Data Mining Activity for Bone Discipline: Calculating a Factor of Risk for Hip Fracture in Long-Duration Astronauts

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The factor-of-risk (Φ), defined as the ratio of applied load to bone strength, is a biomechanical approach to hip fracture risk assessment that may be used to identify subjects who are at increased risk for fracture. The purpose of this project was to calculate the factor of risk in long duration astronauts after return from a mission on the International Space Station (ISS), which is typically 6 months in duration. The load applied to the hip was calculated for a sideways fall from standing height based on the individual height and weight of the astronauts. The soft tissue thickness overlying the greater trochanter was measured from the DXA whole body scans and used to estimate attenuation of the impact force provided by soft tissues overlying the hip. Femoral strength was estimated from femoral areal bone mineral density (aBMD) measurements by dual-energy x-ray absorptiometry (DXA), which were performed between 5-32 days of landing. All long-duration NASA astronauts from Expedition 1 to 18 were included in this study, where repeat flyers were treated as separate subjects. Male astronauts (n=20) had a significantly higher factor of risk for hip fracture Φ than females (n=5), with preflight values of 0.83± 0.11 and 0.36 ± 0.07, respectively, but there was no significant difference between preflight and postflight Φ (Figure 1). Femoral aBMD measurements were not found to be significantly different between men and women. Three men and no women exceeded the theoretical fracture threshold of Φ=1 immediately postflight, indicating that they would likely suffer a hip fracture if they were to experience a sideways fall with impact to the greater trochanter. These data suggest that male astronauts may be at greater risk for hip fracture than women following spaceflight, primarily due to relatively less soft tissue thickness and subsequently greater impact force.

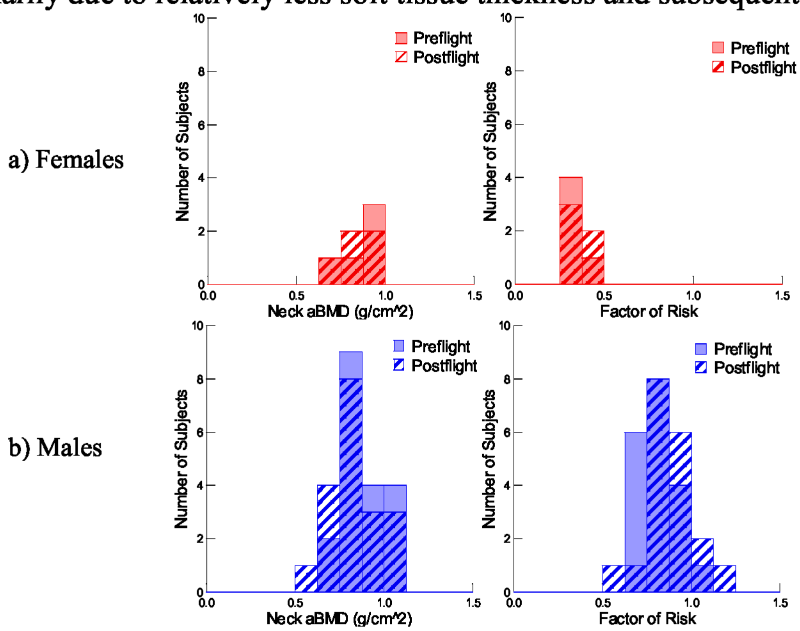

Figure 1. Pre- and postflight calculations of femoral neck aBMD and factor of risk (Φ) for hip fracture in a) females and b) males.

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Introduction

Addresses Risk of Accelerated Osteoporosis and Risk of Bone Fracture

- Motivation: short- or long-term risk of hip fracture in astronauts is unknown
- The factor-of-risk (Φ) is a biomechanical approach to hip fracture risk assessment that incorporates aBMD (as an estimate of femoral strength), body composition and estimated fall forces
- May be used to identify subjects at risk for hip fracture
  - Theoretically, fracture will occur when $\Phi > 1$

$$\text{Factor of Risk } (\phi) = \frac{\text{Fall Force}}{\text{Bone Strength}}$$

Objectives

- Determine the change in factor-of-risk for hip fracture due to long-duration exposure to microgravity
- Assess the time course of recovery of BMD and the factor-of-risk
- Identify gender- or mission length-specific differences in the components that may influence hip fracture risk

Methods

- **Study Design:** Subjects include all NASA long duration astronauts from Expedition 1-18 (2000-2009). Repeat flyers were treated as separate subjects.
- **Study Data:** DXA scans for femoral trochanteric aBMD and soft tissue thickness overlying the greater trochanter. Includes scans at preflight, postflight (within 5 – 32 days of return), and follow-up (of varying duration).

Table 1. Subject data (mean standard deviation)

	n	Age	BMI	Mission Length
Men	20	46 5	26.8 2.0	170 46
Women	5	43 2	23.8 2.2	175 43

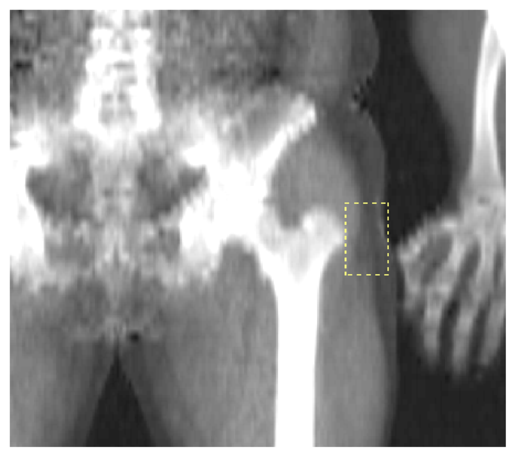


Figure 1. Whole body DXA scan with manual measurement of lateral distance between the trochanter-soft tissue boundary and the soft tissue- air boundary

Methods

- **FOR calculation:**
  - Estimated Failure Load
    - Use cadaver study (n=76) of correlation between femoral failure load and trochanteric aBMD (R^2=0.74) to predict hip fracture strength of subjects (Roberts et al, Bone 2009).
    - Failure Load (N) = 10118 (Trochanteric aBMD)– 1512.5
  - Estimated Fall Force
    - Calculate peak force applied to hip during a sideways fall from standing height as a function of the individual's height, weight, and soft tissue thickness (Bouxsein et al, 2007)
    - $v = \sqrt{2gh_{cog}}$
    - $\text{Fall Force} = v\sqrt{k_{stiff}\frac{m}{2}} - k_{fat}d_{ST}$
    - h_{cog}= height of center of gravity, m = body mass, k_{stiff}= sex-specific stiffness of the femur, k_{fat}= 71 N/(mm of soft tissue), d_{ST}=soft tissue thickness

Methods

- Statistical Analysis
  - Paired t-test to determine difference between preflight and postflight values.
  - Two sample t-test to assess differences between men and women at a single timepoint.
  - Linear regression to assess association between BMD, factor-of-risk and mission length
  - Mixed-effects model with random slope and random intercept of longitudinal data to determine rate of recovery

Results

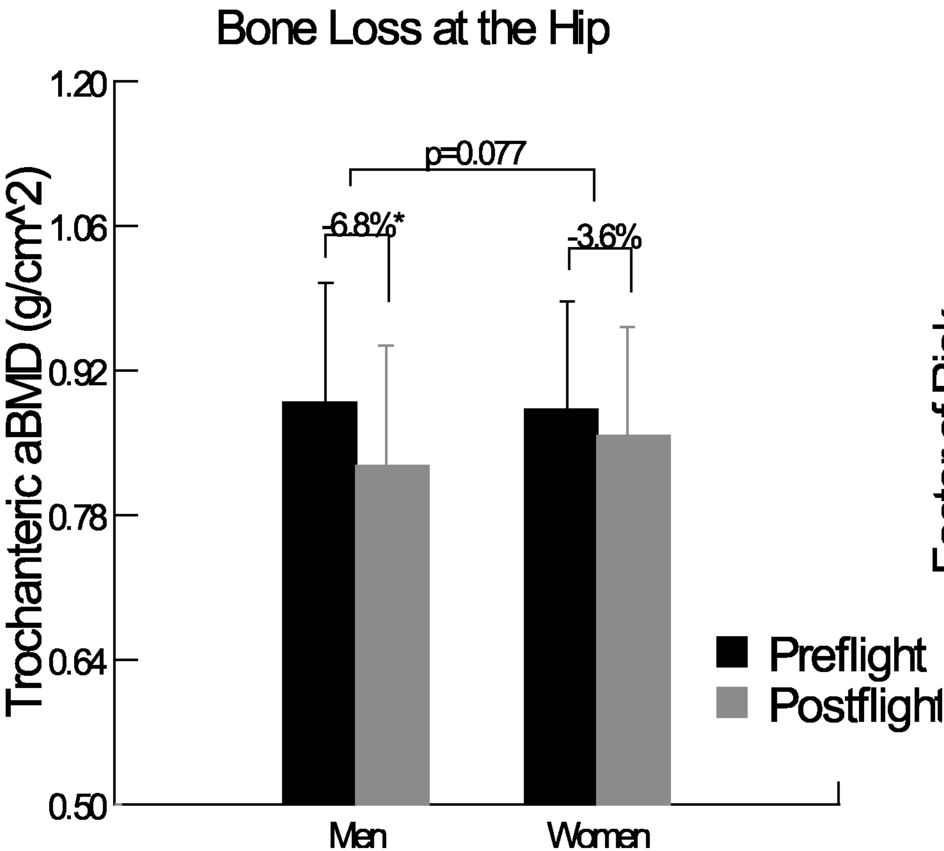


Figure 2. On average, men lost -6.8% of femoral trochanteric aBMD (p<0.001), whereas women lost -3.6% (p = 0.093). Thus, bone loss in men was nearly two-fold greater than in women (p=0.077). Preflight aBMD values did not differ between men and women. *=p<0.001

High risk for hip fracture

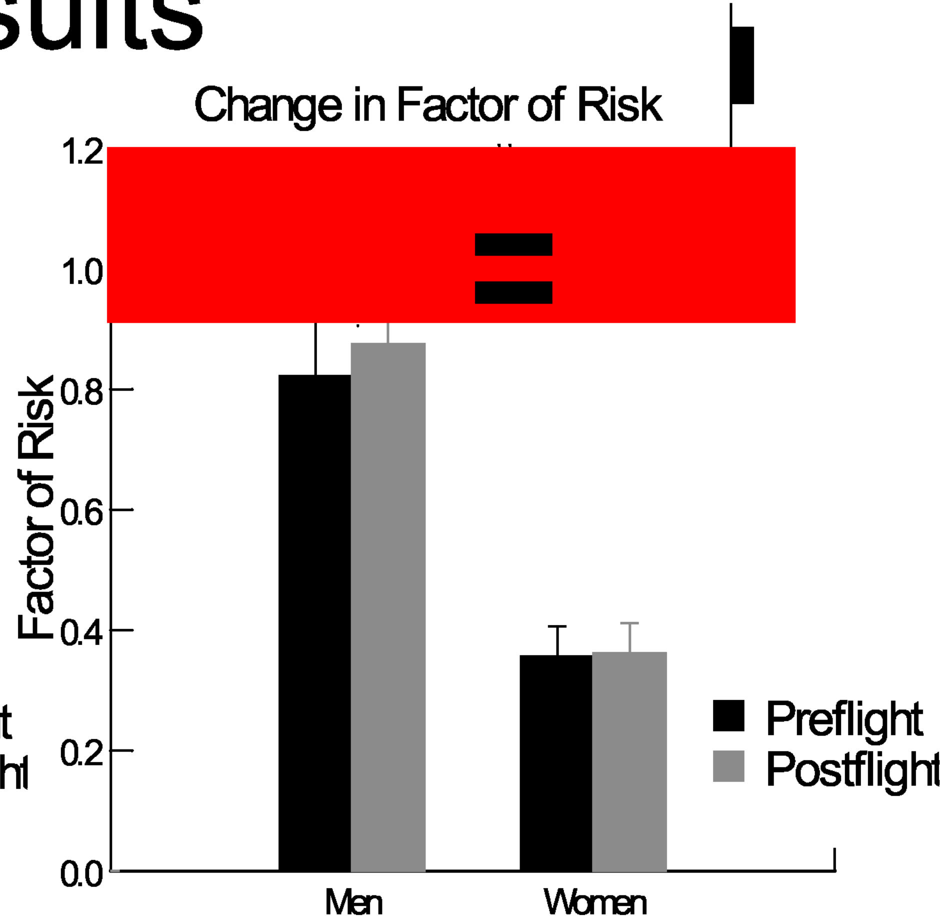


Figure 3. Men have a dramatically higher preflight Φ (0.82 ± 0.12) than women (0.36 ± 0.05, p<0.001). Φ increases as a result of microgravity exposure (p = 0.007) in men but not in women (p = 0.75). *=p<0.01, **= p<0.001

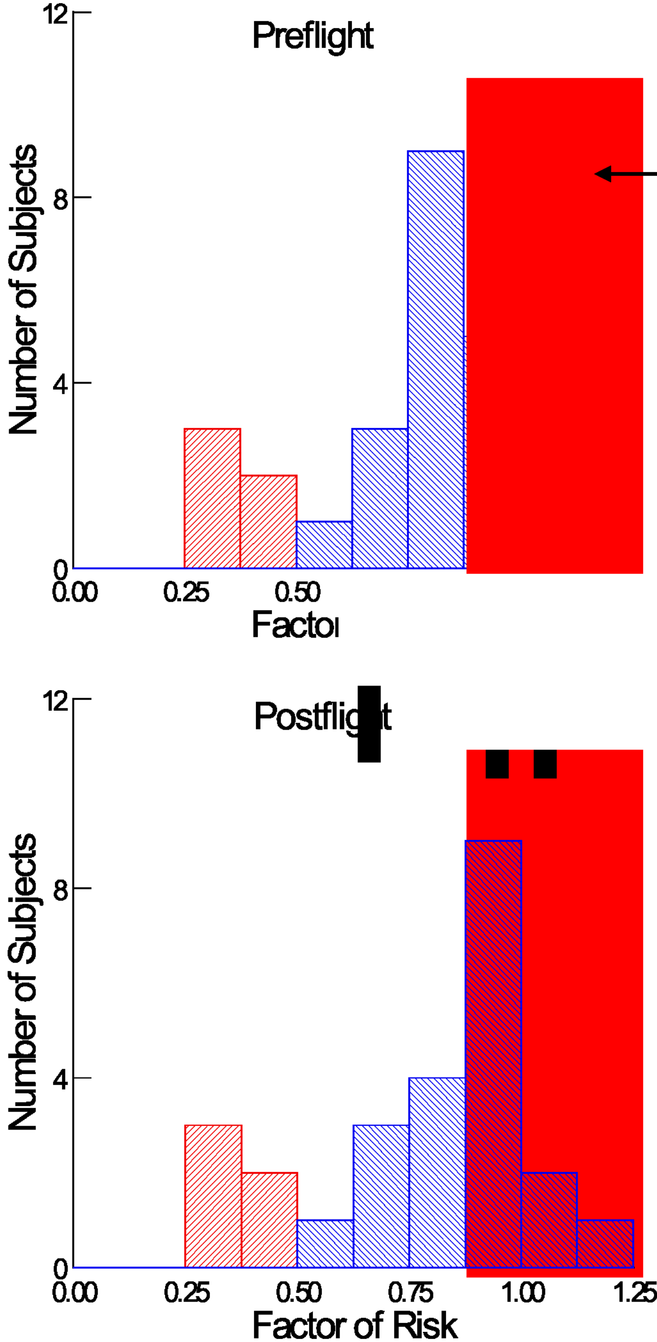
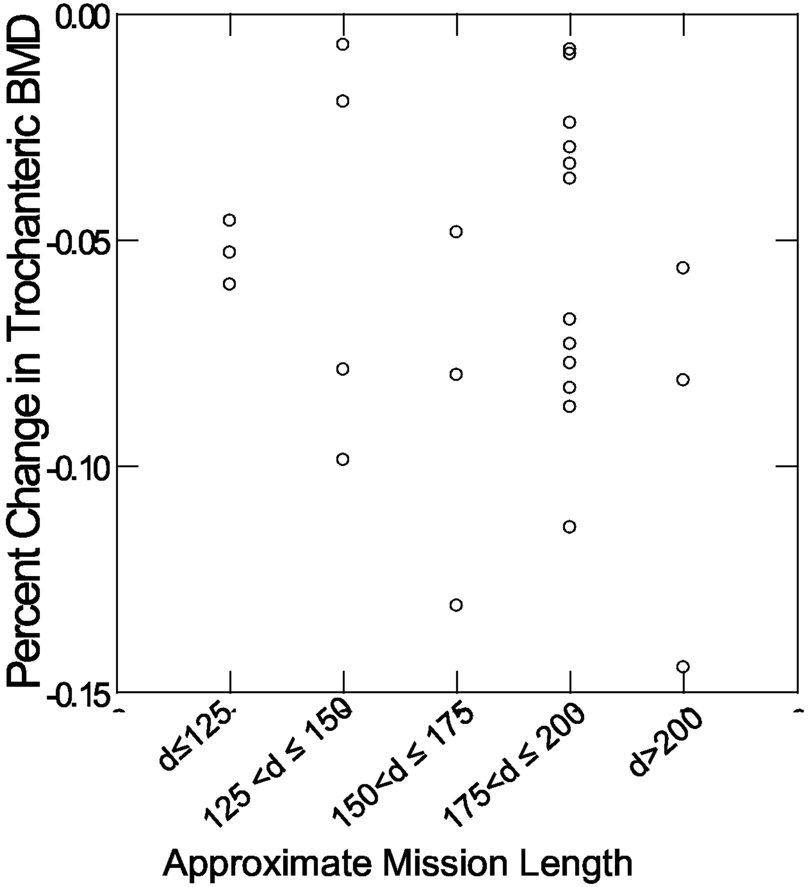
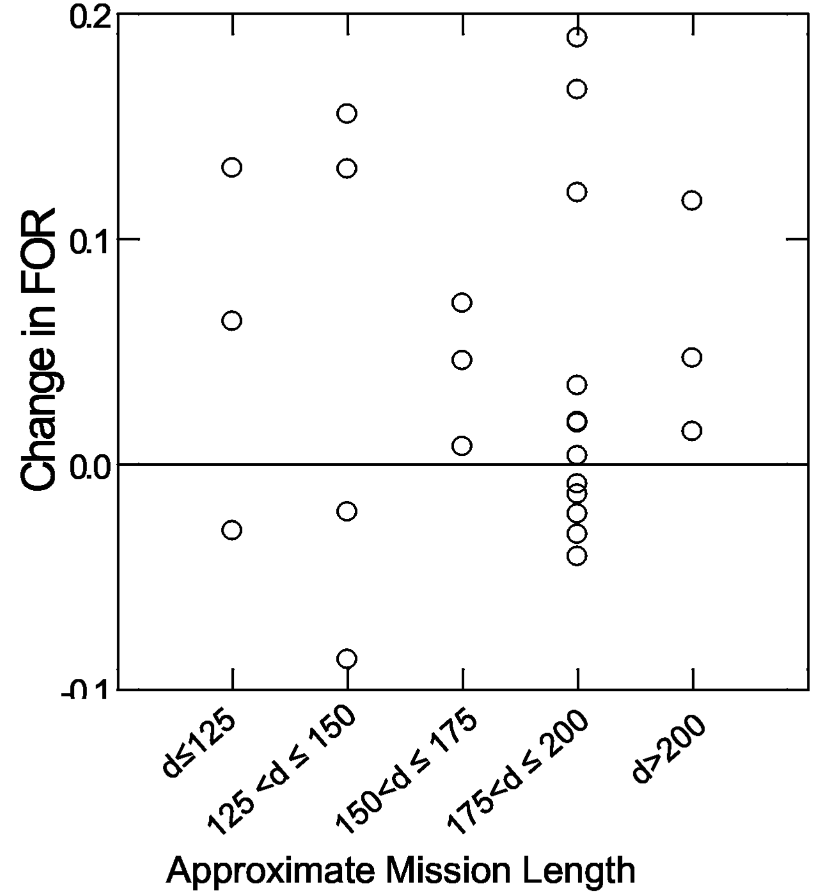


Figure 4. Distribution of the factor-of-risk for hip fracture in men and women pre- and postflight.

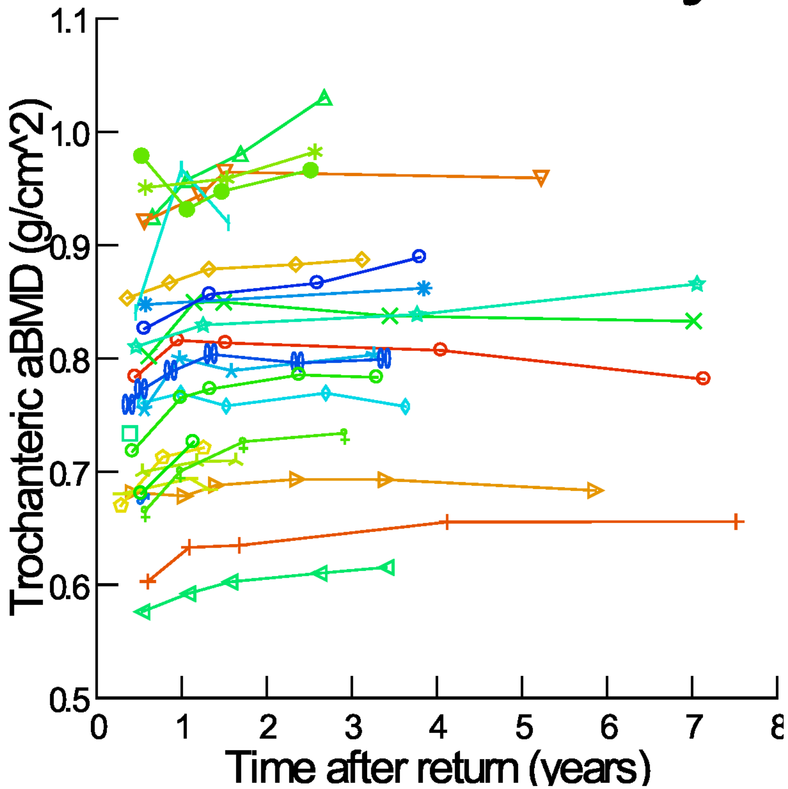
		High risk for fracture (0.9 ≤ Φ < 1.0)	Above fracture threshold (Φ> 1)
Preflight	Men	3	2
	Women	0	0
Postflight	Men	8	3
	Women	0	0

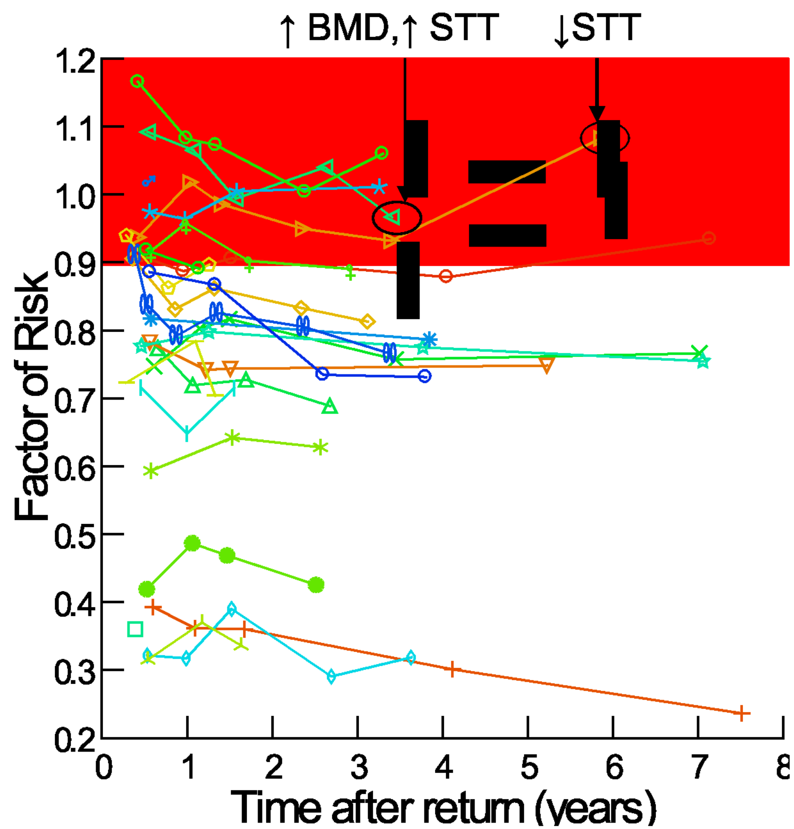
No association between mission length and percent change in trochanteric aBMD or change in factor-of-risk





Recovery





- Bone Mineral Density
  - Most of the recovery of aBMD occurs within the first 1.5 years after return. (avg. slope = +0.038 g/cm^2/year, $p<0.001$)
  - There is no significant change in aBMD after 1.5 years ($p=0.63$)
- Factor of Risk
  - High heterogeneity in postflight recovery of the factor-of-risk and BMD
  - No significant overall trend in factor-of-risk due to competing influences of BMD, weight, soft tissue thickness

Discussion and Conclusion

- Male astronauts experience a greater decrease in BMD than females after exposure to microgravity.
- As a result of lower BMD, less soft tissue padding, and greater height and weight, men have a significantly higher factor-of-risk than women. 44% of the male astronauts would be considered at high risk for hip fracture ($\Phi > 0.9$) immediately postflight.
- Most recovery of BMD occurs within the first 1.5 years after return. Nevertheless, 5 male astronauts continue to be at high risk for hip fracture 3 years after return ($\Phi > 0.9$).

Strengths and Limitations

- Strengths
  - Largest data set to date of long-duration astronauts
  - Accounts for other biomechanical factors leading to hip fracture
- Limitations
  - Assumptions in biomechanical model
    - Femoral strength estimated from DXA aBMD measurement, may be improved if QCT data were available
    - Only for sideways fall
    - Force attenuation from trochanteric soft tissue not dependent on proportion of muscle/fat
  - Small n

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