Executive Summary

Bone density loss in microgravity (skeletal unloading) is a well-documented crew health concern since the Skylab mission, when it was observed that the flight crew had about 1-1.5% mineral loss per month. This was noted as being “significantly faster than normal osteoporotic individuals.” As a result, several technical requirements throughout Volumes 1 and 2 of NASA-STD-3001 provide countermeasures that can aid in the prevention of significant deterioration of overall crew health. This will contribute to overall mission success and benefit other areas including crew mental well-being. Countermeasures such as exercise, adequate nutrition, and medications have been recommended or required in order to prevent demineralization, especially during long-duration missions such as planetary and deep-space exploration. Presently, NASA-STD-3001 Volume 1 Rev C, [V1 4027] Pre-Mission Bone Countermeasures provides the range of acceptable loss. In addition, there is a need for appropriate nutrition to prevent loss from various areas of concern, including that of the skeletal, muscular, and immunological systems.
Background

Post-flight recovery of bone loss and demineralization can occur over a period of time, but the long-term effects (increased risk of osteoporosis) of these changes on the crew are not completely understood, especially in crewmembers’ later years following long-duration flights. As missions increase in duration, the prevention of bone loss is necessary to avoid injuries or fractures to the crew, especially as more strenuous activities are performed, and risks are increased with the exploration of other planetary bodies and longer durations of microgravity.

Exercise as a Countermeasure

It is noted in the Human Integration Design Handbook (HIDH) Section 5.2.4.2 that “it is critical for crewmembers to have frequent access (potentially multiple daily sessions) to exercise equipment that can provide high levels of loading, and diversity in load application, on the skeletal system. These exercise countermeasures should be targeted primarily toward protecting the lower body and hip regions.” It has been observed that the areas of most concern for skeletal unloading are in the lower areas of the body (i.e., hips and trochanter).

As mentioned by Shackelford et al. “Spaceflight can be considered the ultimate model to determine the role of gravity on the human skeleton. There is a consensus among exercise scientists that both endurance (aerobic) and resistance exercises are needed as countermeasures to maintain overall crew health and performance during and after spaceflight. An exercise countermeasure has the advantage of benefiting multiple body systems (musculoskeletal, cardiovascular, immunological) and can be targeted to those body regions needing protection. Maintenance of muscle strength also reduces risk of injury during falls and impact. Increased muscle strength reduces the risk of impact injury by decreasing joint angular velocity, providing damping of impact loads. Muscles protect bone from fracture by resisting bending moments across long bones.”

1. OCHMO-TB-031 Exercise Technical Brief

Risk of Bone Fracture due to Spaceflight-induced Changes to Bone

Grimm et al.
Background

<table>
<thead>
<tr>
<th>Level</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Bone density is within 1 SD (+1 or -1) of the young adult mean.</td>
</tr>
<tr>
<td>Low bone mass</td>
<td>Bone density is between 1 and 2.5 SD below the young adult mean (-1 to -2.5 SD).</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Bone density is 2.5 SD or more below the young adult mean (-2.5 SD or lower).</td>
</tr>
<tr>
<td>Severe (established)</td>
<td>Bone density is more than 2.5 SD below the young adult mean, and there have been one or more osteoporotic fractures.</td>
</tr>
</tbody>
</table>

World Health Organization Definitions Based on Bone Density Levels

Reference Information

“Observations of astronauts and cosmonauts indicate that skeletal unloading causes loss of calcium from the skeleton, which increases the risk of kidney stones and bone fracture (both during the mission and potentially as a lifelong consequence). By using single photon absorptiometry, the bone density of the calcaneus in astronauts aboard Skylabs 2, 3, and 4 had a decrease of as much as 8% with an average of 4% on the longest flights of 59 and 84 days. Similar observations have been made in cosmonauts, where losses in bone density of the calcaneus have been reported to be as much as 19% after 140 days in microgravity” (Holick). Additionally, Shackelford et al. reported “to date, we have collected pre-and post-flight bone densitometry measurements on 47 individuals from such flights. Although losses show significant heterogeneity among individuals and between bones of a given subject, bone loss is a consistent finding after spaceflight. Among astronauts and cosmonauts who participated in long duration (average of 170 days) flights aboard Mir and the ISS, >50% of the crew members had a 10% loss in at least one skeletal site, and 22% of the Mir cosmonauts had a 15–20% loss in at least one site. This bone loss has been shown to be a regional phenomenon in which the areas with the greatest decrease in weight bearing lose the most bone; losses average 1–2%/mo in such regions as the lumbar spine and hip compared with no change in the arms or radius (Mir and ISS astronauts, arms: 0.1%/mo; ISS astronauts, radius and ulna: -0.1%/mo).”
Reference Data

In a review of the information from the Apollo Medical Summit, NASA/TM-2007-214755, it was noted that “the astronauts demanded exercise capability for the Command Module for rest and relaxation purposes,” which supports Volume 1 of NASA-STD-3001 stating that countermeasures should be used to “mitigate undesirable physical, physiological, and psychological effects of space flight upon crewmembers.”

Due to the rarity of persons in microgravity for the purposes of studying bone loss, numerous studies have been performed using bed-rest as an analogue to better understand the physiology during skeletal unloading, as well as efficacy of various prevention techniques (exercise, medications, diet, etc.). The following tables show the results of these studies and the impact of unloading, regardless of the presence of microgravity (Tables 1 and 2 from Grimm et al.).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Recent bed-rest studies investigating the influence of simulated microgravity on bone.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of bed-rest</td>
<td>Duration</td>
</tr>
<tr>
<td>HDT with or without exercise</td>
<td>5 d</td>
</tr>
<tr>
<td>HDT with or without resistive vibration exercise or resistive exercise</td>
<td>60 d</td>
</tr>
<tr>
<td>HDT with or without resistive vibration exercise</td>
<td>60 d</td>
</tr>
<tr>
<td>HDT</td>
<td>35 d</td>
</tr>
<tr>
<td>HDT with or without 30 min centrifugation (1 g at center of mass)</td>
<td>5 d</td>
</tr>
<tr>
<td>HDT</td>
<td>30 d</td>
</tr>
<tr>
<td>HDT</td>
<td>90 d</td>
</tr>
<tr>
<td>HDT with or without vibration training</td>
<td>14 d</td>
</tr>
<tr>
<td>HDT with or without exercise or high-protein nutrition</td>
<td>60 d</td>
</tr>
<tr>
<td>HDT with or without exercise or high-protein nutrition</td>
<td>60 d</td>
</tr>
<tr>
<td>HDT</td>
<td>21–90 d</td>
</tr>
<tr>
<td>HDT with or without resistive vibration exercise or resistive exercise</td>
<td>60 d</td>
</tr>
</tbody>
</table>

BR = bed-rest, HDT = head down tilt, d = days, NTx = amino-terminal collagen crosslinks, PINP = procollagen type I N-terminal propeptide, sCD200 = soluble CD200, sCD200R1 = soluble CD200R1.
Reference Data

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Overview of the bone loss countermeasures used in real and simulated microgravity.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countermeasure</td>
<td>Microgravity stimulates</td>
</tr>
<tr>
<td>RED</td>
<td>Real (ISS)</td>
</tr>
<tr>
<td>ARED</td>
<td>Real (ISS)</td>
</tr>
<tr>
<td>70 mg alendronate once/week + RED orARED</td>
<td>Real (ISS)</td>
</tr>
<tr>
<td>HEM (resistance exercise training)</td>
<td>Simulated (horizontal bed-rest)</td>
</tr>
<tr>
<td>Resitive exercise + vibration</td>
<td>Simulated (HDT bed-rest)</td>
</tr>
<tr>
<td>Supine treadmill exercise within LBNP/flywheel</td>
<td>Simulated (HDT bed-rest)</td>
</tr>
<tr>
<td>Artificial gravity (1g at center of mass)</td>
<td>Simulated (HDT bed-rest)</td>
</tr>
<tr>
<td>Alendronate (10 mg/d)</td>
<td>Simulated (horizontal bed-rest)</td>
</tr>
<tr>
<td>EHDR (5 or 2 x 20 mg/d)</td>
<td>Simulated (horizontal bed-rest)</td>
</tr>
<tr>
<td>Flywheel resistance training + 1 x 60 mg pamidronate</td>
<td>Simulated (HDT bed-rest)</td>
</tr>
</tbody>
</table>

**HEM** = horizontal exercise machine, **BMD** = bone mineral density, **RED** = interim resistive device, **ARED** = advanced resistive exercise device, **HDT** = headdown tilt, **d** = days, **LBNP** = lower body negative pressure, **EHDR** = disodium ethane-1-hydroxy-1,1-diphosphonate or ethane-1-hydroxy-1,1-diphosphonate.

**Application**

Information noted in the NASA-STD-3001 Volumes 1 and 2, along with details from the HIDH, provide reference details and guidance to aid in the understanding of crew needs. Some examples that have helped in the implementation of the exercise equipment include items from ISS, such as the **Advanced Resistive Exercise Device (ARED)** – This device, while similar to the Interim Resistive Exercise Device (iRED), is capable of higher concentric resistance and eccentric-to-concentric ratio close to that recommended by expert panels and confirmed effective by exercise scientists. The aRED also collects data regarding the parameters associated with crew exercise and transmits it to the ground.

![aRED Diagram; NASA, 2012](aRED Diagram; NASA, 2012)

**NASA astronaut Chris Cassidy using the aRED device**
Application

- **Treadmill 2 (COLBERT)** – An exercise treadmill that can also be used to collect data such as body loading, duration of session, and speed for each crewmember.

![COLBERT Diagram; NASA, 2009](image1)

- **Cycle-Ergometer with Vibration Isolation System (CEVIS)** – A structurally isolated aerobic exercise cycle that serves as a countermeasure to cardiovascular deconditioning on orbit.

![CEVIS Diagram; Ambrose et al, 2014](image2)

The crew is required to exercise a minimum of time dependent on the program mission as dictated by the medical team, however previous requirements have been as little as 2.5 hours per workday with a strict exercise program. Additionally, the medical team may instruct the crew to take medication, such as bisphosphonates, to prevent bone loss, but this is not currently required for all crew.

Furthermore, the food lab and nutritionists have developed appropriate nutritional foods to ensure that the crew have enough micro- and macronutrients to promote crew mental and physical health. The interactions of the various technical requirements from both NASA-STD-3001 Volumes 1 and 2, along with the supported information from the appendices, will allow for successful missions.¹

While it is important to review and update the individual technical requirements that address crew health or related areas, considerations should be taken to ensure that all the technical requirements are reviewed holistically so they can be applied appropriately for planning and future requirements.
Back-Up
Major Changes Between Revisions

Rev B → Rev C
- Updated information to reflect the revisions to language throughout both volumes of NASA-STD-3001.
- Updated/added website links due to new NASA website launch

Rev A → Rev B
- Updated information to be consistent with NASA-STD-3001 Volume 1 Rev B and Volume 2 Rev C.

Original → Rev A
- Overview
  - Added executive summary
  - Updated standards to Volume 2 Rev B
- Background
  - Added subcategory “Exercise as a countermeasure” after description in order to have more separation in the information
  - Added picture to support subcategory for more visual interest
- Application
  - Added diagrams of exercise equipment for more visual interest
- Other
  - Added revision page
  - Added referenced standards page
Referenced Technical Requirements

NASA-STD-3001 Volume 1 Revision C

[V1 3002] Pre-Mission Preventive Health Care  Pre-mission preventive strategies shall be used to reduce in-mission and long-term health medical risks, including, but not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3003] In-Mission Preventive Health Care  All programs shall provide training, in-mission capabilities, and resources to monitor physiological and psychosocial well-being and enable delivery of in-mission preventive health care, based on epidemiological evidence-based probabilistic risk assessment (PRA), individual crewmember needs, clinical practice guidelines, flight surgeon expertise, historical review, mission parameters, and vehicle-derived limitations. These analyses consider the needs and limitations of each specific vehicle and design reference mission (DRM) with particular attention to parameters such as mission duration, expected return time to Earth, mission route and destination, expected radiation profile, concept of operations, and more. In-mission preventive care includes, but is not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3016] Post-Mission Health Care  Post-mission health care shall be provided to minimize occurrence of deconditioning-related illness or injury, including but not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3017] Post-Mission Reconditioning  All programs shall provide the planning, coordination, and resources for an individualized post-mission reconditioning program, specific to each crewmember, mission type, and mission duration. The post-mission reconditioning starts with crew egress at landing and includes a guided, phased reconditioning protocol. The goals of the reconditioning program include the following:
   a. To ensure the health and safety of returning crew.
   b. To actively assist the crew’s return to full functional abilities and return-to-flight status.
   c. To actively assist in the crew’s return to pre-mission fitness

[V1 3018] Post-Mission Long-Term Monitoring  Crewmembers returning from spaceflight shall be monitored longitudinally for health, behavioral health, and well-being parameters in a standardized manner.

[V1 4020] In-Mission Nutrient Intake  Programs shall provide each crewmember with 100% of their calculated nutrient and energy requirements, based on an individual’s age, sex, body mass (kg), height (m), and appropriate activity factor.

[V1 4026] Pre-Mission Bone Mineral Density  Crewmembers’ pre-mission bone mineral density (BMD) T-scores for total hip and lumbar spine (L1-L4), as measured by mass dual energy X-ray absorptiometry (DXA) shall be consistent with an age, sex, gender, and ethnic-matched population.

[V1 4027] Pre-mission Bone Countermeasures  Countermeasures shall maintain bone mineral density of the hip and spine at or above 95% of pre-mission values and at or above 90% for the femoral neck.

[V1 4028] Post-Mission Bone Reconditioning  Post-mission reconditioning shall be aimed at returning bone mineral density to pre-mission baseline values.
Referenced Technical Requirements

NASA-STD-3001 Volume 2 Revision D

[V2 7038] Physiological Countermeasures Capability The system shall provide countermeasures to meet crew bone, muscle, sensorimotor, thermoregulation, and aerobic/cardiovascular requirements defined in NASA-STD-3001, Volume 1.

[V2 7043] Medical Capability A medical system shall be provided to the crew to meet the medical requirements of NASA-STD-3001, Volume 1.

[V2 7100] Food Nutrient Composition The system shall provide a food system with a diet including the nutrient composition that is indicated in the Dietary Reference Intake (DRI) values as recommended by the National Institutes of Health, with the exception of those adjusted for spaceflight as noted in Table 7.1-2—Nutrient Guidelines for Spaceflight.

All referenced tables and figures are available in NASA-STD-3001 Volume 2 Revision D.
Reference List

2. Apollo Medical Summit, NASA/TM-2007-214755
7. Internation Space Station Facilites: Research in Space 2017 and Beyond. NP-2017-04-014-B-JSC