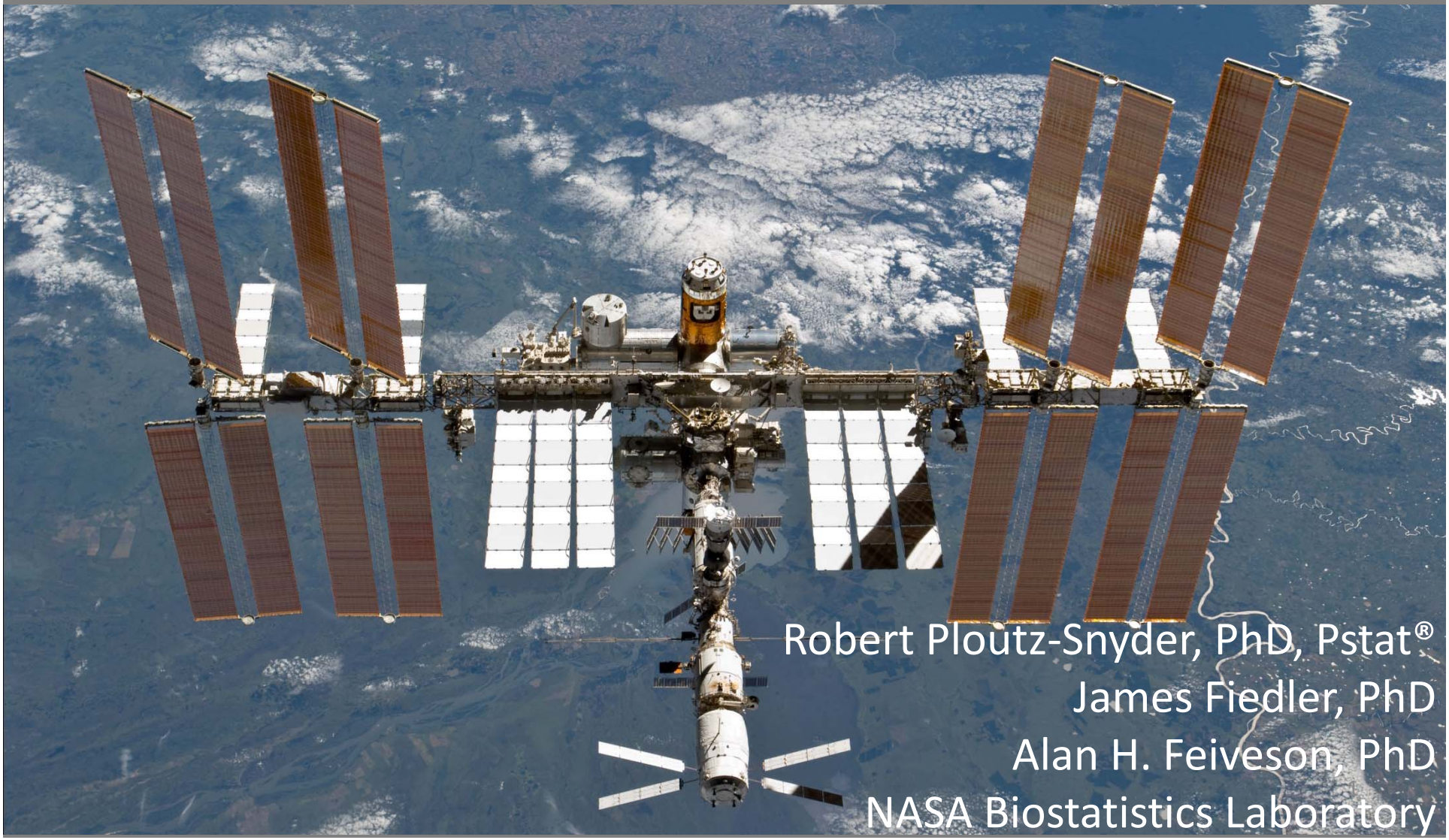
Getting More from (Small-n) Research Data: Getting Clinical instead of Cynical



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The Problem

- ISS (and analog) research sometimes results in low confidence with regard to inferences about the general astronaut population
  - Small-*n*
  - Non-random samples
  - Mission constraints on data acquisition
  - Lack of control over some data acquisition
  - Experimental confounds/competing studies
  - …just to name a few

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Sample Size Issues

- Justifying new research with small-*n*
- Magnified pragmatic concerns (ex. missing data, attrition, protocol constraints)
- Analytic diagnostics testing prior to hypothesis tests
- Limited statistical options for hypothesis tests

- …How can we get more from small-*n* studies?

Mainstream Scientific Approach

- Collect data from a well-designed study
- Test hypotheses about the population of interest
  - Typically focused on the *average* effect for outcomes that are continuously scaled, or a difference in probabilities if the outcome is categorical.
- Results sections of manuscripts emphasize differences between groups and averages.

“Average” Men and Women

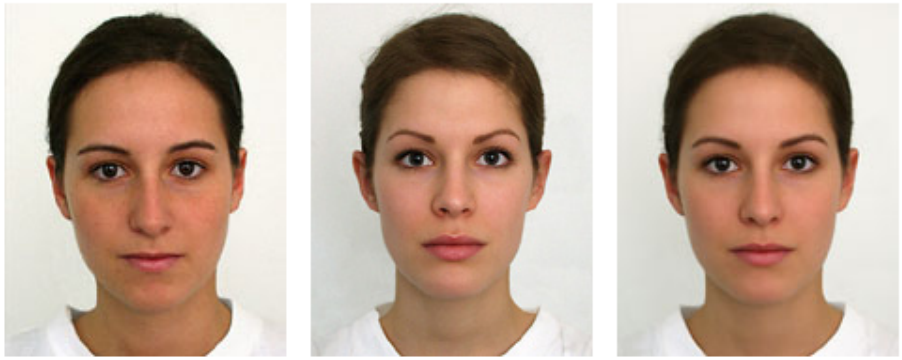
Average female (left) and male (right) composite faces, made from 64 individual female and male images each.

“The attractiveness ratings of the transformed faces depend on the number of original faces that have been used to create them. The more original images were used to create the composite, the more attractive it was rated. (r = 0.57 ** for female faces, r = 0.64 ** for male faces)… Average faces are attractive…”

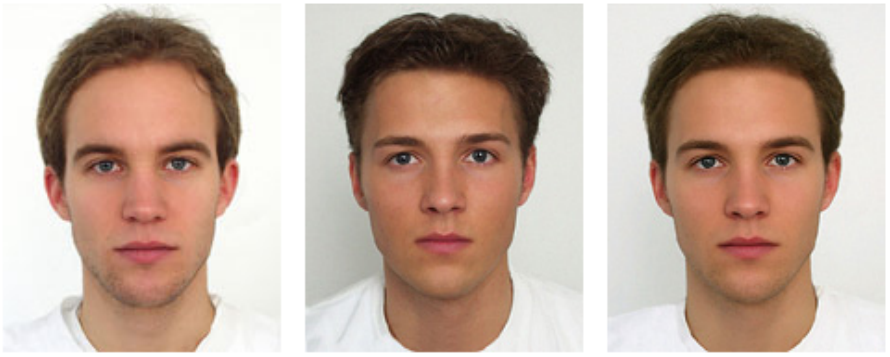
http://tinyurl.com/xr7j

Reality

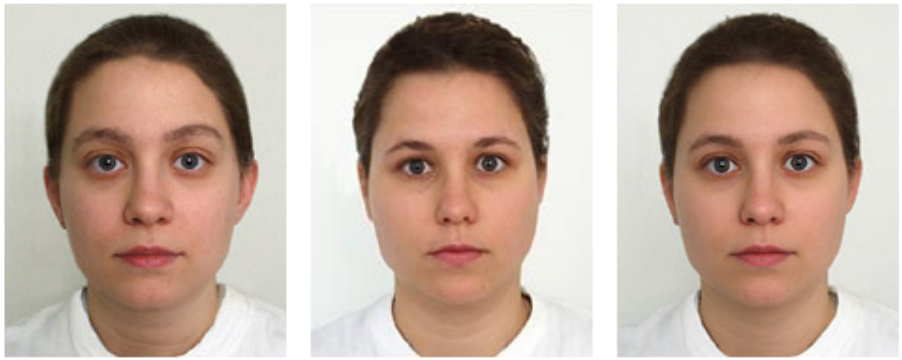
Attractive female faces:



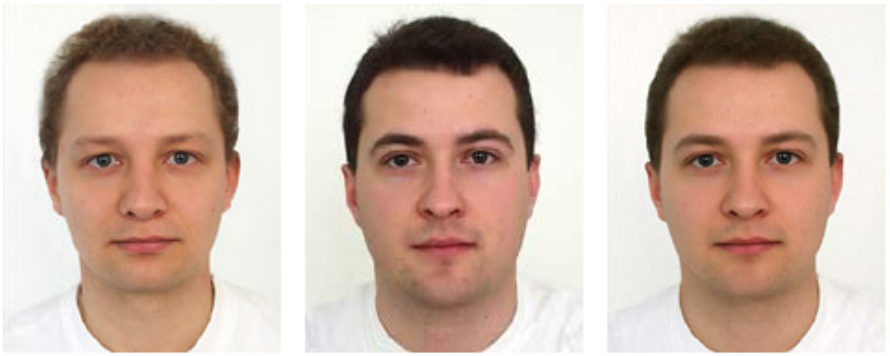
Attractive male faces:



Unattractive female faces:



Unattractive male faces:



The Individual vs. the Average

- Doc treat patients… not averages
- NASA sends astronauts… not composites of available candidates
- When you make personal decisions, you probably consider the consequences to YOURSELF… not the average Joe or Jane Doe.

- How can scientists who emphasize groups and averages move towards individualized knowledge?

How Can Science Become more Clinical/Individualized?

- Continue to apply our current methods
  - *This talk is, by no means, an argument against the scientific method!*
- Augment our current methods (analytics, reports) in ways that help the reader understand the potential consequences to a hypothetical future *individuals*…

Using Data-Driven Simulations to Augment Traditional Analyses

- Perform your usual cadre of statistical tests of hypotheses for manuscripts, etc.
- Consider augmenting your sample data with other *relevant* data if available
- ♥ Consult your discipline knowledge & literatures to improve your theory & assumptions
- Consider the most likely distribution of your outcome variable(s) (ex. Gaussian)
- Calculate summary statistics (ex. mean, sd) from your sample

Simulations (cont.)

- Simulate future samples given the summary statists from your data, and the assumptions that you made about the outcome
  - Ex. Draw a sample from a normal distribution with mean = μ and standard deviation = σ
- Repeat the simulation several hundred times
- Graph the simulated data, along with any relevant clinical, operational, or scientifically meaningful reference values
- Calculate the probability of a future individual falling above/below the relevant reference values

Example: Hip BMD

Shapiro-Wilk W test for normal data

Variable	Obs	W	V	z	Prob>z
TotalHip_B~1	51	0.99122	0.419	-1.855	0.96822

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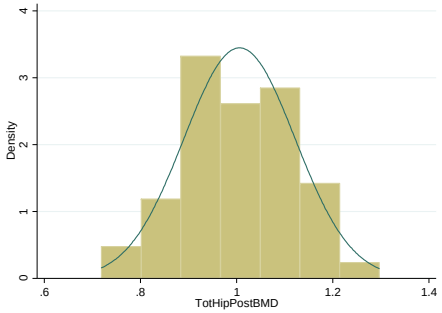
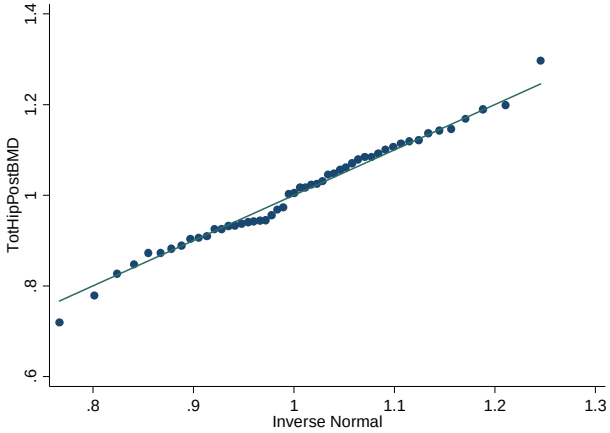
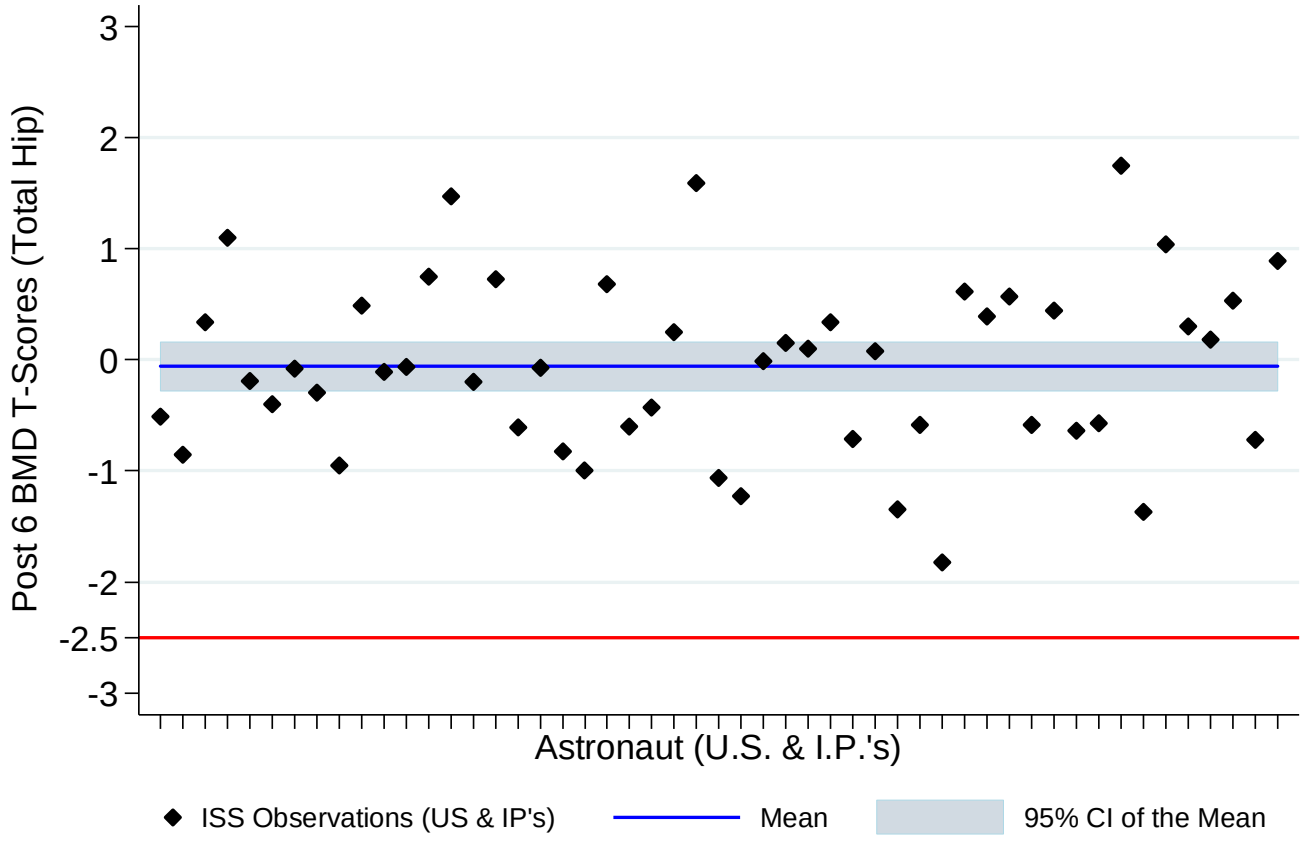




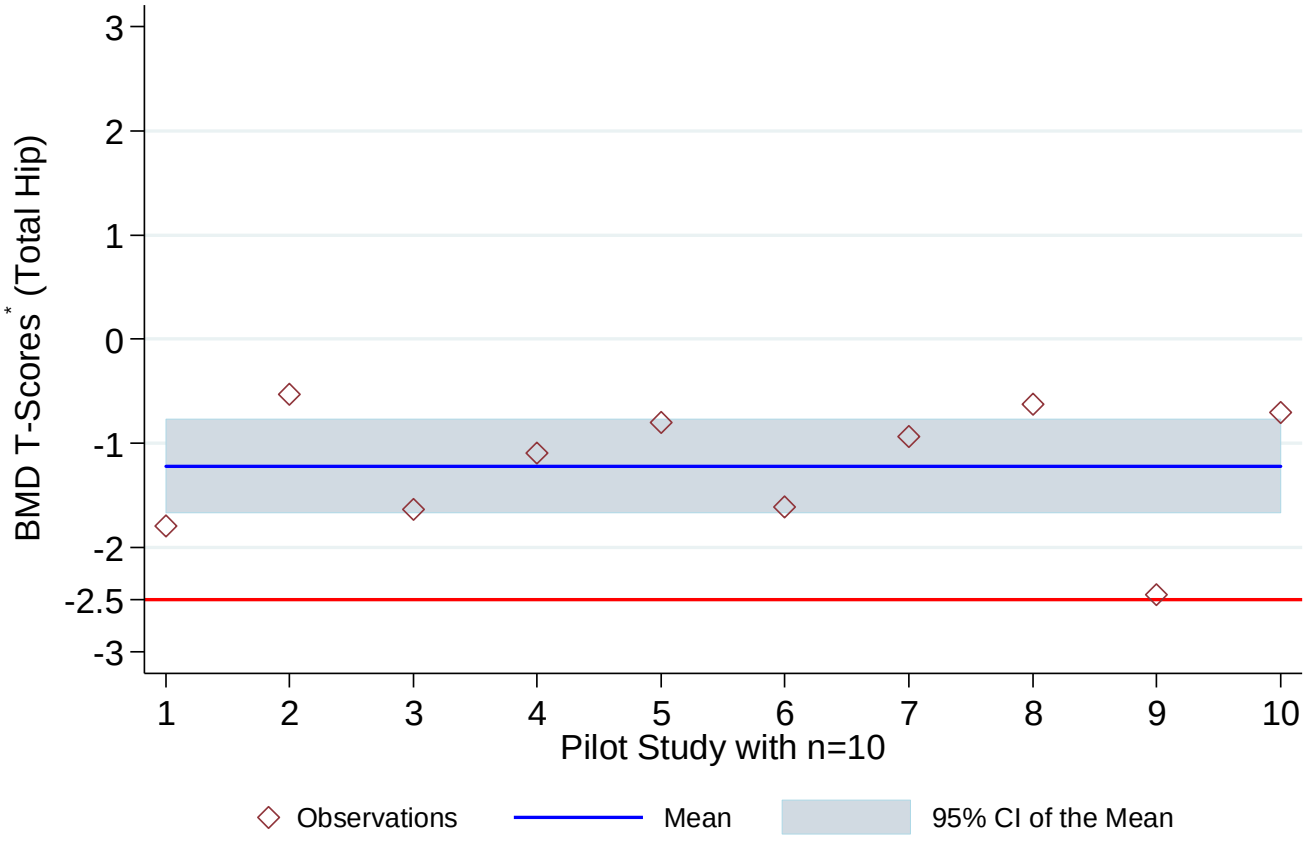
This is just a placeholder slide… will discuss why I chose this example…
T-scores are normally distributed, widely accepted bone measures, and NASA has
A standard for them.

Real Data



Historical data from n=51 US & IP Long Duration Astronauts
μ=-0.60, σ=.79

Hypothetical Pilot Study Under a New Situation

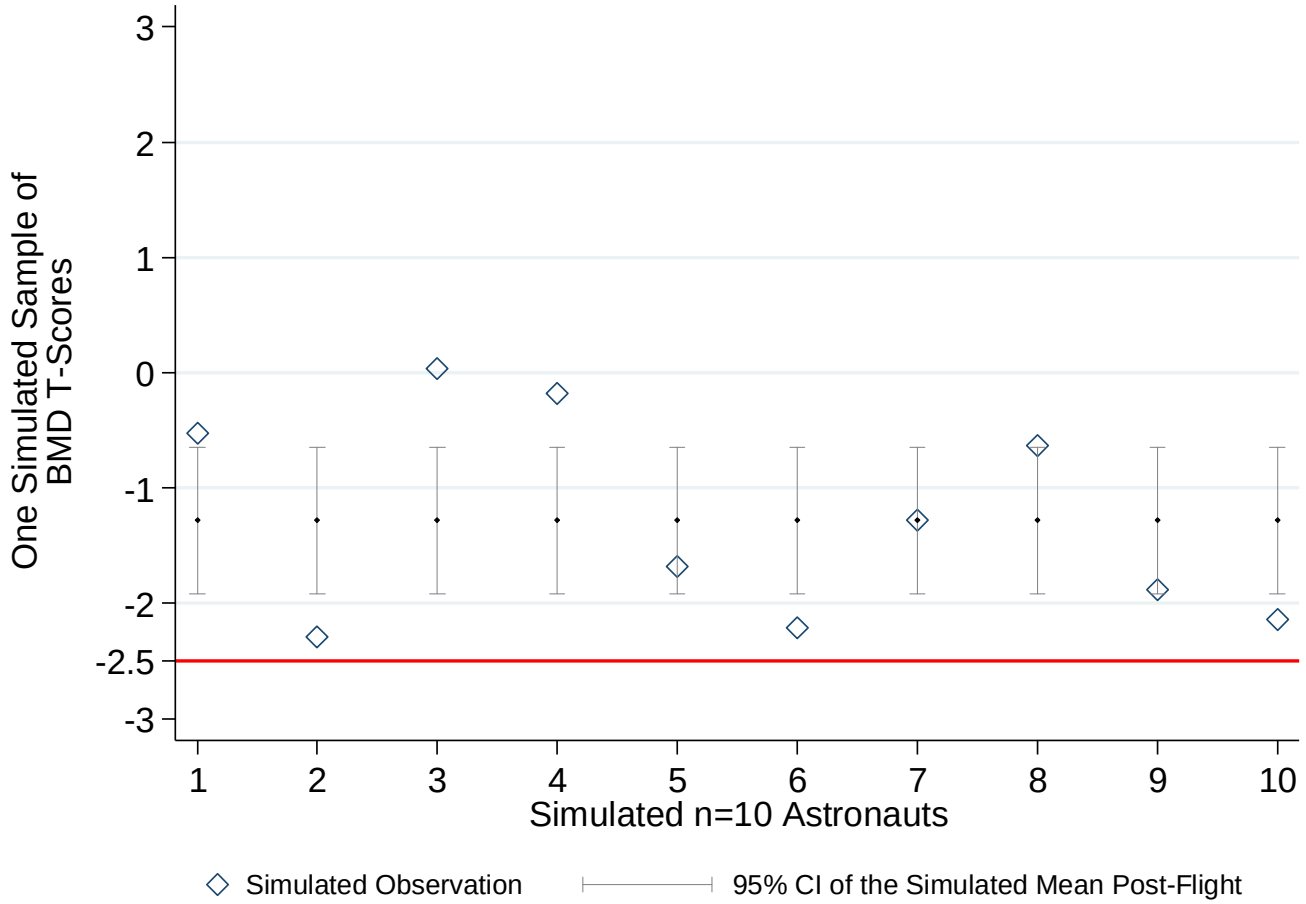


*Hypothetical pilot data showing a reduction in the mean relative to historical data
μ=-.73, σ=1.57

Run Monte Carlo Simulations

- Let's stay consistent with the assumption that t-scores are normally distributed
- Let's assume that the population has variability similar to our larger historical data from n=51 subjects.
- Let's assume that the mean for this new situation is lower by about 20% of the range of historical 6mo data.
  - Informed by our pilot data *and* the literature

One Simulated Dataset



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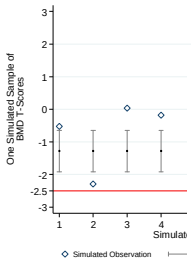
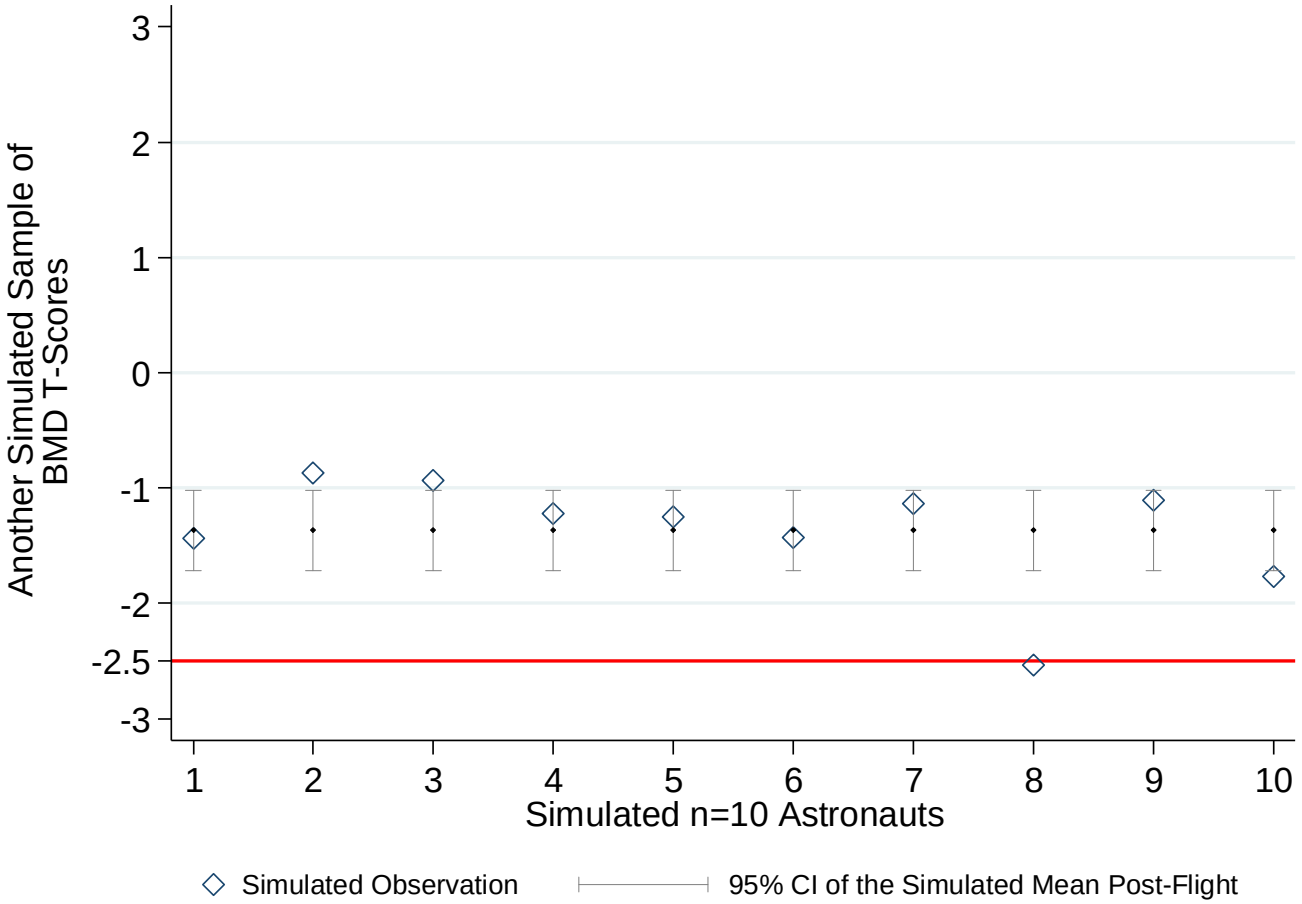
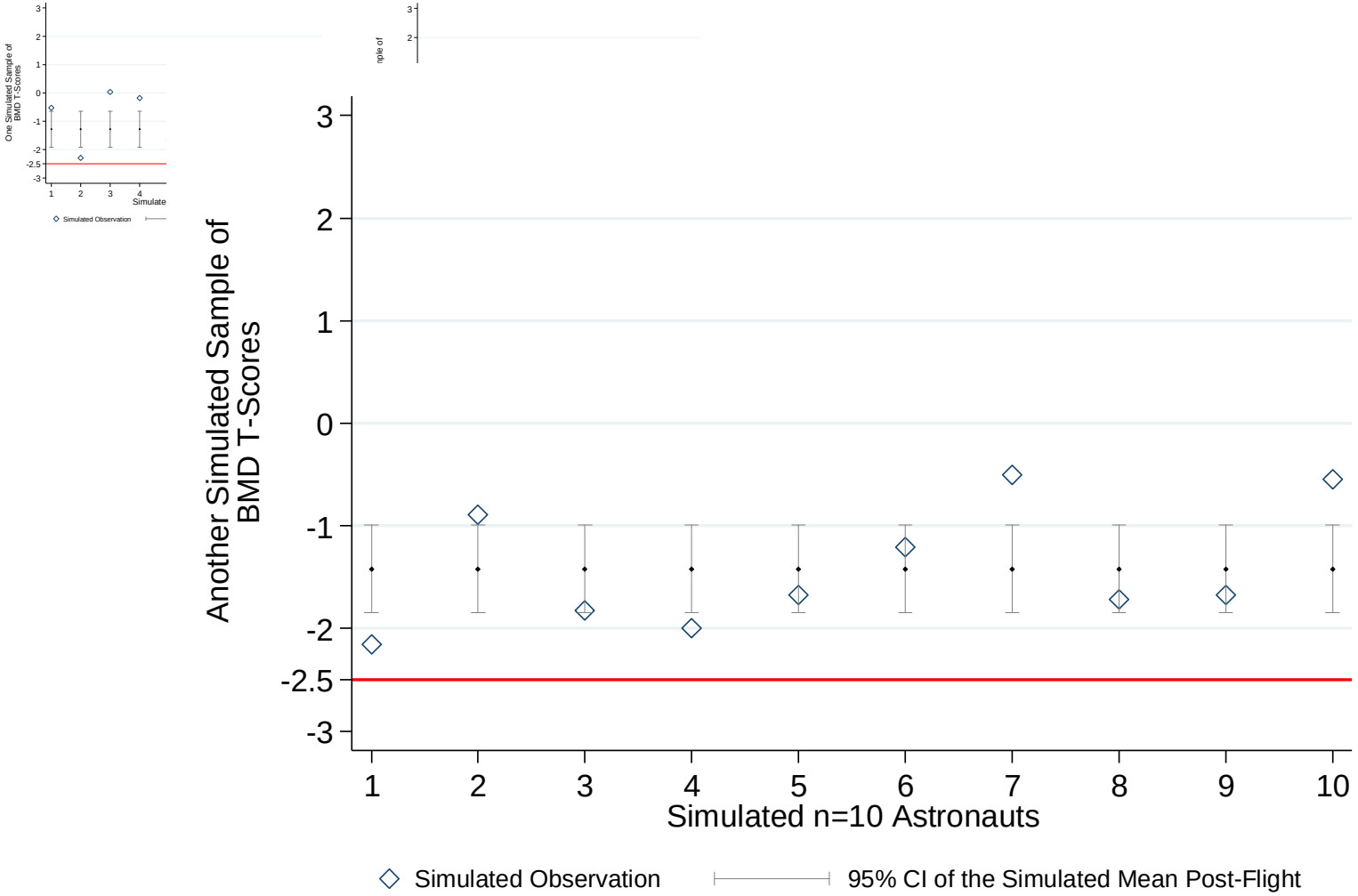
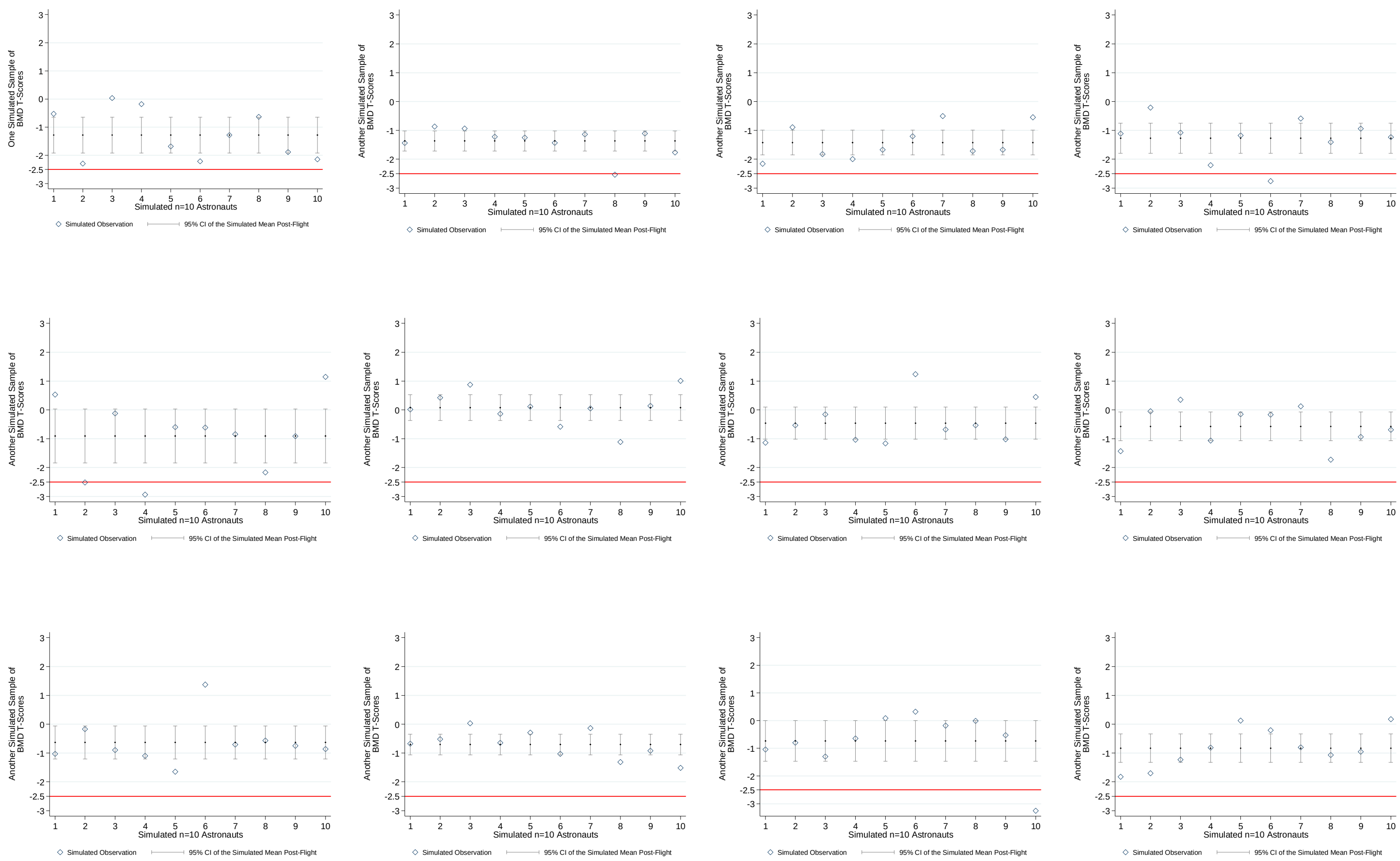




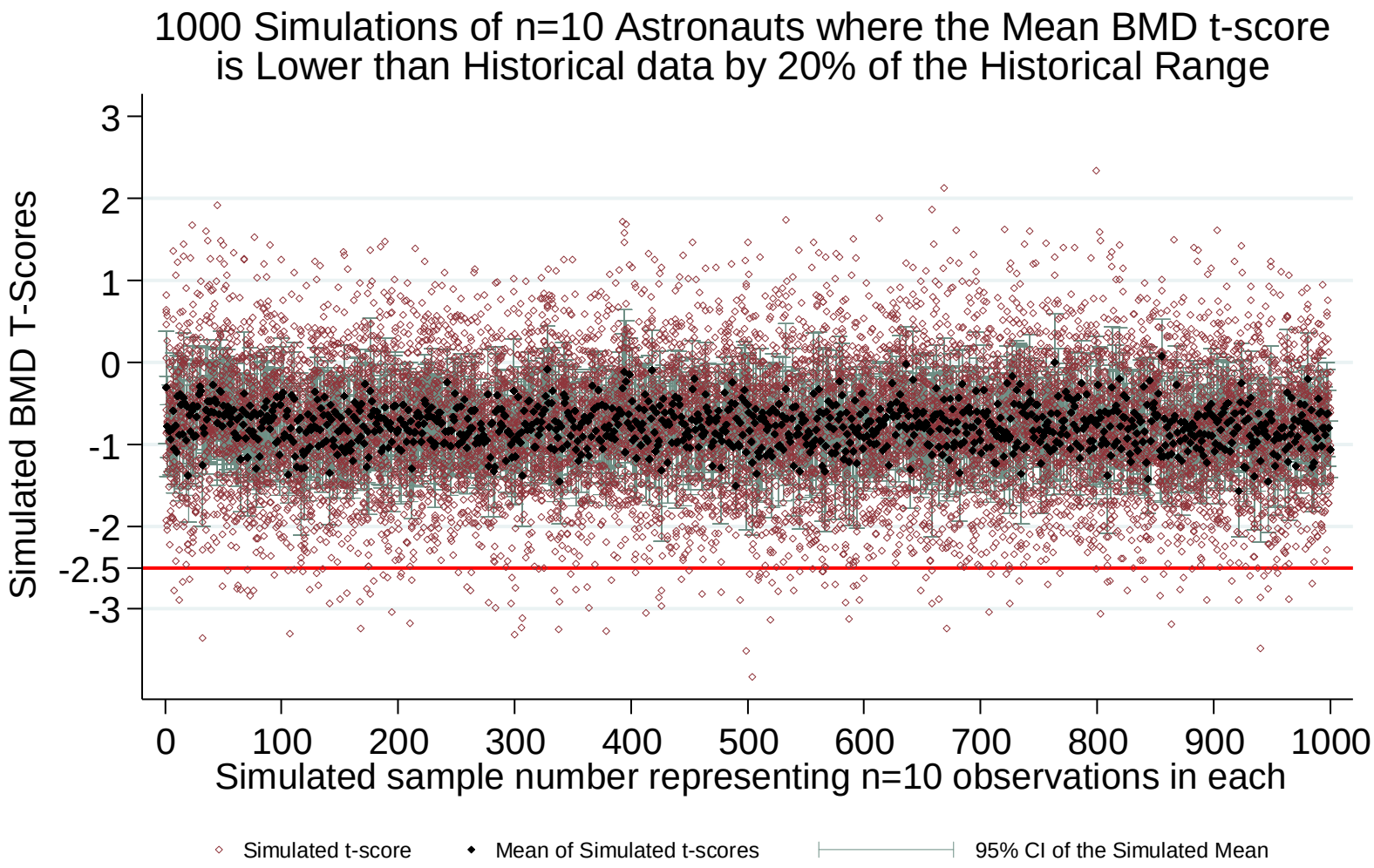
Another Simulated Dataset…



Several Simulated Datasets…



After 1000 Samples



Each column of hollow diamonds along the X-axis represents a simulated sample of n=10.
The probability for any single astronaut to fall under the cut-off = 0.014.

What have we gained?

- A visual representation of the individual risk of falling bellow a pre-established, clinically relevant threshold.
  - P(fail) = 0.014
- A reminder that our single-sample pilot data is just that—a random sample from the larger population.
- An extension of our data, informed also by historical data and the literature, enabling a discussion of next steps.

What did it cost?

- Zero cost for additional subjects
- Zero up mass for spaceflight
- Zero competition with other studies
- …Zero new data!

- Time & expertise for reflection following pilot study to contemplate simulation parameters
- Time & expertise for conducting the Monte Carlo simulations.
  - Minimal software requirements… potentially free

Limitations of MC Simulations

- They are never as good as real data & cannot stand alone
  - Useful as an augmentation tool
- Simulation parameters and assumptions can be tenuous & vulnerable to competing theories
- When pilot studies are small, their contributions to the MC Simulations can be questionable
  - Thus my recommendation to use the literature to help guide model assumptions & parameters

Next..

- Dr. Feiveson is going to take this idea one step further, and discuss the Bayesian approach to statistical analysis.
  - Can Bayes help with small-*n?*