
2014 Bone and Muscle Risks Standing Review Panel

Evidence Reviews for:

*The Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance and
The Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity*

Final Report

I. Executive Summary and Overall Evaluation

The 2014 Bone and Muscle Risks Standing Review Panel (from here on referred to as the SRP) met for a site visit in Houston, TX on December 17 - 18, 2014. The SRP reviewed the updated Evidence Reports for the Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance and (from here on referred to as the 2014 Muscle Evidence Report) and the Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (from here on referred to as the 2014 Aerobic Evidence Report), as well as the Research Plans for these Risks. The SRP agreed the Evidence Reports were comprehensive and described a logical sequence of steps taken by NASA and the scientific community to address the risk of impaired performance as a result of muscle atrophy, i.e., reduced muscle mass, loss of strength and loss of endurance in a microgravity environment. The interdependence of the three physiological systems represented by this SRP (i.e., skeletal, muscular and cardiovascular) supports a level of discussion on system integration that is now appreciated by the Chief Scientist of the Human Research Program (HRP).

The Evidence Reports cover the effects of microgravity on muscle, ranging from the cellular and molecular levels to whole muscle function. The reports also addressed other factors related to muscle (e.g., neural influences, insulin resistance, heat stress, and nutrition) that will serve as a basis for future discussions on the integration of physiological systems and the response to microgravity. The SRP agreed the Evidence Reports were balanced, provided insight to muscle function, and laid the foundation for the integrated approach now taken by the SRP.

II. Review of the Evidence for the Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance

1. *Evaluate the 2014 Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance (Muscle) Evidence Report using the following criteria:*

A. *Does the 2014 Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?*

The SRP agrees that the 2014 Muscle Evidence Report provides sufficient documentation in support of the position that the Risk is relevant to long-term space missions. The 2014 Muscle Evidence Report emphasizes the use of appropriate countermeasure programs that employ informed physical exercise interventions, including aerobic and resistance exercise. For example, a discussion that continues today revolves around the statement “*load capacities for resistance exercise devices for use in space must be able to replace the body loads that are lost in microgravity on top of the normal loads that one would use on the ground.*” The idea that high resistance loads are requisite to attenuate muscle atrophy is one

currently supported by the SRP. Noted in the 2014 Muscle Evidence Report, however, and a current serious challenge to the use of optimal exercise equipment on the International Space Station (ISS) is the lack of availability of current hardware on the ISS for use in the exercise interventions. The 2014 Muscle Evidence Report states, and the SRP agrees, that this situation will have a very negative impact on the maintenance of crew health and physical fitness on the ISS. While the evidence is clear and strongly supports the use of exercise countermeasures the 2014 Muscle Evidence Report also states “*access to the crew members during both short and long-term missions to study the efficacy of the proposed countermeasures has been limited.*” This remains a challenge today.

Additionally, the 2014 Muscle Evidence Report states “*to comprehensively assess this risk, i.e., muscle atrophy, we must fully define mission-specific functional tasks and develop countermeasures to address those task demands.*” This remains a major concern of the SRP, i.e., defining specific task demands.

*B. Are the Risk Title and Statement properly stated in the current version of the HRP Integrated Research Plan (IRP)?**

The SRP thinks the Risk Title in the current version of the IRP is appropriate. The SRP thinks the wording of the Risk Title in the current version of the IRP is appropriate, but the new wording presented at the meeting (page 4 of the Muscle presentation) was not.

C. Is the text of the Risk Context provided in the HRP IRP clear?

The SRP suggests rewording the Risk Content to (suggested edits in bold and strikethrough): There is a growing body of research evidence that indicates skeletal muscles, particularly muscles of the lower limb, undergo atrophy and structural and metabolic alterations during spaceflight. However, the associations between in-flight exercise, muscle changes, and performance levels are not well understood. Efforts should be made to understand the current status of **pre-flight**, in-flight, and post-flight exercise performance capability and what goals/target areas for protection are needed for the in-flight exercise program. Pre-flight data are critical and should be included where possible to be more informative.

D. Does the evidence base make the case for the knowledge-type gaps presented?

Yes. The section of the 2014 Muscle Evidence Report on Human Ground-Based Evidence presents an excellent overview of the various models, such as bed rest, not only addressing the common element of a rapid loss and reduced but continued decrements in muscle volume in microgravity, but also the psychological adjustments that exacerbate physiological stressors. Additionally, the nutritional factors, such as nutritional inadequacies/less energy intake, that influence decreases in muscle mass were discussed. Women seem to lose muscle volume at a slightly faster rate than men, but the data on this potentially important sex difference are rather sparse.

Finally, the 2014 Muscle Evidence Report outlines several content-related areas that should be considered when discussing muscle function and the challenges in microgravity to

maintain muscle mass and muscle strength. Neural influences, muscle protein synthesis, changes in muscle fibers and enzyme activity, insulin resistance and heat stress/thermoregulation are all discussed and summarized along with a discussion of appropriate human and animal models for use as surrogate models for the human experience in space.

E. Are there any additional knowledge-type gaps that should be considered for this specific Risk?

The SRP does not think there are any additional knowledge-type gaps that should be considered at this time.

F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP IRP?

The 2014 Muscle Evidence Report does address relevant interactions between the Muscle Risk and others in the HRP IRP. The muscle response to microgravity was studied in detail with respect to fiber types (muscle quality), motor unit function, morphology, size, and mechanical output (e.g., power production), but more summary statements were needed “along the way.” There is no integration of muscle function with either bone or the central nervous system. The newly formed emphasis on integration of information, while still a challenge to the HRP, is strongly supported by the SRP.

G. Are the qualifications of the author(s) appropriate for identifying the evidence base necessary to characterize the given Risk?

Yes, the team of authors is knowledgeable and qualified.

H. Is there information from other HRP disciplines that need to be included in the 2014 Evidence Report?

The SRP does not think additional information from other HRP disciplines is needed at this time. The 2014 Muscle Evidence Report covers a great deal of information and does review related areas in Section B.

I. Is the breadth of the cited literature sufficient?

Yes, the 2014 Muscle Evidence Report cites all relevant studies/literature published over the past four to five decades providing an excellent review on the effect of microgravity on skeletal muscle from the level of molecules and cells to the level of whole muscle and its’ ability to perform tasks requisite to successful missions in space.

J. What is the overall quality and readability of the 2014 Evidence Report?

The overall quality and readability of the 2014 Muscle Evidence Report is good. Organization of the 2014 Muscle Evidence Report indicates strong progress in developing

questions informed by actual data, albeit limited, from the Mercury to the Apollo Programs, Skylab and subsequently the Space Shuttle program and the ISS. New technologies were created to study muscle response to microgravity and selected exercise countermeasures.

2. *Provide comments on any important issues that are not covered by the criteria in #1 above.*

The 2014 Muscle Evidence Report is comprehensive and reasonably complete. Indeed, the 2014 Muscle Evidence Report may well serve as a basis for the SRP's continued discussion regarding the integration of evidence produced by all SRPs and the generation of the next level of hypotheses needed to study the integration of physiological systems in response to the challenges of microgravity.

III. Review of the Evidence for the Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity

1. *Evaluate the 2014 Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (Aerobic) Evidence Report using the following criteria:*

- A. *Does the 2014 Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?*

Yes, the SRP thinks the 2014 Aerobic Evidence Report provides sufficient evidence that the Risk is relevant to long-term space missions.

- B. *Are the Risk Title and Statement properly stated in the current version of the HRP Integrated Research Plan (IRP)?**

The Risk Title is appropriate in the current version of the IRP. The SRP suggests rewording the Risk Statement to (suggested edit in bold): Given the condition of reduced aerobic capacity as measured by $VO_{2\max}$ /**peak**, there is a possibility of reduced physical performance.

- C. *Is the text of the Risk Context provided in the HRP IRP clear?*

The SRP suggests rewording the Risk Content to (suggested edits in bold and strikethrough): Astronauts' physical performance during a mission, including activity in microgravity and fractional gravity, is critical to mission success. Setting minimum ~~fitness standards~~ **VO_2 standards (ml/kg)** and measuring whether crew can maintain these standards will document the effectiveness of maintenance regimens.

- D. *Does the evidence base make the case for the knowledge-type gaps presented?*

The SRP thinks the evidence base in the 2014 Aerobic Evidence Report makes the case for the knowledge-type gaps presented.

E. Are there any additional knowledge-type gaps that should be considered for this specific Risk?

The SRP does not think there are any additional knowledge-type gaps that should be considered at this time.

F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP IRP?

The SRP thinks the 2014 Aerobic Evidence Report addresses relevant interactions, but this could be improved as mentioned by the Integration Panel discussion.

G. Are the qualifications of the author(s) appropriate for identifying the evidence base necessary to characterize the given Risk?

Yes, the team of authors is knowledgeable and qualified.

H. Is there information from other HRP disciplines that need to be included in the 2014 Evidence Report?

The SRP does not think additional information from other HRP disciplines is needed at this time.

I. Is the breadth of the cited literature sufficient?

The SRP thinks the breadth of the cited literature in the 2014 Aerobic Evidence Report is sufficient.

J. What is the overall quality and readability of the 2014 Evidence Report?

The overall quality and readability of the 2014 Aerobic Evidence Report is good.

2. *Provide comments on any important issues that are not covered by the criteria in #1 above.*

The SRP has no additional comments at this time.

IV.2014 Bone and Muscle Risks SRP Evidence Review: Statement of Task for the Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance (Muscle) and the Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (Aerobic)

In 2008, the Institute of Medicine (IOM) reviewed NASA's Human Research Program (HRP) Evidence Books that describe the Risks that were identified in NASA's Human Research Program Requirements Document (PRD). The 2014 Evidence Reports for the Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance (Muscle) and the Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (Aerobic) have not been reviewed since the last IOM review and there have been significant changes to the evidence base for the Risks.

The 2014 Bone and Muscle Risks Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist to review the Evidence Reports for the Muscle and Aerobic Risks. The 2014 Bone and Muscle Risks SRP will evaluate the Evidence Reports and generate a final report of your analyses of the evidence base, including any recommendations on how to improve the current Evidence Report, and submit it to the HRP Chief Scientist. Your report will also be made available on the Human Research Roadmap (HRR) website.

The 2014 Bone and Muscle Risks SRP is charged to:

1. Separately evaluate the 2014 Muscle and Aerobic Evidence Reports based on each of the following criteria:
 - A. Does the 2014 Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?
 - B. Are the Risk Title and Statement properly stated in the current version of the HRP Integrated Research Plan (IRP)?*
 - C. Is the text of the Risk Context provided in the HRP IRP clear?*
 - D. Does the evidence base make the case for the knowledge-type gaps presented?
 - E. Are there any additional knowledge-type gaps that should be considered for this specific Risk?
 - F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP IRP?
 - G. Are the qualifications of the author(s) appropriate for identifying the evidence base necessary to characterize the given Risk?
 - H. Is there information from other HRP disciplines that need to be included in the 2014 Evidence Report?
 - I. Is the breadth of the cited literature sufficient?
 - J. What is the overall quality and readability of the 2014 Evidence Report?
2. Provide comments on any important issues that are not covered by the criteria in #1 above.

** Please be aware that any suggested changes to the Risk Title, Statement, and Risk Context by the SRP may need to be approved by the Human Systems Risk Board (HSRB). The HSRB has the overall responsibility to implement and maintain a consistent, integrated process for assessing, documenting, and tracking all risks to the human system associated with spaceflight activities (both in flight and post flight).*

Additional information regarding this review:

1. Attend a meeting in Houston, TX on December 17 - 18, 2014 to discuss the Evidence Report with the Human Health Countermeasures (HHC) Element. At this meeting, prepare a draft report for each risk that addresses each of the evaluation criteria listed in the panel charge (A-J) including any recommendations on how to improve the Evidence Report. Debrief the HRP Chief Scientist and a representative from the HHC Element on the salient points that will be included in the final report and specifically the items in the panel charge.
2. Prepare a draft final report for each risk (within one month of the site visit debrief) that contains a detailed evaluation of the Evidence Report specifically addressing items #1 and #2 of the SRP charge. The draft final report will be sent to the HRP Chief Scientist and he will forward it to the appropriate Element for their review. The HHC Element and the HRP Chief Scientist will review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP within two weeks of receipt of the draft report. If any misunderstandings or errors of fact are identified, the SRP will be requested to address them and finalize the 2014 SRP Final Report as quickly as possible. The 2014 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the HHC Element that sponsors the muscle and aerobic disciplines and also made available to the other HRP Elements. The 2014 SRP Final Report will be made available on the HRR website (<http://humanresearchroadmap.nasa.gov/>).

To clarify, the Risk Statement and Risk Context are defined as follows:

Risk Statement:

“Given the CONDITION, there is a possibility that a CONSEQUENCE will occur”.

Condition: a single phrase briefly describing current key circumstances, situations, etc., that are causing concern, doubt, anxiety, or uncertainty – something that keeps you up at night.

Consequence: a single phrase or sentence that describes the key, negative outcome(s) of the current conditions.

Notes:

The condition-consequence format provides a more complete picture of the Risk, which is critical during mitigation planning. The condition component focuses on what is currently causing concern. This is something that is true or widely perceived to be true. This component provides information that is useful when determining how to mitigate a Risk.

The consequence component focuses on the intermediate and long-term impact of the risk. Understanding the depth and breadth of the impact is useful in determining how much time, resources, and effort should be allocated to the mitigation effort.

A well-formed Risk Statement usually has only one condition, and has one or more consequences.

Risk Context:

Purpose: provide enough additional information about the Risk to ensure that the original intent of the Risk can be understood by other personnel, particularly after time has passed.

Description: capture additional information regarding the circumstances, events, and interrelationships not described in the Risk Statement.

An effective context captures the what, when, where, how, and why of the Risk by describing the circumstances, contributing factors, and related issues (background and additional information that are NOT in the Risk Statement).

V. 2014 Bone and Muscle Risks Standing Review Panel Roster

Panel Chairs:

Julie Glowacki, Ph.D.

Brigham and Women's Hospital
Orthopedic Research
75 Francis Street
Boston, MA 02115
Ph: 617-732-6855

Email: jglowacki@partners.org

Robert Gregor, Ph.D.

University of Southern California
Division of Biokinesiology and Physical
Therapy
22910 Cheyenne Drive
Valencia, CA 91354
Ph: 661-904-7239

Email: rgregor@usc.edu

Panel Members:

Diane Cullen, Ph.D.

Creighton University
Osteoporosis Research Center
Crisis II, Room 313
2500 California Plaza
Omaha, NE 68178
Ph: 402-280-3855

Email: dcullen@creighton.edu

Almond Drake, M.D.

Brody School of Medicine
Division of Endocrinology
600 Moyer Boulevard
Room 3E-129
Greenville, NC 27834
Ph: 252-744-2567

Email: Drakea@ecu.edu

Roger Enoka, Ph.D.

University of Colorado
Department of Integrative Physiology
Mail Stop 354 UCB
Boulder, CO 80309
Ph: 303-492-7232

Email: enoka@colorado.edu

Edward Hanley Jr., M.D.

Carolinas Medical Center
Department of Orthopaedic Surgery
1025 Morehead Medical Drive, Suite 300
Charlotte, NC 28204
Ph: 704-355-5026

Email: edward.hanley@carolinashealthcare.org

William Kraemer, Ph.D.

The Ohio State University
Department of Human Sciences/Kinesiology
Room A054, PAES Building
305 W. 17th Avenue
Columbus, OH 43210
Ph: 614-688-3432

Email: kraemer.44@osu.edu

Peter Raven, Ph.D.

University of North Texas Health Sciences
Center at Fort Worth
Department of Integrative Physiology
3500 Camp Bowie Boulevard
Mail Stop RES-302
Fort Worth, TX 76107
Ph: 817-735-2074

Email: praven@hsc.unt.edu

D. Rick Sumner, Ph.D.

Rush Medical College
Department of Anatomy and Cell Biology
600 South Paulina, Suite 507
Chicago, IL 60612
Ph: 312-942-5744

Email: Rick_Sumner@rush.edu