

# Sleep, Health, and Society

FROM AETIOLOGY TO PUBLIC HEALTH

Edited by

Francesco P. Cappuccio, Michelle A. Miller, and Steven W. Lockley



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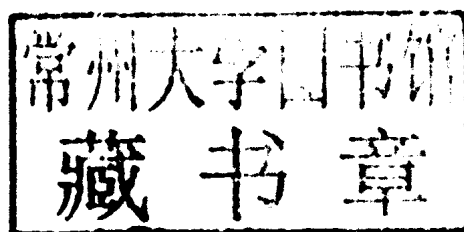
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## **Sleep, Health, and Society**

# Foreword

*Macbeth does murder sleep, the innocent sleep,  
Sleep that knits up the ravell'd sleeve of care,  
The death of each day's life, sore labour's bath,  
Balm of hurt minds, great nature's second course,  
Chief nourisher in life's feast.*

W. Shakespeare, *Macbeth*, Act 2 Scene 2

Is sleep a cause, a consequence, or a symptom? Shakespeare says it rather well: all three. Lack of sleep is a **cause** of distress and ill health. If we miss sleep we miss the balm of hurt minds, the chief nourisher in life's feast. Second, Macbeth's actions and his distress murder sleep. Sleep disturbance is a **consequence** of the circumstances of people's lives. Macbeth thinks he will sleep no more because he has just murdered King Duncan. More prosaically, shift work, overtime, and poor living conditions can all affect sleep with the likely ill-effects that causes. Third, Lady Macbeth's heart is sorely charged and her sleep is disturbed. Sleep disturbance is a **symptom** of depression and perhaps other illness.

These three – cause, consequence, and symptom – can all interact. Too much sleep, too little, or poor quality sleep can be the result of other problems but can, in their turn, cause other problems. Although the possibility of interaction must be always considered, it is important to sort out which of the three is operating, as interventions might be quite different. Sleep research has mostly been the subject of specialized small scale studies. This volume builds on and brings together epidemiological studies of sleep. It is greatly to be welcomed. Shakespeare knew sleep to be important and we know sleep to be important, but with what consequences and what we can do about it, has been unclear.

The first issue, of course, is the difficulty of measurement. It is said that for anyone who has had a baby or been a junior doctor on call, or both, the concept of a “normal” night's sleep is forever changed. Epidemiological studies described here rely for the most part on self-report. People are inaccurate enough in reporting what they do when they are awake, let alone when consciousness is doubtful or absent. That said, measurement error is a challenge to be overcome not a counsel of despair. People can report how long they slept and if they have disturbed nights. The results are extraordinarily interesting. Short sleep, overly long sleep, and sleep disturbance all seem to play a role in disease.

Second, it is not at all surprising that sleep should be intimately bound up with hormonal and metabolic changes and that these will have effects on health and disease. The surprise is that we should not have given sleep, this fundamental part of life, all the attention it deserves. The link between short sleep and obesity via an effect of short duration on leptin and ghrelin and hence on appetite regulation is an elegant example. As the book makes clear we now need much more work to explore both the nature of the link between aspects of sleep and chronic disease and the mechanisms by which they occur.

This leads to the third big issue. If, as seems likely, the evidence firms up that sleep quality and duration are important, what is to be done? As an example, we know that shift work and

overtime work with their impact on sleep, have deleterious health effects. There will be other features of the circumstances in which people live and work with impacts on sleep. How should they be addressed?

One in particular relates to children. As this book makes clear sleep in childhood is likely to be important. Yet data from Britain show that the likelihood of a regular bed time for children diminishes the lower the socioeconomic position of their parents. This was highlighted by the Review we conducted of Health Inequalities in England. We emphasized the likely consequences on child development and hence on health inequalities in adult life.

The big achievement of this volume is to bring together research on the health consequences of sleep and put sleep on the agenda for research in epidemiology and public health. It is timely indeed.

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# Foreword

There are currently 6.85 billion people on Earth, and every one of them is subject to the biological imperative of daily sleep. Our genetic code instantiates this imperative in a circadian rhythm of sleep and waking, which reflects evolutionary adaptation that extends back to the oldest complex animals. Modern societies often question the need to sleep each day, and many social factors (e.g., television viewing, commute time to/from work) result in reduction of time for sleep in exchange for time spent in work, leisure, and other more socially and economically valued pursuits. However, this modern view of sleep as a low-value, nonessential activity is increasingly contradicted by a steady flow of scientific evidence on the physiological and neurobehavioural effects of sleep deprivation, suggesting that sleep serves critical biological needs. However, experimental evidence such as this has not stemmed the tide of political, social, and economic pressure to have more people awake for more amount of time, especially in nonstop industrialized societies with their heavy reliance on electronic technologies and machine automation.

What has begun to give pause to the view that sleep is merely an archaic arbitrary activity that has no meaningful relation to health and lifespan is the recent explosion of population science on sleep health, sleep duration, and sleep timing, relative to obesity, disease, and mortality. While epidemiological studies of self-reported sleep time and health status began to appear more than 40 years ago, many of the hundreds of published population studies on sleep in relation to public health have appeared in the past 15 years, and have come from all over the globe, as population science and sleep science have matured in parallel in academic institutions, and as obesity has increased around the world, as time has become more valuable, and as stress and psychological uncertainty have become normative for many humans. Collectively, these post-Cold War global changes have caused concern that public health may require attention to factors other than the traditional focus on sanitation and clean water, vaccinations, management of toxins, etc. As a result of widespread evidence that sleep duration in particular has an association with obesity, serious common diseases, and mortality, sleep and sleep disorders have become visible as possible significant contributors to the health of both children and adults.

What has been missing in the scientific and policy debates about whether adequate sleep is important for public health is a thoughtful integration of the rapidly expanding epidemiological literature on sleep. Fortunately, this marvelously comprehensive book, *Sleep, Health, and Society: From Aetiology to Public Health*, edited by Cappuccio, Miller, and Lockley, is a much-needed integration of the burgeoning data on sleep need and public health. It is the first systematic review of this literature by content experts in their fields, and it provides an overdue and essential critical evaluation of the strengths and weaknesses of the data, the conclusions that can be drawn from the available evidence, the limitations of arguments used pro and con relative to sleep need in relation to obesity, health, accidents, and mortality, and the need for specific types of studies going forward.

The extensive evidence reviewed in the well-written chapters of this text reveals that sleeping 7–8 hours per night may be optimal for health for a great many people, but the authors conclude that, in many cases, this general statement cannot be asserted as factual causality until prospective studies, mechanistic studies, and intervention studies confirm it. On the other hand, public health policy does not always have to wait for conclusive evidence of causality, especially if an epidemic is moving rapidly and in vulnerable populations, as is the case with obesity in children. There is

ample evidence that reduced sleep duration and obesity are associated in children. As reviewed by Gozal and Spruyt in Chapter 10, chronic inadequate sleep may contribute not only to obesity in children but also to neurobehavioural problems, which appear to be increasing in frequency. Whether there is a direct or indirect causal relationship between sleep duration and obesity in children, it would seem unwise to avoid doing the needed prospective interventional studies with objective measures of sleep and obesity.

It is well established that inadequate sleep – whether voluntary or from disorders that disrupt sleep continuity or duration – often leads to significant risk of accidents relative to driving and other safety-sensitive activities. As a result, public policies continue to evolve in many countries regarding treatment of sleep disorders, fatigue management in the work place, and improved schedules for those who work nights, rotating shifts, and prolonged and irregular duty periods. The public health and policy response to inadequate sleep and increased risk to safety is by no means sufficient, however, as the last seven chapters of this text reveal. Nevertheless, these policy responses are further along than the as-yet-nonexistent public policies regarding the need for healthy adequate sleep duration. This text highlights the importance of public health research mobilized around objective measures of sleep and health, using study designs superior to extensive cross-sectional research conducted to date.

Surprisingly, it is often argued that large-scale population-based intervention trials to evaluate the benefits of extending sleep time are too costly or infeasible. This perspective is somewhat needlessly pessimistic and reminds one of reasoning used to avoid studying women and myocardial infarcts, minorities in health-related outcome studies, and interventions for weight loss. Yet, in all of these cases, when public health research was properly conducted, the resulting science provided definitive answers regarding actual risks and benefits. Why should assessing the benefits of improving sleep quality or extending sleep time be any different than evaluating diets, or exercise, or other interventions? As many of the authors argue in chapters throughout the book, we must push the science beyond reliance on self-report measures of sleep and cross-sectional designs. Even if prospective intervention studies demonstrate that cost-benefits argue in favour of allowing sleep to be curtailed (likely) for economic reasons, public health understanding of the scope of the problems posed by sleep loss for the most vulnerable populations will be enriched, and public awareness may affect behavioural changes.

*Sleep, Health, and Society* presents a comprehensive and critical look at the remarkable accumulation of data on the association between sleep and public health risks. It points out the most promising paths to follow scientifically to determine why these associations continue to be found globally. What is needed now is the public policy will and resources to resolve these important and promising opportunities for improving public health by understanding how alterations in sleep quality and quantity affect weight gain, cardiovascular and respiratory health, metabolism, neurological status, and mortality. The text offers the first comprehensive public health focus on what we know about sleep and its potential criticality for healthy populations. It points to the path that enlightened societies should take relative to one of nature's oldest and most important biological imperatives.

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# Acknowledgements

We are delighted to see the publication of this book which represents one of the first comprehensive textbooks of Sleep Epidemiology. The seeds were laid in late 2005 with the establishment of the *Sleep, Health, & Society Programme* at the University of Warwick in close collaboration with the Division of Sleep Medicine at Brigham and Women's Hospital and Harvard Medical School. The ambition was to close important gaps in medical teaching and research in the area of sleep medicine and to expand our knowledge of the population implications of sleep disturbances and sleep disorders. It is extraordinary to reflect on the speed with which this discipline has developed and gained momentum in just a few years. It goes without saying that this book would not have been possible without the scholarly and highly professional contributions of many authors who gave time, expertise, and enthusiasm to the project. Our gratitude and appreciation go to them primarily.

Such an achievement, however, would not have been reached without the aid of many others. The *Sleep, Health, & Society Programme* has been supported by a multidisciplinary team of researchers and we wish to thank, in particular, Anne Bakewell, Lanfranco D'Elia, Richard Donahue, Joan Dorn, Mair Edmunds, Chen Ji, N-B Kandala, Pasquale Strazzullo, Jason Sullivan, Frances Taggart, Maurizio Trevisan, and Geraldine Ward for their fundamental role in the development of the *Sleep, Health, & Society* research programme.

First and foremost, our particular thanks go to Yvonne Carter, founding Dean of Warwick Medical School, who provided encouragement and support to us: sadly she is no longer with us to enjoy this book. We also thank Ed Peile, who had the foresight to develop the first formal medical school training course in Sleep Medicine nationwide in 2004. Over 60 medical students have now completed the Special Study Module in Sleep Medicine, initiating a new generation of physicians to the importance of getting good sleep for keeping good health. We are grateful for their positive feedback and the participation that makes our teaching module a continuing success. Each year we have had students who have developed a keener interest in research aspects of the discipline. In particular, we wish to thank Daniel Cooper, Andrew Currie, and Alex Lowe who have participated more actively in several research projects in their own time with commendable commitment and professionalism.

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# Abbreviations

%SEI	Sleep efficiency index in %	COR	Chain of responsibility
95% CI	95% confidence interval	Cox-2	Cyclooxygenase-2
A	Actigraphy	CPAP	Continuous positive airways pressure
AASM	American Academy of Sleep Medicine	CPSI	American Cancer Society's Cancer Prevention Study I (baseline 1959–60)
ABMS	American Board of Medical Specialties	CPSII	American Cancer Society's Cancer Prevention Study II (baseline 1982)
ACGME	Accreditation Council for Graduate Medical Education	CR	Constant routine
ACQ	Asthma Control Questionnaire	CRH	Corticotropin-releasing hormone
ACTH	Adrenocorticotrophic hormone	CRSD	Circadian rhythm sleep disorders
AD	Alzheimer's disease	CRY	Cryptochrome
ADHD	Attention-deficit hyperactivity disorder	CSA	Central sleep apnoea
AEE	Activity-related energy expenditure	CSF	Cerebrospinal fluid
AF	Atrial fibrillation	CSHQ	Children's Sleep Habits Questionnaire
AHI	Apnoea-hypopnoea index	CVD	Cardiovascular disease
AIDS	Auto immuno-deficiency syndrome	DI	Disposition index
AIRG	Acute insulin response to glucose	DIMS	Difficulties of initiating and maintaining sleep
AMI	Acute myocardial infarction	DLB	Dementia with Lewy bodies
aMT6s	6-Sulphatoxymelatonin	DSM	Diagnostic and statistical manual of mental disorders
ApoE4	Apolipoprotein E4	DSPD	Delayed sleep phase disorder
AQOL	Asthma quality of life	DSPS	Delayed sleep phase syndrome
ASDA	American Sleep Disorders Association	ED	Excessive sleepiness
ASPS	Advanced sleep phase syndrome	EDS	Excessive daytime sleepiness
BMA	British Medical Association	EEG	Electroencephalogram or Electroencephalography
BMI	Body mass index	EMG	Electromyogram or electromyography
BT	Bedtime	EOG	Electrooculogram or electrooculography
CAC	Coronary artery calcification	ER	Emergency room
CAD	Coronary artery disease	ERV	Expiratory reserve volume
CAR	Cortisol awakening response	ESS	Epworth Sleepiness Scale
CARDIA	Coronary artery risk development in young adults	EU	European Union
CBT	Core body temperature	EWTD	European Working Time Directive
CDC	Centres for Disease Control	FAI	Fatigue assessment instrument
cGMP	Cyclic guanosine monophosphate	FDA	Federal Drugs Authority
CHD	Coronary heart disease	FEV <sub>1</sub> %	Forced expiratory volume in one second as % of predicted value
CI	Confidence interval	FFI	Fatal familial insomnia
CMS	Centers for Medicare and Medicaid Services	fMRI	functional magnetic resonance imaging
CNS	Central nervous system		
CO <sub>2</sub>	Carbon dioxide		
COPD	Chronic obstructive pulmonary disease		

FMSCA	Federal Motor Carrier Safety Administration	LVEF	Left ventricular ejection fraction
FRC	Functional residual capacity	m	Metre
FVC%	Forced vital capacity as % of predicted value	M	Method
GERD	Gastroesophageal reflux disease	MetS	Metabolic syndrome
GH	Growth hormone	MG	Myasthenia gravis
GHRH	Growth hormone releasing hormone	MI	Myocardial infarction
GME	Graduate Medical Education	MRE	Mortality risk estimates
GWS	Genome wide scan	MS	Multiple sclerosis
H@N	Hospital at Night	MSA	Multiple system atrophy
HbA1c	Haemoglobin A1c	MSLT	Multiple sleep latency test
HDL	High-density lipoprotein	MVA	Motor vehicle accidents
HIV	Human immunodeficiency virus	MVV	Maximum minute ventilation
HLA	Human leukocyte antigen	MWT	Maintenance of wakefulness test
HOMA-IR	Homeostasis model assessment-estimated insulin resistance	N1	Stage 1 sleep
HOS	Hours of service	N2	Stage 2 sleep
HPA axis	Hypothalamic-pituitary-adrenal axis	N3	Stage 3 sleep
HR	Hazard ratio	NADPH	Nicotinamide adenine dinucleotide phosphate
HRT	Hormone replacement therapy	NAEPP	National Asthma Education and Prevention Program
hs-CRP	C-reactive protein (high-sensitivity)	NCSDR	National Commission of Sleep Disorders Research
HVDF	Heavy vehicle driver fatigue	NDD	Neurodevelopmental disorders
ICAM-1	Intracellular adhesion molecule-1	NFLE	Nocturnal frontal lobe epilepsy
ICS	Inhaled corticosteroid	NF- B	Nuclear factor-Kappa B
ICSD-2	International Classification of Sleep Disorders, 2nd Edition	ng/mL	Nanograms per millilitre
ICU	Intensive care unit	NHANES	National Health and Nutrition Examination Survey (USA)
IFN- $\gamma$	Interferon-gamma	NHLBI	National Heart, Lung and Blood Institute
IH	Intermittent hypoxia	NHS	National Health Service
IL-1	Interleukin-1	NMD	Neuromuscular disorders
ILD	Interstitial lung disease	NO	Nitric oxide
ILO	International Labour Organization	NOS	Nitric oxide synthase
IMT	Intima-media thickness	NREM	Non-rapid eye movement
IOM	Institute of Medicine	NSF	National Sleep Foundation
ISR	Insulin secretory rate	NTSB	National Transport Safety Board
ivGTT	Intravenous glucose tolerance test	O <sub>2</sub>	Oxygen
JACC	Japan Collaborative Cohort study	OAD	Obstructive airway disease
Kcal	Kilocalorie	OCP	Oral contraceptive pill
KDT	Karolinska drowsiness test	ODI	Oxygen desaturation index
kg	Kilogram	OHS	Obesity hyperventilation syndrome
KLS	Kleine-Levin syndrome	OR	Odds ratio
KSS	Karolinska Sleepiness Scale	OSA	Obstructive sleep apnoea
LDL	Low-density lipoprotein	OSAS	Obstructive sleep apnoea syndrome
LPL	Lipoprotein lipase	PaCO <sub>2</sub>	Arterial CO <sub>2</sub> pressure
LPS	Lipopolysaccharide		

PAI-1	Plasminogen activator inhibitor	SD	Standard deviation
PaO <sub>2</sub>	Arterial O <sub>2</sub> pressure	SDB	Sleep-disordered breathing
PCI	Percutaneous coronary intervention	SES	Social economic status
PCOD	Polycystic ovary disease	SEWS	Standardized early warning score
PEF	Peak expiratory flow	SF-36	Short form of medical outcomes study questionnaire (36 questions)
PEFR	Peak expiratory flow rate	SGRQ	St. George's Respiratory Questionnaire
Per	Period gene	SHHS	Sleep Heart Health Study
Pes	Esophageal pressure (measured on esophageal manometry)	SI	Insulin sensitivity
PET	Positron emission tomography	SOL	Sleep onset latency
PFT	Pulmonary function test	SpO <sub>2</sub>	Oxyhaemoglobin saturation
PGO	Ponto-geniculo-occipital	SpRs	Specialist Registrars
PH	Pulmonary hypertension	SPT	sleep period time
PKG	Protein kinase G	SRS	Sleep regulatory substance
PLMD	Periodic limb movement disorder (nocturnal myoclonus)	SSM	Special Study Module
PLMS	Periodic limb movements of sleep	SSRI	Structured sleep-related interview
PNE	Primary nocturnal enuresis	SSRIs	Selective serotonin re-uptake inhibitors
PRC	Phase response curve	SSS	Stanford Sleepiness Scale
PSG	Polysomnography	SWS	Slow wave sleep
PSQI	Pittsburgh Sleep Quality Index	SWSD	Shift-work sleep disorders
PTSD	Post-traumatic stress disorder	T2DM	Type 2 diabetes mellitus
PVT	Psychomotor vigilance test	TD	Time-diary
PYY	Peptide YY	TEE	Total energy expenditure
Q	Questionnaire	TEM	Thermic effect of meals
QOL	Quality of life	TI	Telephone interview
RA	Rheumatoid arthritis	TIB	Time in bed
RBD	REM sleep behaviour disorder	TLC%	Total lung capacity as % of predicted value
RCP	Royal College of Physicians	TLRs	Toll-like receptors
RDI	Respiratory disturbance index	Tmin	Temperature minimum
REM	Rapid eye movement	TNF- $\alpha$	Tissue necrosis factor-alpha
RHT	Retinohypothalamic tract	TSH	Thyroid-stimulating hormone
R <sub>L</sub>	Total airway resistance	TST	Total sleep time
R <sub>LL</sub>	Lower airway resistance	TST <sub>SaO<sub>2</sub>&lt;90%</sub>	Total sleep time with oxyhaemoglobin saturation<90%
RLS	Restless legs syndrome	TV	Tidal volume
RMR	Resting metabolic rate	U.S.	United States
RNA	Ribonucleic acid	U.K.	United Kingdom
ROS	Reactive oxygen species	UAW	Upper airway
RR	Relative risk	UK	United Kingdom
R <sub>UAW</sub>	Upper airway resistance	UPPP	Uvulopharyngopalatoplasty
RV	Residual volume	US	Unites States
S	Survey	UTR	Untranslated region
SAH	Sleep apnoea-hypopnoea	V/Q	Ventilation/perfusion ratio
SCI	Spinal cord injury		
SCN	Suprachiasmatic nucleus/nuclei		

VCAM-1	Vascular cell adhesion molecule-1	WASE	Wakefulness after sleep end
V <sub>E</sub>	Minute ventilation	WGBH	A Boston-based public broadcasting station
VEGF	Vascular endothelial growth factor	WHO	World Health Organization
VNTR	Variable number tandem repeat	WHR	Waist-hip ratio
V <sub>T</sub>	Tidal volume	WU	Wake-up time

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