

CFT70 Data Review

Testosterone Supplementation as a Countermeasure against Musculoskeletal Losses during Space Exploration

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William J. Durham, PhD

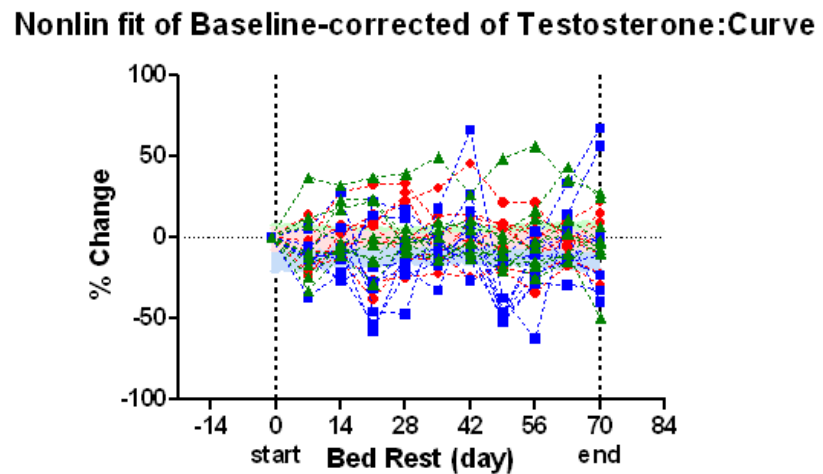
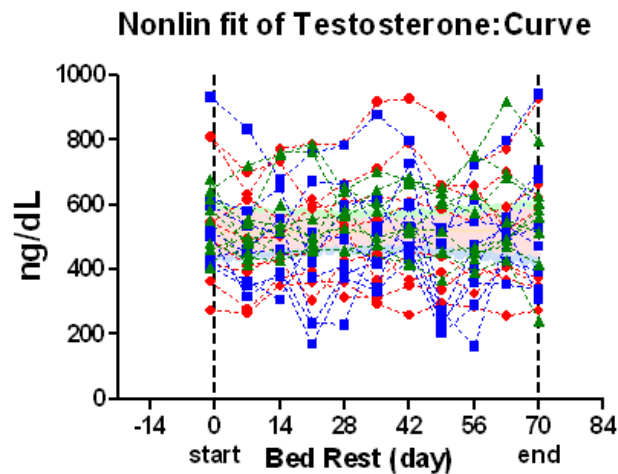
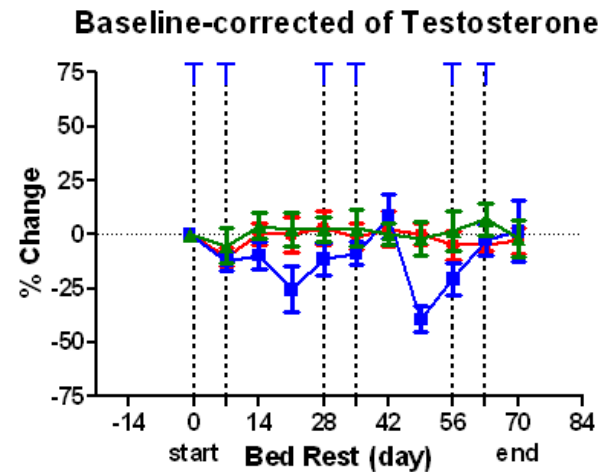
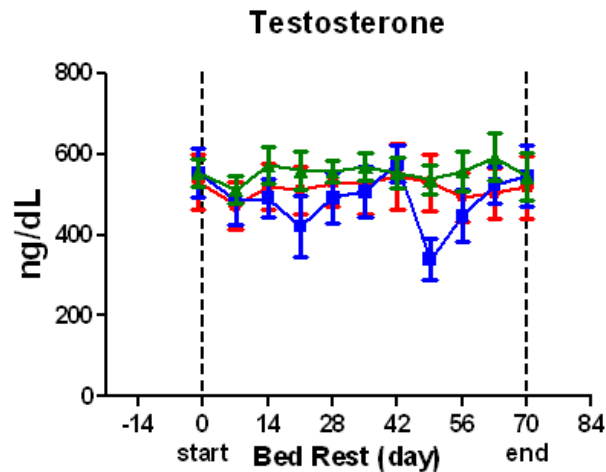
Proposed Outcome Measures

- **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)

Data included in this review

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

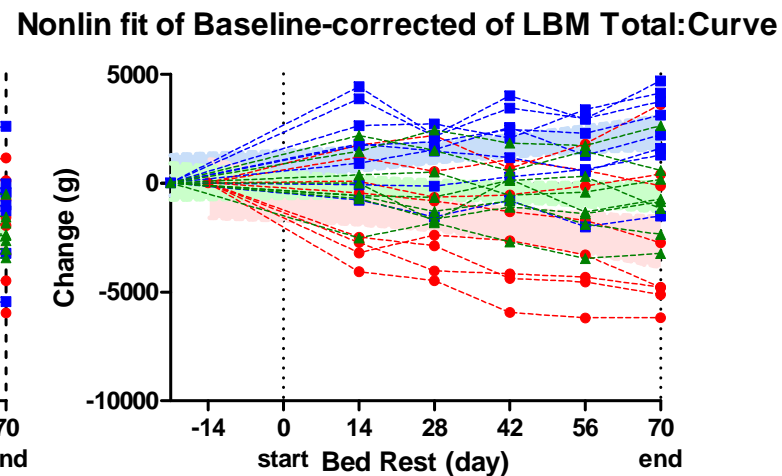
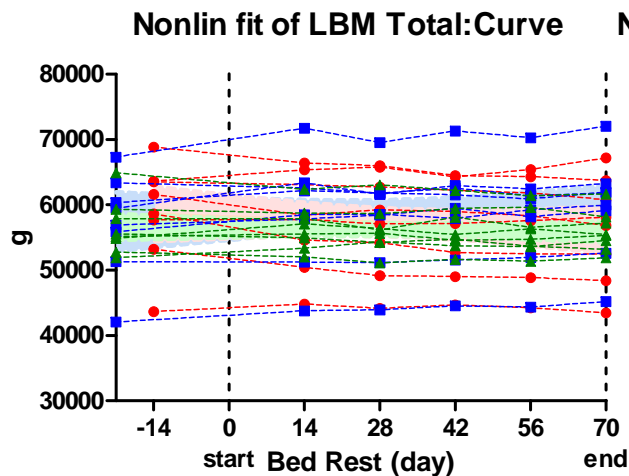
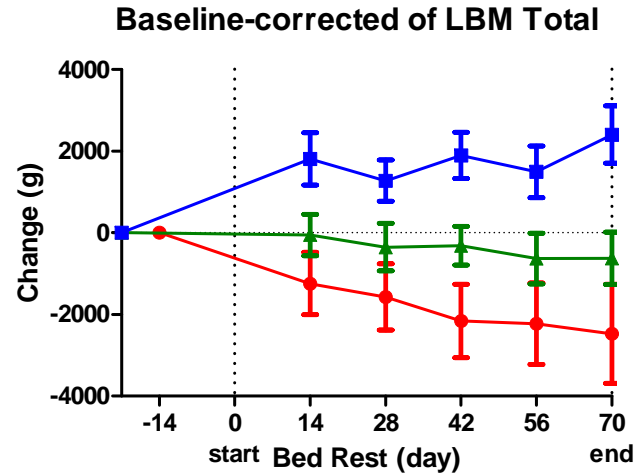
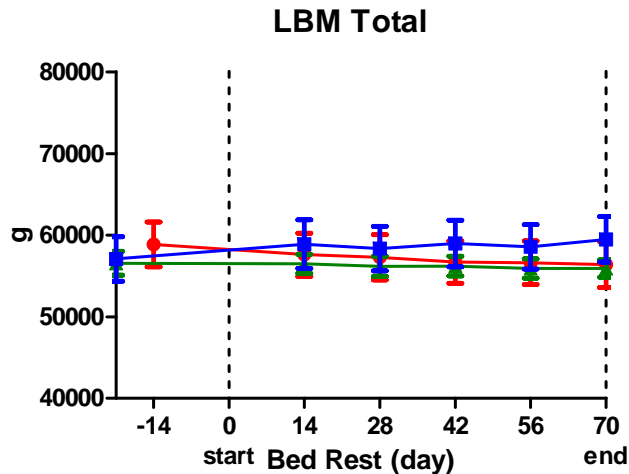
Testosterone



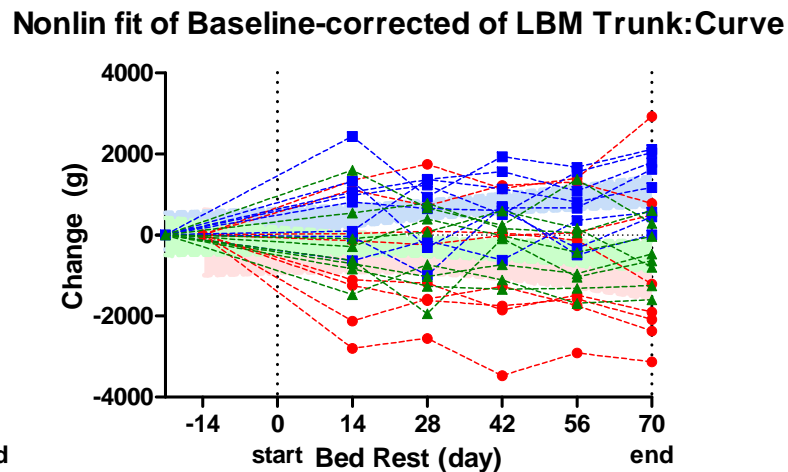
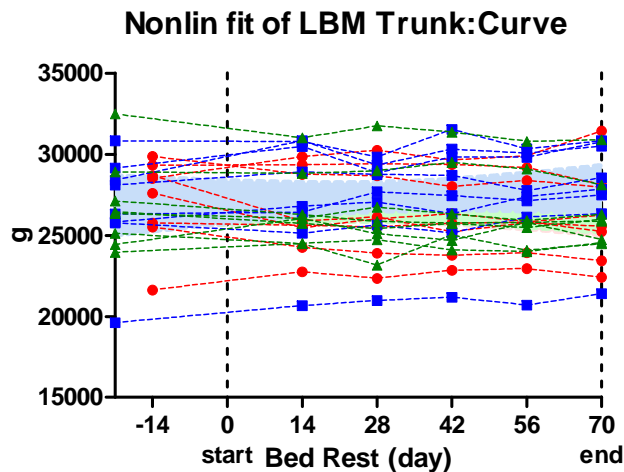
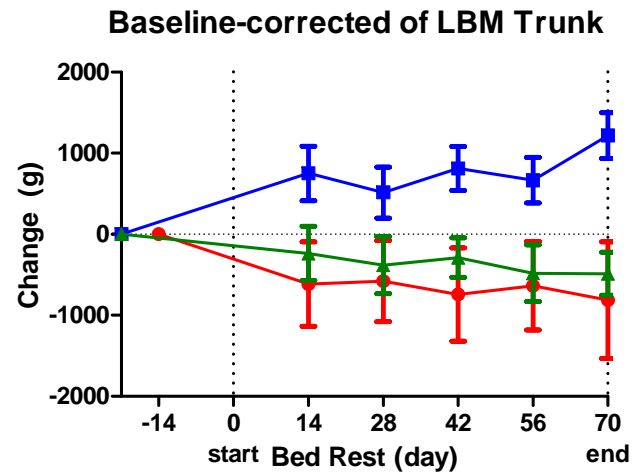
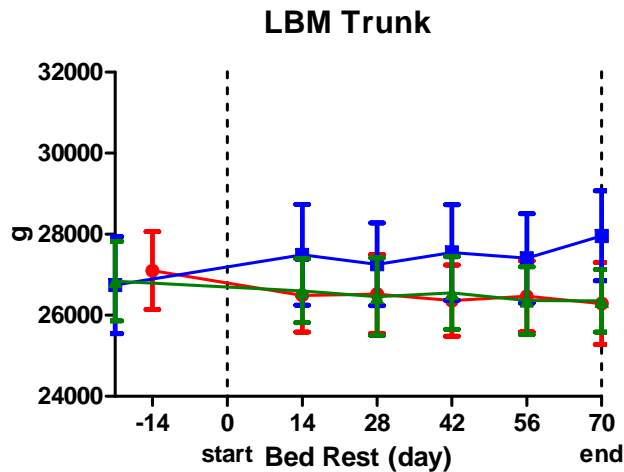
Body Composition (iDXA)

- **Lean Body Mass**
 - Total
 - Trunk
 - Legs
 - Arms
- **Fat Mass**
 - Total
 - Trunk
 - Legs
 - Arms
- **Bone Mineral Density**
 - Total
 - Spine
 - Pelvis
 - Legs
 - Arms
- **Bone Mineral Content**
 - Total
 - Legs

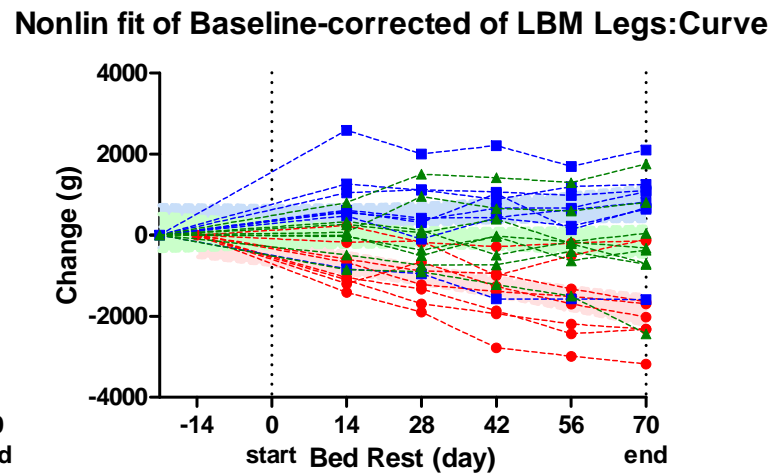
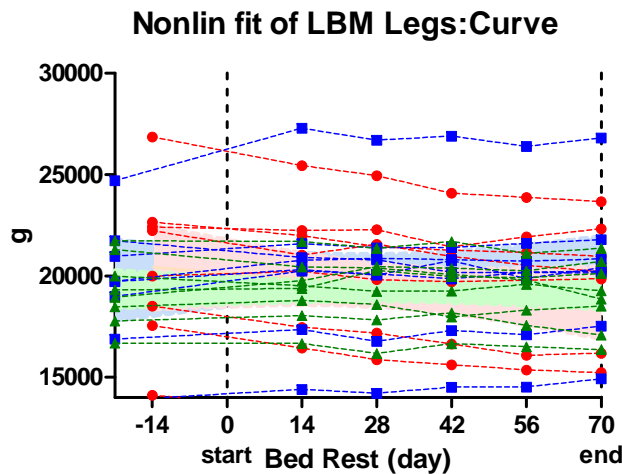
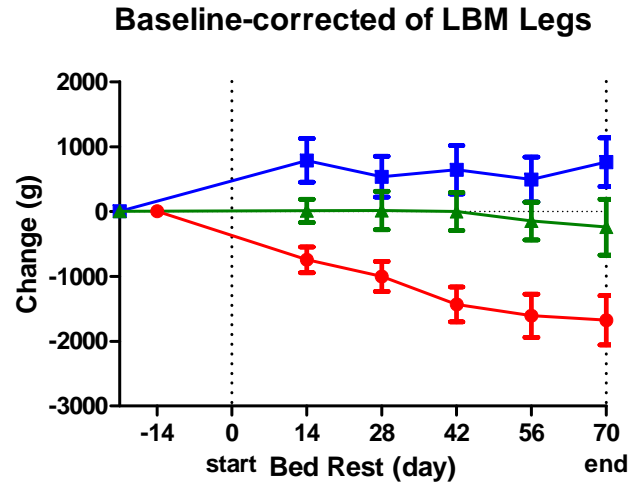
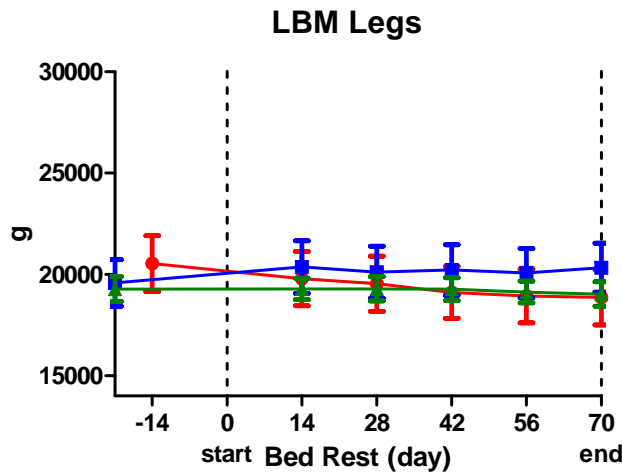
Lean Body Mass - Total



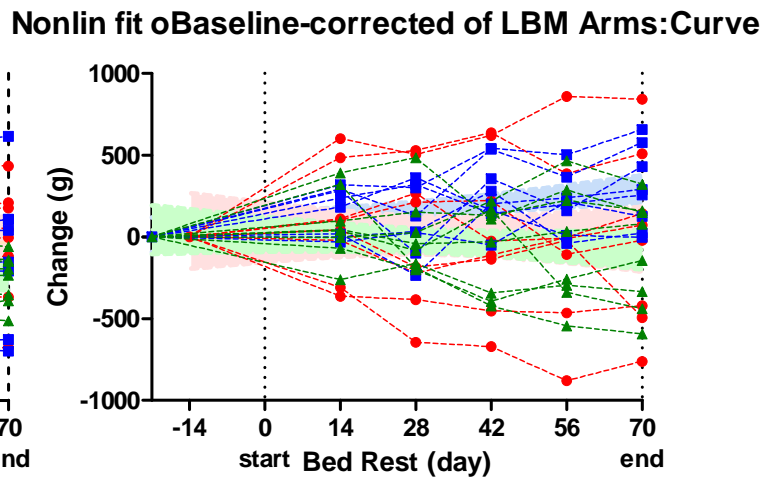
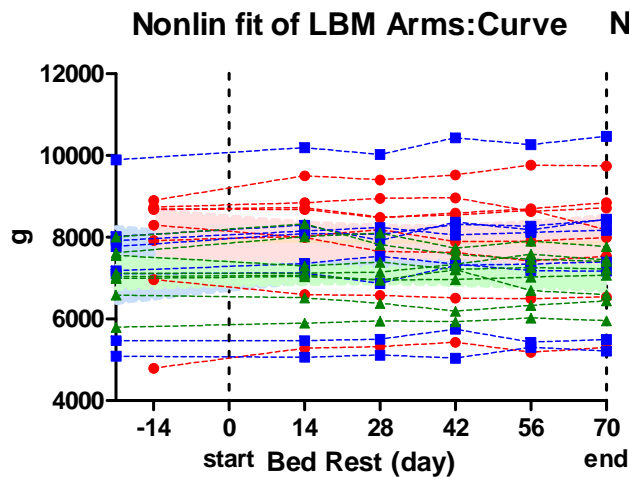
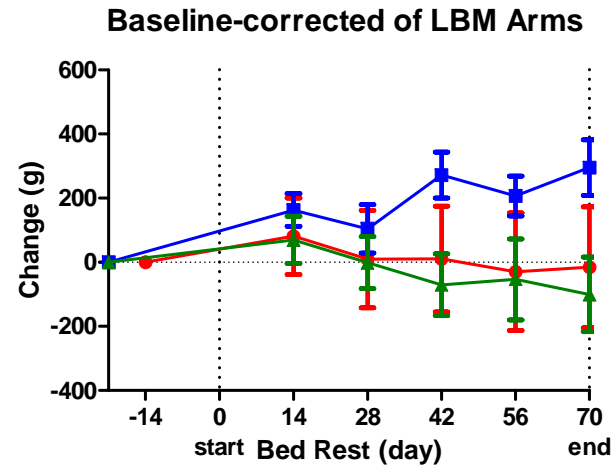
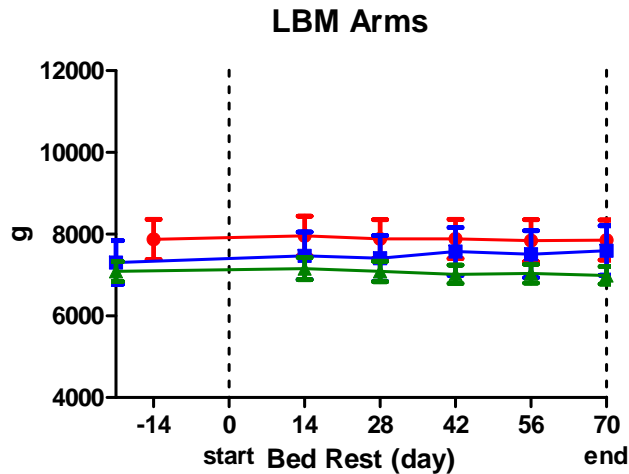
Lean Body Mass - Trunk



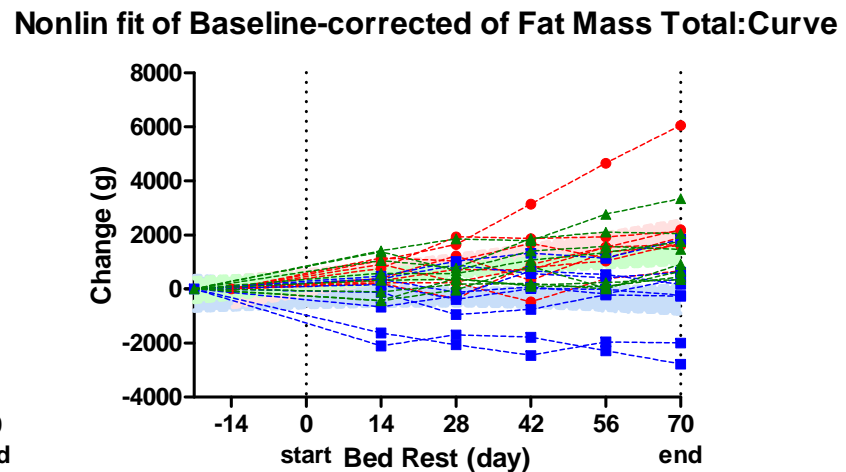
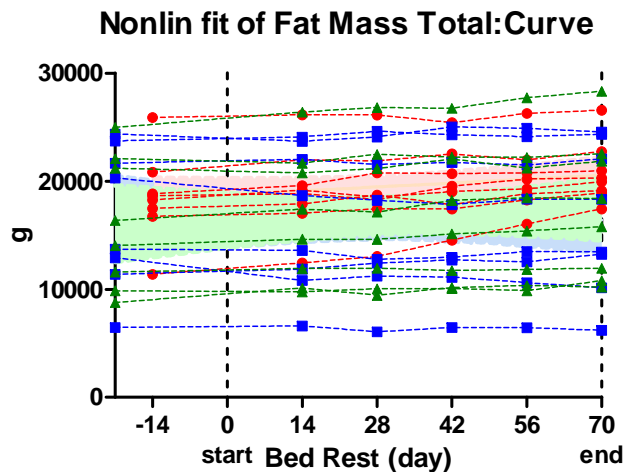
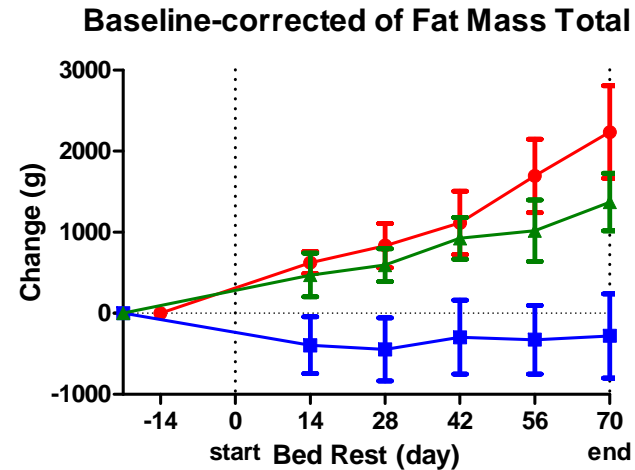
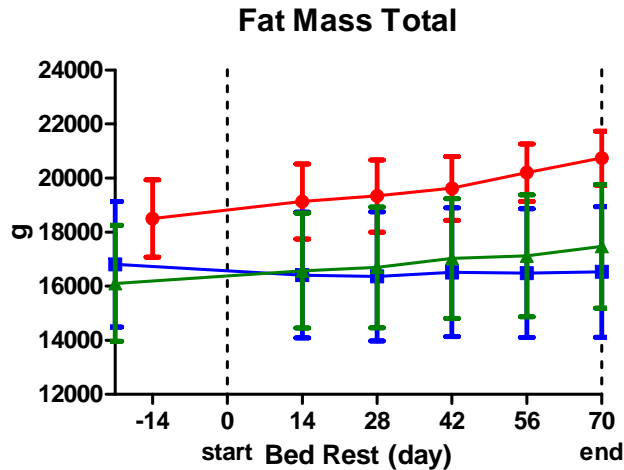
Lean Body Mass - Legs



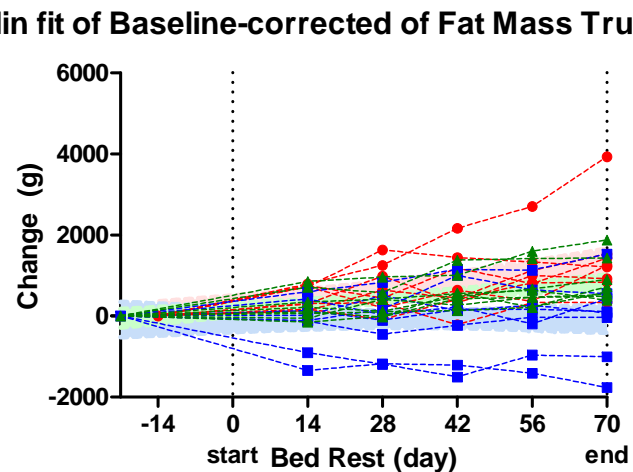
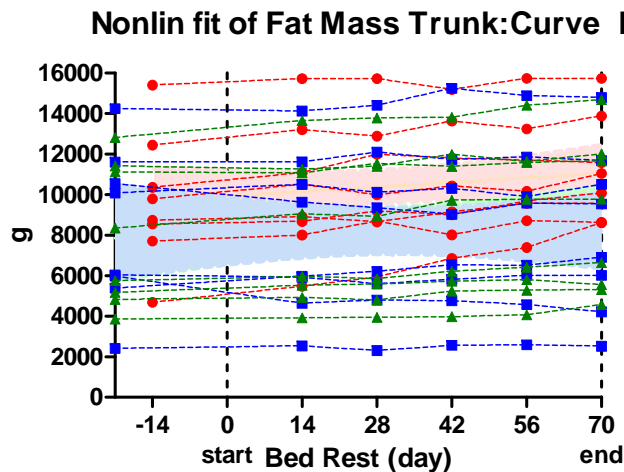
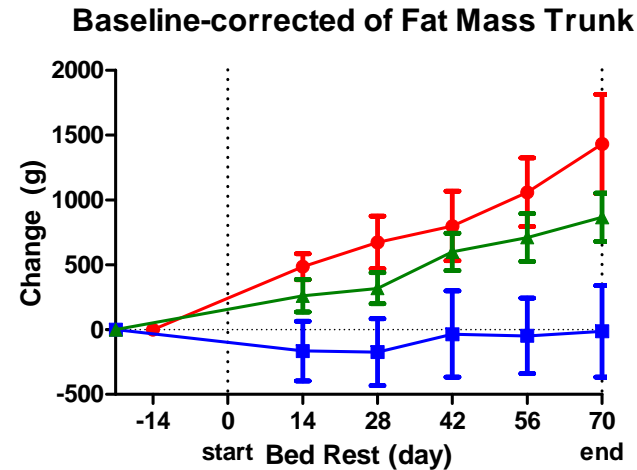
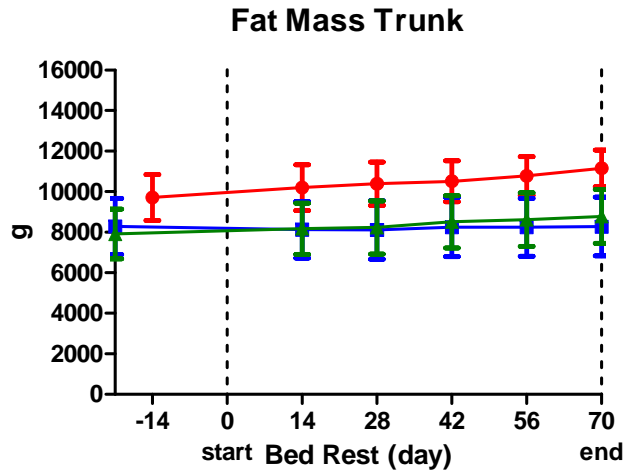
Lean Body Mass - Arms



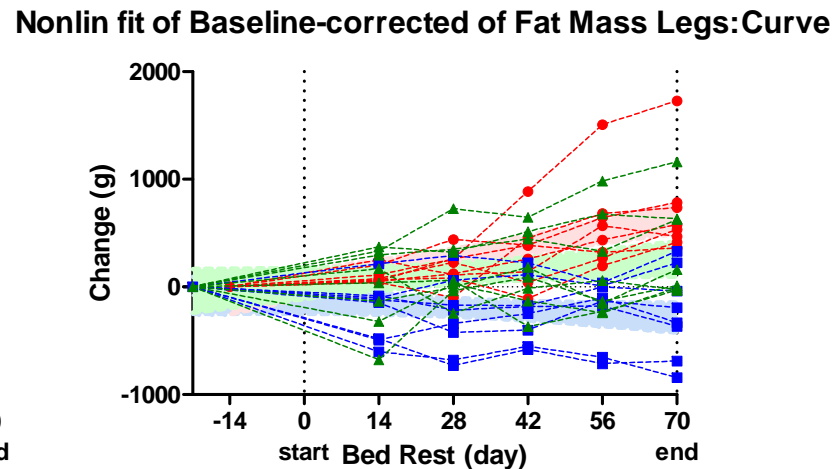
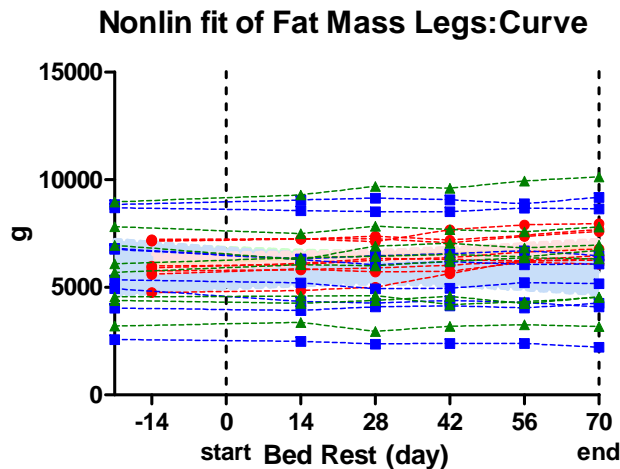
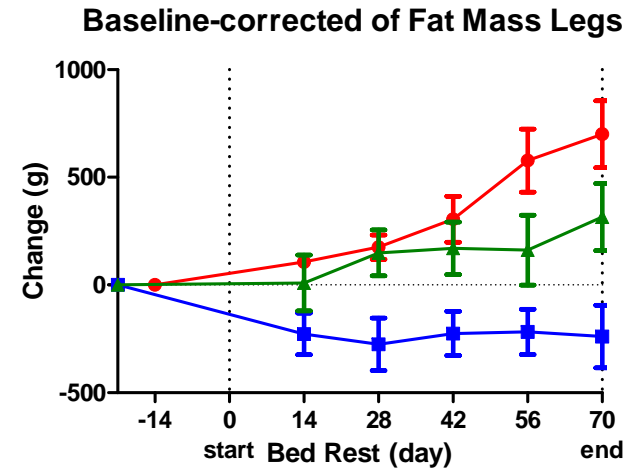
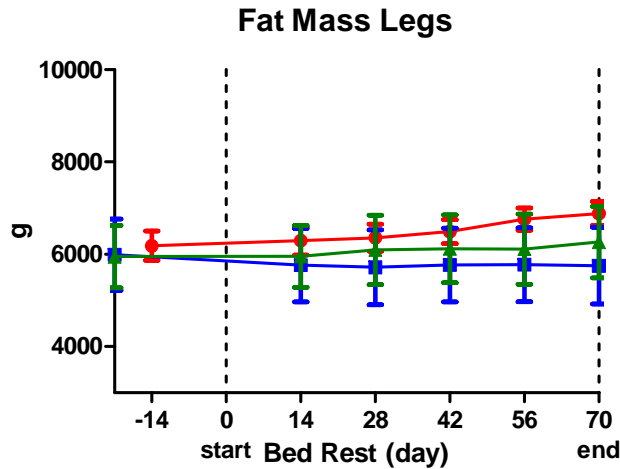
Fat Mass - Total



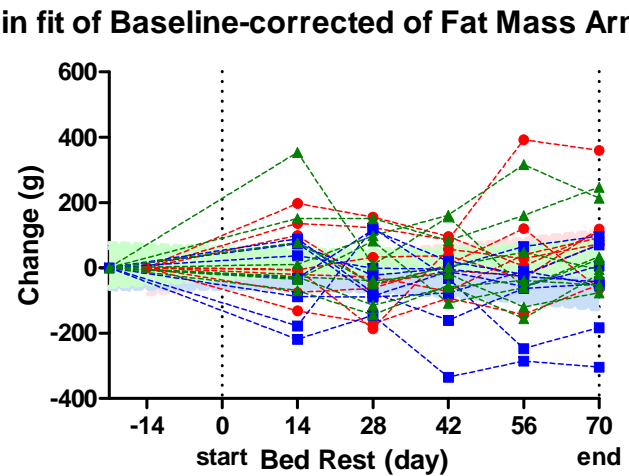
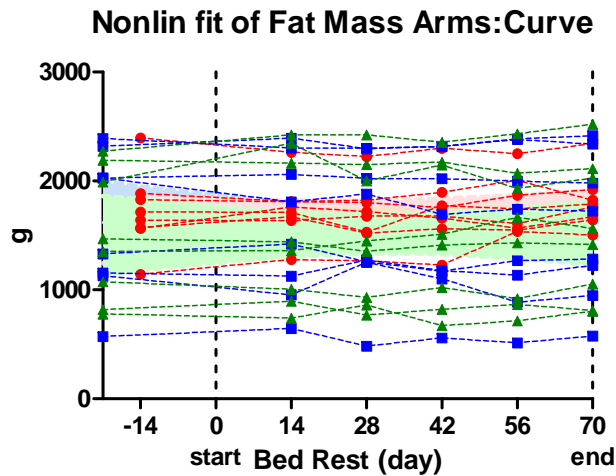
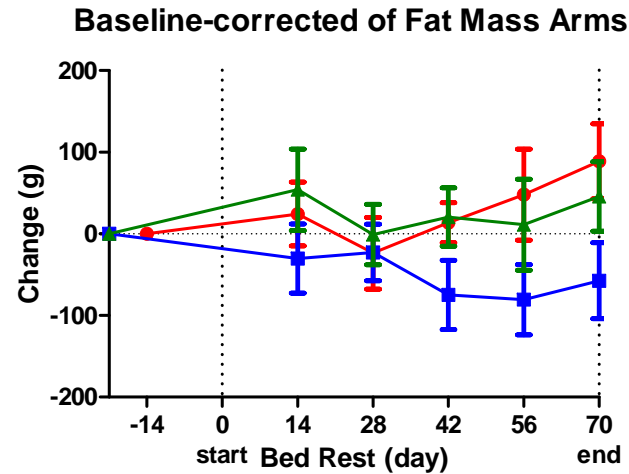
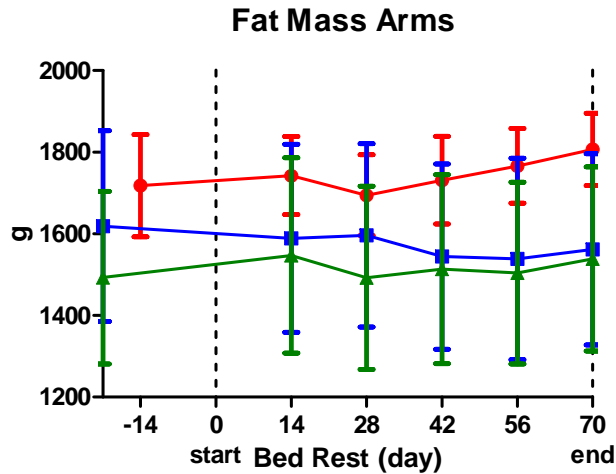
Fat Mass - Trunk



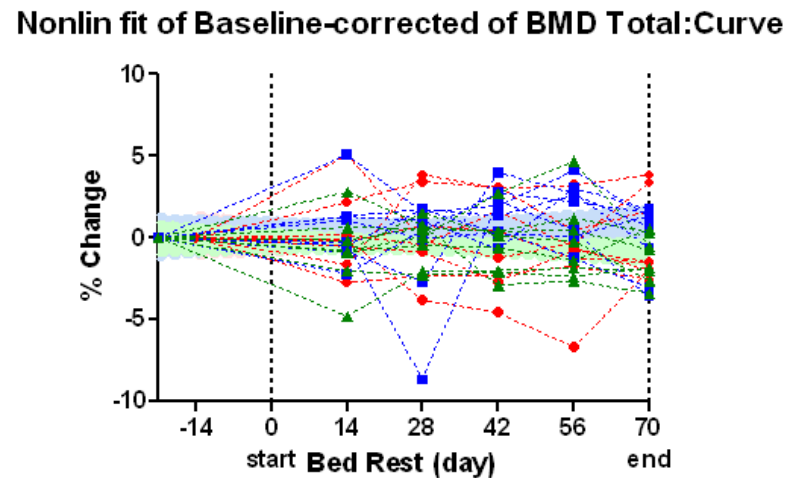
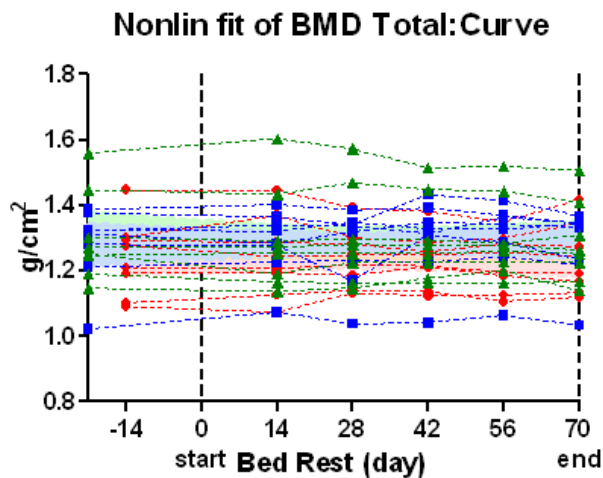
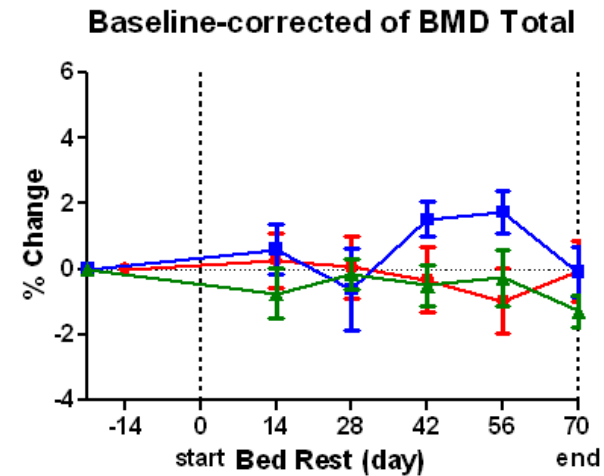
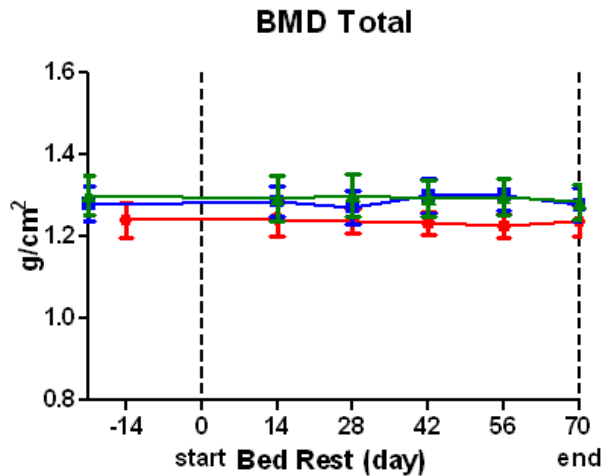
Fat Mass - Legs



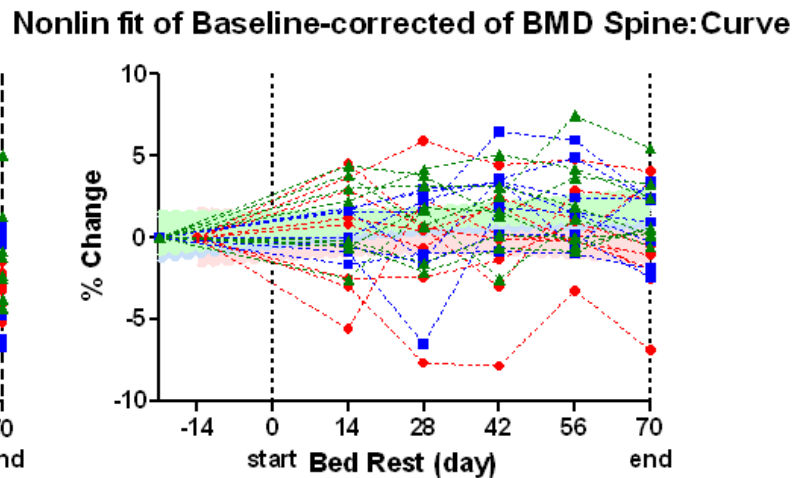
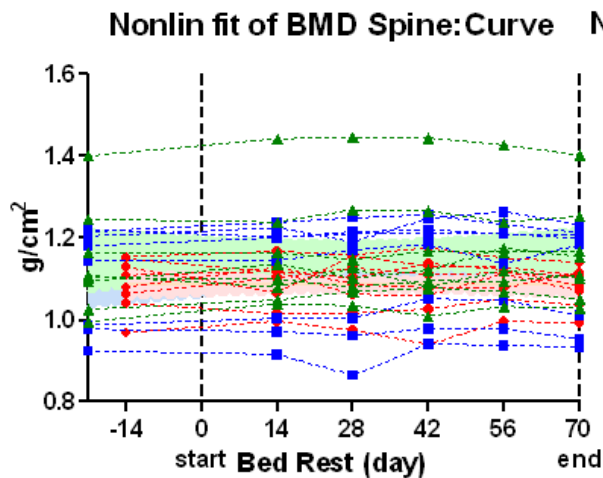
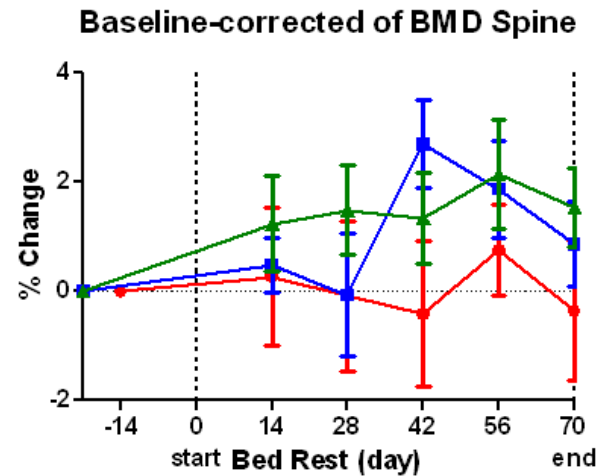
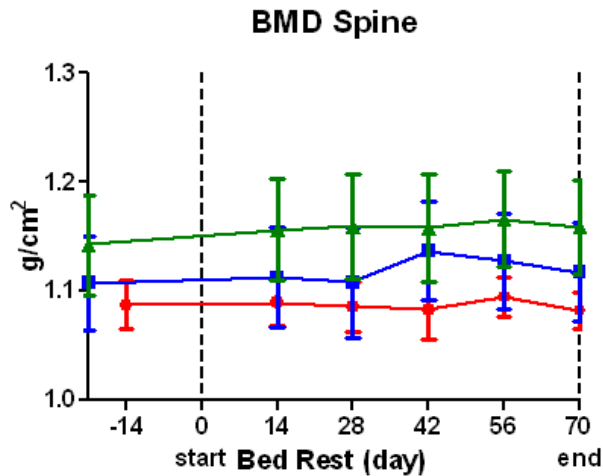
Fat Mass - Arms



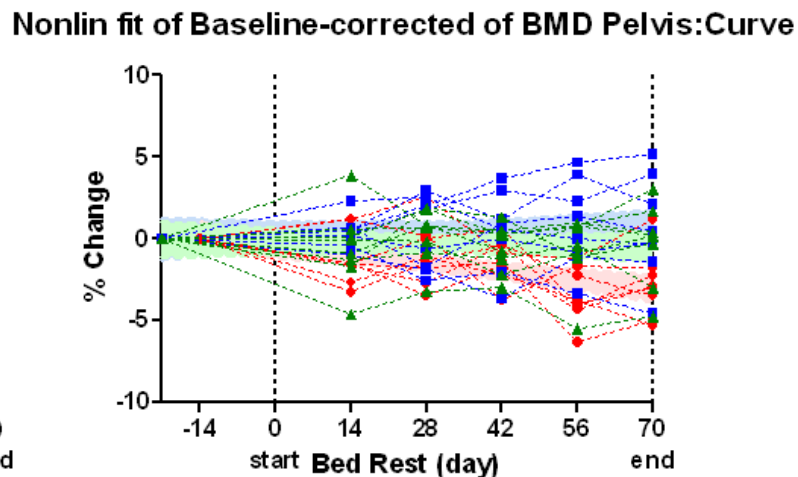
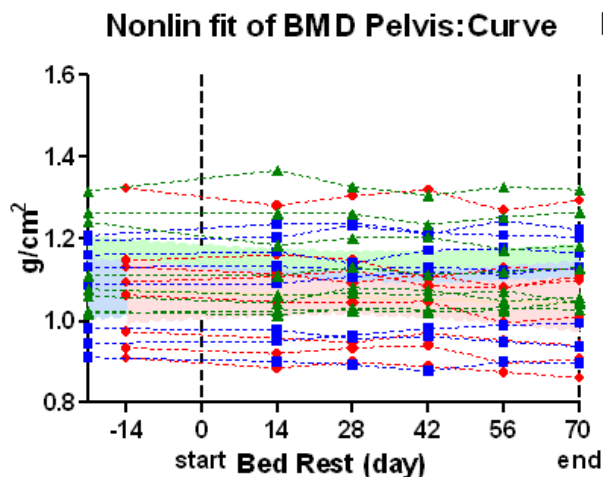
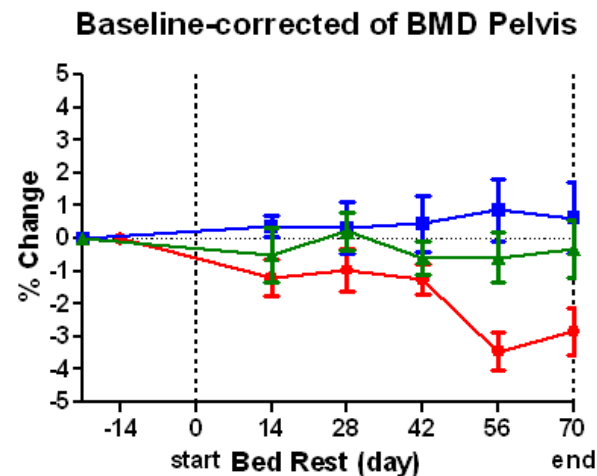
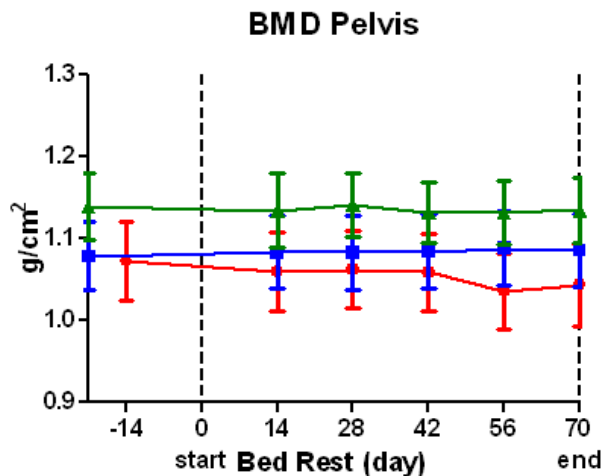
Bone Mineral Density - Total



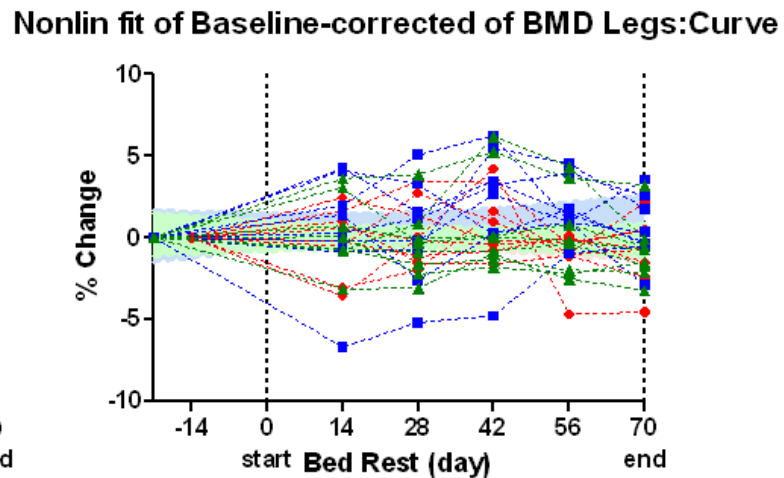
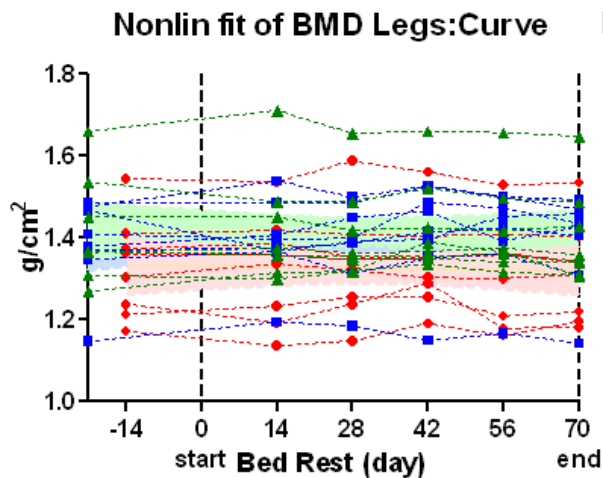
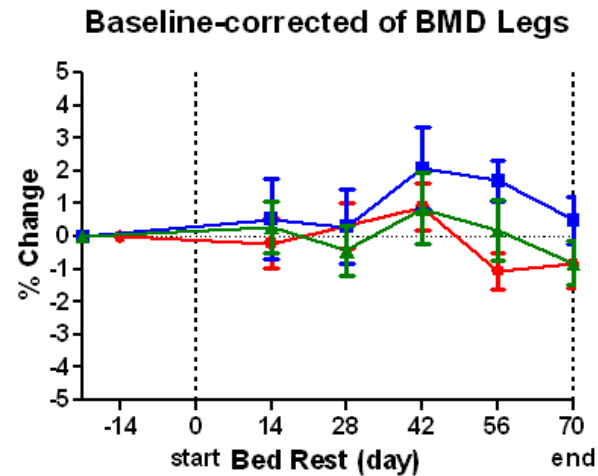
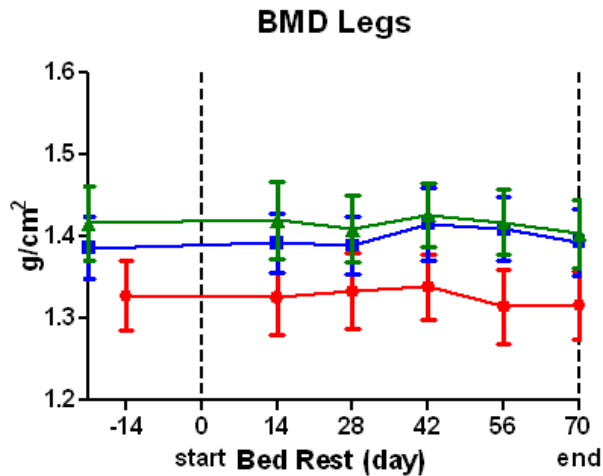
Bone Mineral Density - Spine



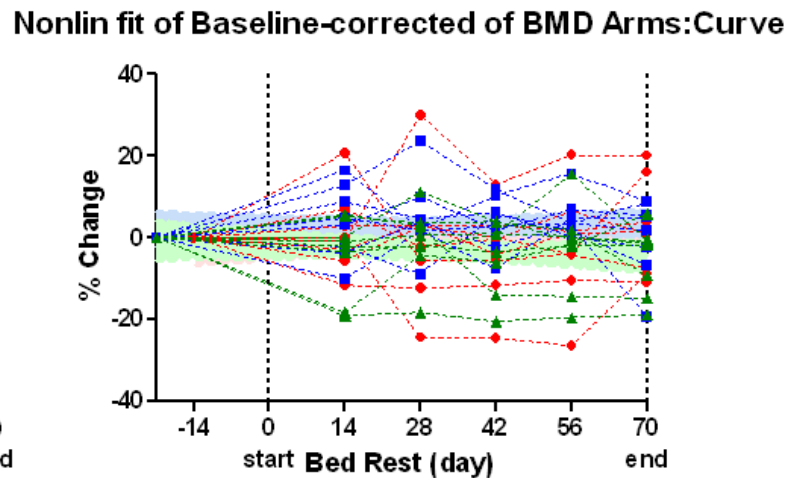
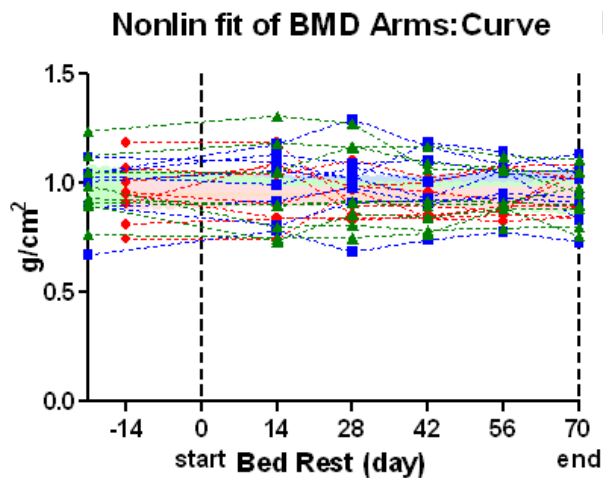
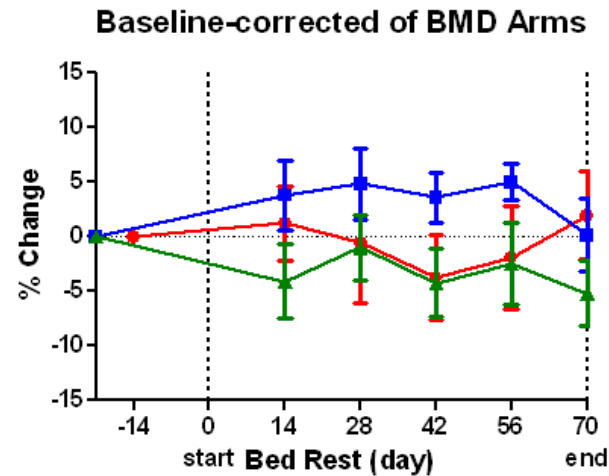
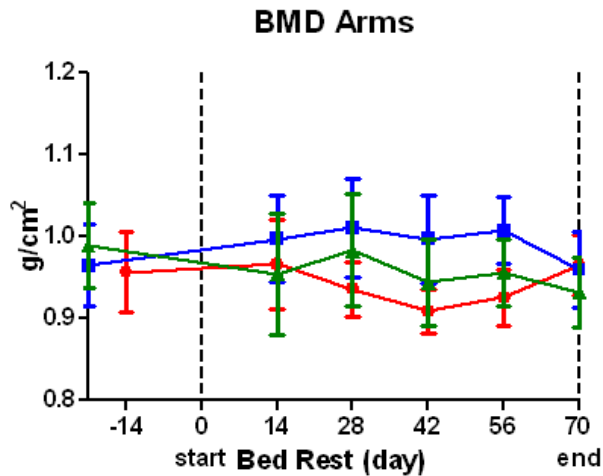
Bone Mineral Density - Pelvis



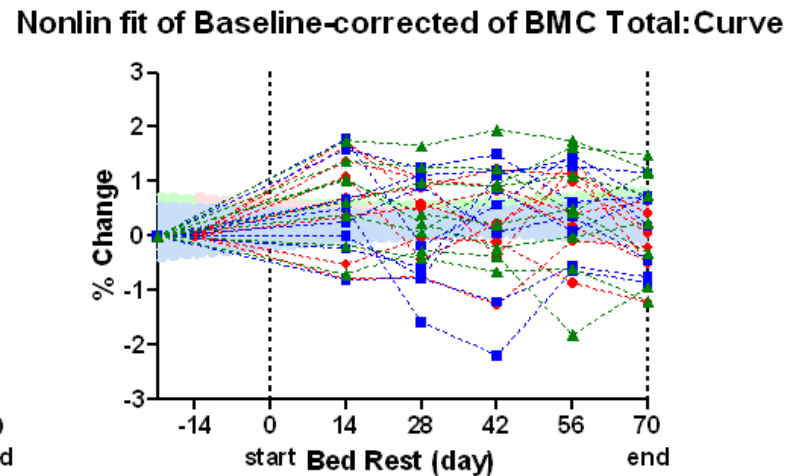
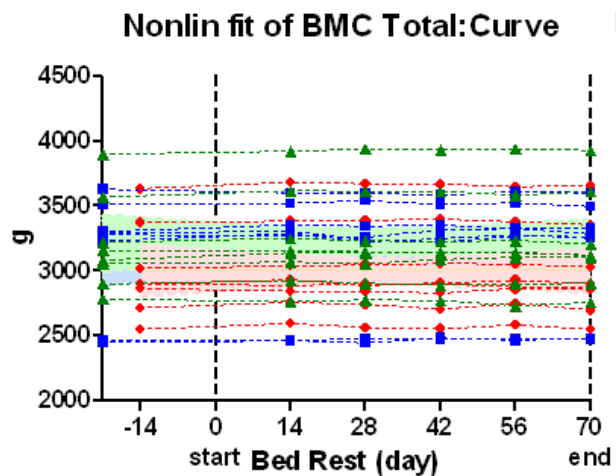
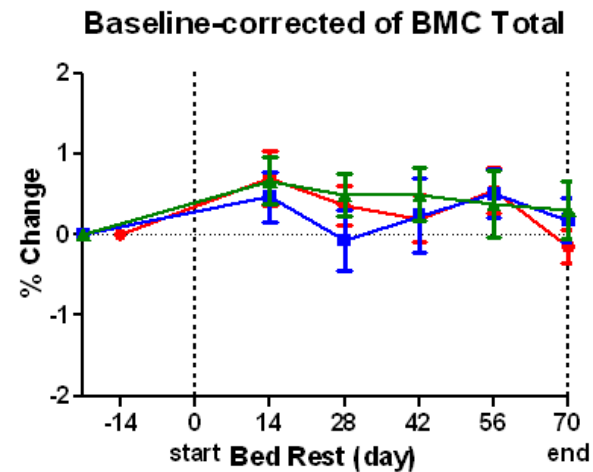
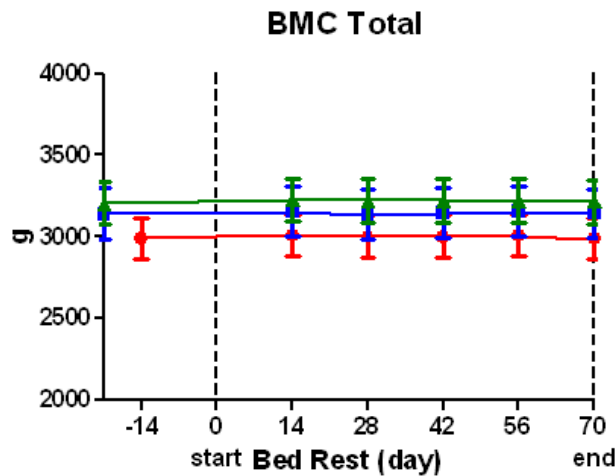
Bone Mineral Density - Legs



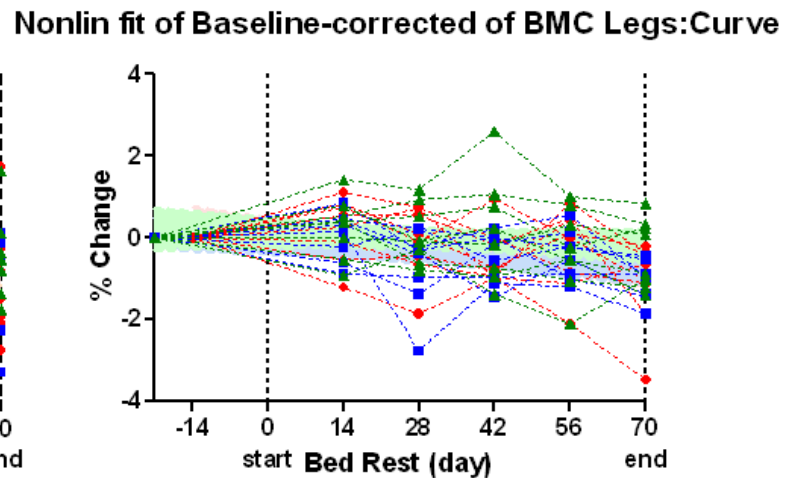
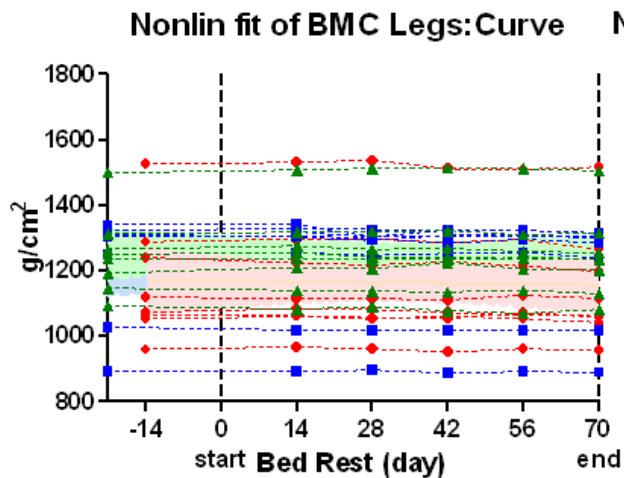
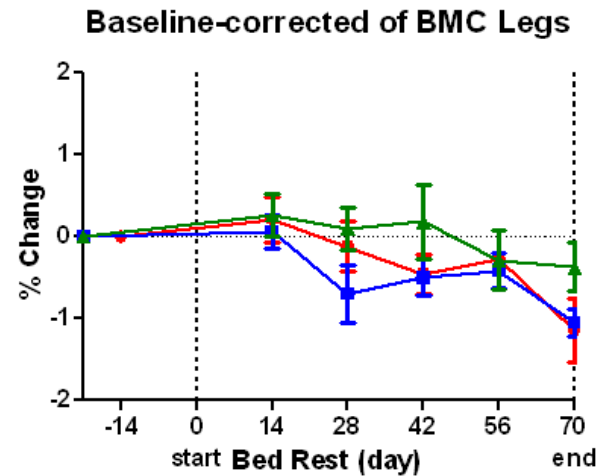
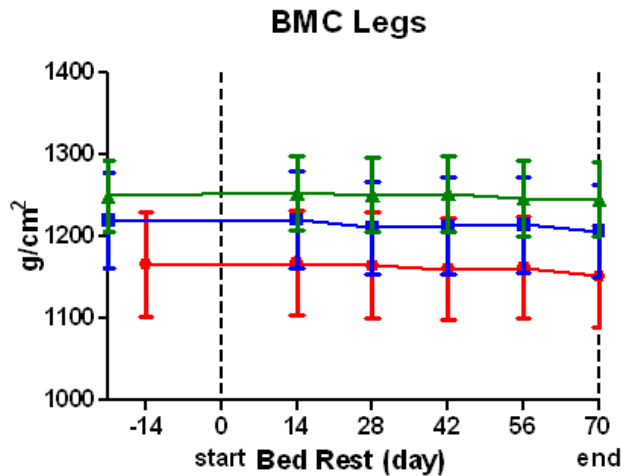
Bone Mineral Density - Arms



Bone Mineral Content - Total



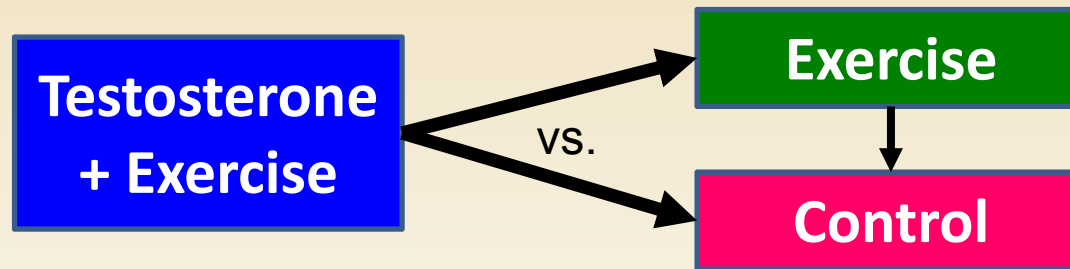
Bone Mineral Content - Legs



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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- Randall J. Urban, M.D.
- Melinda Sheffield-Moore, Ph.D.
- Lichar Dillon, Ph.D.
- Bill Durham, Ph.D.
- Chris Danesi, MS
- Kate Randolph, B.S.
- John Quisenberry, BS
- Charlie Gilkison, R.N., M.S.N.
- ITS-CRC & FARU Staff
- FAP Team
- CFT70 Colleagues



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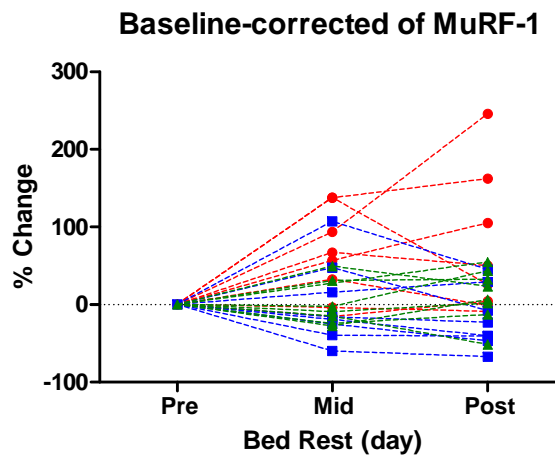
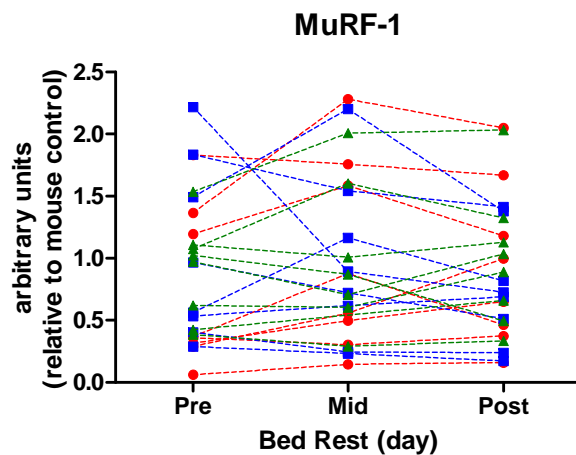
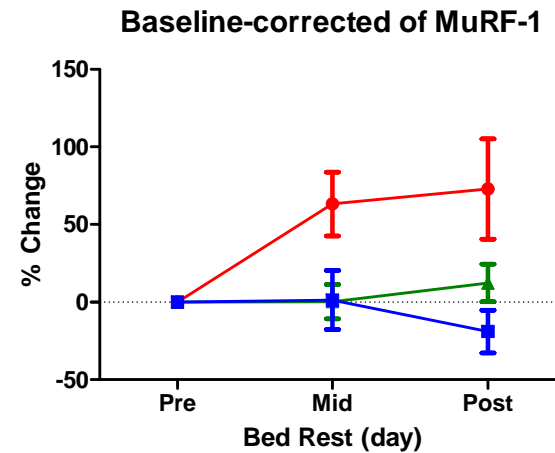
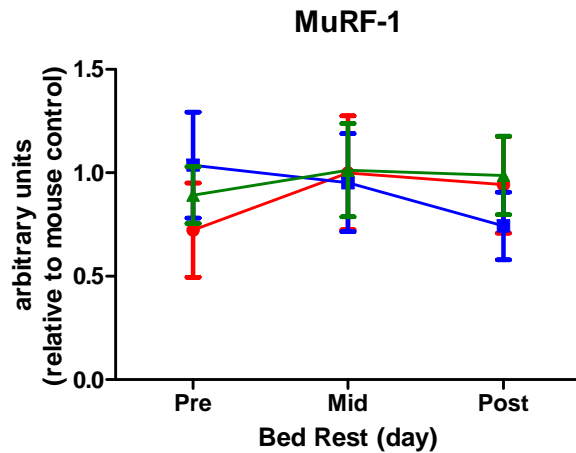
- NASA Flight Analogs Project



Backup Slides



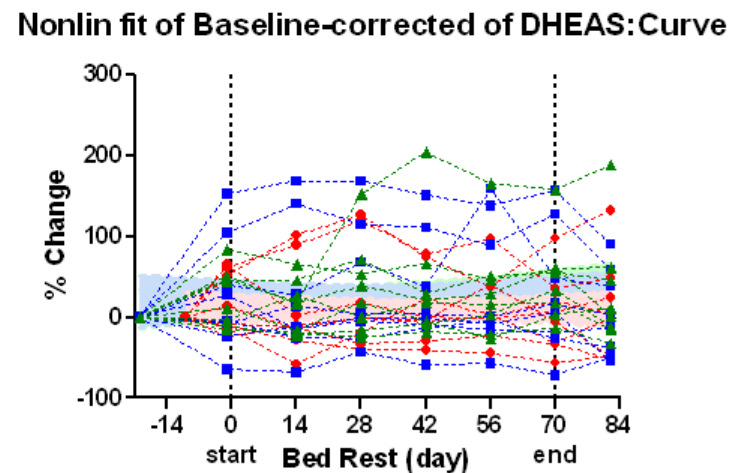
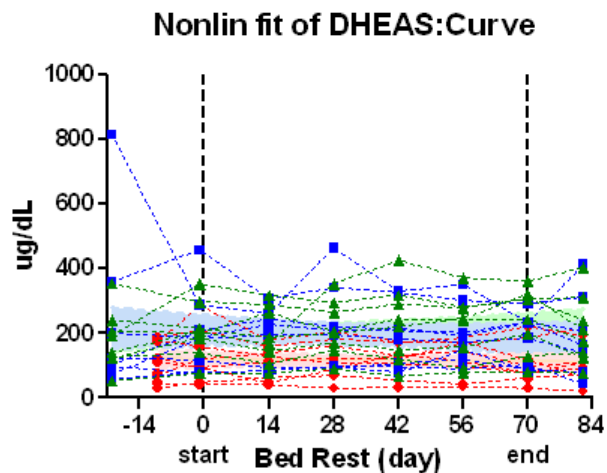
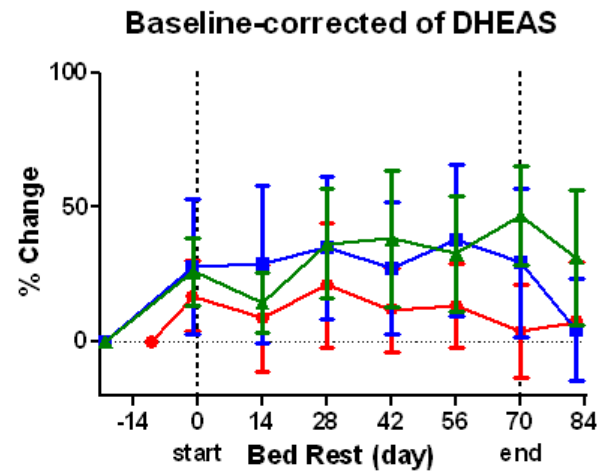
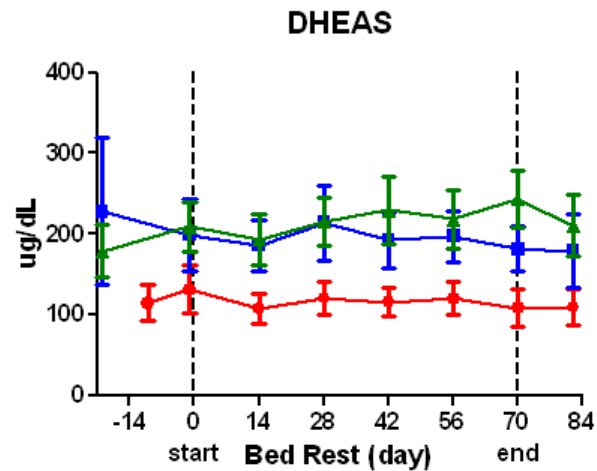
Leg Skeletal Muscle Protein Catabolism: MuRF-1



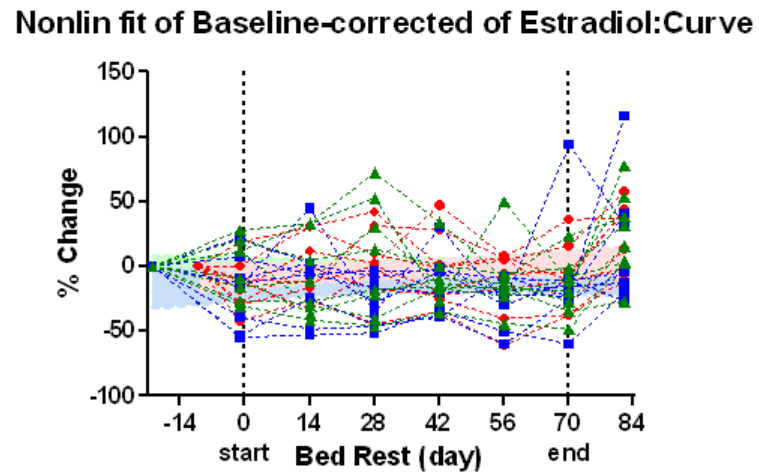
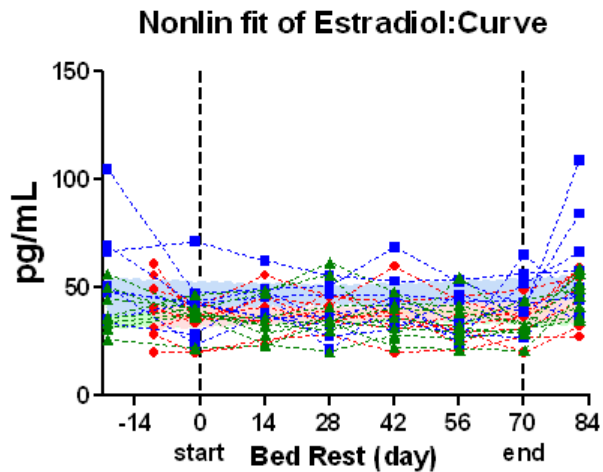
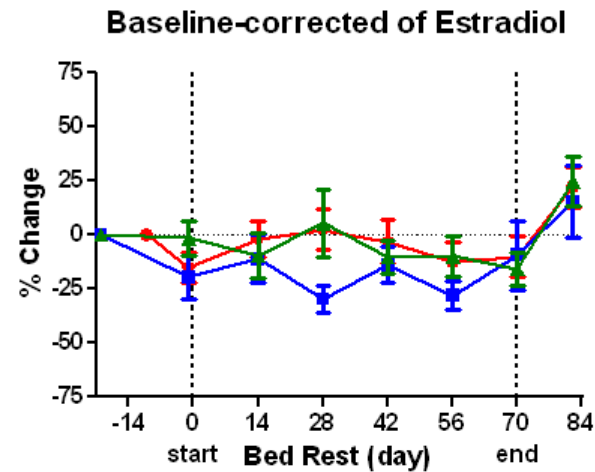
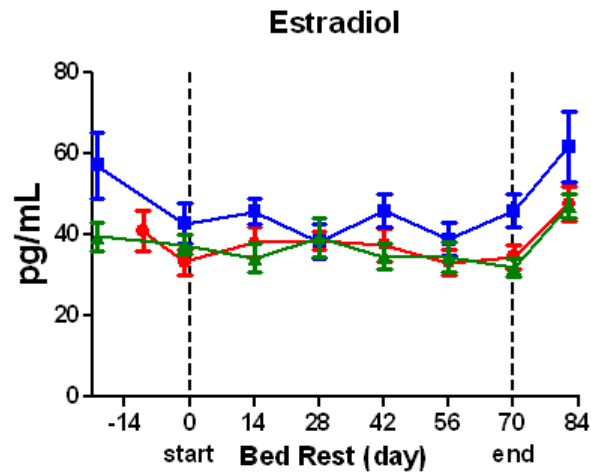
Hormones (Immulite)

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

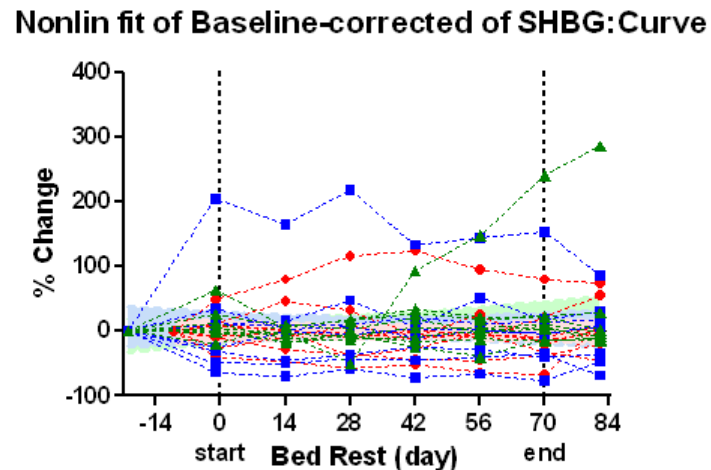
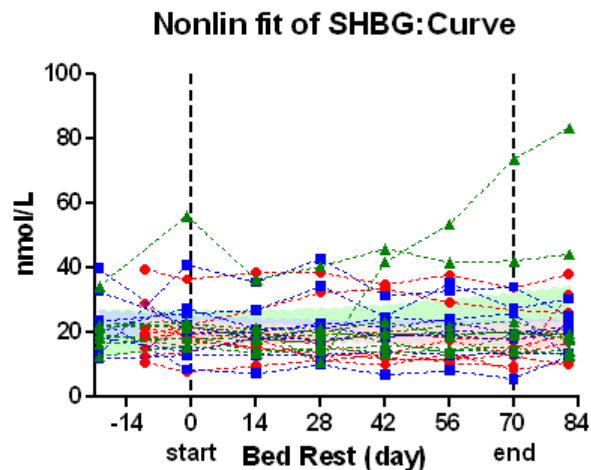
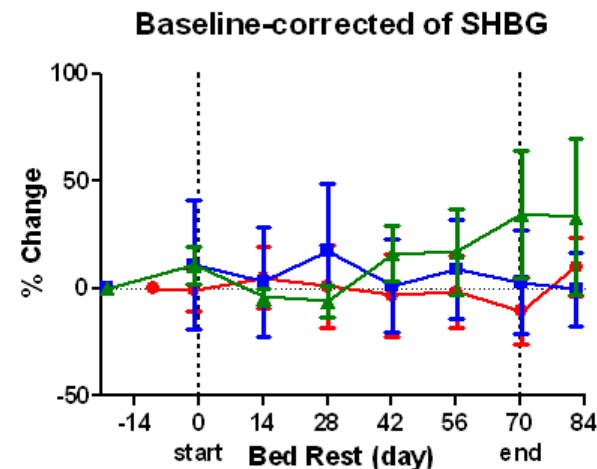
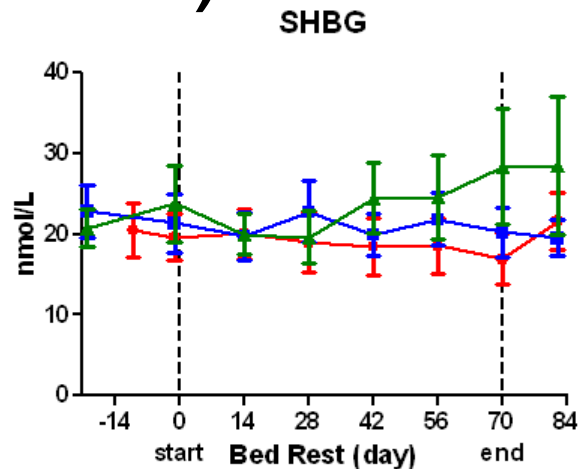
DHEAS



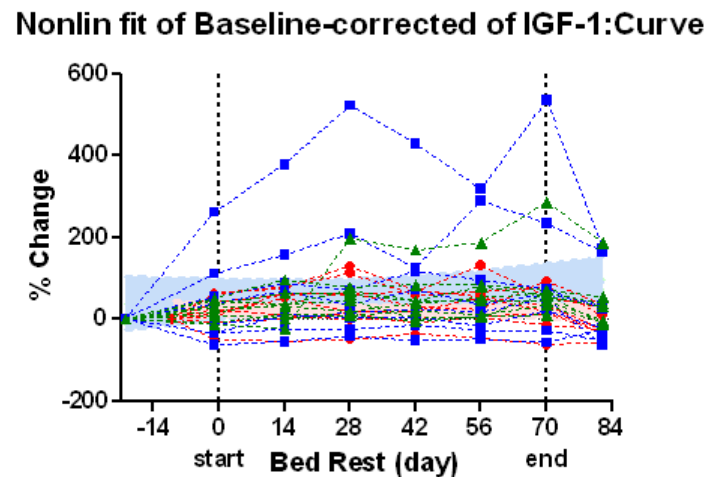
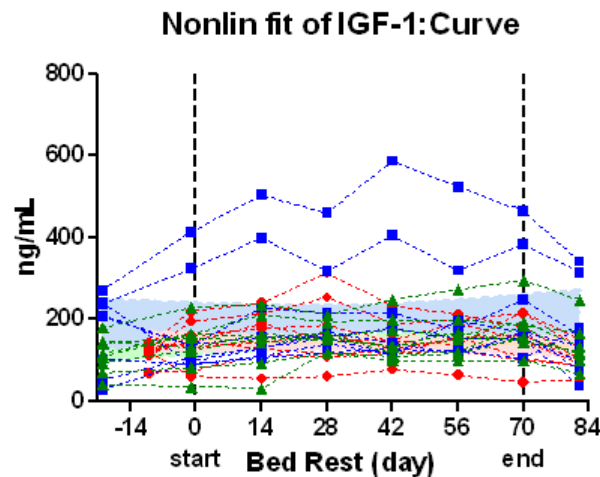
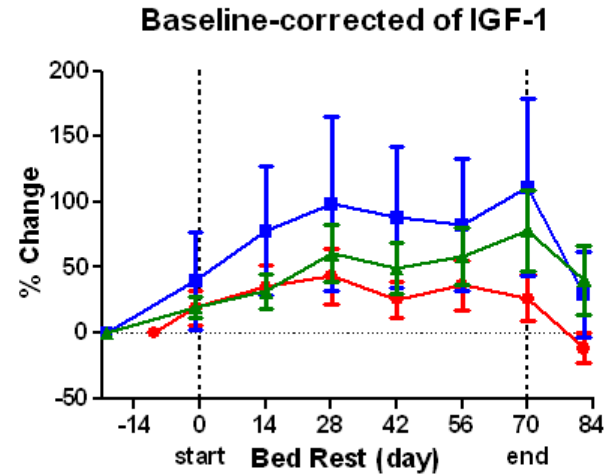
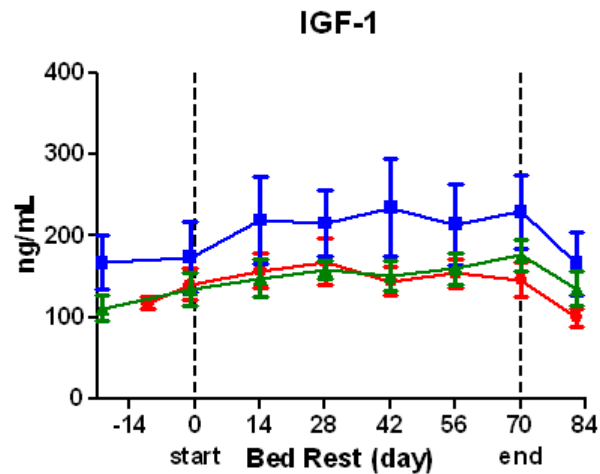
Estradiol



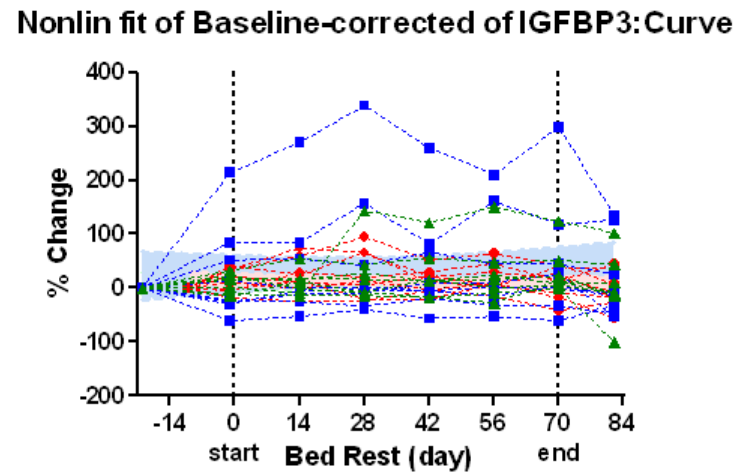
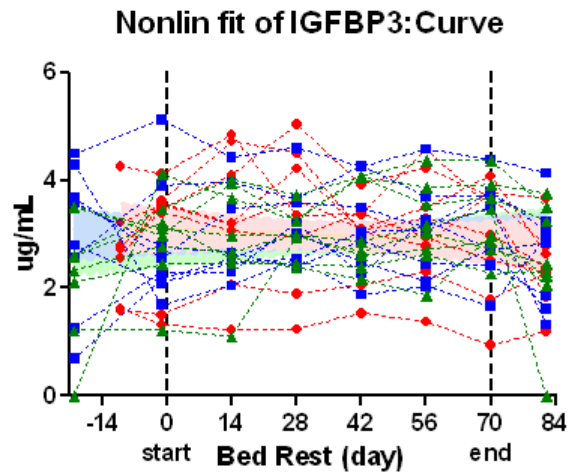
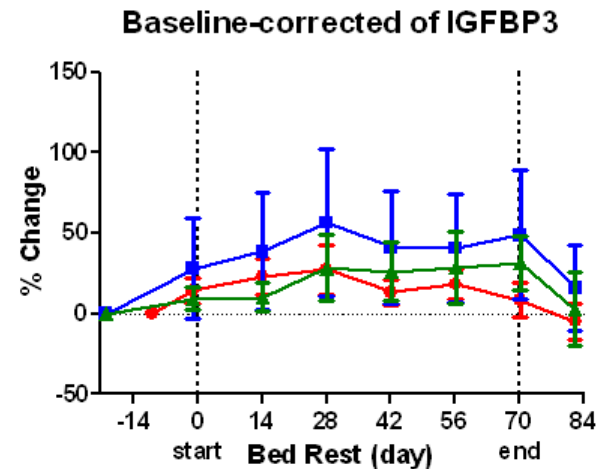
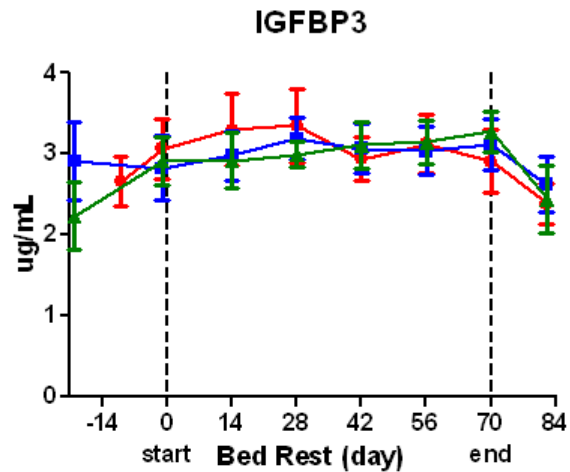
Sex Hormone Binding Globulin (SHBG)



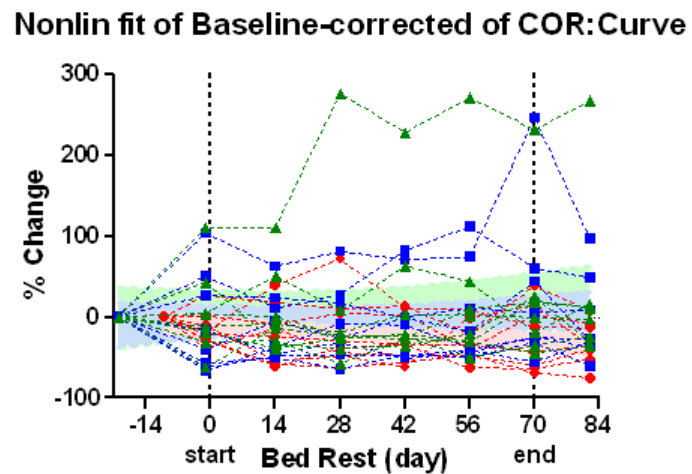
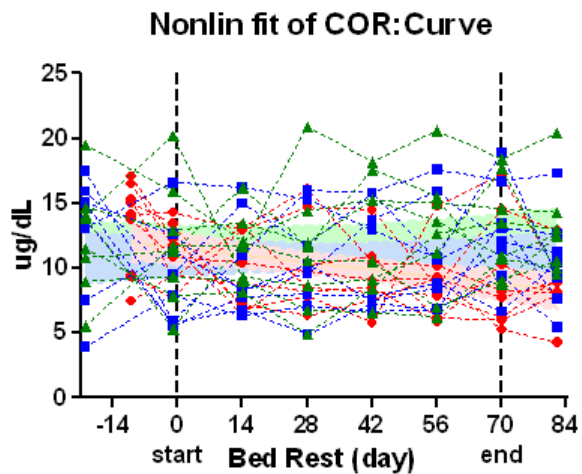
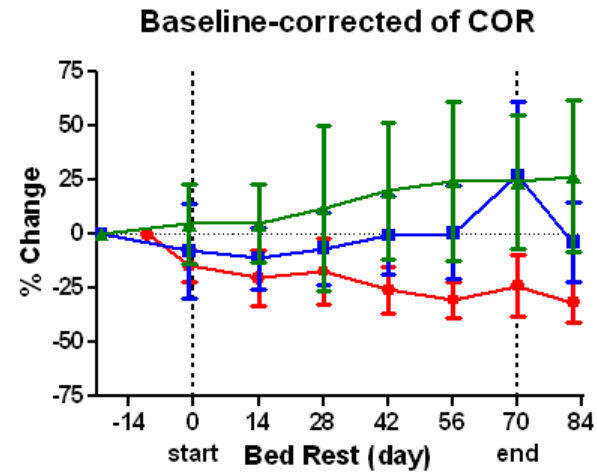
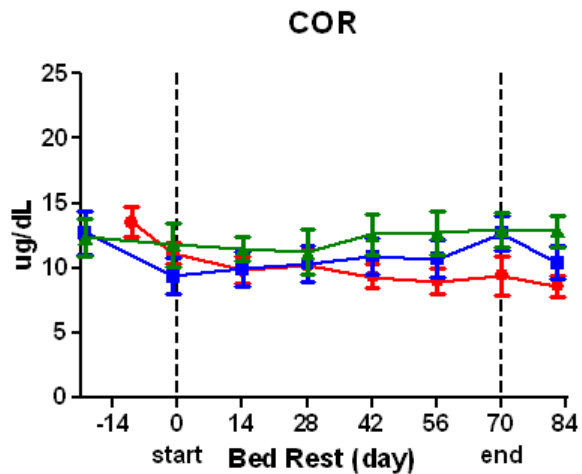
IGF-1



IGFBP-3

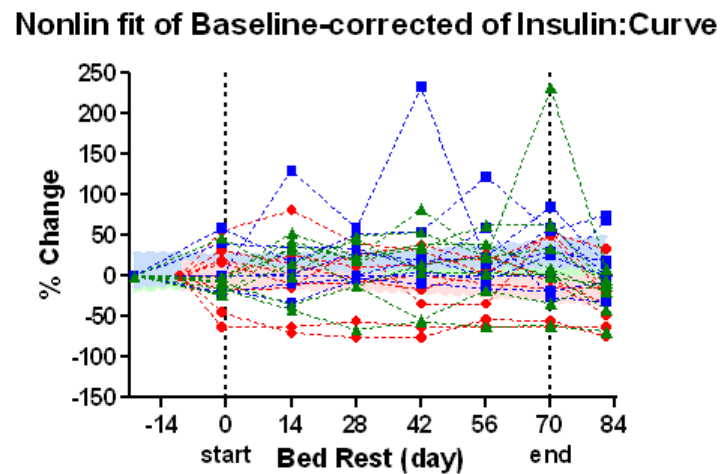
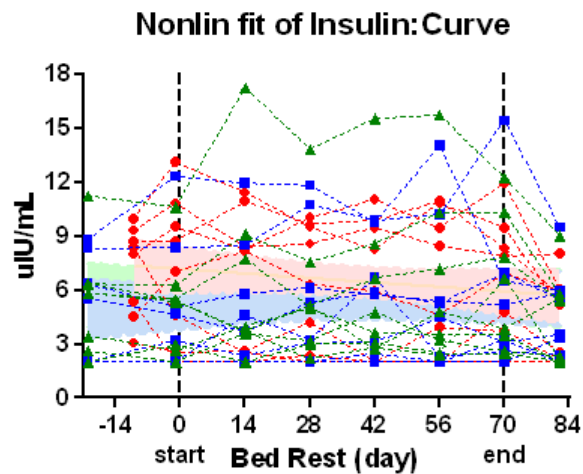
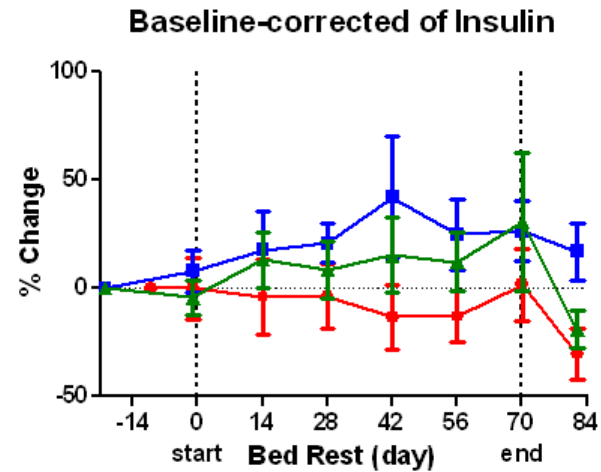
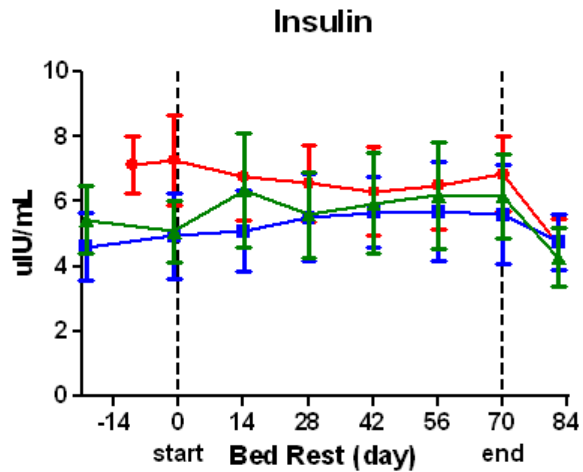


Cortisol

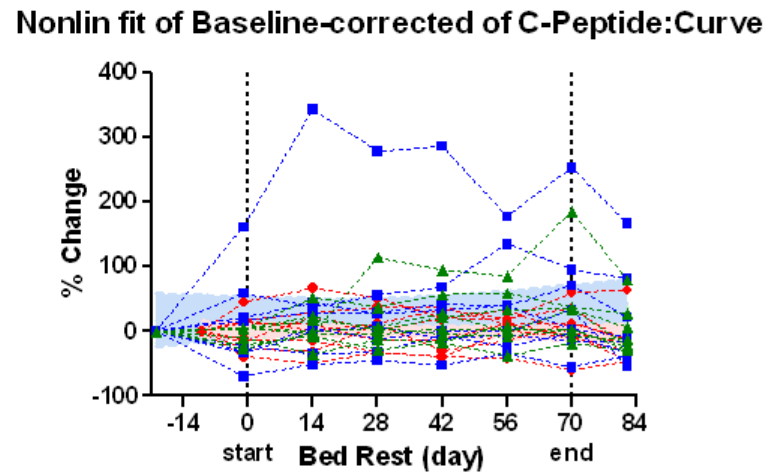
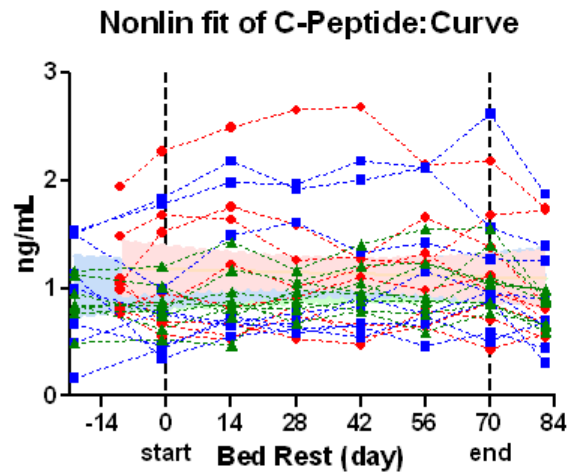
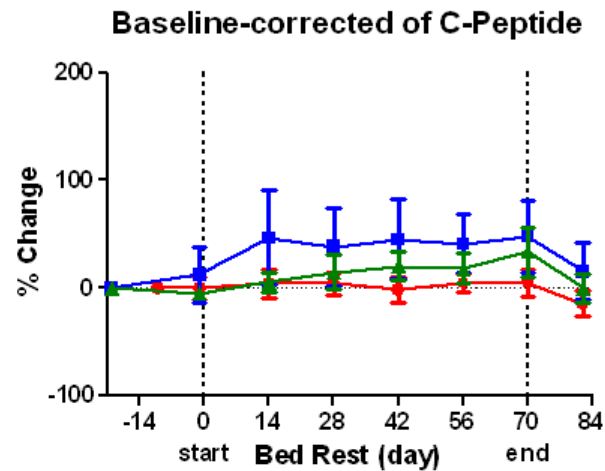
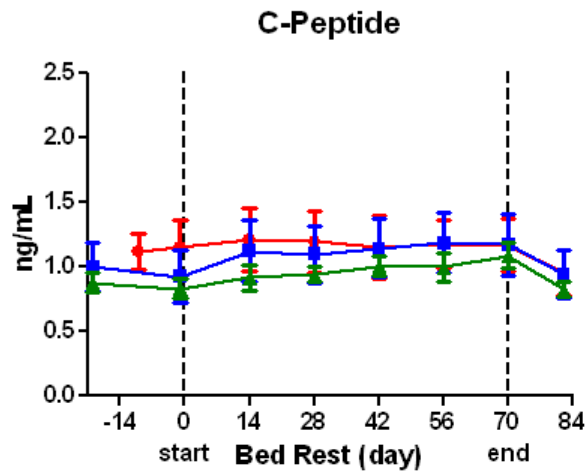


- Control
- ▲ Exercise
- Exercise + Testosterone

Insulin



C-Peptide

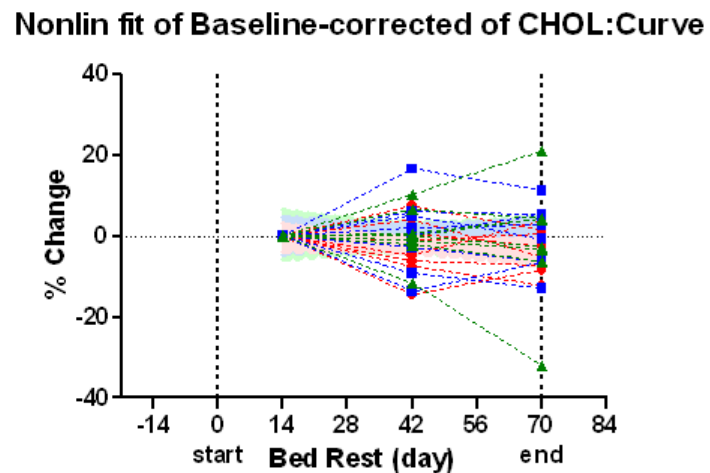
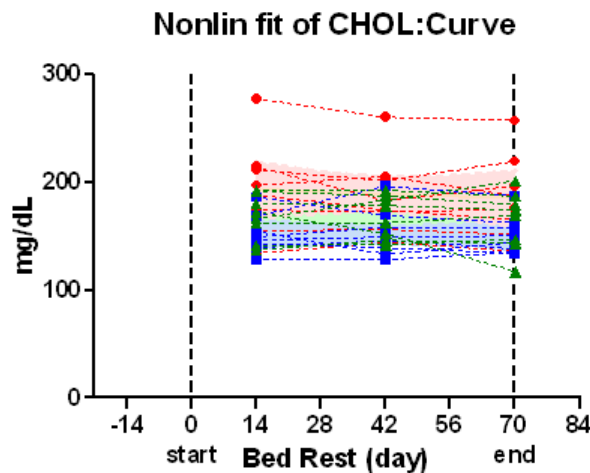
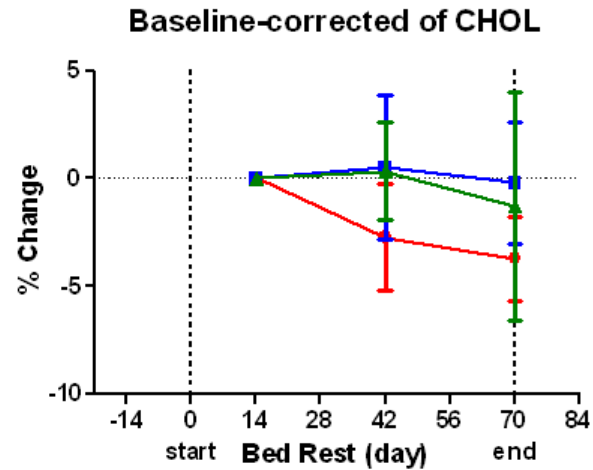
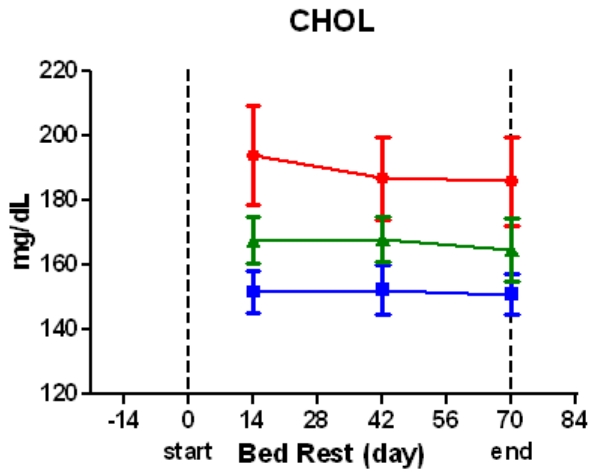


Hormones Summary

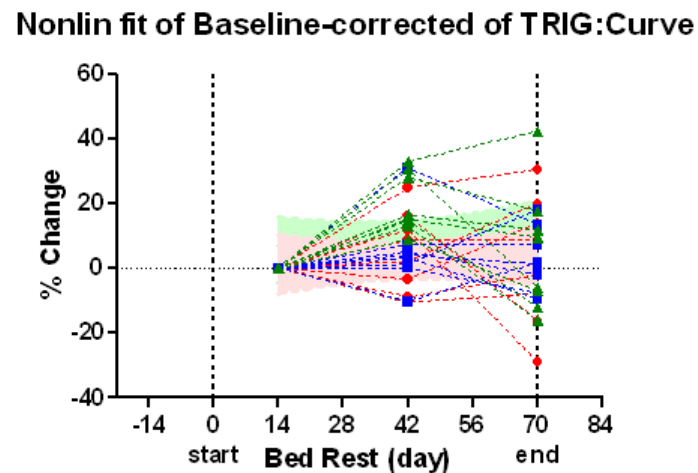
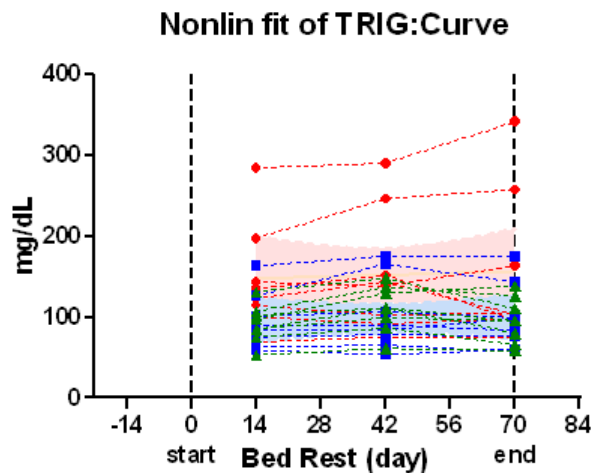
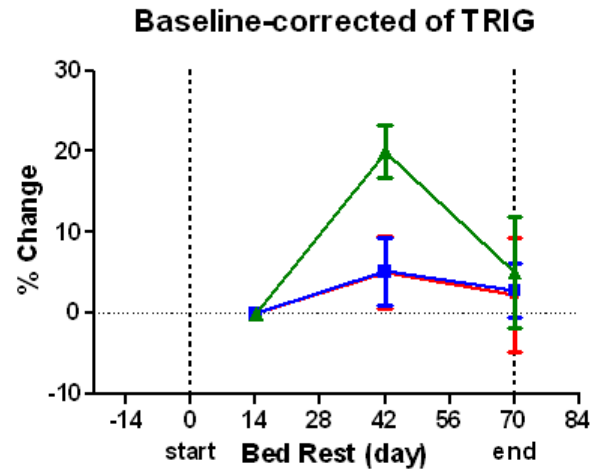
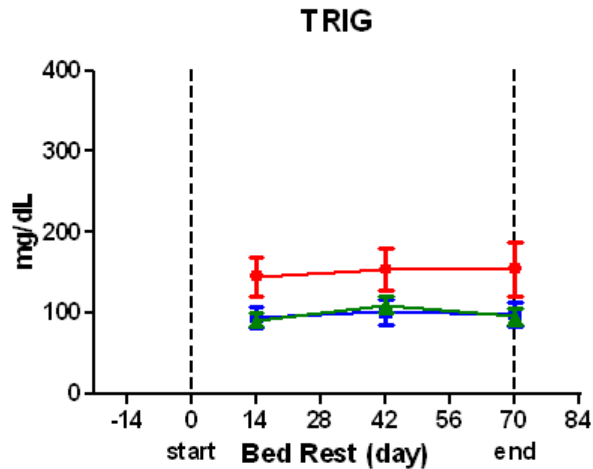
Lipid panels

- 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

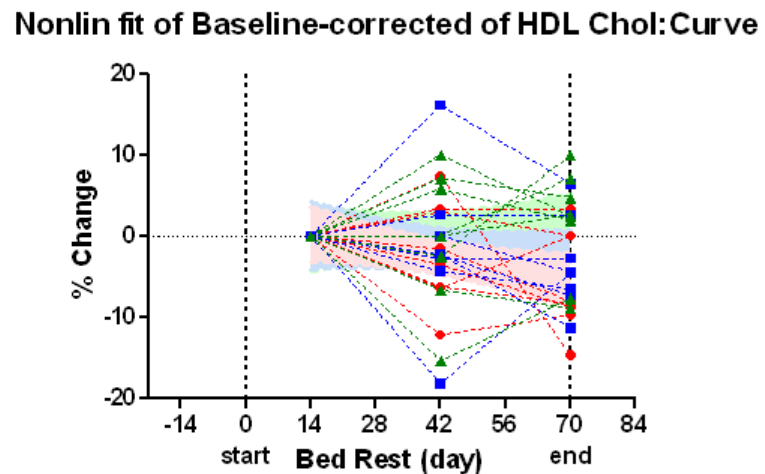
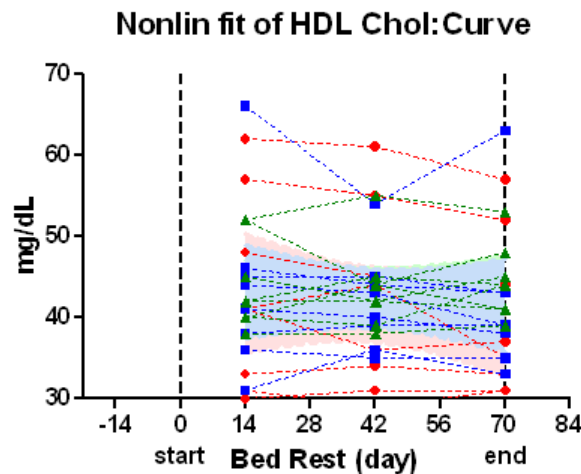
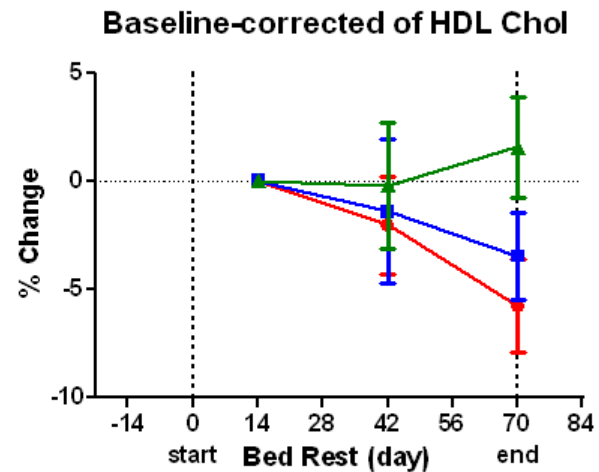
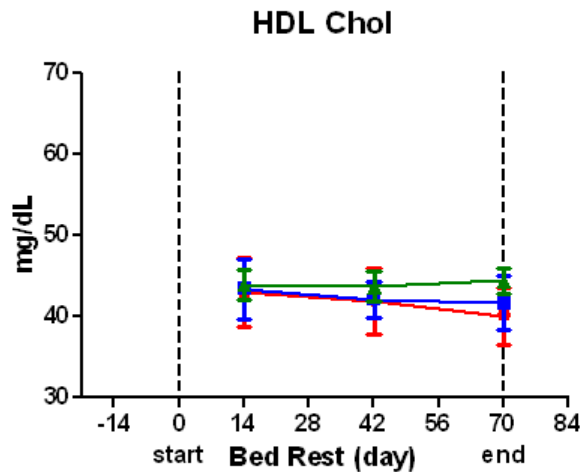
Cholesterol



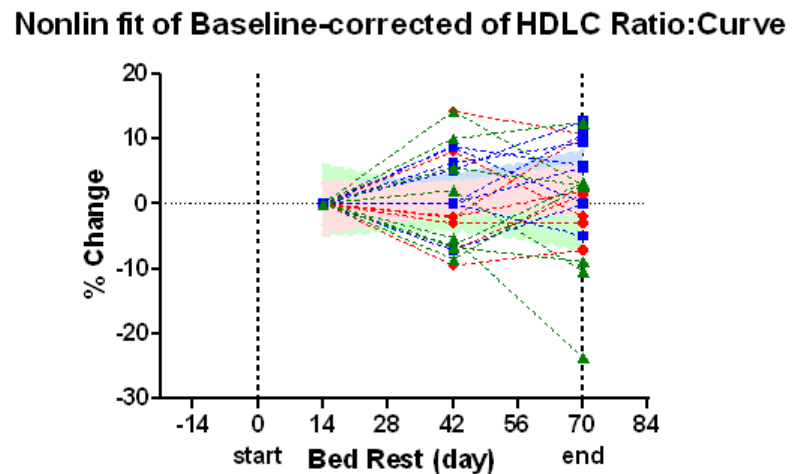
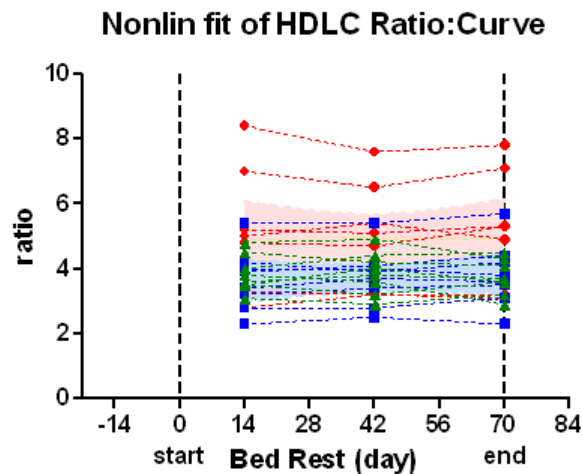
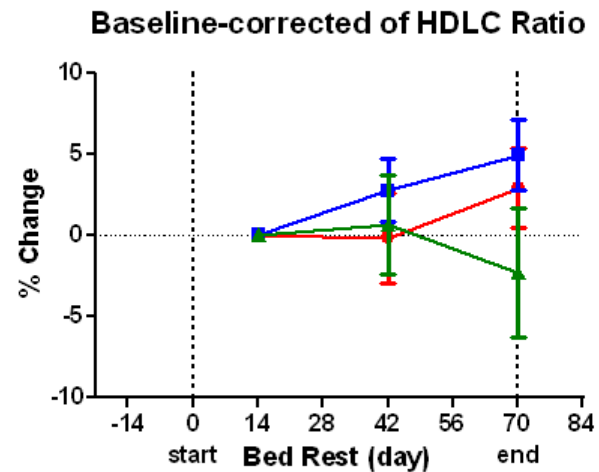
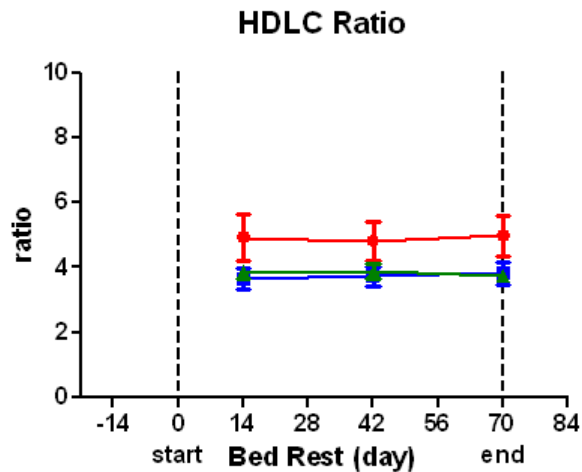
Triglycerides



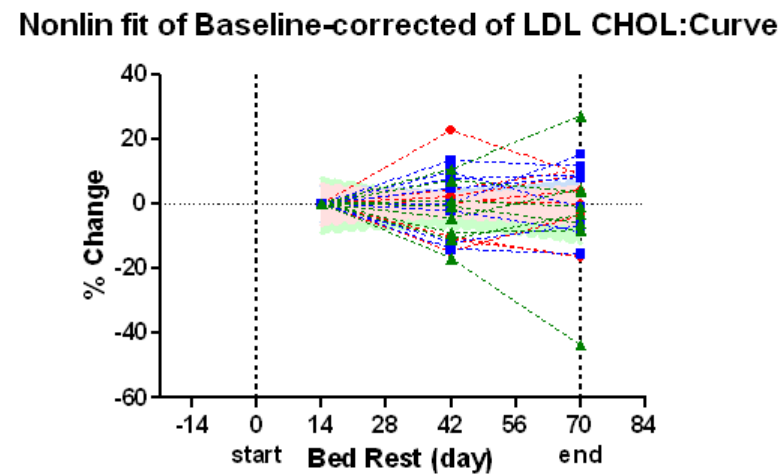
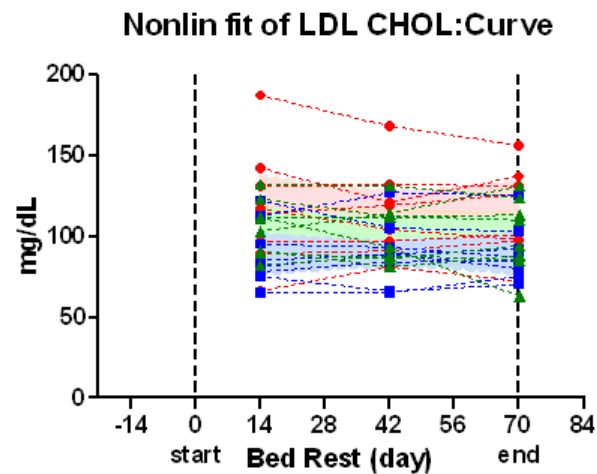
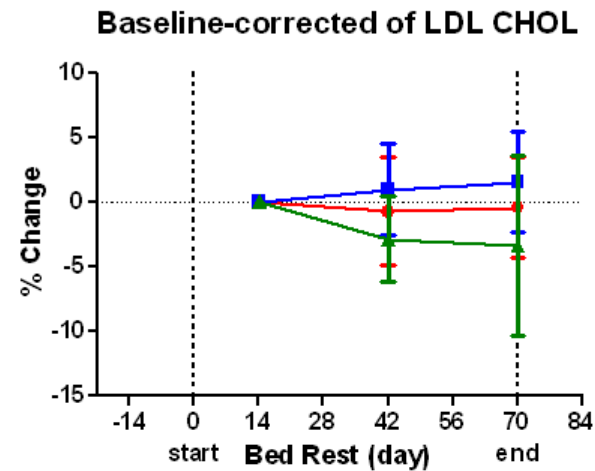
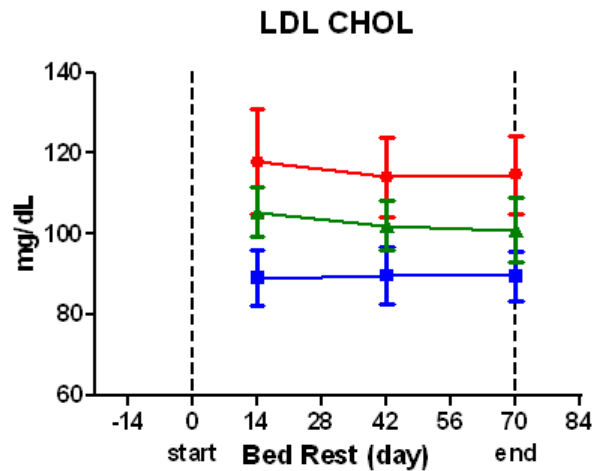
HDL Cholesterol



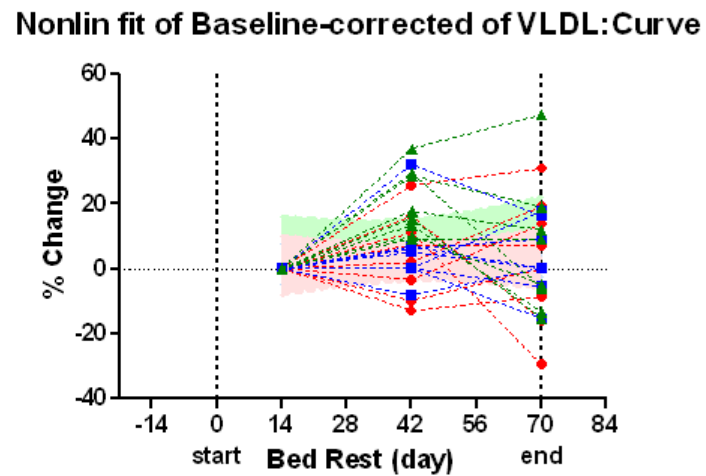
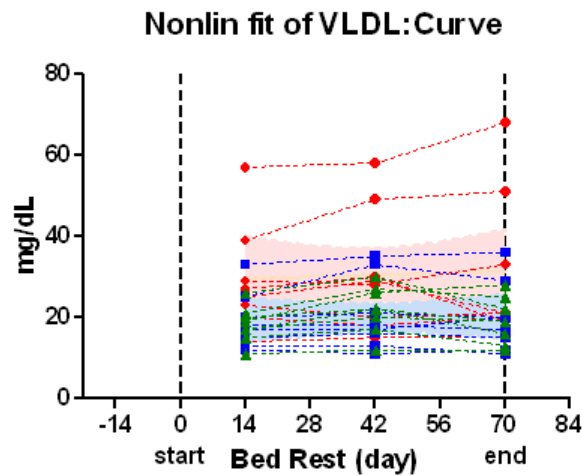
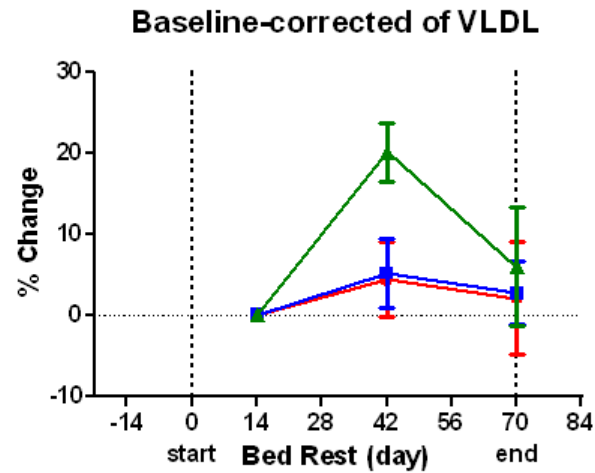
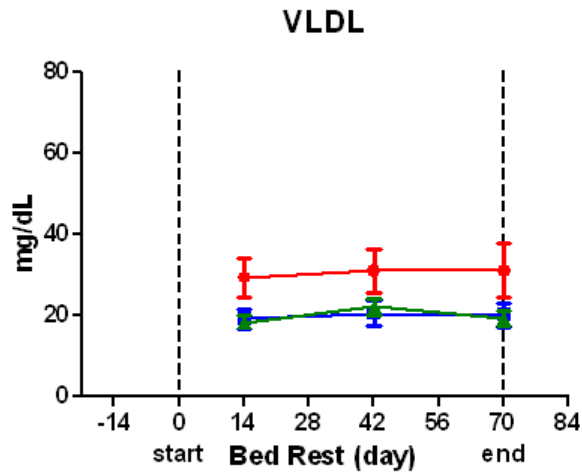
HDL Chol Ratio



LDL Cholesterol



VLDL



Lipid Panel Summary



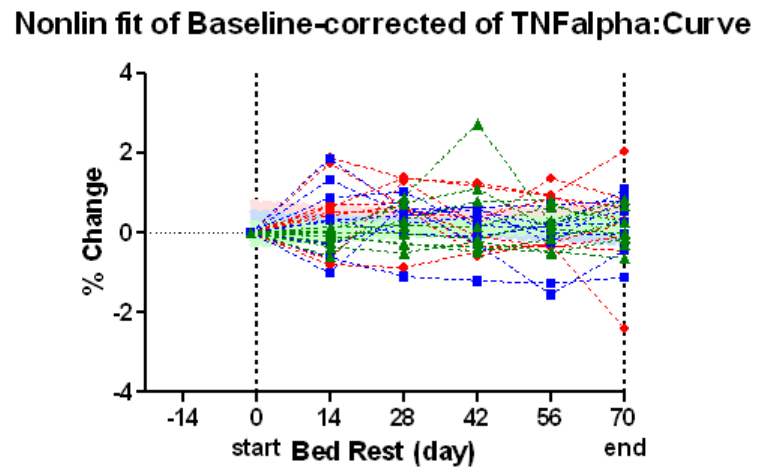
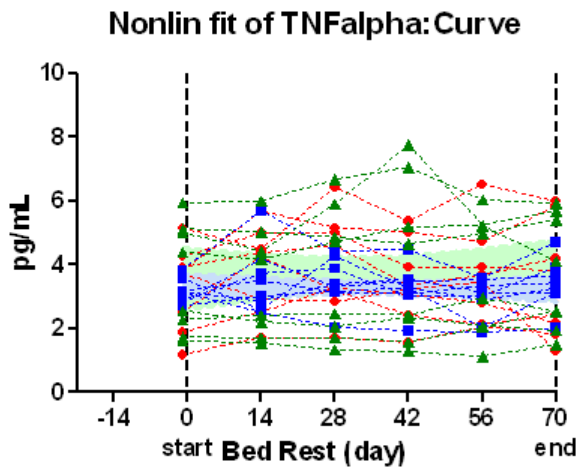
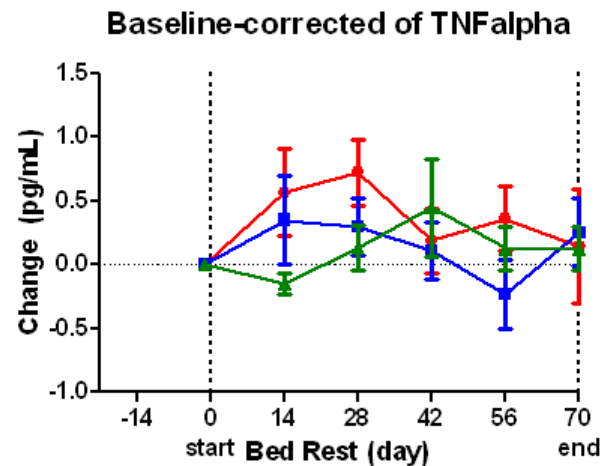
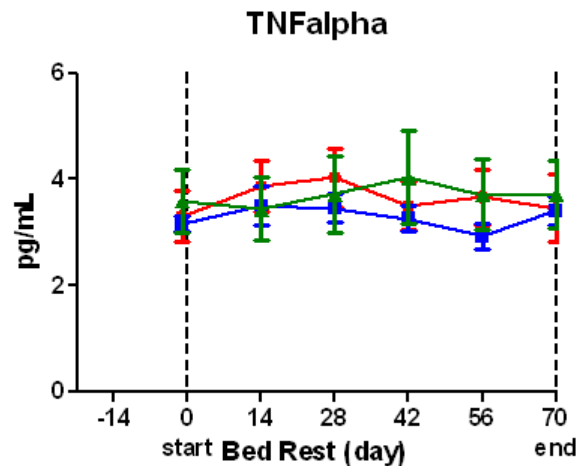
Bone Panel

Milliplex

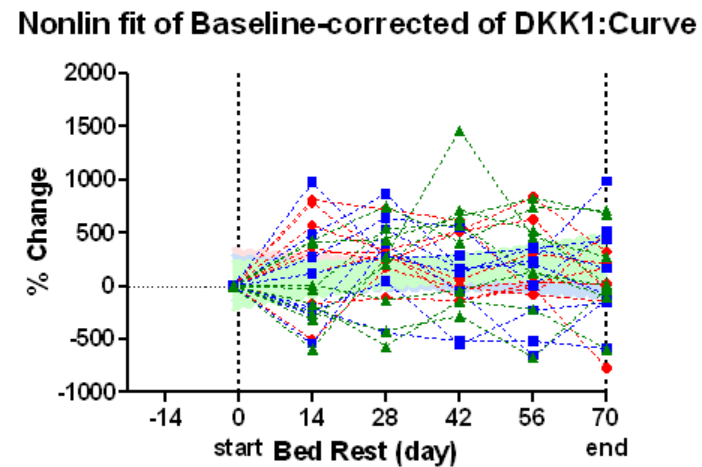
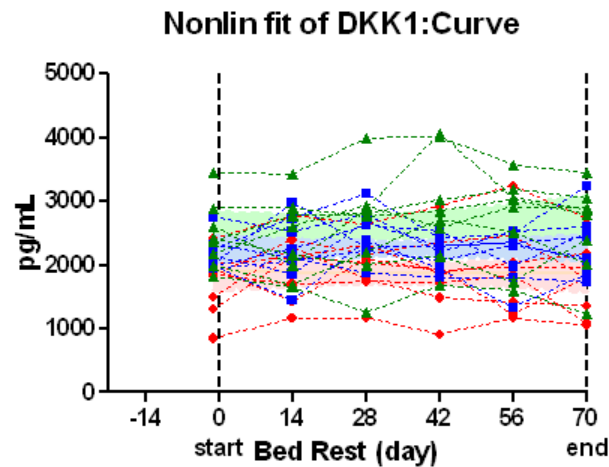
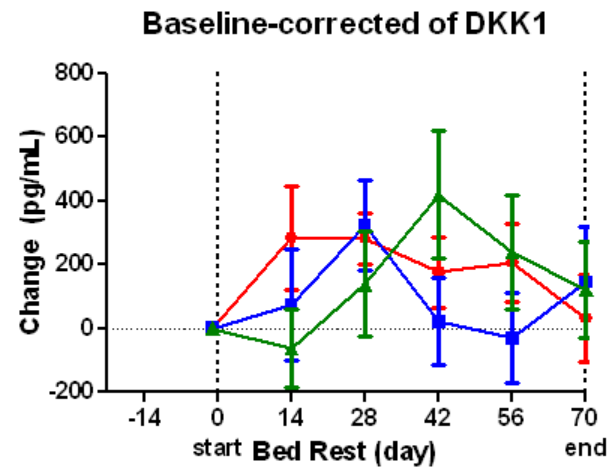
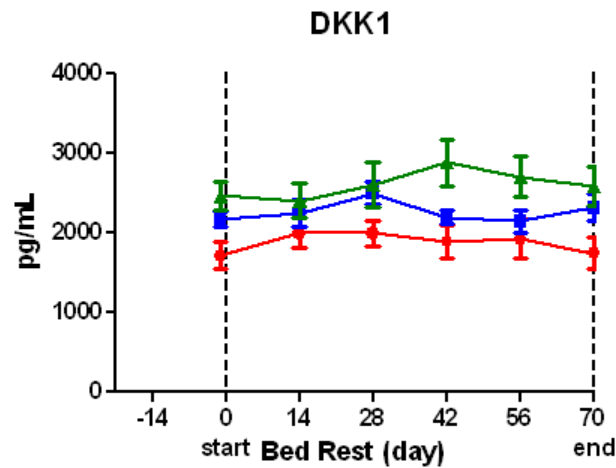
- TNF- α
- ACTH*
- DKK-1
- FGF-23
- IL-1 β *
- IL-6*
- RANKL*
- Insulin
- Leptin
- Osteocalcin (OC)
- Osteopontin (OPN)
- Osteoprotegerin (OPG)
- Parathyroid hormone (PTH)
- Sclerostin (SOST)

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

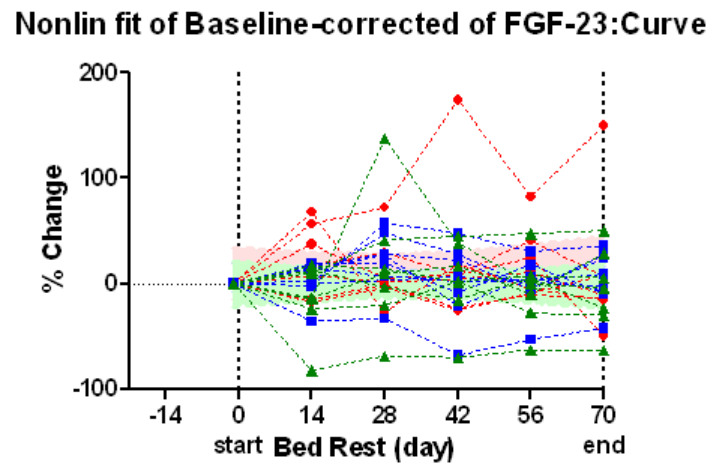
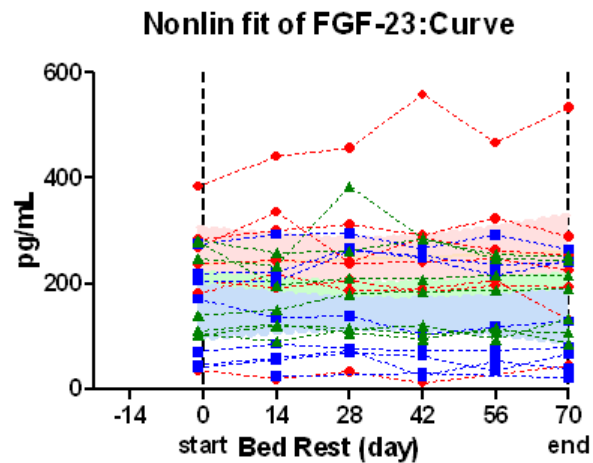
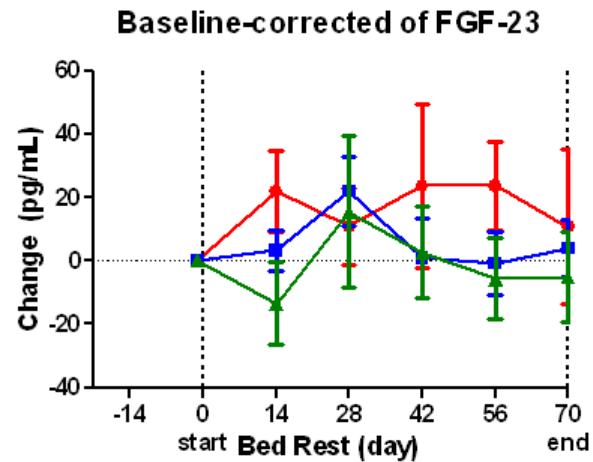
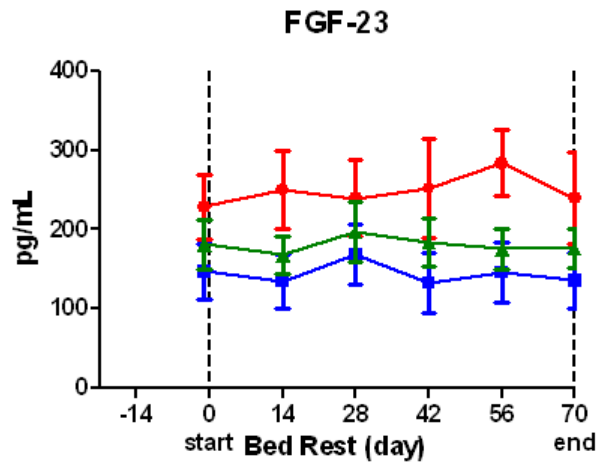
TNF-alpha



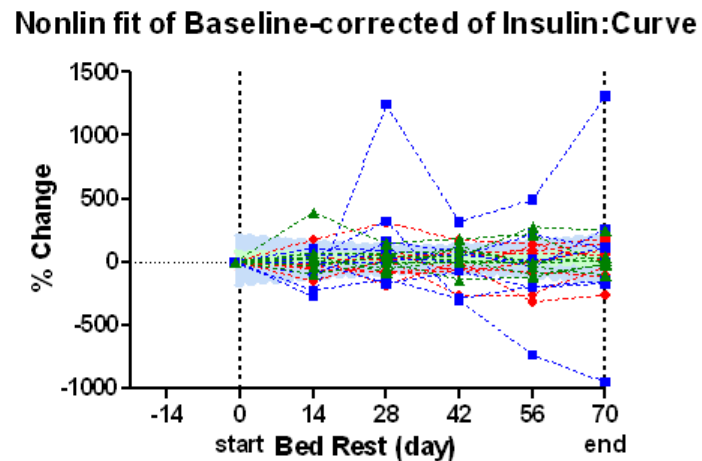
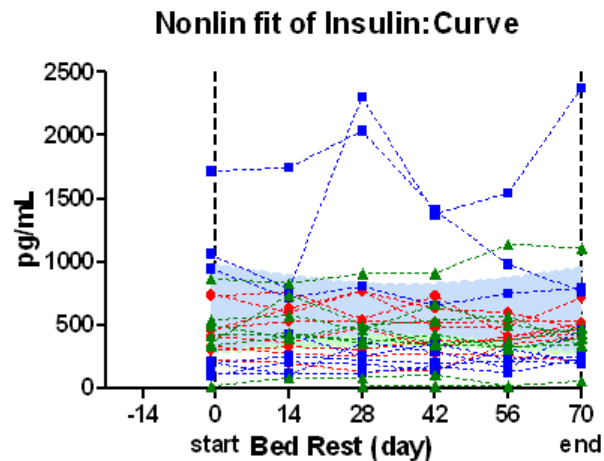
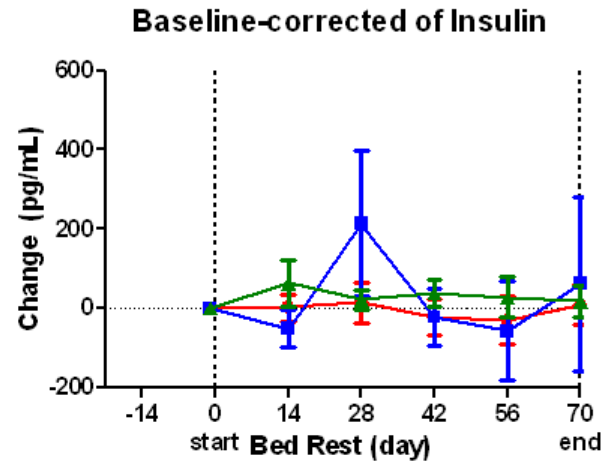
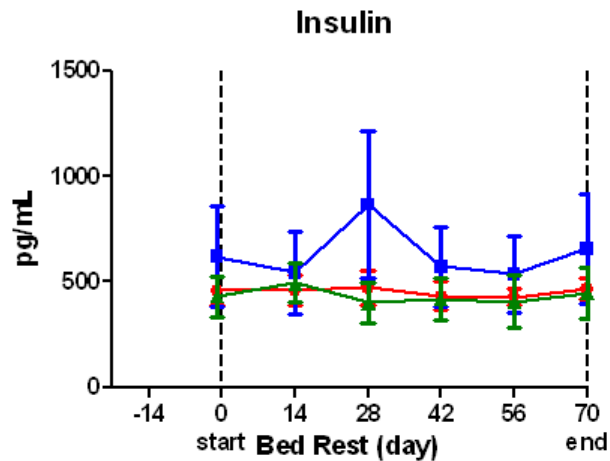
DKK1



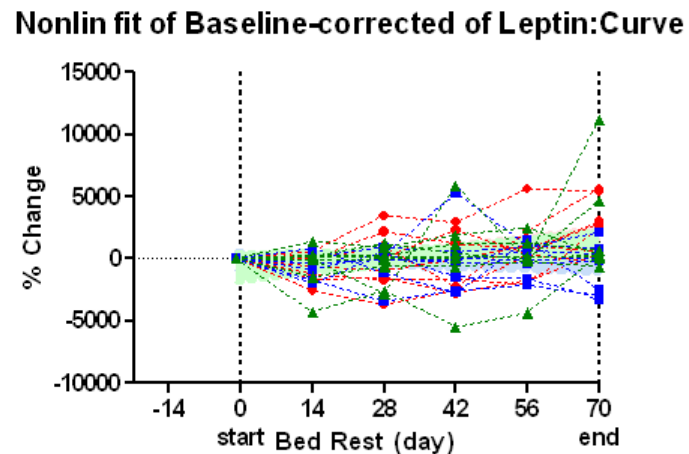
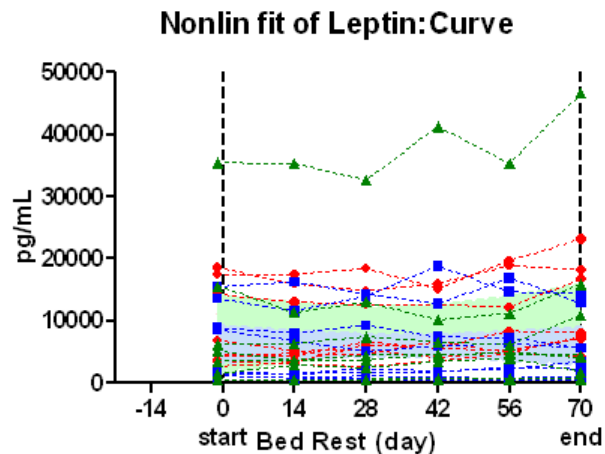
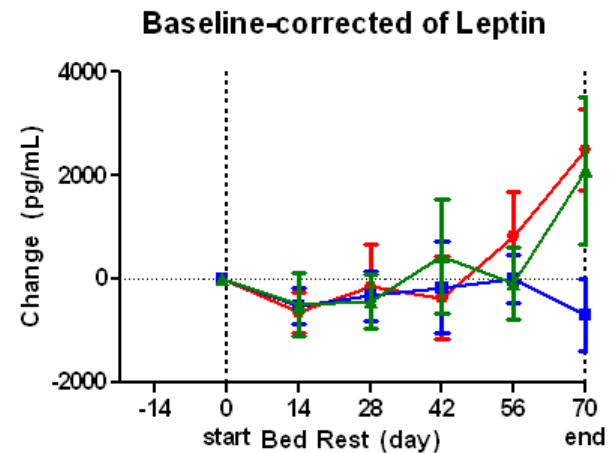
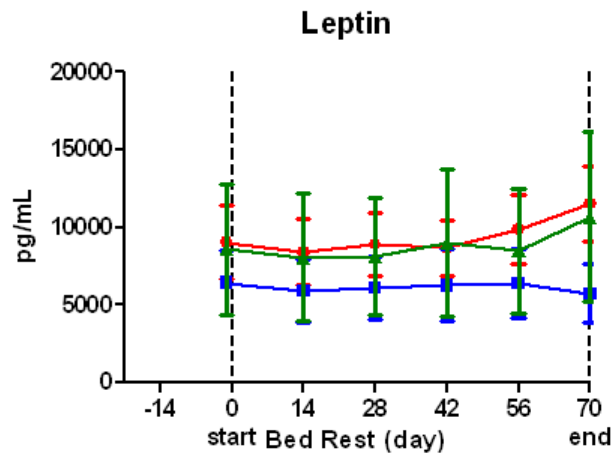
FGF-23



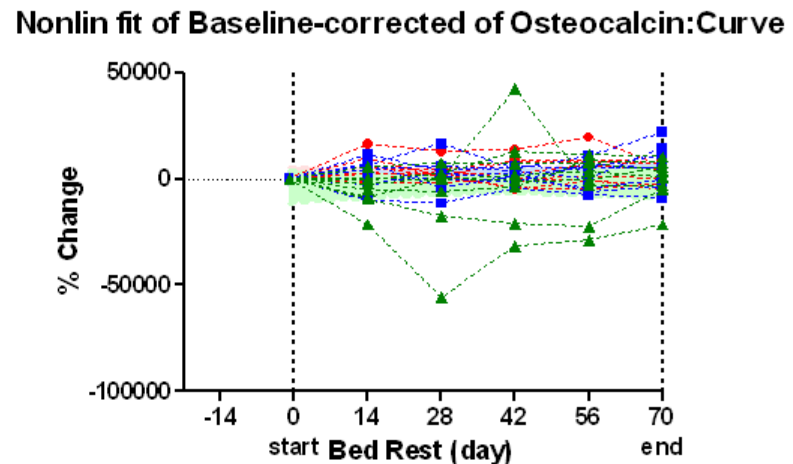
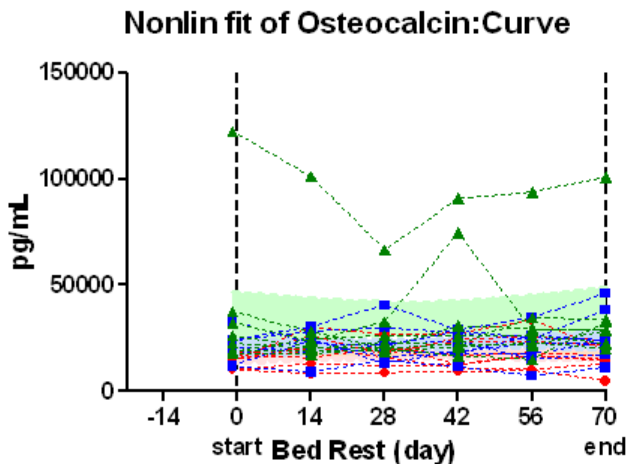
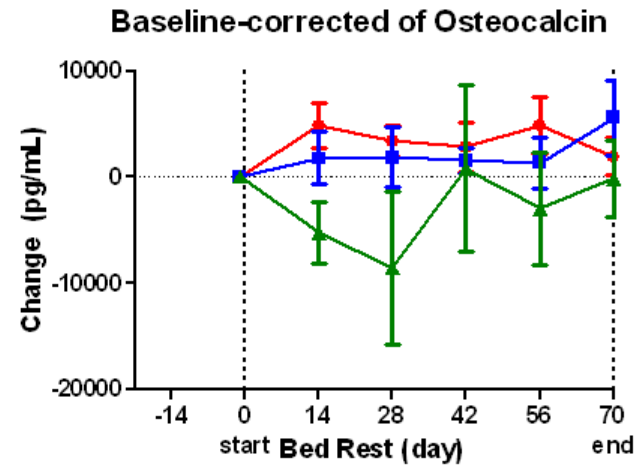
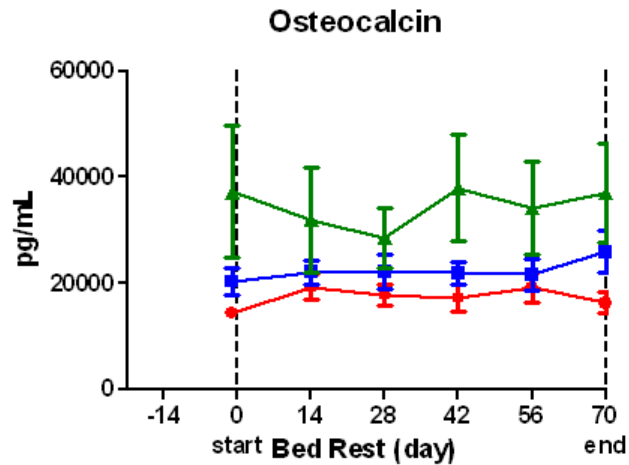
Insulin



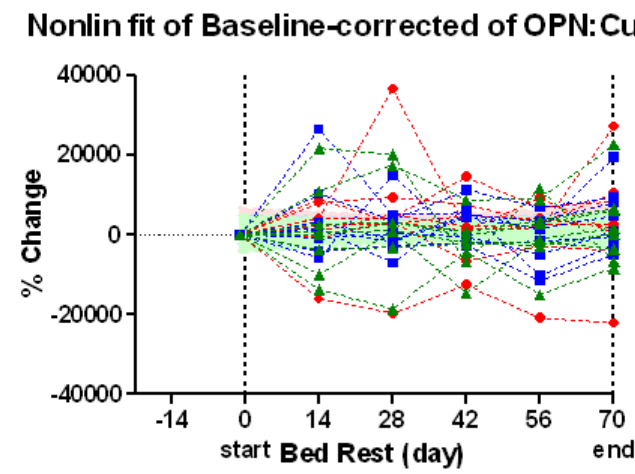
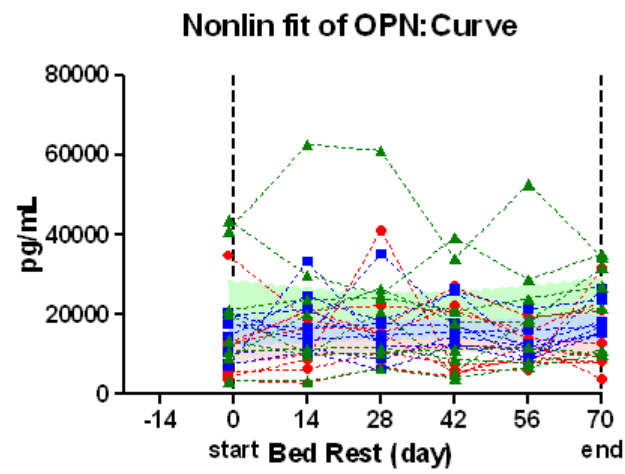
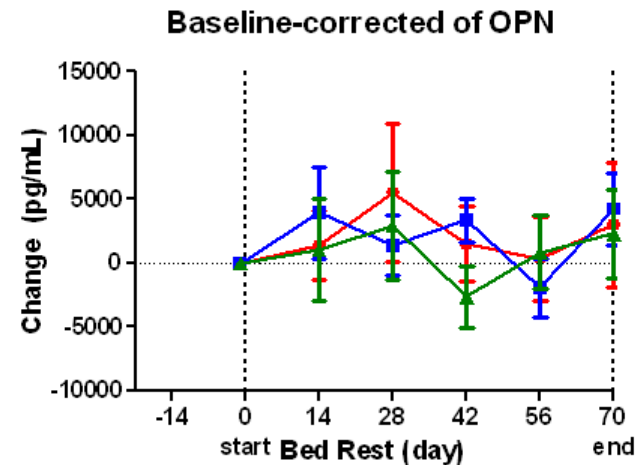
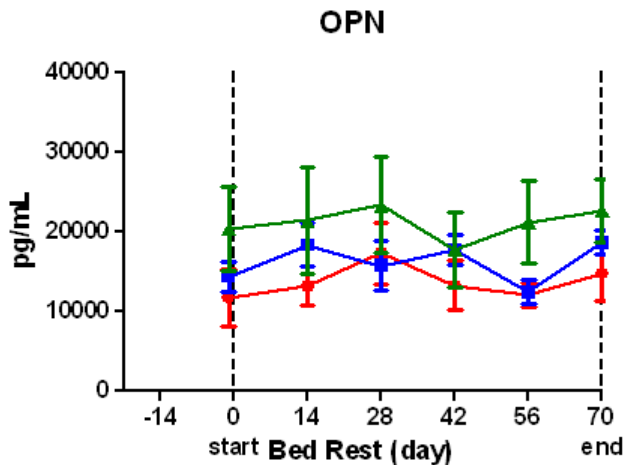
Leptin



Osteocalcin (OC)

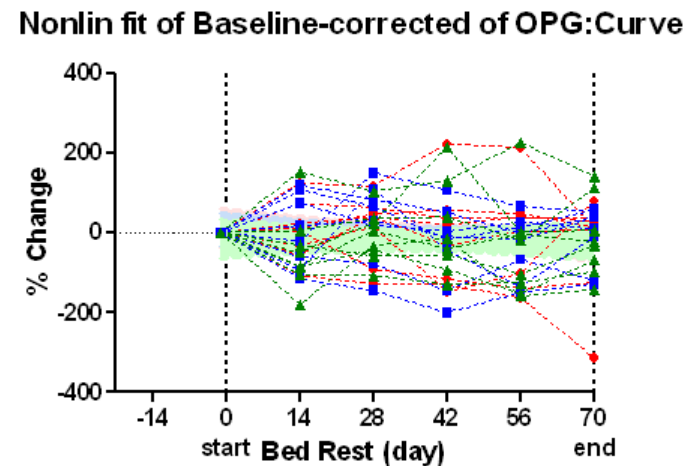
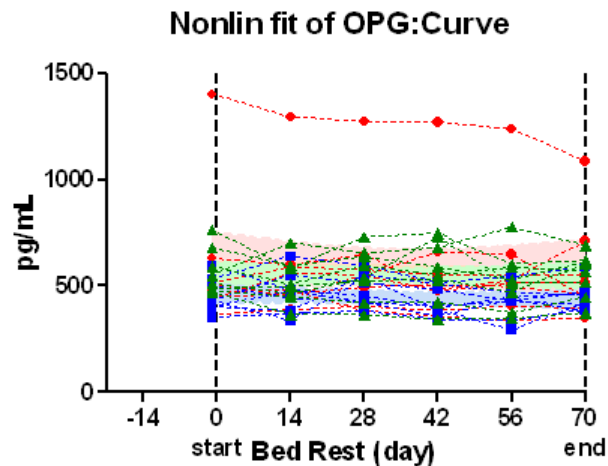
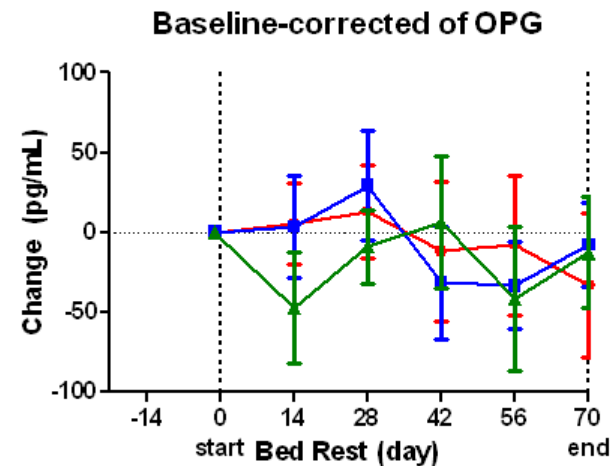
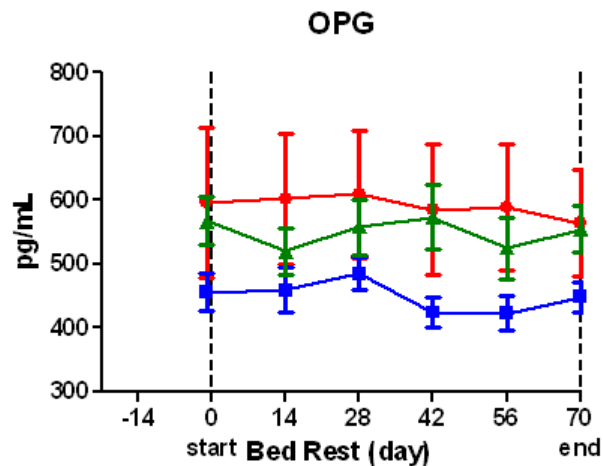


Osteopontin (OPN)

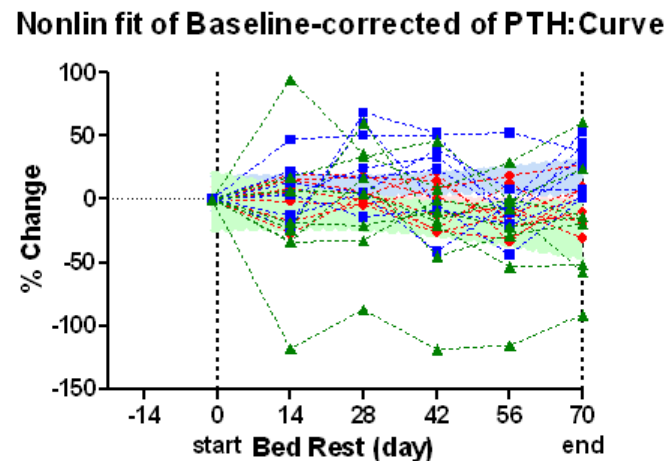
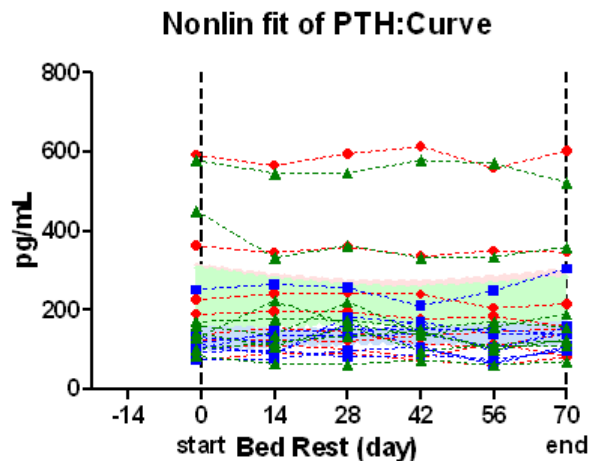
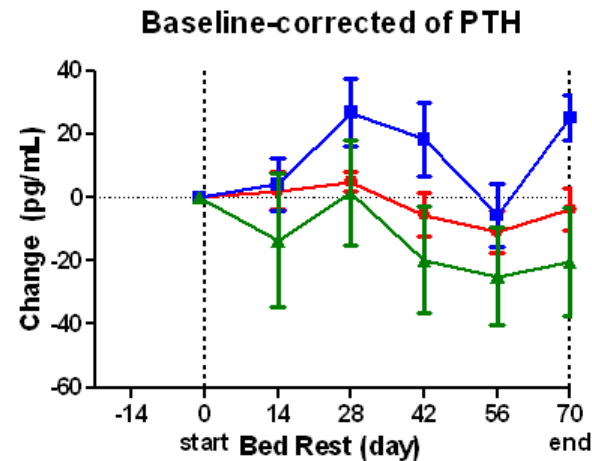
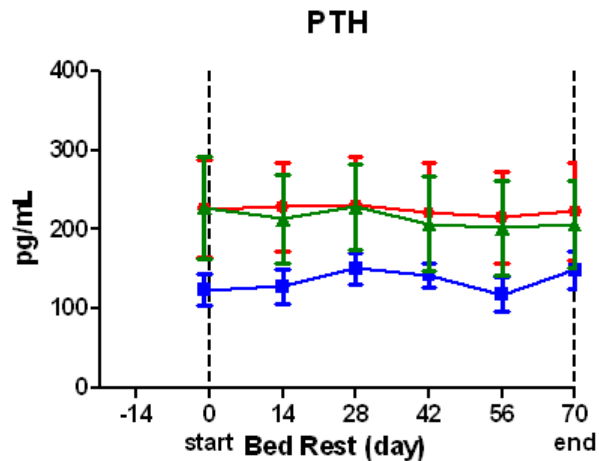


- Control
- ▲ Exercise
- Exercise + Testosterone

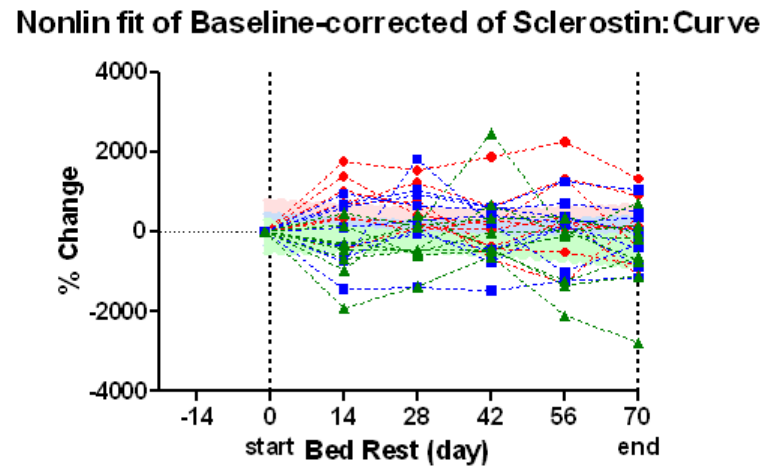
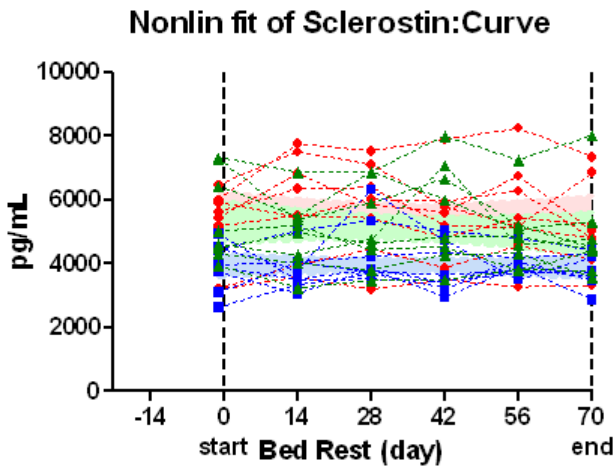
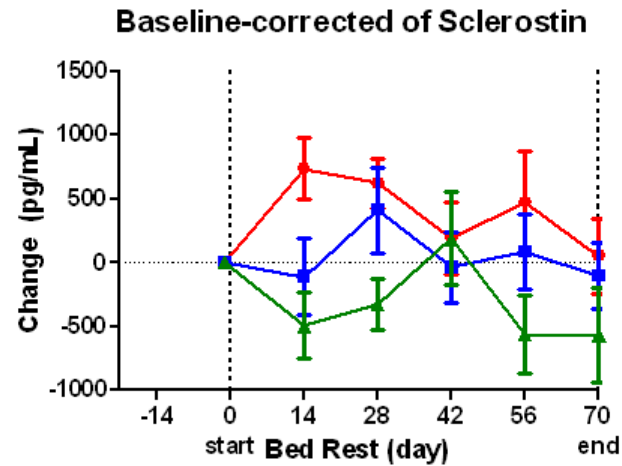
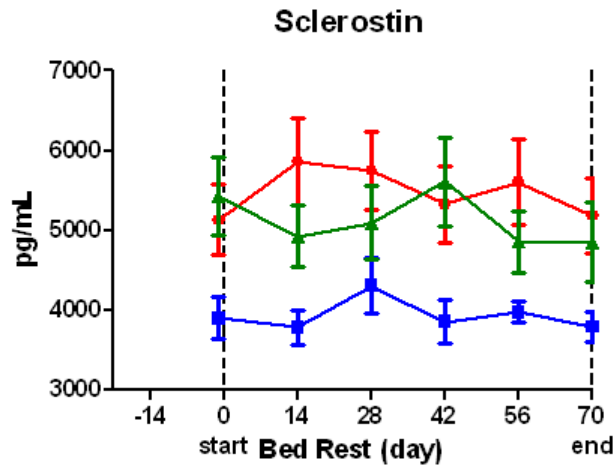
Osteoprotegerin (OPG)



Parathyroid Hormone (PTH)



Sclerostin (SOST)



Bone Panel Summary



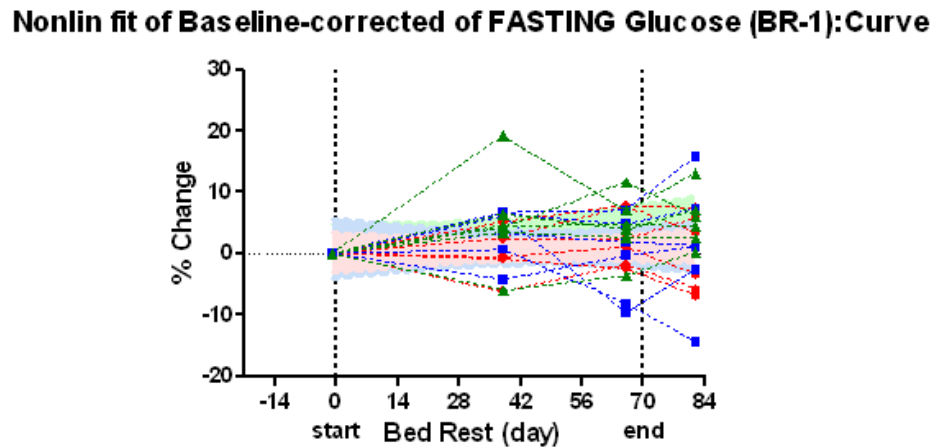
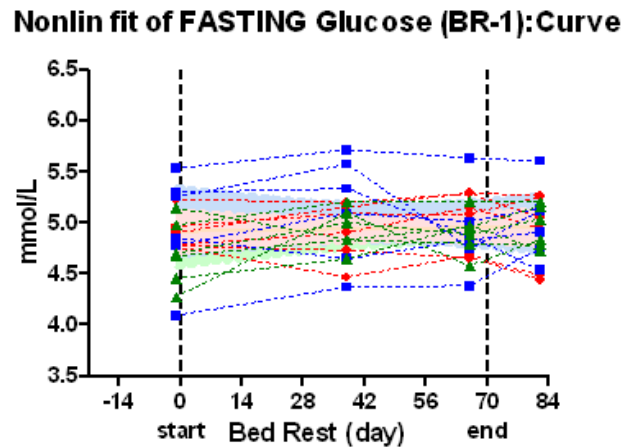
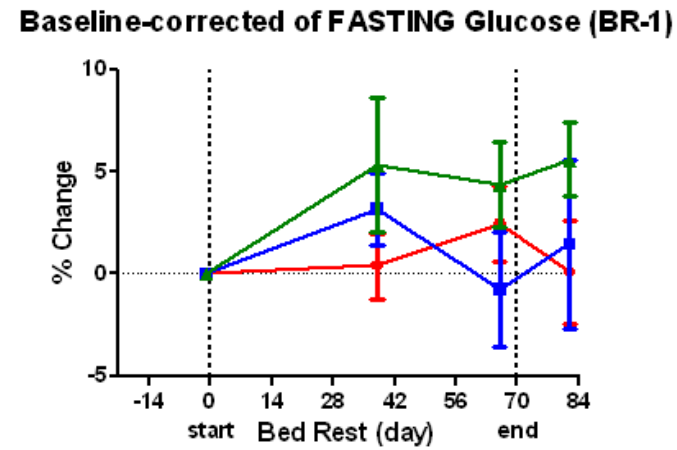
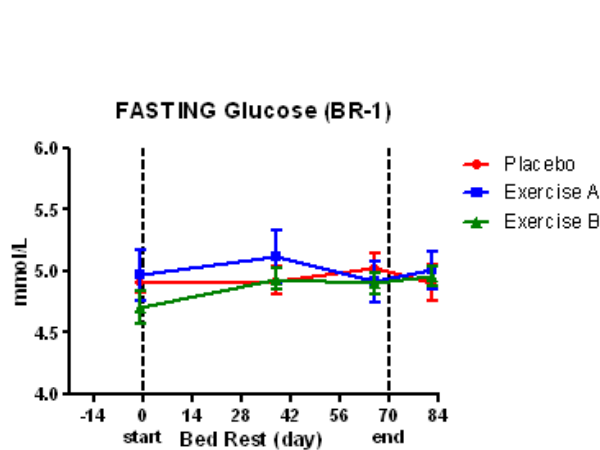
Glucose Tolerance

- 2Hr Oral Glucose Tolerance Test (OGTT)
 - Glucose
 - Insulin

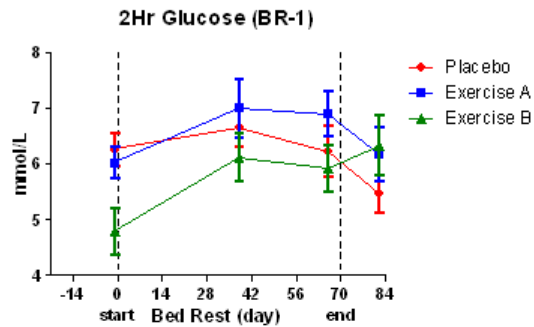
 - Insulin Resistance (HOMA-IR)
 - Insulin Sensitivity (Matsuda Index)

 - Lactate
 - Glucose oxidation

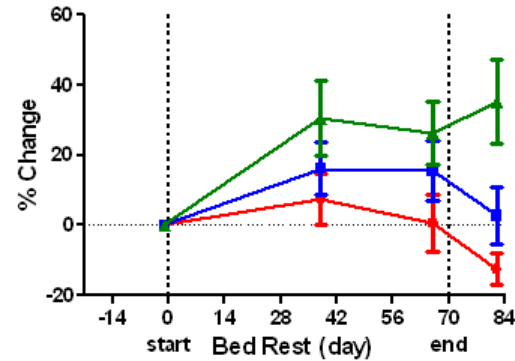
OGTT – Fasting Glucose



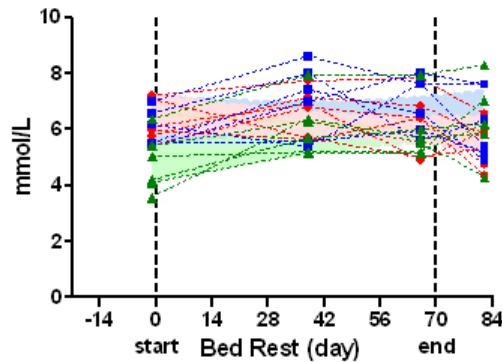
OGTT – 2Hr Glucose



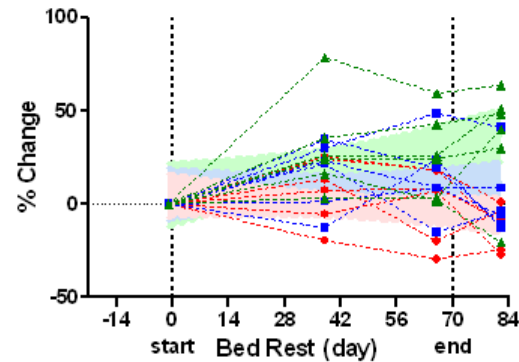
Baseline-corrected of 2Hr Glucose (BR-1)



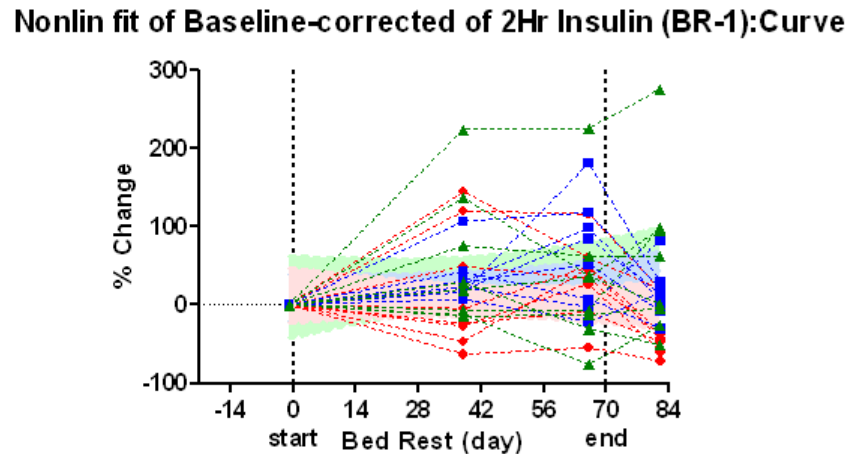
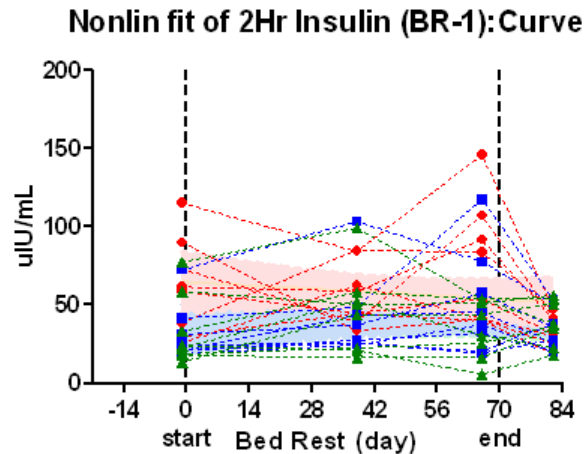
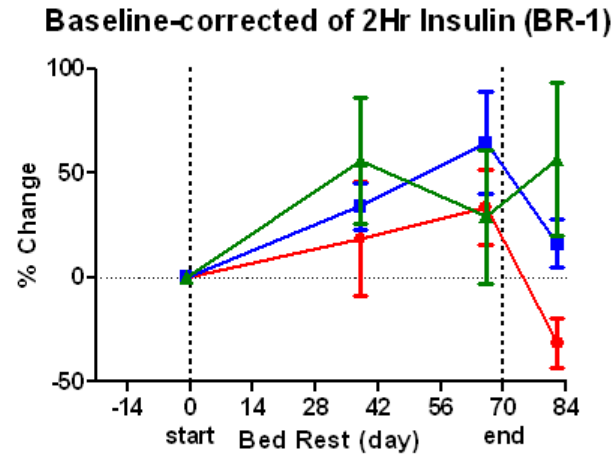
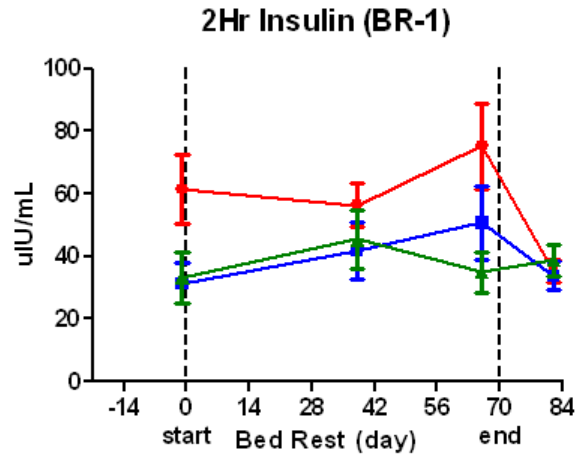
Nonlin fit of 2Hr Glucose (BR-1):Curve



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

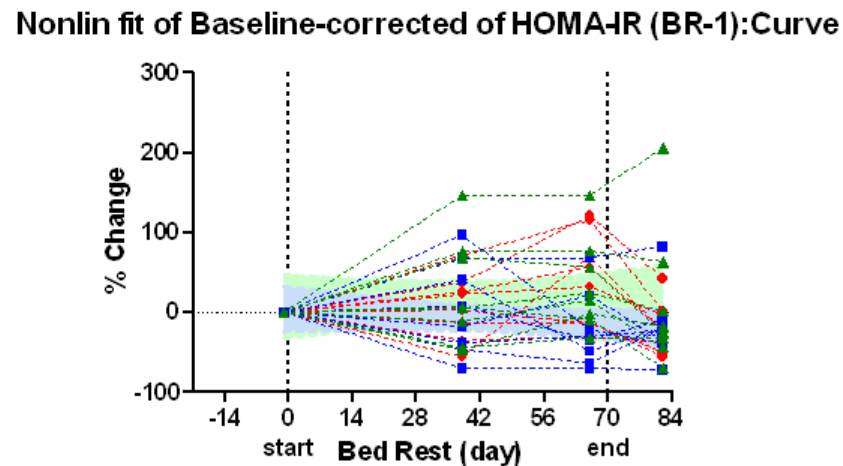
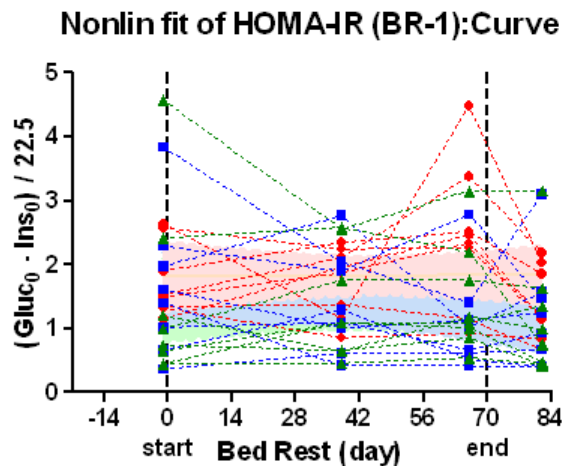
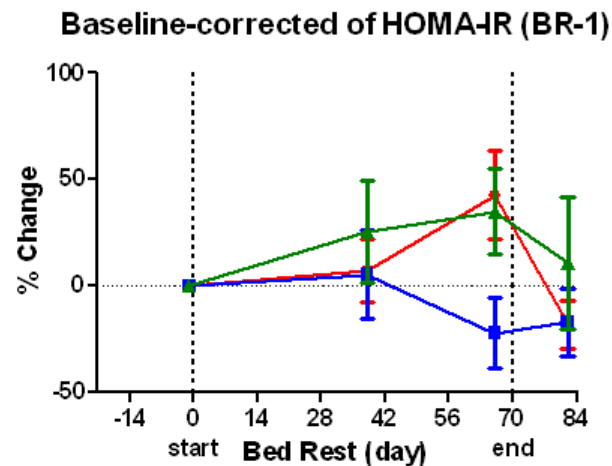
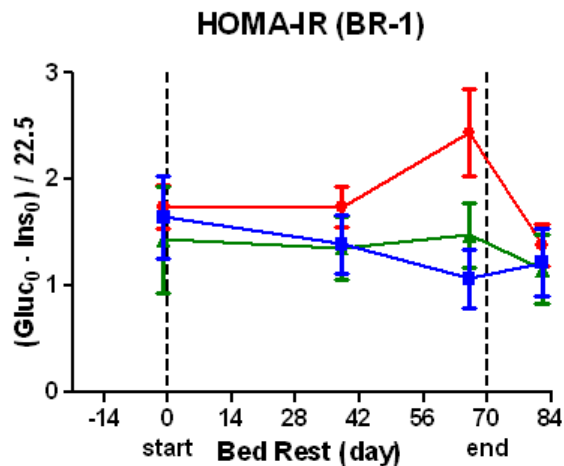


OGTT – 2Hr Insulin

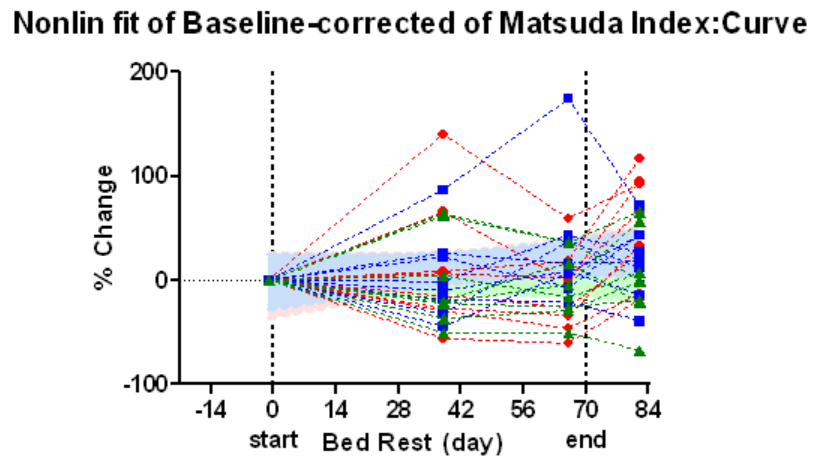
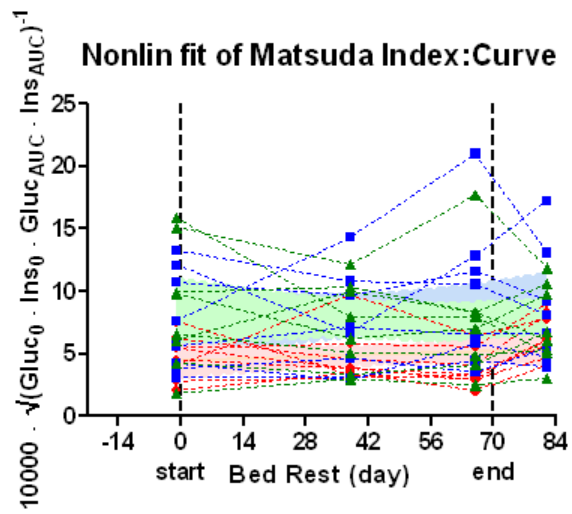
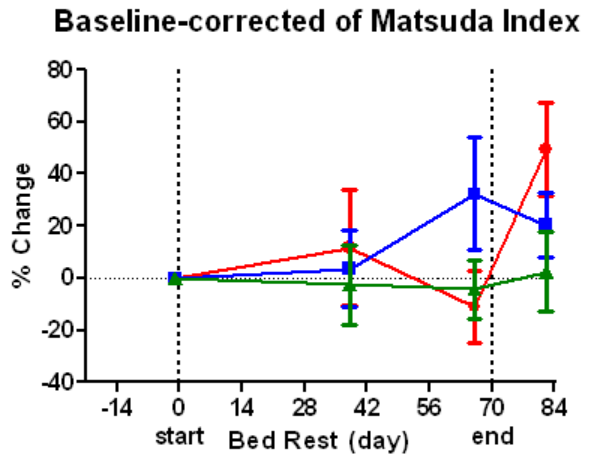
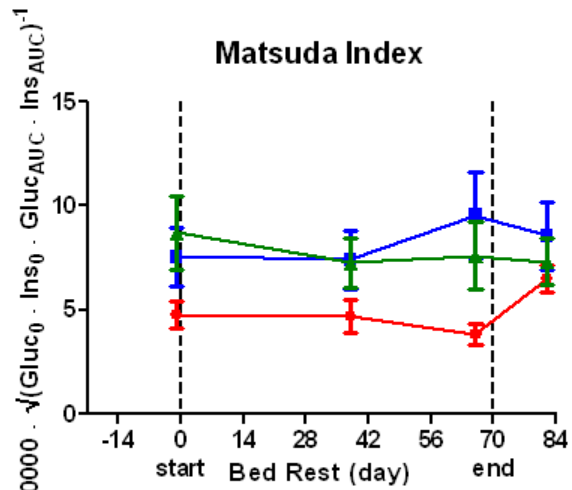


- Control
- ▲ Exercise
- Exercise + Testosterone

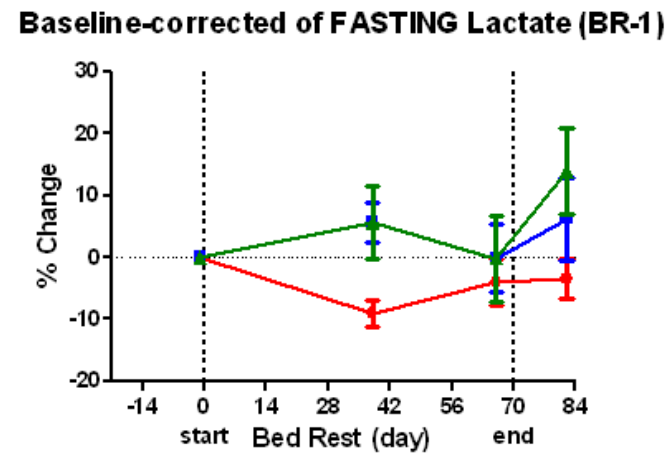
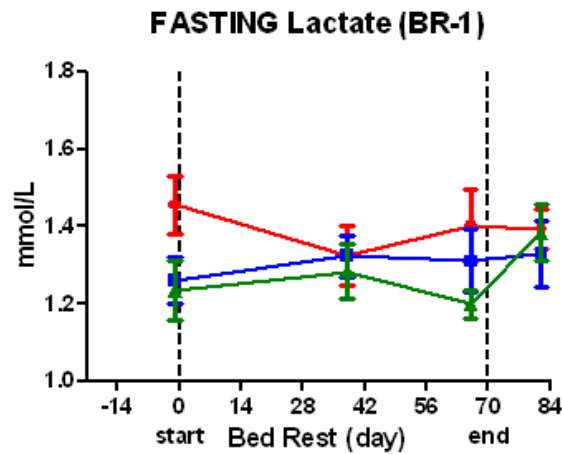
OGTT- Insulin Resistance



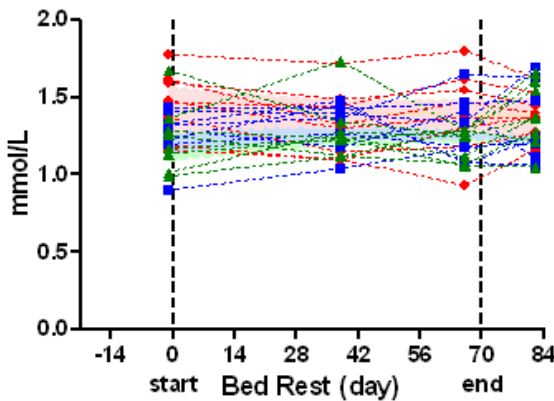
OGTT – Insulin Sensitivity



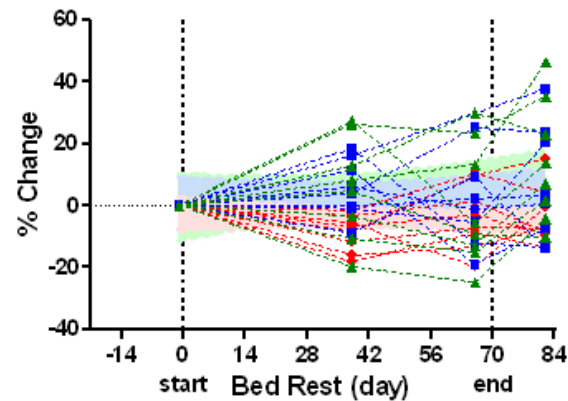
OGTT - Fasting Lactate



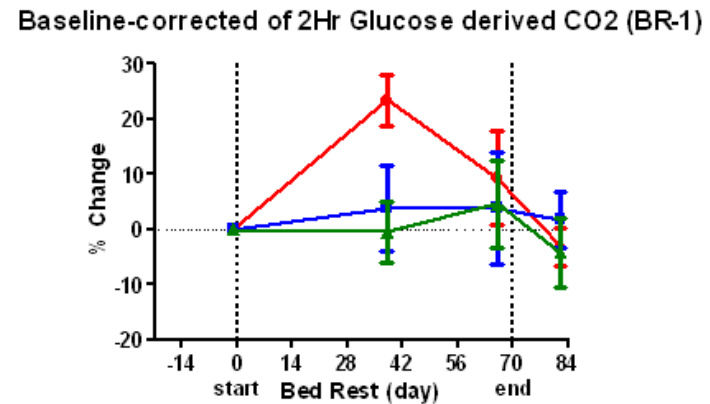
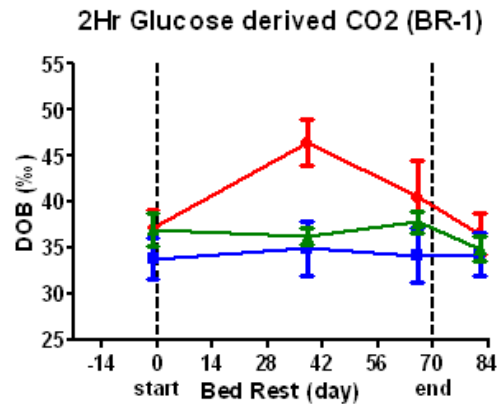
Nonlin fit of FASTING Lactate (BR-1):Curve



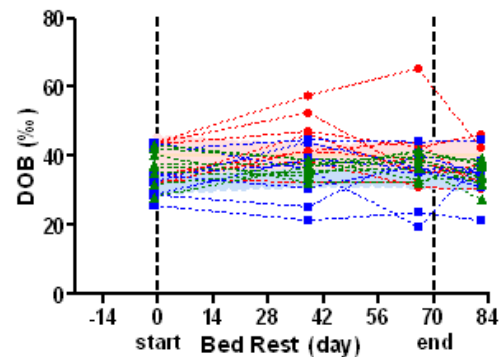
Nonlin fit of Baseline-corrected of FASTING Lactate (BR-1):Curve



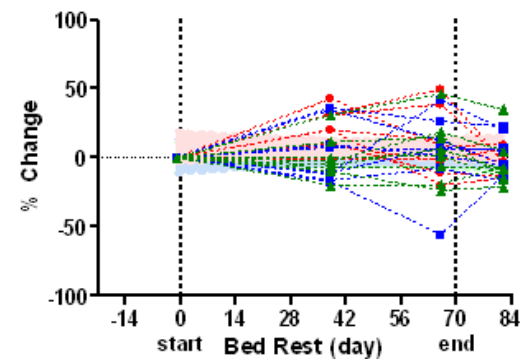
OGTT - Glucose Oxidation



Nonlin fit of 2Hr Glucose derived CO2 (BR-1):Curve



Nonlin fit of Baseline-corrected of 2Hr Glucose derived CO2 (BR-1):Curve



OGTT Summary
