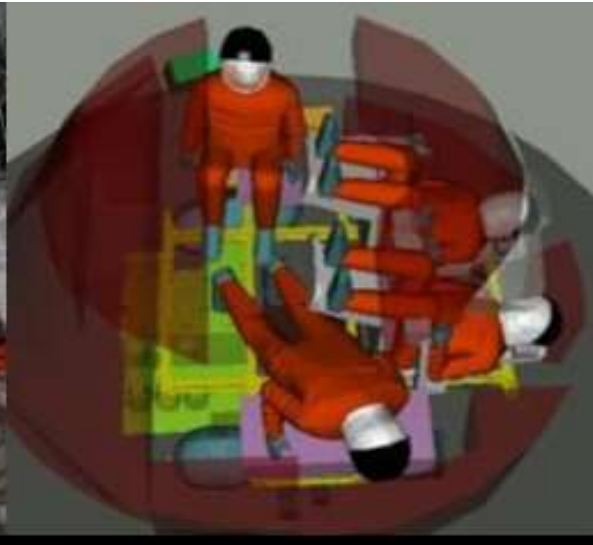
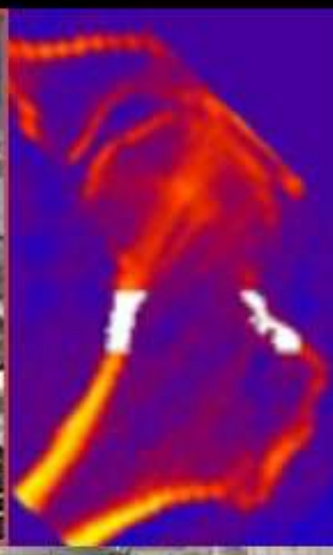


Human Research Program Utilization Plan for the International Space Station



2014 Update

Human Research Program
Utilization Plan for the International Space Station
2014 Update

Verify this is the correct version before use
For correct version go to:
https://sashare.jsc.nasa.gov/sites/HRP/HRP%20Pages/HRP%20Document%20Management%20System.aspx

April 2015
Baseline

National Aeronautics and Space Administration
Lyndon B. Johnson Space Center
Houston, Texas

Human Research Program
Utilization Plan for the International Space Station
2014 Update

Submitted By:

4/30/2015

Lisa Milstead, M.S.
Integration Engineer
Program Science Management Office
Human Research Program

Date

Concurred By:

4/30/2015

Michele Perchonok, Ph.D.
Manager
Program Science Management Office
Human Research Program

Date

Approved By:

4/30/15

William Paloski, Ph.D.
Program Manager
Human Research Program

Date

		DOCUMENT CHANGE/ REVISION LOG	PAGE 1 OF 1
Change/ Revision	**Date**	**Description of Change**	**Pages Affected**
Baseline	4/30/2015	Initial Release approved by HRPCB per HHPD-HRPCB-15-008	All

TABLE OF CONTENTS

Section Page

1 INTRODUCTION 1

2 SUMMARY OF PROGRESS SINCE 2012 3

3 HUMAN HEALTH AND PERFORMANCE RISKS 7

3.1 Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities (ExMC) 7
3.2 Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (BHP) 10
3.3 Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team (BHP) 12
3.4 Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload (BHP) 14
3.5 Risk Factor of Inadequate Nutrition (HHC) 16
3.6 Risk of Adverse Health Event Due to Altered Immune Response (HHC) 18
3.7 Risk of Early Onset Osteoporosis Due to Spaceflight (HHC) 19
3.8 Concern of Intervertebral Disc Damage Upon and Immediately after Re-Exposure to Gravity (HHC) 21
3.9 Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (HHC) 23
3.10 Risk of Orthostatic Intolerance During Re-Exposure to Gravity (HHC) 24
3.11 Risk of Cardiac Rhythm Problems (HHC) 25
3.12 Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance (HHC) 26
3.13 Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (HHC) 28
3.14 Risk of Impaired Control of Spacecraft/Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight (HHC) 29
3.15 Risk of Ineffective or Toxic Medications Due to Long Term Storage (HHC) and Concern of Clinically Relevant Unpredicted Effects of Medication (HHC) 31
3.16 Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations (HHC) 33
3.17 Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System (SHFH) 35
3.18 Risk of Adverse Health Effects Due to Host-Microorganism Interactions (SHFH) 37
3.19 Risk of an Incompatible Vehicle/Habitat Design (SHFH) 38
3.20 Risk of Inadequate Human-Computer Interaction (SHFH) 40
3.21 Risk of Injury from Dynamic Loads (SHFH) 42
3.22 Risk of Performance Errors due to Training Deficiencies (SHFH) 43

4 SUMMARY 44

APPENDIX A: CROSS-REFERENCE OF RISKS AND TASKS (EXPERIMENTS) 46

APPENDIX B: SELECT PRODUCTS AND PUBLICATIONS FROM ISS 62

APPENDIX C: ACRONYMS AND ABBREVIATIONS 66

1 INTRODUCTION

NASA's Human Research Program (HRP) goal is to provide human health and performance countermeasures, knowledge, technologies, and tools to enable safe, reliable, and productive human space exploration. To meet that goal, the value and necessity of the International Space Station (ISS) was analyzed to quantify and address the human health and performance risks for crews during exploration missions. Based on a set of exploration risks, the HRP defined a research and technology development plan to address the risks. This plan is documented in the Human Research Roadmap (HRR) (http://humanresearchroadmap.nasa.gov) and sets the following goals to be completed by the end of the ISS in 2024:

- to perform the research needed to identify and quantify risks to human health and performance
- to identify potential countermeasures
- to flight validate those countermeasures

NASA's Human Research Program has a comprehensive Integrated Research Plan (IRP) that includes both flight and ground experiments and facilities that are primarily focused on the Mars mission. The plan also addresses precursor missions, such as visiting an asteroid or lunar distant retrograde orbit, that serve as a proving ground for Mars by expanding deep space exploration capabilities. Annually, HRP analyzes the risks cataloged in the HRR and determines the required next steps in research and technology development activities to quantify the risks and, wherever possible, reduce these risks to acceptable levels. HRP established and maintains a Path to Risk Reduction (PRR completed prior to the initiation of the one year mission) for each risk. The PRR lays out a notional timeline of product deliveries that are expected to reduce the likelihood or consequence of an adverse event, thus reducing the overall risk. Products used to reduce the risk can include standards, countermeasures, technologies, tools or knowledge to help understand and mitigate risks. The Integrated PRR (iPRR) is shown in Figure 1, communicating the high-level PRRs for all HRP risks. The PRR/iPRR also identifies the products in the path that require the use of ISS.

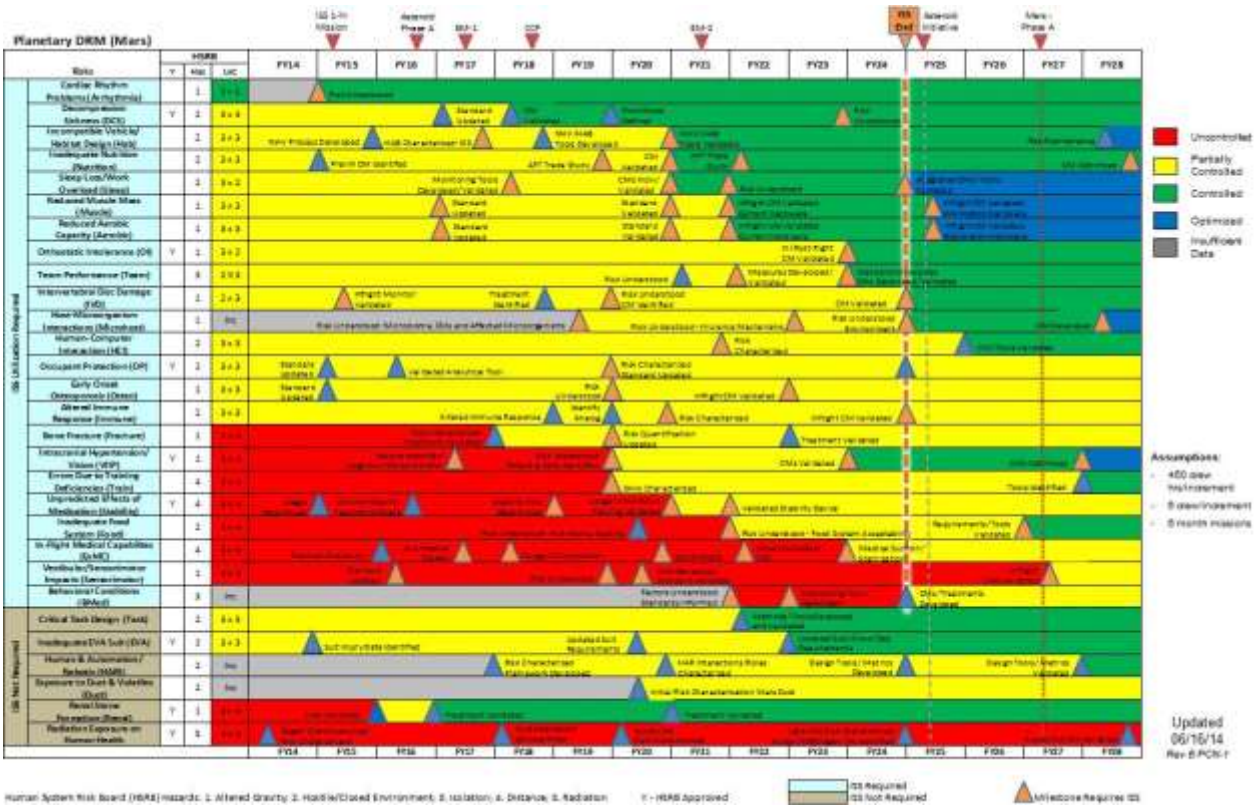


Figure 1. Integrated Path to Risk Reduction (iPRR)

Notes: Decompression Sickness no longer requires ISS;
Unpredicted Effects of Medication consists of a HRP-managed Human Health Countermeasure Risk and Concern;
Radiation Exposure on Human Health consists of four HRP-managed Space Radiation Risks.

The ISS, as an orbiting, microgravity laboratory, provides an invaluable platform to secure knowledge, test countermeasures, and evaluate technologies important for the development and validation of risk mitigation techniques for exploration missions. The research plan for HRP risks is laid out as a progression of activities that are designed to address critical gaps in our knowledge or capabilities that must be filled in order to reduce the risk.

As indicated by the yellow milestones in each PRR, the ISS is in the critical path to risk reduction if there is no effective ground-based analog in which to conduct the work on Earth, or the research activity needs the complete operational environment of spaceflight to validate the countermeasure (CM) or technology. The ISS is necessary to mitigate 22 of the 33 human health risks and concerns anticipated on exploration missions (blue background on iPRR). Only those human system risks that require use of the ISS are discussed in this document.

HRP uses an iterative approach to research, and the IRP and PRR will continue to be revised and updated based on consideration of new evidence gained, available resources, new opportunities, exploration needs, and other driving schedule constraints. As such, the risks that require ISS is expected to change over time as research results either reduce the risk to an acceptable level, identify new questions that now require ISS, or identify alternative approaches to address the risk. This document represents the best plan available at this time and is based on annual assessments of progress since August 2012.

NASA is increasing efficient use of ISS resources through more cooperative research with ISS international partners (IPs). NASA established a Multilateral Human Research Panel for Exploration (MHRPE) to aggressively work with the ISS IPs, facilitating a multilateral approach to human risk reduction. The MHRPE is comprised of representatives from the European Space Agency (ESA), Russian Space Agency (RSA), Canadian Space Agency (CSA), and the Japan Aerospace Exploration Agency (JAXA) all working to coordinate human research plans, remove barriers to collaboration, and facilitate multilateral research collaborations between international scientists.

2 SUMMARY OF PROGRESS SINCE 2012

NASA continues to implement the ISS flight studies identified in the 2012 plan and has made significant progress in the following areas:

1) Understanding the likelihood of cardiac rhythm problems when existing exercise protocols are maintained;
2) Understanding the magnitude of sleep disruptions and potential performance impacts on ISS;
3) Understanding the kinematic differences in running on a treadmill in microgravity;
4) Management of crewmember orthostatic intolerance;
5) Understanding the effectiveness of current practices in monitoring and maintaining aerobic capacity; and
6) Adding in-flight capabilities to measure microgravity-induced changes in fluid distribution and ocular anatomy to better understand the Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations (Short Title: VIIP).

Between 2012 and 2014, the HRP has completed or started the following ISS research and technology development activities given below. [format: IRP long task title (Fly-off Plan task title)]. The investigations marked with an asterisk were selected to obtain one year mission data for comparison to their six month results.

<u>Tasks Completed Between 2012 – 2014</u>

- Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capacity, and Risk of Cardiac Arrhythmias (Integrated Cardiovascular)
- Maximal Oxygen Uptake (VO2max) and Submaximal Estimates of VO2max Before, During and After Long Duration International Space Station Missions (VO2max)
- Biomechanical Analysis of Treadmill Locomotion on the International Space Station (Treadmill Kinematics)
- Validation of Procedures for Monitoring Crewmember Immune Function (Integrated Immune)*
- Nutritional Status Assessment: SMO-016E (Nutrition)

- Physiological Factors Contributing to Postflight Changes in Functional Performance (Functional Task Test, FTT)*
- Psychomotor Vigilance Test (PVT) on ISS (Reaction Self Test)*
- Feasibility Study: QCT Modality for Risk Surveillance of Bone – Effects of In-flight Countermeasures on Sub-regions of the Hip Bone (Hip QCT)*
- Sonographic Astronaut Vertebral Examination (Spinal Ultrasound)
- Assessing the Impact of Communication Delay on Performance: An Examination of Autonomous Operations Utilizing the International Space Station (Comm Delay Assessment)

Tasks Started Between 2012 – 2014

- Study of the impact of long-term space travel on the astronaut's microbiome (Microbiome)
- Prospective Observational Study of Ocular Health In ISS Crews (Ocular Health)*
- Space Biochemistry Profile (Biochem Profile)*
- Quantification of In-Flight Physical Changes – Anthropometry and Neutral Body Posture (Body Measures)
- The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity (Salivary Markers)
- Defining the relationship between biomarkers of oxidative and inflammatory stress and atherosclerosis risk in astronauts during and after long-duration spaceflight (Cardio Ox)*
- In-flight Demonstration of Portable Load Monitoring Devices – Phase I: XSENS ForceShoe™ (Force Shoes)
- Factors Contributing to Food Acceptability and Consumption, Mood and Stress on Long-term Space Missions (Astro Palate)
- Risk of Intervertebral Disc Damage After Prolonged Spaceflight (IVD)
- Manual Control (two merged investigations: Assessment of Operator Proficiency Following Long-Duration Spaceflight; Effect of Sensorimotor Adaptation Following Long-Duration Spaceflight on Perception and Control of Vehicular Motion) (Manual Control)
- Behavioral Issues Associated with Long Duration Space Missions: Review of Astronaut Journals – Extension (Journals)*
- Risk of Visual Impairment and Intracranial Hypertension after Space Flight: Evaluation of the Role of Polymorphism of Enzymes Involved in One-Carbon Metabolism
- Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases (NeuroMapping)*

In 2013, NASA and Russia announced their intent to fly two crewmembers, one Russian and one US, to the ISS for one year. HRP worked with Russia's Institute of Biomedical Problems (IBMP) to develop a joint science program for this increment planned to launch in March 2015. The one year mission (1YM) provides a unique opportunity to assess the effectiveness of countermeasures beyond six months and understand the potential time course of several microgravity related risks. Several investigations that were already underway or recently completed were selected to participate in the one-year opportunity (marked above with an asterisk). Additionally, the following experiments are included in the 1YM: Sprint, Cognition, Fine Motor Skills, Habitability, Training Retention, Fluid Shifts, and Field Test. More details are given on these experiments throughout Section 3.

Selection of Scott Kelly, as the US crewmember to participate in this one year mission, provided another unique opportunity to understand the effects of spaceflight on humans. Scott Kelly has an identical twin brother, who has also flown in space. Following this mission, Scott Kelly will have completed 540 days in space, while his twin brother Mark will have completed 54. The launch of an identical twin with a ten-fold difference in space exposure provides an opportunity to assess the genetic, proteomic and epigenetic effects of spaceflight. HRP and the National Space Biomedical Research Institute (NSBRI) jointly solicited investigations targeted at understanding the impact of spaceflight on these identical twins. Ten studies were selected. The studies will investigate differences in deoxyribonucleic acid (DNA) (sequence, telomere length, epigenetics (e.g., methylation), ribonucleic acid (RNA), protein, metabolites); the 'microbiome' (i.e., the bacteria) that live in our gut; whole body physiology; and mental performance (e.g., the ability to mentally manipulate spatial objects). Studying identical twins potentially allows scientists to separate "nature versus nurture." In this case, we will look at the effect of spaceflight on one twin while the other twin remains on earth. Since the twins have essentially almost identical DNA, and DNA controls the biomolecular workings of the body, then any difference is likely due to spaceflight and not because the two subjects are genetically distinct. Although the Twins Study does not specifically address an HRP risk, it will provide additional insight into the effects of spaceflight that may allow a better understanding of multiple risks. Four of the ten investigations are part of tasks directly mapped to HRP risks in the IRP and are marked "Twins Study" in the risk updates throughout Section 3.

The Human System Risk Board (HSRB) continues to be an important aspect of human system risk management. Since 2012, the HSRB established a new process and new risk scales based on defined operational and long term health consequences and the likelihood of their occurrence (see Figure 2).

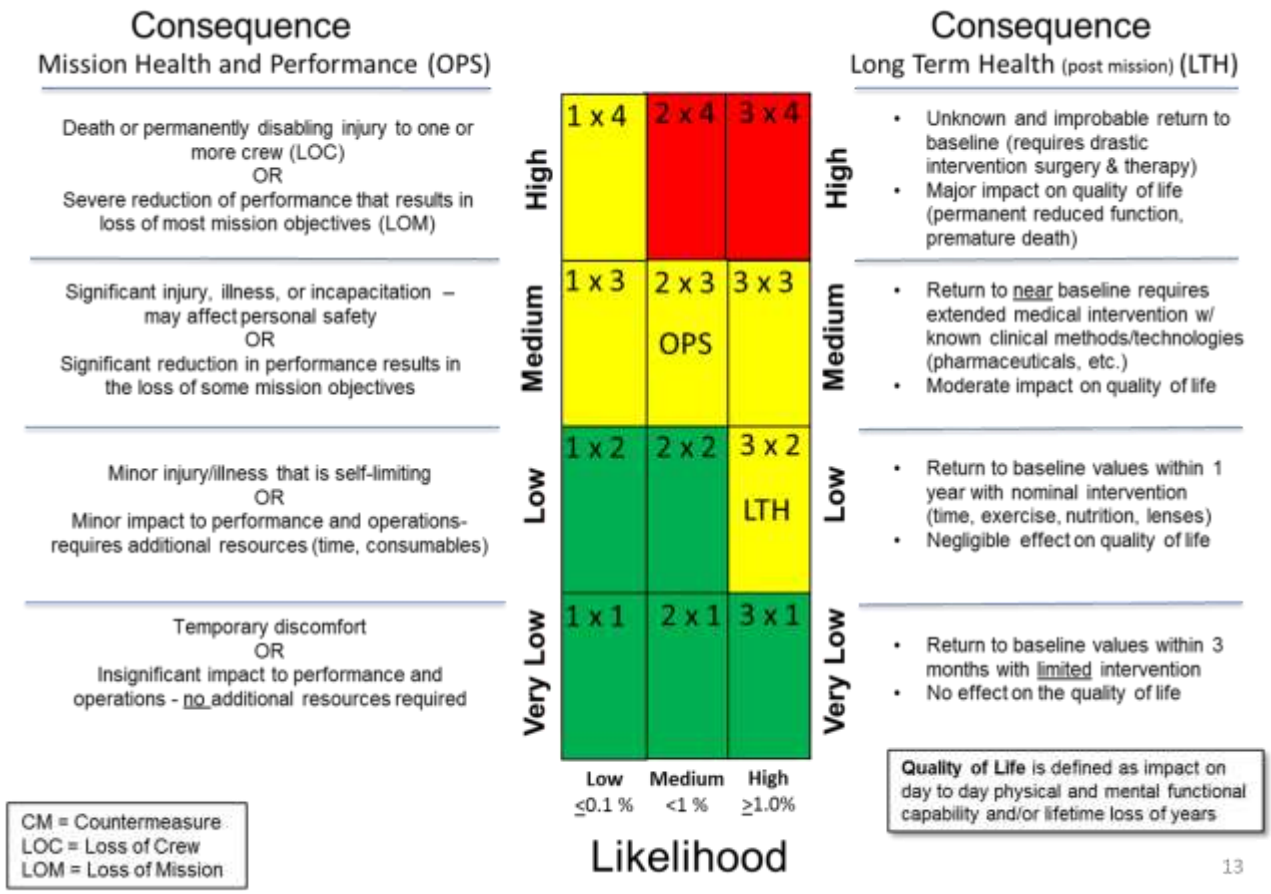


Figure 2: HSRB Risk Scale

All HRP risks were re-evaluated against the new HSRB criteria and are in the process of being reviewed and baselined by the HSRB. The re-evaluation resulted in the identification of new risks and different approaches for some of the existing risks previously covered in this document. Table 1 identifies the changes in the risks covered in this document since 2012.

Risks that now require the use of ISS:
• Risk of inadequate human-computer interaction
• Risk of injury from dynamic loads
• Risk of performance errors due to training deficiencies
Risks that no longer require ISS:
• Risk of radiation carcinogenesis from space radiation
• Risk of compromised EVA performance and crew health due to inadequate EVA suit systems
• Risk of renal stone formation
• Risk of decompression sickness

Table 1. Changes in Risks that Require ISS

Currently, HRP is conducting approximately 14-16 studies per increment pair. Each crewmember has a unique complement of research they have consented to perform. Results are made publicly available as soon as practical, while maintaining priority of publication for the investigators if practical. Results are published in scientific and technical journals, NASA technical publications, and the HRP Evidence Reports. HRP Evidence Reports are available at http://humanresearchroadmap.nasa.gov/Evidence/.

NASA is continually updating both its strategic and tactical plans to optimize ISS experiment throughput and maximize crew participation in biomedical flight experiments. The HRP strategic plans associated with each risk area are contained in the Integrated Research Plan (IRP). The IRP is available via the Human Research Roadmap (http://humanresearchroadmap.nasa.gov/) and is updated on at least an annual basis. The tactical ISS plans list the current and planned human research experiments that will be undertaken in each ISS increment and is updated continually throughout the year. The implementation of this plan is documented in Appendix A.

The following sections describe the risks, progress since 2012, and updates to planned activities that require use of the ISS. After each risk title, the responsible HRP Element is identified. The Elements of HRP are Space Radiation (SR), Human Health Countermeasures (HHC), Exploration Medical Capability (ExMC), Behavioral Health and Performance (BHP), Space Human Factors and Habitability (SHFH), and ISS Medical Projects (ISSMP). All tasks highlighted in these sections follow the format of "*IRP long task title* (*Fly-off Plan task title*)."

Appendix A traces the IRP, Rev F, ISS experiments to HRP risks, Appendix B lists select products and publications from work on ISS since 2012, and Appendix C lists acronyms and abbreviations used in this document.

3 HUMAN HEALTH AND PERFORMANCE RISKS

3.1 Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities (ExMC)

Mission architecture limits the amount of equipment, consumables, and procedures that will be available to prevent, diagnose, and treat medical conditions during human exploration missions. Given these constraints, there is a possibility of unacceptable health and mission outcomes. Allocated resources, such as mass, power, volume, and crew time must be used efficiently to optimize the delivery of in-flight medical care.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

To overcome the challenges of prevention, diagnosis, and treatment of medical conditions during exploration missions, NASA will develop and test technologies using ISS to make the best possible use of the limited mass, volume, power, and crew training time.

Figure 3. NASA astronaut Mike Fossum, Expedition 29 commander, performs a leg muscle self-scan in the Columbus laboratory of the International Space Station using the Ultrasound 2 (USND-2) unit and Video Power Converter (VPC) hardware.

Technologies, which are smaller, lighter, reliable, and more user-friendly, will be required to fit within the limited space of exploration vehicles. Specifically, ISS will be used to demonstrate systems for providing medical oxygen, medical suction, in-flight laboratory analysis, electrocardiogram (ECG) using dry electrodes, and medical inventory tracking. Currently on the ISS, the crewmember's source of contingency oxygen, if needed, is 100% continuous oxygen from the onboard oxygen tanks. To avoid a local oxygen bubble near the crewmember, a fan is used to disperse the oxygen-rich air. The oxygen limits of the spacecraft could also be exceeded within hours. For future spacecraft, a contingency system, which concentrates the oxygen within the cabin environment and safely provides the required concentration of oxygen to the crewmember, will be necessary. The ISS will be used to demonstrate an oxygen concentration capability, which is small, lightweight, and requires low power usage.

A medical suction and fluid containment system will also be demonstrated on the ISS to ensure that the gravity-independent technology is capable of meeting the needs for future missions. Medical suction capability for exploration missions should be more robust than the current manual system allows, which limits suction levels and flow rates that may be necessary to appropriately clear biofluids. In addition, the collection mechanism does not separate gas from fluid, limiting its usage volume.

ISS will also be important to establish that blood and urine analytical devices can be operated routinely in the microgravity environment. Analyzing bodily fluids (urine, blood, saliva) in-flight will reduce launch and return mass and volume, and it will provide the data near real-time in lieu of post-flight results. A system to perform real-time laboratory analyses is necessary to meet these requirements.

The monitoring of crewmembers' physiologic data can indicate a medical problem during intravehicular and extravehicular activity. For an exploration mission, NASA needs a health monitoring system of small biomedical sensors that can measure, store, and transmit data and that utilize less consumables than current modalities. One device of interest is the ECG with re-usable dry electrodes. The ISS will be used to demonstrate the success of the technology, which will be aided by the use of a comfortable garment that neatly places each dry electrode in the appropriate location for measurement.

Progress in addressing the risk.

In 2013, an electronic stethoscope carried on the ISS by JAXA was studied by NASA astronaut Tom Marshburn and nine other physicians on the ground. Results showed that this stethoscope can be used to successfully auscultate, record, and transmit body sounds in the noisy ISS environment. As missions aim to explore further from Earth, telemedicine will play a larger role in medical care. This technology will be important to ensure that the medical ground support has diagnostic quality auscultation recordings. A Medical Consumables Tracking (MCT) system will be launched to ISS in 2015 to demonstrate the use of radio frequency identification (RFID)

technology to electronically track consumable contents within an ISS medical kit and report the information to the ground to determine usage over time. This system will reduce the need for manual inventories by the crew via visual inspection or digital photography. In turn, the accurate inventory of the medical kits will ensure that the crew's medical equipment is not under- or oversupplied and that they house the appropriate contents for the crew to support their mission and maintain their health.

Planned research to support **Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.2 Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (BHP)

Cognitive and behavioral issues are inevitable among groups of people, no matter how well selected and trained. Spaceflight demands can heighten these issues. The extended duration and the isolated, extreme and confined environments of future missions present the possibility that adverse cognitive and behavioral conditions or mental disorders could develop should adverse cognitive and behavioral conditions go undetected and unmitigated.

Figure 7. Crewmembers participating in Journals use laptops aboard the ISS to make entries of their thoughts for the day. The focus of the Journals investigation is to help the crew cope with isolation during long duration exploration and to provide information on issues affecting crew cognitive and behavioral health.

Scientific studies demonstrate, that if left unmitigated, issues, such as those listed below, can erode individual mood, motivation, morale and performance.

- Worry/anxiety over conditions of mission or on Earth
- Insufficient training (pre-, in- or post-flight) relating to cognitive and behavioral health
- Depression/loneliness due to isolation from friends and family
- Chronic stress from continued high performance demand while living in an isolated, confined, and extreme environment
- Lack of proper sensory and cognitive stimulation due to monotony, confinement, and isolation

Acute or chronic conditions during spaceflight and environmental effects, such as microgravity and radiation, may also exacerbate the risk of developing a psychiatric disorder from these adverse cognitive or behavioral conditions.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS is used to emulate some of the aspects of the transit environment to Mars to further characterize the risk of cognitive and behavioral conditions and psychiatric disorders that can develop during long-duration space travel so that validated and reliable tools that predict, detect, and assess this risk can be identified and/or developed, and the appropriate countermeasures can be developed.

Progress in addressing the risk.

The first data collection via audio recording was successfully implemented on ISS as an alternative to electronic written records for “Behavioral Issues Associated with Long Duration Space Missions: Review of Astronaut Journals - Extension (Journals (6-crew)),” a study that collects information on behavioral and human factor issues that are relevant to living in the confined and isolated environment of a spacecraft. This study focuses on the journals of astronauts of six-person ISS crews, in comparison to the previous Journals study that focused on members of two and three-person ISS crews. Results support the design of equipment, habitat and processes to sustain performance during extended-duration missions. A comprehensive, software-based, neurocognitive toolkit is being developed to permit evaluation of a full range of

cognitive functions using brief (1-5 min), validated procedures ("Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue (Cognition))." It is slated to begin testing on the 1YM mission. The toolkit will also be used as part of the Twins Study to evaluate cognitive changes in response to acute and prolonged exposure to microgravity and other spaceflight stressors on the same astronaut before and in-flight as well as between an astronaut on the ground and an astronaut in space. A new experiment "Standardized Behavioral Measures for Detecting Behavioral Health Risks during Exploration Missions (Standardized Behavioral Measures)" has recently been selected for funding to provide standardized cognitive and behavioral measures aboard for future ISS missions starting in 2017, including those that are being used in the current Journals and Cognition experiments.

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders										

3.3 Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team (BHP)

Risk of performance errors due to poor team cohesion, inadequate selection/team composition, inadequate training, and poor psychosocial adaptation is yet undetermined. Although research on teams has been well documented and identifies strong relationships among factors within the general population, the vast majority of this research is conducted using terrestrial samples over very short durations. Little to no quantitative data is available that specifically addresses issues that relate to an astronaut population in a space environment.

Quantitatively identifying factors that are salient to defining team functioning in the astronaut population under spaceflight conditions will provide direction to future operational research studies, which are necessary to reduce risk, as well as inform current operations.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS will be used for flight validation of methods and technologies, including sociometric badges, a standardized package of behavioral measures including measures of team functioning, and lexical analysis technology, that can be used to monitor individuals and crews for issues related to poor team cohesion, inadequate selection/team composition, inadequate training, and poor psychosocial adaptation. In addition, the ISS crews will be used to collect data and gather evidence on the effects of increased autonomy on group cohesion and performance and the effects of long periods of task entrainment on individuals shifting to and from tasks requiring teamwork. The data will help determine the most effective methods for mitigating conflict and low morale, and investigate countermeasures to optimize team performance (e.g., on-board training, team debriefs).

Figure 14. Five of the six Expedition 36 crewmembers are pictured in the International Space Station's Kibo laboratory during a daily planning conference.

Progress in addressing the risk.

Much of the research required to address specific knowledge gaps are better implemented using ground-based analogs or laboratories. Several studies are currently on-going in laboratories and the new Human Exploration Research Analog (HERA), which will lead to the development and ground validation of training and monitoring tools that will then be validated on the ISS.

Flight data collection has completed for "Assessing the Impact of Communication Delay on Performance: An Examination of Autonomous Operations Utilizing the International Space Station (Comm Delay Assessment)" to determine whether communication delays impact individual and crew performance of tasks and whether that impact is related to task criticality or novelty.

Planned research to support	15	16	17	18	19	20	21	22	23	24
Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team										

3.4 Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload (BHP)

Evidence indicates that fatigue has been an issue for many crewmembers dating back to the Apollo missions. Research using objective measures demonstrates that, despite countermeasures, chronic sleep loss and circadian misalignment was common on the Shuttle and on ISS. Sleep loss, circadian desynchronization, extended wakefulness and work overload occur to some extent for ground and flight crews, prior to and during spaceflight missions. Ground evidence indicates that fatigue, as experienced by ground and flight crews, may lead to performance errors, which could potentially compromise mission objectives and consequently the mission itself. Additionally, there is a growing body of evidence indicating that health decrements are associated with sleep loss, circadian misalignment, and work overload. Understanding the nature of sleep in space and developing mitigation strategies is, therefore, relevant in the current context and in preparing for future space missions. Efforts are needed to identify the environmental and mission conditions that interfere with sleep and circadian alignment, as well as to identify the individual vulnerabilities and resiliencies to sleep loss and circadian desynchronization. Research areas to mitigate this risk also include development of standardized measures of sleep, circadian phase, workload and performance; light therapy for circadian alignment, phase shifting, alertness and behavioral health; individualized protocols for sleep-wake medication use; validated models of performance based on sleep-wake data to inform scheduling decisions and countermeasure implementation; and other evidence-based means to improve individual circadian phase, sleep quantity and quality, and workload.

Figure 19. Jeffrey Williams, Expedition 22 Commander, performing Reaction Self Test (PVT) in the U.S. Laboratory.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Terrestrial evidence demonstrates that configurations of specific light intensity and wave length, administered at certain times and for appropriate durations, can serve as a potent countermeasure for maintaining circadian alignment, hastening circadian shifting, and promoting optimal sleep. Given physiological changes that have been shown in the microgravity environment, the ISS will be used to assess artificial and transmitted light exposure on circadian rhythms and performance to validate lighting as a countermeasure in-flight. A planned investigation, led by the Pharmacology discipline, seeks to evaluate the pharmacokinetics and pharmacodynamics of commonly used sleep medications in the ISS environment. Planned studies, using standardized measures on the ISS, will help to characterize individual vulnerabilities and resiliencies to sleep loss and circadian desynchronization in the spaceflight environment, as well as further characterize workload. The ISS will be used to collect data and subsequently validate a self-assessment tool for cognitive function and fatigue and other means to improve sleep quality and reduce fatigue. Rodent studies may help further identify whether changes in the eye observed in spaceflight may have a circadian implication. The ISS is required to investigate the sleep-related

issues associated with microgravity and to ensure the tools and methods are appropriate for the spaceflight environment.

Progress in addressing the risk.

Findings from the decade long "Sleep-Wake Actigraphy and Light Exposure During Spaceflight (Sleep Long)" investigation on 64 Shuttle and 21 ISS astronauts were published in the Lancet Neurology. Wrist actigraphy and daily logs showed that astronauts slept less than six hours per night nearly 50% of the time for both ISS and Shuttle flights and that use of sleep medications was common. A study using the "Psychomotor Vigilance Test (PVT) on ISS (Reaction Self Test (PVT))" was completed for 24 six-month crewmembers in 2014. The portable 3-minute test enabled astronauts to monitor the effects of fatigue on performance, as well as evaluated the extent to which performance feedback is perceived as useful for assessing performance capability. Both investigations will be conducted during the 1YM to determine if sleep deprivation or performance changes from six months to one year.

Planned research to support **Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.5 Risk Factor of Inadequate Nutrition (HHC)

Adequate nutrition is a key factor in all physiological functions and spaceflight has been shown to alter many of these physiological functions in humans. Countermeasures for individual systems may alter the nutritional status with a possibility that inadequate nutrition will compromise crew health, including endurance, muscle mass and strength, immune function, bone mass and strength, cardiovascular (CV) performance, gastrointestinal function, endocrine function, and ocular, psychological and physical health, and the ability to mitigate oxidative damage. In general, nutritional risks increase with duration of exposure to a closed (or semi-closed) food system. Understanding nutrient requirements in micro- or partial gravity environments and the effect of countermeasures on nutrient requirements is critical to ensure crew health and safety and mission success. Provision of these nutrients in safe amounts (neither high nor low) depends on provision of appropriate, palatable foods with the stability of nutrients for the duration of the mission, actual intake of the nutrients, and knowledge that countermeasures are not altering requirements. It is critical that crewmembers be adequately nourished before and during missions. Critical research areas within this risk include validation of the correct nutritional needs, assessment of the stability of nutrients during long duration flight, correct packaging and preservation techniques, effects of countermeasures on nutrition, and use of nutrients as countermeasures.

Figure 4. Japan Aerospace Exploration Agency astronaut Akihiko Hoshide, Expedition 32 flight engineer, poses for a photo after undergoing a generic blood draw in the Columbus laboratory. These blood samples are used for various experiments, including ones on nutrition.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS is used to improve the nutritional content of the food when consumed, identify the variety, acceptability, and ease of use for long-duration missions, validate correct nutritional needs, and quantify the stability of nutrients during long-duration flight. The ISS is required to ensure that the data represents space normal and for validation of potential countermeasures to inadequate nutrition. Flight validation of nutritional requirements was completed in 2013, and updates to the nutrition standard will be made in 2018.

Progress in addressing the risk.

The recently completed “Nutritional Status Assessment: SMO-016E (Nutrition/SMO-016E)” study yielded numerous insights regarding human nutrition in spaceflight. One finding was that iron stores increase early in spaceflight and then return to pre-flight concentrations by the end of a six month mission. Increased iron stores during flight were associated with increased oxidative damage to DNA, and also correlated with bone loss. Crewmembers that consumed more iron had a greater iron response during flight (and a greater oxidative damage, and regional bone loss). Additionally, data from the Nutrition SMO also showed that increased urinary calcium excretion during flight was the source of clogging of the ISS Urine Processor Assembly (UPA). Continued tracking of urine calcium concentrations showed that recommendations to increased astronaut fluid intake were sufficient to maintain a 74% water recovery rate. These data were utilized by the ISS Program to make decisions regarding operational limits for the UPA. A new flight study,

the “Space Biochemistry Profile (Biochemical Profile)” (*Twins Study*) will continue to provide a broad spectrum of biochemistry profiles from blood and urine to support operational and research activities.

The “Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Space Flight and Recovery (Pro K)” experiment concluded flight operations in late 2014, with final sample return and post flight data collection planned for 2015. This effort seeks to examine the relationship between dietary animal protein and potassium and effects on acid/base balance and bone health. Other systems (e.g., muscle, renal) will likely also benefit from this project.

Working with the Space Food Systems Lab, efforts continue to develop and fly a healthier food system, one focused on several nutrients known to provide health benefits. This integrated approach would maximize the remaining time on ISS for this type of research and would likely have benefits for many (if not all) physiological systems, while also benefitting morale and performance. Studies are planned for the future to further clarify the impact of nutrition on other risks.

Planned research to support **Risk Factor of Inadequate Nutrition**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.6 Risk of Adverse Health Event Due to Altered Immune Response (HHC)

Human immune function is altered during and after spaceflight, but it is unclear if this change leads to an increased susceptibility to disease. Reactivation of latent viruses has been documented in crewmembers, though this reactivation has not been directly correlated with immune changes or with observed disease and is usually asymptomatic.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

ISS will be used to characterize the magnitude and specific types of immune dysregulation. These data are necessary to ascertain any clinical risks to crewmembers that may be present, related to immune dysregulation, during deep space exploration class missions. The ISS will be used to develop and validate an immune monitoring strategy consistent with operational flight requirements and constraints. Following terrestrial development, ISS will be used to validate potential countermeasures (e.g., benign nutritional supplements or possibly pharmacological interventions) to mitigate any adverse effects of spaceflight on the immune system.

Progress in addressing the risk.

Figure 17. European Space Agency astronaut Andre Kuipers, Expedition 30 flight engineer, prepares vials in the Columbus laboratory of the International Space Station for venous blood sample draws during an immune system investigation.

Results from "Validation of Procedures for Monitoring Crewmember Immune Function (Integrated Immune)" indicate that some alterations in immunity persist during spaceflight and are not merely related to the transitional stress of launch or landing. Ongoing immune dysregulation and reduced immune cell function, in conjunction with elevated radiation exposure and limited clinical care, may increase specific clinical risks for crewmembers during exploration-class space missions. Depressed immune responses can result in asymptomatic viral shedding, which means dormant viruses in the body reawaken, but without symptoms of illness. Heightened immune activity can result in increased allergy symptoms and persistent rashes. Studies, which will begin on ISS within the next several years, include characterization of innate immune function, the effects of hypoxia on immune function during spaceflight, and assessment of accelerated telomere shortening and changes in telomerase activity associated with spaceflight (*Twins Study*).

Planned research to support **Risk of Adverse Health Event Due to Altered Immune Response**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.7 Risk of Early Onset Osteoporosis Due to Spaceflight (HHC)

Osteoporosis is a skeletal syndrome characterized by low bone mass and severe structural deterioration. This condition can be due to aging (Primary Osteoporosis) or to extrinsic factors (Secondary Osteoporosis). Spaceflight-induced bone loss is classified as the latter. Bone mineral loss occurs in microgravity due to unloading of the skeletal system and is monitored by evaluating the difference in bone mineral density (BMD) measured before and after a spaceflight mission of at least 30 days duration. For the typical four to six month mission, the averaged loss rate is approximately 1% per month. It is unclear whether this decline in bone mineral density will stabilize at a lower level, and at what duration of microgravity exposure this would occur. It is unknown if fractional gravity, present on the moon and Mars, would mitigate the loss. Animal models of fractional weight-bearing, however, suggest that bone mineral declines proportionally to the fraction of 1-g weight-bearing. Likewise, the impact of multiple long-duration missions or of cumulative time in space is not yet established. Space exposure could be a risk factor for Secondary Osteoporosis after return to Earth and could put crewmembers at greater risk of osteoporosis-related, low trauma fractures at an earlier age than expected for a terrestrial peer group. Greater understanding of the mechanisms of bone atrophy in microgravity, and for recovery after return, is necessary to frame this risk, as well as to understand how current and future osteoporosis treatments may be employed. This risk deals specifically with the likelihood of developing post-mission osteoporosis.

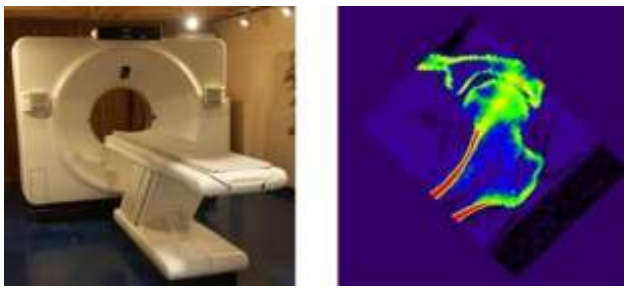


Figure 8. Representative image of a clinical Quantitative Computed Tomography [QCT] instrument (left side) with its capability of detecting the transmission of x-rays in hip bone over three dimensions. Representative QCT scan of hip (right side) with mineral-dense cortical bone in red and the trabecular "spongy" bone compartment in blue.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

ISS is required to evaluate whether spaceflight-induced changes to bone persist after return, which could predispose astronauts to premature osteoporosis. The ISS will be used to validate effective nutritional, pharmaceutical and exercise countermeasures to mitigate physiological deconditioning and protect against bone changes during spaceflight.

Progress in addressing the risk.

Sixteen participating subjects have completed the in-flight and almost all post-flight protocols for the nutritional study, “Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Space Flight and Recovery (Pro K).” This investigation has examined the hypothesis that a diet with a decreased ratio of animal protein to potassium will lead to decreased bone resorption and decreased percentage of bone mineral loss during flight. These data could provide the necessary foundation to make dietary recommendations to minimize the extent of bone loss during spaceflight exploration. The last subject is scheduled for completion in FY 2015.

In 2014, the "Feasibility Study: QCT Modality for Risk Surveillance of Bone - Effects of In-flight Countermeasures on Sub-regions of the Hip Bone (Hip QCT)" completed pre- and post-flight quantitative computed tomography (QCT) scanning of the hips in ISS astronauts. This study described the effects of pharmacological and resistive exercise countermeasures to space-induced changes to hip structure. Structural parameters are known contributors to hip bone strength and hip fracture risk above and beyond bone mineral density.

HRP has two additional ongoing ISS investigations to assess nutritional countermeasures to changes in bone metabolism and a planned experiment to study mechanisms for bone loss during spaceflight using a well-characterized mouse model.

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of Early Onset Osteoporosis Due To Spaceflight										

3.8 Concern of Intervertebral Disc Damage Upon and Immediately after Re-Exposure to Gravity (HHC)

Evidence from medical operations indicates that astronauts have a higher incidence of intervertebral disc (IVD) damage than the general population. Extended exposures to microgravity (and possibly fractional gravity) may lead to an increased risk of spinal nerve compression and back pain. Lengthening of the spine has been shown to occur during exposure to microgravity and may lead to IVD damage or other detrimental changes to the IVD, such as protrusion, herniation, degeneration or tear. Muscle weakness, muscle atrophy, and postural disturbances associated with exposure to microgravity may also be contributors. Although there appears to be a correlation between IVD damage and spaceflight, a causal relationship has yet to be definitively established.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Additional evidence will be gathered from ISS crewmembers in order to establish whether the lengthening of the spine exacerbates the risk for IVD damage with loading. The ISS will be used to determine the extent of this problem, and the data will guide the design of re-entry and post-flight protocols, as well as future re-entry spacecraft. If significant issues are found, the ISS will be required to validate countermeasures.

Progress in addressing the concern.

The "Sonographic Astronaut Vertebral Examination (Spinal Ultrasound)" study was completed in 2014 and the "Risk of Intervertebral Disc Damage After Prolonged Spaceflight (Intervertebral Disc Damage)" was initiated in 2013. The purpose of these studies is to understand what causes spontaneous back pain during spaceflight and disc herniation after return to Earth.

Figure 16. In the International Space Station's Columbus laboratory, NASA astronaut Chris Cassidy, Expedition 36 flight engineer, performs an ultrasound on European Space Agency astronaut Luca Parmitano, flight engineer, for the Spinal Ultrasound investigation.

The Intervertebral Disc Damage study is describing the disc structure and looking for signs of tissue degradation before and after ISS missions to see if spaceflight might be causing changes that could lead to injury. State-of-the-art imaging technologies are being used to evaluate the lumbar discs of 12 astronauts before and after prolonged spaceflight. The Spinal Ultrasound study examined the anatomic and compositional changes in the vertebrae during long-duration spaceflight. Ground-based pre- and post-flight magnetic resonance imaging (MRI) and high fidelity ultrasound, combined with in-flight ultrasound, was used to capture the progression of changes, as well as characterize and assign a mission health risk to microgravity-associated spinal alterations for back pain and injury.

Currently, changes seen immediately following spaceflight indicate a risk of IVD damage. However, because the etiology of the changes is unknown, both of the above studies help to define the extent of the problem and its relationship to space exposure, which is presently a

major knowledge gap in this area. Data from these studies will determine the need for additional studies to develop and validate countermeasures.

Planned research to support **Concern of Intervertebral Disc Damage Upon and Immediately after Re-Exposure to Gravity**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.9 Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (HHC)

Bone mineral loss occurs in microgravity due to unloading of the skeletal system and is monitored by evaluating the difference in BMD measured before and after a spaceflight mission of at least 30 days duration. For the typical four to six month mission, the averaged loss rate is approximately 1% per month. It is unclear whether this decline in bone mineral density will stabilize at a lower level and at what duration of microgravity exposure this would occur. It is unknown if fractional gravity, present on the moon and Mars, would mitigate the loss. Animal models of fractional weight-bearing, however, suggest that bone mineral declines proportionally to the fraction of 1-g weight-bearing. Likewise, the impact of multiple long-duration missions or of cumulative time in space is not yet established. A Probabilistic Risk Assessment model for bone fracture suggests that the risk for fracture is due to the total number of loading events encountered by an astronaut over a mission. Hence, the probability of bone fracture during an ISS mission is acceptable, but increases with missions of longer duration and with more frequent loading activities. The risk of fracture during a mission cannot be accurately estimated until the condition of bones and probabilities of bone overloading are better defined.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Pre- and post-flight data will be gathered from ISS crews to supplement the current Space Human Health bone standard, which is based upon bone mineral density. Skeletal outcomes with some validation as fracture predictors in terrestrial studies will be recommended to monitor the integrity of the hip in astronauts during and after spaceflight. A flight study will also be conducted to assess spine health before and after ISS missions. The ISS will be used to validate the efficacy of exercise regimens to mitigate physiological declines in space using these expanded measures of skeletal health and function for surveillance.

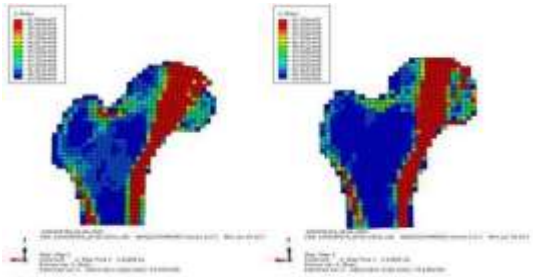


Figure 20. Representative analyses of hip QCT images by Finite Element Modeling. This mathematical model of the 3-D hip structure can be used to calculate the force required to fracture the hip, based upon the 3-D geometry and mechanical properties computed from each astronaut's QCT bone density. These plots illustrate the von Mises stress distributions in two proximal femora of males representing typical control subjects (left) and fracture subjects (right).

Progress in addressing the risk.

Finite Element models of the hip are being evaluated as a surveillance tool to monitor changes in hip bone strength in response to in-flight bone countermeasures. The analysis of these Finite Element Models, generated from data from the "Feasibility Study: QCT Modality for Risk Surveillance of Bone - Effects of In-flight Countermeasures on Sub-regions of the Hip Bone (Hip QCT)," will describe how in-flight countermeasures influence hip bone strength and/or whether rehabilitation after return to Earth is sufficient to restore crewmembers to preflight status. Unlike the current medical test, hip bone strength, derived from the analysis of Finite Element models, is an index that integrates multiple factors associated with fracture (e.g., bone mineral density, bone geometry, loading, and bone material properties).

Planned research to support **Risk of Bone Fracture due to Spaceflight-induced Changes to Bone**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.10 Risk of Orthostatic Intolerance During Re-Exposure to Gravity (HHC)

Post-flight orthostatic intolerance, the inability to maintain an appropriate blood pressure while in an upright position, is an established, space-related medical problem. The cardiovascular system adaptations during spaceflight have resulted in orthostatic intolerance upon re-exposure to gravity in some crewmembers. Orthostatic intolerance has been shown to progress to presyncope (inability to maintain cerebral perfusion) in ~20% of Shuttle astronauts and up to 80% of long-duration crewmembers during a post-flight tilt test. Currently, in-flight countermeasures are not effective in all crewmembers; in particular, women are more susceptible to post-flight orthostatic intolerance than are men.

Figure 9. Anti-gravity suits. The US antigravity suit (left) contains air bladders, which are pressurized to produce compression. The Russian antigravity suit, Kentavr (right), utilizes an elastic compressive material and lacings to produce compression.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

To better understand orthostatic intolerance, the ISS will be used to determine the magnitude and importance of cardiac atrophy associated with long duration spaceflight, and to relate this atrophy to measures of physical activity and cardiac work in-flight. Researchers will identify changes in ventricular conduction, depolarization, and repolarization before, during and after long duration spaceflight, and relate these to changes in cardiac mass and function.

A number of countermeasures have been successfully identified and are under study for eliminating or minimizing the risk of orthostatic intolerance upon landing (e.g., fluid loading, re-entry compression garments, post-flight compression garments, etc.). The currently performed countermeasure for orthostatic intolerance, fluid loading, has been shown to improve a Cardiac Stress Index after short-duration Space Shuttle missions, but does not completely restore plasma volume. The ISS will be used to improve this countermeasure.

Progress in addressing the risk.

Results from "Evaluation of Commercial Compression Garments as a Countermeasure to Post-Spaceflight Orthostatic Intolerance (Alternative Compression Garments)," conducted on Shuttle crewmembers, suggests that the use of compression garments can significantly improve orthostatic tolerance in short-duration crewmembers, and a follow-on study corroborates those results in a bed rest cohort. These alternative (gradient) compression garments will be tested for efficacy in long-duration ISS crewmembers as a part of the "Recovery of Functional Performance Following Long Duration Space Flight (Field Test)" study.

Planned research to support	15	16	17	18	19	20	21	22	23	24
Risk of Orthostatic Intolerance During Re-Exposure to Gravity										

3.11 Risk of Cardiac Rhythm Problems (HHC)

Heart rhythm disturbances have been seen among astronauts. Some of these may have been related to cardiovascular disease, but it is not clear whether this was due to pre-existing conditions or effects of spaceflight. It is hoped that advanced screening for coronary disease has greatly mitigated this risk. Other heart rhythm problems, such as atrial fibrillation, can develop over time, necessitating periodic screening of crewmembers' heart rhythms. Beyond these terrestrial cardiac risks, some concern exists that prolonged exposure to microgravity may lead to heart rhythm disturbances. Although this has not been observed to date, further surveillance is warranted.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Figure 15. Japan Aerospace Exploration Agency astronaut Koichi Wakata, Expedition 38 Flight Engineer, uses ultrasound to perform self-scans of the carotid artery, right brachial artery, and heart while being remotely guided from the ground for the Cardio Ox investigation.

ISS is required as the Mars transit analog for initial work to define "space normal" and subsequent countermeasure validation. Scientists will use the ISS to measure the time course of changes in cardiac structure and function over six months of spaceflight. They will define the potassium, magnesium, and phosphorus changes in relation to cardiovascular issues.

Progress in addressing the risk.

The "Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capacity, and Risk of Cardiac Arrhythmias (Integrated Cardiovascular Study)" was completed in 2013. Preliminary results indicate that given current training programs and ground-based interventions, cardiac morphology (right and left ventricular mass and volume) and function are preserved after six months of spaceflight. Long duration spaceflight may exacerbate cardiac arrhythmias in those crewmembers with existing pathologies.

In 2013, the first in-flight sessions for "Defining the Relationship Between Biomarkers of Oxidative and Inflammatory Stress and Atherosclerosis Risk in Astronauts During and After Long-Duration Spaceflight (Cardio Ox)" (*Twins Study*) began collecting data to determine whether markers of oxidative stress and inflammation in the blood and urine are elevated in astronauts participating in long-duration spaceflight and whether they are related to changes in vascular structure and function, which may be precursors of cardiovascular disease. The combined Fluid Shifts study was selected for flight as a joint US/Russian investigation that will begin in-flight data collection in 2015. Although this study focuses on changes that occur in eye morphology and visual function, cardiac measures (such as cardiac output) that are relevant to the cardiovascular risk portfolio are being collected as well.

Planned research to support **Risk of Cardiac Rhythm Problems**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.12 Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance (HHC)

There is a growing body of research evidence, which suggests that skeletal muscles, particularly postural muscles of the lower limb, undergo atrophy and structural and metabolic alterations during spaceflight. However, the relationships between in-flight exercise, muscle changes, and performance levels are not well understood. Efforts should be made to try to understand the current status of in-flight and post-flight exercise performance capability and what goals/target areas for protection are needed for the in-flight exercise program.

Figure 10. NASA astronaut Chris Cassidy, Expedition 36 flight engineer, gets a workout on the Advanced Resistive Exercise Device (ARED) in the Tranquility node of the International Space Station.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

ISS will be required to evaluate and validate optimized exercise countermeasures and hardware (e.g., resistance exercise device, treadmill, cycle ergometer). Optimized countermeasures are those that need minimal exercise to free crewmember time for other tasks required for mission success and need minimal volume and hardware to maintain muscle mass, strength, and endurance. The ISS will be used to evaluate an integrated set of functional and physiological tests on returning crewmembers, and these tests will determine how post-flight changes in sensorimotor, CV, and muscle physiology impact post-flight functional performance. Computational tools will be generated that will be useful in quantification of the physiological cost of exploration tasks, including quantifying joint kinematics during treadmill locomotion on the ISS, to compare the data to treadmill locomotion on Earth and develop a computer model that will assess locomotion speed and external loading condition influence upon joint torque.

Progress in addressing the risk.

An engineering evaluation of a portable load monitoring device, the XSENS ForceShoe™, was initiated in July 2014 to evaluate it as a potential method to measure exercise loads on the Advanced Resistive Exercise Device (ARED) during exercise sessions on ISS.

The “Biomechanical Analysis of Treadmill Locomotion on the International Space Station (Treadmill Kinematics)” investigation compared hip, knee, and ankle sagittal motion trajectories, gait temporal kinematics, and ground reaction force parameters between exercise sessions in 1G and 0G. The effects of speed and bungee load on ground reaction force parameters were also examined. Results indicate that joint motion trajectories and gait temporal kinematics remained relatively consistent between 0G and 1G at a given speed. Ground reaction force parameters, however, were significantly decreased in 0G, but did increase with increased speed and bungee load. Furthermore, the relationship between peak ground reaction forces and speed and bungee load were subject-dependent, suggesting that individual variations exist in adaptation strategies to the microgravity environment. The data suggest that subject-specific relationships can be developed that allow practitioners to prescribe exercise that may more effectively recreate 1G-like ground reaction forces, and that subjects performing exercise at higher speeds obtain ground reaction forces similar to exercising at lower speeds on Earth.

The “Integrated Resistance and Aerobic Training Study (SPRINT)” is in the process of developing and testing new interval protocols designed to maintain bone and muscle, while reducing the time required for exercise. Once the exercise prescription is optimized, it will be used to validate new exploration exercise devices designed to provide similar loads to those on ISS, but within a much smaller resource foot print.

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance										

3.13 Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (HHC)

Figure 11. Japan Aerospace Exploration Agency astronaut Koichi Wakata, Expedition 38 flight engineer, performs a VO2max session for the SPRINT investigation while using the Cycle Ergometer with Vibration Isolation System (CEVIS) in the Destiny laboratory of the International Space Station. VO2max uses the Portable Pulmonary Function System (PPFS), CEVIS, Pulmonary Function System (PFS) gas cylinders and mixing bag system, plus multiple other pieces of hardware to measure oxygen uptake and cardiac output.

Astronauts' physical performance during a mission, including activity in microgravity and fractional gravity, is critical to mission success. In addition to reduced skeletal muscle strength and endurance, reduced aerobic capacity may put mission success at risk. Sustained sub-maximal activities (even walking on a planetary surface) could become difficult to perform given large enough decrements in aerobic capacity. Setting minimum fitness standards and measuring whether crew can maintain these standards will document the effectiveness of exercise regimens.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Aerobic capacity (VO2max) and cardiac output will be measured during and after long term spaceflight on ISS. In addition, the ISS will be used to optimize, and subsequently to validate, effective exercise prescriptions to mitigate physiological deconditioning during spaceflight, including aerobic capabilities as it relates to functional capacity and exercise volume, regimens, and equipment.

Progress in addressing the risk.

The HHC Element completed the "Maximal Oxygen Uptake (VO2max) and Submaximal Estimates of VO2max Before, During and After Long Duration International Space Station Missions (VO2 Max)" experiment designed to quantify the risk of reduced physical performance capabilities due to reduced aerobic capacity. Results from this investigation indicate that VO2 peak declines during the first few weeks of ISS missions and slightly recovers, but, as a group, ISS astronauts are still aerobically deconditioned at the end of their missions. Despite the average findings of our subjects, examination of the individual test results shows that some of the astronauts were able to attain VO2 peak values at or above pre-flight levels during their missions. Following ISS missions, aerobic capacity is reduced, but recovers over the 30 days following flight. The study also found that the current method of estimating aerobic fitness was unreliable when applied to an individual, thus an alternative method is recommended. The "Integrated Resistance and Aerobic Training Study (SPRINT)" will help ensure an exercise prescription that also maintains aerobic capacity.

Planned research to support **Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.14 Risk of Impaired Control of Spacecraft/Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight (HHC)

It has been shown that long duration spaceflight alters vestibular/sensorimotor function, which manifests as changes in eye-head-hand control, postural and/or locomotor ability, gaze function, and perception. The risk of impairment is greatest during and soon after g-transitions when performance decrements may have high operational impact (e.g., landing, immediate egress following landing). The possible alterations in sensorimotor performance are of interest for Mars. These changes have not been specifically correlated with real-time performance decrements. Thus, this risk must be better documented and vestibular/sensorimotor changes must be better correlated with performance issues.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Since long-duration operational scenarios are still to be determined, the ISS will be used to gather the data required to define the research that might be needed to enable anticipated long-duration mission operations. This data includes the Space Station Remote Manipulator System, docking, glove box operations, Soyuz landings, and performance neurosensory dysfunction. If countermeasures for Mars missions are warranted, the ISS, as the Mars transit analog, will be required for countermeasure validation. The ISS will be used to collect data to determine individual capability for rapid sensorimotor adaptation, develop a sensorimotor adaptability training program that can be integrated into astronaut pre-flight exercise programs, and enhance in-flight exercise programs to include a sensorimotor adaptability component. The ISS will be used to collect data on crew performance during operationally relevant functional tasks, and researchers will identify physiological systems that require countermeasures in order to preserve performance of functional tasks, as well as identify which physiological systems contribute the most to impaired performance on these functional tests. The ISS will also be used to investigate volumetric, structural and functional changes in task-relevant brain structures and map changes in brain structures to changes in performance of cognitive and functional tasks. Results from this study would link changes in cognitive and functional performance with the degree of neuronal remodeling and determine if structural changes persist for an extended time period.

Figure 18. Subject demonstrating the Seat Egress and Walk Test at Johnson Space Center, Houston, TX.

Progress in addressing the risk.

The final subjects for "Physiological Factors Contributing to Postflight Changes in Functional Performance (Functional Task Test (FTT))" returned for post-flight testing in 2014. This study previously collected pre- and post-flight data on seven short duration subjects, and upon completion of post-flight Baseline Data Collection (BDC) in 2014, data were collected on 13 long-duration subjects since Increment 22. Crewmembers were tested on an integrated suite of functional and physiological tests before and after long-duration spaceflight. The study identified critical mission tasks that may be impacted and mapped physiological changes to alterations in functional performance. Preliminary data showed that functional tests requiring a greater demand for dynamic control of postural equilibrium (e.g., fall recovery, seat egress/obstacle avoidance

during walking, object translation, jump down) showed the greatest decrement in performance. Functional tests with reduced requirements for dynamic postural stability (e.g., hatch opening, ladder climb, manual manipulation of objects and tool use) showed less reduction in performance. These data, along with a corresponding bed rest study, point to the importance of providing significant axial body loading during in-flight treadmill and resistive exercise along with pre- and in-flight balance training. The results will aid in the design of countermeasures that specifically target the physiological systems responsible for impaired functional performance. This study will continue collecting a subset of immediate post-flight data on crewmembers until the new joint NASA-Russian "Recovery of Functional Performance Following Long Duration Space Flight (Field Test)" investigation becomes operational during Increment 43/44. FTT will also be performed with a 1YM crewmember before and after the mission.

Planned research to support	15	16	17	18	19	20	21	22	23	24
Risk of Impaired Control of Spacecraft/ Associated Systems and Decreased Mobility Due to Vestibular/ Sensorimotor Alterations Associated with Spaceflight										

3.15 Risk of Ineffective or Toxic Medications Due to Long Term Storage (HHC) and Concern of Clinically Relevant Unpredicted Effects of Medication (HHC)

Because the human body undergoes a variety of physiological changes during spaceflight, there is a risk that terrestrial medications may not perform as expected when used during spaceflight. It could be that the spaceflight environment may require different therapeutic agents or prescribing tactics. Alterations in physiology due to spaceflight could result in unexpected drug action on the body (pharmacodynamics) or in unusual drug absorption, distribution, metabolism, or excretion (pharmacokinetics). The spaceflight environment may also have direct effects on stored drugs themselves, leading to premature inactivation or degradation of drugs.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk and concern.

The ISS will be used to perform pharmacokinetic, pharmacodynamic and medication storage studies in a spaceflight environment. There are no existing ground analogs that adequately reproduce the microgravity and radiation effects associated with spaceflight, as far as multi-system pharmacological measures are concerned.

Figure 12. NASA astronaut Michael Hopkins, Expedition 37 flight engineer, prepares to insert samples into a Minus Eighty Laboratory Freezer for ISS (MELFI) dewar tray in the International Space Station's Destiny laboratory.

Progress in addressing the risk.

ISS medications beyond or approaching their expiration dates have typically been removed from the supply chain and destroyed, but SpaceX Dragon missions have permitted return of these ISS-aged samples to Earth for laboratory analysis. Through this ad hoc mechanism, a few data points regarding stability of certain medications during extended on-orbit aging were collected. In order to prepare for longer duration missions, these data have been used to design a systematic examination of medication stability over longer time periods. This six year stability study is expected to begin in 2016.

Progress in addressing the concern.

Several tasks are ongoing or planned to address aspects of medication usage in flight. The "Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions (Dose Tracker)" investigation, selected for flight in 2014 and beginning data collection in 2015, is one of several existing iOS (Apple's mobile operating system) applications in development within HRP. Medication usage data will be collected from astronauts in-flight and compared to their medication usage prior to flight. This will permit a top-level examination of in-flight changes in pharmacokinetics (PK) and pharmacodynamics (PD), as well as unusual side effects. A more rigorous examination of spaceflight effects on PK/PD is planned for 2015-2019. This collaborative study involves

Figure 13. Dose Tracker application for iOS systems.

university researchers at Harvard and the University of Florida and will evaluate pharmacokinetics of six frequently used medications, both on the ground and in-flight, with simultaneous measurements of medication effects on one important aspect of PD during spaceflight missions, the sleep/wake system.

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of Ineffective or Toxic Medications Due to Long Term Storage and Concern of Clinically Relevant Unpredicted Effects of Medication										

3.16 Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations (HHC)

Some crewmembers on long duration ISS missions experienced ophthalmic anatomical changes and visual performance decrements of varying degrees, which are temporary in some cases and permanent in others. This constellation of eye-related signs and symptoms has been titled the Visual Impairment Intracranial Pressure (VIIP) syndrome. The pathophysiology underlying these changes is unknown and is under investigation by several studies, but is hypothesized to involve elevation of intracranial pressure (ICP) due to cephalad fluid shifts and elevated levels of carbon dioxide in the ISS atmosphere. Some experts hypothesize that the problem may be eye-centric. Observed physical findings in long-duration crewmembers include optic disc edema, choroidal folds, increased optic nerve sheath diameter and optic nerve kinking, and a posterior flattened globe.

Visual acuity changes occur at a rate much higher than expected in spaceflight crews. Persistent increased post-flight ICP has been inferred in several cases, consistent with a root cause of intracranial hypertension (IHT) possibly secondary to microgravity-induced fluid shifts. The mechanisms that cause IHT in microgravity are not known, and the processes by which eye damage occurs, as a result of IHT, are not well understood. Decreased visual acuity, IHT, and other findings are present months and, in some cases, years, after return, indicating that damage may be permanent. Visual acuity and some changes have also been noted in short-duration crewmembers, indicating that the process starts early in spaceflight, although this group has not been closely examined. It is unknown if fractional gravity would mitigate the hazard. Likewise, the impact of multiple missions or of cumulative time in space is not yet established. Greater understanding of the mechanisms for these eye changes is necessary in order to mitigate this condition.

Figure 21. Expedition 36/37 flight engineer Karen Nyberg of NASA uses a fundoscope to take still and video images of her eye while in orbit. This was the first use of the hardware and new vision testing software.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Space Medicine Operations conduct eye and vision evaluations on all crewmembers before, during and after flight. Several modalities for improved in-flight measurements of ocular structure and function have been developed and launched (e.g., visual acuity testing software, ocular ultrasound, improved fundoscopy, and optical coherence tomography (OCT)). While significant progress has been made by Space Medicine Operations on the in-flight hardware that evaluates ocular structure and function, VIIPs research arm is working on the identification and implementation of techniques and technologies for measuring in-flight ICP, either invasively or noninvasively. Improved diagnostic tools are an important step toward understanding the etiology and risk factors that contribute to VIIP development.

Progress in addressing the risk.

In 2013, NASA initiated the “Prospective Observational Study of Ocular Health in ISS Crews (Ocular Health)” to systematically gather physiological data to characterize the Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations on crewmembers assigned to a

six month ISS increment. The data collected will mirror testing performed by Space Medicine Operations, but with an increase in the frequency of in-flight and post-flight testing to more accurately assess changes that occur in the visual, vascular, and central nervous systems upon exposure to microgravity and the resulting fluid shifts. Research-only tests have been added as well. Monitoring in-flight visual changes, in addition to post-flight recovery, is the main focus of this protocol.

The Cerebral and Cochlear Fluid Pressure (CCFP) device was certified for flight on the ISS in support of the combined Fluid Shifts investigation scheduled to begin flight operations in 2015. The Fluid Shifts investigation measures how much fluid shifts from the lower body to the upper body, in or out of cells and blood vessels, and determines the impact these shifts have on ICP, as well as changes in vision and eye structures. Preliminary analysis of data from “Risk of Visual Impairment and Intracranial Hypertension after Space Flight: Evaluation of the Role of Polymorphism of Enzymes Involved in One-Carbon Metabolism (One-Carbon Metabolism)” showed elevations in four metabolites of the one-carbon metabolism pathway in ISS crew with vision changes. Additional crew subjects were recruited in 2013, and results are being matched to medical record data.

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations										

3.17 Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System (SHFH)

If the food system does not adequately provide for food safety, nutrition, and acceptability, then crew health and performance and the overall mission may be adversely affected. Furthermore, if the food system uses more than its allocated mission resources, then total required mission resources may exceed capabilities, the mission may not be deemed feasible, or allocation of resources to other systems may be unduly constrained.

Figure 5. NASA astronaut Karen Nyberg is pictured near fresh fruit floating freely in the Unity node of the International Space Station during Expedition 36.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS will be used to develop an acceptable food system by providing evidence upon which to base requirements. This includes both how the food is perceived by crew (acceptability in flight over shelf life), and the nutrition provided to the crew over shelf life. Researchers may determine if certain taste perceptions (salty, sweet, sour, bitter, umami) differ significantly in microgravity compared to perception on Earth, determine if spice intensity differs significantly when perceived in microgravity as compared to Earth, and recommend recipe modifications and/or condiment additions to improve the acceptability of the food system in microgravity. The data may be used to quantitatively confirm or rebut the commonly held notion that foods taste different in space and provide direction on how to improve acceptability of menu items in space.

The ISS is used to identify methods to enhance the eating experience on orbit. Researchers investigate how special meals and eating occasions, as well as “cooking” on orbit, can impact mood, stress, and behavior; identify trigger foods and determine the relative impact on mood of these foods; determine the effect of communal dining as compared to solo dining on mood state; determine the role of food preparation on mood and stress; and recommend dining behaviors and practices that positively affect the mood, stress, and behavior of crew on extended missions. The ISS is used to provide a quantitative assessment of the impact of food and dining on crew mood, stress, and behavior.

Given the requirement to minimize mass use on future missions, calorically dense meal replacement bars with the potential to decrease food system mass are being investigated. The ISS may be used to provide validation for the acceptability of these foods over extended flight durations when used on different meal replacement schedules. This data will ensure that food system changes will support adequate food consumption and crew health. Researchers may also study the physiological state of crew in relation to dietary choices (tracked by ISS Food Intake Tracker (FIT), shown below) as crew adapt to spaceflight. Food and nutrition are expected to affect all aspects of human health and performance, including immune, muscle, bone, cardiovascular, and psychological health. Studies that associate nutritional intake with physiological impacts during human adaptation to spaceflight may begin to characterize a healthy status in relation to diet, and indicate where alterations in diet may best improve physiological status. The data will guide future food system development efforts towards efficient dietary interventions and improved overall health, and ultimately the success of long duration human exploration missions.

Progress in addressing the risk.

Exploration food systems require low mass, high quality, and long shelf life. Packaging failures, excess material, or oxygen trapped within the package can be detrimental to this system. Ground-based research continues to identify methods to reduce mass and extend the shelf life of an integrated food system while maintaining adequate nutrition and quality. ISS will be used to assess the impact of microgravity on taste, smell and mood, as well as validate food system concepts and provision of healthier shelf-stable food choices. "Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions (Astro Palate)" began in-flight operations in 2014. The ISS FIT iPad Application (App) is planned to be installed on iPads on the ISS to more accurately and efficiently track food consumption to support Nutritional Biochemistry and Food research studies.

Figure 6. ISS Food Intake Tracker.

Planned research to support **Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.18 Risk of Adverse Health Effects Due to Host-Microorganism Interactions (SHFH)

Because consequences of infectious disease could include loss of mission and loss of crew, recent findings that spaceflight can increase virulence of microorganisms indicates that the extent of the risk of adverse health effects due to infectious disease or allergic response may be greater than previously expected. Therefore, additional characterization of the determinant of infectious disease in long duration missions is imperative if mitigation strategies are to be sufficiently robust to ensure crew health and mission success.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS will be used to evaluate changes in host and microbial cellular response to spaceflight; assess the likelihood and consequence of risk to crew health that is posed by increases in virulence of microbial pathogens as they are exposed to conditions of space travel; and determine if changes in crew flora is occurring during spaceflight.

Figure 22. NASA astronaut Michael Barratt, Expedition 20 flight engineer, conducts a Surface, Water and Air Biocharacterization (SWAB) water sampling from the Potable Water Dispenser (PWD) in the Destiny laboratory of the International Space Station.

Progress in addressing the risk.

In 2013, active monitoring of both the crewmembers' microbiome and immune systems, along with their interaction within the unique ISS environment, was initiated to support “Study of the Impact of Long-Term Space Travel on the Astronaut’s Microbiome (Microbiome).” Periodic samples will be taken from different parts of the crewmembers’ bodies and the surrounding ISS environment. As part of this study, the likelihood and consequences of alterations in the microbiome due to extreme environments, and the related human health risk, will be assessed. Follow-on flight studies are planned to address changes in microbial virulence, microbial controls, and the efficacy of antimicrobial medications and probiotic supplements in spaceflight.

Planned research to support **Risk of Adverse Health Effects Due to Host-Microorganism Interactions**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.19 Risk of an Incompatible Vehicle/Habitat Design (SHFH)

The habitability of space architectures and pressurized environments and the usability of tools and equipment are critical for the existence of humans in space. Any inadequacies in the design of the environment can restrict or prevent the user from surviving in extreme conditions and may impact safety and performance. Factors that affect the habitability must be assessed and properly addressed to ensure all potential hazards are mitigated or monitored. The improper planning and design of space environments introduces the possibility of errors or decreases the ability of the crew to complete tasks in a timely manner. Inconsistent design among subsystems and vehicles leads to negative transfer of training and increases risks.

Figure 23. NASA astronaut Karen Nyberg, Expedition 36/37 flight engineer, enjoys the view of Earth from the windows in the Cupola of the International Space Station. A blue and white part of Earth is visible through the windows.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Designing habitable environments in confined, isolated, and unforgiving conditions, restricted by launch capability, and mass and power constraints is difficult. The ISS is a perfect platform to provide insight to future space habitat designs and will be used to evaluate the effect of architecture on crew performance, including how net habitable volume, functional layout, and traffic patterns affect the crew; the effects of environmental factors on crew performance, including how lighting, noise, temperature, air flow, or other environmental factors affect the crew; and the effects of time for self-sustaining activities, including how time for personal hygiene, meals, recreation, medical conferences, family conferences, and other non-operational activities affect crew safety and performance.

The physiological response of the human body to micro-gravity presents challenges to spacecraft, spacesuit, and equipment designers. Historical data indicates that spinal elongation occurs when crewmembers are subjected to microgravity. In as little as two days, the typical crewmember will exhibit increases in stature of up to 3 percent. However, to date, data has been collected only for crewmembers in standing postures, and a limited pool of subjects was available. Seated height data in microgravity is considered necessary to identify correctly the seated height projections of the crew for future spacecraft configurations. Additionally, data concerning the effects of spinal elongation on seated height would aid in the design of suit components, as well as requirements for habitats and other vehicles. The ISS will be used to collect seated height due to spinal growth for subjects exposed to microgravity environments and seated height rate of change over time.

Progress in addressing the risk.

The Space Habitability Observation Reporting Tool (iSHORT) is an iOS application that was designed to allow ISS crewmembers to document habitability observations by text, voice, pictures, and/or video. During the NASA Extreme Environment Mission Operations (NEEMO)

16 mission, participants used iSHORT, as well as targeted video data collection methods (using head-worn cameras and iPad cameras), to report observations during the 12-day mission. These tools will also be put to use for data collection in the "Vehicle NHV and Habitability Assessment (Habitability)" task to document net habitable volume (NHV) and habitability issues during the 1YM, six month flight exploratory study, or other venues, such as the Human Exploration Research Analog (HERA).

Planned research to support	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Risk of an Incompatible Vehicle/Habitat Design										

3.20 Risk of Inadequate Human-Computer Interaction (SHFH)

Figure 24. European Space Agency astronaut Luca Parmitano, Expedition 36 flight engineer, enters data on a computer in the Destiny laboratory of the International Space Station.

While much is known about designing systems that provide adequate human-computer interaction, exploration missions bring new challenges and risks. Whereas the space shuttle had hundreds of hard switches and buttons, exploration vehicles will feature primarily glass-based interfaces, requiring crew to rely on an input device to interact with software displays and controls. All information potentially needed by crew during a mission will have to be available onboard, since the ground may not be an available or timely resource during long-duration missions. Due to mass restrictions, the real estate for displayed information is likely to be limited, but the amount of information available for display will be greatly increased, posing challenges for information design and navigation schemes. Future vehicles will also fly many new technologies that must be usable with pressurized gloves in microgravity and under vibration.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

The ISS will be used to evaluate aspects of human-computer interaction and information architecture designs that must support crew tasks, Exploration crewmembers will rely heavily on information-rich displays for commanding and monitoring vehicles and habitats during autonomous long-duration missions. They will interact with displays using fine motor skills for pointing, touching, and actuating hardware and software controls. We do not know the impacts of extended microgravity on the cognitive functions and fine motor skills required to interact with computer-based systems. Flight studies will also be used to validate the type and level of detail of information that will be required for long-duration missions and how to organize the information for adequate retrieval and consumption. This includes development and validation of methods or tools for unobtrusively measuring Crew Resource Management (CRM), Situational Awareness (SA), and Workload in-situ.

Progress in addressing the risk.

In 2014, the “Effects of Long-duration Microgravity on Fine Motor Control Skills (Fine Motor Skills)” flight study began to determine the effects of long-duration microgravity and different gravitational transitions on fine motor performance and functional task performance (human interaction with computer-based systems). Fine Motor Skills utilizes a series of tests designed to evaluate various aspects of fine motor control, as indicated by reciprocal pointing, dragging, geometric tracing, and object manipulation. Data obtained from this study will add to our knowledge base and provide improved capabilities to judge the risk of fine motor performance decrements due to long-duration microgravity. This study will be performed by 1YM and six month ISS crewmembers.

Planned research to support **Risk of Inadequate Human-Computer Interaction**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.21 Risk of Injury from Dynamic Loads (SHFH)

Because all crewmembers must endure dynamic phases of flight, detailed understanding of the human body response to such environments is critical. In addition, because spaceflight deconditioning causes decreases in bone strength, decreases in muscle strength, and increases in bone fracture risk, the criticality of this understanding is greater with longer duration spaceflight missions.

Figure 25. Digital still and video imagery and a tape measure to measure segmental length, height, depth, and circumference data for all body segments (i.e., chest, waist, hip, arms, legs, etc.) from astronauts for pre-, post-, and in-flight conditions. Subject outfitted with body markers and positioned in one of the three poses that will be used for photographic measurements.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Crewmembers experience varying levels of deconditioning related to exposure to microgravity, including changes to the musculoskeletal system. ISS will be used to collect data on changes in body measurements in microgravity and pre- and post-flight measurements of the lumbar, thoracic and cervical spine. These data will be used to model bone strength, as well as develop or update deconditioning scaling factors used in several risk assessment models.

Progress in addressing the risk.

In-flight operations began in 2013 for "Quantification of In-Flight Physical Changes - Anthropometry and Neutral Body Posture (Body Measures)." This study is co-sponsored by the Space Human Factors and Habitability (SHFH) Element of the Human Research Program and by the Johnson Space Center Extravehicular (EVA) Project Office and aims to collect microgravity-induced changes in anthropometry (body measurements). Digital still and video imagery and a tape measure will be used to measure length, height, depth, and circumference data for all body segments (i.e., chest, waist, hip, arms, legs, etc.) from astronauts for pre-, post-, and in-flight conditions. Body size and shape changes due to spaceflight can be used in design and verification of vehicle and habitat design, EVA suit sizing, and occupant protection during dynamic phases of flight.

Planned research to support **Risk of Injury from Dynamic Loads**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**

3.22 Risk of Performance Errors due to Training Deficiencies (SHFH)

Currently, the training flow begins years before the mission, and crews have commented on the impact of early and drawn-out training on the level of training retention. Historically, spaceflight operations have mitigated potential execution errors in at least two ways: specially-trained crewmembers are assigned to missions or rotated into the operational environment when complex, mission-critical tasks must be performed; and, execution of tasks are closely monitored and supported by ground personnel, who have access to far more information and expertise than an individual operator. However, emerging future mission architectures include long-duration operations in deep space. Simply increasing the pre-mission ground training time will not address the need for increased training retention and may even exacerbate the issue. Deep space operations do not allow for assignment of new crew or rotation of crew to ground for training. Further, delays in communication will have a disruptive effect on the ability of Earth-based flight controllers to monitor and support space operations in real time. Consequently, it is necessary to develop an understanding of how training can be tailored to better support long-duration deep space operations. This includes appropriate methods for Just-In-Time (JIT) training, and the extent to which materials, procedures, and schedules of training should be modified. Performance errors of critical tasks may result in crew inefficiencies, failed mission objectives, and both short and long-term crew injuries.

Figure 26. Canadian Space Agency astronaut Robert Thirsk, Expedition 20 flight engineer, participates in Crew Health Care Systems (CHeCS) medical emergency training in the U.S. Laboratory of the International Space Station.

Role of the ISS in quantifying the level of risk or acquiring additional information to confirm or eliminate risk.

Earth-based studies have shown that skills that are retained over long time intervals are highly specific and not generalized, whereas skills that generalize easily are not always retained well. Thus, determining basic skills that could both be retained and generalized across tasks remains a significant challenge. ISS will be used to quantify the retention and decay functions of skills, knowledge, and materials currently trained.

Progress in addressing the risk.

The "Effects of Long-Duration Spaceflight on Training Retention (Training Retention)" will be conducted on both six month and 1YM crewmembers in 2015. The study will be used to develop the operational understanding of training retention and transfer, as well as JIT training requirements, under the conditions of a long-duration space mission. A three-pronged approach will allow data collection on training effectiveness while on orbit. It includes testing for retention and transfer, a comparison between on-orbit and on-Earth performance, and a qualitative recording of training-related events.

Planned research to support	15	16	17	18	19	20	21	22	23	24
Risk of Performance Errors Due to Training Deficiencies										

4 SUMMARY

In summary, the ISS remains an invaluable asset in addressing human risks sufficiently to enable NASA to safely proceed with mission goals and objectives. It will be used through 2024 to complete the studies necessary to understand the severity of certain risks, to gather evidence to quantify the risks, and to complete the development of key countermeasures. The ISS research allows validation of techniques and technologies needed for long duration flight with particular interest in the transit phase of a Mars mission.

		15	16	17	18	19	20	21	22	23	24
3.1	Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities	■	■	■	■	■	■	■	■	■	■
3.2	Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders	■	■	■	■	■	■	■	■	■	■
3.3	Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team	■	■	■	■	■					
3.4	Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload	■	■	■	■	■	■	■	■	■	■
3.5	Risk Factor of Inadequate Nutrition	■	■	■	■	■	■	■	■	■	■
3.6	Risk of Adverse Health Event Due to Altered Immune Response	■	■	■	■	■	■	■	■	■	■
3.7	Risk of Early Onset Osteoporosis Due To Spaceflight	■	■	■	■	■					
3.8	Concern of Intervertebral Disc Damage upon and immediately after re-exposure to Gravity	■	■	■	■	■	■	■	■	■	■
3.9	Risk of Bone Fracture due to Spaceflight-induced Changes to Bone	■	■	■	■	■					
3.10	Risk of Orthostatic Intolerance During Re-Exposure to Gravity	■	■	■	■	■	■	■	■	■	
3.11	Risk of Cardiac Rhythm Problems	■	■	■	■	■	■	■	■	■	
3.12	Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance	■	■	■	■	■	■	■	■	■	■
3.13	Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity	■	■	■	■	■	■	■	■	■	■
3.14	Risk of Impaired Control of Spacecraft/ Associated Systems and Decreased Mobility Due to Vestibular/ Sensorimotor Alterations Associated with Spaceflight	■	■	■	■	■	■	■	■	■	■
3.15	Risk of Ineffective or Toxic Medications Due to Long Term Storage and Concern of Clinically Relevant Unpredicted Effects of Medication	■	■	■	■	■	■	■			
3.16	Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations	■	■	■	■	■	■	■	■	■	■
3.17	Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System	■	■	■	■	■	■	■	■	■	■
3.18	Risk of Adverse Health Effects Due to Host-Microorganism Interactions	■	■	■	■	■	■	■	■	■	■
3.19	Risk of an Incompatible Vehicle/Habitat Design	■	■	■	■	■					
3.20	Risk of Inadequate Human-Computer Interaction	■	■	■	■	■	■	■	■	■	■
3.21	Risk of Injury from Dynamic Loads	■	■	■	■	■	■				
3.22	Risk of Performance Errors Due to Training Deficiencies	■	■	■							

Table 2. Summary of HRP Risks Being Addressed Using ISS by FY

Note: Data derived from the Jan/Feb 2015 analysis (by ISSMP) of flight experiments identified in the IRP, Rev F, and associated discussions with HRP Elements.

APPENDIX A: CROSS-REFERENCE OF RISKS AND TASKS (EXPERIMENTS)

This appendix traces the HRP risk to the IRP Rev F investigation associated with HRP "Fly-off Plan" experiment title and shows the required number of subjects ("N") that are being accommodated or remain unmet. ISS increments are indicated within fiscal years. Some experiments do not require human subjects, but do require crew time for set-up and other operational activities. The colors used throughout the appendix are defined as follows:

L	Launch of experiment hardware
~~0~~	In definition phase
	Includes in-flight operations; in current flight queue; select for flight process complete
	Includes in-flight operations; in current flight queue; select for flight process in work
	Projected experiment anticipated to complete given current schedule, resources, and priorities
	Pre/post operations only; in current flight queue
	Delayed start due to limitations
	Anticipate experiment will be incomplete in 2020 given current schedule, resources, and priorities
	Anticipate experiment will be incomplete in 2020, but will be complete by 2024, given current schedule, resources, and priorities

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015		2016		2017		2018		2019		2020		2021		2022		2023		2024		Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44		I45-48		I49-52		I53-56		I57-60		I61-64		I65-68		I69-72		I73-76		I77-80			I81-84	I85-88	I89-92	I93-96	
3.1	Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities	a	Biosensors for Exploration Medical System	Biosensors for Medical Systems (ExMC)	1	θ	θ	θ	L	1	θ															0					0
		b	Exploration Laboratory Analysis	Exploration Lab Analysis (ExMC)	N/A								θ	θ	θ	L	1	θ								0					0
		c	Risk of Intervertebral Disc Damage After Prolonged Spaceflight	Intervertebral Disc Damage/ Hargens (p/p) (HHC/Bone)	12	2	1	0	1	1	1	1	1	1	θ											0					0
		d	Medical Consumables Tracking	Medical Consumables Tracking/ Zoldak (ExMC)	N/A	θ	θ	1	θ																	0					0
		e	Development of Medical Suction Technology	Medical Suction (ExMC)	N/A															θ	θ	θ	L	1	θ	0					0
		f	Study of the impact of long-term space travel on the astronaut's microbiome	Microbiome/ Lorenzi (SHFH)	9	1	3	1	θ																	0					0
		g	Oxygen Delivery System	Oxygen Delivery System (ExMC)	N/A							θ	θ	θ	L	1	θ									0					0
3.2	Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders	a	Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions	Astro Palate/Vickers (SHFH)	8	1	1	1	1	1	2	1	θ													0					0
		b	Integrated Tools and Technologies Testing, Verification, and Validation (Flight)	Behavior/ Performance Monitoring Tools (BHP)	12									θ	θ	θ		2	2	2	2	2	2	θ		0					0
		c	Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue	Cognition/ Basner (BHP/NSBRI)	6	1	3	2	θ																	0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015		2016		2017		2018		2019		2020		2021		2022		2023		2024		Unmet "N"	2025		2026		2027		2028		Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44		I45-48		I49-52		I53-56		I57-60		I61-64		I65-68		I69-72		I73-76		I77-80			I81-84		I85-88		I89-92		I93-96		
3.2	Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders	d	Assessing the Impact of Communication Delay on Performance: An Examination of Autonomous Operations Utilizing the International Space Station	Comm Delay Assessment/ Palinkas (BHP)	3	0																				0									0
		e	Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions	Dose Tracker (HHC/Multi)	24	0	0	2	2	2	3	2	3	2	3	2	3	0								0									0
		f	Vehicle NHV and Habitability Assessment	Habitability/ Thaxton (SHFH)	6	0	1	2	2	1	0															0									0
		g	Behavioral Issues Associated with Long Duration Space Missions: Review of Astronaut Journals - Extension	Journals (6-crew)/Stuster (BHP)	10 (US)	2	0																			0									0
		h	Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases	NeuroMapping/Seidler (HHC/EP+BHP)	13	1	1	1	1	1	1	1	1	1	1	2	1	0								0									0
		i	Inflight pharmacokinetic and pharmacodynamic responses to medications commonly used in spaceflight	Pharmacokinetics /Pharmacodynamics (HHC/Multi)	6	0	0	0			1	2	0	2	0	1	0									0									0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
		IRP Rev F Title		Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.2	Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders	j	Testing solid state lighting countermeasures to improve circadian adaptation, sleep, and performance during high fidelity analog and flight studies for the International Space Station	SSLA Lighting Effects (BHP)	12	θ	θ θ	L 2	1 2	2 2	2 1	θ				0					0
		k	Standardized Behavioral Measures for Detecting Behavioral Health Risks during Exploration Missions	Standardized Behavioral Measures (BHP)	8		θ θ	θ L	2 2	2 2	θ					0					0
3.3	Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team	a	Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions	Astro Palate/Vickers (SHFH)	8	1 1	1 1	1 2	1 θ							0					0
		b	Assessing the Impact of Communication Delay on Performance: An Examination of Autonomous Operations Utilizing the International Space Station	Comm Delay Assessment/ Palinkas (BHP)	3	θ										0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.3	Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team	c	Understanding and Preventing Crew Member Task Entrainment Team Task Switching in Astronaut Crews on the International Space Station: Integrating Multiteam Membership, Multiteam Systems, Multitasking, & Multidimensional Networks to Monitor & Enable Functional Work Shifts in Astronaut Crews	Team Task Switching (BHP)	6		θ θ	θ 2	2 2	θ						0					0
		d	Effects of Long-Duration Spaceflight on Training Retention	Training Retention/ Barshi (SHFH)	6	θ 1	1 2	2 θ								0					0
3.4	Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload	a	Integrated Tools and Technologies Testing, Verification, and Validation (Flight)	Behavior/ Performance Monitoring Tools (BHP)	12					θ θ	θ	2 2	2 2	2 2	θ	0					0
		b	Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue	Cognition/ Basner (BHP/NSBRI)	6	1 3	2 θ									0					0
		c	Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions	Dose Tracker (HHC/Multi)	24	θ θ	2 2	2 3	2 3	2 3	2 3	θ				0					0
		d	Behavioral Issues Associated with Long Duration Space Missions: Review of Astronaut Journals - Extension	Journals (6-crew)/Stuster (BHP)	10 (US)	2 θ										0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.4	Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload	e	Inflight pharmacokinetic and pharmacodynamic responses to medications commonly used in spaceflight	Pharmacokinetics /Pharmacodynamics (HHC/Multi)	6	θ θ	θ	1	2 0	2 0	1 θ					0					0
		f	Testing solid state lighting countermeasures to improve circadian adaptation, sleep, and performance during high fidelity analog and flight studies for the International Space Station	SSLA Lighting Effects (BHP)	12	θ	θ θ	L 2	1 2	2 2	2 1	θ				0					0
		g	Standardized Behavioral Measures for Detecting Behavioral Health Risks during Exploration Missions	Standardized Behavioral Measures (BHP)	8		θ θ	θ L	2 2	2 2	θ					0					0
		h	Validation of unobtrusive Crew Resource Management (CRM), Situation Awareness (SA), and Workload	Unobtrusive Measures (SHFH)	6							θ	θ θ	2 2	2 θ	0					0
3.5	Risk Factor of Inadequate Nutrition	a	Space Biochemistry Profile	Biochemical Profile/Smith (HHC/Multi)	as many as possible	2 3	2 2	2 Contained in Standard Measures								N/A					N/A
		b	Risk of visual impairment and intracranial hypertension after space flight: Evaluation of the role of polymorphism of enzymes involved in one-carbon metabolism	N/A (not a flight study implemented by ISSMP)	72																

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.5	Risk Factor of Inadequate Nutrition	c	Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Space Flight and Recovery	Pro K/Smith (HHC/Multi)	16	0										0					0
3.6	Risk of Adverse Health Event Due to Altered Immune Response	a	Space Biochemistry Profile	Biochemical Profile/Smith (HHC/Multi)	as many as possible	2 3	2 2	2 Contained in Standard Measures								N/A					N/A
		b	Immune Countermeasures Validation - Flight	Immune Countermeasures (HHC/Multi)	10							0 0	0 2	2 2	2 2	0	0				0
		c	Functional Immune	Functional Immune (HHC/Multi)	17	0	0 0	2	2 2	2 2	2 2	2 1	0			0					0
		d	Deep Space Exploration Atmosphere Effects on Hematologic, Immunologic, and Oxidative Stress and Damage Parameters in Astronauts: An ISS Flight Study	Exploration Atmosphere (HHC/CVV)	17	0	0 0	0	2 0	2 0	2 0	2 0	2 0	2 0	2 0	3	2 0	2 0			0
		e	The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity	Salivary Markers/ Simpson (HHC/Multi)	6	2 1	1 0									0					0
		f	Assessing Telomere Lengths and Telomerase Activity in Astronauts	Telomeres/ Bailey (HHC/Multi)	10	0 2	2 2	2 2	0							0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.7	Risk Of Early Onset Osteoporosis Due To Spaceflight	a	Space Biochemistry Profile	Biochemical Profile/Smith (HHC/Multi)	as many as possible	2 3	2 2	2 Contained in Standard Measures								N/A					N/A
		b	Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss: SMO-021	Bisphosphonates Controls/E255-SMO021/Matsumoto-LeBlanc (HHC/Bone)	10	2 1	1 θ									0					0
		c	Integrated Resistance and Aerobic Training Study	Sprint (Control Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	1 0	1 0	1 1	1 θ						0					0
				Sprint (Active Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	0 1	0 1	θ							0					0
		d	Vertebral Compression Fracture Assessment	N/A (not implemented by ISSMP; part of Medical Requirement-035L Bone Densitometry)	12																
3.8	Concern of Intervertebral Disc Damage Upon and Immediately after Re-Exposure to Gravity	a	Disc Damage Countermeasure	Disc Damage Countermeasure (HHC/Bone)	3				θ θ	θ		1	0 1	0 1	θ	0					0
		b	Risk of Intervertebral Disc Damage After Prolonged Spaceflight	Intervertebral Disc Damage/ Hargens (p/p) (HHC/Bone)	12	2 1	0 1	1 1	1 1	1 θ						0					0
3.9	Risk of Bone Fracture due to Spaceflight-induced Changes to Bone	a	Vertebral Compression Fracture Assessment	N/A (not implemented by ISSMP; part of Medical Requirement-035L Bone Densitometry)	12																
3.10	Risk of Orthostatic Intolerance During Re-Exposure to Gravity	a	Recovery of Functional Performance Following Long Duration Space Flight	Field Test/Reschke (p/p) (HHC/EP)	15	θ 1	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 θ		0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.11	Risk of Cardiac Rhythm Problems	a	Defining the relationship between biomarkers of oxidative and inflammatory stress and atherosclerosis risk in astronauts during and after long-duration spaceflight	Cardio Ox/Platts (HHC/CVV)	12	2 2	2 2	1 θ								0					0
		b	Recovery of Functional Performance Following Long Duration Space Flight	Field Test/Reschke (p/p) (HHC/EP)	15	θ 1	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 θ		0					0
		c	Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance	Fluid Shifts/Stenger, et al. (HHC/CVV)	10	θ 1	0 2	1 1	θ							0					0
			Microgravity Associated Compartmental Equilibration (MACE)																		
			Fluid Distribution before, during and after Prolonged Space Flight-NNX13AJ12G																		
3.12	Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance	a	Advanced Exercise Concepts Device Flight Demonstration 1	Advanced Exercise Demo 1 (HHC/EP)	8		θ θ	θ θ	L 1	2 1	2 2	θ				0					0
		b	Advanced Exercise Concepts Device Flight Demonstration 2	Advanced Exercise Demo 2 (HHC/EP)	8					θ θ	θ θ	L 2	1 2	1 1	1 θ	0					0
		c	Advanced Exercise Concepts Device Flight Demonstration 3 with Integrated Countermeasures Suite	Advanced Exercise Demo 3 (HHC/EP)	8								θ θ	θ θ	L 2	6	1 2	1 2	θ		0

Sec No	HRP Risk with Tasks on ISS		Associated Tasks		FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.12	Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance	d	Biomechanical Analyses of Resistance Exercise Using the Advanced Resistive Exercise Device	ARED Kinematics (HHC/EP) (implemented by ESA)	16																
		e	Recovery of Functional Performance Following Long Duration Space Flight	Field Test/Reschke (p/p) (HHC/EP)	15	θ 1	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 θ		0					0
		f	Flight Mission Task Assessments	Flight Mission Tasks Assessments (p/p) (HHC/EP)	12			θ θ	θ	1	2 1	2 1	2 1	2 θ		0					0
		g	In-flight Demonstration of Portable Load Monitoring Devices-Phase I: XSENS ForceShoe™	Force Shoes/Hanson (HHC/EP)	4	1 1	θ									0					0
		h	Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases	NeuroMapping/Seidler (HHC/EP+BHP)	13	1 1	1 1	1 1	1 1	1 1	2 1	θ				0					0
		i	Integrated Resistance and Aerobic Training Study	Sprint (Control Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	1 0	1 0	1 1	1 θ						0					0
				Sprint (Active Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	0 1	0 1	θ							0					0
3.13	Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity	a	Advanced Exercise Concepts Device Flight Demonstration 1	Advanced Exercise Demo 1 (HHC/EP)	8		θ θ	θ θ	L 1	2 1	2 2	θ				0					0
		b	Advanced Exercise Concepts Device Flight Demonstration 2	Advanced Exercise Demo 2 (HHC/EP)	8					θ θ	θ θ	L 2	1 2	1 1	1 θ	0					0
		c	Advanced Exercise Concepts Device Flight Demonstration 3 with Integrated Countermeasures Suite	Advanced Exercise Demo 3 (HHC/EP)	8								θ θ	θ θ	L 2	6	1 2	1 2	θ		0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.13	Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity	d	Flight Mission Task Assessments	Flight Mission Tasks Assessments (p/p) (HHC/EP)	12			θ θ	θ	1	2 1	2 1	2 1	2 θ		0					0
		e	Integrated Resistance and Aerobic Training Study	Sprint (Control Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	1 0	1 0	1 1	1 θ						0					0
				Sprint (Active Subjects)/ Ploutz-Snyder (HHC/EP)	9	0 1	0 1	0 1	θ							0					0
3.14	Risk of Impaired Control of Spacecraft/ Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight	a	Recovery of Functional Performance Following Long Duration Space Flight	Field Test/Reschke (p/p) (HHC/EP)	15	θ 1	2 2	2 2	2 2	2 2	2 2	2 2	2 2	2 θ		0					0
		b	Effects of Long-duration Microgravity on Fine Motor Control Skills	Fine Motor Skills/Holden (SHFH)	8	θ 1	2 2	2 1	θ							0					0
		c	Assessment of Operator Proficiency Following Long-Duration Spaceflight	Manual Control (p/p)/Moore (HHC/EP)	8	1 θ										0					0
			Effect of Sensorimotor Adaptation Following Long-Duration Spaceflight on Perception and Control of Vehicular Motion																		
		d	Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases	NeuroMapping/Seidler (HHC/EP+BHP)	13	1 1	1 1	1 1	1 1	1 1	2 1	θ				0					0
		e	Development of Countermeasures to Enhance Sensorimotor Adaptation - ISS Flight Validation	Sensorimotor Adaptation Countermeasures (HHC/EP)	12			θ θ	θ		2 0	2 1	2 1	2 1	1 θ	0	θ				0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.14	Risk of Impaired Control of Spacecraft/ Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight	f	Developing Predictors of Sensorimotor Adaptability - ISS Flight Validation	Sensorimotor Predictors (HHC/EP)	12			0 0	0		2	1 2	1 2	1 2	1 0	0	0				0
		g	Sensorimotor Countermeasure Evaluation Suite	Sensorimotor Countermeasure Evaluation (HHC/EP)	12						0 0	0			2	10	1 2	1 2	1 2	1 0	0
		h	Space Motion Sickness Countermeasures in Spaceflight	Space Motion Sickness (HHC/EP)	12				0 0	0		2 1	2 1	2 1	2 1	0	0				0
3.15	Risk of Ineffective or Toxic Medications Due to Long Term Storage and Concern of Clinically Relevant Unpredicted Effects of Medication	a	Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions	Dose Tracker (HHC/Multi)	24	0 0	2 2	2 3	2 3	2 3	2 3	0				0					0
		b	Medical Consumables Tracking	Medical Consumables Tracking/ Zoldak (ExMC)	N/A	0 0	1 0									0					0
		c	Medication In-flight Analysis/ Flight Validation	Medication Analysis (HHC/Multi)	N/A	0	0 0	L 1	0							0					0
		d	Inflight pharmacokinetic and pharmacodynamic responses to medications commonly used in spaceflight	Pharmacokinetics /Pharmacodynamics (HHC/Multi)	6	0 0	0	1	2 0	2 0	1 0					0					0
3.16	Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations	a	Human Cerebral Vascular Autoregulation and Venous Outflow in Response to Microgravity-Induced Cephalad Fluid Redistribution	Cephalad Fluid Redistribution/Roberts (p/p) (HHC/CVV)	8	0 0	0 1	2 1	2 1	1 0						0					0
		b	Direct Intracranial Pressure Measurement	Direct Intracranial Pressure (HHC/CVV)	4		0	0 0		1 1	1 1	0				0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.16	Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations	c	Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance Microgravity Associated Compartmental Equilibration (MACE) Fluid Distribution before, during and after Prolonged Space Flight-NNX13AJ12G	Fluid Shifts/Stenger, et al. (HHC/CVV)	10	θ 1	0 2	1 1	θ							0					0
		d	Validation of in-flight non-invasive ICP as compared to a direct measurement of intracranial pressure	Non-Invasive Intracranial Pressure (HHC/CVV)	N/A								θ θ	θ L	1 1	0	θ				0
		e	Prospective Observational Study of Ocular Health in ISS Crews	Ocular Health/Otto (HHC/CVV)	12	1 3	2 θ									0					0
		f	Effects of Long Duration Spaceflight on Venous and Arterial Compliance in Astronauts	Vascular Compliance (HHC/CVV)	8	θ θ	θ 1	2 2	2 1	θ						0					0
		g	VIIP Biomarker Analysis - Flight	Visual Impairment/ Intracranial Pressure Biomarkers (HHC/CVV)	6		θ θ	θ		1 1	1 1	1 1	θ			0					0
		h	VIIP Countermeasures Development	Visual Impairment/ Intracranial Pressure Countermeasure (HHC/CVV)	10				θ	θ θ	L 2	0 2	0 2	0 2	0 2	0	θ				0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.16	Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations	i	Risk of visual impairment and intracranial hypertension after space flight: Evaluation of the role of polymorphism of enzymes involved in one-carbon metabolism	N/A (not a flight study implemented by ISSMP)	72																
3.17	Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System	a	Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions	Astro Palate/Vickers (SHFH)	8	1 1	1 1	1 2	1 θ							0					0
		b	Contribution of factors affecting food acceptability and satiety in spaceflight	Integrated Food Acceptability (SHFH)	15			θ θ	θ		1 2	1 2	1 2	1 2	1 2	0	θ				0
		c	Pick-and-Eat Salad-Crop Productivity, Nutritional Value, and Acceptability to Supplement the ISS Food System	Bioregeneration (SHFH)	6			θ θ θ	1 1	2 2	θ					0					0
		d	Pick and Eat - System Integration	Pick and Eat (SHFH)	6					θ	θ θ	2 2	2 θ			0					0
3.18	Risk of Adverse Health Effects Due to Host-Microorganism Interactions	a	Antimicrobial Efficacy Flight	Antimicrobial Efficacy (SHFH)	N/A		θ	θ θ	L 1	θ						0					0
		b	Flight Validation of Ground Based Dose-Response Analog	Dose Response Characterization (SHFH)	N/A					θ	θ θ	L 1	θ			0					0
		c	Microbial Control Methods	Microbial Control Methods (SHFH)	12							θ	θ θ		2 2	8	2 2	2 2	θ		0
		d	Study of the impact of long-term space travel on the astronaut's microbiome	Microbiome/ Lorenzi (SHFH)	9	1 3	1 θ									0					0
		e	Microbiome Flight Validation	Microbiome Validation (SHFH)	12					θ	θ θ	2 2	2 2	2 2	θ	0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.18	Risk of Adverse Health Effects Due to Host-Microorganism Interactions	f	Probiotic Flight Validation	Probiotic (SHFH)	12						θ	θ θ	2	2 2	2 2	2	2 θ				0
		g	Flight Validation of Virulence Mechanisms	Virulence Mechanisms (SHFH)	N/A							θ	θ θ	L 1	θ	0					0
3.19	Risk of an Incompatible Vehicle/Habitat Design	a	Quantification of In-flight Physical Changes - Anthropometry and Neutral Body Posture (NBP)	Body Measures/ Rajulu (SHFH)	12	1 2	1 2	1 θ								0					0
		b	Vehicle NHV and Habitability Assessment	Habitability/ Thaxton (SHFH)	6	θ 1	2 2	1 θ								0					0
		c	Wearable Kinematic Systems for Quantifying 3-D Space Utilization in the Microgravity Environment	Habitat Utilization (SHFH)	8	θ θ	θ	1 2	2 2	1 θ						0					0
3.20	Risk of Inadequate Human-Computer Interaction	a	Validation of Autonomous information system - flight	Autonomous Info Systems (SHFH)	12							θ	θ θ	1 0	2 1	8	2 2	2 2	θ		0
		b	Electronic Procedures (eProc) Validation - Flight	Electronic Procedures (SHFH)	2						θ	θ θ	2 θ			0					0
		c	Effects of Long-duration Microgravity on Fine Motor Control Skills	Fine Motor Skills/Holden (SHFH)	8	θ 1	2 2	2 1	θ							0					0
		d	Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases	NeuroMapping/Seidler (HHC/EP+BHP)	13	1 1	1 1	1 1	1 1	1 1	2 1	θ				0					0
		e	Evaluation of Crew-Centric Onboard Mission Operations Planning and Execution Tool	On-board Planning (SHFH)	5		θ	θ θ		2	1 2	θ				0					0
		f	Validation of unobtrusive Crew Resource Management (CRM), Situation Awareness (SA), and Workload	Unobtrusive Measures (SHFH)	6							θ	θ θ	2 2	2 θ	0					0

Sec No	HRP Risk with Tasks on ISS	Associated Tasks			FY	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	Unmet "N"	2025	2026	2027	2028	Unmet "N"
			IRP Rev F Title	Fly-off Plan Title	Subj Req	I41-44	I45-48	I49-52	I53-56	I57-60	I61-64	I65-68	I69-72	I73-76	I77-80		I81-84	I85-88	I89-92	I93-96	
3.21	Risk of Injury from Dynamic Loads	a	Quantification of In-flight Physical Changes - Anthropometry and Neutral Body Posture (NBP)	Body Measures/ Rajulu (SHFH)	12	1 2	1 2	1 θ								0					0
		b	Risk of Intervertebral Disc Damage After Prolonged Spaceflight	Intervertebral Disc Damage/ Hargens (p/p) (HHC/Bone)	12	2 1	0 1	1 1	1 1	1 θ						0					0
3.22	Risk of Performance Errors Due to Training Deficiencies	a	Effects of Long-Duration Spaceflight on Training Retention	Training Retention/ Barshi (SHFH)	6	θ 1	1 2	2 θ								0					0
*	Not assigned to a Risk	a	N/A	Repository/ McMonigal	as many as possible	2 2	2 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	3 3	N/A	3 3	3 3	3 3	3	N/A
		b	N/A	MARES Protocol (HHC/Intl)	4	θ	θ θ	1 1	1 1	θ						0					0

Table 3. Cross-reference of HRP Risks with Their Associated Tasks on ISS

APPENDIX B: SELECT PRODUCTS AND PUBLICATIONS FROM ISS

Sample Results from ISS Research

1. NASA HRP research shows that long duration space flight may temporarily alter the immune systems of astronauts, leaving them more vulnerable to illnesses.
   Crucian BE, Zwart SR, Mehta S, Uchakin P, Quiriarte HA, Pierson DL, Sams CF, Smith SM. Plasma cytokine concentrations indicate in-vivo hormonal regulation of immunity is altered during long-duration spaceflight. J Interferon Cytokine Res 34:778-86, 2014.

2. Based on data from astronauts serving from 120 to 180 days a panel of bone experts recommended that NASA use QCT and finite element modeling to study the effects of spaceflight (and recovery) on bone health.
   Orwoll, E. S., Adler, R. A., Amin, S., Binkley, N., Lewiecki, E. M., Petak, S. M., Shapses, S. A., Sinaki, M., Watts, N. B. and Sibonga, J. D. (2013), Skeletal health in long-duration astronauts: Nature, assessment, and management recommendations from the NASA bone summit. J Bone Miner Res, 28: 1243–1255.

3. Bone mineral density and urinary supersaturation risk in response to spaceflight was not different for men and women.
   Smith, S. M., Zwart, S. R., Heer, M., Hudson, E. K., Shackelford, L. and Morgan, J. L. (2014), Men and Women in Space: Bone Loss and Kidney Stone Risk After Long-Duration Spaceflight. J Bone Miner Res, 29: 1639–1645. doi: 10.1002/jbmr.2185

4. Crewmembers were able to obtain diagnostic-quality examinations of the cervical and lumbar spine that would provide essential information about acute or chronic changes to the spine
   Marshburn TH, Hadfield CA, Sargsyan AE, Garcia K, Ebert D, Dulchavsky SA.New heights in ultrasound: First report of spinal ultrasound from the International Space Station. J Emerg Med. 2014 Jan;46(1):61-7

5. Although headache incidence was not high, results suggest an increased susceptibility to physiological effects of CO(2) in-flight.
   Law J, Van Baalen M, Foy M, Mason SS, Mendez C, Wear ML, Meyers VE, Alexander D. Relationship between carbon dioxide levels and reported headaches on the international space station. J Occup Environ Med. 2014 May;56(5):477-83. doi: 10.1097/JOM.0000000000000158

6. Increases in stored iron and dietary intake of iron during space flight have raised concern about the risk of excess iron and oxidative damage, particularly in bone.
   Zwart SR, Morgan JL, Smith SM. Iron status and its relations with oxidative damage and bone loss during long-duration space flight on the International Space Station. Am J Clin Nutr. 2013 Jul;98(1):217-23.

7. Data indicate that, while VO2peak may be difficult to maintain during long-duration ISS missions, aerobic deconditioning is not an inevitable consequence of long-duration spaceflight. aerobic capacity; weightlessness.
   Moore AD, Jr, Downs ME, Lee SMC, Feiveson AH, Knudsen P, Ploutz-Snyder L. Peak exercise oxygen uptake during and following long-duration spaceflight. J Appl Physiol. 2014. 117: 231–238.

8. Extended exposure to microgravity compromised torso stability beyond that found in bed rest subjects using walk on floor/ eyes closed, a standard sensorimotor test of dynamic postural stability.
   Mulavara, A.P. Feiveson, A. H. Reschke, M. F., Bloomberg, J.H. A cpmarison of torso stability between bed rest subjects and astronuats druing tandem walk. Preliminary findings. 37th Am. Soc. Biomechanics. 2013. Sept.: 4-7.

9. Bisphosphonates as a supplement to exercise protect bone during long-duration spaceflight.
   Leblanc AD, Matsumoto T, Jones JA, Shapiro J, Lang TF, Shackelford LC, Smith SM, Evans HJ, Spector ER, Ploutz-Snyder RJ, Sibonga JD, Keyak JH, Nakamura T, Kohri K, Ohshima H. Osteoporosis International. 2013 July; 24(7): 2105-2114. DOI: 10.1007/s00198-012-2243-z.

10. Central retinal artery (CRA) blood flow was measured using Doppler before, during, and after long-term microgravity exposure in astronauts compared with data from a control group of nonastronauts subjected to head-down tilt (HDT).
    Sirek AS, Garcia KM, Foy M, Ebert D, Sargsyan AE, Wu JH, Dulchavsky SA. Doppler ultrasound of the central retinal artery in microgravity. Aviation, Space, and Environmental Medicine. 2014 January 1; 85(1): 3-8. DOI: 10.3357/ASEM.3750.2014.

11. Using NASA's models of risks and uncertainties, we predicted that central estimates for radiation induced mortality and morbidity could exceed 5% and 10% with upper 95% CI near 10% and 20%, respectively for a

Mars mission. Additional risks to the central nervous system (CNS) and qualitative differences in the biological effects of GCR compared to terrestrial radiation may significantly increase these estimates.

Cucinotta FA, Kim M-HY, Chappell LJ, Huff JL (2013) How Safe Is Safe Enough? Radiation Risk for a Human Mission to Mars. PLoS ONE 8(10): e74988. doi:10.1371/journal.pone.0074988.

12. Protocol to conduct a controlled prospective longitudinal study to investigate the effects of spaceflight on the sensorimotor and cognitive performance in ISS astronauts and ground based subjects.

    Koppelmans V, Erdeniz B, De Dios YE, Wood SJ, Reuter-Lorenz PA, Kofman I, Bloomberg JJ, Mulavara AP and Seidler RD (2013). Study Protocol to Examine the Effects of Spaceflight and a Spaceflight Analog on Neurocognitive Performance: Extent, Longevity, and Neural Bases. BMC Neurology 13(1): 205. 2.564

13. Crewmembers tend to lose body mass during flight, and determinations are reliable on both the US and Russian devices. While the average body mass loss is 3-5% of preflight body mass, many recent crewmembers have managed to maintain body mass, along with bone mass and likely other health benefits.

    Zwart SR, Launius R, Coen GK, Charles JB, Smith SM. Body mass changes during long-duration spaceflight. Aviat Space Environ Med 85:897-904, 2014. Associated Letter to the Editor and response: Aviat Space Environ Med 85:1229-30, 2014.

14. Summary of nutrition-related findings obtained from ISS studies during 2009-2014.

    Smith, S. M., Zwart, S. R., Heer. M. 2014. Human Adaptation to Spaceflight: The Role of Nutrition (NP-2014-10-018-JSC) http://go.nasa.gov/QS1KW1

Publications in High Impact Factor Journals

1. Barger, L. K., Flynn-Evans, E. Kubey, A., Walsh, L., Ronda, J. M., Wang, W., Wright, K. P., Czeisler, C. A. 2014. Prevalence of sleep deficiency and use of hypnotic drugs in astronauts before, during, and after spaceflight: an observational study. Lancet Neurology. Published online August 8, 2014 http://dx.doi.org/10.1016/S1474-4422(14)70122-X.

2. Leblanc AD, Matsumoto T, Jones JA, Shapiro J, Lang TF, Shackelford LC, Smith SM, Evans HJ, Spector ER, Ploutz-Snyder RJ, Sibonga JD, Keyak JH, Nakamura T, Kohri K, Ohshima H. Bisphosphonates as a supplement to exercise to protect bone during long-duration space flight. Osteoporosis International. 2013 July; 24(7): 2105-2114. DOI: 10.1007/s00198-012-2243-z.

3. Zwart, S.R., J.L. Morgan, and S.M. Smith, Iron status and its relations with oxidative damage and bone loss during long-duration space flight on the International Space Station. Am J Clin Nutr, 2013. 98(1): p. 217-23.

4. Smith SM, Abrams SA, Davis-Street JE, Heer M, O'Brien KO, Wastney ME, Zwart SR. Fifty years of human space travel: implications for bone and calcium research. Annu Rev Nutr. 2014. 34:377-400.

5. Mehta, S. K. Laudenslager,, M.L., Stowe R.P. Crucian B.E., Sams, C.F. Peirson, D. L. Multiple latent viruses reactivate in astronuats during Space Shuttle missions. Brain, Behavior, and Immunity. Brain Behav Immun. 2014 Jun 2. pii: S0889-1591(14)00136-6. doi: 10.1016/j.bbi.2014.05.014. [Epub ahead of print]

6. Orwoll, E. S., Adler, R. A., Amin, S., Binkley, N., Lewiecki, E. M., Petak, S. M., Shapses, S. A., Sinaki, M., Watts, N. B. and Sibonga, J. D. (2013), Skeletal health in long-duration astronauts: Nature, assessment, and management recommendations from the NASA bone summit. J Bone Miner Res, 28: 1243–1255.

7. Smith, S. M., Zwart, S. R., Heer, M., Hudson, E. K., Shackelford, L. and Morgan, J. L. (2014), Men and Women in Space: Bone Loss and Kidney Stone Risk After Long-Duration Spaceflight. J Bone Miner Res, 29: 1639–1645. doi: 10.1002/jbmr.2185.

8. Moore AD, Downs ME, Lee SM, Feiveson AH, Knudsen P, Ploutz-Snyder LL. Peak Exercise Oxygen Uptake During and Following Long-Duration Spaceflight. Journal of Applied Physiology, 117:231-8, 2014.

Cover Publications

Area: Bone
June 2013. Skeletal Health in Long-Duration Astronauts. Because of the limitations of DXA in describing the effects of spaceflight on bone strength, the panel recommended that the U.S. space program use QCT and finite
element modeling to further study the unique effects of spaceflight (and recovery) on bone health in order to better inform clinical decisions.

Area: Vision

August 2014. Gene expression analysis in isolated retina identified 139 differentially expressed genes in spaceflight. These results suggest a concerted change in gene expression in the retina of mice flown in space, possibly leading to retinal damage, degeneration, and remodeling. These results suggest a concerted change in gene expression in the retina of mice flown in space, possibly leading to retinal damage, degeneration, and remodeling.

Area: Circadian Misalignment and Fatigue in Space
September 2014. Sleep deficiency in astronauts was prevalent not only during space shuttle and ISS missions, but also throughout a 3 month preflight training interval. Despite chronic sleep curtailment, use of sleep-promoting drugs was pervasive during spaceflight. Because chronic sleep loss leads to performance decrements, our findings emphasize the need for development of effective countermeasures to promote sleep.

Patents Issued (2012-2014)

Title	Contract
Systems and methods for evaluating neurobehavioural performance from reaction time tests	NCC 9-58-NBPF00805
Streamline-based microfluidic device	NCC 9-58-317

Recent Patents Filed (2013-2014)

Filed 8/27/13. Pulsar Informatics, Inc. Calibration System With Human-Like Response Actuator

Filed 6/17/13. D. Mollicone et al. Methods & Systems for Circadian Physiology Predictions

Filed 2/28/13 Pulsar Informatics, Inc (Mollicone) Physiological And Neurobehavioral Status Monitoring

Filed 1/17/2013 Pulsar Informatics, Inc. (Mollicone) Systems and Methods for Inter-Population Neurobehavioral Status Assessment Using Profiles Adjustable to Testing Conditions

Filed 5/9/2014 Progressive Lighting and Radiometrics, LLC. (Brainard) Method and Apparatus for determining circadian input.

New NASA/HRP-developed Technologies

2014 Force Shoes
2014 Dose tracker iOS application
2014 ISS Food Intake Tracker (ISS Fit) iOS food consumption application
2014 Space Habitability Observation Reporting Tool – iSHORT (iOS application)
2014 Sensorimotor Assessment and Rehabilitation Apparatus (SARA)
2014 BHP Dashboard and software for individualized stress detection
2014 Integrated Medical Model (IMM) v. 3.0
2014 Psychomotor Vigilance (PVT) Self Test (Reaction Self Test)
2014 Human Factors Analysis Support Tool (H-FAST)
2014 Semantic Language and Tools for Reporting Human Factors Incidents
2014 Serial Coronary Artery Calcium scanning for astronaut risk assessment
2013 Team Dimensional Training - debriefing strategy for use by flight directors
2013 Flexible Ultrasound system
2013 Behavioral Competencies Tool for astronaut selection process
2013 NASA Space Radiation Cancer Risk Model 2012 Runner-Up for the 2013 Software of the Year Award
2013 Lunar Neutron Environmental model on OLTARIS design tool web-site
2013 Spaceflight Resource Management (SFRM) training tool update for expeditionary skills
2013 Computation tool to assess locomotion speed and external loading condition influences upon joint torque (tech pipeline)

New NASA/HRP Technology Spin-offs

2014 Cerebrotech Medical Systems JSC/NSBRI
2014 Eye tracking algorithm "EyeBox" JSC/NSBRI
2014 Pear Therapeutics "e "pharmaceutical formulation software JSC/NSBRI
2014 ACell, space-compatible gel formulation JSC/NSBRI
2013 ASTRO-CHARM integrated Cardiovascular risk calculator JSC/NSBRI
2013 Android Psychomotor Vigilance self test for commercial trucking JSC/NSBRI
2013 vMetrics
2013 NASA's research on Neutral Body Posture used to design new car seats for the 2013 Nissan Altima

APPENDIX C: ACRONYMS AND ABBREVIATIONS

ACRONYMS AND ABBREVIATIONS

1YM	One Year Mission
ARED	Advanced Resistance Exercise Device
ASTRO-CHARM	Astronaut Cardiovascular Health and Risk Modification Tool
BDC	baseline data collection
BHP	Behavioral Health and Performance Program Element
BMD	bone mineral density
CCFP	cerebral and cochlear fluid pressure
CEVIS	Cycle Ergometer with Vibration Isolation System
CHeCS	Crew Health Care Systems
CM	countermeasure
Comm	communication
CRM	crew resource management
CSA	Canadian Space Agency
CV	cardiovascular
CVV	Cardiovascular and Vision (HHC Portfolio)
DCS	decompression sickness
DNA	deoxyribonucleic acid
DXA	Dual Energy X-ray Absorptiometry
ECG	Electrocardiogram
E/P	Exercise and Performance (HHC Portfolio)
ESA	European Space Agency
EVA	extravehicular activity
ExMC	Exploration Medical Capability Program Element
FIT	Food Intake Tracker
FTT	Functional Task Test
FY	fiscal year
g	gravity
HERA	Human Exploration Research Analog
H-FAST	Human Factors Analysis Support Tool
HHC	Human Health Countermeasures Program Element
HRP	Human Research Program
HRR	Human Research Roadmap
HSRB	Human System Risk Board
IBMP	Institute of Biomedical Problems
ICP	intracranial pressure
IHT	intracranial hypertension
IMM	Integrated Medical Model
iOS	Apple’s mobile operating system
IP	international partner
iPRR	Integrated Path to Risk Reduction
IRP	Integrated Research Plan
iSHORT	Space Habitability Observation Reporting Tool
ISS	International Space Station
ISSMP	International Space Station Medical Projects Program Element
IVD	intervertebral disc
JAXA	Japan Aerospace Exploration Agency
JSC	Johnson Space Center
JIT	Just-In-Time
MARES	Muscle Atrophy Research and Exercise System
MCT	Medical Consumables Tracking
MELFI	Minus Eighty Laboratory Freezer for ISS

ACRONYMS AND ABBREVIATIONS

MHRPE	Multilateral Human Research Panel for Exploration
MRI	Magnetic Resonance Imaging
Multi	Multisystem (HHC Portfolio)
NASA	National Aeronautics and Space Administration
NEEMO	NASA Extreme Environment Mission Operations
NHV	net habitable volume
NSBRI	National Space Biomedical Research Institute
O2	oxygen
OCT	Optical Coherence Tomography
OLTARIS	On-Line Tool for the Assessment of Radiation in Space
PD	pharmacodynamics
PFS	Pulmonary Function System
PK	pharmacokinetics
p/p	pre/post
PPFS	Portable Pulmonary Function System
PRR	Path to Risk Reduction
PSMO	Program Science Management Office
PVT	Psychomotor Vigilance Test
PWD	Potable Water Dispenser
QCT	Quantitative Computed Tomography
Rev F	Document Revision F
RFID	radio frequency identification
RNA	ribonucleic acid
RSA	Russian Space Agency
SA	situational awareness
SARA	Sensorimotor Assessment and Rehabilitation Apparatus
SFRM	Spaceflight Resource Management
SHFH	Space Human Factors and Habitability Program Element
SR	Space Radiation Program Element
SWAB	Surface, Water and Air Biocharacterization
UPA	Urine Processor Assembly
USND-2	Ultrasound-2
VIIP	Visual Impairment/Intracranial Pressure
VO2max	maximal oxygen uptake
VPC	Video Power Converter