glucose ➢ insulin ➢ inhibitory / excitatory electrical activity	Chronic sleep debt caused by low SES is partially associated with metabolic diseases that increase comorbidity.

Table 1: Details of studies included in the results

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RESULTS

Relation between allostatic load and sleep

Experiences from our environment stimulate our perception and our training capabilities. These training capabilities are improved by quality and length of our sleep [46,47]. Recent results showed that repetitive stimuli trigger cortical neurons and their mechanisms of synaptic plasticity, mediating training and consolidation during sleep [12,13]. SD such as insomnia, narcolepsy and sleepwalking are frequently associated with cognitive impairment, both in healthy people and in those with neurological disorders such as parkinsonian syndromes or MD [48,49]. Such SD may result from MD or neurodegenerative diseases at an early stage, and may be the initial manifestations of neuropsychiatric syndromes [17,18,50]. Insomnia (e.g. frequent and early alarm clocks, difficulty sustaining sleep) and excessive diurnal somnolence (e.g. attacks of sleep, frequent drowsiness lasting the day) are important examples of disordered brain function and may have several different causes like some forms of parkinsonism, medications and psychiatric disorders [6,51].

Stress is an important feature associated with SD. Environmental stress results from exposure to multiple environmental stressors (e.g. housing, income, social relationships) and varies according to SES, and needs to be distinguished from psychological stress in the development of MD such as anxiety and depression [15,52-54]. In older people, the level of exposure to environmental stressors influences psychological stress. Thus, development of SD may be affected by several external factors (environmental and socioeconomic) and biological factors (hormones, circadian cycle, practices of life, medical history, medication) [6,15,51-54].

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Current literature describes the rise of psychological, environmental and socioeconomic factors in several populations [55,56]. The combined interaction of socioeconomic and psychobiological factors over SD has not been studied in depth. As much as the prevalence of SD is higher in the population over 50 years-old, these issues have not been addressed in much depth in younger adults. Current epidemiological data also show higher incidence of neurological diseases and mental illness for elders, compared to adults under 40 years-old [54,57]. It is important to understand the simultaneous effects of environmental stimuli and psychological profiles on the evolution of SD according to different age ranges, because stressors are the same and probably start to affect people at an early age. The allostatic load is a manifestation of this long exposure to stress, and people in the same community are affected differently even with the same stressors [58-60].

Relation between socioeconomic status, sleep and mood disorders

As is the case with any biological feature, health status is highly variable for any person in a given population. Certain individuals die at a very early age; others have chronic diseases, and many live up until a very advanced age. Health differences may be analyzed according to geographic region, race, age ranges, and according to SES [60,61]. These factors reveal systematic trends in the distribution of health so that, from birth, each person is not as likely as the other to live in good health for a long time. The SES indicates the position that a person holds in the community. One cannot measure this status directly, but there are some indirect indicators, for example, income, education, occupation, household or the social class (SC) [60,61]. Whatever the indicator used, there is a universal tendency for people from lower socioeconomic groups to die younger and to get sick more often during their lives. The concept of "socioeconomic groups" is identical to the term "socioeconomic category". A socioeconomic category is generally defined as a class in which members of a community or a population have similar features in common, such as professional indicators, age, sex, social position, income, education, environmental stress and psychological stressors [61].

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Social position and economic disparity are strong predictors of health inequalities. Exposure to low income, low levels of education and precarious employment status may impair indicators of health in a population by way of several indirect mechanisms that limit access to better lifestyles and proper healthcare [23,60,62].

Predisposing risk factors are recurring elements that increase the odds of development of a disease, usually present in the environment or being part of the lifestyle [61,63]. Such risk factors may be environmental, [63] biological and psychosocial [62,64,65]. Among biopsychosocial risk factors we have metabolic heredity, tobacco addiction, sedentarism, and diseases such as diabetes *mellitus*, obesity, arterial hypertension, hypercholesterolemia, and stress [1,20,66]. Arterial hypertension is the most important risk factor for stroke, whereas environmental and psychological stress are major psychosocial risk factors for MD (depression and anxiety) and SD such as insomnia. When several risk factors are present, the risk may result from the product of them rather than the sum.

Certain risk factors (genetic or environmental) or unforeseen events in our daily lives often escape our control. There is a pressing need for more research on prevention, pharmacological therapy and rehabilitation of patients with SD. SD are usually progressive and strongly correlated with living conditions [53]. SES is considered in the diagnosis and in the response to therapy of SD by way of psychological stress, which is a mediator of environmental stress [67,68].

In older people, the level of exposure to the environmental stressors exerts an influence on psychological stress [54,69]. There is a strong relation between environmental stress and SD, but also between environmental stress and MD such as depression and anxiety [2,25]. A similar relation would also exist between stress and cognition, more importantly for young adults. Young adults are more prone to psychological stressors, therefore prone to MD and cognitive disorders, incidentally more frequent in people under 40 years [20,70]. MD usually impair academic performance, social and professional relationships.

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Psychological stress, moderated by MD, would be a mediator of the effect of environmental stress over SD, which can become chronic [25,26,59,71-73]. Physical and emotional balance are required for proper functionality. Manifestations of stress are associated with the appearance or aggravation of MD and SD [74,75]. Psychological stress induced by some professional (for example night shift work, building jobs, customer relations) or academic environments (for example graduated studies, medical school) results in a combination of risk factors which worsen cognitive impairments and SD [18,50,76]. The risk of cognitive impairment is more important for people who have difficulty to fall asleep. People with cognitive disorders often have reduced length of sleep, but also difficulty falling asleep, cardiovascular and respiratory dysfunction, and neurological impairment including memory dysfunction [17]. Cognitive disorders may also worsen when neuropsychiatric conditions are present (anxiety, depression, general discomfort) and result in light sleep disturbances [9,10]. Overall, cognitive decline is accelerated when there is a disturbance of the quality and the duration of sleep. MD probably play a central role in the cognition of young adults who, however, do not have as many comorbidities or diagnoses of neurodegenerative diseases as older people; and reduced psychological stress will, hypothetically, lead to decreased incidence or aggravation of cognitive disorders [1,17,18]. Improved living conditions (including professional environments, psychosocial and financial support) would reduce the devastating effects of stress on cognition. In this context, SD would be indicators of cognitive decline well before the diagnoses of depression and anxiety [77,78]. In the current state of knowledge and scientific findings, the most recurrent psychological and social stressors related to sleep disturbances are the following: ethnicity, well-being, households, obesity, social ties and support, discrimination, education, low-SC or low-incomes and multiple comorbidities [1,15,16,20,40,55,63,67,79]. Overall, the risk of SD increases when an individual has a lower SES, one or multiple comorbidities (like obesity and mood disorders), and is exposed to permanent stressors (i.e. discrimination, lack of social support, low income) in his environment leading to allostatic load. In the same logic, an individual living in relatively good conditions (i.e. healthy habits, no chronic diseases) with a satisfactory income (middle

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and higher SES) and very little stress in his environment has a small risk of SD in his lifetime (except when induced by physiological dysfunctions). Figure 2 summarizes these interactions, with their influences one by one or in association with sleep.

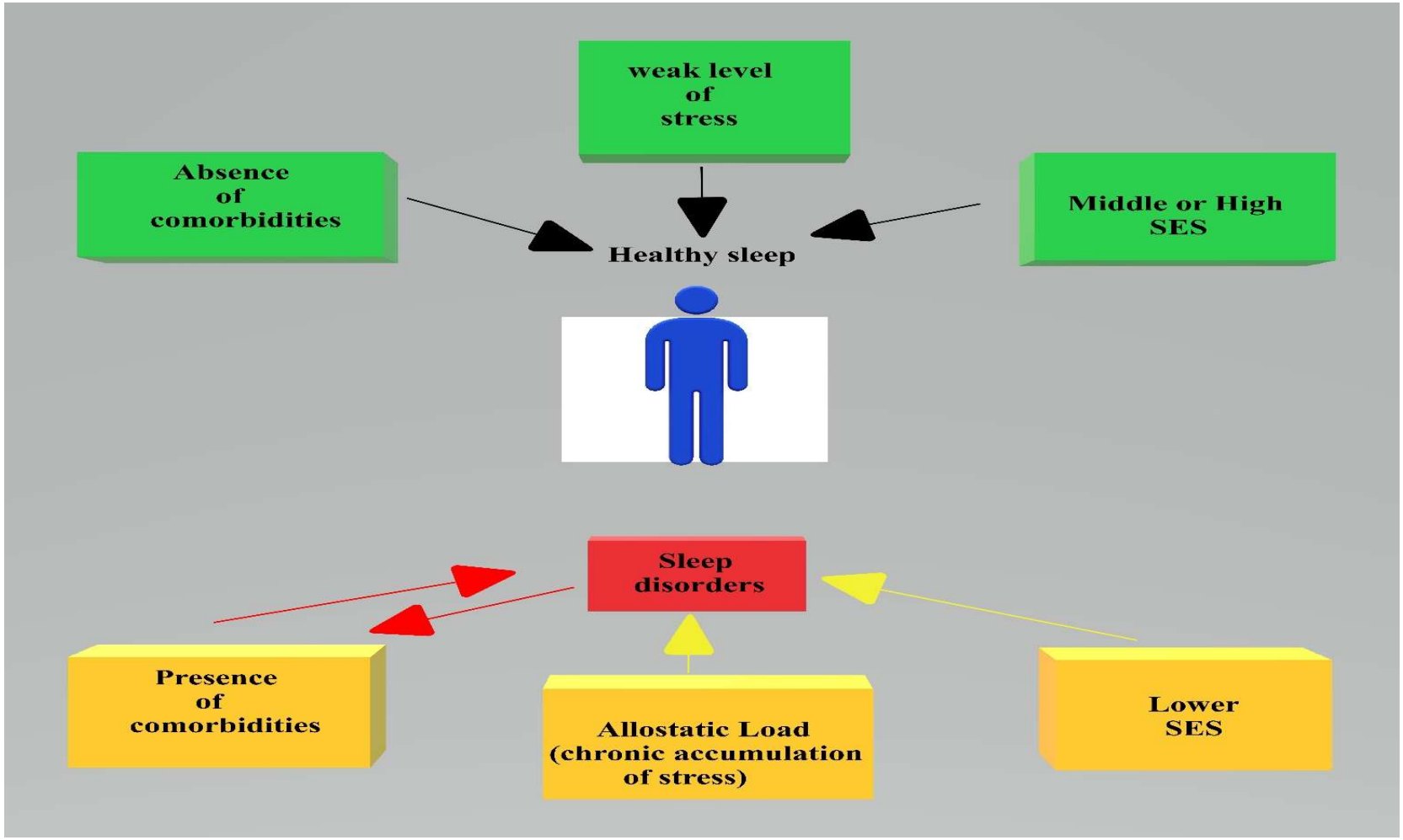

Fig. 2: Theoretical relation between comorbidities, Socioeconomic status (SES) and stress.

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Relation between socioeconomic status and circadian rhythms

CRs are 24h cycles in physiology and behaviour that are driven by an internal molecular clock. The molecular mechanism underlying this rhythm is the cell autonomous transcription-translation feedback loop (TTFL). In mammals, the transcription factors CLOCK and BMAL1 drive the expression of *Period (Per1/2)* and *Cryptochrome (Cry1/2)*, whose protein products repress the function of CLOCK and BMAL1 [80]. CLOCK and BMAL1 bind to DNA elements known as E-boxes that lie within the promoters of about 1/3 of the genome, which as result, can oscillate with a 24h rhythm to regulate tissue-specific metabolic and physiological functions. This molecular clock exists within most cells of the body, which are maintained in synchrony by a master pacemaker, the SCN, residing within the hypothalamus. The SCN receives direct input on the environmental light dark cycle from the retino-hypothalamic tract, thus ensuring that internal time is coordinated with the external world [81]. The SCN then synchronises peripheral circadian clocks throughout the body through multiple signals, with the hypothalamic pituitary adrenal axis, through the hormone cortisol, providing one of the most powerful synchronising signals. As the circadian clock regulates on average about 15% of the transcriptome of any tissue [82-84], it has a profound effect on the function of that tissue, resulting in appropriately timed physiology. It is therefore no surprise that sleep and CR disruption, that occurs for example as a consequence of stressors such as shift-work or jet-lag, can contribute to the development of a range of disorders. Much of our evidence comes from the study of night shift workers and offshore workers, where CRs of cortisol can be dampened and shifted [85,86], and resulting in comorbidity with insomnia, anxiety and depression [87], and impacting normal metabolism, incidence of cancer and mental health disorders [88,89].

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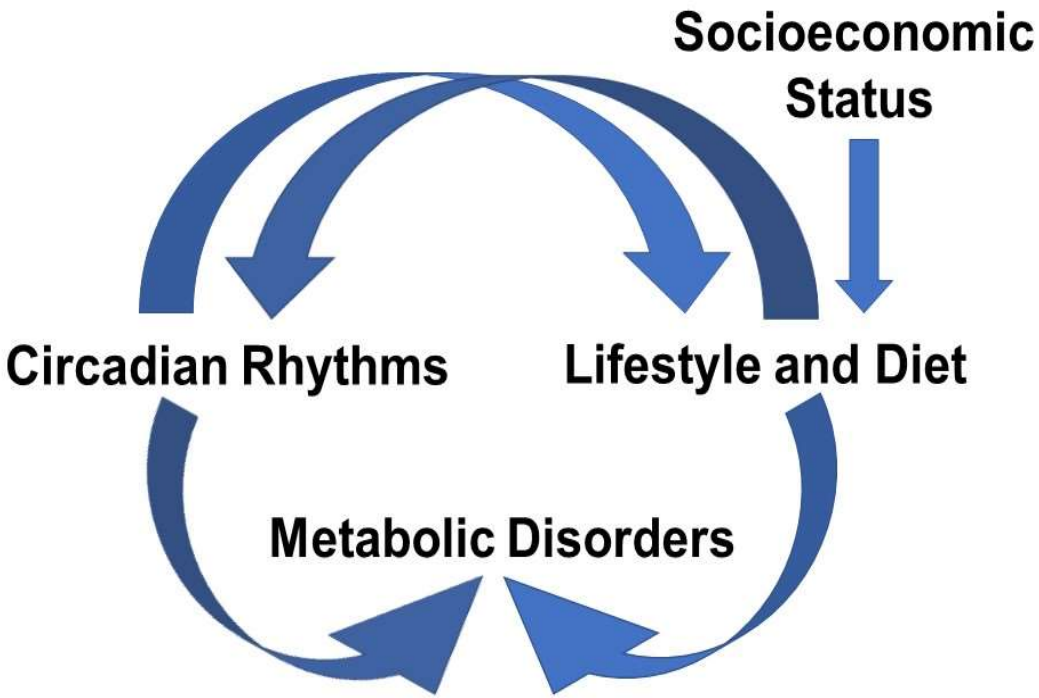

Fig. 3: Theoretical relation between circadian rhythms, socioeconomic status, lifestyle and metabolic disorders.

FUTURE DIRECTIONS AND CONCLUSIONS

SD have been under intense study in the last two decades and remain a subject of interest at the borders of several disciplines such as psychology, neurology and psychiatry. Incidence and prevalence of SD are increasing, while their determinants as well as their

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associated psychopathological mechanisms are not well understood. More than the other external factors, the interaction between the SES and sleep must be understood better. Living conditions strongly influence the trajectory of SD by inducing allostatic load which affects differently adolescents, adults and older people, in an unknown speed and for a non-determined period. The combined effects of environmental and psychological stressors seem noxious for mood disorders and sleep. Future work should identify the combined effect of psychological factors, stress and lifestyle on the development and progression of SD, such that behavioural and pharmacological interventions, including those promoting a healthy lifestyle, can be implemented to reduce the incidence of SD and develop novel therapies. This would be effective when a full definition of SES is known, allowing researchers of different fields to understand each other and apply mixed methodologies to assess collected data, which can be used by everyone.

Practice Points

- Socioeconomic status affects the development of sleep disorders in low-income populations, independently of gender, age, education and country.
- Socioeconomic status can induce allostatic load through daily stressors, sleep disorders and MD.
- Sleep disorders can be a consequence of MD but may also be indicators of high levels of stress.
- Circadian rhythms and circadian cycle are affected by socioeconomic status and their influences vary from one individual to another inside the same community.
- Socioeconomic status and circadian disruption are associated with metabolic diseases such as diabetes and cancer.
- Socioeconomic status has almost no effect on SD in the normal aging population but increase SD symptoms of older people suffering from neurodegenerative diseases.
- The most widely correlated measures of socioeconomic status related to sleep disorders are social class, discrimination, ethnicity, low-income, occupation, education, obesity, neurodevelopmental and motor disabilities and households.
- The most well-studied sleep disorders in association with socioeconomic status are insomnia, sleepiness, circadian rhythms sleep disorders, obstructive sleep apnea and sleep disorders induced by some substance (caffeine, opioid, nicotine, etc..)

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Research Agenda

It will be worthy for future generations of researchers to think about the following points:

- A clear and conventional definition of socioeconomic status should be developed to allow cross-comparisons between different studies.
- A novel mixed methodology to assess level of stress without cortisol.
- Development of fundamental theories and biomedical applications of an index of measure of sleep disorders related to socioeconomic status.
- Wide investigations of prevalence and incidence of other sleep disorders in low- and middle-income countries and their populations should be performed in the future.
- Associations between circadian rhythm and metabolic syndromes should be deeply explored.
- Development of mixed-programs to increase socioeconomic status and sleep disorders should be considered by leaders, as tools to prevent public health crises.

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