Executive Summary

In 1993, the U.S. Congress established the National Center on Sleep Disorders Research (NCSDR), located within the National Heart, Lung, and Blood Institute (NHLBI), because of the tremendous toll sleep deficiency and sleep disorders had begun taking on productivity, morbidity, and mortality. Part of the legislation mandated the development of a comprehensive National Sleep Research Plan [1].

Although sleep is a critical requirement for overall health and well-being across the lifespan, some 30–40% of U.S. adults and 65–80% of teens report sleep deficiency (e.g., insufficient sleep, irregular timing of sleep, poor quality of sleep) each year, according to the Centers for Disease Control and Prevention. Scientific evidence has consistently linked sleep deficiency and sleep disorders to disease pathology in almost every tissue in the human body. An economic analysis of health costs associated with sleep deficiency — including the burden of disease, accidents, and lost productivity — indicated losses that amounted to nearly \$411 billion a year, or about 2.3% of U.S. gross domestic product [2].

Since the NCSDR was established, the sleep and circadian fields have advanced from basic knowledge about how sleep impacts safety, to a deeper understanding of sleep disorders. Research has also explored the genetics of narcolepsy and the heterogeneity of sleep apnea, as well as the multisystem effects of sleep and sleep deficiency on health and disease.

Major scientific accomplishments, particularly the discovery of molecular mechanisms controlling circadian rhythms — which earned the 2017 Nobel Prize in Physiology or Medicine [3] — have illustrated how basic mechanistic studies and medicine can help promote health and well-being. However, investigation of sleep and circadian biology across the basic, clinical, and translational science spectrum is necessary to further these advances with high translational value. This work will be critical to improving our scientific knowledge, transforming health care, and advancing public health and safety and the well-being of the nation. Foundational to this science will be the development of a diverse and interdisciplinary workforce that can stimulate the application of sleep and circadian scientific advances into crosscutting areas.

In developing the 2021 NIH Sleep Research Plan, the following Strategic Goals were identified, each of which are high-priority research areas that list specific opportunities for investigation:

Goal 1:	Elucidate the Sleep and Circadian Mechanisms Underlying Health and Disease
Goal 2:	Improve the Treatment of Sleep and Circadian Disorders and Reduce the Risk Associated with Sleep Deficiency and Circadian Misalignment
Goal 3:	Identify Gaps and Opportunities to Accelerate the Clinical Implementation of Sleep and Circadian Research and Protect Public Health
Goal 4:	Advance the Scientific Understanding of Sleep and Circadian Contributions to Health Disparities in Diverse Populations, and Their Different Impacts on the Public Safety of These Populations
Goal 5:	Foster the Development of a Strong and Diverse Workforce for Sleep and Circadian Research



In addition, nine Critical Opportunities (CO) related to the strategic goals are featured. These COs were deemed timely and actionable, with potential for the highest transformative value to medicine and public health:

- **CO1:** Identify biomarkers in sleep and circadian physiology to indicate the severity of medical conditions and the effectiveness of therapeutic interventions. **(Goal 1)**
- CO2: Elucidate the significance of sleep and circadian biology to immune function and the microbiome. (Goal 1 and Goal 2)
- **CO3:** Elucidate the relationships between sleep and circadian rhythms and dementia pathobiology and clinical outcomes, including Alzheimer's disease and related dementias. **(Goal 1 and Goal 4)**
- CO4: Identify the neurobiological mechanisms underlying the perception of sleep quality, sleepiness, and fatigue. (Goal 1)
- CO5: Develop chronotherapeutic approaches to prevent and treat chronic diseases. (Goal 3)
- **CO6:** Develop tools and/or methods for the early prediction, detection, and treatment of sleep deficiency and sleep and circadian disorders in children and adolescents to promote lifelong health and well-being and prevent disease. **(Goal 1 and Goal 3)**
- **CO7:** Standardize measurements and data and demonstrate how dissemination and implementation of high-quality care for sleep and circadian disorders can be improved by data science approaches in adaptive healthcare systems. **(Goal 2, Goal 4, and Goal 5)**
- **CO8:** Embed omics-based approaches in real-world healthcare settings to facilitate personalizing treatments and cures for sleep and circadian rhythm disorders. (Goal 2, Goal 3, and Goal 5)
- **CO9:** Identify people-driven approaches to improve awareness of sleep and circadian rhythms and promote healthy sleep behaviors for the benefit of public health and safety. **(Goal 3 and Goal 4)**

The plan incorporates crosscutting NIH priorities that address minority health and health disparities, <u>sex as a biological</u> <u>variable</u>, <u>inclusion across the lifespan</u>, the opioid epidemic, and how the loss of sleep health may exacerbate the risk and outcome of infectious diseases such as COVID-19. The plan also covers the development of personalized treatments for sleep and circadian disorders. That said, the opportunities identified in this research plan are not meant to be inclusive of every important research topic in sleep and circadian biology, and they do not preclude the scientific exploration of any other significant topic in this field.