

AN INTERACTIVE SHINY APPLICATION FOR USING BIOMARKER CHANGES IN EARLY DECISION-MAKING IN PSORIASIS

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Janssen R&D

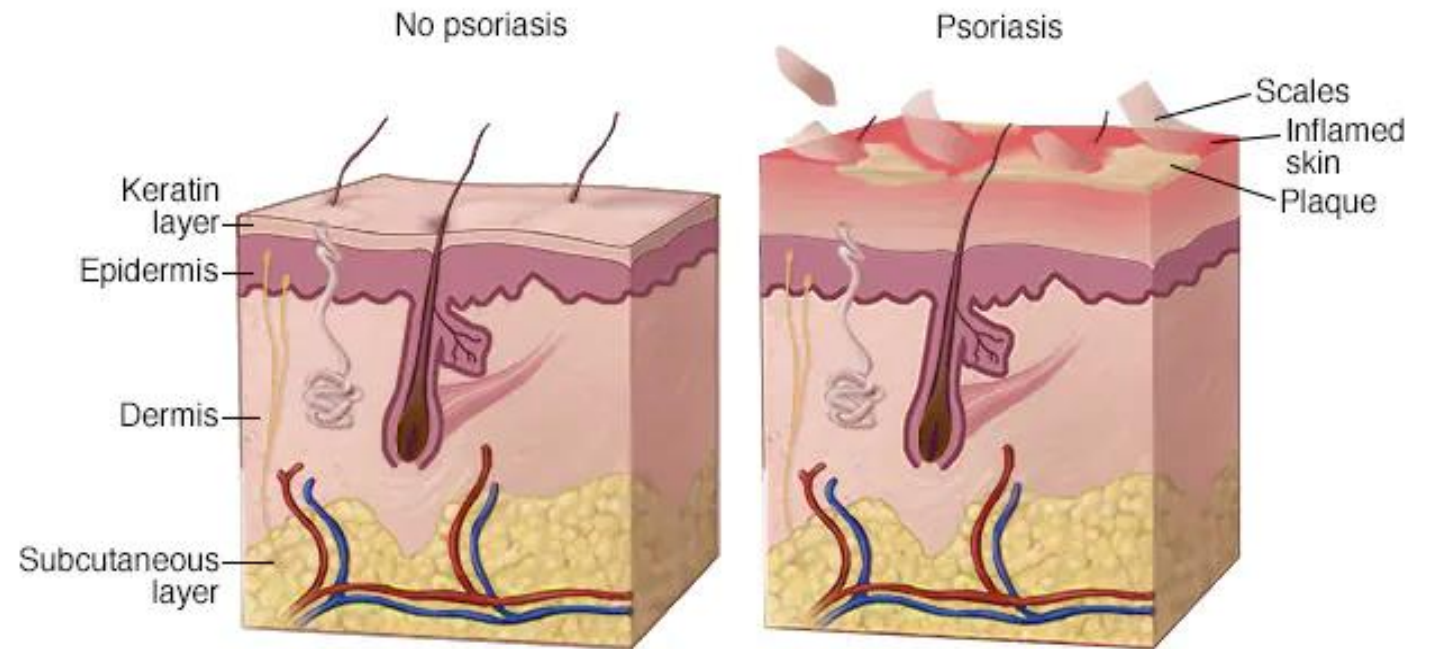
Psoriasis & Biomarkers

Takes up to **12 weeks** to see clinical improvement

Biomarkers like IL-17A, IL-22, Beta-defensin start changing much earlier

Can biomarker change be used at **week 4** to

1. Show the treatment is different from placebo
2. Assess the similarity of the treatment of interest to existing compounds



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Data?

Biomarker	Placebo	Compounds
MADPsoUp	2	6
KC IL-17A Up	1	3
IL-17A	2	4
IL-22	2	4
IL-17F	2	4
Beta-defensin 4B	1	3
KC IL-22 Up	1	3
KC TNF Up	1	3
Mph TNFa Up	1	3
Fibroblasts IL17 Up	1	3
Monocytes IL17 Up	1	3
EB13	1	3
IL-23R	1	2
S100A7A	1	2
CEACAM5	1	2
C15orf48	1	2
FZF5	1	2
S100P	1	2
ETHE1	1	2
PHLDA2	1	2
FERMT1	1	2
WARS	1	2
FGFBP1	1	2
KLK6	1	2

□ Skin Biopsy

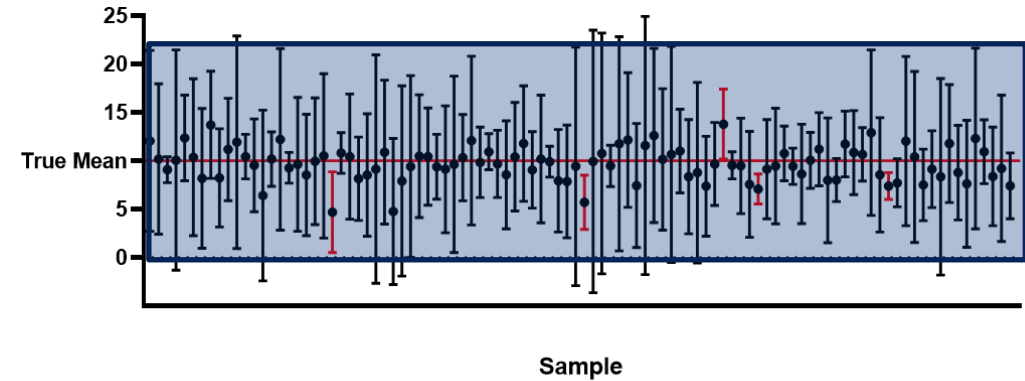
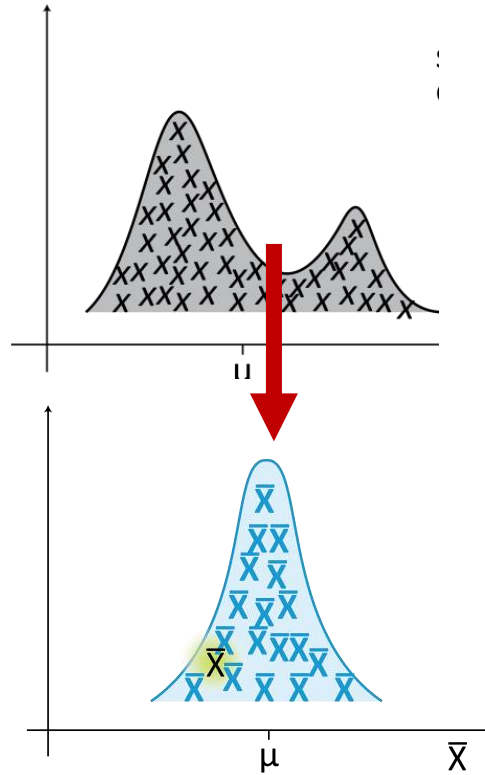
- Very small sample sizes (~10)
- 24 biomarkers
 - most internal
 - Placebo limited to 1-2 studies

Biomarker	Placebo	Compounds
Beta-Defensin 2	2	3
IL-17A	2	3
IL-17F	2	3
IL-22	2	3
IL-23	1	2
IL-8	1	2
MDC	1	2
MIP1b	1	2

• Serum Biomarkers

- Large sample sizes (~40)
- 8 biomarkers, internal data only (until recently)

The process



Population distribution created by combining samples with mixed normal distribution

Sample distributions constructed from populations

Tolerance intervals

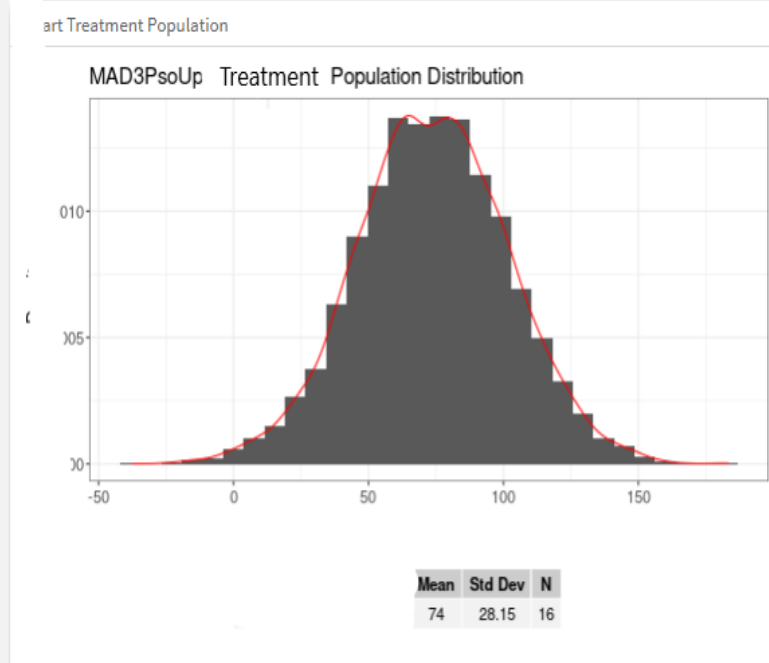
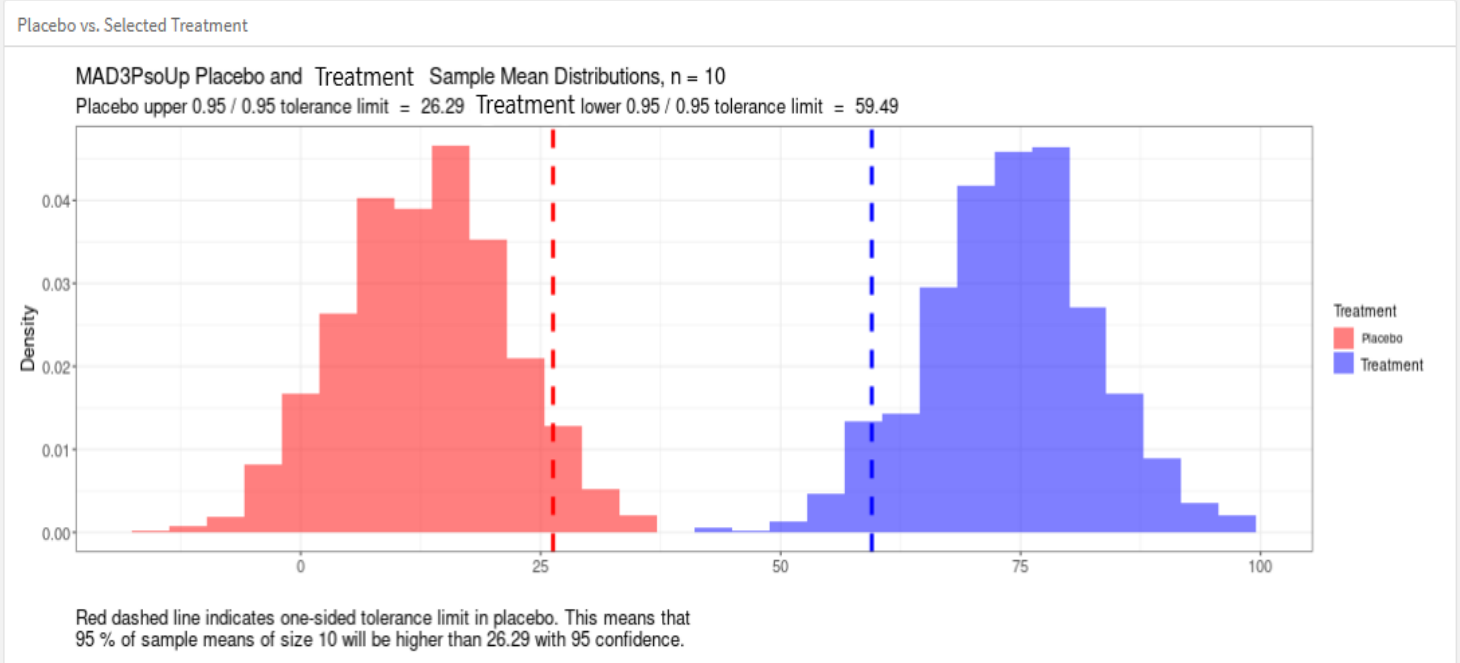
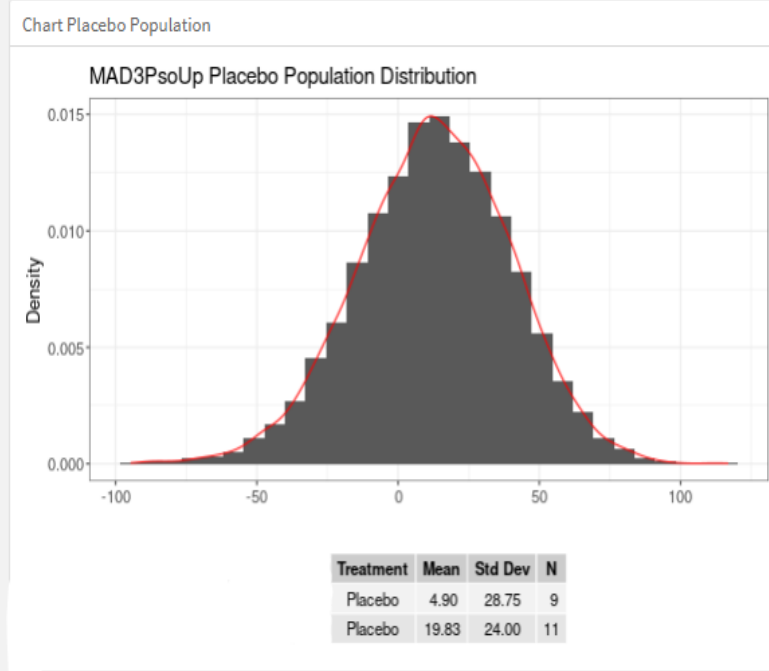
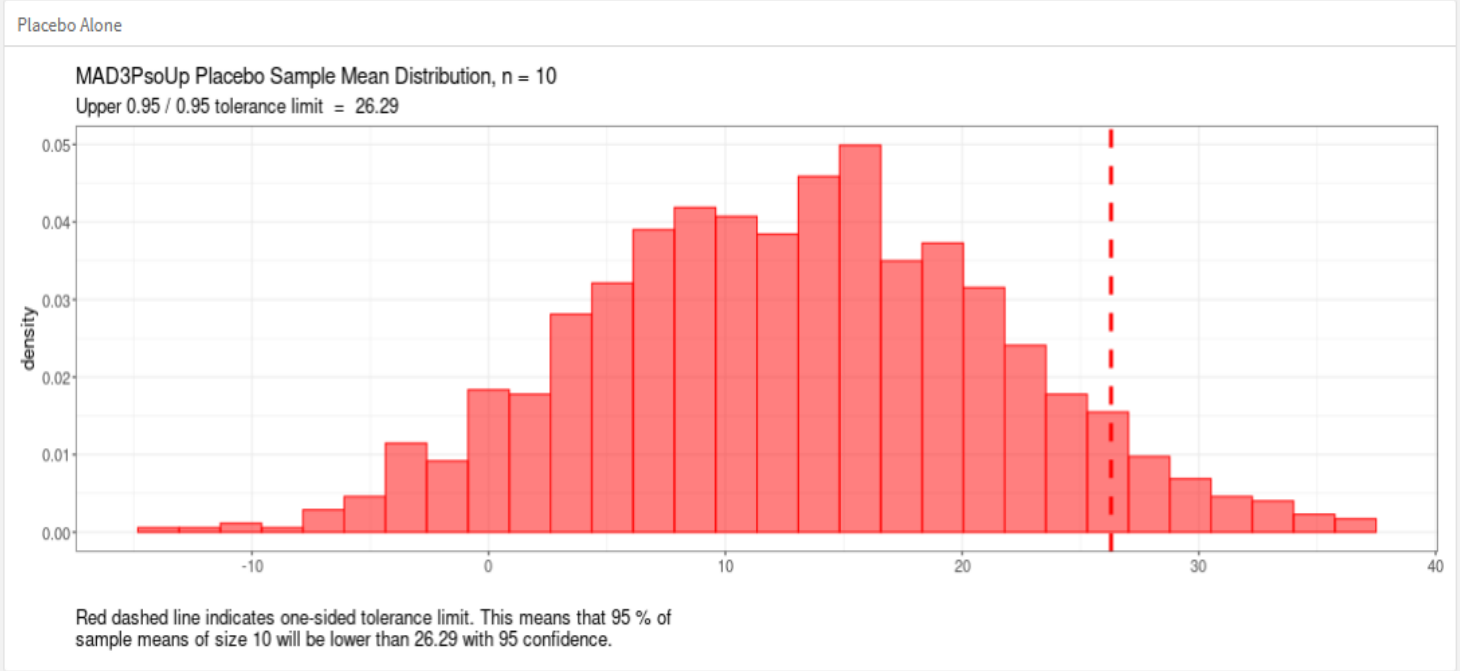
Biomarker:
 MAD3PsoUp

Treatment:
 [Dropdown]

Sample Size:
 [Slider: 1 to 50, set to 10]

Tolerance Interval Confidence:
 [Slider: 0.5 to 1, set to 0.95]

Tolerance Interval Coverage:
 [Slider: 0.5 to 1, set to 0.95]



Skin: Comparisons of Placebo and Treatments

Serum: Comparisons of Placebo and Treatments

Interactive Biomarker Toleran

Biomarker:

MAD3PsoUp

MAD3PsoUp

KC_IL17_Up_

IL22

IL17A

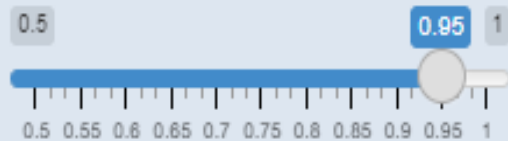
IL17F

DEFB4A

KC_IL22_Up_

KC_TNF_Up_

Tolerance Interval Confidence:



Tolerance Interval Coverage:

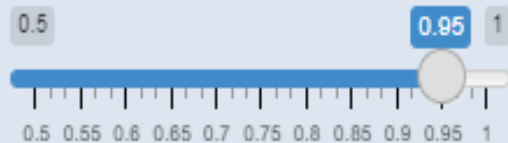
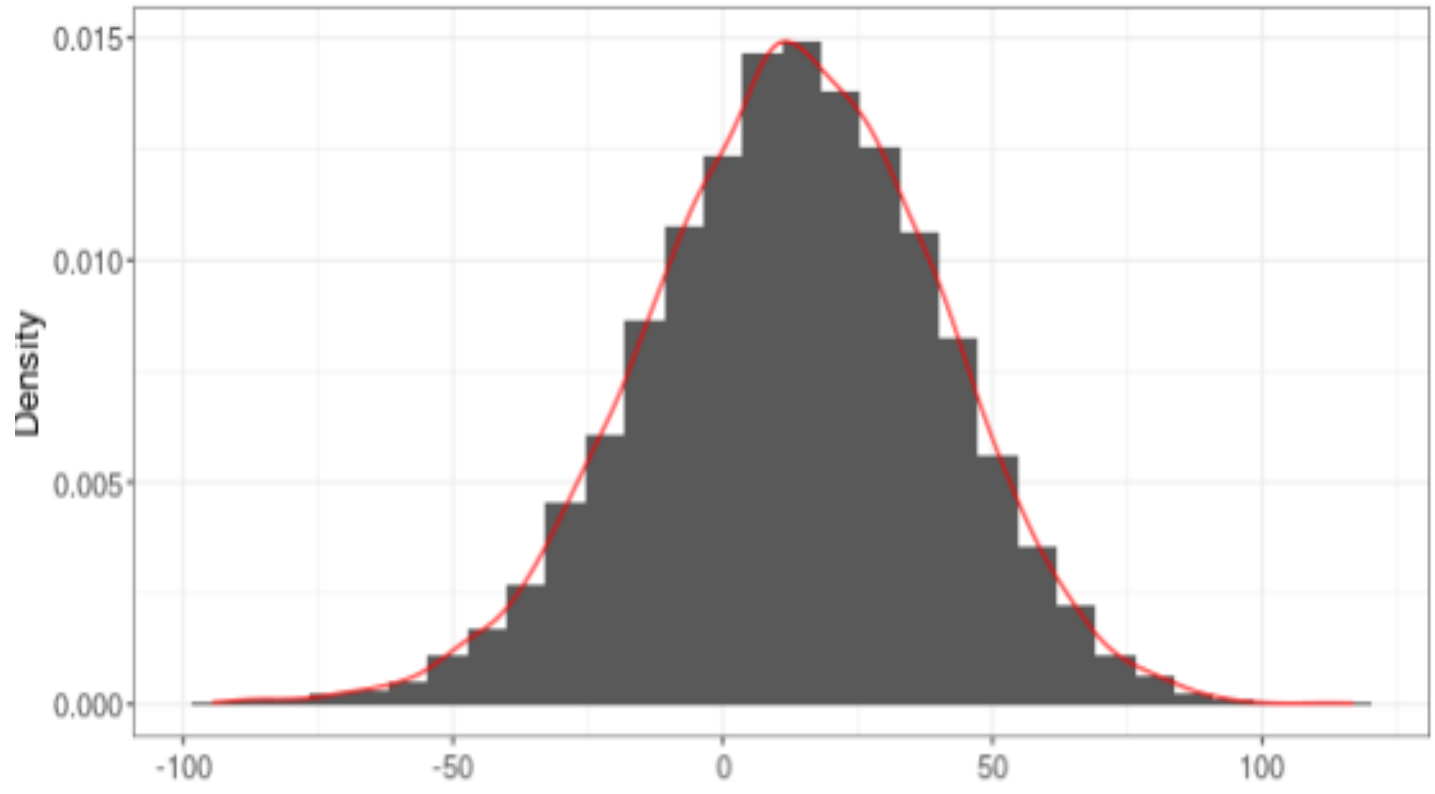


Chart Placebo Population

MAD3PsoUp Placebo Population Distribution

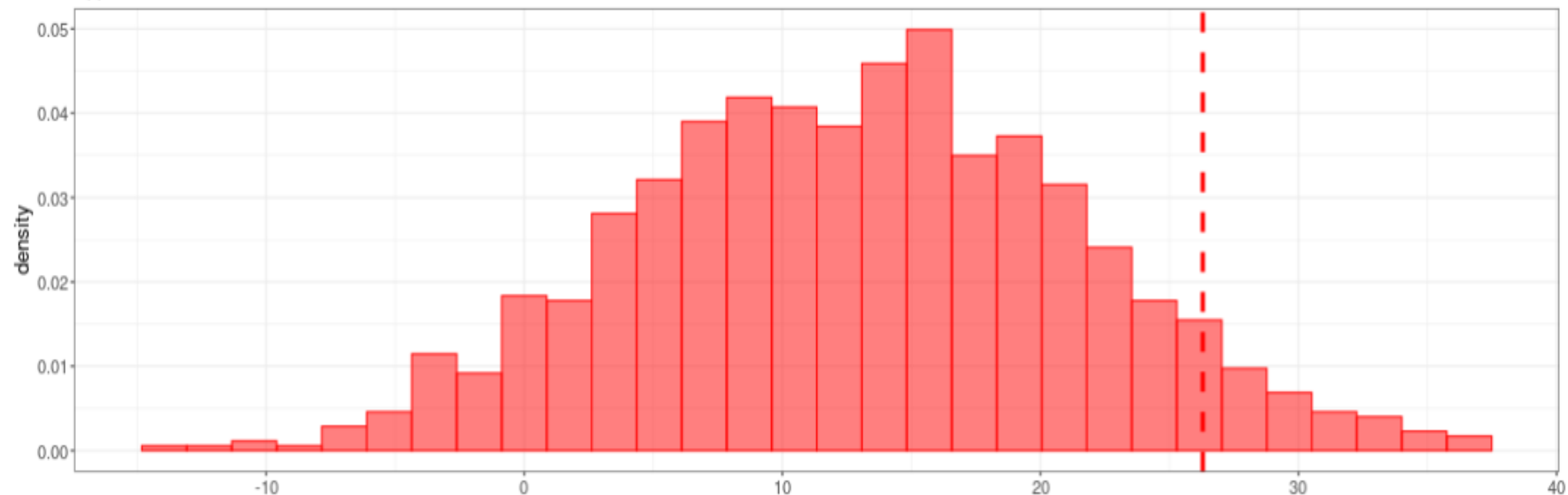


Treatment	Mean	Std Dev	N
Placebo	4.90	28.75	9
Placebo	19.83	24.00	11

Placebo Alone

MAD3PsoUp Placebo Sample Mean Distribution, $n = 10$

Upper 0.95 / 0.95 tolerance limit = 26.29

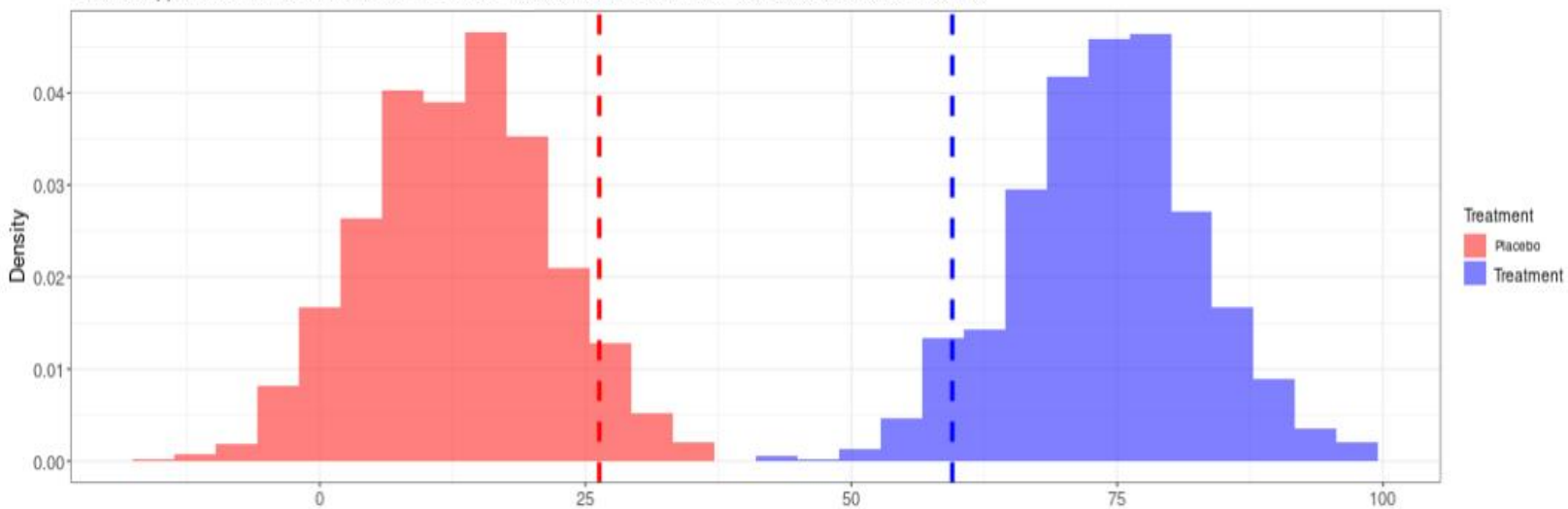


Red dashed line indicates one-sided tolerance limit. This means that 95 % of sample means of size 10 will be lower than 26.29 with 95 confidence.

Placebo vs. Selected Treatment

MAD3PsoUp Placebo and Treatment Sample Mean Distributions, n = 10

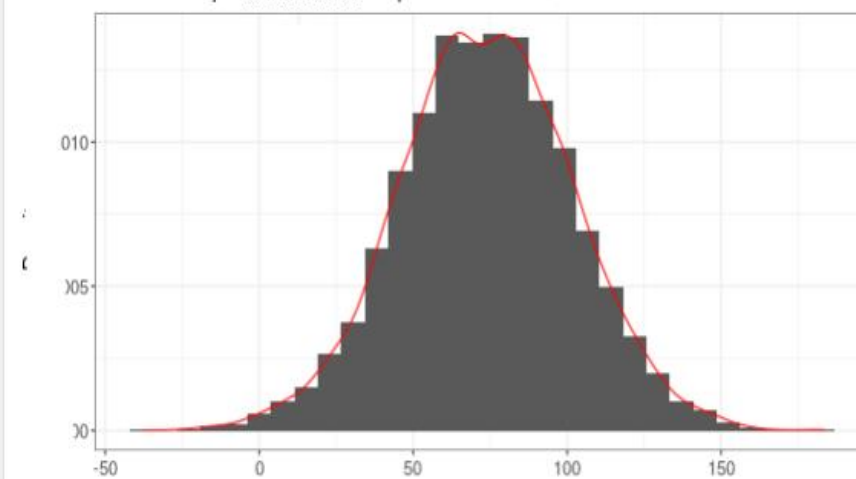
Placebo upper 0.95 / 0.95 tolerance limit = 26.29 Treatment lower 0.95 / 0.95 tolerance limit = 59.49



Red dashed line indicates one-sided tolerance limit in placebo. This means that 95 % of sample means of size 10 will be higher than 26.29 with 95 confidence.

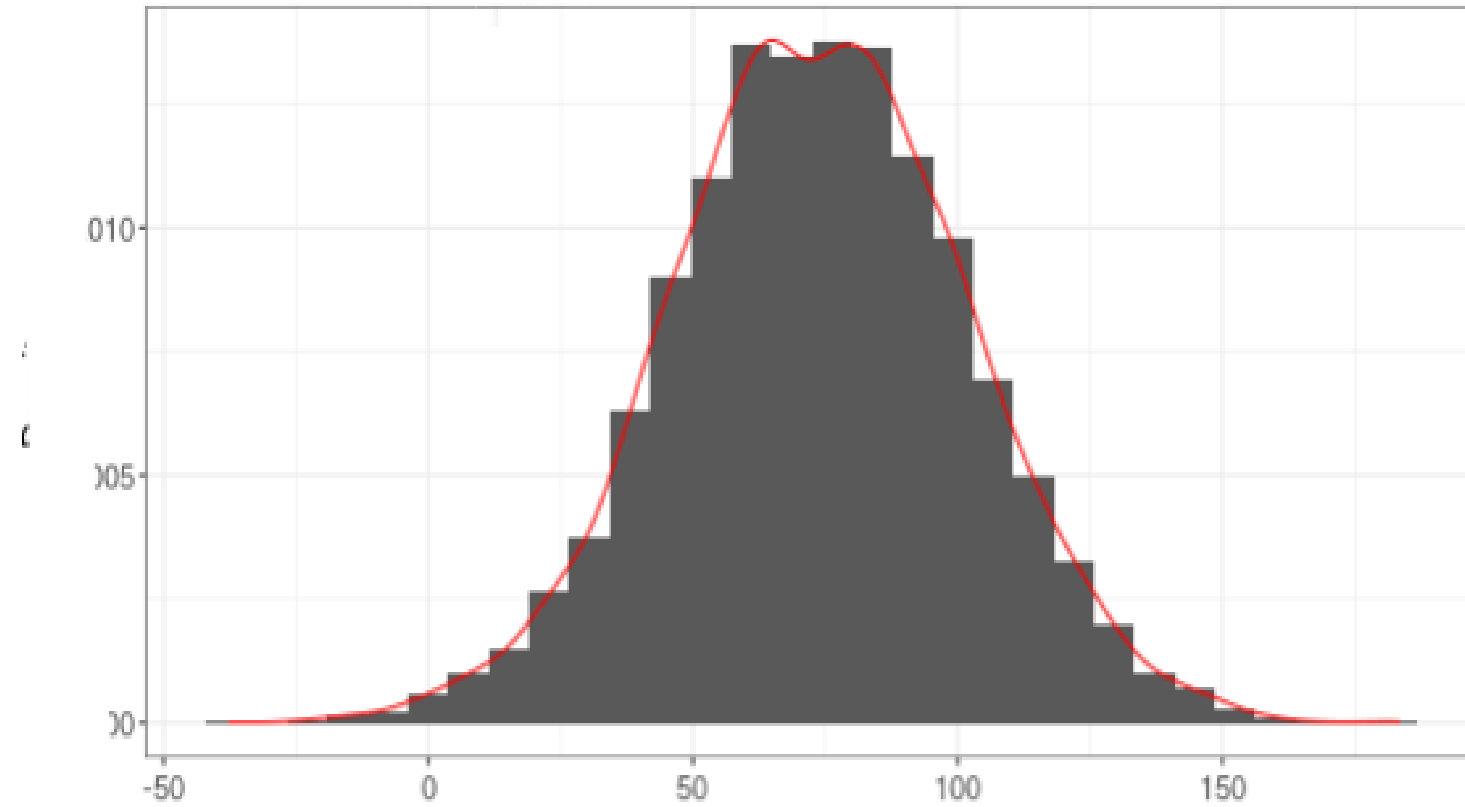
art Treatment Population

MAD3PsoUp Treatment Population Distribution



Mean	Std Dev	N
74	28.15	16

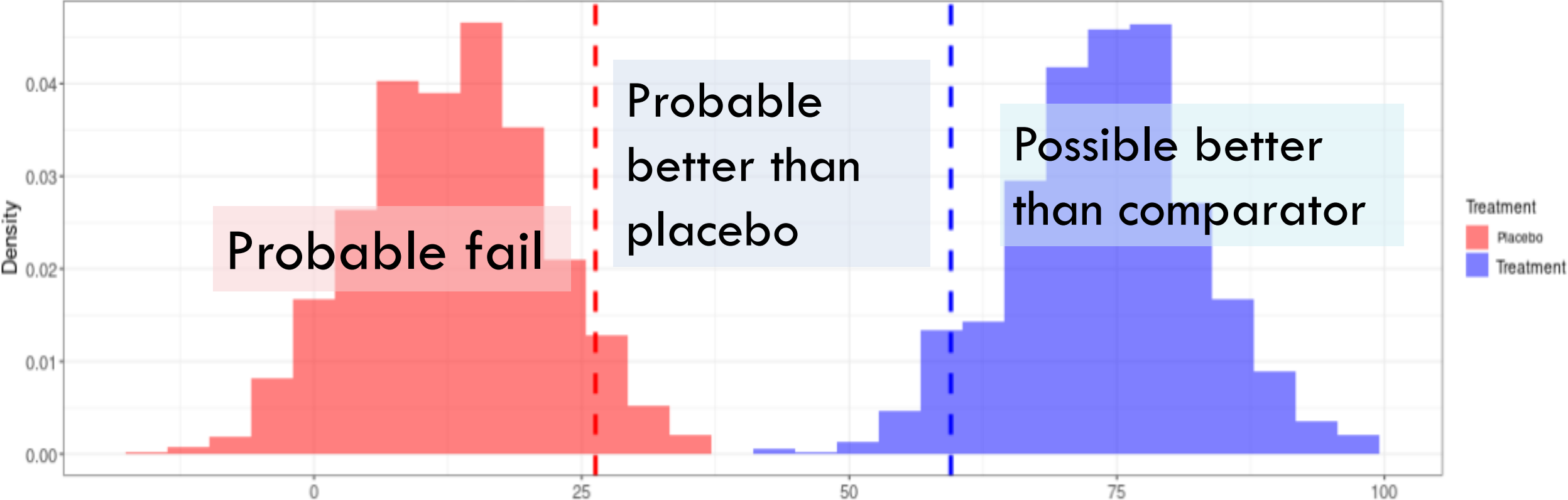
MAD3PsoUp Treatment Population Distribution



Mean	Std Dev	N
74	28.15	16

Placebo vs. Selected Treatment

MAD3PsoUp Placebo and Treatment Sample Mean Distributions, n = 10
Placebo upper 0.95 / 0.95 tolerance limit = 26.29 Treatment lower 0.95 / 0.95 tolerance limit = 59.49



Red dashed line indicates one-sided tolerance limit in placebo. This means that 95 % of sample means of size 10 will be higher than 26.29 with 95 confidence.

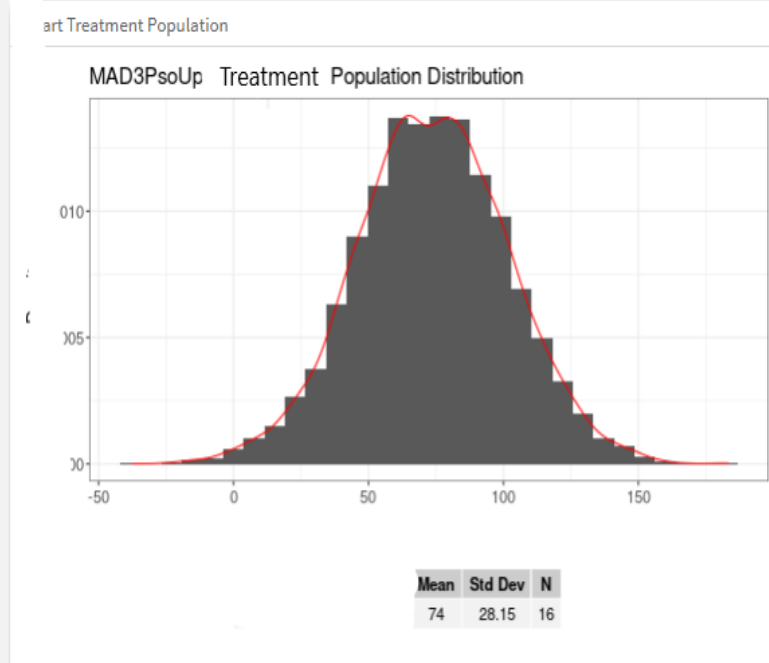
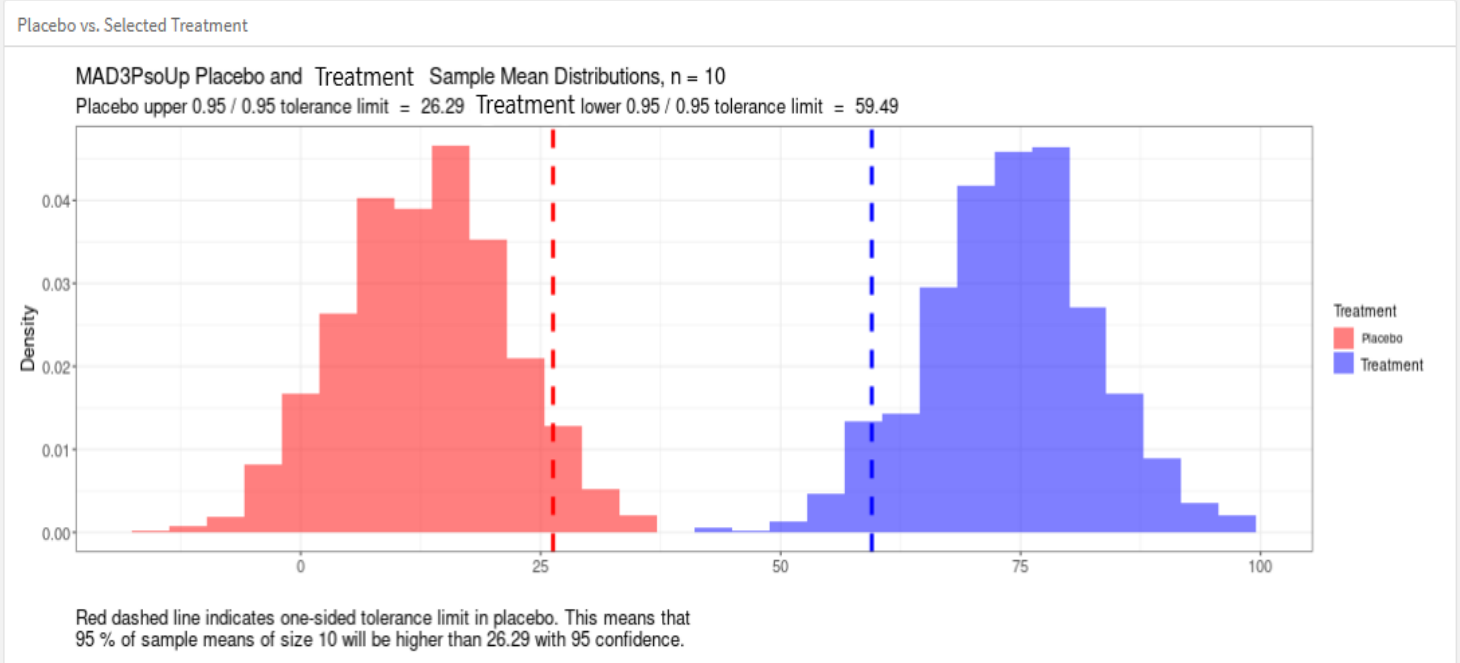
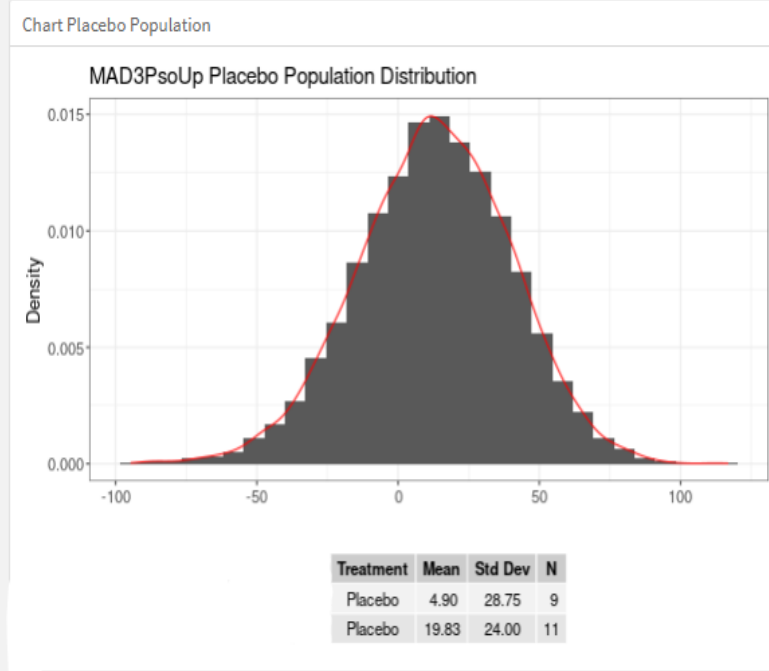
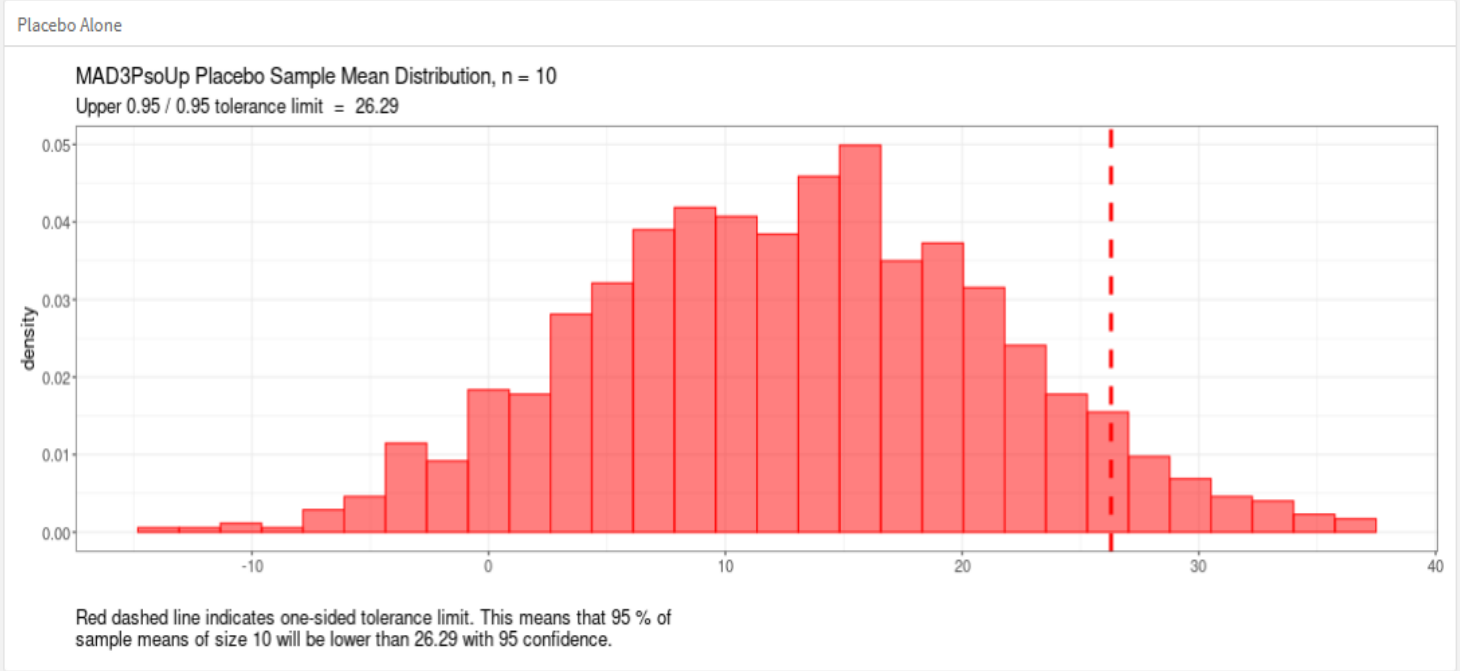
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Treatment:
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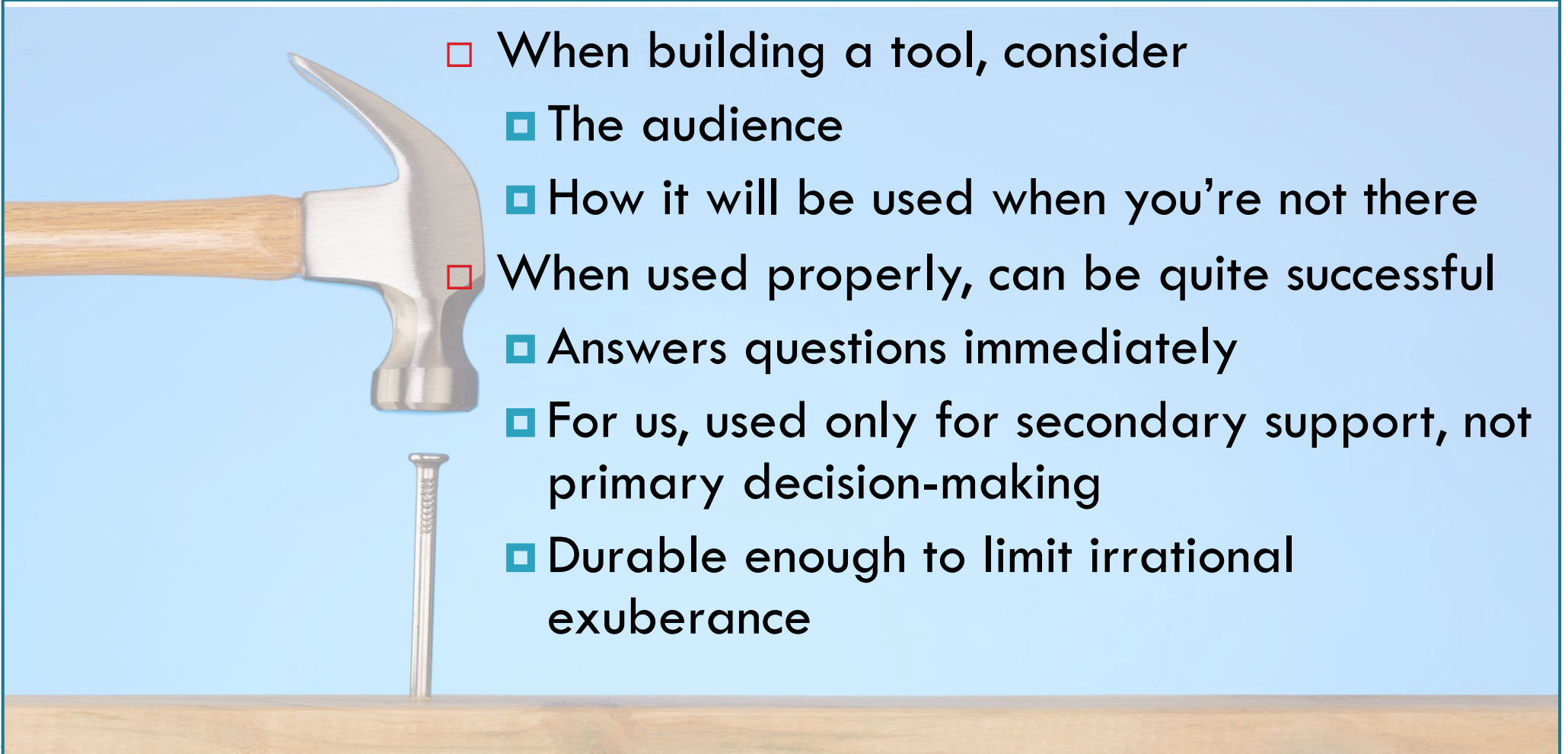
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 [Slider: 0.5 to 1, set to 0.95]

Tolerance Interval Coverage:
 [Slider: 0.5 to 1, set to 0.95]



To Conclude



- When building a tool, consider
 - ▣ The audience
 - ▣ How it will be used when you're not there
- When used properly, can be quite successful
 - ▣ Answers questions immediately
 - ▣ For us, used only for secondary support, not primary decision-making
 - ▣ Durable enough to limit irrational exuberance