CFT70 Data Review

Testosterone Supplementation as a Countermeasure against Musculoskeletal Losses during Space Exploration

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Proposed Outcome Measures

• Primary dependent measures
  - Muscle cross-sectional area and volume (MRI)
  - Lean body mass (iDXA)
  - Fat mass (iDXA)
  - Muscle strength (Exercise Std Measures)

• Secondary dependent measures
  - Bone mineral density (iDXA)
  - Cardiac Compliance (ECHO, Cardio Std Measures)
  - Muscle fatigue (Ex Std Measures and Questionnaires)
  - Hormones and lipid profiles (UTMB and Nutr/Clin Std Measures)
  - Glucose tolerance and insulin sensitivity (OGTT)
  - Bone metabolism (bone panel and Nutr Std Measures)
  - Skeletal muscle signaling and inflammation
  - Skeletal muscle proteomics
  - Quality of Life (Questionnaires)

Analyses completed/available
Analyses in progress
Shared/LSDW data not yet received
Data included in this review

- Body Composition (iDXA)

- Backup slides:
  - Hormones (Immulite)
  - Lipid Panels (UTMB Clinical Lab)
  - Bone Panel (Milliplex)
  - Glucose Tolerance (OGTT)
Testosterone

Nonlin fit of Testosterone: Curve

Nonlin fit of Baseline-corrected of Testosterone: Curve

- Control
- Exercise
- Exercise + Testosterone
## Body Composition (iDXA)

<table>
<thead>
<tr>
<th>Lean Body Mass</th>
<th>Bone Mineral Density</th>
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<tbody>
<tr>
<td>Total</td>
<td>Total</td>
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<tr>
<td>Trunk</td>
<td>Spine</td>
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<td>Legs</td>
<td>Pelvis</td>
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<td>Arms</td>
<td>Legs</td>
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<th>Fat Mass</th>
<th>Bone Mineral Content</th>
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<tr>
<td>Arms</td>
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<table>
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<tr>
<th>Bone Mineral Content</th>
<th>Total</th>
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<tbody>
<tr>
<td>Total</td>
<td>Legs</td>
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**utmb Health**  
Department of Internal Medicine
Lean Body Mass - Total

**LBM Total**

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**Baseline-corrected of LBM Total**

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<td>70</td>
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**Nonlin fit of LBM Total:**

**Nonlin fit of Baseline-corrected of LBM Total:**

- Control
- Exercise
- Exercise + Testosterone
Lean Body Mass - Trunk

Graphs showing changes in LBM Trunk and Baseline-corrected LBM Trunk during bed rest.

- **LBM Trunk**: Graph showing the trend in LBM Trunk from -14 to 70 days of bed rest.
  - Baseline: 28000 g
  - End: 26000 g
  - Change: -400 g

- **Baseline-corrected LBM Trunk**: Graph showing the trend in Baseline-corrected LBM Trunk from -14 to 70 days of bed rest.
  - Baseline: 28000 g
  - End: 24000 g
  - Change: -4000 g

Non-linear fits of LBM Trunk and Baseline-corrected LBM Trunk are also shown in the graphs.

Legend:
- Red: Control
- Green: Exercise
- Blue: Exercise + Testosterone
Lean Body Mass - Legs

**LBM Legs**

- Graph showing LBM Legs over time from -14 to 70 days of bed rest.

**Baseline-corrected of LBM Legs**

- Graph showing baseline-corrected LBM Legs over time from -14 to 70 days of bed rest.

**Nonlin fit of LBM Legs: Curve**

- Graph showing non-linear fit of LBM Legs over time from -14 to 70 days of bed rest.

**Nonlin fit of Baseline-corrected of LBM Legs: Curve**

- Graph showing non-linear fit of baseline-corrected LBM Legs over time from -14 to 70 days of bed rest.

Legend:
- **Control**
- **Exercise**
- **Exercise + Testosterone**
Lean Body Mass - Arms

**LBM Arms**

- Baseline-corrected of LBM Arms

**Nonlin fit of LBM Arms:Curve**

- Baseline-corrected of LBM Arms:Curve

Legend:
- Red: Control
- Green: Exercise
- Blue: Exercise + Testosterone
Fat Mass - Total

Fat Mass Total

Baseline-corrected of Fat Mass Total

Nonlin fit of Fat Mass Total: Curve

Nonlin fit of Baseline-corrected of Fat Mass Total: Curve
Fat Mass - Trunk

- Fat Mass Trunk
- Baseline-corrected of Fat Mass Trunk
- Nonlin fit of Fat Mass Trunk: Curve
- Nonlin fit of Baseline-corrected of Fat Mass Trunk: Curve

Legend:
- Control
- Exercise
- Exercise + Testosterone
Fat Mass - Legs

Fat Mass Legs

Baseline-corrected of Fat Mass Legs

Nonlin fit of Fat Mass Legs: Curve

Nonlin fit of Baseline-corrected of Fat Mass Legs: Curve
Fat Mass - Arms

**Fat Mass Arms**

- Baseline-corrected of Fat Mass Arms

**Nonlin fit of Fat Mass Arms:Curve**

- Nonlin fit of Baseline-corrected of Fat Mass Arms:Curve

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Control
Exercise
Exercise + Testosterone
Bone Mineral Density - Total

- BMD Total
- Baseline-corrected of BMD Total
- Nonlin fit of BMD Total: Curve
- Nonlin fit of Baseline-corrected of BMD Total: Curve

- Control
- Exercise
- Exercise + Testosterone
Bone Mineral Density - Spine
Bone Mineral Density - Pelvis

BMD Pelvis

Baseline-corrected of BMD Pelvis

Nonlin fit of BMD Pelvis: Curve

Nonlin fit of Baseline-corrected of BMD Pelvis: Curve

- Control
- Exercise
- Exercise + Testosterone
Bone Mineral Density - Legs

BMD Legs

Baseline-corrected of BMD Legs

Nonlin fit of BMD Legs:Curve

Nonlin fit of Baseline-corrected of BMD Legs:Curve

- Control
- Exercise
- Exercise + Testosterone
Bone Mineral Density - Arms

BMD Arms

Baseline-corrected of BMD Arms

Nonlin fit of BMD Arms: Curve

Nonlin fit of Baseline-corrected of BMD Arms: Curve

Control
Exercise
Exercise + Testosterone
Bone Mineral Content - Total

BMC Total

Baseline-corrected of BMC Total

Nonlin fit of BMC Total: Curve

Nonlin fit of Baseline-corrected of BMC Total: Curve

- Control
- Exercise
- Exercise + Testosterone
Bone Mineral Content - Legs

BMC Legs

Baseline-corrected of BMC Legs

Nonlin fit of BMC Legs: Curve

Nonlin fit of Baseline-corrected of BMC Legs: Curve

Control
Exercise
Exercise + Testosterone
Body Composition Summary

- Exercise promotes LBM maintenance
- Testosterone + Ex promotes gains in LBM
- Testosterone + Ex prevents FM increases
- Effects of bed rest on bone unclear
  - pelvis (BMD) and legs (BMC)?
Publication Plan

Effects of countermeasures on:
- Muscle mass and volume
  - iDXA, MRI, Hormones, Lipids,
- Muscle Function and fatigue
  - Muscle strength/fatigue, Cardiac Function, QOL Questionnaires
- Bone metabolism
  - iDXA, Bone panels, Hormones, Cytokines
- Muscle metabolism
  - Skeletal muscle proteomics
Team & Support

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- Chris Danesi, MS
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- Charlie Gilkison, R.N., M.S.N.
- ITS-CRC & FARU Staff
- FAP Team
- CFT70 Colleagues

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- NASA Flight Analogs Project
Leg Skeletal Muscle Protein Catabolism: MuRF-1

MuRF-1

Baseline-corrected of MuRF-1

Bed Rest (day)

arbitrary units (relative to mouse control)

Bed Rest (day)

% Change

Baseline-corrected of MuRF-1

Bed Rest (day)

% Change

Control
Exercise
Exercise + Testosterone
# Hormones (Immuleite)

- DHEA-SO4
- Estradiol
- Sex Hormone Binding Globulin (SHBG)
- IGF-1
- IGFBP-3
- Cortisol
- Insulin
- C-Peptide
DHEAS

DHEAS

Baseline-corrected of DHEAS

Nonlin fit of DHEAS: Curve

Nonlin fit of Baseline-corrected of DHEAS: Curve

Control
Exercise
Exercise + Testosterone
Estradiol

- Estradiol
- Baseline-corrected of Estradiol
- Nonlin fit of Estradiol: Curve
- Nonlin fit of Baseline-corrected of Estradiol: Curve

Control
Exercise
Exercise + Testosterone
Sex Hormone Binding Globulin (SHBG)
IGF-1

**IGF-1**

**Baseline-corrected of IGF-1**

**Nonlin fit of IGF-1:Curve**

**Nonlin fit of Baseline-corrected of IGF-1:Curve**

- **Control**
- **Exercise**
- **Exercise + Testosterone**
IGFBP-3
Cortisol

**COR**

**Baseline-corrected of COR**

**Nonlin fit of COR: Curve**

**Nonlin fit of Baseline-corrected of COR: Curve**

- Control
- Exercise
- Exercise + Testosterone
Insulin

Insulin

Baseline-corrected of Insulin

Nonlin fit of Insulin: Curve

Nonlin fit of Baseline-corrected of Insulin: Curve

- Red: Control
- Green: Exercise
- Blue: Exercise + Testosterone
C-Peptide

![Graphs showing C-Peptide levels and baseline-corrected C-Peptide levels over time.](image)
Hormones Summary
Lipid panels

- Measured by UTMB Clinical lab during bed rest phase for monitoring of normal values during testosterone treatment
  - Cholesterol
  - HDL Chol
  - HDL/Chol Ratio
  - LDL Chol
  - VLDL
  - Triglycerides
Cholesterol

**CHOL**

- Control
- Exercise
- Exercise + Testosterone

**Baseline-corrected of CHOL**

- Control
- Exercise
- Exercise + Testosterone

**Nonlin fit of CHOL:Curve**

- Control
- Exercise
- Exercise + Testosterone

**Nonlin fit of Baseline-corrected of CHOL:Curve**

- Control
- Exercise
- Exercise + Testosterone
Triglycerides
HDL Cholesterol

- HDL Chol
- Baseline-corrected of HDL Chol
- Nonlin fit of HDL Chol: Curve
- Nonlin fit of Baseline-corrected of HDL Chol: Curve

- Control
- Exercise
- Exercise + Testosterone
HDL Chol Ratio

**HDLC Ratio**

**Baseline-corrected of HDLC Ratio**

**Nonlin fit of HDLC Ratio: Curve**

**Nonlin fit of Baseline-corrected of HDLC Ratio: Curve**

- Control
- Exercise
- Exercise + Testosterone
LDL Cholesterol

LDL CHOL

Baseline-corrected of LDL CHOL

Nonlin fit of LDL CHOL:Curve

Nonlin fit of Baseline-corrected of LDL CHOL:Curve

- Control
- Exercise
- Exercise + Testosterone
Lipid Panel Summary
Bone Panel

Milliplex

- TNF-α
- ACTH*
- DKK-1
- FGF-23
- IL-1β*
- IL-6*
- RANKL*

- Insulin
- Leptin
- Osteocalcin (OC)
- Osteopontin (OPN)
- Osteoprotegerin (OPG)
- Parathyroid hormone (PTH)
- Sclerostin (SOST)

*Not presented: Incomplete/inconclusive results due to values below the detectable range in most samples
TNF-alpha

TNFalpha

Baseline-corrected of TNFalpha

Nonlin fit of TNFalpha: Curve

Nonlin fit of Baseline-corrected of TNFalpha: Curve

Control
Exercise
Exercise + Testosterone
DKK1

Nonlin fit of DKK1: Curve

Nonlin fit of Baseline-corrected of DKK1: Curve

Control
Exercise
Exercise + Testosterone
FGF-23
Insulin
Leptin
Osteocalcin (OC)

Osteocalcin

Baseline-corrected of Osteocalcin

Nonlin fit of Osteocalcin:Curve

Nonlin fit of Baseline-corrected of Osteocalcin:Curve

- Control
- Exercise
- Exercise + Testosterone
Osteopontin (OPN)
Osteoprotegerin (OPG)
Parathyroid Hormone (PTH)
Sclerostin (SOST)
Glucose Tolerance

- 2Hr Oral Glucose Tolerance Test (OGTT)
  - Glucose
  - Insulin
  - Insulin Resistance (HOMA-IR)
  - Insulin Sensitivity (Matsuda Index)
  - Lactate
  - Glucose oxidation
OGTT – Fasting Glucose
OGTT – 2Hr Glucose
OGTT – 2Hr Insulin

2Hr Insulin (BR-1)

Baseline-corrected of 2Hr Insulin (BR-1)

Nonlin fit of 2Hr Insulin (BR-1): Curve

Nonlin fit of Baseline-corrected of 2Hr Insulin (BR-1): Curve

Legend:
- Red: Control
- Green: Exercise
- Blue: Exercise + Testosterone
OGTT- Insulin Resistance
OGTT – Insulin Sensitivity

Matsuda Index

Baseline-corrected of Matsuda Index

Nonlin fit of Matsuda Index: Curve

Nonlin fit of Baseline-corrected of Matsuda Index: Curve

Legend:
- Control
- Exercise
- Exercise + Testosterone
OGTT - Fasting Lactate

Nonlin fit of FASTING Lactate (BR-1): Curve

Nonlin fit of Baseline-corrected of FASTING Lactate (BR-1): Curve

- Control
- Exercise
- Exercise + Testosterone
OGTT - Glucose Oxidation
OGTT Summary