National Aeronautics and Space Administration

Skeletal Health Risks Due to Spaceflight: Recommended Research Directions by a Clinical Advisory Panel

Northeast Ohio Medical University, Dept. of Anatomy and Neurobiology 2012 Spring Seminar Series

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Center for Space Medicine, Cleveland Clinic

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Overview

- Defining the risks in atypical conditions (The 3 C's)
- Novel skeletal adaptation
- Directions for Bone Research

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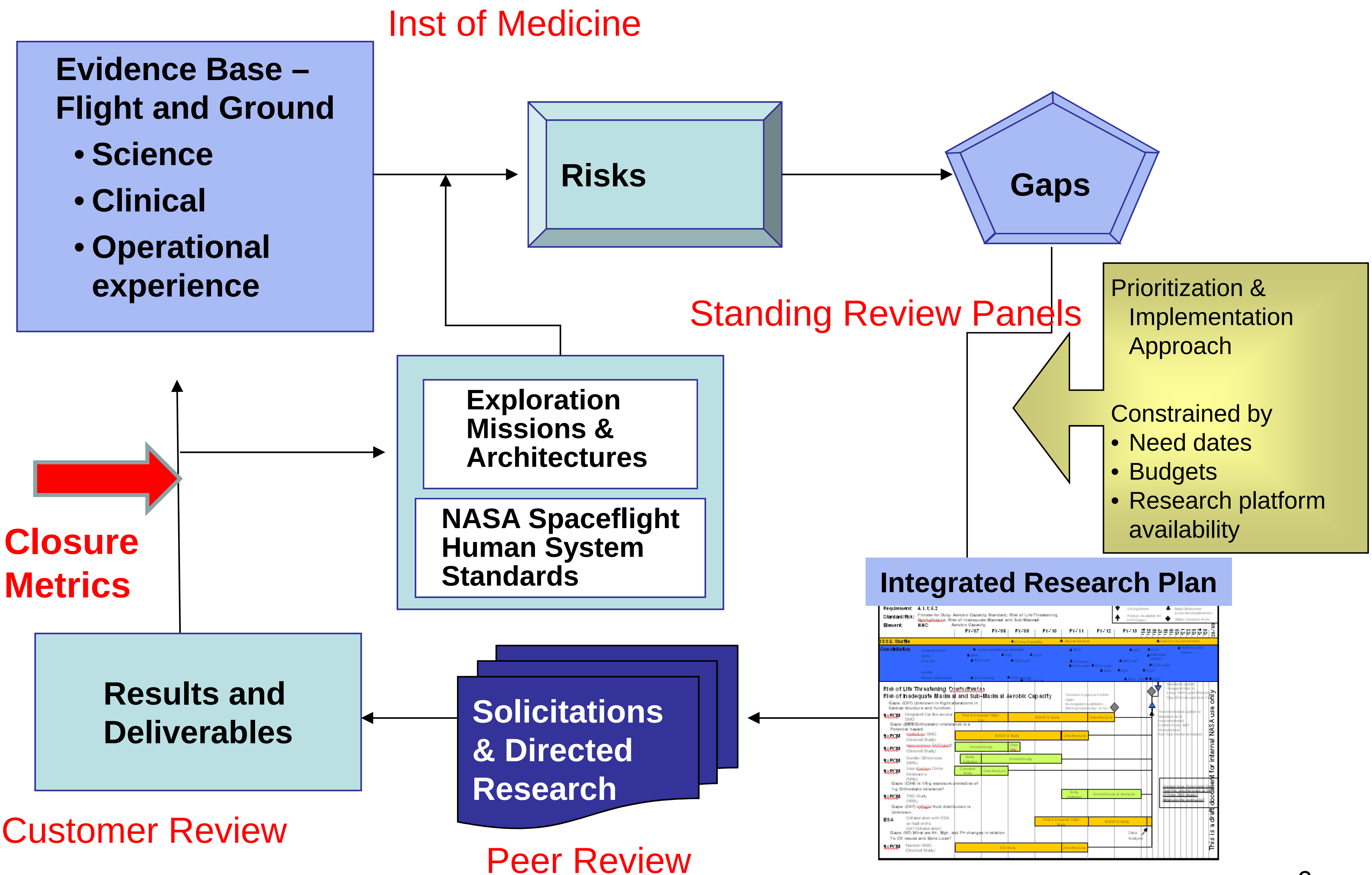
- Defining the risks in atypical conditions
- Novel skeletal adaptation
- Directions for Bone Research

Not a health care institution.

NASA CULTURE

NASA Human Research Program:

Mitigating Risk for the Human System



Adapted HRP 2012

Identified HRP "Bone" health risks due to space exploration.

1. Early Onset Osteoporosis

   Long-term health issue

2. Bone Fracture
3. Formation of Renal Stones
4. Intervertebral Disc Injury *(or Damage)*

   #2-4 Greater risk to mission operations.

Two Risks Associated with Fracture*

- Risk of Early Onset <u>Osteoporosis</u> Due to Spaceflight

  Osteoporosis: Condition of ***low bone mass*** and ***severe structural disruption*** <u>leading</u> to fractures under *normal* physical activities -- "fragility or atraumatic" fractures (fracture with fall from standing height)

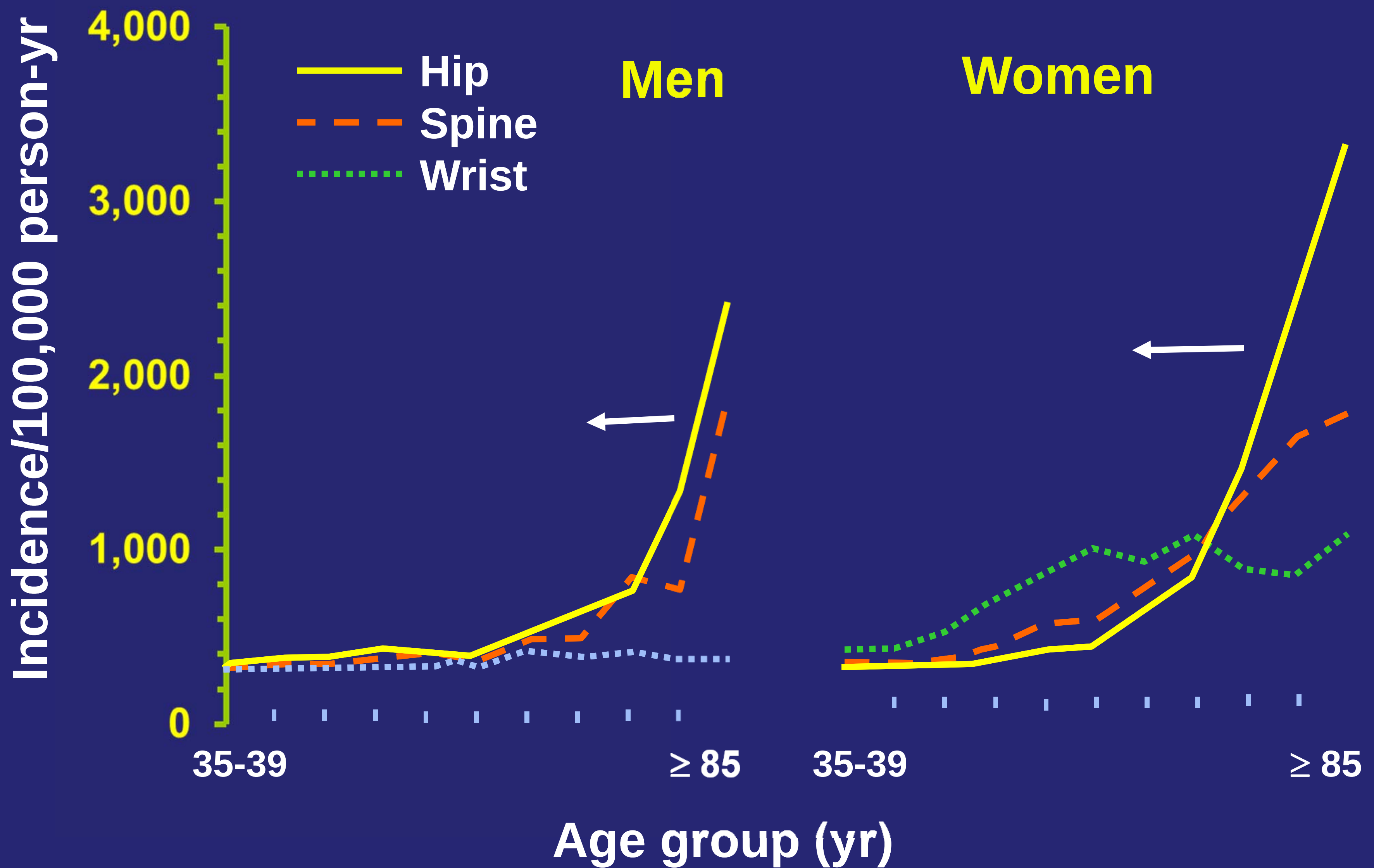
  Osteoporosis is the INTERMEDIATE condition.

- Risk of Bone Fracture

  Factor of Risk = Ratio of **Applied Load/Bone Failure Load** ("Bone Strength")

  Includes TRAUMATIC FRACTURE - Biomechanics

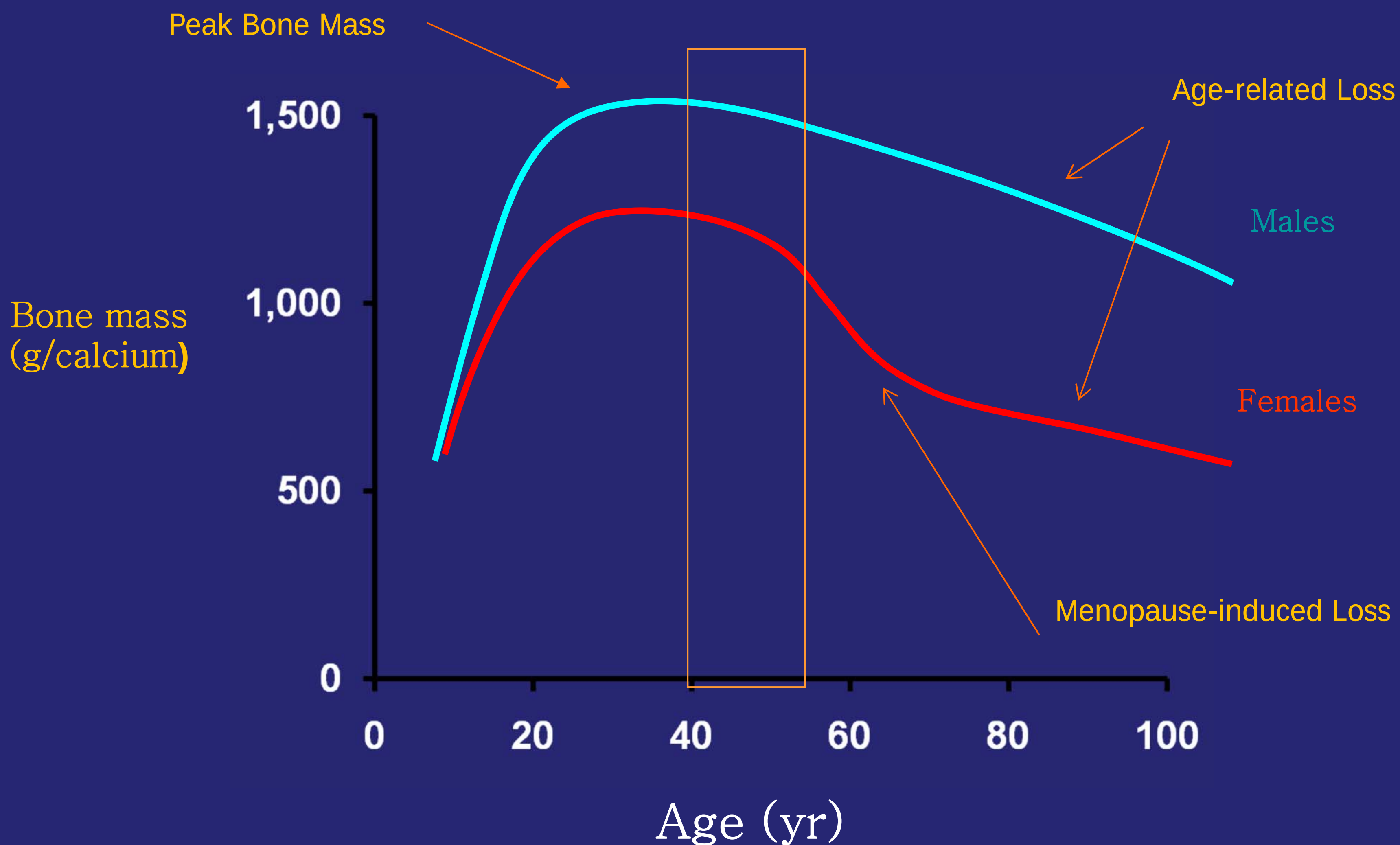
Premature Osteoporosis fractures in astronauts?



SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992

Does spaceflight result in irreversible changes to bone that combine with age-related losses?



Riggs BL, Melton LJ: Adapted from Involutional osteoporosis
Oxford Textbook of Geriatric Medicine
ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Given that osteoporosis is not a geriatric condition…

WHAT SHOULD NASA MEASURE *NOW* TO ADDRESS AN OCCUPATIONAL HEALTH RISK THAT MAY MANIFEST *LATER*?

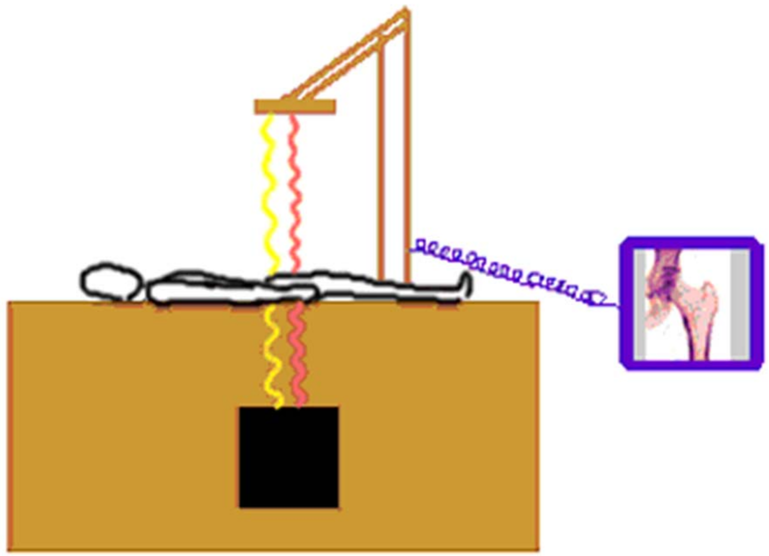
Requirement for Evaluating Bone Strength

- "Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. <u>Bone strength reflects the integration of two main features: bone density and bone quality</u>." JAMA 2001
- What is an index of Bone Quality? – any bone parameter that can influence bone strength independent of DXA BMD. *Supplement BMD as a predictor of fracture.*

Dual-energy X-ray Absorptiometry [DXA] BMD @ Johnson Space Center

- Monitor astronaut skeletal health
- Characterize skeletal effects of long-duration spaceflight
- Evaluate efficacy of bone loss countermeasures
- Verify restored health status

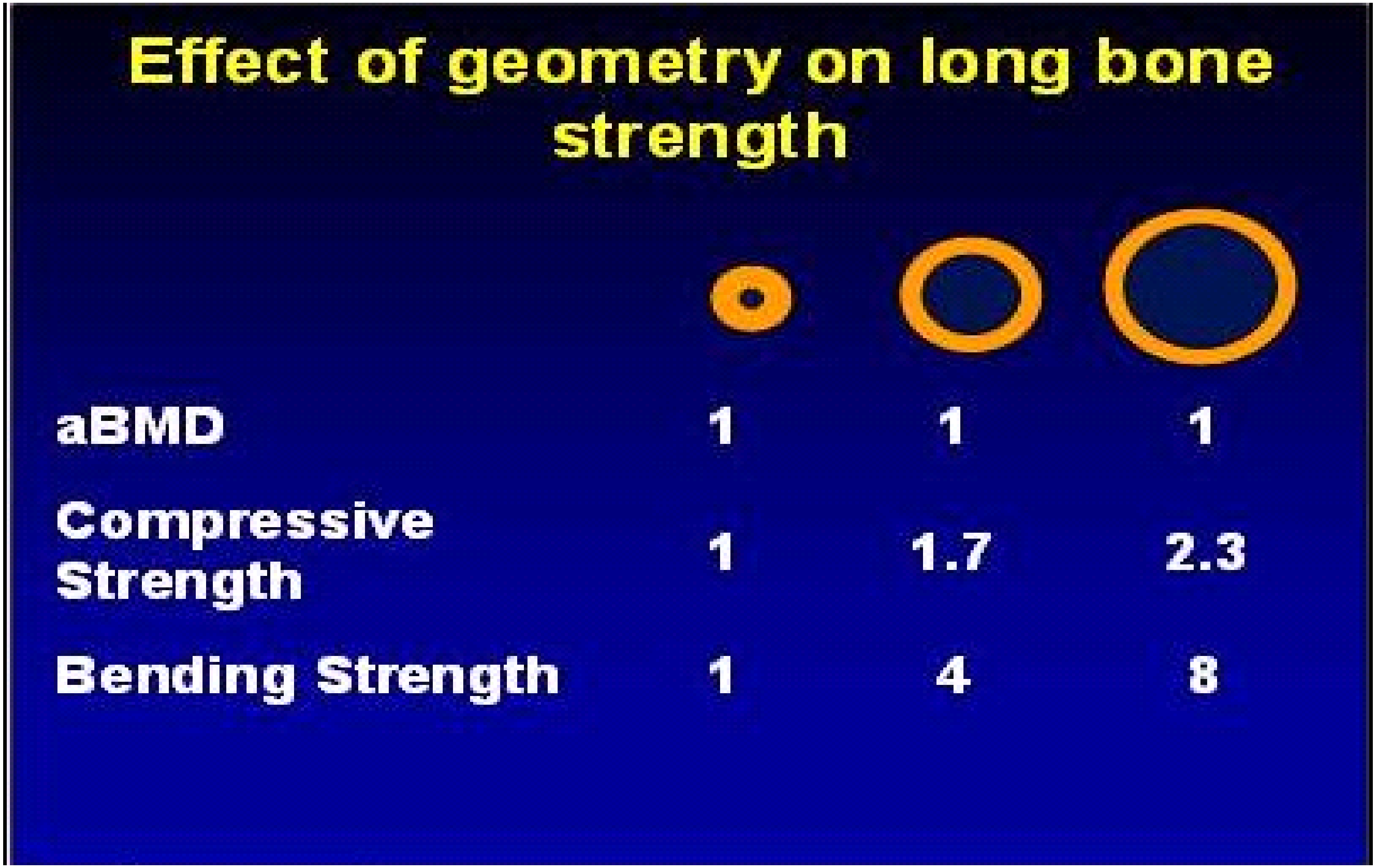
Dual-energy X-ray Absorptiometry-DXA



DXA measurement of areal BMD [BMD_a] – a 3d measure in 2d units

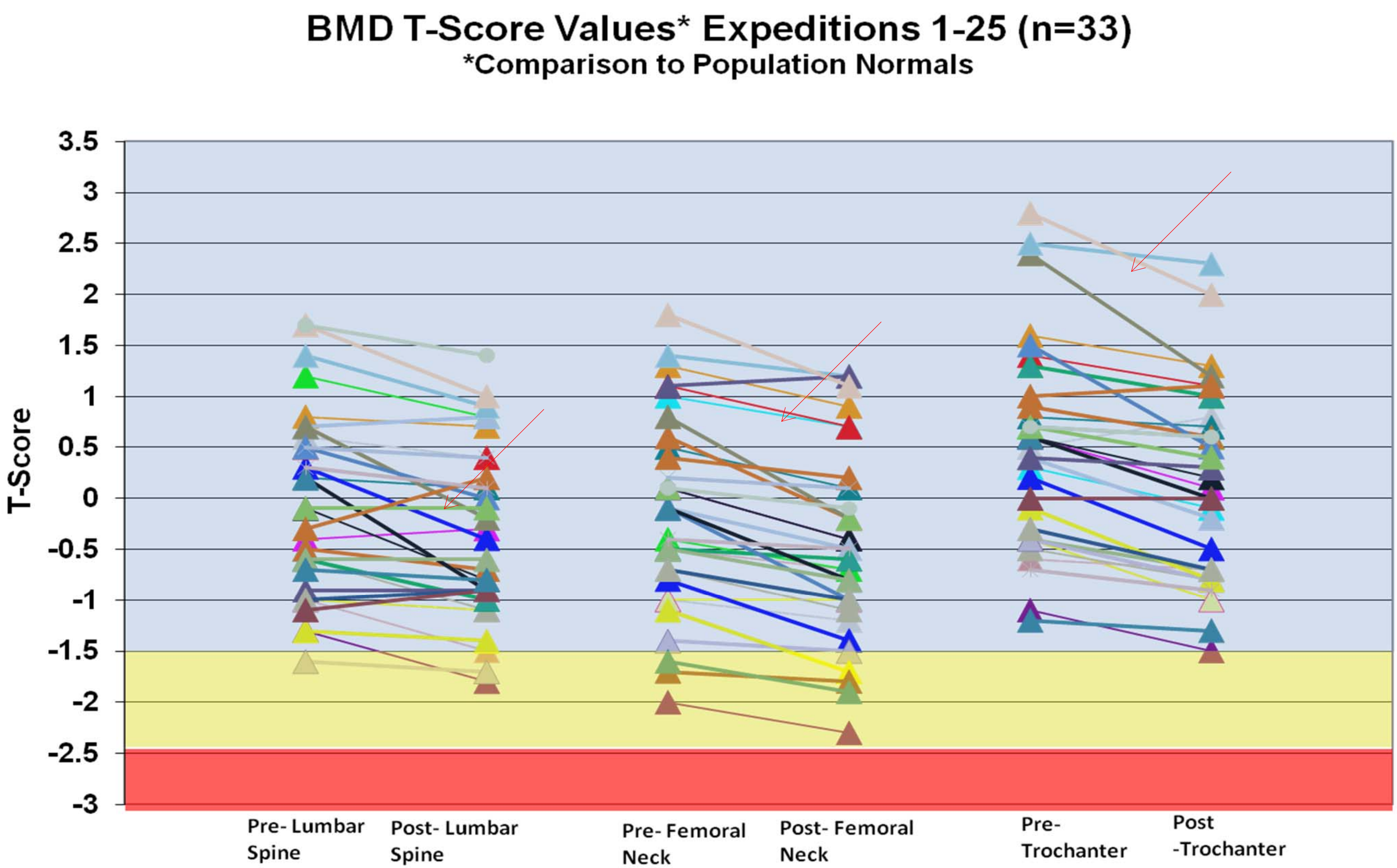
- Improved precision
- Low radiation
- Shorter scan times
- BMD measures over multiple skeletal sites
- Used in large prospective studies for fracture prediction
- Long established, widely-applied surrogate for bone strength

Limitation of DXA: cannot distinguish different geometries of bone and thus cannot reflect different levels of bone strength.



Mary Bouxsein, Ph.D. Bone Geometry and Skeletal Fragility, May 2005

DXA-based T-scores not appropriate, informative or predictive for fracture in astronaut population.



Understudied population for osteoporosis/novel risk factors

ASTRONAUT COHORT

The Long-duration Astronaut

- Typical space mission duration – 164 ± 33d (range 58-215d)
- Average Age – 46.9 ± 4.2 y (range 36.8 – 55.3)
- Male to Female Ratio – 3.9 : 1
- Current total # per astronauts in corps – 44 of 331
- # repeat fliers – 4
- BMI – Male BMI 26.4 ± 2.0 *(range 22.3 to 30.7);* Female BMI 21.7 ± 1.9 *(range 20.1 to 25.8)*
- Wt and Ht- Males: Males: 82 ± 9 kg *(range 63 to 101 kg),* 177 ± 6 cm *(range 163 to 188 cm)*;
- Wt and Ht Females: 61 ± 6 kg *(52 to 72 kg),* 168 ± 3 cm *(range 163 to 173 cm)*

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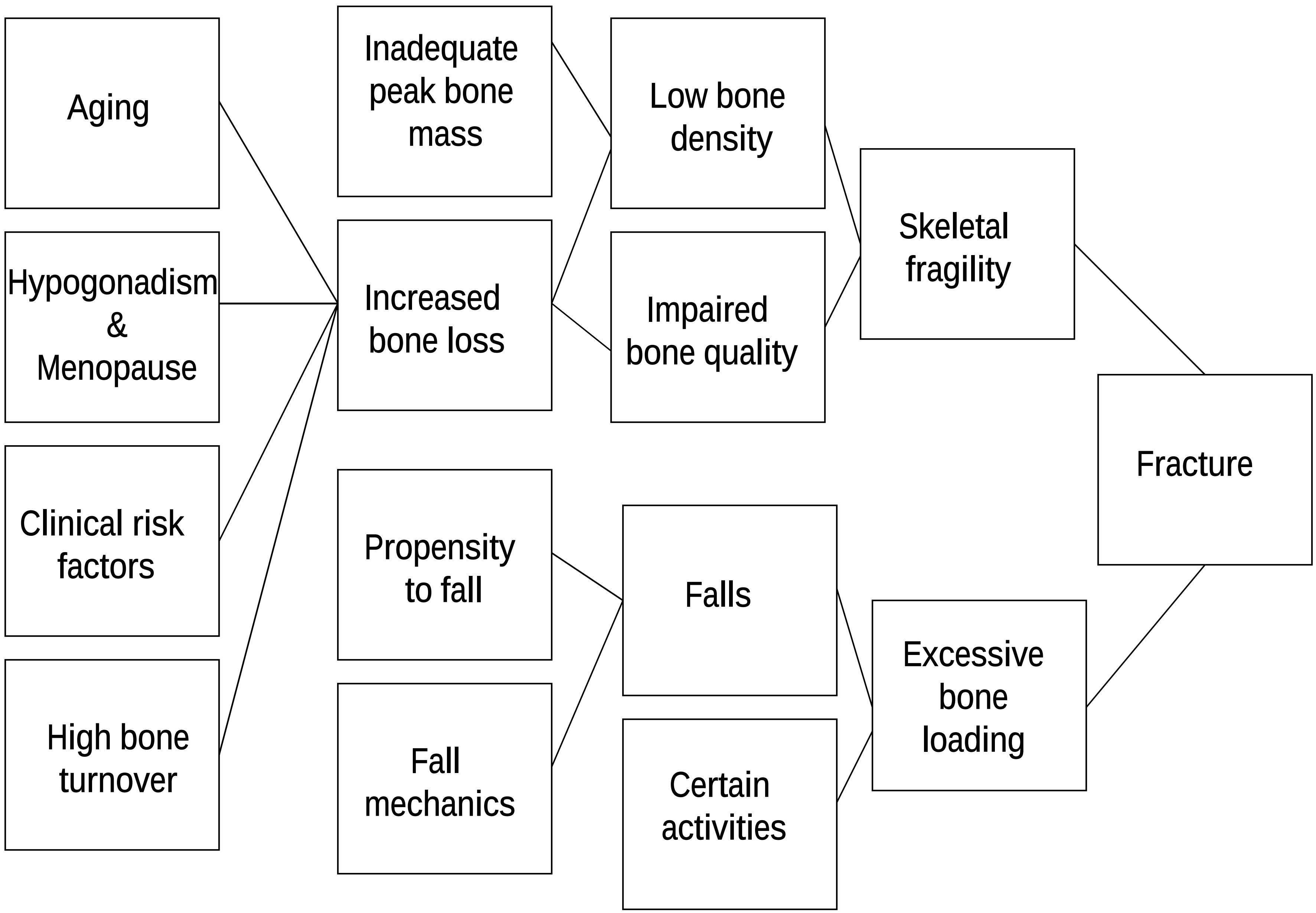
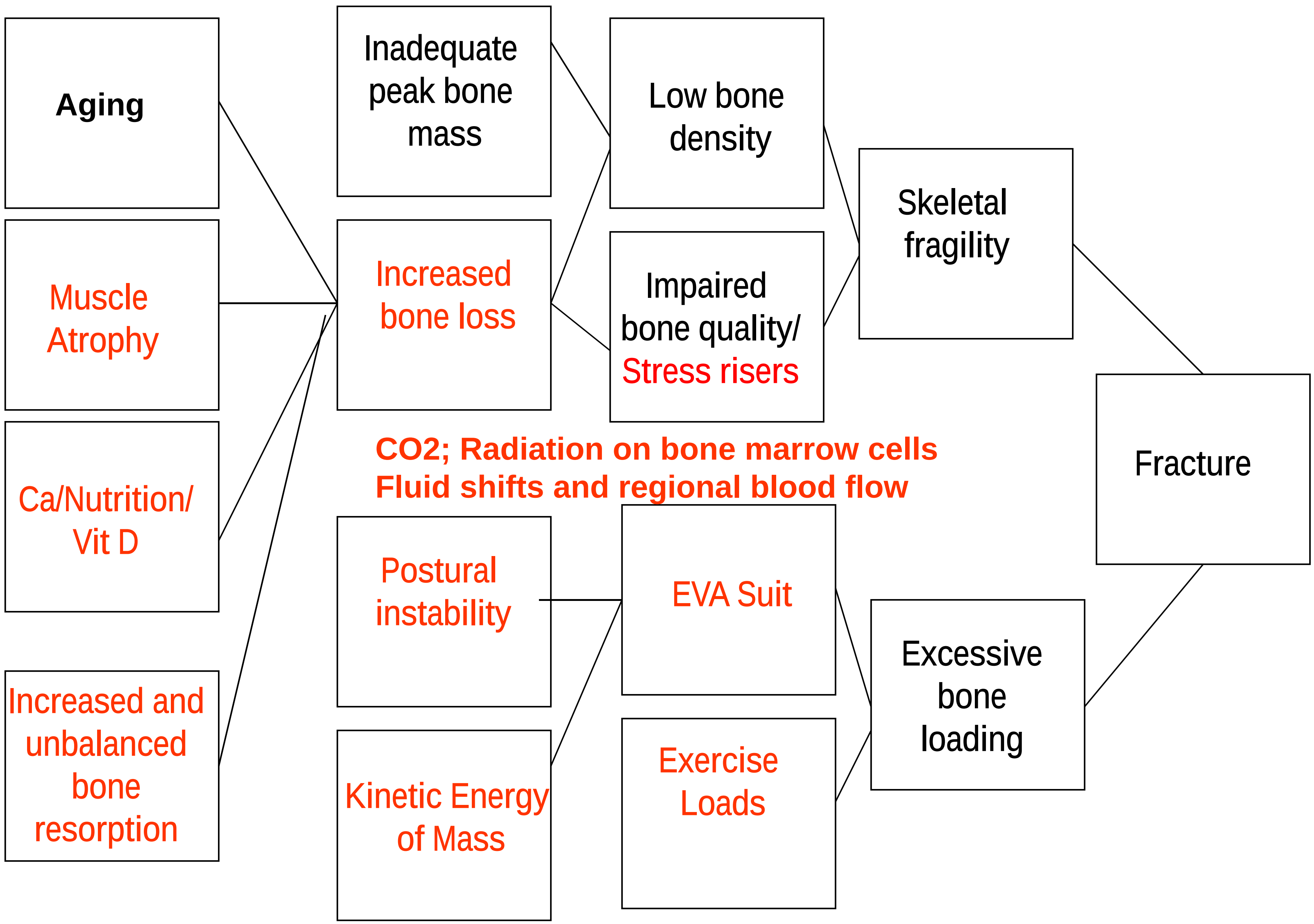


Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ



ASTRONAUTS EXPOSED TO UNIQUE SET OF RISK FACTORS DURING SPACEFLIGHT

Subject Numbers/Scheduling/Budget/Platform Availability/
Therapeutic Windows

NASA CONSTRAINTS

The long-duration astronaut – Constraints to clinical practice guidelines

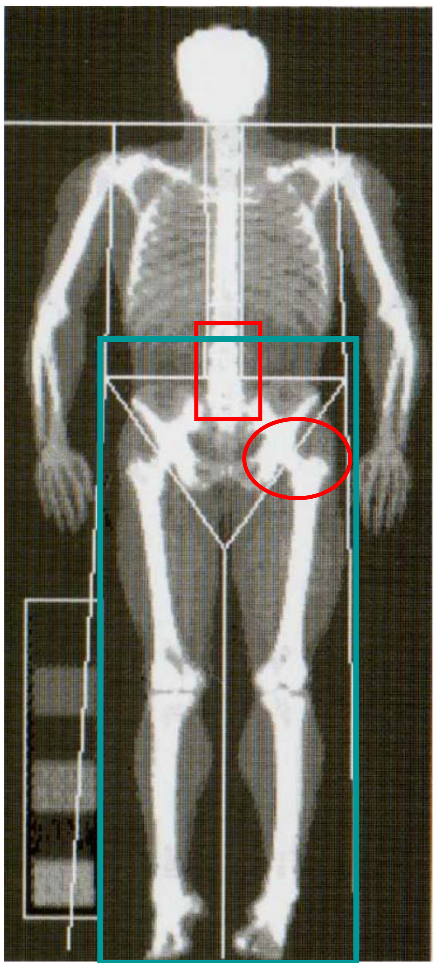
- Current total # per astronauts in corps – 44 of 331
- # repeat fliers – 4
- Male to Female Ratio – ~4:1
- Restricted presentation of sex-specific data – *Medical privacy*
- Limited Medical Assessment Tests – DXA, Biochemical bone turnover markers
- Limited expeditions/yr – 3 to 4
- Limited platform availability – 2020

Overview

- Defining the risks in atypical conditions
- Novel Skeletal Adaptation
- New Directions for Research

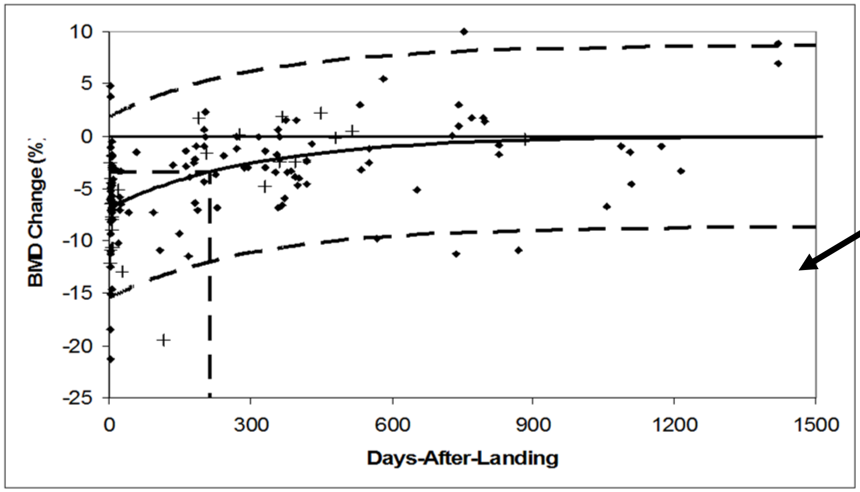
DXA BMD reveals changes that are unique & complex. Drives requirement for research.

Rapid (1-1.5%/mo) and site-specific BMD loss (means local regulation occurring).



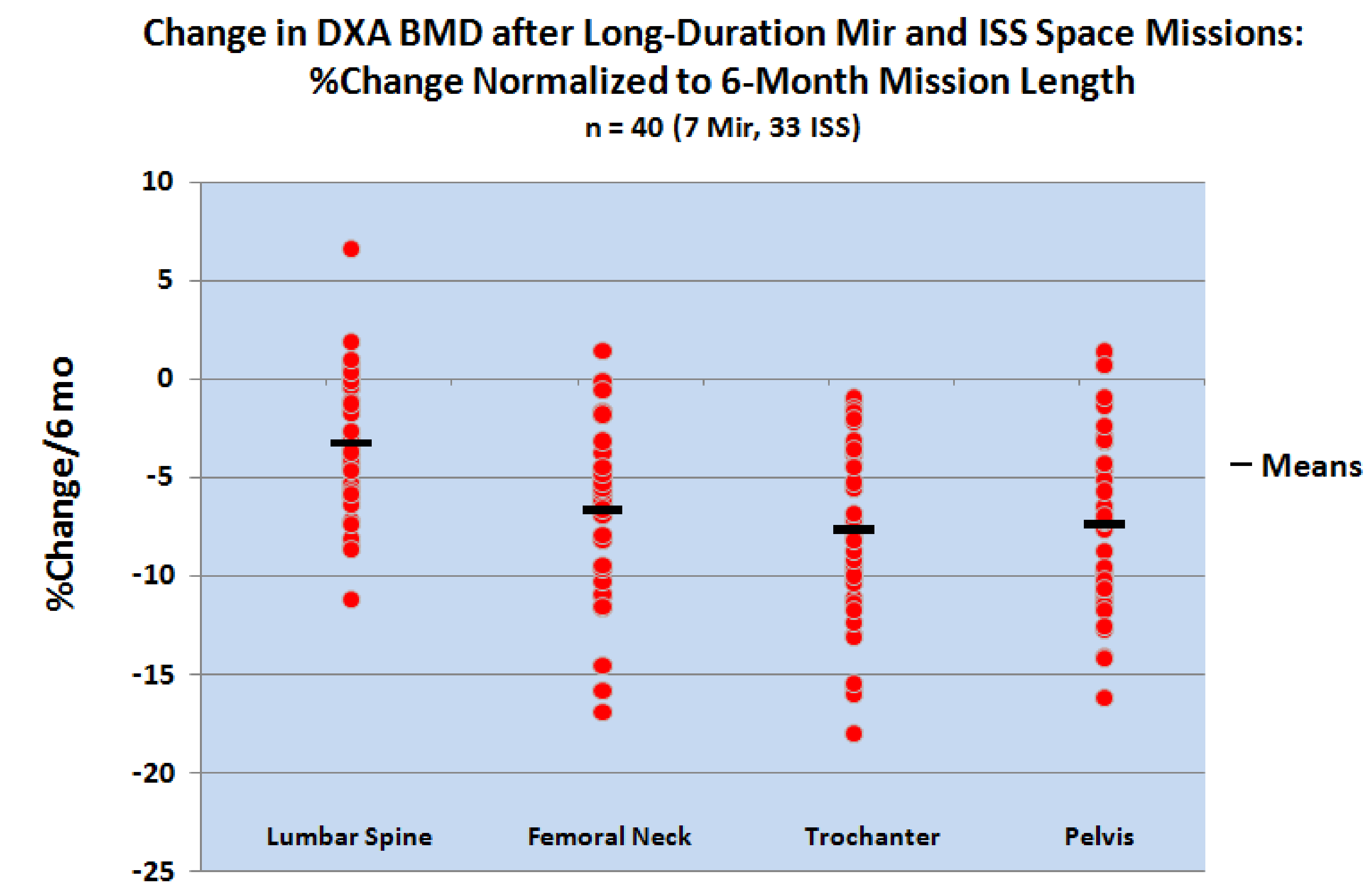
BMD Site	Mean Immediate Post Flight BMD (% change/month)			Mean Three Year Post Flight BMD (% change/month)		
	Predicted	Observed	p-value	Predicted	Observed	p-value
Total Hip	1.063 (0.05)	0.994 (-0.76)	<0.001	1.066 (0.02)	1.047 (-0.03)	<0.001
Lumbar Spine	1.081 (0.11)	1.016 (-0.58)	<0.001	1.085 (0.03)	1.069 (-0.00)	0.11
Ultra-Distal Radius	0.558 (-0.05)	0.550 (-0.20)	0.12	0.541 (-0.08)	0.551 (-0.04)	0.005
Mid-Shaft Radius	0.755 (0.19)	0.741 (-0.00)	0.04	0.749 (0.02)	0.741 (0.00)	0.28
Total Body	1.288 (-0.04)	1.262 (-0.26)	0.009	1.284 (-0.01)	1.261 (-0.05)	0.19

Total BMD **loss** greater and **persist** compared to BMD changes predicted from algorithms derived from earth-based population

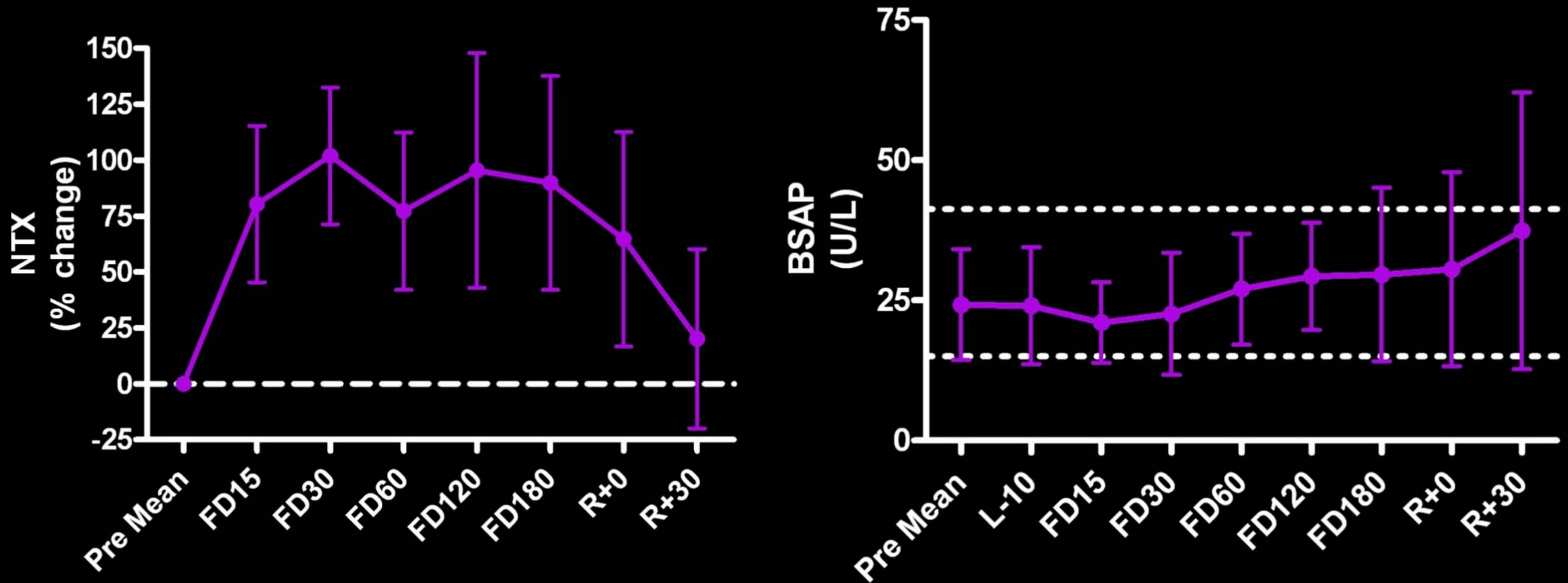


Loss is variable.
Recovery is variable.
Recovery is prolonged.
Indicates: Multiple Risk Factors at play.

More informative. – but how do we translate to fracture risk in astronauts?



Bone Turnover Markers suggest a net loss in bone mass in the skeleton



Slide Courtesy of Dr. SM Smith; Adapted by Sibonga