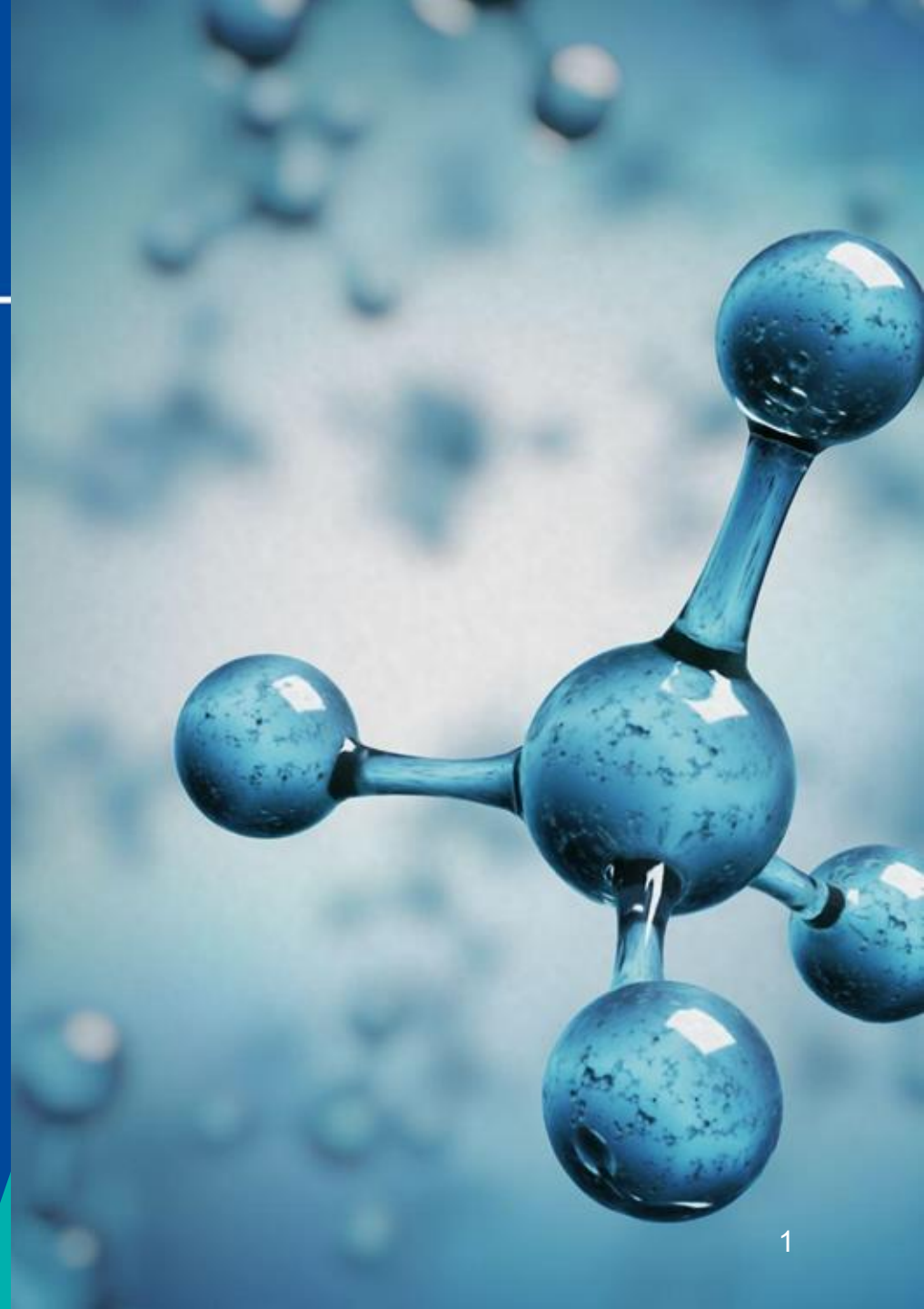
Webinar Session

Quality Tolerance Limits (QTLs): Setting the Threshold

PHUSE Working Group QTL Thresholds
June 23, 2026



Disclaimer: The views and opinions expressed in this slide deck and in the oral presentation belong to the working group members and do not necessarily reflect the views and opinions of companies of the working group members
Presentations are intended for informational purposes only and do not replace independent professional judgment. Statements of fact and opinions expressed are those of the working group members only and are not the opinion or position companies of the working group members.

Welcome

2-Session Webinar on QTL Monitoring

Webinar 1: Setting the QTL Threshold (23 June 2026)

- Presentation
- Round Table
- Please enter your questions into the chat.

Webinar 2: Action Limits (1 September 2026)

- Presentation
- Round Table
- Q&A Session

QTL Threshold Working Group

connect·share·advance

Marcus E. Muli
Market Access
Organon

Anandavalli Thiagarajan
Manager, Centralized Monitoring
PPD, Part of Thermo Fisher Scientific

Stefano Saino
Sr. Clinical Quality Operations Manager,
MSD

Debra Jendrasek
Sr. Director, Data Review and Reporting,
Daiichi Sankyo

Nathalie van Borrendam
Working Group Co-Lead
Ass Director, Data Management – Central Monitoring
Johnson & Johnson

We also want to acknowledge the working group team members for their contribution to this session.

Agenda Topics

- **Setting the Foundation**
  - Quality by Design (QbD)
  - Critical to Quality (CtQ) Factors
  - Critical Data and Processes (CD&Ps)
- **Quality Tolerance Limit (QTL) Parameters**
- **Methods for Setting Thresholds for QTL Parameters**

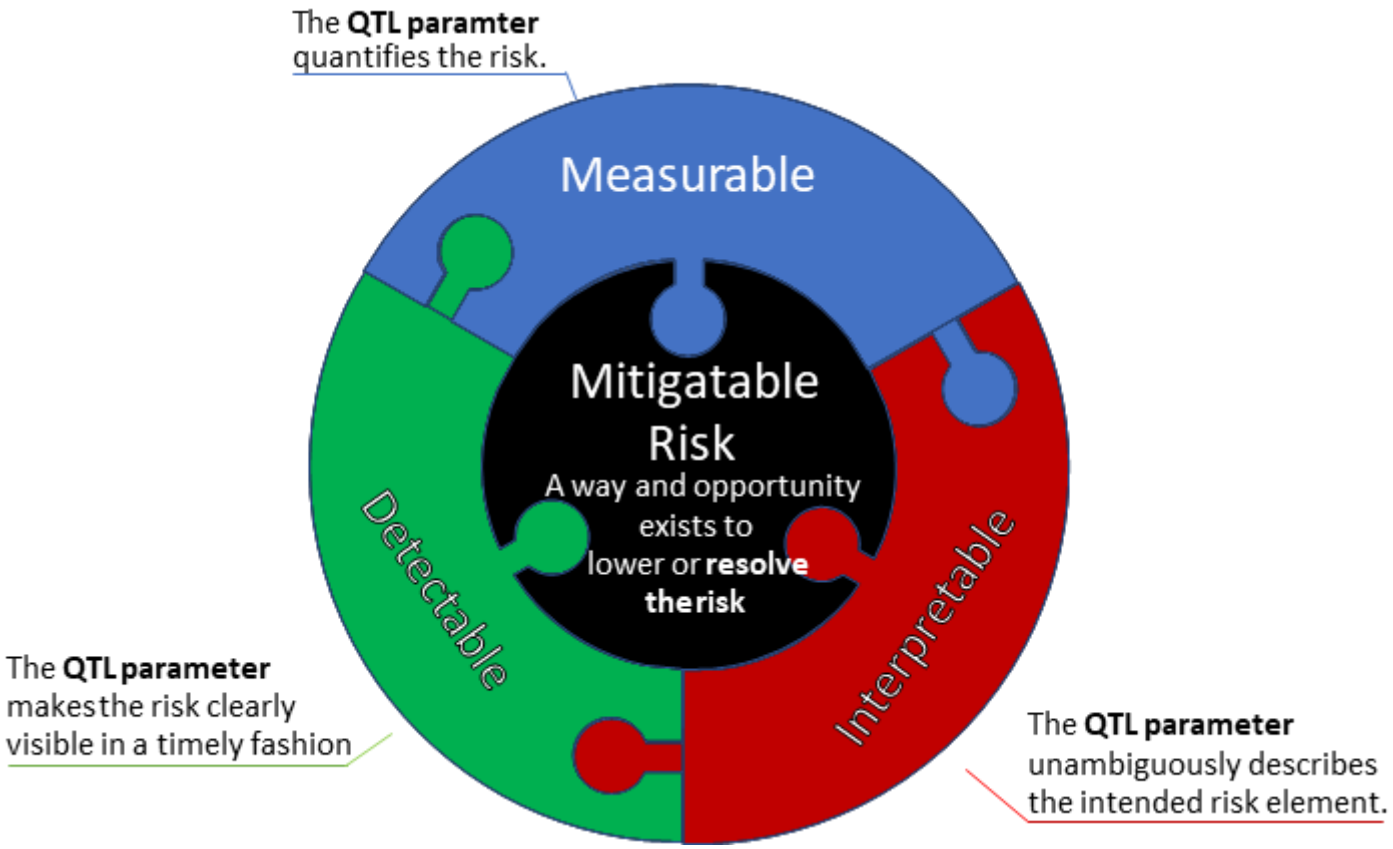
Getting Started...

- **Quality by Design (QbD)**
- **Critical to Quality (CtQ) Factors**
  - Quality Attributes of the trial
  - Data or Processes that are key to scientific question of the trial or Subject Safety
- **Activities focus on those hazards that may introduce harm to the CtQ Factors**

Measurable Variable

- **Allows for monitoring of the risk exposure over time**
- **Thresholds can depend on data expectations such as:**
  - Ensuring acceptance of the trial by regulatory agencies
  - Ensuring acceptance of the trial results by journal editors and subject matter experts
  - Ensuring statistical power for the primary and key secondary endpoints focusing on data integrity

Quality Tolerance Limit (QTL) Parameter

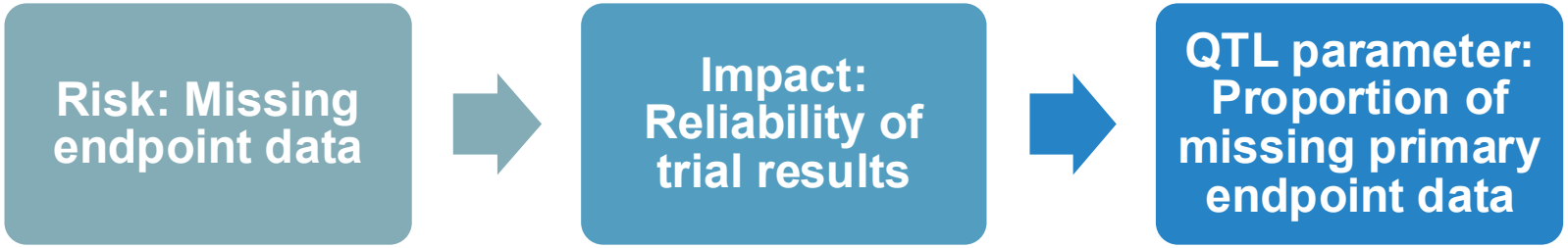


Examples:

- Counts such as number of days
- Proportions/rates such as dropout rate
- Event rates adjusted for treatment times

Considerations for Setting QTL Parameters

- **Trial Design/Objectives**
- **Trial Phase (limited duration, small sample size, fast enrollment)**



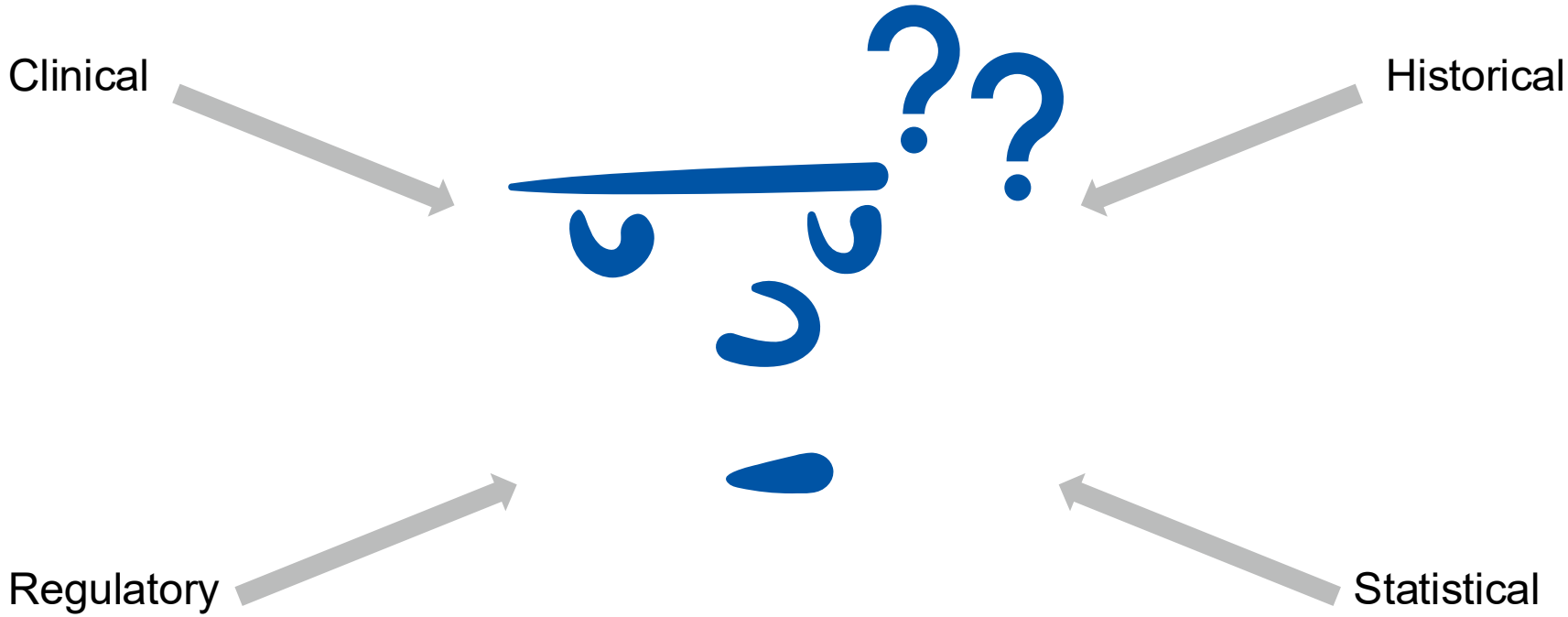
- **Number of QTL Parameters**

Industry Examples

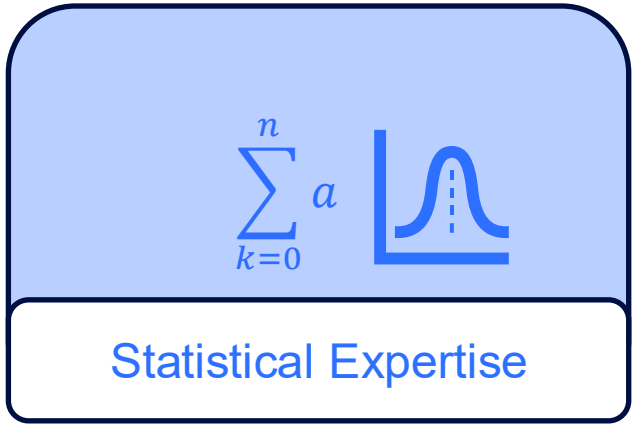
connect·share·advance

CtQ Category	Risk	QTL Parameter	Threshold Setting Method
Data integrity of primary endpoint	Too many dropouts negatively affect the power of the trial Too few events observed to detect a certain hazard ratio with power of at least 90%	Annual dropout rate (%) Proportion (%) of subjects with two or more missed consecutive disease evaluation assessments	Sample size calculation in the design stage of the trial based on earlier dropout rates in the anticipated trial population Simulation of trial scenarios and validation with reference trials
Eligibility of subjects	Scientific question of the trial cannot be answered due to too many subjects not being part of the targeted population.	Proportion (%) of randomized subjects who did not meet one or more of the inclusion or exclusion criteria.	Expert knowledge and statistical methods

So… What Number Do We Choose?



Four Doors To A Threshold

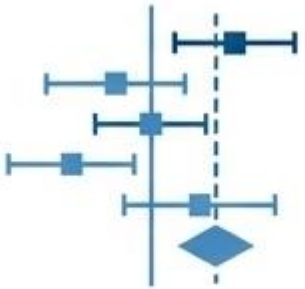


Statistical Considerations For Setting QTLs

1. Research
Gather similar historical trials

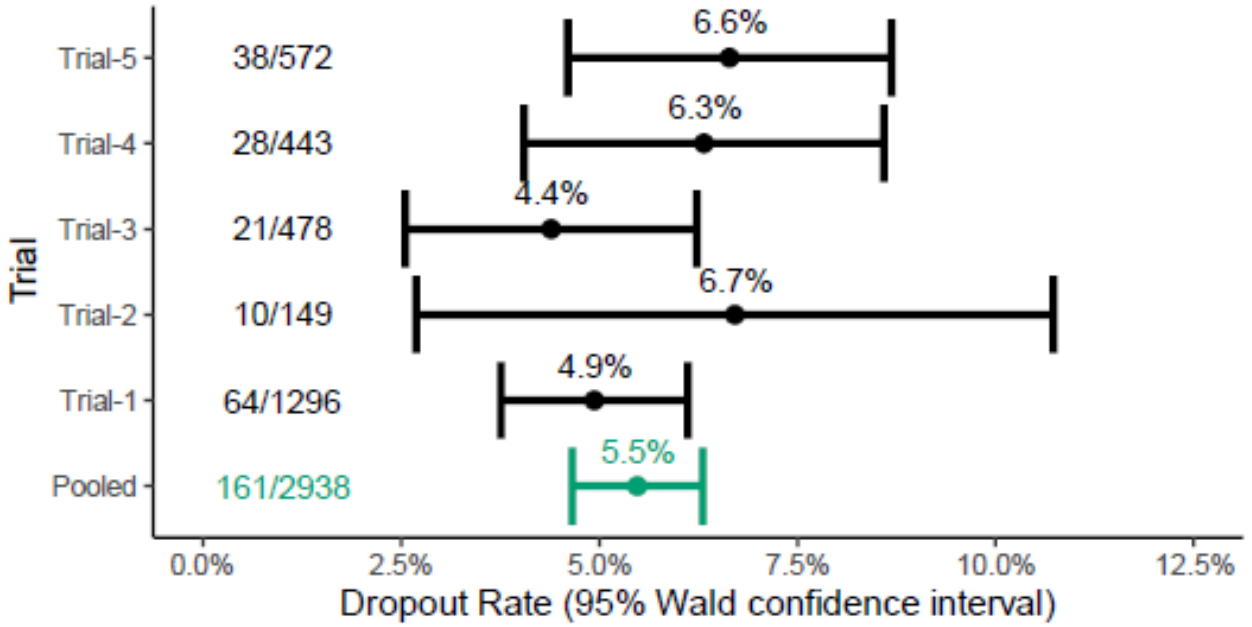
2. Inference
Pool the data, Quantify uncertainty

3. Prediction
Simulate the new trial to set the threshold



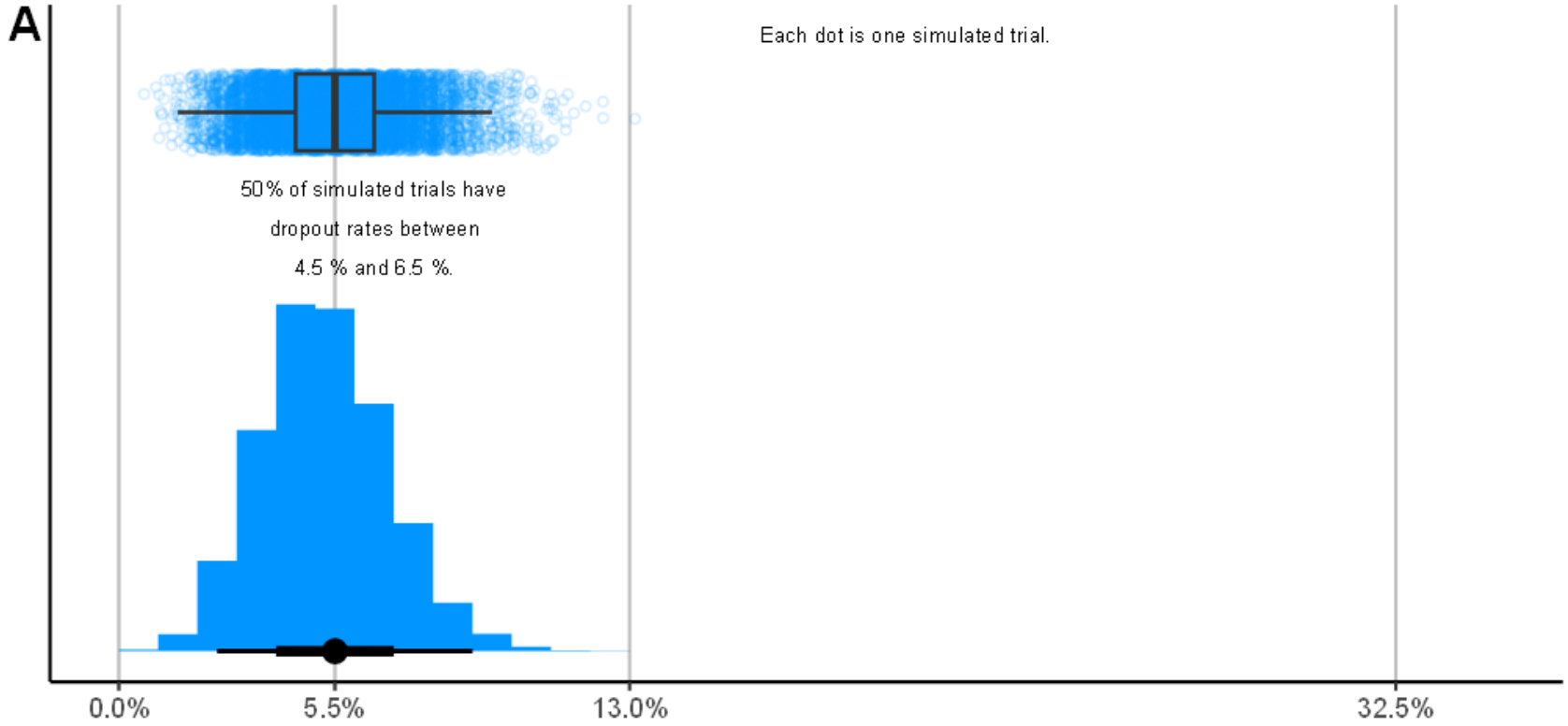
Case Study: Research & Inference

Phase 2 plaque psoriasis trial, 12 weeks, 200 subjects. Parameter: dropout rate



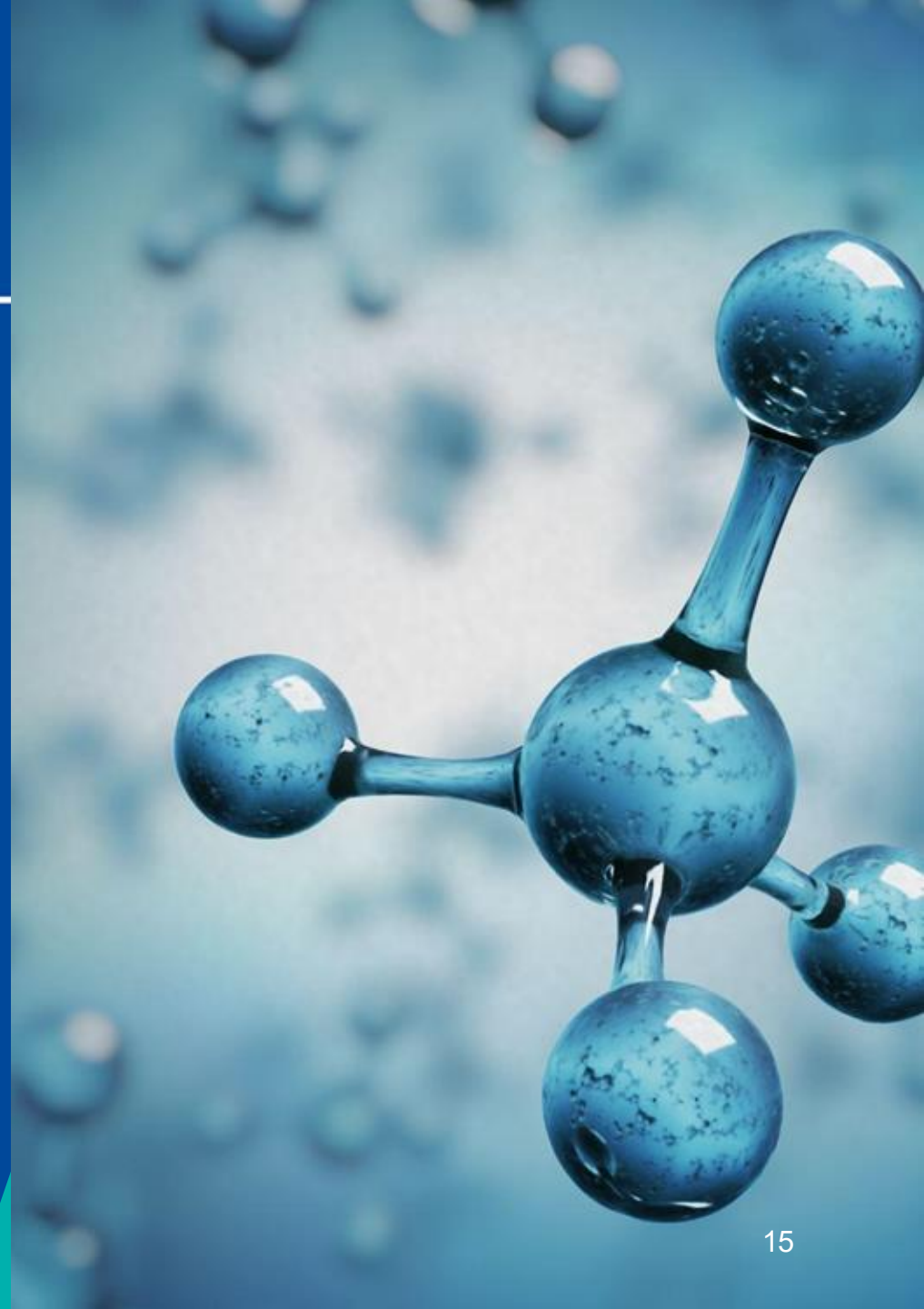
Case Study: From Prediction To Decision

Phase 2 plaque psoriasis trial, 12 weeks, 200 subjects. Parameter: dropout rate



Conclusion

1. A QTL threshold is a decision, not a calculation
2. Statistics does not replace judgement; it helps narrow the range
3. Research → Inference → Prediction



Round Table Discussion

Round Table Discussion 1

Would you share with us:

- Which functions/roles are involed in defining and conducting QTL Monitoring?
  That is, who initiates, who is responsible and who contributes to the process?

- Which challenges do you face with your QTL monitoring process?

Round Table Discussion 2

Would you share with us:

- Which data (sources) do you use for QTL Monitoring?
- Who is
  - conducting the programming, e.g., setting up the dashboards and runs the analysis during the study,
  - looking at the numbers and takes decision?

- Which challenges do you face with this data analysis process?

connect·share·advance

THANK YOU!