

Application of BDA Methodologies in Clinical Trials Focus on Neurology

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Disclosures

- Full time employee and share holder of Signant Health
- Practice Leader for Data Analytics at Signant Health
- Signant Health provides a number of services including data analytics, eligibility reviews and rater oversight
- The views and opinions expressed in this presentation are solely my own and do not necessarily reflect the official policies or positions of Signant Health

Introduction

- In-study -endpoint focused- blinded data analytics have been increasingly adopted in clinical trials in and outside of CNS indications
- The questions are:
 - Whether Blinded Data Analytics are needed?
 - What is the impact of data concerns on trial data?
 - What are the limitations of implementing Blinded Data Analytics?

Agenda

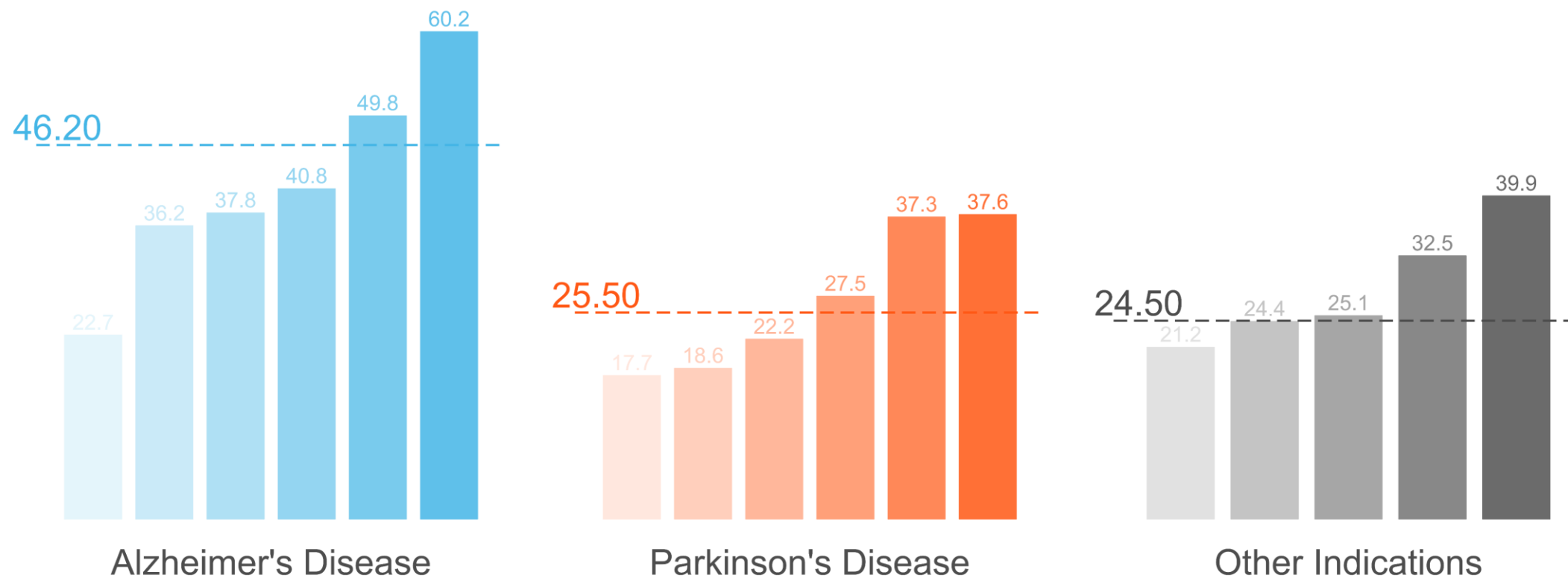
Data concerns in neurological clinical trials

Impact of data concerns

Case examples

Conclusions

Clinically Meaningful Data Concerns



Most Frequent Data Concerns

AD data concerns

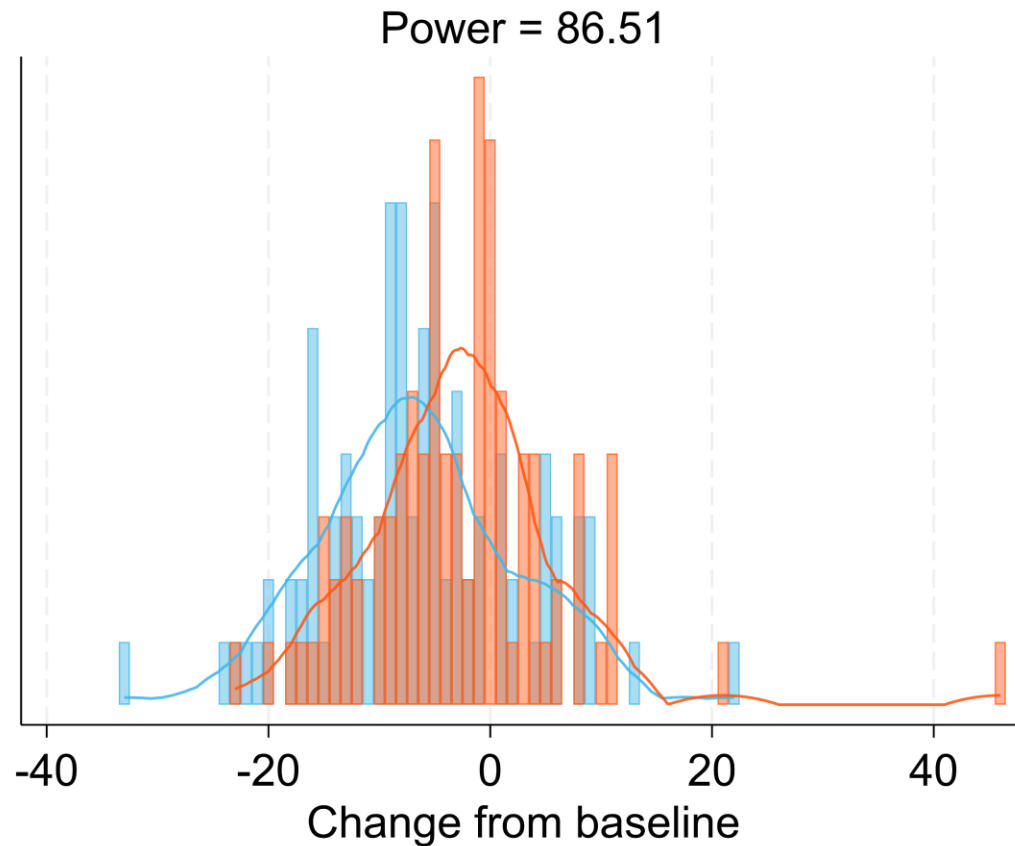
- Inclusionary concerns
- Scoring errors
- Admin errors
- Assessment duration
- Excessive variability

PD data concerns

- Between scale discordance
- Excessive variability
- Assessment duration
- Inclusionary concerns
- Low variability

Impact of Data Concerns

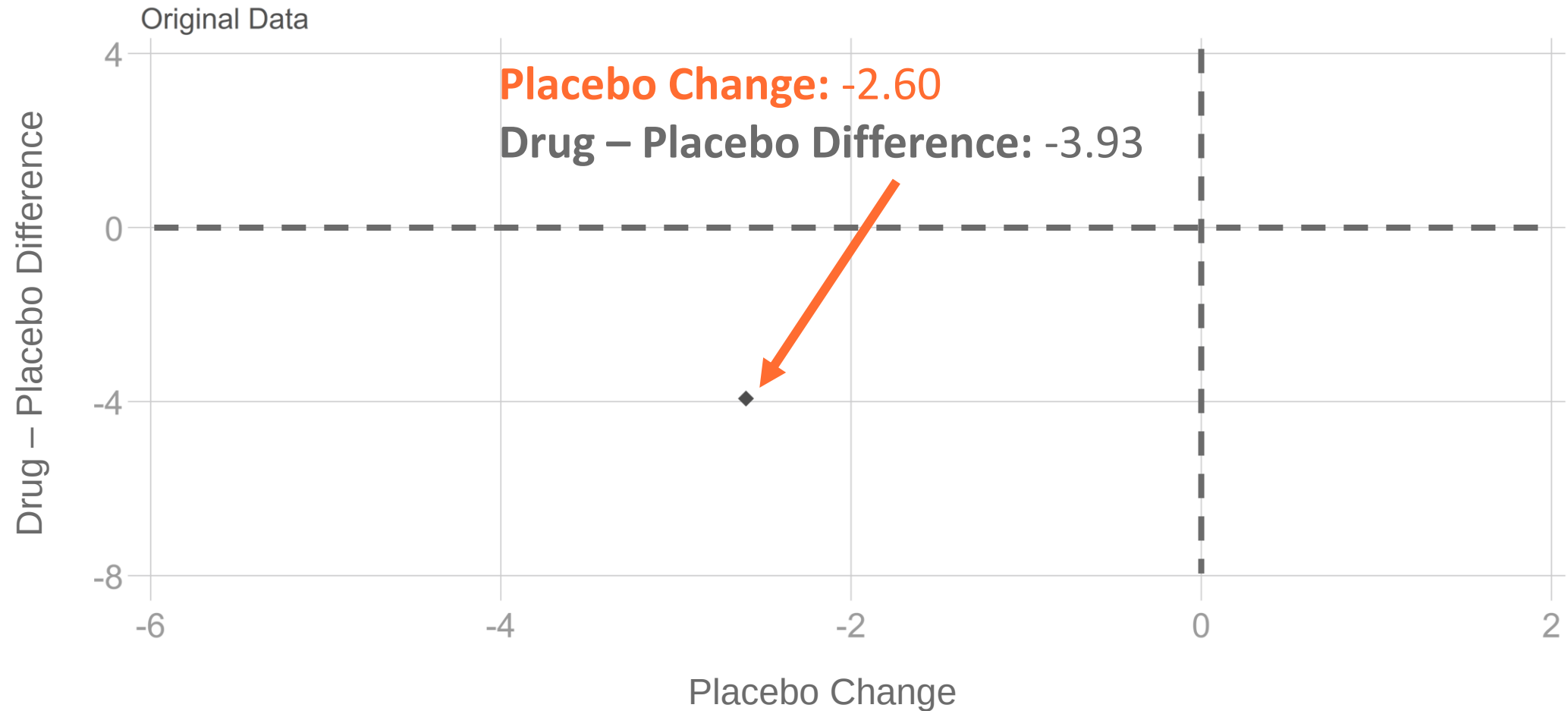
Simulation – Original Data



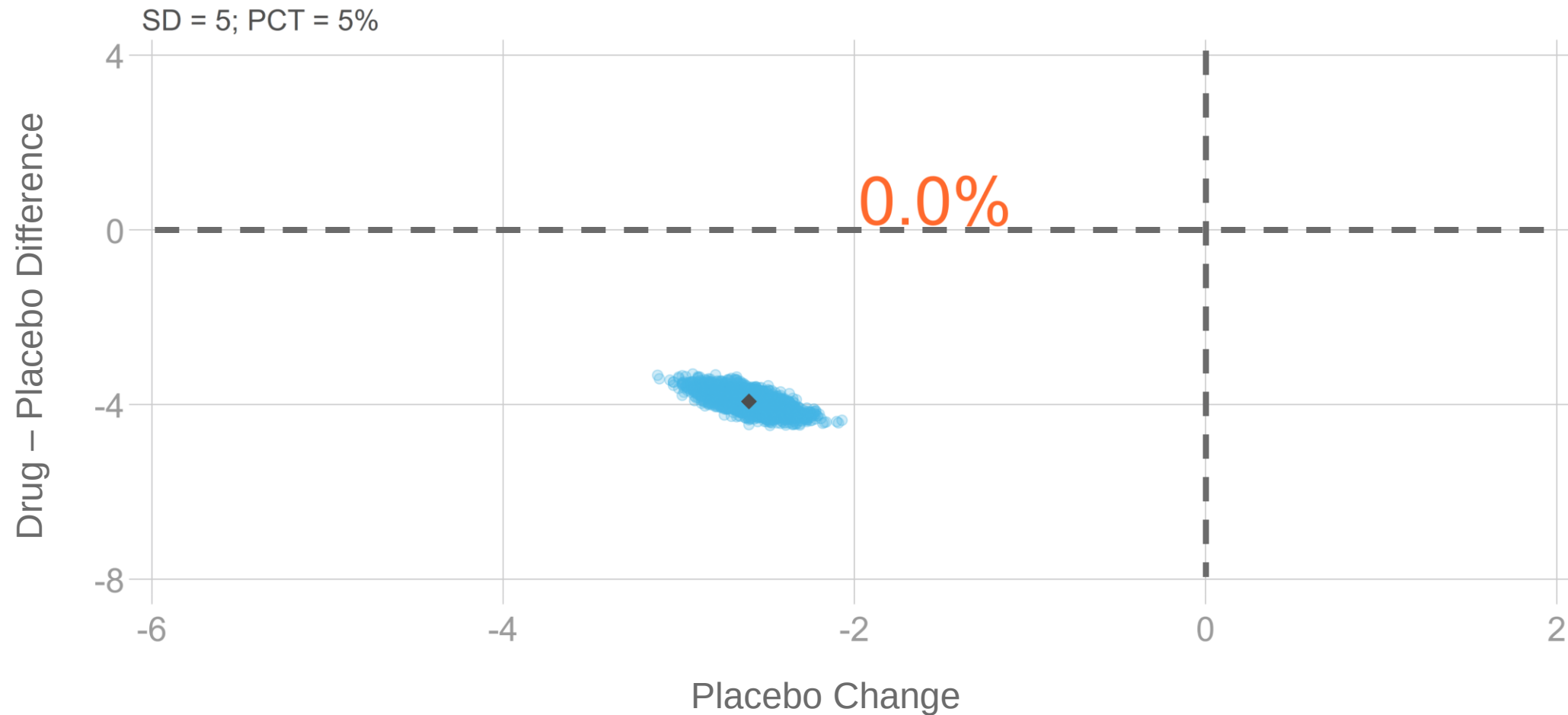
- 10000 clinical trials simulated
- 1:1 randomization
- 100 subjects per arm

	Mean change (SD)
Placebo	-2.60 (9.06)
Treatment	-6.53 (9.00)
Difference	-3.93; p = .0023

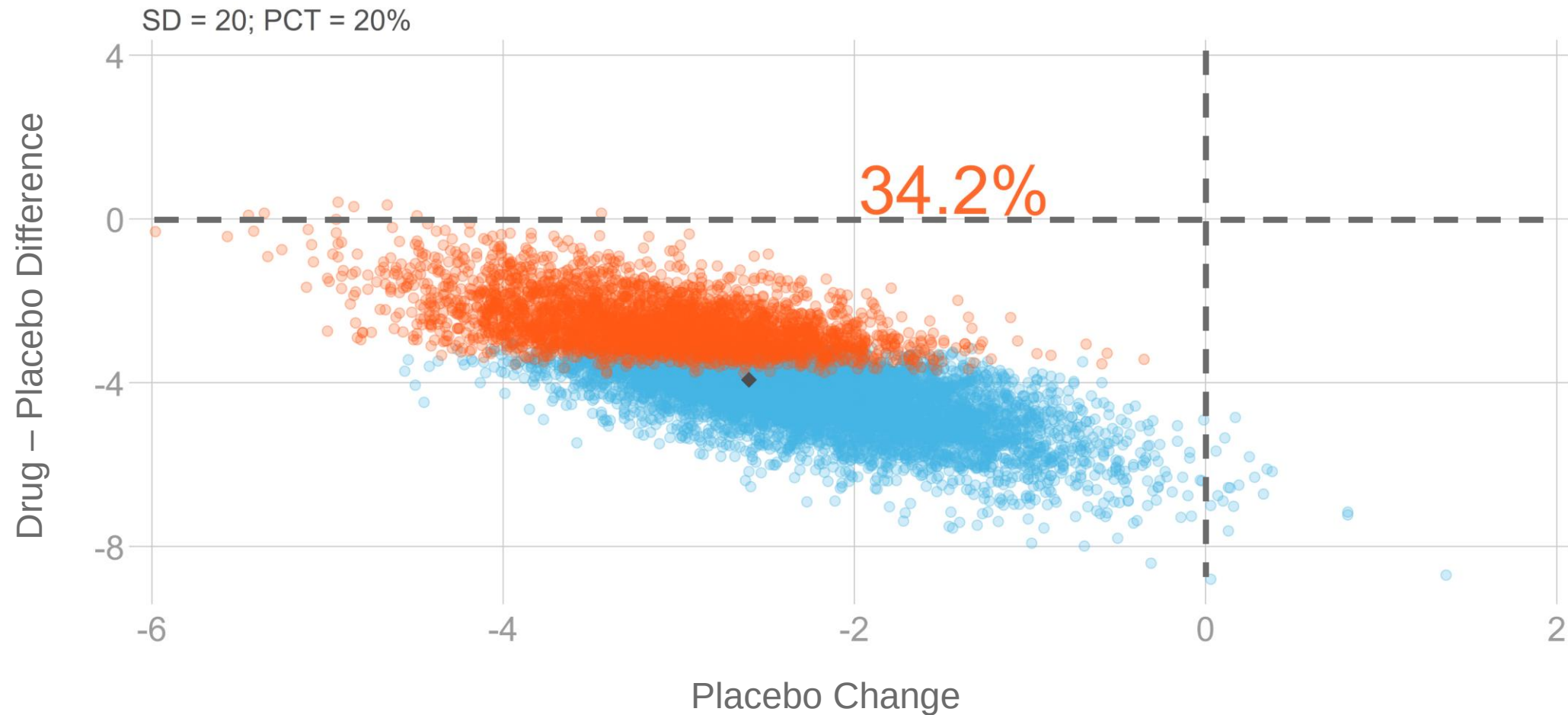
Simulation – Original Data



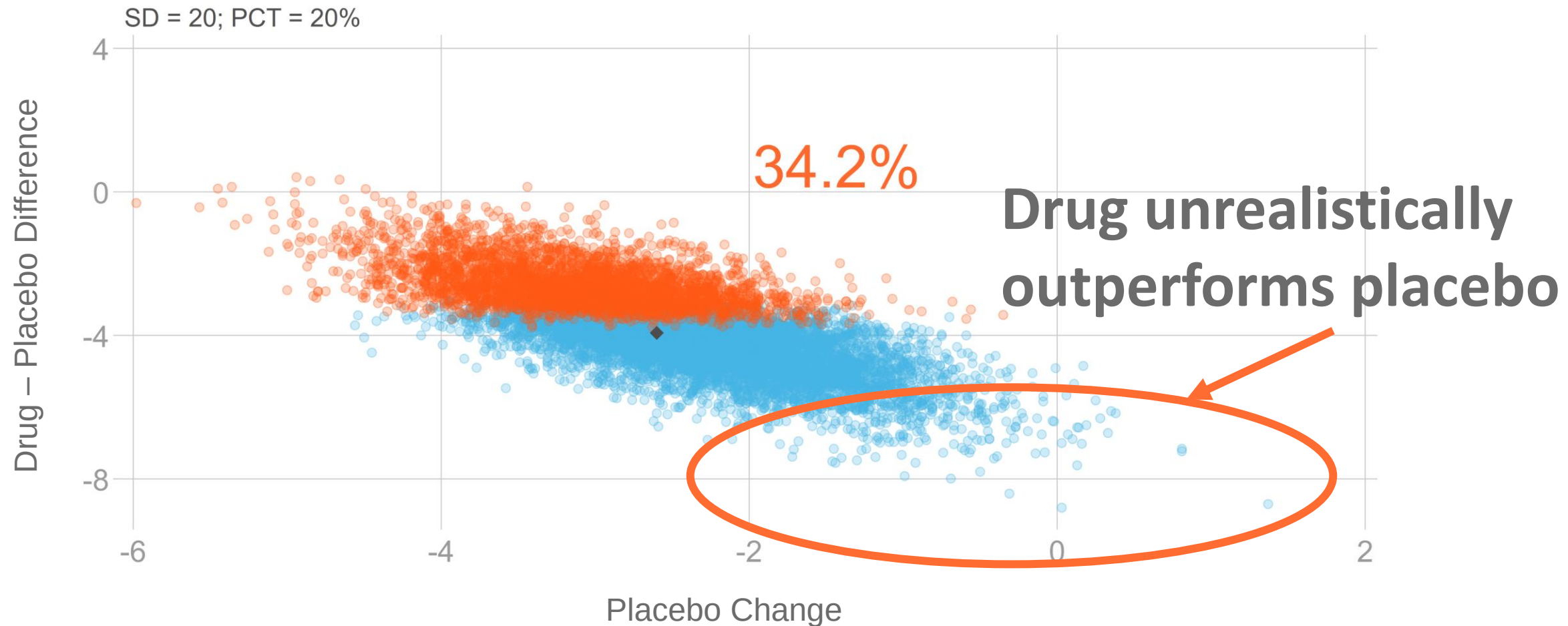
Simulation – Introducing Error



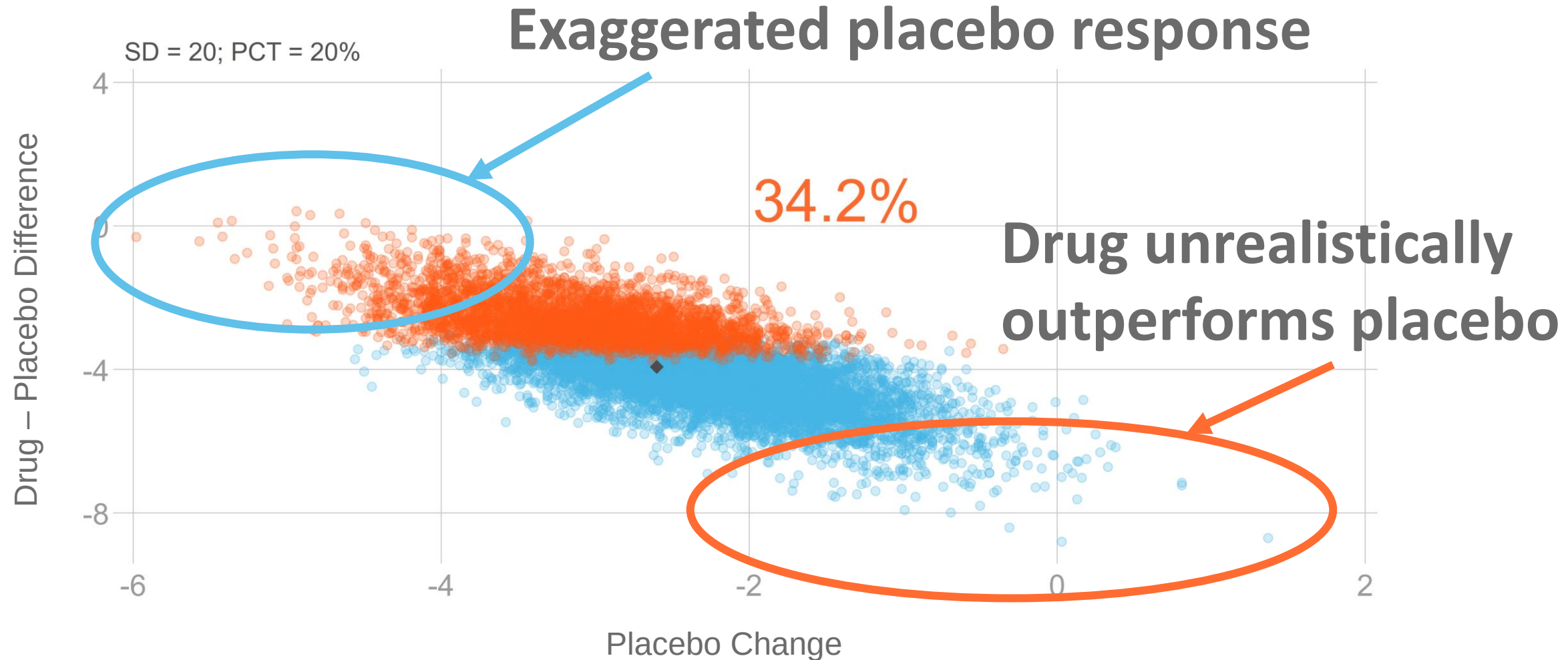
Simulation – Introducing More Error



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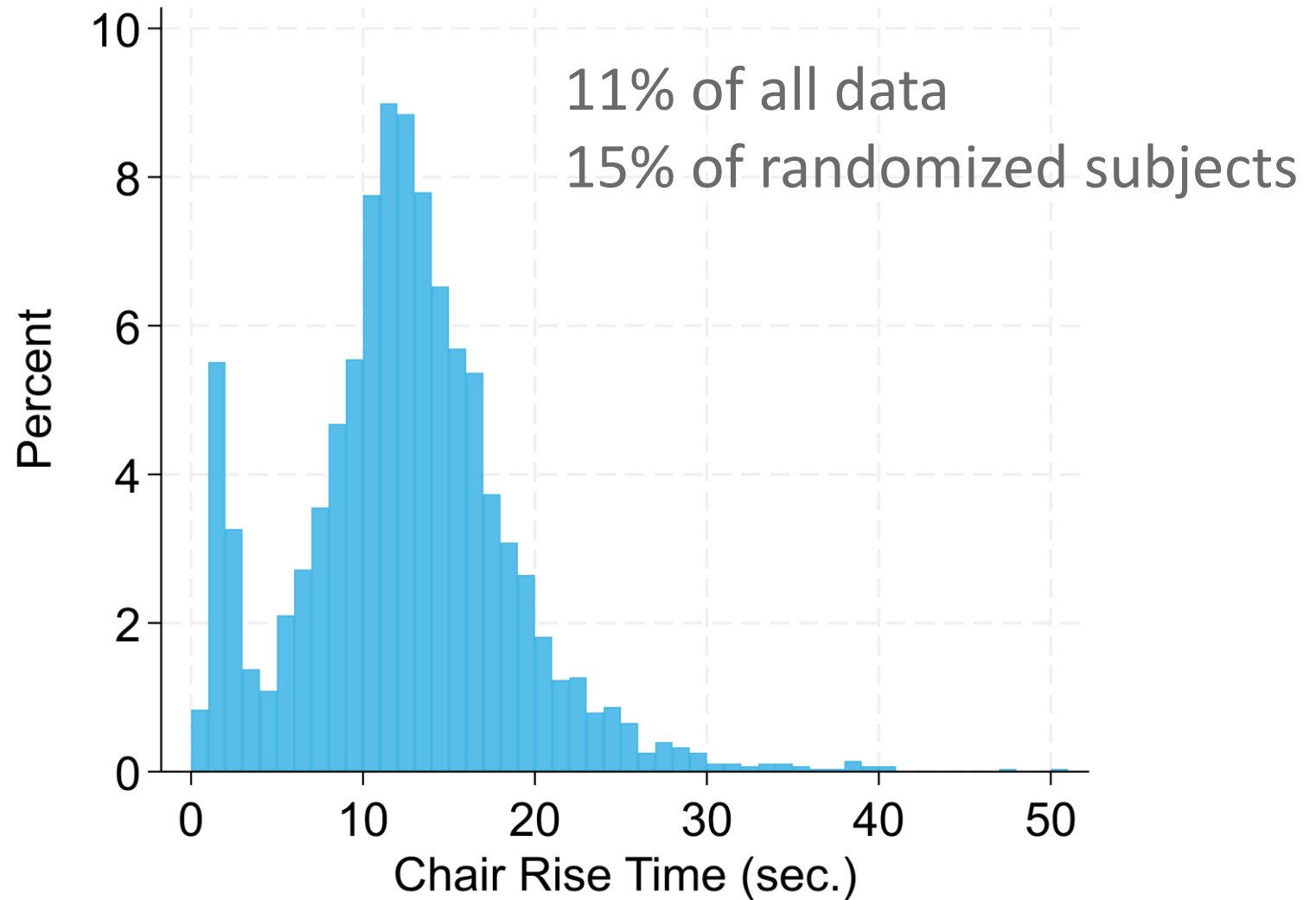
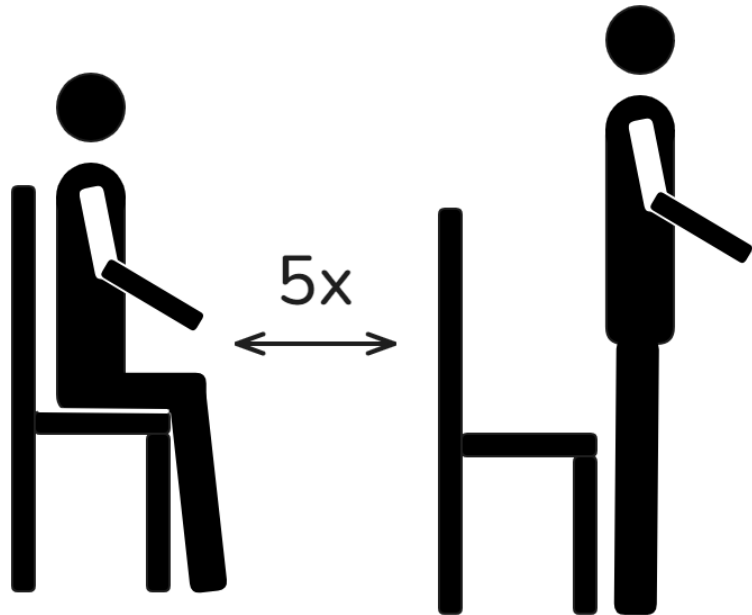


Simulation – Introducing More Error

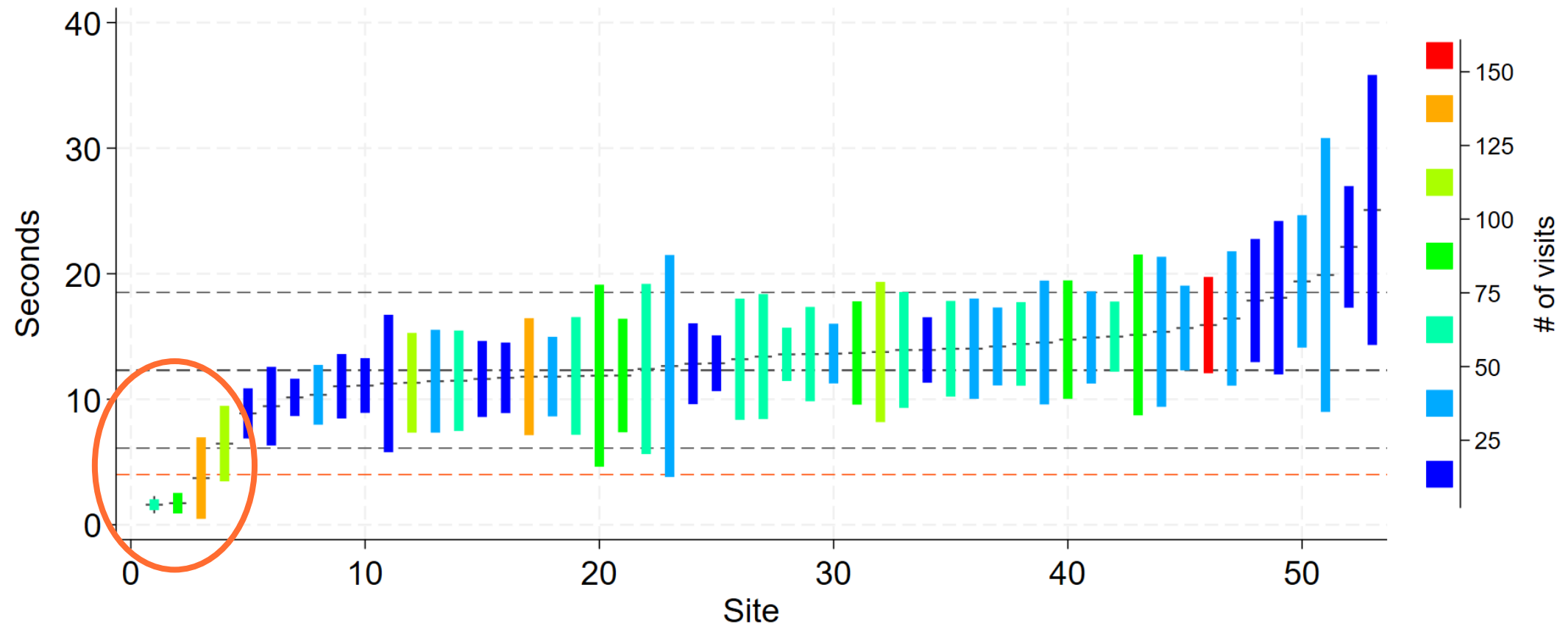


Case Example #1

mPPT Assessment – Chair Rise

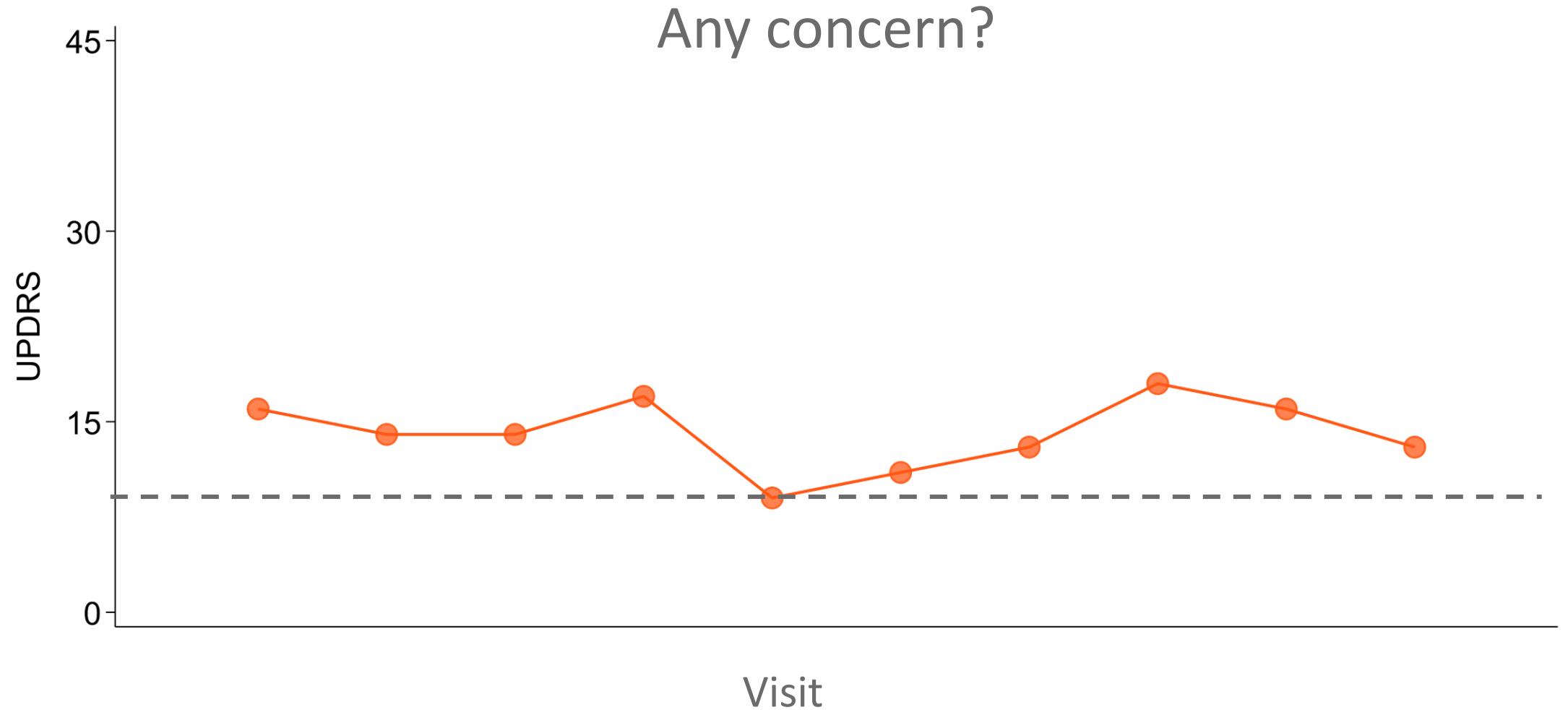


Data Concerns are Clustered

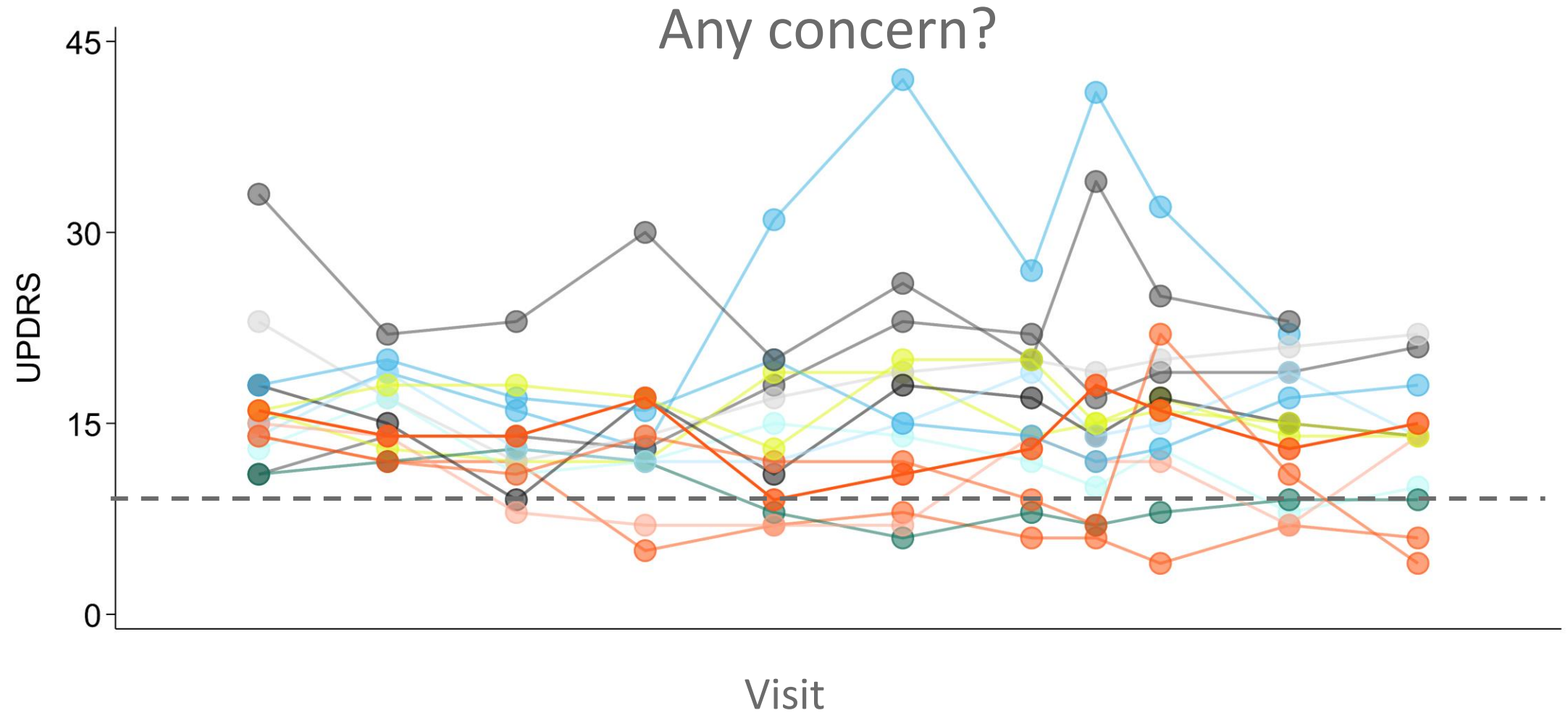


Case Example #2

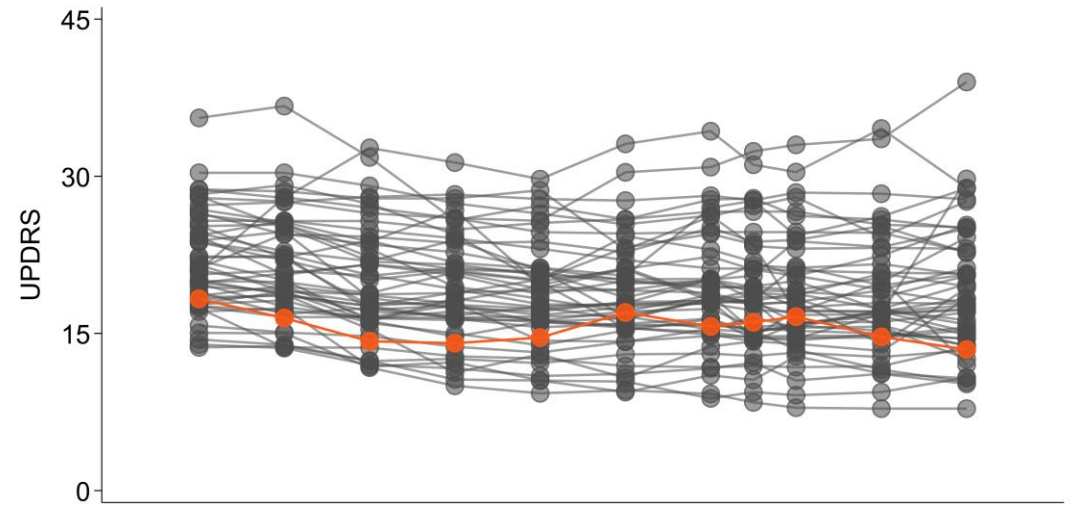
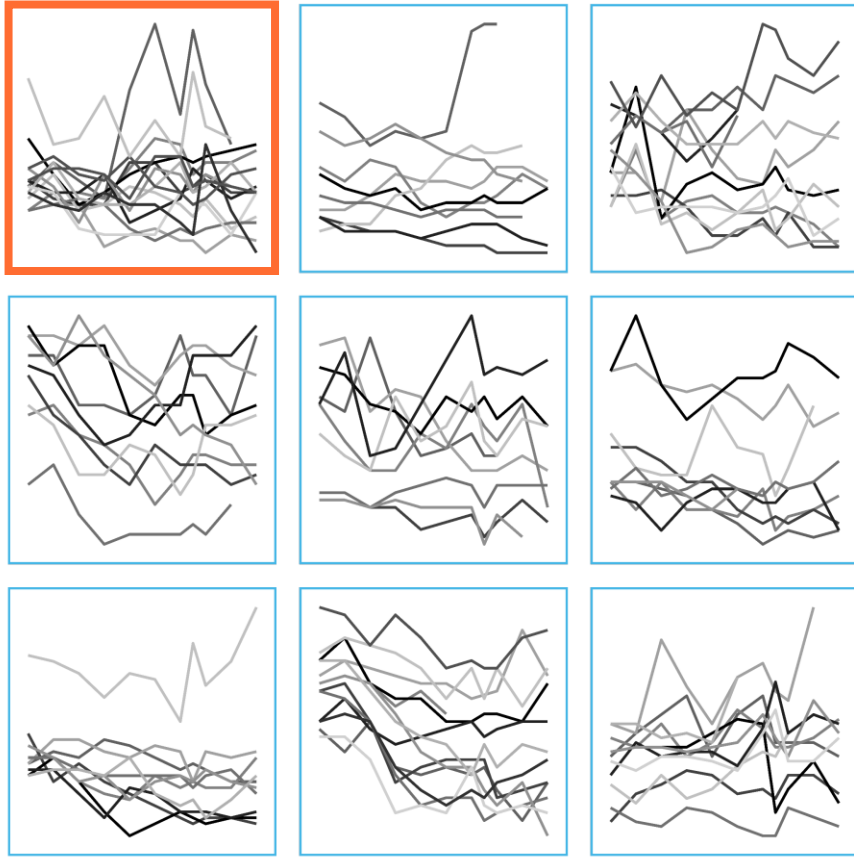
UPDRS Trajectory: Subject A



UPDRS Trajectories: Site ABC



Visual and Statistical Inspection

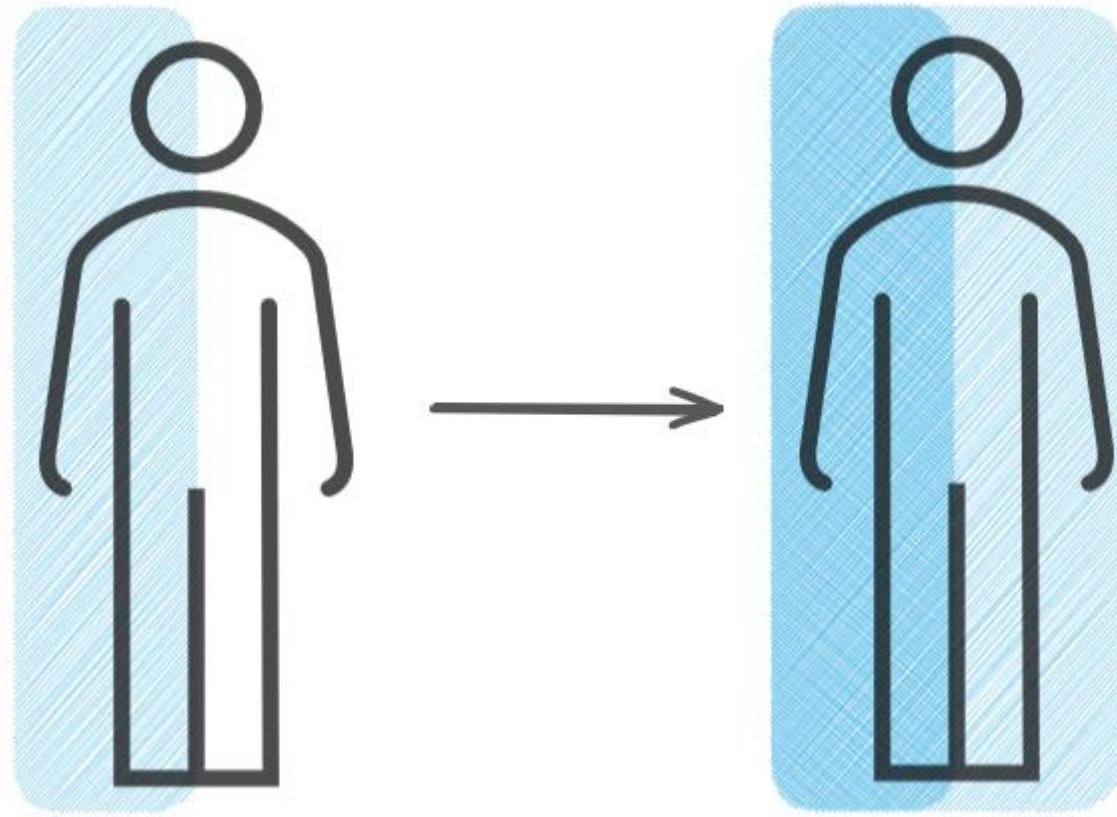


Visual inspection ✗

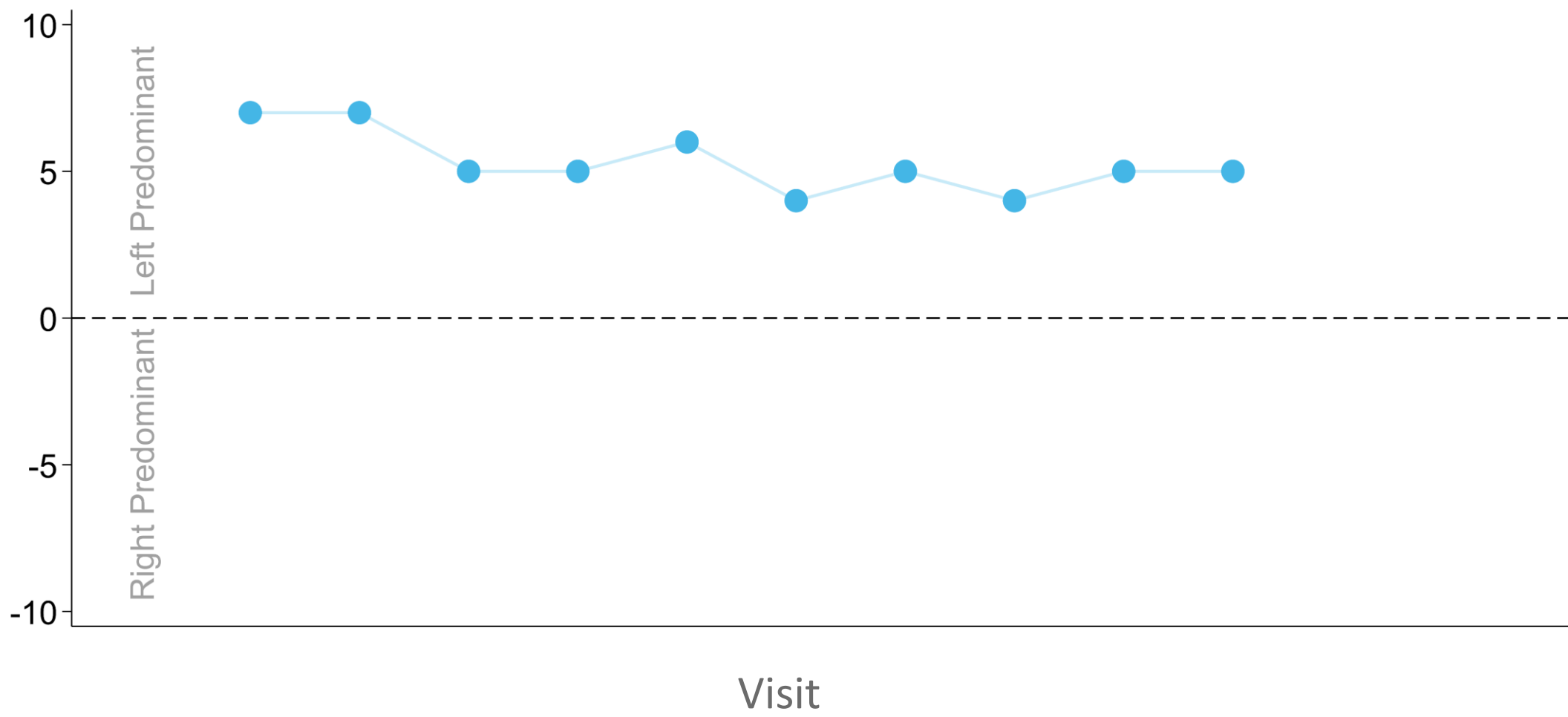
Statistical analysis ✗

Lateral Predominance

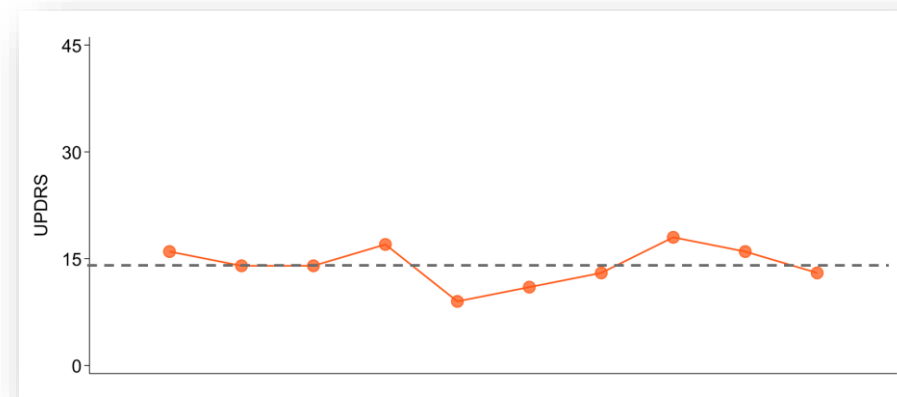
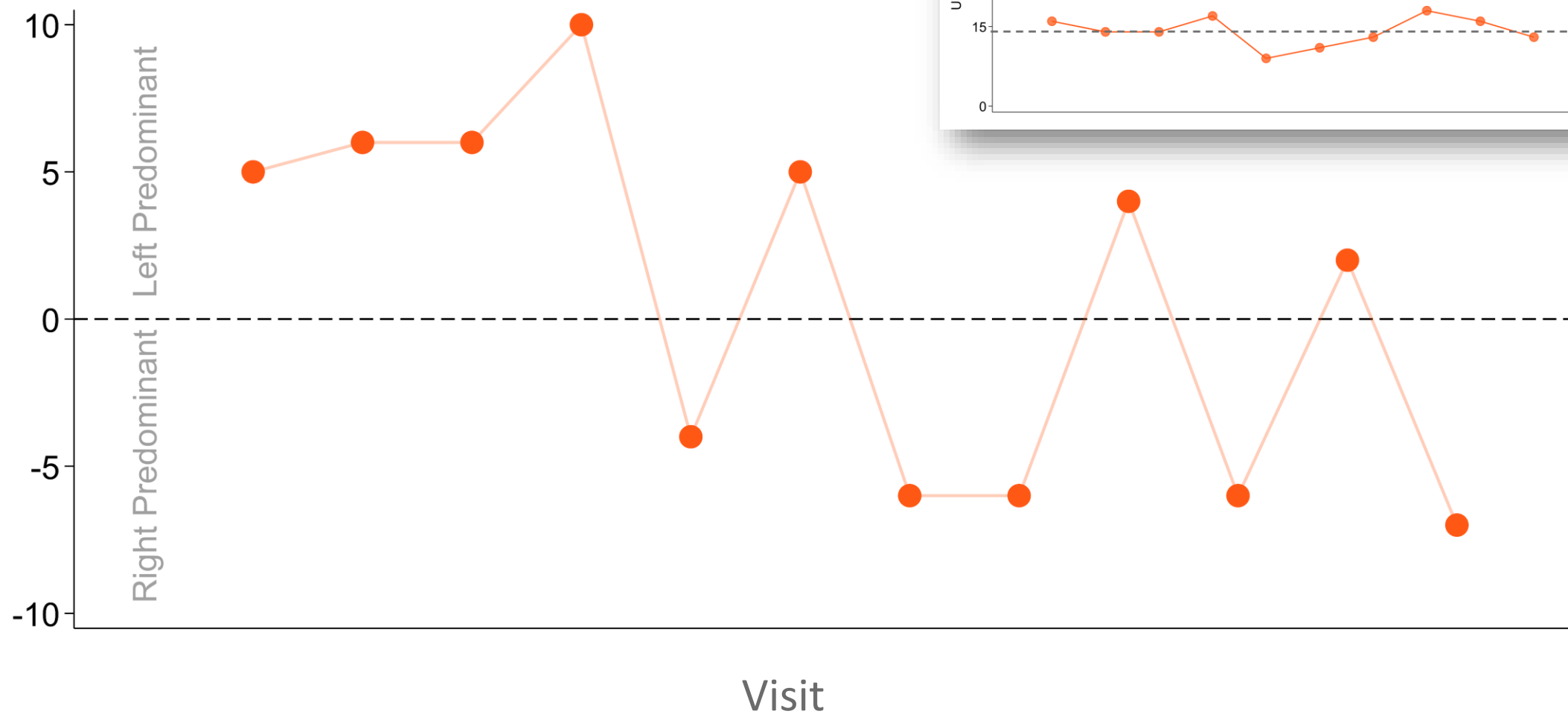
Asymmetry of motor signs is a cardinal feature of Parkinson's disease



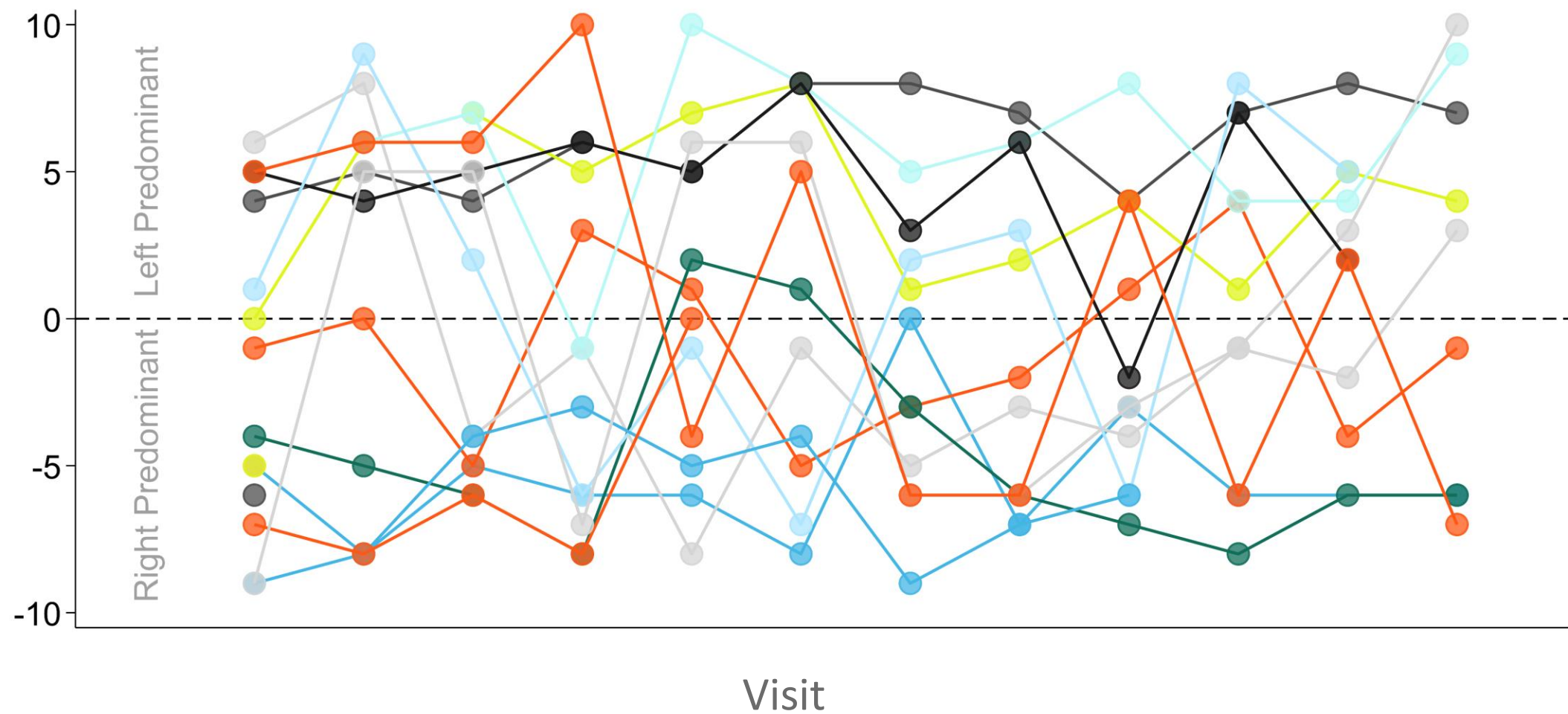
Typical PD Patient



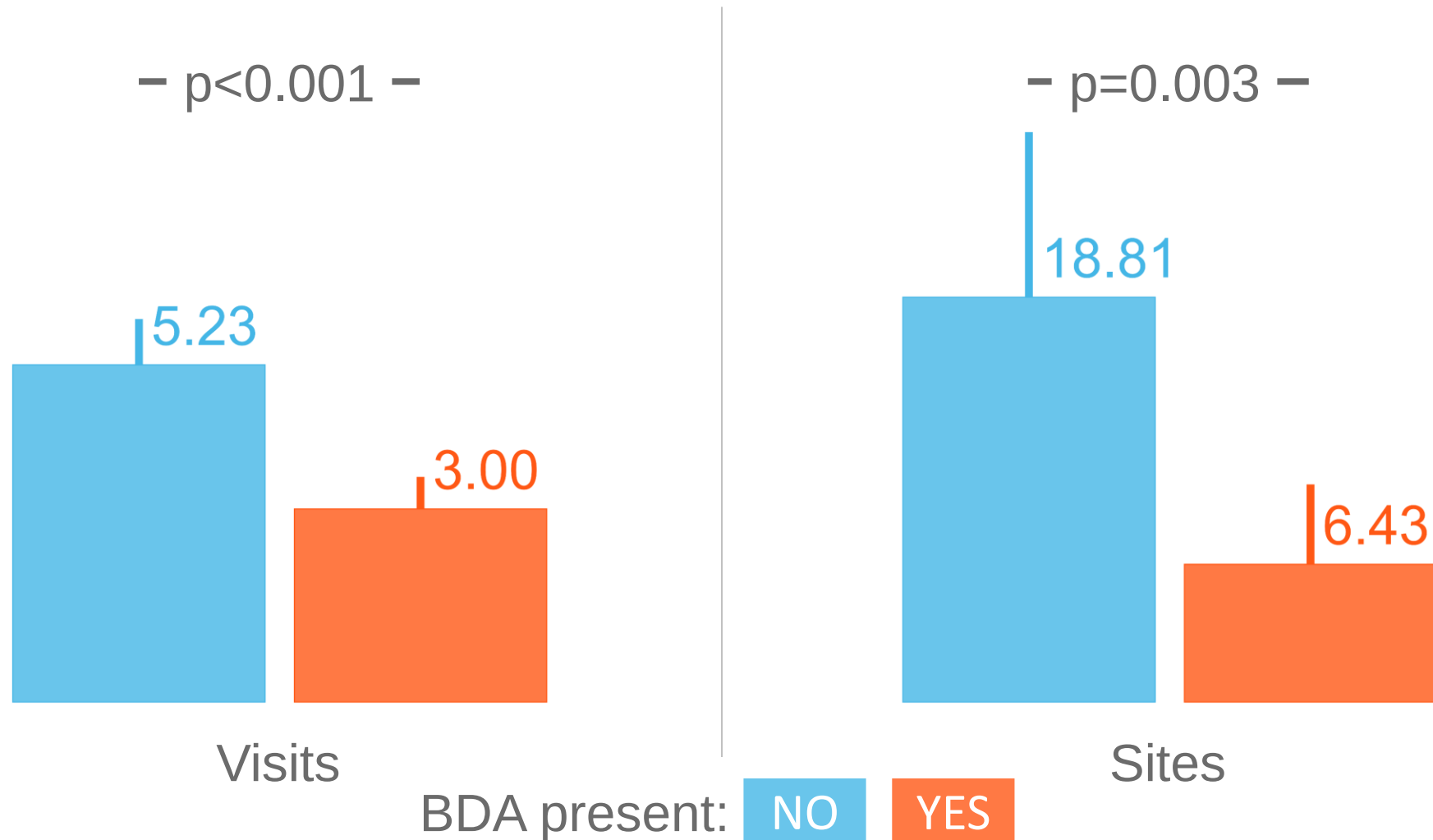
Subject A



Site ABC

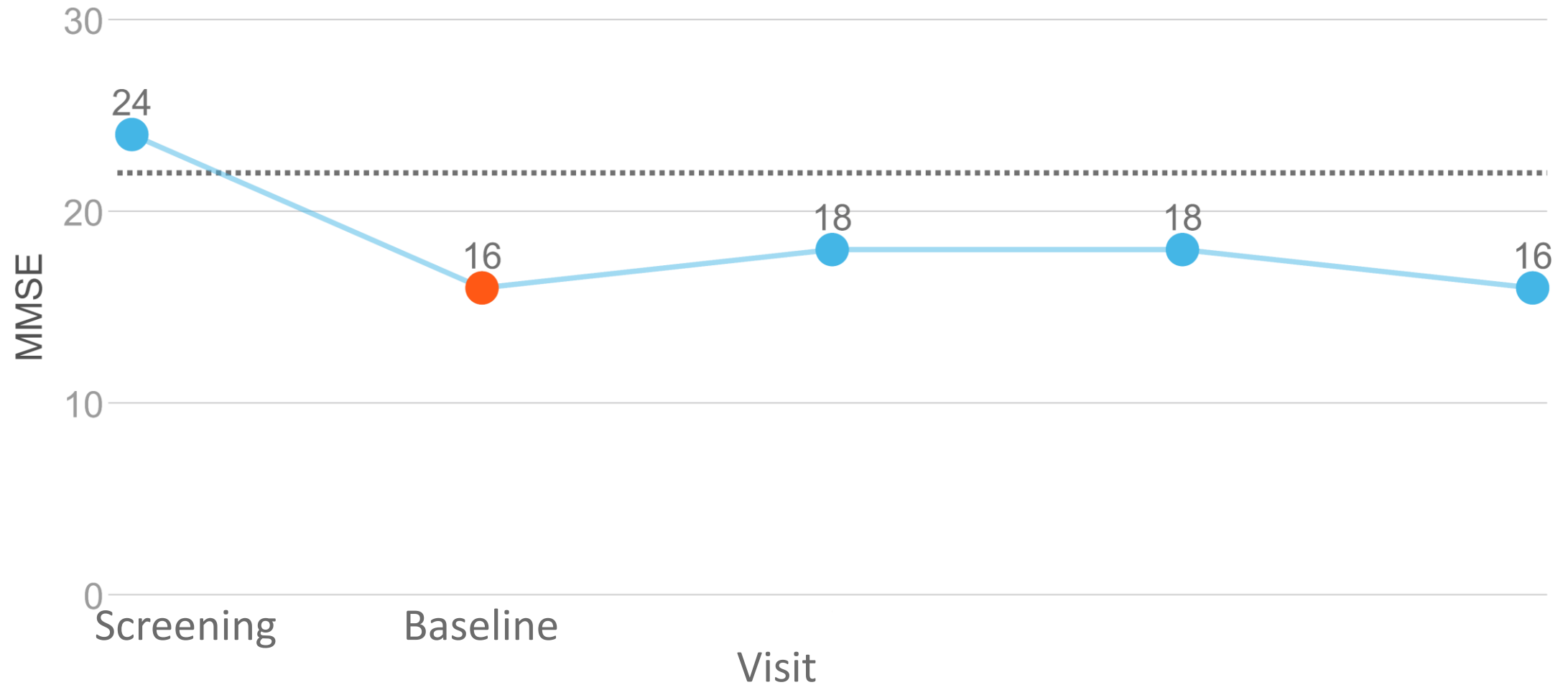


BDA Impact on Laterality Changes

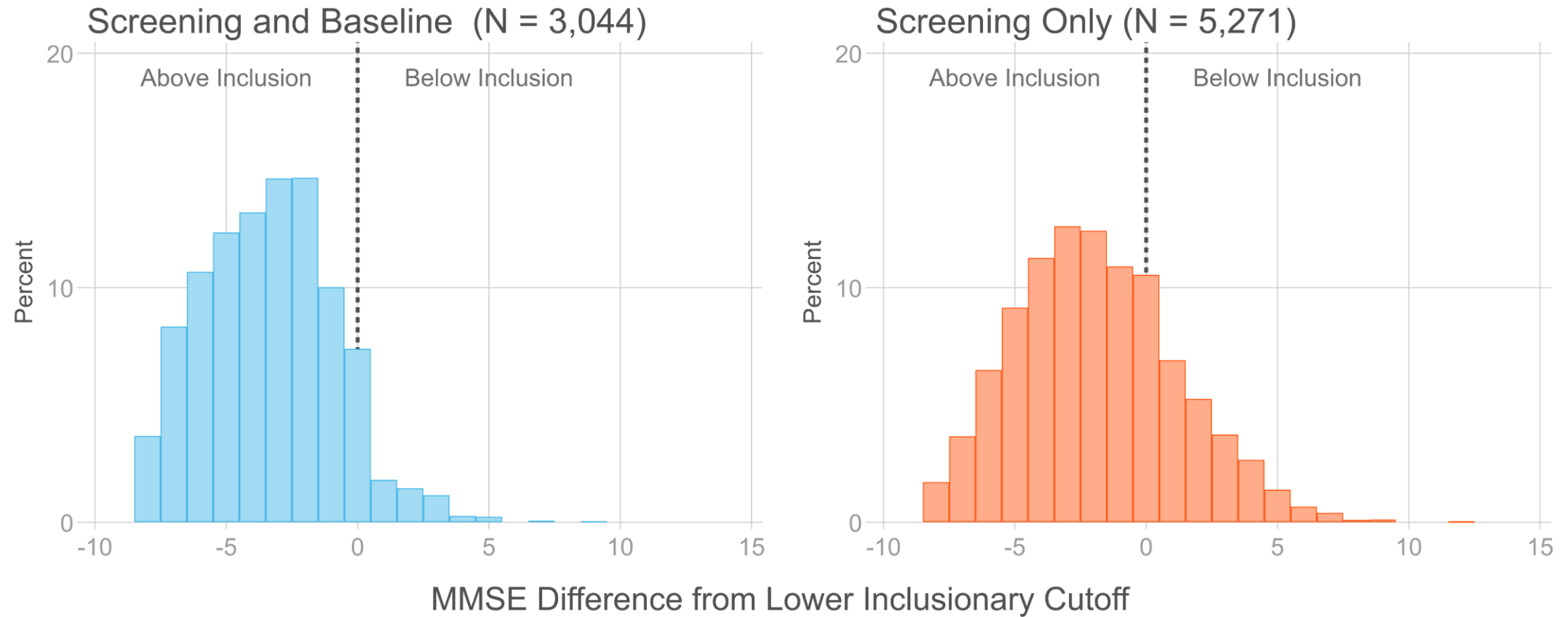


Case Example #3

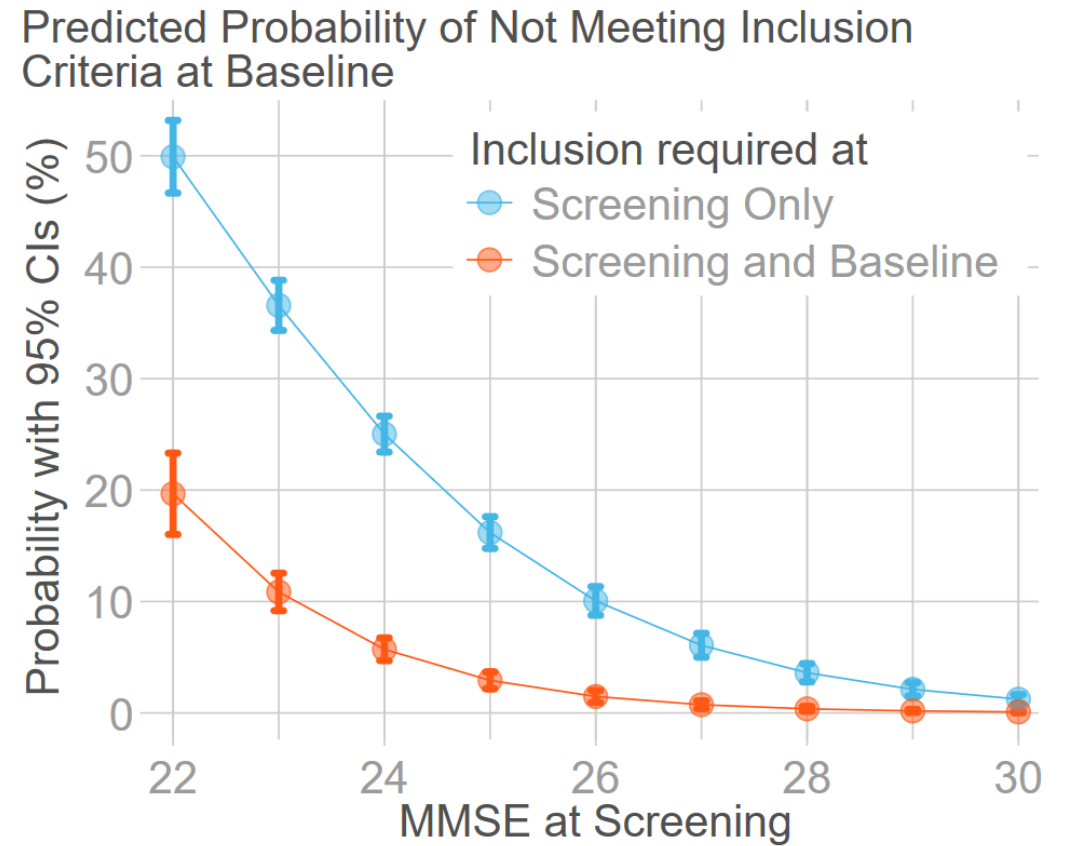
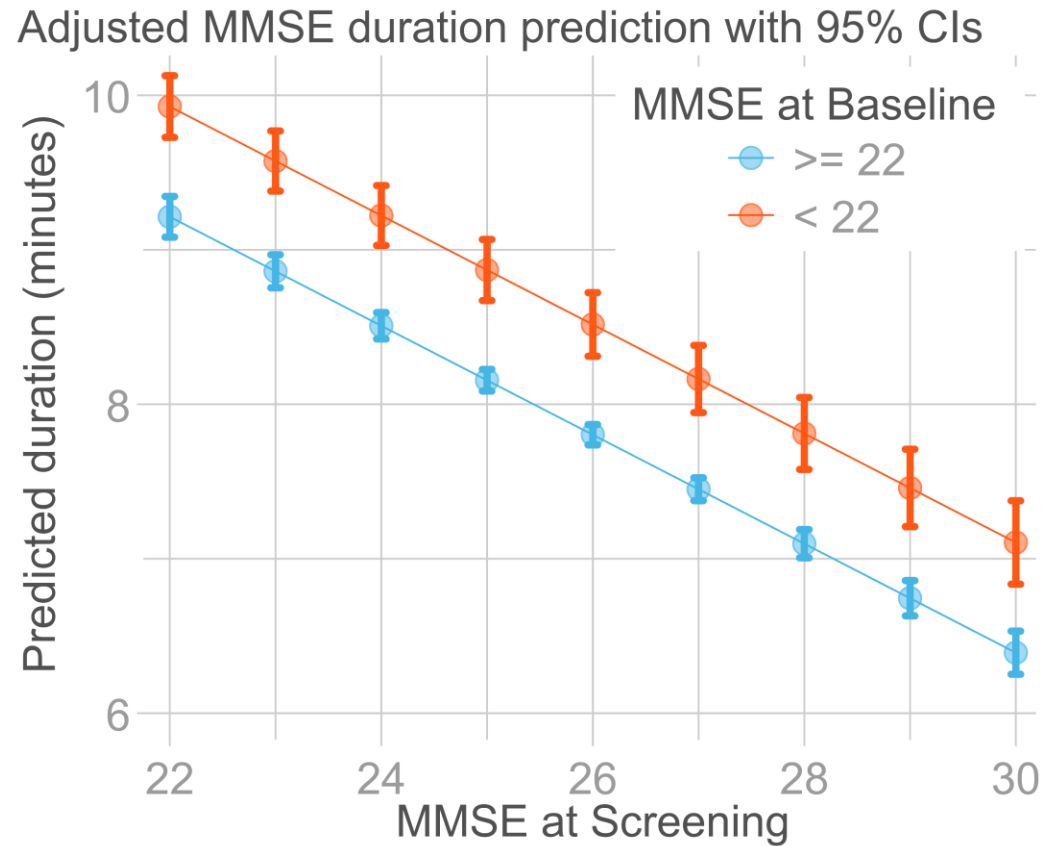
Eligible Subject into Early AD Trial



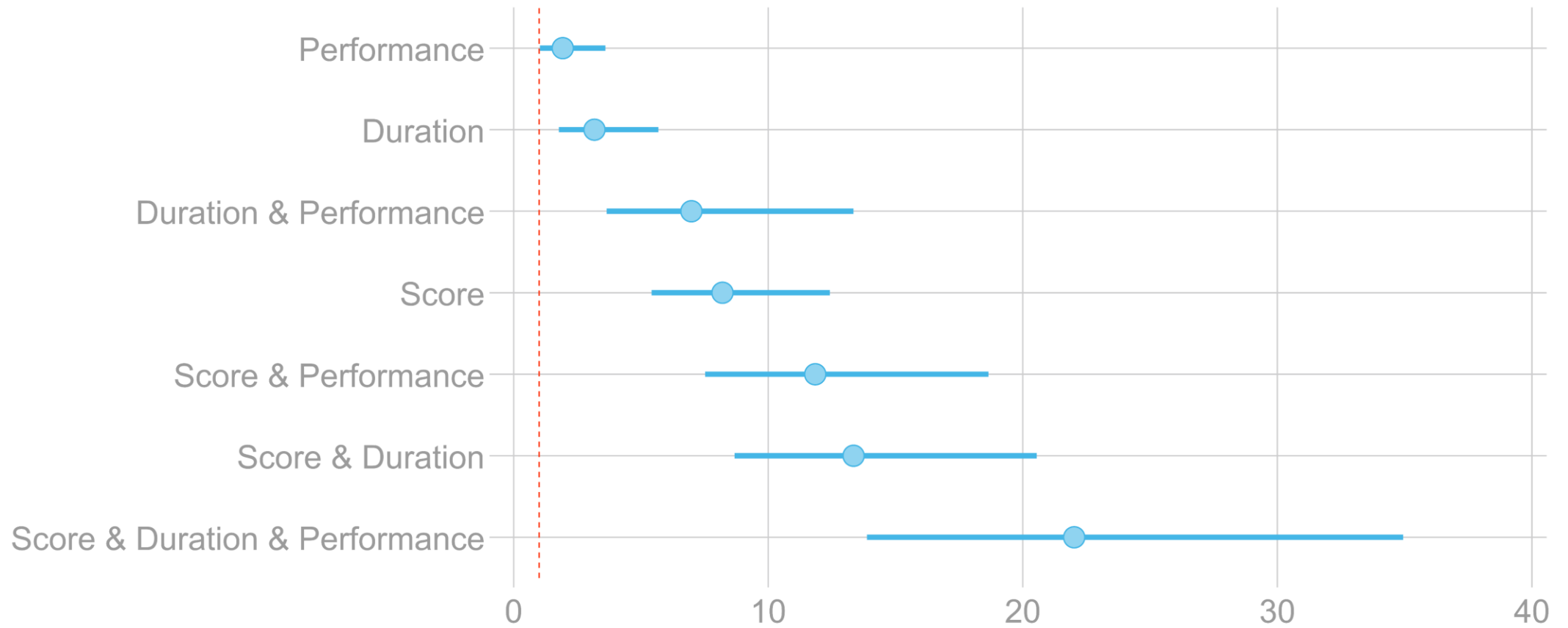
Impact of Protocol on Baseline MMSE



Risk Factors



Predicting Baseline MMSE Score



Conclusions

Conclusions

- Data concerns are frequent in clinical trials in neurology
- Data concerns are often non-randomly distributed in the data
- Data concerns impact on signal detection
 - may unrealistically inflate or attenuate the signal
- Data concerns have substantially higher impact in poorly powered trials

Conclusions

- Data analytics offer a powerful solution to identify and address data concerns

To overcome limitations

- Data analytics need to be immediate
- Data analytics need to be clinically informed
- Data analytics need to be actionable

Thank you