# SPACE RADIATION RISK MODELING – THE MULTI-MODEL ENSEMBLE RISK ASSESSMENT (MERA) PROJECT

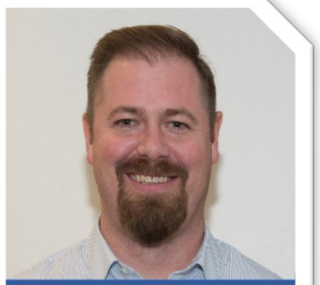
Tony Slaba
on behalf of the MERA team


NASA Human Research Program Investigator's Workshop
February 12, 2024

# The MERA Team: *125+ years of space radiation research experience*

**Janice Huff**

***MERA Project Scientist***
*Individual risk assessment*



**Ryan Norman**

***MERA Project Manager***
*Lung cancer*

**Tony Slaba**

*Cancer ensemble risk model*
*Galactic cosmic ray simulator design*

**Charles Werneth**

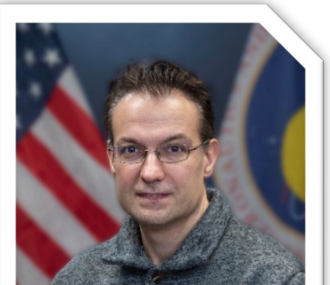
*Medical countermeasure & Mitigation assessment*
*Biologically-based risk models*

**Steve Blattnig**

*CVD risk models*
*Late CNS risk assessment*
*Combined spaceflight risks*

**Martha Clowdsley**

***MERA Project Manager***
*Engineering design*

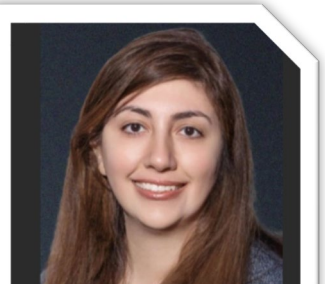


**Ianik Plante**

*Track structure & biophysics*
*CVD clinical prediction models*
*CNS risk modeling*

**Floriane Poignant**

*Chromosome aberration modeling*
*Track structure & biophysics*



**Shirin Rahmanian**

*Risk communication*
*Radiation transport*

**Xiaojing Xu (Sharon)**

*Dose response modeling*

# Space Radiation Major Health Risks

## Carcinogenesis

*Solid cancers (lung, breast, colon, stomach, esophagus, liver, ovaries, bladder, skin, brain) and leukemias*

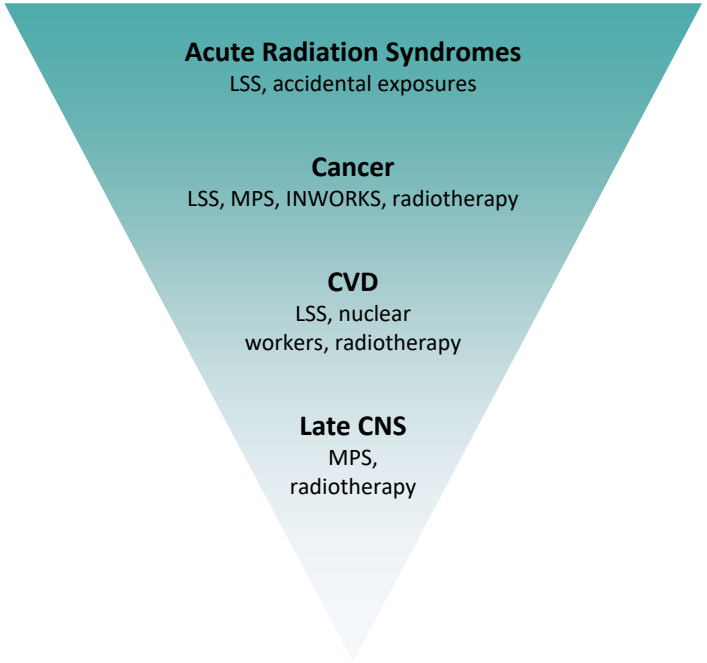
## Cardiovascular Diseases (CVD)

*Accelerated atherosclerosis, ischemic heart disease, and stroke*

## Neurodegeneration (Late CNS)

*Changes in cognition, motor function, behavior, and neurodegenerative disorders such as Parkinson's disease, vascular dementia and Alzheimer's disease*

- ***Current space radiation risk models are population-based and extrapolate from terrestrial data***
- ***Level of evidence in terrestrial data correlates with maturity of risk assessment models***




**The NASA cancer risk model is the most mature model of the three risk areas**

- Uses data from the atomic bomb survivor Life Span Study (LSS)
- Scales LSS for mixed field and low dose rate space radiation using experimental animal and cell culture data
- Used to set PELs and communicate risks to crewmembers and other stakeholders

**CVD risk models are not used operationally but are currently in development**

- Currently scaling from low linear energy transfer (LET) exposures
- Individualized risk models for primary prevention and medical management
- Approaches for assessment of multiple spaceflight hazards

**No risk models are available for CNS effects at this time**

- Research underway to determine whether space radiation poses a significant risk in humans

INWORKS – International Nuclear Workers Study  MPS – Million Person Study  PEL – Permissible Exposure Limit  CNS – Central Nervous System

# MERA Project Goals

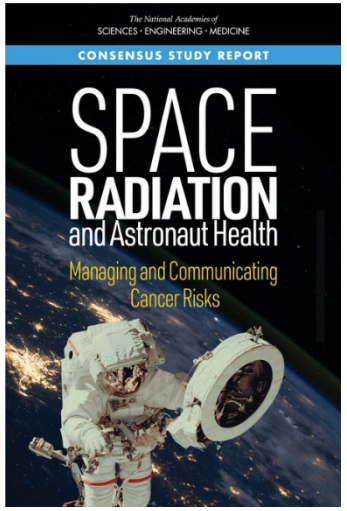
## To develop robust and accurate tools for evaluating space radiation health risks to support mitigation strategies, informed consent, and operations

- Ensemble risk assessment models
- Methodology for assessing medical countermeasures (MCM) and other mitigation approaches
- Individualized risk assessments supporting primary prevention and medical management
- Assessment of combined spaceflight hazards
- Risk communication

## Research activities guided by and aligned with

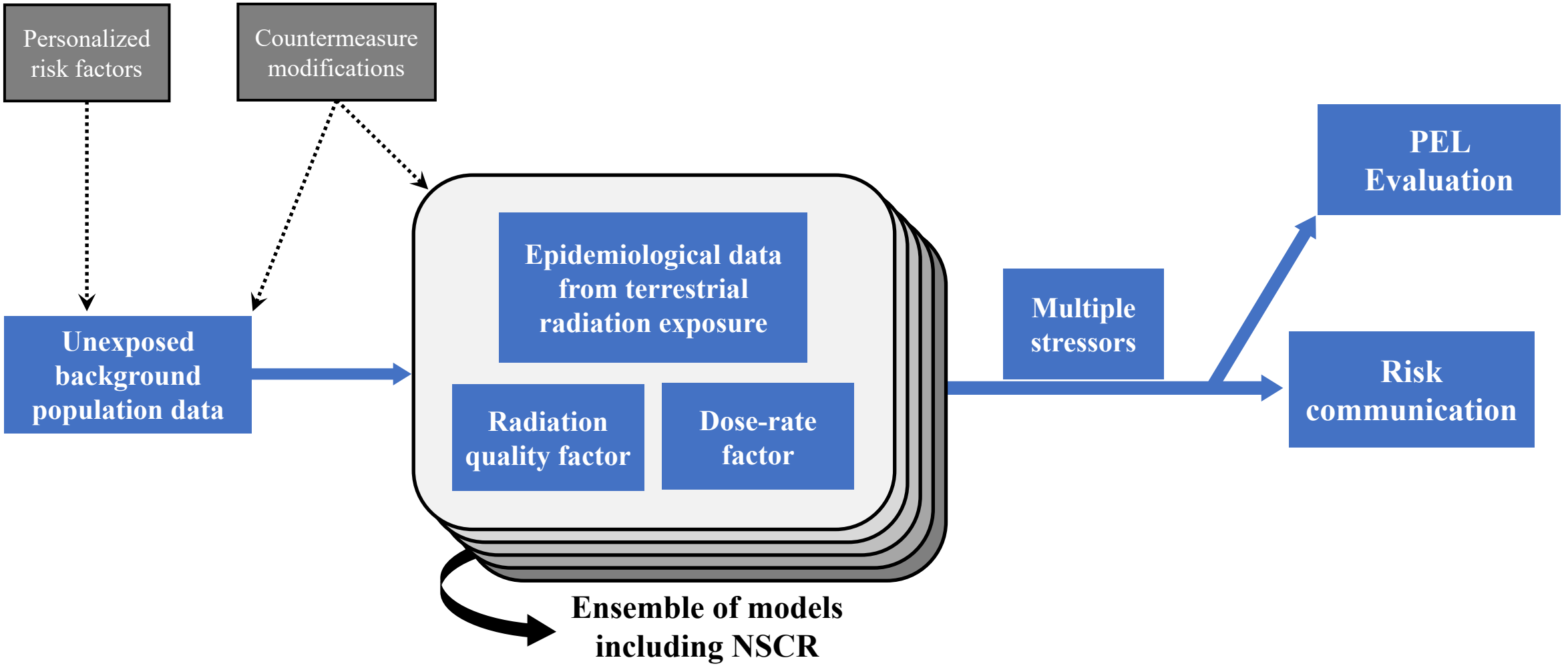
- Human Research Program (HRP) space radiation element
- Agency roadmaps and gaps
- External advisory panel recommendations

NASEM (2021) *Space radiation and astronaut health: managing and communicating cancer risks* https://www.nap.edu/download/26155




NASEM – National Academies of Sciences, Engineering, and Medicine

# Risk Assessment Model Framework




Notional diagram of space radiation risk model framework to assess and communicate the increased risks of radiogenic cancers, cardiovascular disease, and late neurogenerative diseases from mission exposures.

# Quantitative Evaluation of Medical Countermeasures

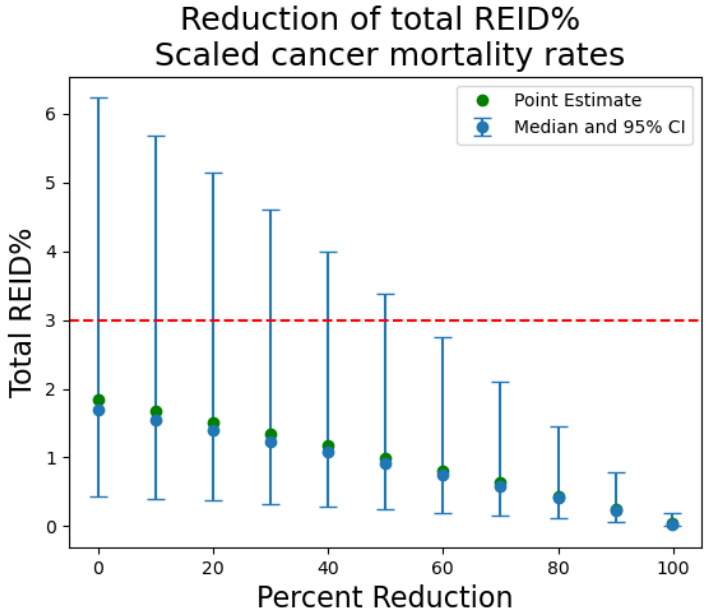
- **Develop methodologies to quantify impact of medical countermeasures**
- **Support agency goals of space radiation risk mitigation**


- Initial demonstration considering aspirin* or warfarin*

  ** Proof of Concept Study - Does not reflect endorsement of these drugs for use in spaceflight*

- Additional sensitivity study performed to scope MCM requirements needed to reach PELs for Mars missions

- It is unlikely these types of MCM will allow PELs to be met for Mars missions
  - Need to consider if MCM benefits outweigh possible health detriments
  - MCM should be considered as part of holistic approach to risk reduction




**Recent Publications:**

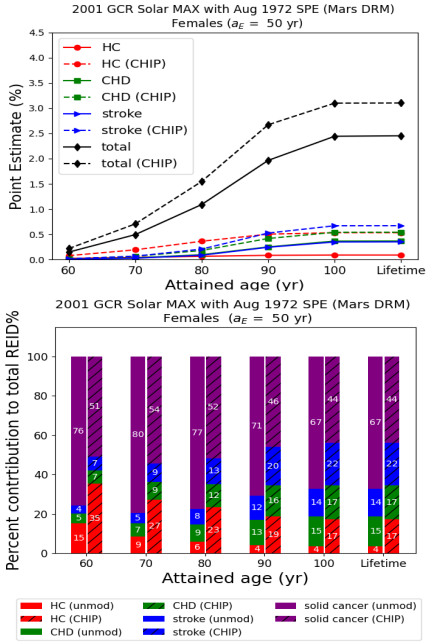
Werneth, Slaba, Huff, Patel, Simonsen, Medical Countermeasure Requirements to Meet NASA's Space Radiation Permissible Exposure Limits for a Mars Mission Scenario. *Health Physics* 123, 116 (August 2022)

Werneth, Slaba, Blattnig, Huff, Norman, A Methodology for Investigating the Impact of Medical Countermeasures on the Risk of Exposure Induced Death. *Life Sci Space Res* 25, 72 (May 2020)

# Toward Personalized Risk Models

- **Develop methodologies to incorporate and evaluate personalized risk factors**
- **Consideration of clinical tools along with modifiable and non-modifiable risk factors**

## Clonal Hematopoiesis of Indeterminate Potential (CHIP)




- Common age-related blood condition in older individuals
- Large increase in the total lifetime REID for CHIP carriers compared to average US population
- **Identifying individuals with higher risk profiles provides opportunities for tailored interventions**


Werneth, Patel, Thompson, Blattnig, Huff, Considering Clonal Hematopoiesis of Indeterminate Potential in Space Radiation Risk Analysis for Hematologic Cancers and Cardiovascular Disease." *Communications Medicine,* In press (2024)

REID – Risk of Exposure Induced Death

## Astro-CHARM Clinical CVD Model Integrated with NSCR

- Astronaut cardiovascular health and risk modifications (Astro-CHARM)
- Calculates risk factor and biomarker-based individualized disease rates from Astro-CHARM and combined with baseline population rates
- **Extends risk modeling capability to support primary prevention and medical management**


https://astrocharm.org (Khera et al. *Circulation* 2018)


161947 - INTEGRATION OF THE CARDIOVASCULAR RISK MODEL ASTRO-CHARM IN THE NASA RADIATION RISK MODEL
Wednesday February 14
Exhibit Hall A 2:45 PM
Poster Session B

# Scaling Terrestrial Exposures to Space

- **Improve capability to extrapolate limited experimental data to complex space radiation environment**
- **Address main drivers of uncertainty in cancer risk projections – radiation quality and dose-rate**

## Ensemble Dose Response and Quality Factor

- Leveraging existing data sets and empirical models
- Developing new models
  - Statistical approach (Xu et al.)
  - Microdosimetric approach (Rahmanian et al.)
- **Prepared for GCRsim dose response data**
- Robust uncertainty quantification
- Statistical weighting of ensemble dose response models




1646319 - A GENERALIZED MICRODOSIMETRIC DOSE RESPONSE MODEL
Wednesday February 14
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Poster Session B

## Track Structure and Biophysical Modeling

- Develop computational models to simulate initial damage, repair processes, and intermediate surrogate endpoints
- Track structure and chromosome aberration models
- Models will inform dose response and quality factor research

**Recent Publications:**


- Poignant, Plante, Patel, Huff, Slaba, Geometrical Properties of the Nucleus and Chromosome Intermingling Are Possible Major Parameters of Chromosome Aberration Formation. *Int J Mol Sci* **23**, 8638 (2022).
- Poignant, Plante, Crespo, Slaba, Impact of Radiation Quality on Microdosimetry and Chromosome Aberrations for High-Energy (>250 MeV/n) Ions. *Life (Basel)* **12**, 358 (2022).
- Plante, Poignant, Slaba, Track Structure Components: Characterizing Energy Deposited in Spherical Cells from Direct and Peripheral HZE Ion Hits. *Life (Basel)* **11**, 1112 (2021).
- Plante, I. A review of simulation codes and approaches for radiation chemistry. *Phys Med Biol* **66**, 03TR02 (2021).



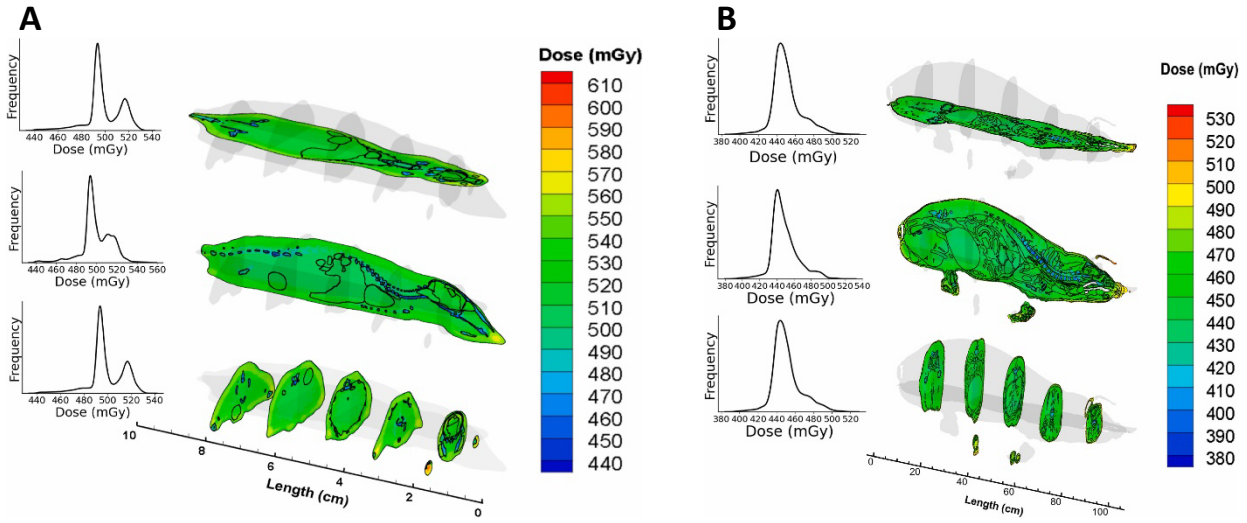
1642088 - PREDICTING CELL SURVIVAL, CHROMOSOME ABERRATIONS AND THEIR TRANSMISSIBILITY
Thursday February 15
3:15 Exhibit Hall B


1619480 - SIMULATION OF RADIATION-INDUCED DNA DAMAGE SHOWS HISTONE PROTECTION
Thursday February 15
3:55 PM - 4:05 PM
Exhibit Hall B

# GCRsim and Space Environment Modeling

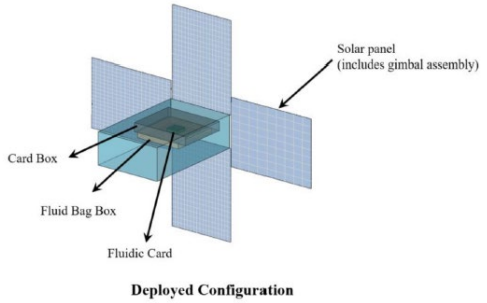
- **Validation of GCRsim for multiple experimental platforms at NSRL**
- **Provide GCR environmental prediction capabilities for space-based experimental platforms**

## GCRsim Beam Analysis

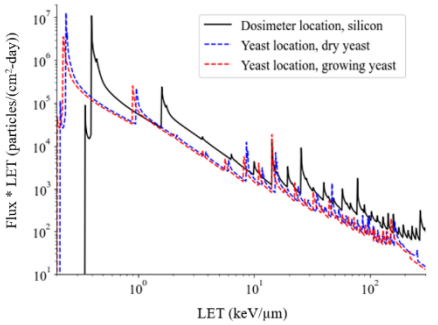



*Voxel dose distribution (dose contour) in (A) Digimouse and (B) Digipig models exposed to the GCR beam.*

## BioSentinel Exposure Prediction




*Geometry set up of the BioSentinel nanosatellite in HZETRN2020*




*Flux spectrum for the deployed configuring at the dosimeter location*

**Recent Publications:**


Rahmanian, Slaba, Applicability of the NASA galactic cosmic ray simulator for mice, rats, and minipigs. *Acta Astronautica* **208**, 111–123 (2023)

Rahmanian, Slaba, Braby, Santa Maria, Bhattacharya, Straume, T. Galactic cosmic ray environment predictions for the NASA BioSentinel mission. *Life Sci Space Res.* **38**, 19–28 (2023)

Huff, Poignant, Rahmanian, Khan, Blakely, Britten, et al. Galactic cosmic ray simulation at the NASA space radiation laboratory – Progress, challenges and recommendations on mixed-field effects. *Life Sci Space Res.* **36**, 90–104 (2023)


# CNS and Combined Spaceflight Hazards

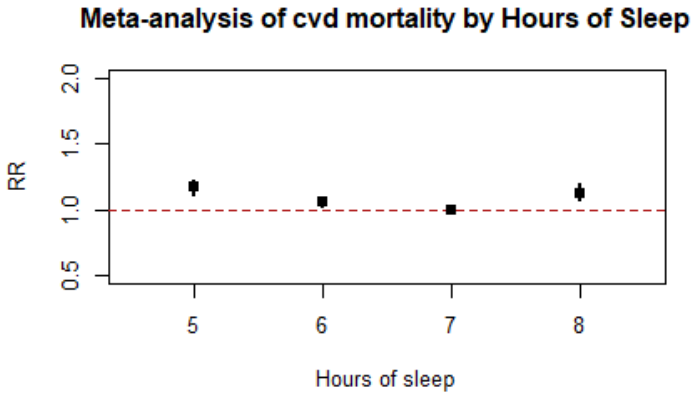
- **Evaluate combined risks for multiple spaceflight hazards using human data**
- **Investigate potential for CNS hazard due to space radiation exposure using human terrestrial data**

## Sleep Deficiency CVD Risk for Astronauts

- Short sleep duration is a known risk factor for CVD on Earth

Barger et al. *Lancet* **13**: 904-912; 2014.

- Sleep deficiency is pervasive among crewmembers
- Average 6 hours/night – shuttle, long-duration ISS crew members
- Significant sleep deficiency during preflight intensive training




Reynolds, Butler, Blattnig, Norman, Patel, Flynn-Evans, Werneth, Huff, An Approach to Quantitative Risk Assessment for Combined Radiation and Spaceflight Hazards: Preliminary Findings of the Potential Impact of Sleep Durations on Space Crew Cardiovascular Health, *In preparation; 2023.*



## MPS evaluation of CNS and Multi-Stressors

- CNS
  - Large number of workers who received both low and high linear energy transfer (LET) exposures
  - Cohorts being evaluated for dementia and cognitive decrements
  - Linkage between career exposures and recorded diagnoses, neuropsychological test scores, and mortality
- Multi-stressor
  - MPS has begun studying submariners to evaluate hazards for astronaut-like population experiencing a multi-stressor environment analogous to space



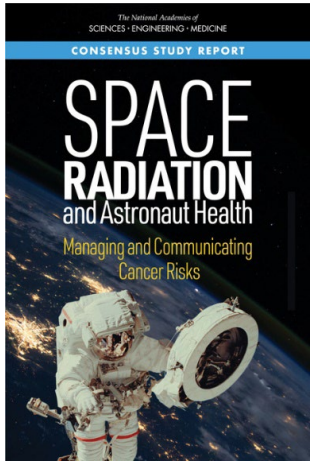
1643947 - THE U.S. MILLION PERSON STUDY OF LOW-DOSE-RATE HEALTH EFFECTS: INNOVATIONS IN EVALUATING COGNITION AND MULTIPLE STRESSORS
Tuesday February 13th
Exhibit Hall B 3:35 PM

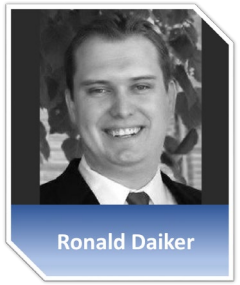
# Risk Communication

- **Space radiation induced health risks must be effectively communicated to a diverse audience of stakeholders**

- ***The need for more effective communications was highlighted in recent NASEM report***

  NASEM (2021) *Space radiation and astronaut health: managing and communicating cancer risks* https://www.nap.edu/download/26155





Ronald Daiker


Rania Ghatas

- **Surveying NASA flight surgeons and retired astronauts via questionnaire**
  - Better understand key information that stakeholders need to make decisions regarding radiation exposure risks


Shirin Rahmanian

- **Additional risk metrics will be added to the MERA framework**
  - International partner risk metrics
  - Metrics accounting for quality of life
  - Potentially incorporate available 5-year survival data

# Summary

**MERA Goal: To develop robust and accurate tools for evaluating space radiation health risks to support mitigation strategies, informed consent, and operations**

## Research activities guided by and aligned with

- HRP space radiation element
- Agency roadmaps and gaps
- External advisory panel recommendations

## Ongoing and future work

- Updated ensemble quality factor model for evaluation in cancer risk model accounting for multiscale and biophysical modeling inputs
- Development and implementation of additional risk metrics beyond lifetime incidence and mortality
- Forthcoming initial personalized risk estimates for space radiation induced CVD (Astro-CHARM)
- Continue initial characterization of space radiation CNS hazard/risk through MPS
- Evaluation of cancer clinical prediction tools to enable more personalized risk assessment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