An Approach to Quantitative Risk Assessment for Combined Spaceflight Hazards: Evaluating the Impact of Short Sleep Durations on Space Crew Cardiovascular Health

Jennifer L. Butler[1], Robert J. Reynolds[4], Steve Blattnig[2], Ryan B. Norman[2], Erin Flynn-Evans[5], #Zarana S. Patel[3,4], Janice L. Huff[2]

1 National Institute of Aerospace, Hampton VA 23666, USA, 2 NASA Langley Research Center, Hampton VA 23681, USA, 3 NASA Johnson Space Center, Houston TX 77058, USA, 4 KBR Inc., Houston TX 77058, USA, 5 NASA Ames Research Center, Moffett Field, CA 94035, USA

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Introduction

- Astronauts embarking on long-duration missions will be exposed to multiple spaceflight hazards including radiation, isolation and confinement, distance from Earth, hostile closed environments, and altered gravity. These hazards pose health risks to the crew in-mission and postflight, including risks to cardiovascular health. For radiation, quantitative risk models have been developed that are based on large-scale epidemiological evidence from exposed terrestrial populations, which are extrapolated to account for the difference in radiological effectiveness between ground-based and in-flight exposures.
- Cardiovascular diseases (CVD) are multifactorial, therefore multiple risk factors can influence disease risk estimates.
- Astronauts with spaceflight experience is a very small population.
- To overcome limitations of cohort, population data from presumed equivalent stressors on Earth can be used to quantitatively assess possible risks.
- Sleep disruption and short sleep duration are known consequences of spaceflight and are also established risk factors for cardiovascular disease on earth (Patel et al., 2020).
- Coronary Heart Disease (CHD), Myocardial Infarction (MI), and stroke are negative health effects due to short sleep durations and sleep disruptions (Yin et al., 2017); (Cappuccio et al., 2010).
- A combined CVD risk model including spaceflight stressor such as sleep, stress, radiation, etc.) will provide more precise estimate of risks.

Background

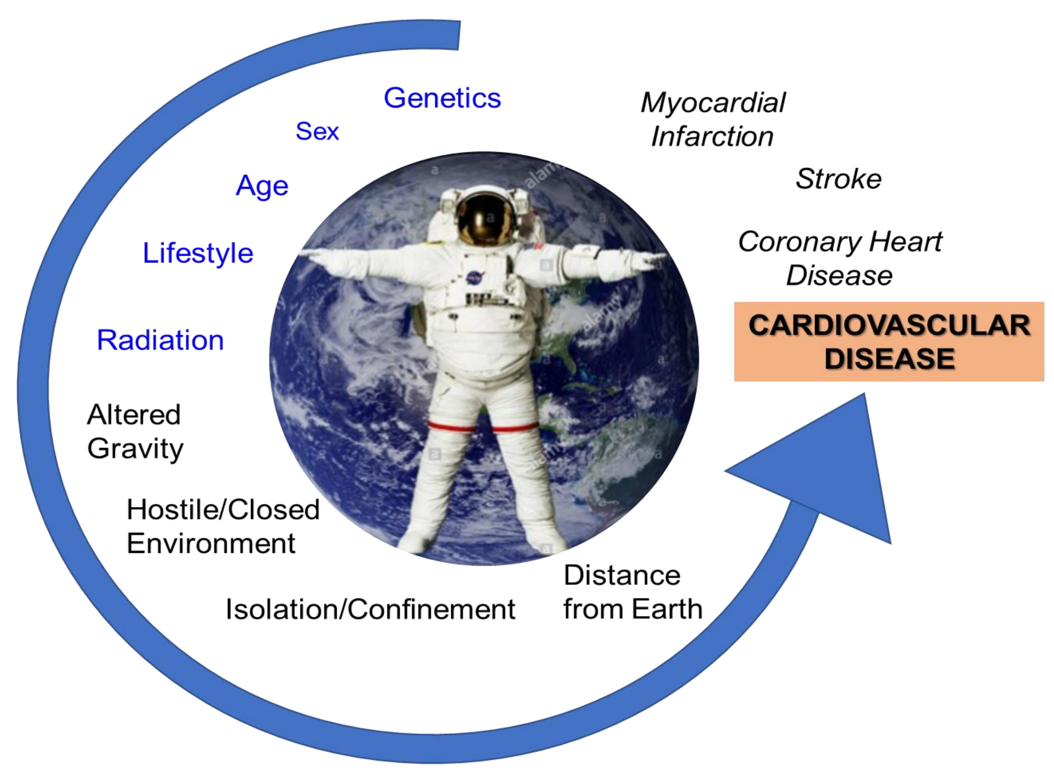


Figure 1. Cardiovascular disease is a human systems risk. In blue are the known risk factors for CVD and in black are the other spaceflight stressors that may also contribute to disease development. Image used in this figure is courtesy of NASA.(Patel et al., 2020)

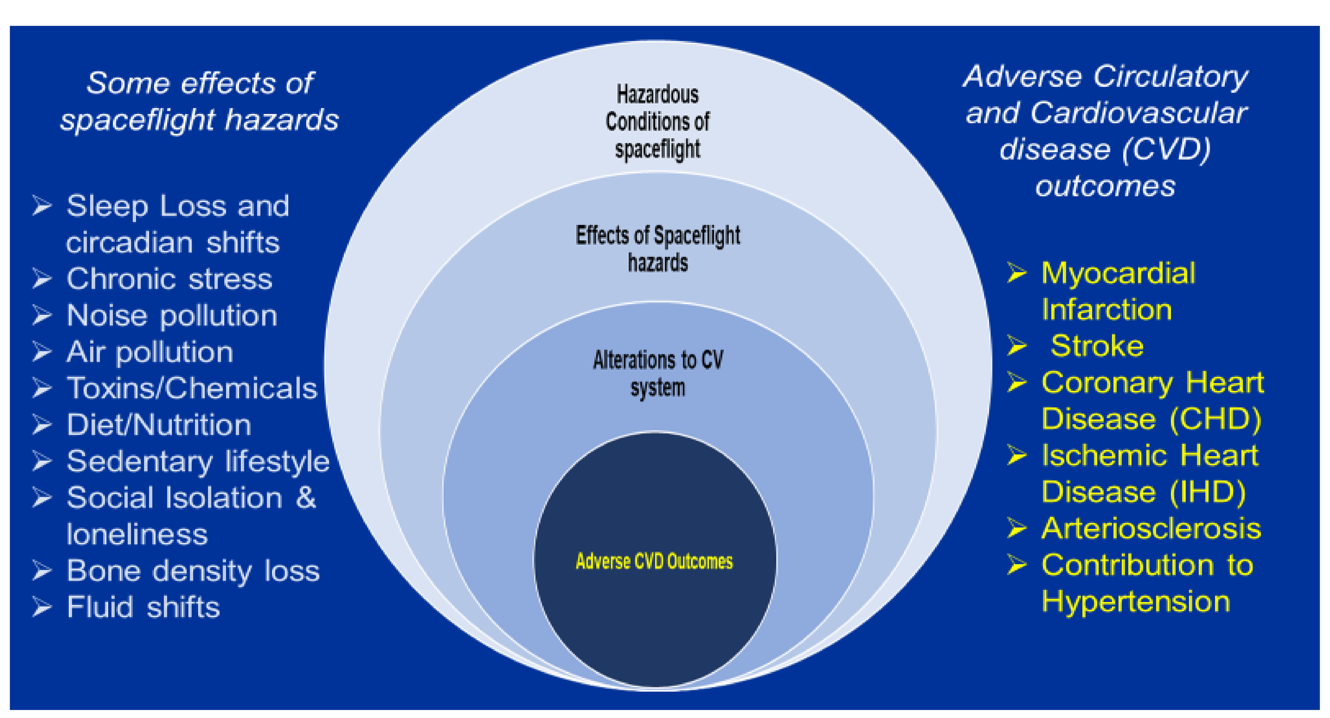


Figure 2. Multiple spaceflight hazards attribute to conditions that may result in adverse cardiovascular disease outcomes. Data from terrestrial cohorts with equivalent stressors can be used for estimating risks when spaceflight data is sparse,

Materials and Methods

A comprehensive systematic review from 67 cohort studies on sleep duration and cardiovascular outcomes was conducted, and 39 cohorts were selected for meta-analysis.

1. Study Design

- Utilized a design that examines patient/population, intervention, comparison, and outcomes (PICO).
- Patient population was defined as healthy adults without known CVD who were exposed to chronic short sleep durations
- Comparison population was health adults without known CVD who were not exposed to chronic short sleep durations.

2. Search Strategy

- PubMed and Google Scholar were used to search for articles with exposures to chronic sleep durations and cardiovascular outcomes that were predefined by Little et al. (2016).

3. *Study Selection*

- Studies were selected if inclusion criteria were met (human studies only, adult populations, English language, conducted on both men and women).
- Selected studies required sufficient data defined as hazard ratios (HR) or risk ratios (RR), with confidence intervals (CI's).
- Omitted studies with missing data, or not clearly defined.
- Omitted studies on subjects with known sleep disorders such as Obstructed Sleep Apnea (OSA).
- Where multiple studies used same cohort, the study with the longest follow-up time was used.

4. *Data Extraction and Quality Assessment*

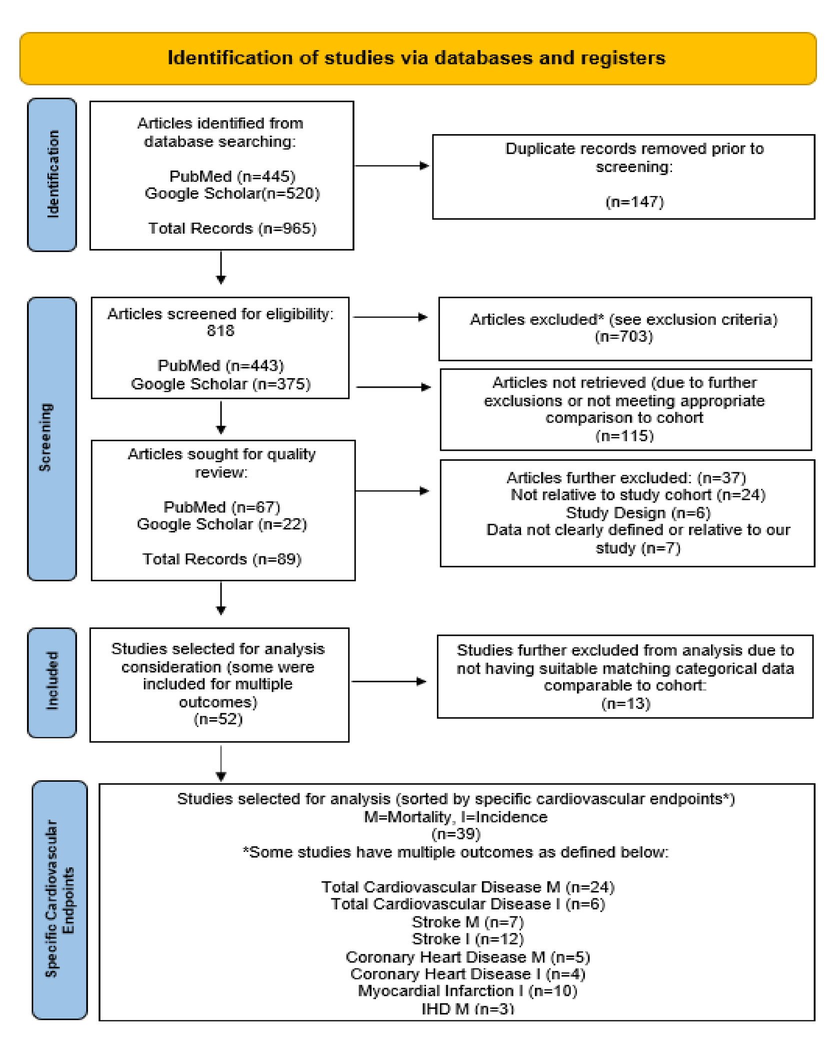
- Studies were examined using a 3- pass approach (by title, author, and article content). Risk ratio data was extracted for categorical values of sleep duration. Duplicate cohorts were removed. Two authors (JB & SB) independently extracted data based on the predefined inclusion/exclusion criteria and assessed for quality using the National Heart Blood Lung Institute (NHBLI) quality assessment tool (NHBLI, 2021). Studies were then divided into disease outcome categories based on the predefined ICD codes.

5. *Meta-analysis Methods*

- For initial risk summary estimates, we computed simple pooled risk ratios for each outcome as the person-year weighted mean of the log relative risks within sleep duration categories and by sex. For formal meta-analysis we fit mixed effects models for each outcome, which adjusted for study sex ratio, average age at study start, average length of follow-up, and sleep duration. Additional factors, such as country of origin, were entered into the model as random effects. This model provides a dose-response estimate for sleep duration adjusted for the potential confounding variables, while controlling for random variation due to country in which the study was conducted and various other factors being used as random effects. Heterogeneity was examined through forest plots.

Results

Systematic Review using PRISMA guidelines



Preliminary Pooled Ratios

Incident Disease Outcome	Pooled Hazard Ratio (HR)	95% Confidence Interval (CI)
Coronary Heart Disease (CHD)	1.33	0.10-1.43
Myocardial Infarction (MI)	1.12	0.79-1.44
Stroke	1.05	0.15-1.95
Total Cardiovascular disease (CVD)	1.08	0.80-1.35

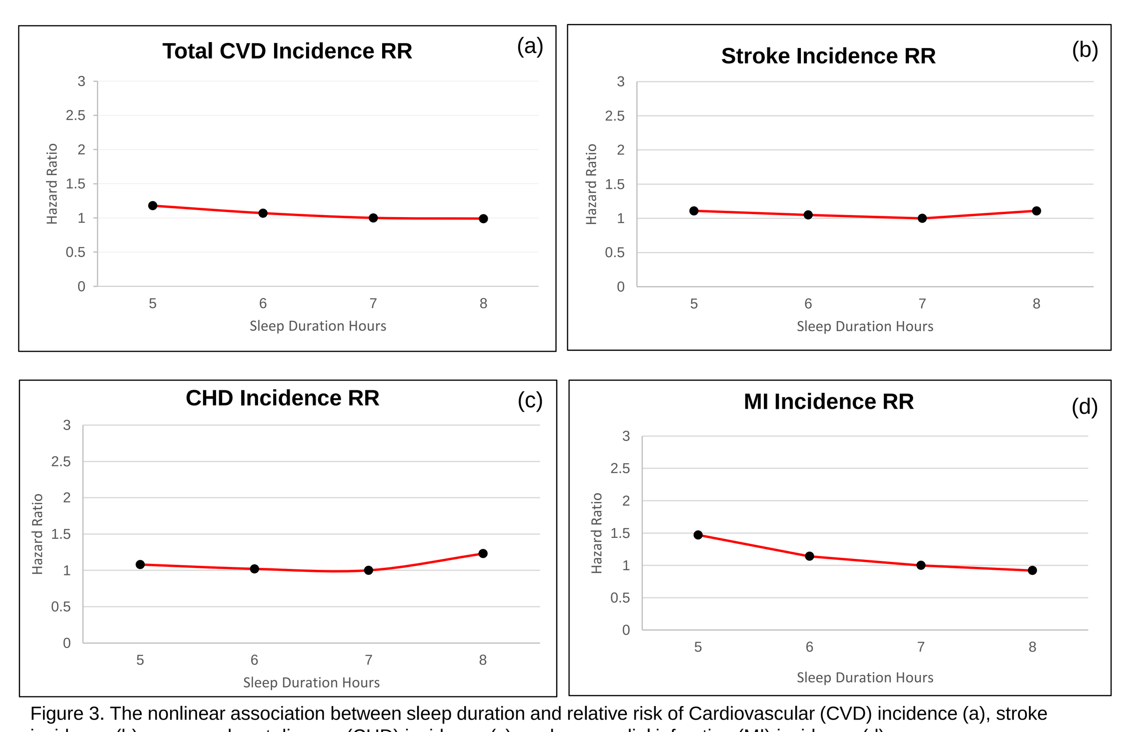


Figure 3. The nonlinear association between sleep duration and relative risk of Cardiovascular (CVD) incidence (a), stroke incidence (b), coronary heart disease (CHD) incidence (c), and myocardial infarction (MI) incidence (d).

Preliminary pooled hazard ratios confirmed an association between short sleep durations and increased risk of adverse cardiovascular disease.

Discussion

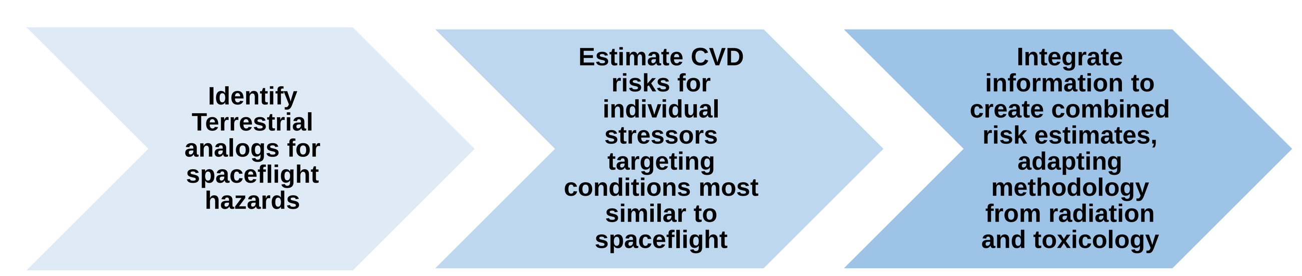
- Shortcomings of some of the studies included the following:

1. Inconsistent use of short and long sleep duration categories (also noted by Yin et al., 2017).
2. Inconsistent reference categories relative to the definition of "good sleep".
3. Inconsistent follow-up times.
4. Lack of use of objective measurements such as actigraphy to measure and validate sleep duration (also noted by Cappuccio et al., 2010).

- Additional considerations for sleep risk in astronauts include individual circadian cycles and other metabolic considerations that may be influenced by genetics, age, sex, or other factors, as well as noise, temperature and mistimed lighting cues (Flynn-Evans et al., 2016).
- Many of the additional risk factors of short sleep are also known contributors to adverse cardiovascular outcomes.
- By using a mathematical model to calculate the combined risks, we can gain a more precise estimate of the overall risk to the astronaut cohort which will be crucial as they embark on longer duration space missions such as to the moon and Mars.

Conclusion

The current research aimed to use terrestrial cohort data on sleep durations to gain a more precise estimate of effect to adverse cardiovascular outcomes. Hazard ratios resulting from the systematic review and meta-analysis will serve as surrogate data for spaceflight sleep durations that will be combined with radiation data in a computational model to provide an overall estimated effect of the total risk to the cardiovascular system. This approach can serve as a template for risk assessment of other health systems.



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