Decision making in drug development: An opportunity for model-based knowledge integration and scenario evaluation

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Acknowledgements

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Abstract

Drug development decision makers are typically faced with the challenge of making accurate decisions in the face of considerable uncertainty about the disease, patient population, and likely efficacy and safety of new therapeutics. Compounding this challenge are the constraints of time, patient access, and direct/opportunity costs. Model based methods allow for a transparent expression of the current state of knowledge, including key assumptions or knowledge gaps. Evaluation of scenarios depicting different decision pathways is possible via model-based simulation and may lead to more effective decision making. Rationale and a general framework will be presented and illustrated with hypothetical examples.

“As to methods, there may be a million and then some, but principles are few. The man who grasps principles can successfully select his own methods. The man who tries methods, ignoring principles, is sure to have trouble.”

- Ralph Waldo Emerson

Outline

Psychology of Decision-Making: Relevance to Drug Development

Precision / Consistency

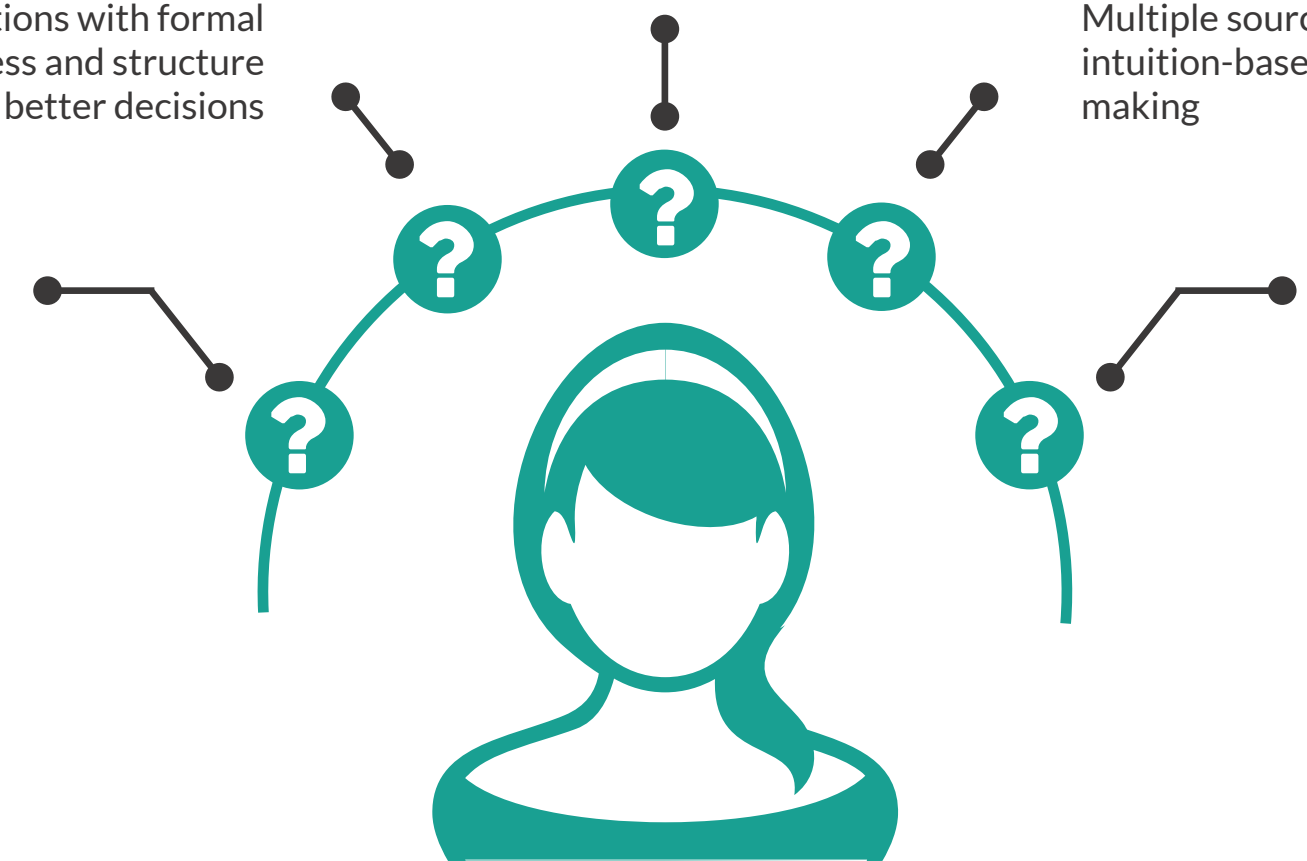
Inconsistency (poor precision) in organizational decision making may be bigger problem than bias

Structure / Process

Organizations with formal decision process and structure make better decisions

Bias

Multiple sources of bias affect intuition-based “expert” decision making



Individuals vs. Groups

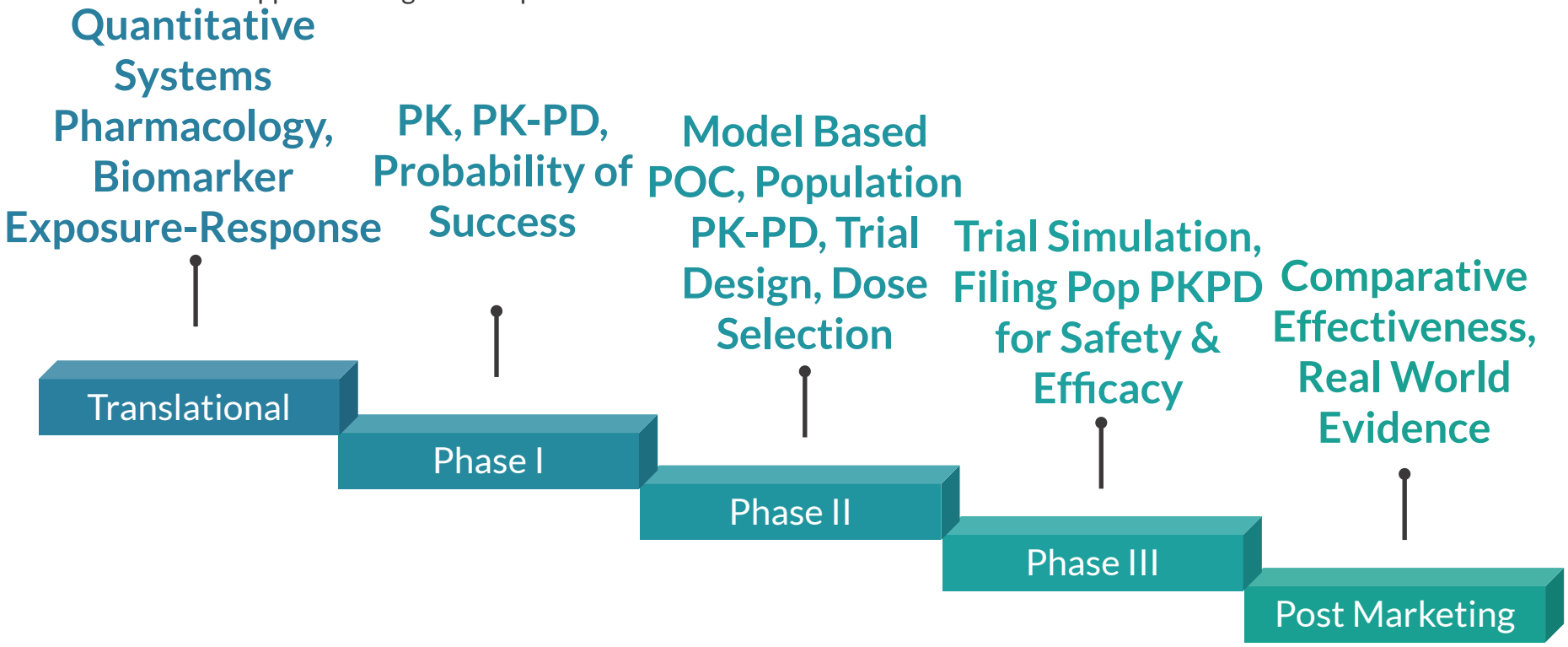
Decision performance for the most-informed individual is better than the group

Intuition vs. Scenarios

Objective (data driven) exploration of scenarios improves decision-making performance

Model-Based Drug Development

Some of the typical methods and activities applied throughout the process



Off-The-Shelf Disease Area Platform Content: Disease Progression, Quantitative Systems Pharmacology, Competitor Model-Based Meta-Analysis, Trial Simulation Tools

Modeling and Simulation Based Decision Making

Start with Key Questions and Potential Decision Paths

- Probability of target product profile
- Treatment regimens
- Trial designs
- Development strategies
- Indications
- Selection of lead candidates

Models

- Drug & disease models
- Treatment population models
- Trial models
- Financial & market models

Other Information Sources

- Public evidence
- Expert opinion / belief

Simulate Outcomes of each Path or Question

Decision Criteria

- Consider cost/benefit trade-offs
  - Safety
  - Clinical utility/efficacy
  - Health Economic
  - Commercial
- Adjusted to consider the value systems of the key stakeholders
  - Patients
  - Health care providers
  - Drug developer
  - Regulators

Assumption Checking

Assess sensitivity of conclusions to uncertainties and assumptions.

Decision

Select highest value path given the current state of knowledge.

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Defining the Question

The question should guide model development and evaluation.

- What model structure and components are needed?
- What data features must be reproduced?

The question to be answered also guides simulation design.

- What simulation structure / components are needed?

Listen and Understand

Listening is not done until you can re-state the specific problem or questions, constraints and concerns, accurately.

"Whoever best describes the problem is the one most likely to solve it"

Dan Roam

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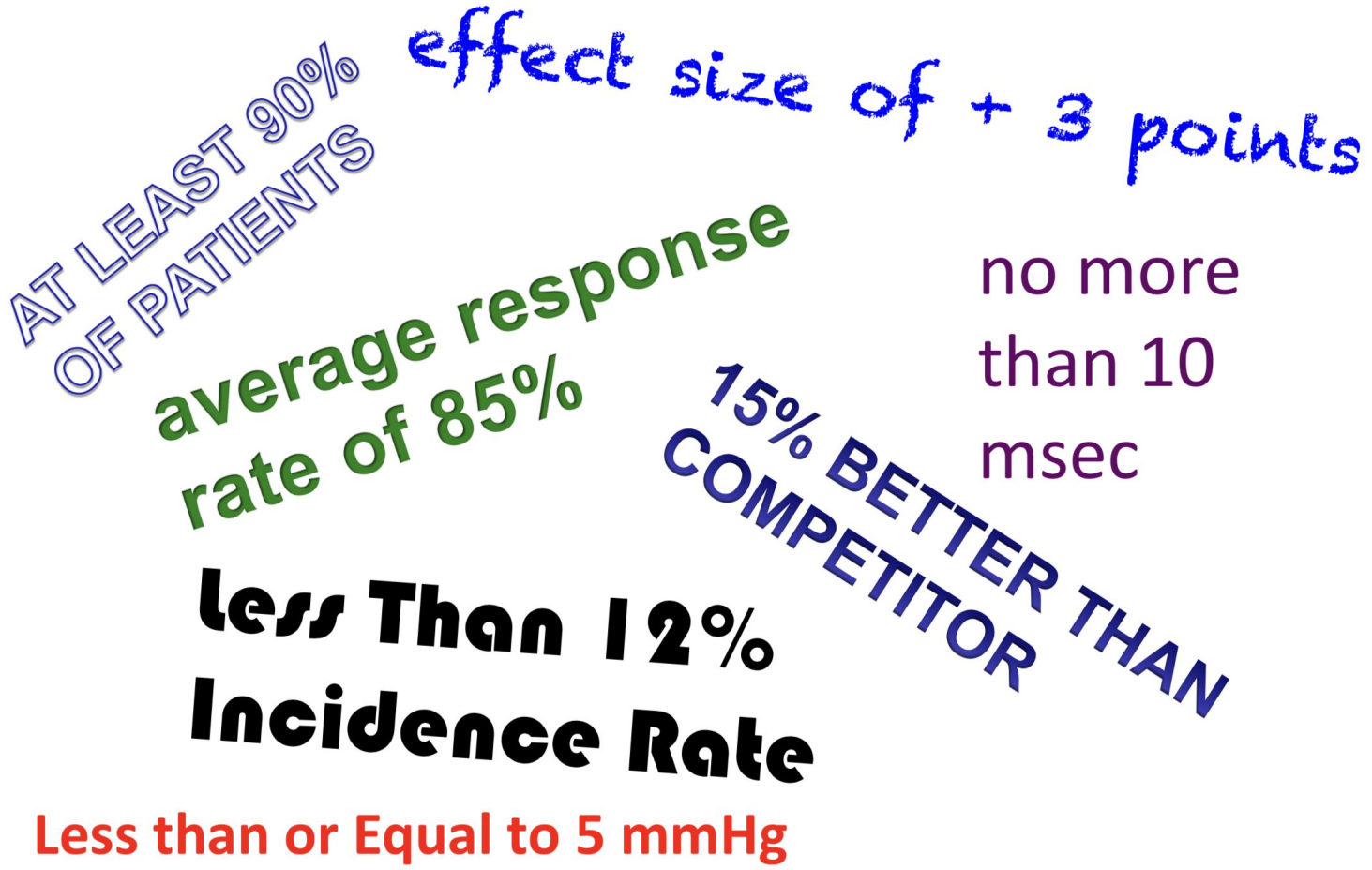
Quantitative Specification of Decision Criteria

The question must be translated into quantitative terms prior to simulation.

Requires specific quantitative definitions of clinically relevant effect size or response rate.

Quantitative questions are often best framed as a probabilistic statement.



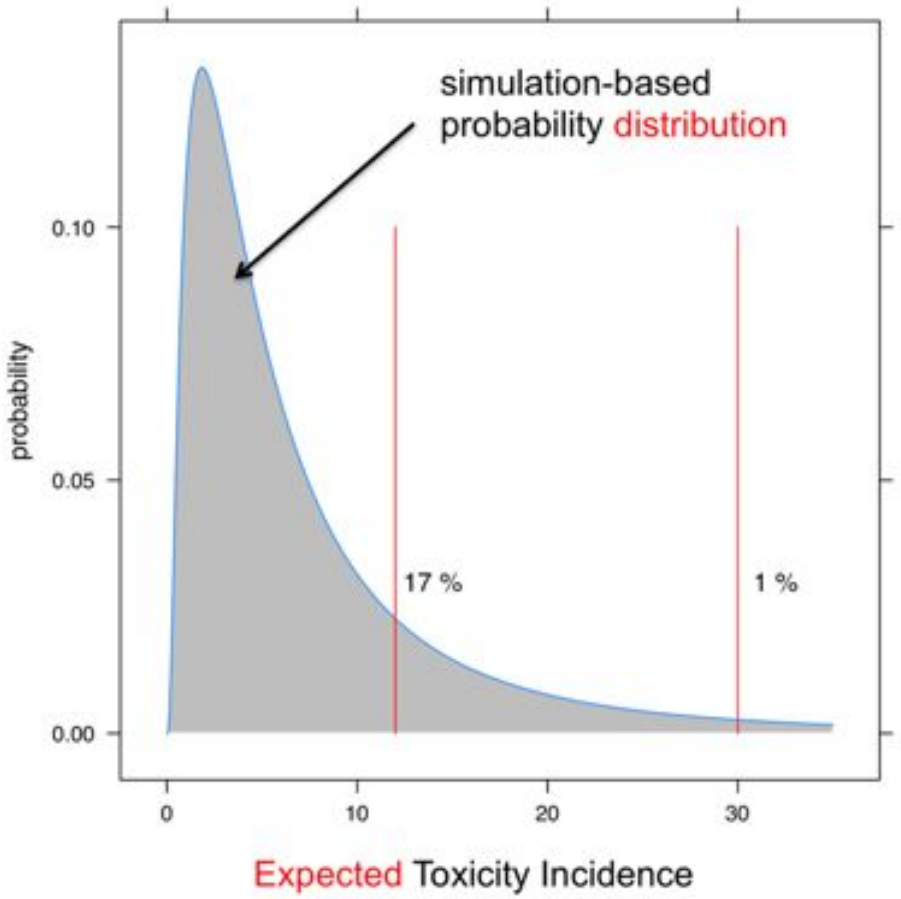
Probability of Achieving Quantitative Criteria

Key Question: Is toxicity a concern at this dose?

Quantitative Translation: To be competitive with SOC, toxicity incidence must be less than 30%. What's the probability?

What's the probability that tox incidence < 12%?

Defining quantitative criteria is key to formulating M&S strategy.



“So often people are working hard at the wrong thing. Working on the right thing is probably more important than working hard.”

– Caterina Fake

Shared Ownership in Decision-Making Collaboration

"Which dose(s) provides the best balance of safety and efficacy according to these criteria?"

Endpoints	Target Criteria (minimum)	Target Criteria (optimum)
EFFICACY_A	80% of patients with response >= competitor response at week 24	80% of patients with response at least 10% better than competitor response at week 24
EFFICACY_B	Mean response of at least 15% change from baseline	Mean response of at least 25% change from baseline
SAFETY_1	Incidence < 10%	Incidence < 5%
SAFETY_2	80% of patients with response <= competitor	80% of patients with response 10% better than competitor

Shared Ownership in Decision-Making Collaboration

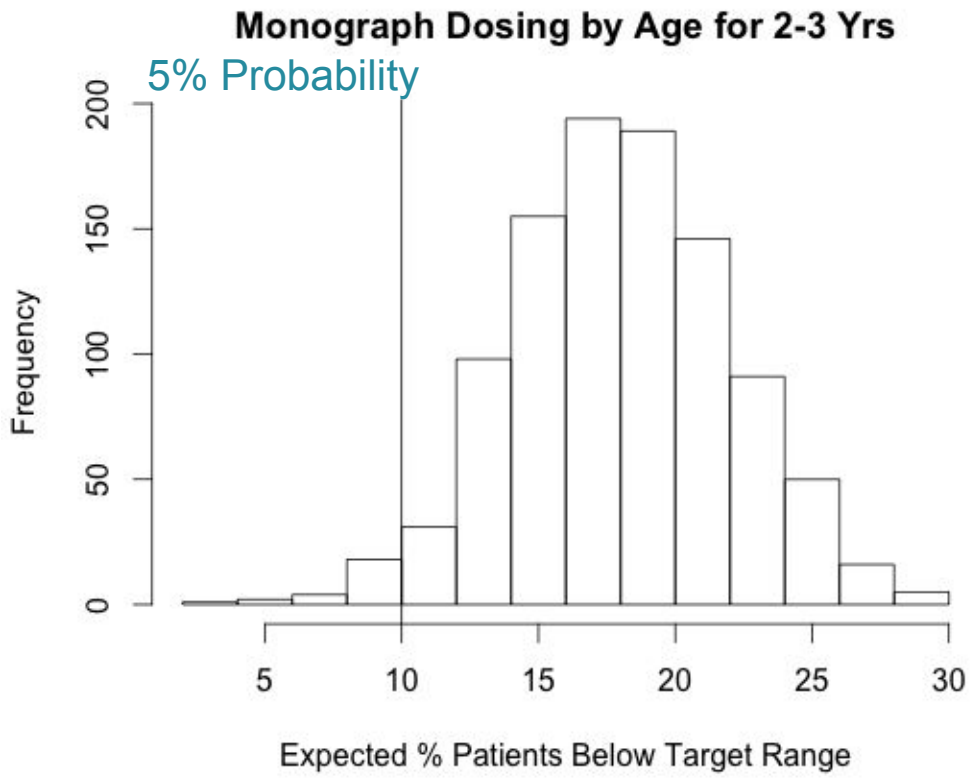
Quantitative specification of weighted clinical utility function.

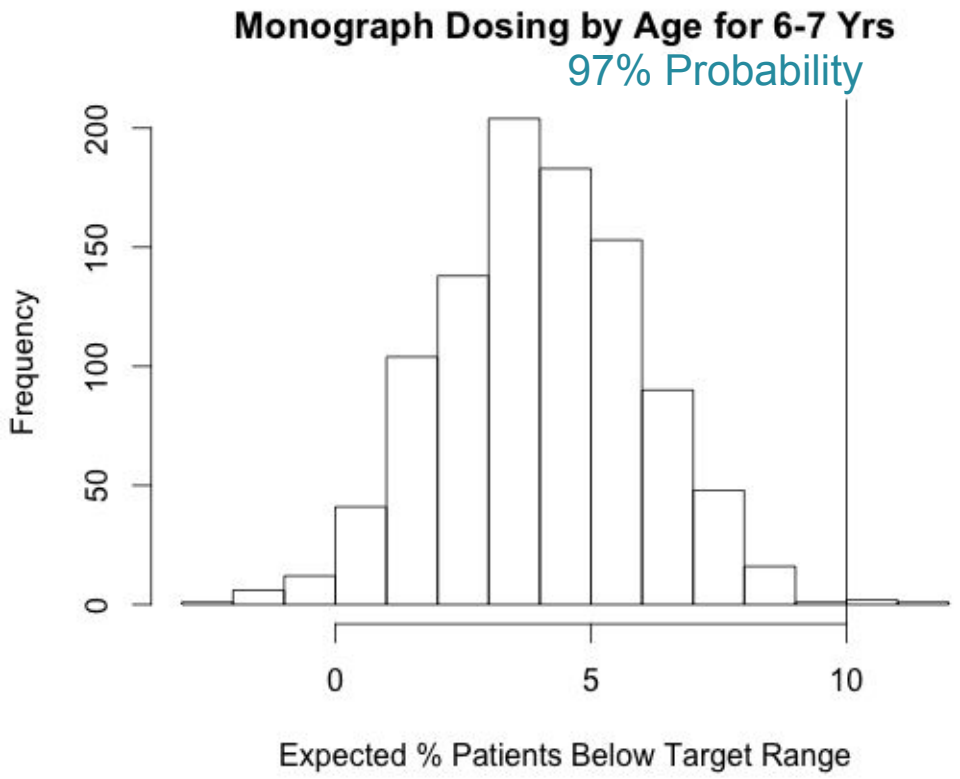
Endpoints	Target Criteria (minimum)	Target Criteria (optimum)	Weight
EFFICACY_A	80% of patients with response >= competitor response at week 24	80% of patients with response at least 10% better than competitor response at week 24	0.3
EFFICACY_B	Mean response of at least 15% change from baseline	Mean response of at least 25% change from baseline	0.2
SAFETY_1	Incidence < 10%	Incidence < 5%	0.3
SAFETY_2	80% of patients with response <= competitor	80% of patients with response 10% better than competitor	0.2

Probability of Achieving Target Exposure

Key Question: Are exposures in children similar to adults with this dosing rule?

Quantitative Criteria: What's the probability fewer than 10% of patients will be below target with this dosing rule?





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Decision

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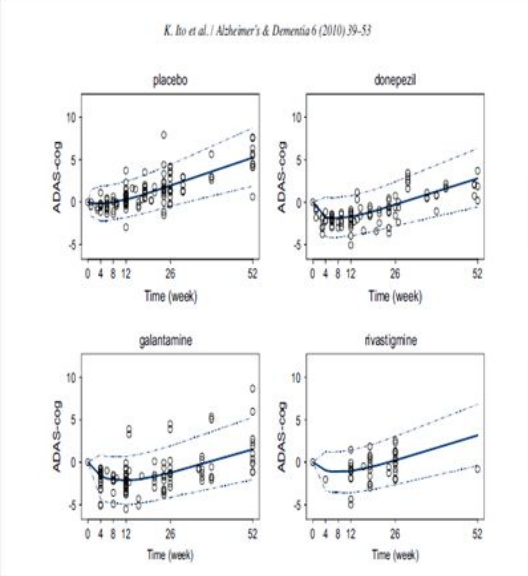
Model Based Decision-Making: Alzheimer's Disease

Literature Meta-Data

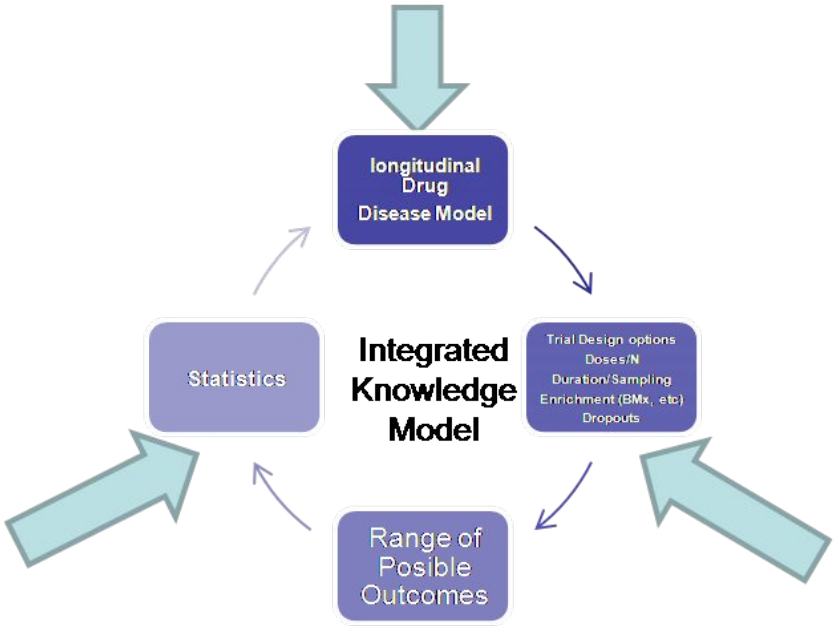


- 73 Trials (1990 to Present)
- Interstudy variability
- Estimate of drug treatment effects (magnitude, onset, offset)

ADNI Defining Alzheimer's Disease
www.adni-info.org

- Natural History
- Interpatient Variability
- Patient Specific Factors
- Imaging and CSF Biomarkers

Sub-populations
Normal (N=200)
MCI (N=400)
Mild AD (N=200)



CAMD
CRITICAL PATH INSTITUTE
c-path.org/programs/cpad/

- 9 trials, 3223 patients
- Interpatient Variability
- Patient Specific Factors
- Placebo Effect

J Pharmacokinet Pharmacodyn
DOI 10.1007/s10928-012-9263-3

ORIGINAL PAPER

Combining patient-level and summary-level data for Alzheimer's disease modeling and simulation: a beta regression meta-analysis

James A. Rogers · Daniel Polhamus · William R. Gillespie · Kaori Ito · Klaus Romero · Ruolun Qiu · Diane Stephenson · Marc R. Gastonguay · Brian Corrigan

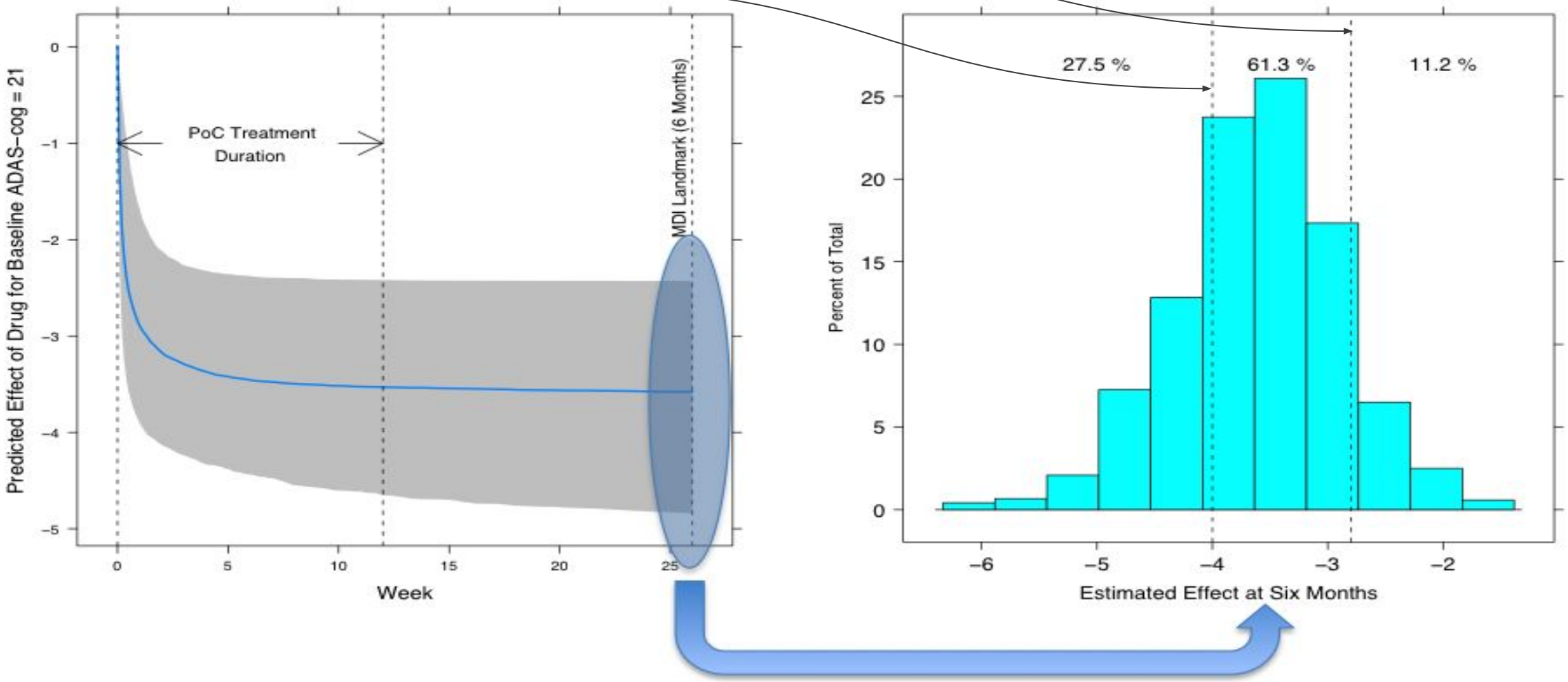
Objective:

Develop a model to describe the longitudinal progression of ADAS-cog in Alzheimer's disease patients in both natural history and randomized clinical trial settings, utilizing both IPD and AD.

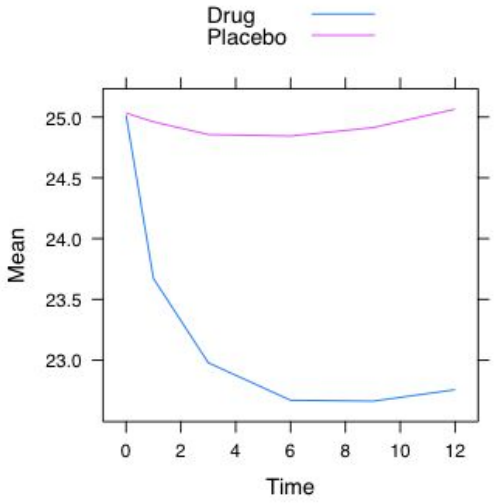
Model-Based Projection of Decision Criteria

Target product response for change in typical ADAScog score at 6 months:

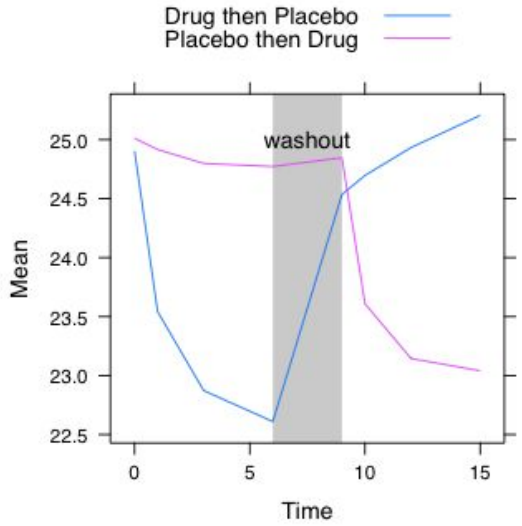
- must have -2.5 units
- wish for -4 units



Exploring POC Trial Design Performance



Given quantitative criteria, explore decision making performance under different assumptions about true drug characteristics.



Assuming drug reaches 50% of maximal effect at 4 weeks:

12 Week Parallel Design

Truth	Decision GO	NO GO
$E(6) = 2$	0%	100%
$E(6) = 4.5$	92%	8%

6 Week Cross-over Design

Truth	Decision GO	NO GO
$E(6) = 2$	10%	90%
$E(6) = 4.5$	92%	8%

$E(6)$ denotes placebo-adjusted drug effect at 6 months;
Table percentages based on 100 simulations

Polhamus D, Rogers J, Gillespie W, French J, and Gastonguay M. From Evidence Synthesis to Trial Optimization: The adsim Package for Model-based Simulation in Alzheimer's Disease PAGE 21 June 2012 (http://metrumrg.com/assets/pubs/page_2012_polhamus.pdf)

Model-Based Indirect Comparison of Efficacy

- Linagliptin (10 trials) vs. Sitagliptin (15 trials)
- No trials with head-to-head comparison

- **Key Question**: Are these drugs different with respect to efficacy?
- **Quantitative Translation**: What's the **probability** that the placebo-adjusted difference in mean change from baseline HbA1c at 24 weeks between Linagliptin (5mg) and Sitagliptin (100mg) is less than +/- 0.1%?

Indirect Comparative Efficacy

Open Access Research

BMJ open accessible medical research

A novel model-based meta-analysis to indirectly estimate the comparative efficacy of two medications: an example using DPP-4 inhibitors, sitagliptin and linagliptin, in treatment of type 2 diabetes mellitus

Jorge Luiz Gross,[1] James Rogers,[2] Daniel Polhamus,[2] William Gillespie,[2] Christian Friedrich,[3] Yan Gong,[4] Brigitta Ursula Monz,[4] Sanjay Patel,[5] Alexander Staab,[3] Silke Retlich[3]

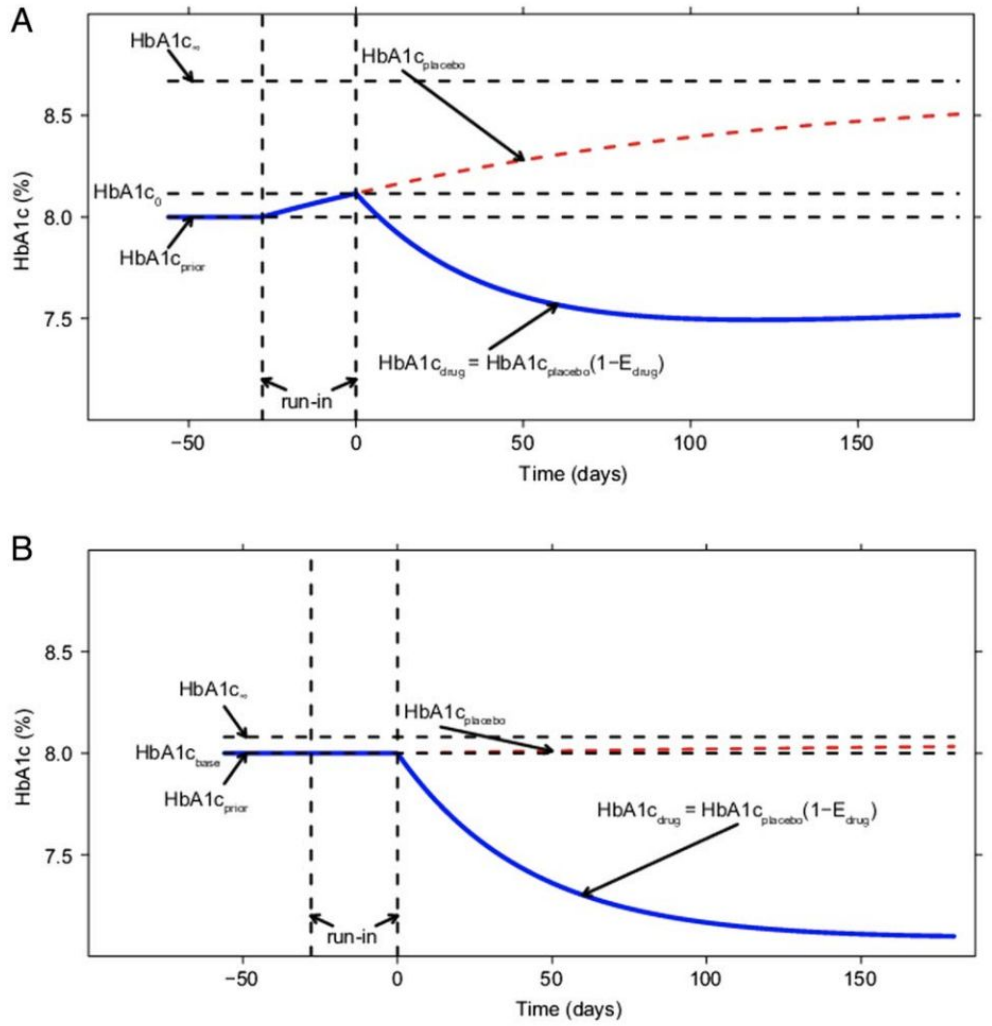
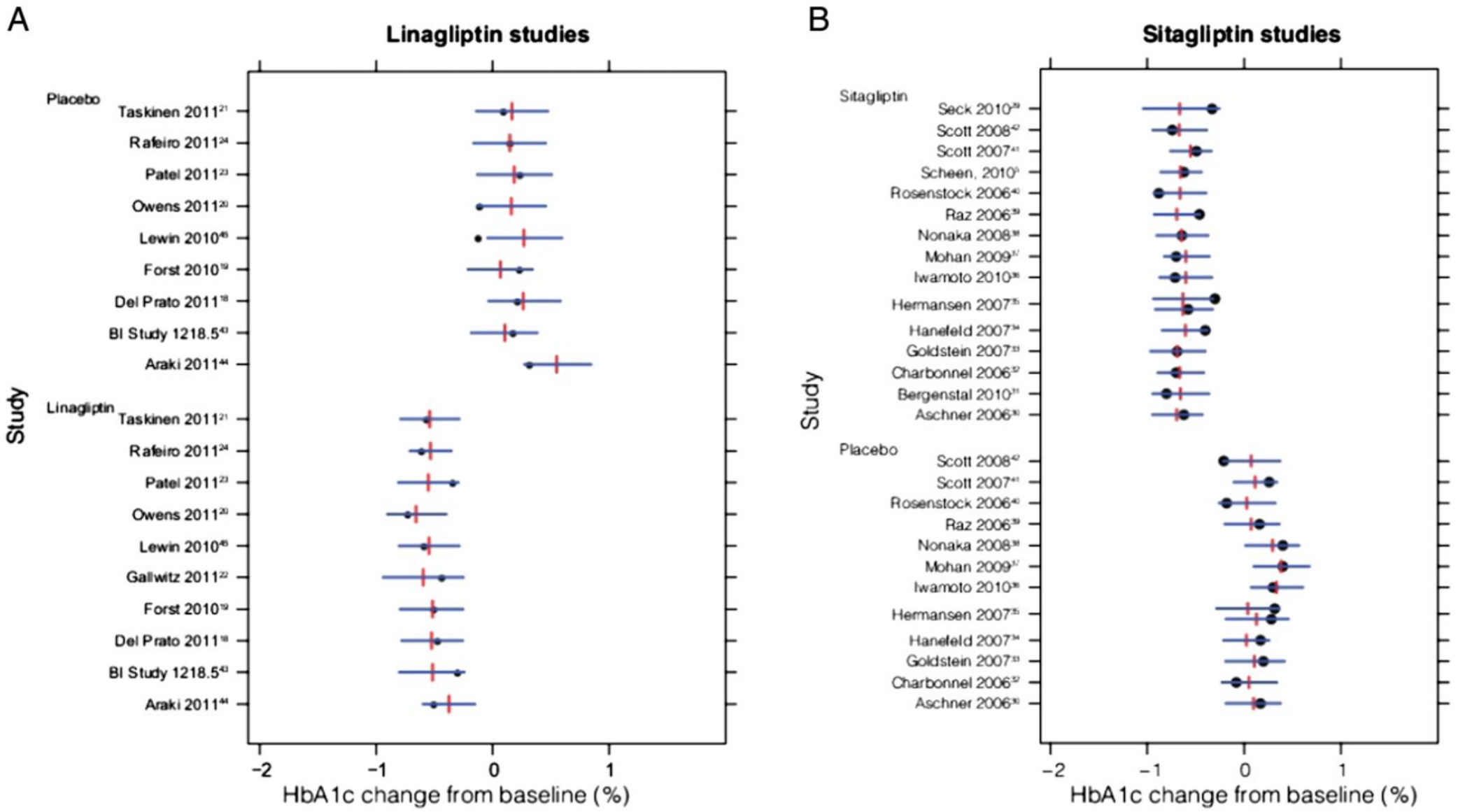


Figure 1 (A) Graphic representation of the components of the final model, for study arms that included patients washing out their prior antihyperglycaemic medication in the run-in period. (B) Graphic representation of the components of the final model, for study arms that included patients who were treatment-naïve or had completely washed out their prior antihyperglycaemic medication before enrolment.

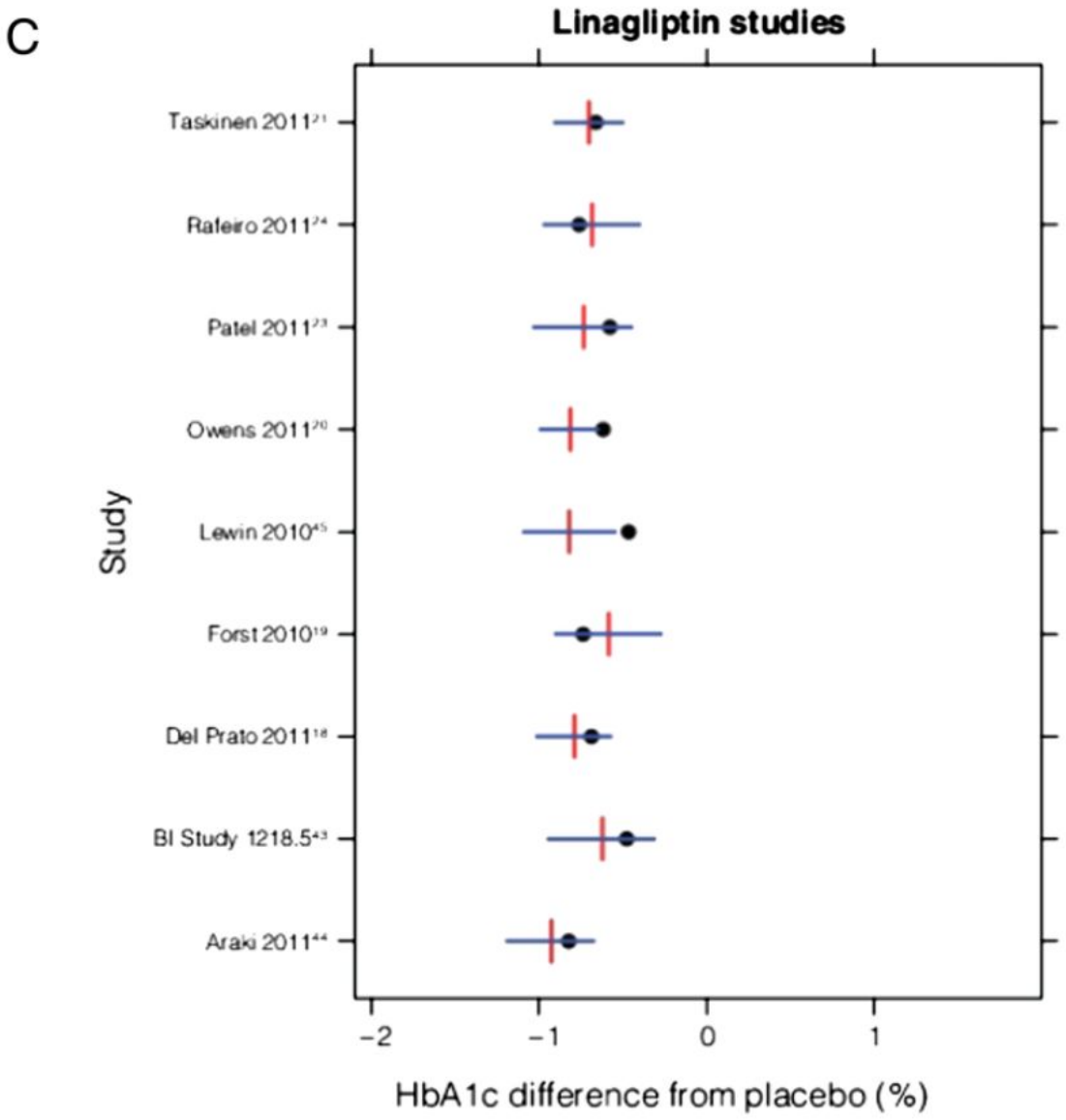
Gross JL, Rogers J, Polhamus D, Gillespie W, Friedrich F, Gong Y, Monz BU, Patel S, Staab A, Retlich S. A novel model-based meta-analysis to indirectly estimate the comparative efficacy of two medications: an example using DPP-4 inhibitors, sitagliptin and linagliptin, in treatment of type 2 diabetes mellitus. BMJ Open 2013, 3:e001844.

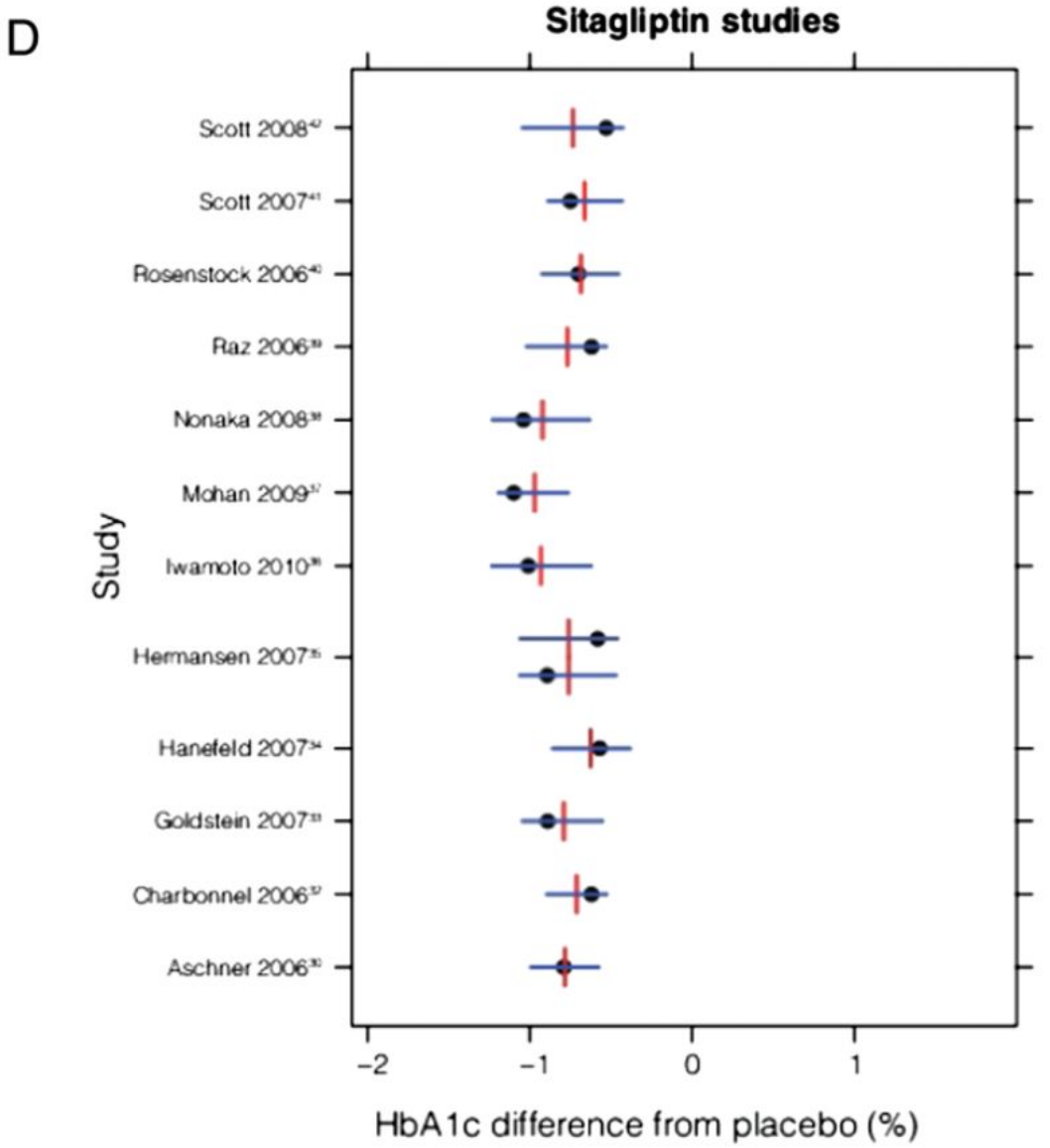
Trial Summary Data: HbA1c Change from Baseline



Gross et al BMJ Open 2013, 3:e001844.

Trial Summary Data: HbA1c Difference from Placebo





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Probability Distribution for Expected Response Difference

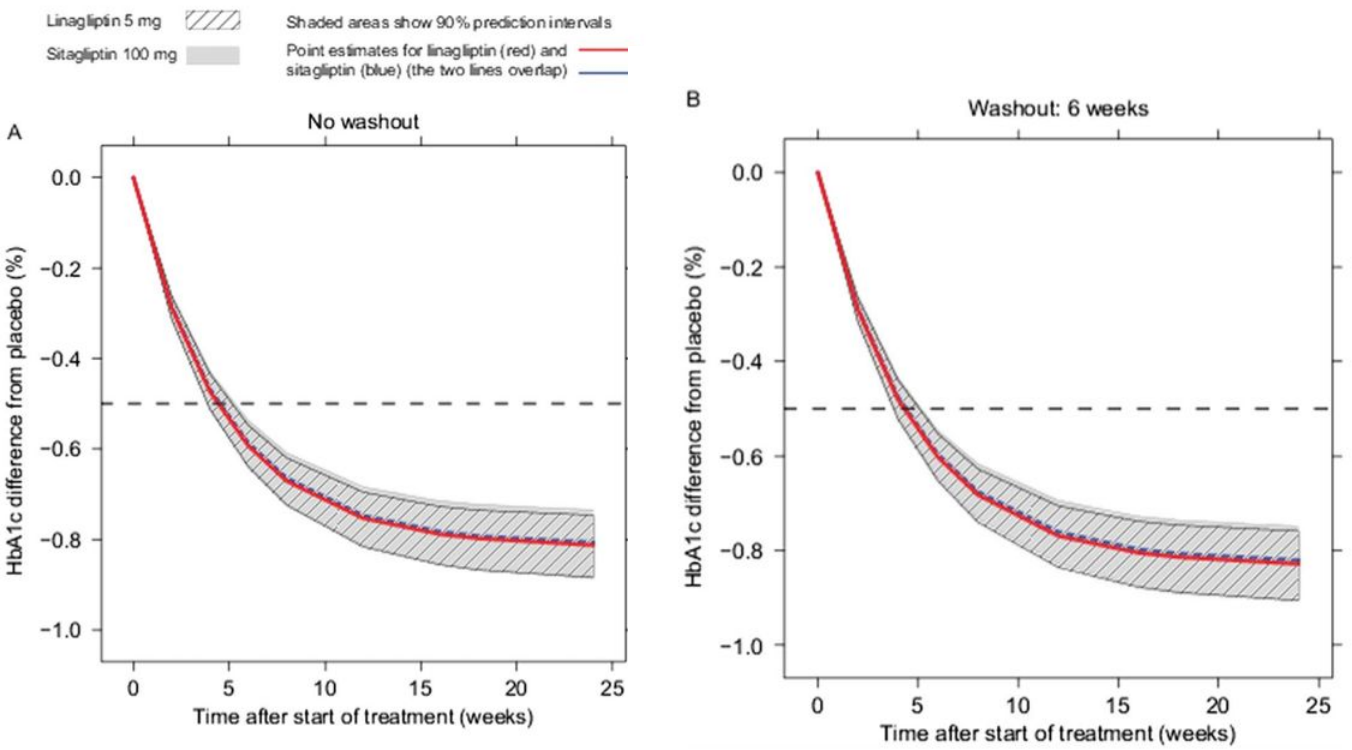


Figure 4 (A) Estimated drug effects on glycated haemoglobin (HbA1c) for reference population, with no pretreatment washout, over 24 weeks (difference from placebo). (B) Estimated drug effects on HbA1c for reference population, with 4-week washout plus 2-week placebo run-in period, over 24 weeks (difference from placebo). Reference population of 1000 participants, baseline HbA1c: 8%, racial composition: 61.5% White, 1.5% Black, 37% Asian.

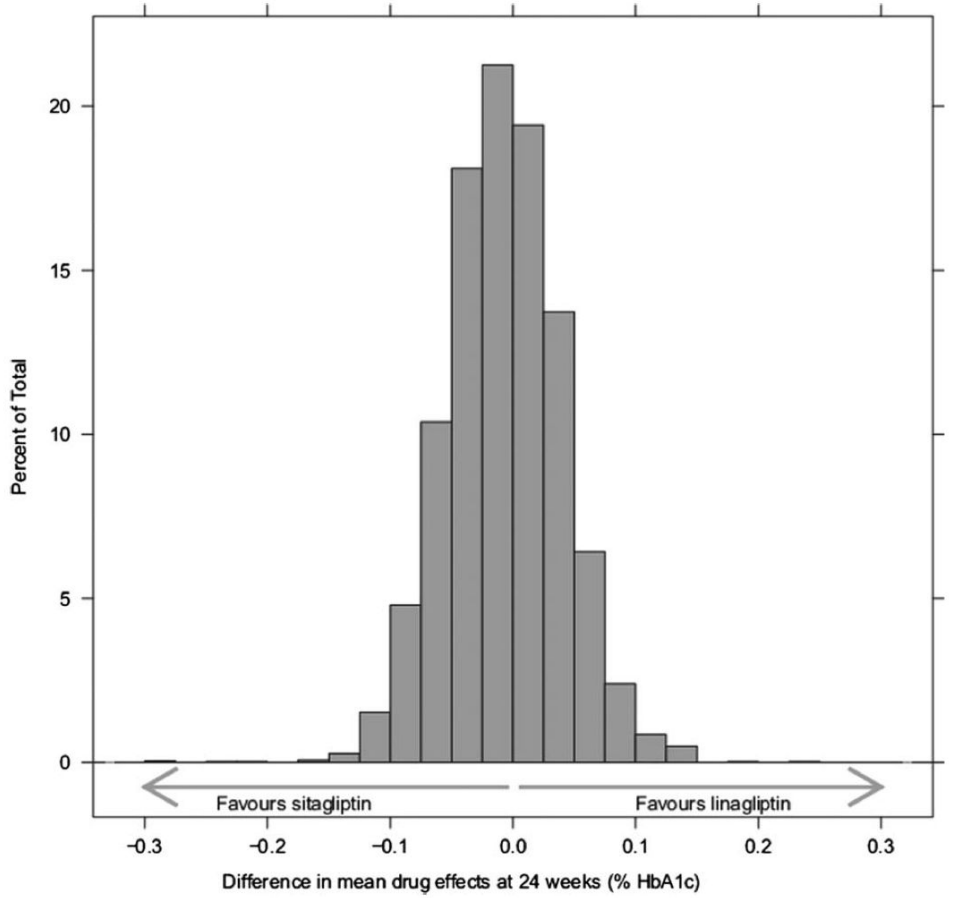
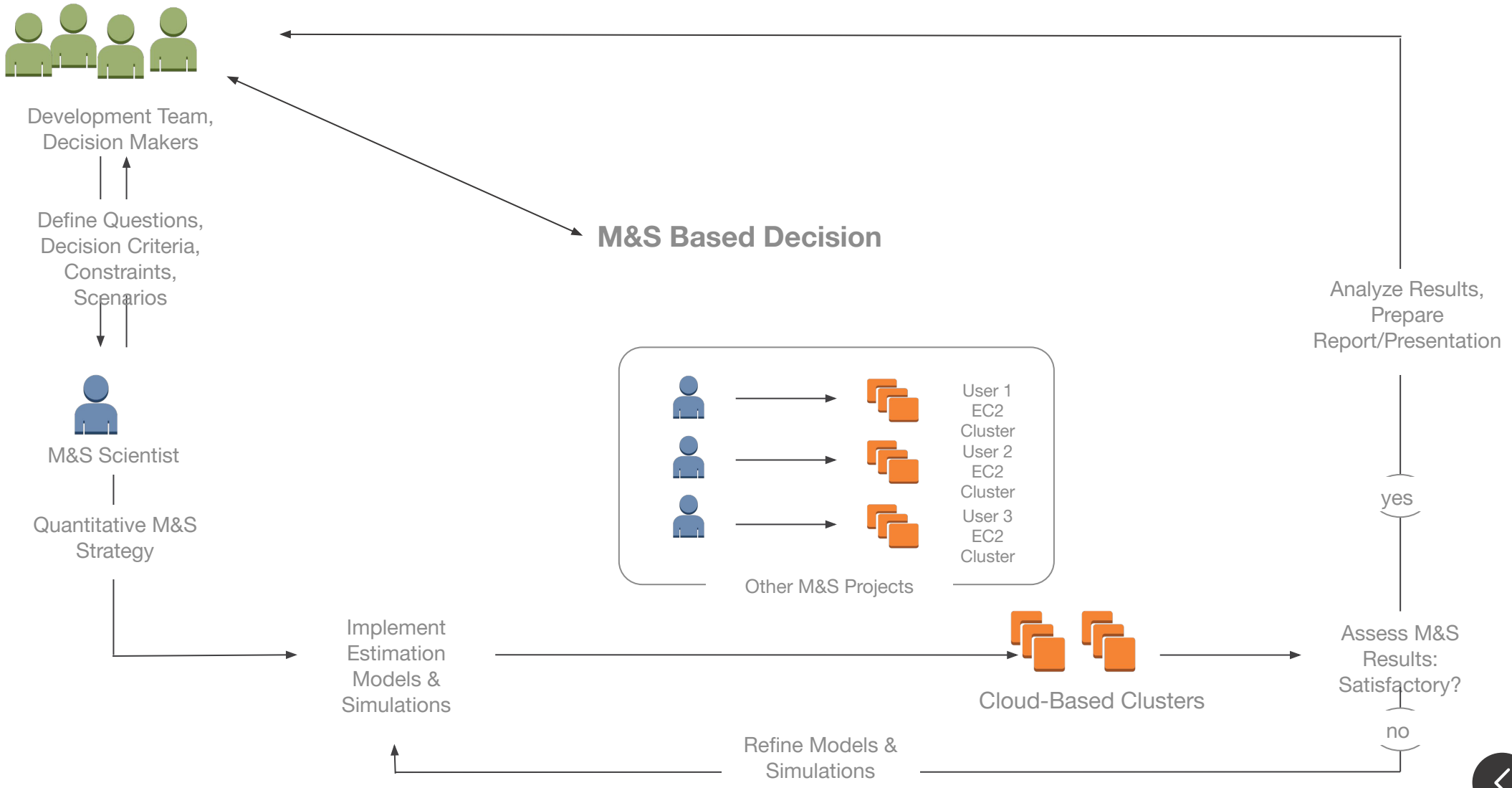


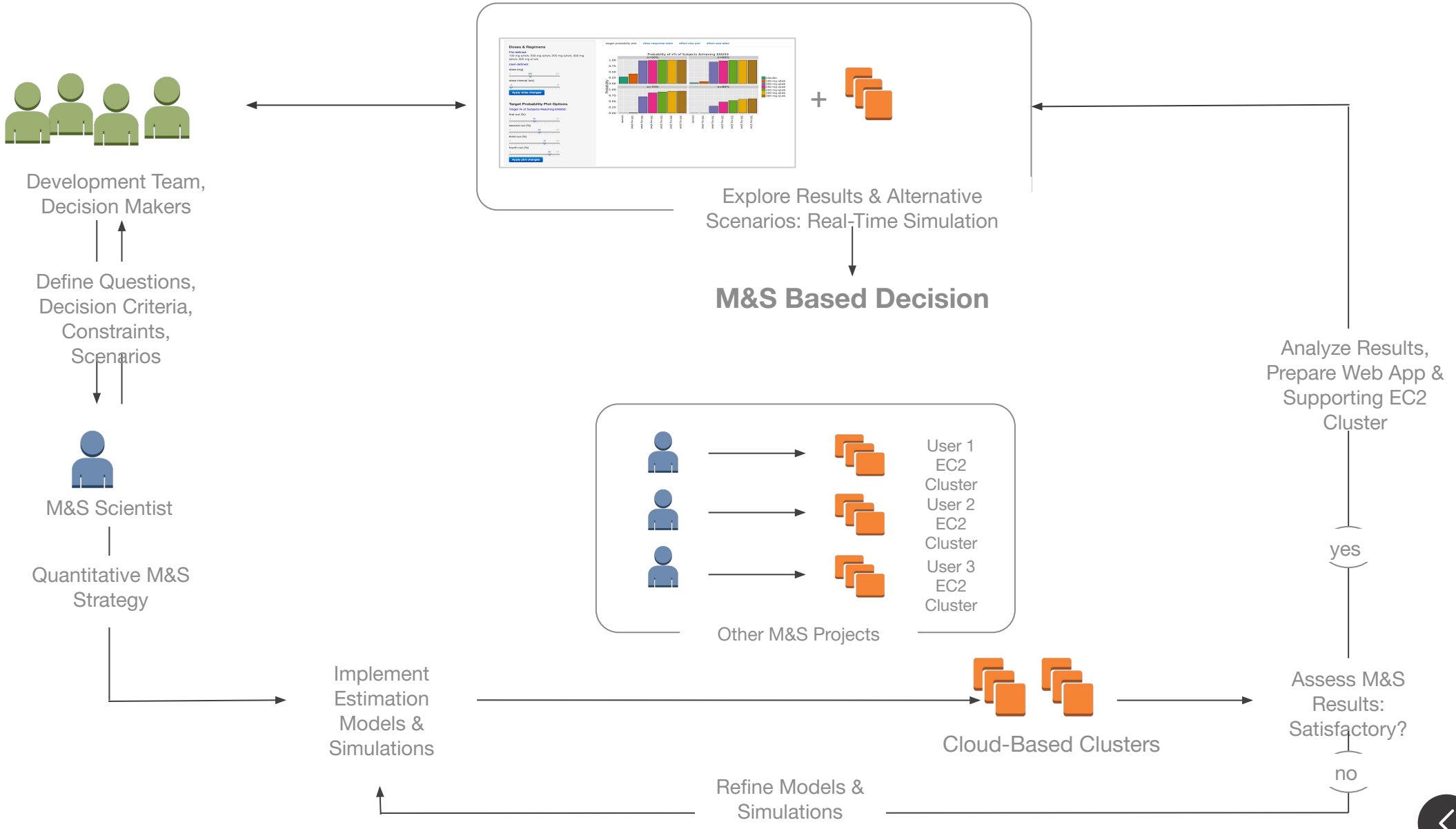
Figure 5 Posterior distribution for the difference in effect estimates between linaglitpin (5 mg) and sitagliptin (100 mg) at 24 weeks. Reference population of 1000 participants (therefore involving 10^6 simulated patients), baseline glycated haemoglobin (HbA1c): 8%, racial composition: 61.5% White, 1.5% Black, 37% Asian.

Gross et al BMJ Open 2013, 3:e001844.

Simulation Based Scenario Evaluation



Interactive Scenario Evaluation



Toujeo Real World Evidence Trial Simulation: Data Sources

(4 studies, ~26 Gb of SAS data)

4,681 patients over 4 trials

126,548 relevant lab records →
29,012 HgbA1c labs

(> 300 GB, ~2 billion records of structured data & metadata)

~ 3,000,000 patients

~ 400,000 HgbA1c labs

314,292 patients → ~ 65, 000 T2DM patients
4917 patients with ≥2 long acting Insulin outpatient prescriptions that are at least 30D apart (life)

Slide courtesy of Jeffrey Barrett, ACoP 2017

Dashboard | RStudio - git-SAN0101F | RWE Simulator | James

https://i-e7be0648.metworx.com/envision/rwe_simulator/

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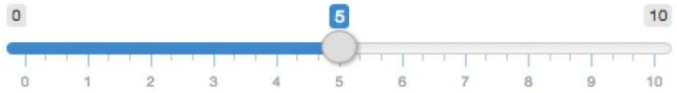
RWE Simulator | Data Sources | Demographics | Lantus / SOC | Toujeo | Simulation Summary | Advanced

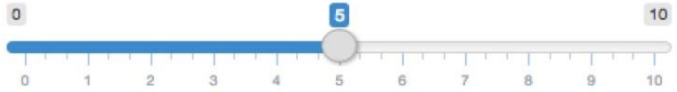
Population Specification

Weight for each data source

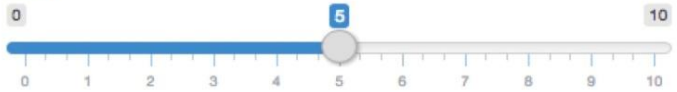
Edition3



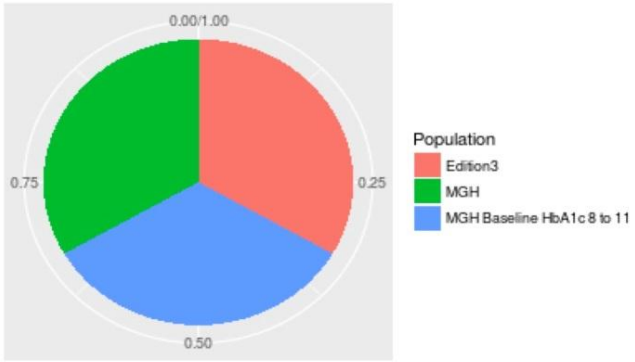
MGH Baseline HbA1c 8 to 11



MGH



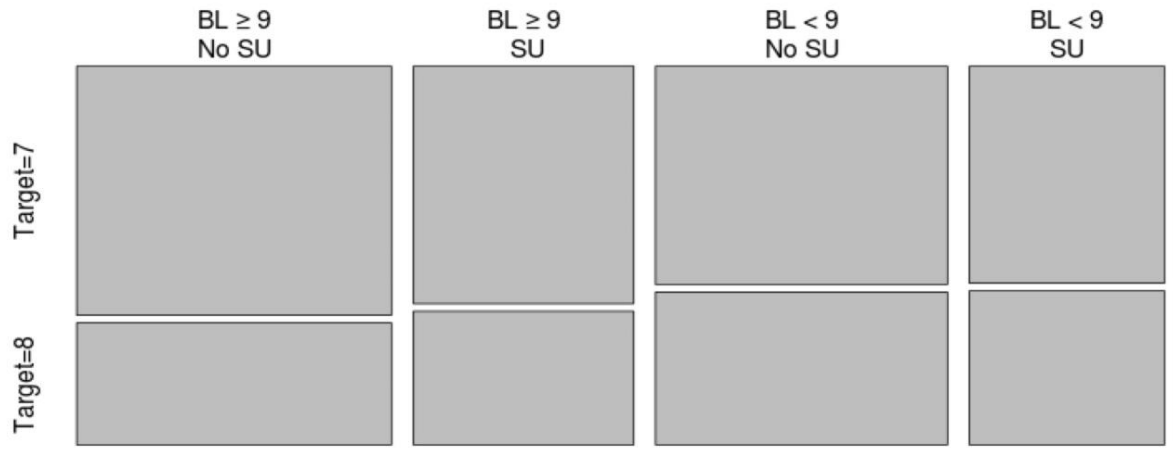
Summary of relative weights



Relative weighting of populations

Summary of Specified Population

%	BL ≥ 9 No SU	BL ≥ 9 SU	BL < 9 No SU	BL < 9 SU	Marginal Total
Target=7	20.7	13.8	16.8	11.2	62.5
Target=8	10.1	7.8	11.8	7.9	37.5
Marg. Tot.	30.8	21.6	28.6	19.1	100.0



Slide courtesy of Jeffrey Barrett, ACoP 2017

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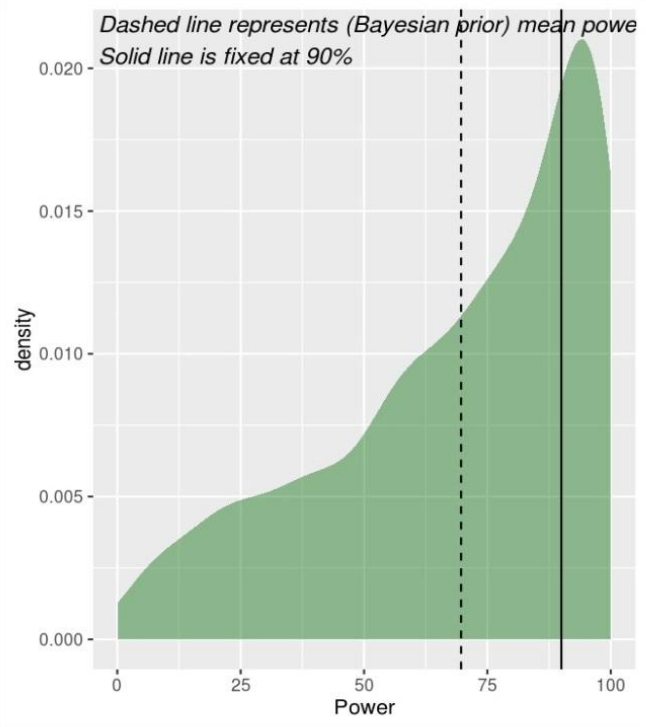
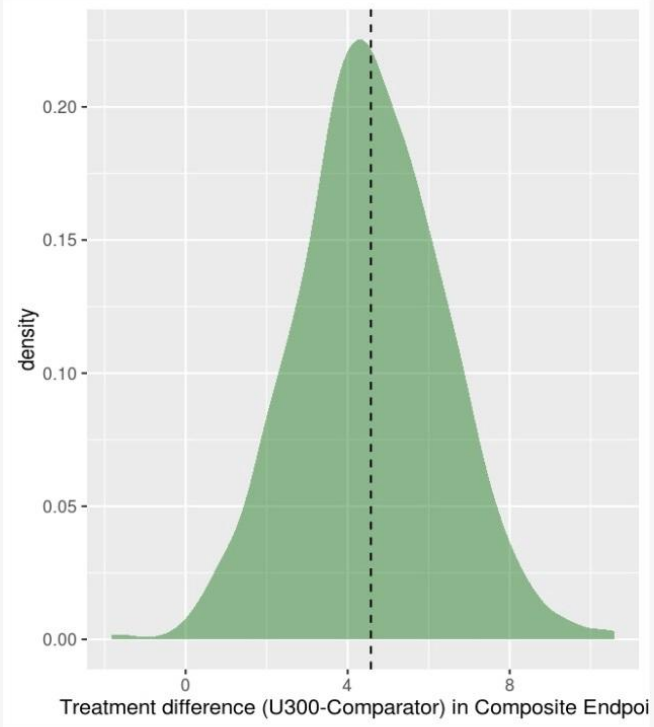
RWE Simulator | Data Sources | Demographics | Lantus / SOC | Toujeo | Simulation Summary | Advanced

Probability of Success



Difference in Composite Event Rates



Current Scenario Statistics

	Estimate (%)
Toujeo Composite Endpoint Rate	38.96
Lantus / SOC Composite Endpoint Rate	34.38
Expected Treatment Difference (U300-Comparator)	4.57
Average (Bayesian Predictive) Power	69.70

EDITION 3

Save Scenario

Saved scenarios can be reviewed by toggling to "Multi-scenario Summary" on the Navigation Bar

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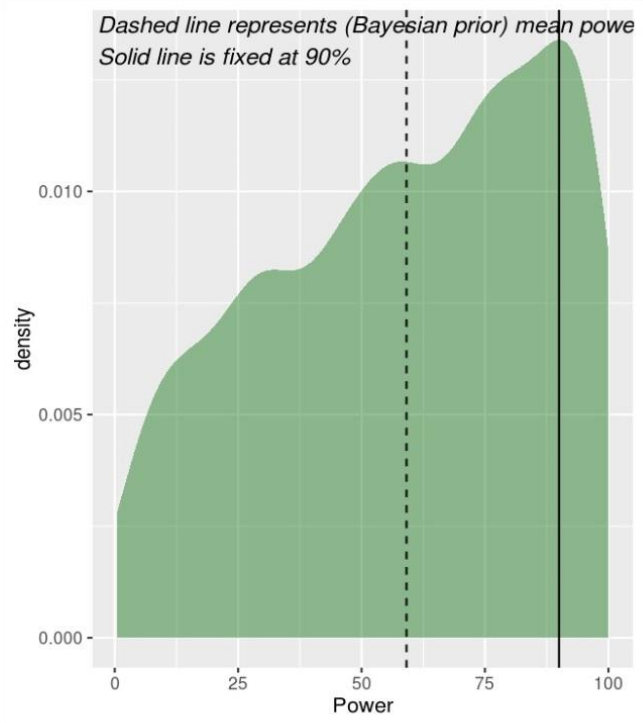
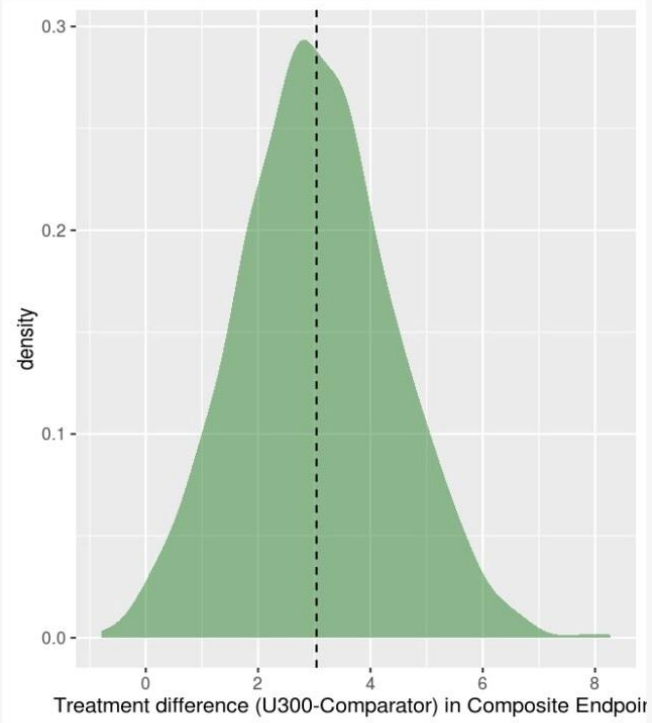


Difference in Composite Event Rates



Current Scenario Statistics

	Estimate (%)
Toujeo Composite Endpoint Rate	18.68
Lantus / SOC Composite Endpoint Rate	15.64
Expected Treatment Difference (U300-Comparator)	3.04
Average (Bayesian Predictive) Power	59.10

MGH 8-11 with E3 Effect

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Slide courtesy of Jeffrey Barrett, ACoP 2017

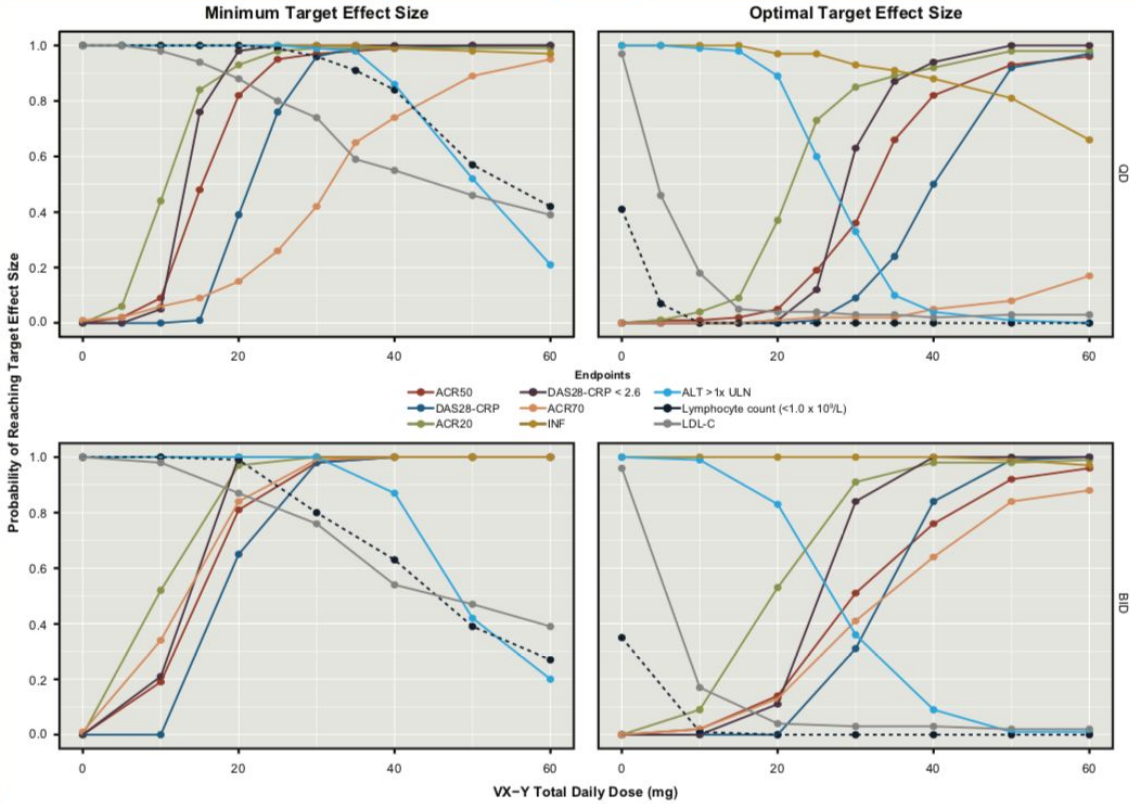
Interactive Simulation for Dose Selection

Table 1. Minimum and Optimal Target Effect Sizes and Weights for Efficacy and Safety Endpoints

Efficacy/Safety Endpoint	Minimum Target Effect Size	Optimal Target Effect Size	Weight for Efficacy or Safety Alone	Weight for Efficacy and Safety Combined (0.55 for Efficacy and 0.45 for Safety)
Efficacy endpoints				
ACR20	> +20%	> +30%	0.30	0.165
ACR50	> +15%	> +25%	0.30	0.165
ACR70	> +7%	> +15%	0.10	0.055
DAS28-CRP	< -1.0	< -1.5	0.20	0.11
DAS28-CRP < 2.6	> 7.5%	> 20%	0.10	0.055
Safety endpoints				
Serious infections	≤ 5%	≤ 2%	0.40	0.18
ALT >1x ULN	< 5%	< 2%	0.25	0.1125
Lymphocyte count (<1.0 x 10^9/L)	< 7.5%	< 3%	0.25	0.1125
LDL-C (>130 mg/dL)	< 25%	< 10%	0.10	0.045

All efficacy and safety endpoints were measured vs placebo. ULN, upper limit of normal.

Figure 2. Simulated Probabilities to Achieve Minimum and Optimal Effect Size for Efficacy and Safety Endpoints



Poster PI-127

A Novel Clinical Utility Analysis Combining Multiple Efficacy and Safety Endpoints to Support Dose Selection in Patients With Rheumatoid Arthritis

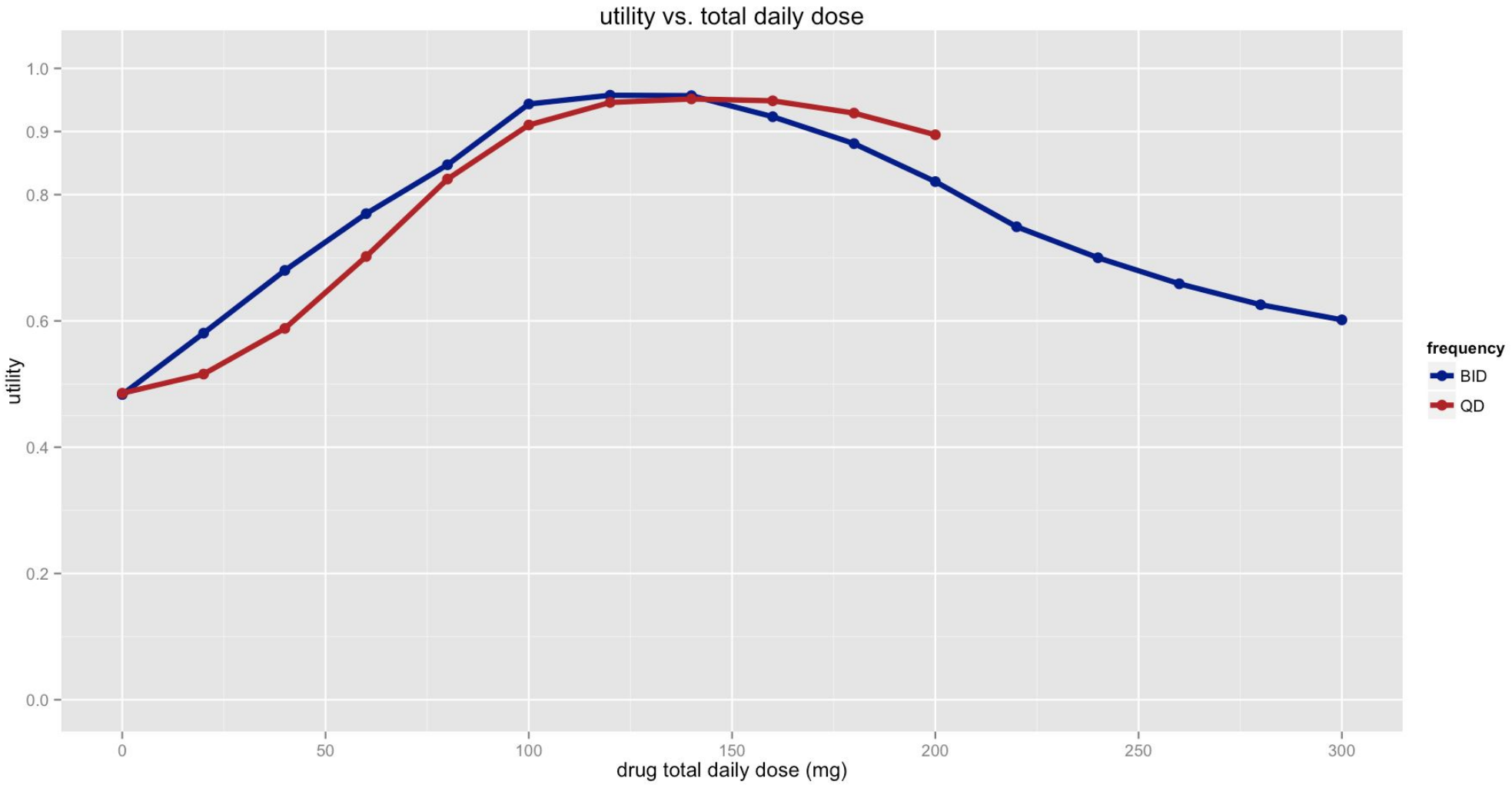
Jiayin Huang, PhD[1*]; Budda Balasubrahmanyam, PhD[1]; Matthew Riggs, PhD[2]; Kyle T. Baron, PharmD, PhD[2]; Marc R. Gastonguay, PhD[2]; Bradley Bloom, MD[3]; Nils Kinnman, MD, PhD[1]; Yanqiong Zhang, PhD[1]; Thomas Hoock, PhD[1]; Jinshan Shen, PhD[1]

1. Vertex Pharmaceuticals Incorporated, Boston, MA, USA; 2. Metrum Research Group LLC, Tariffville, CT, USA; 3. Covance Inc., Princeton, NJ, USA

ASCPT 2016.

Weighted Clinical Utility for Dose-Selection

utility plot | data view | efficacy weights | safety weights | weight summary | endpoint summary



Interactive Simulation for Pediatric Scaling

Model Inputs

Pediatric dose (mg)

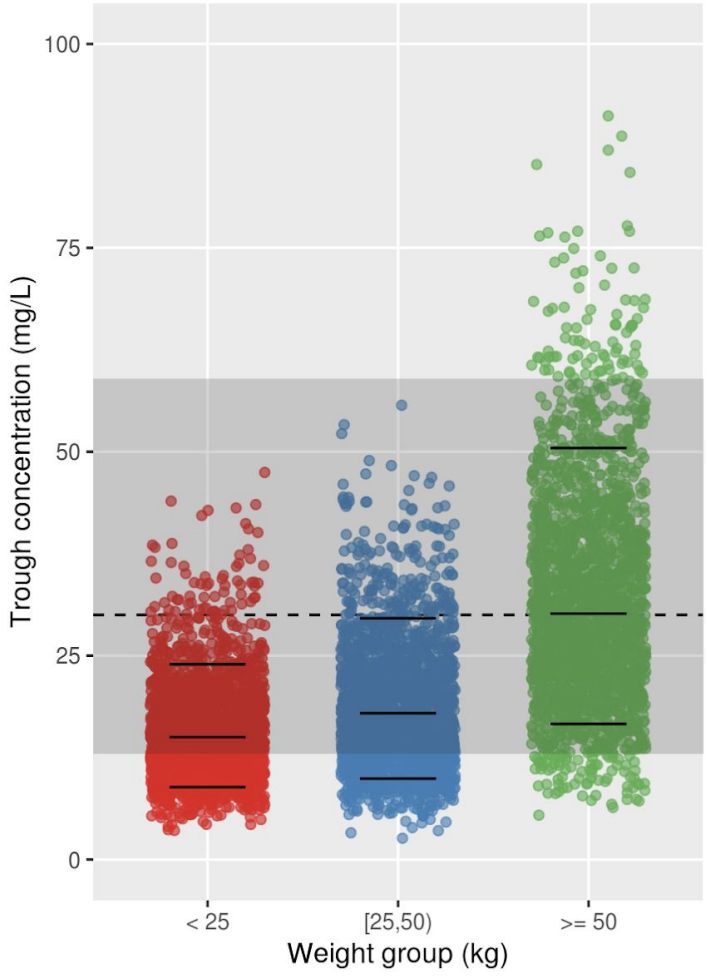
25 50 150

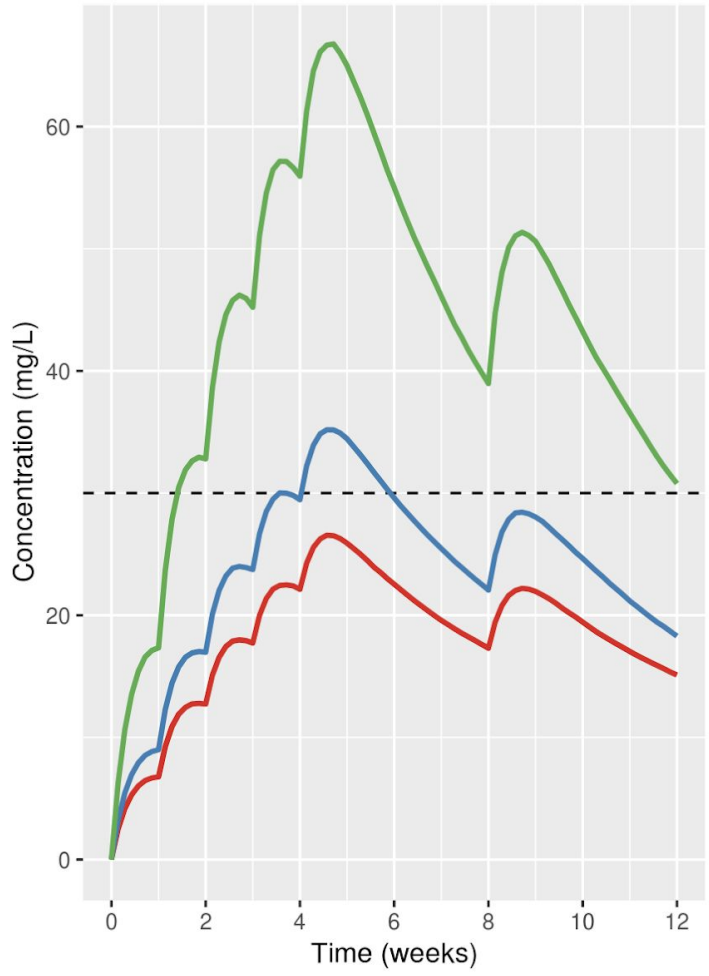
Weight groups (kg)

25 50

Model Results Up to Date

PROBLEM PLAN EXPOSURE OUTCOME





Access to Interactive Simulator Demos

Pediatric Dose Selection https://metrumrg.shinyapps.io/mrgsolve-demo-acop7/

Therapeutic Drug Monitoring https://metrumrg.shinyapps.io/tdmdosing/

AUC/MIC Target Attainment https://metrumrg.shinyapps.io/moxi/

mrgsolve & Shiny (look under the hood) https://metrumrg.shinyapps.io/getstarted/

Open Training Material https://github.com/metrumresearchgroup/model-vis-tutorial

Modeling and Simulation Based Decision Making

Start with Key Questions and Potential Decision Paths

- Probability of target product profile
- Treatment regimens
- Trial designs
- Development strategies
- Indications
- Selection of lead candidates

Models

- Drug & disease models
- Treatment population models
- Trial models
- Financial & market models

Other Information Sources

- Public evidence
- Expert opinion / belief

Simulate Outcomes of each Path or Question

Decision Criteria

- Consider cost/benefit trade-offs
  - Safety
  - Clinical utility/efficacy
  - Health Economic
  - Commercial
- Adjusted to consider the value systems of the key stakeholders
  - Patients
  - Health care providers
  - Drug developer
  - Regulators

Assumption Checking

Assess sensitivity of conclusions to uncertainties and assumptions.

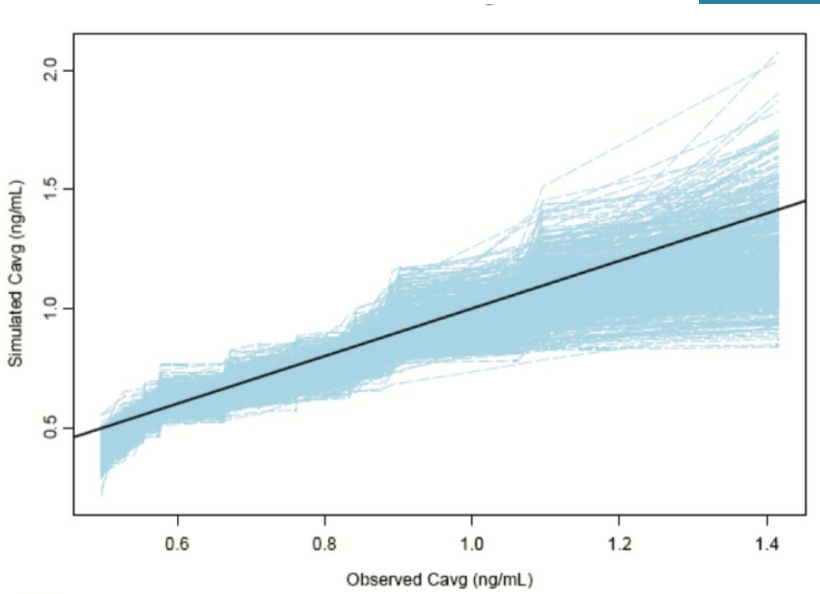
Decision

Select highest value path given the current state of knowledge.

Model and Assumption Checking

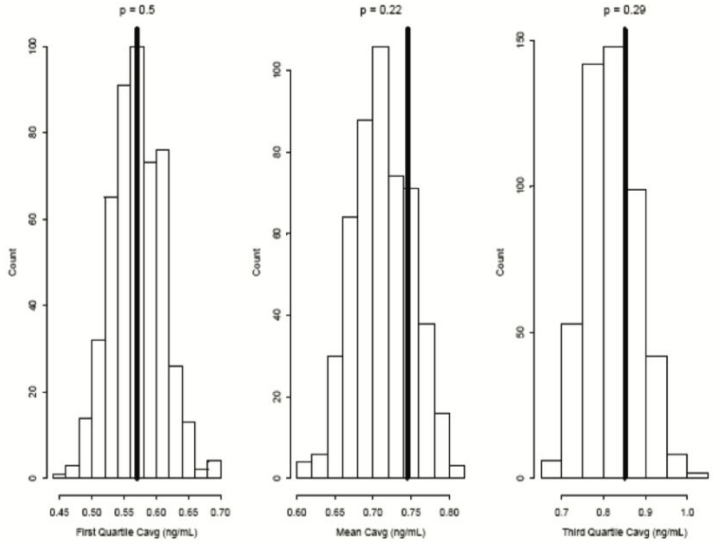
Basic Model Evaluation

- Plausibility of parameter estimates and model structure
- Compare with prior knowledge
- Convergence, global minimum, stable parameter estimates
- Goodness of fit diagnostic plots



Focused Predictive Checks

- What data features are important for decision-making?
- Raw endpoint vs change from baseline.
- Are particular timepoints critical?
  Longitudinal vs snapshot model.



Probabilistic Statements

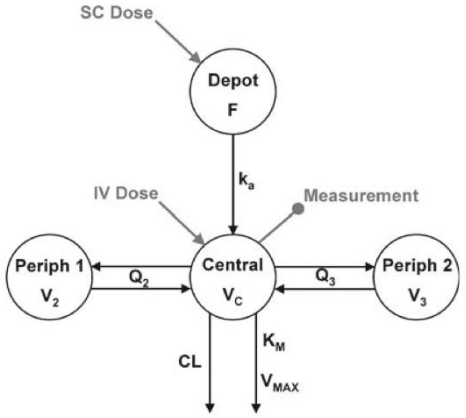
- Requires joint probability distribution of parameter uncertainty

Parameter Uncertainty & Global Sensitivity Analysis

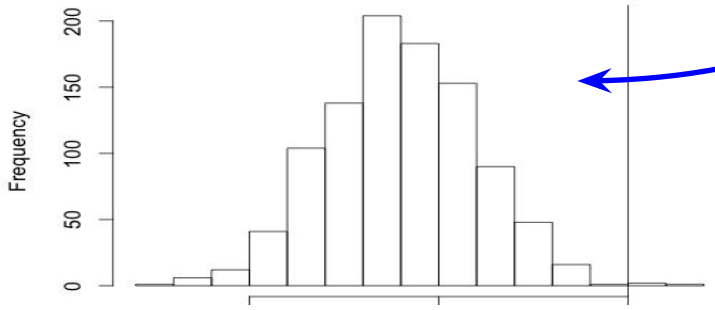
- Simulations include parameter uncertainty (e.g. posterior distributions)
- Explore sensitivity of simulation outcomes (conclusions) to range of parameter uncertainty
- Are conclusions robust to lack of knowledge?
- Which parameters are most influential?
- Are there opportunities to reduce uncertainty?

PK-PD of Fc-Osteoprotegrin and Projected Response

Fig. 1 Final compartmental model for Fc-OPG pharmacokinetics. V_C is the central compartment volume of distribution, V_2 and V_3 are the peripheral compartments' volumes, Q_p is the intercompartmental clearance between the central compartment and compartment p, CL is the linear clearance from serum, and V_{max} and K_M describe Michaelis–Menten elimination. Subcutaneously injected compound had a first-order absorption rate of k_a and a bioavailability of F. See text for more details



$$\frac{dNTX(t)}{dt} = k_{syn}\left(1 - \frac{I_{MAX}C_{OPG}(t)}{IC_{50} + C_{OPG}(t)}\right) - k_{\deg}NTX(t)$$



Typical change from baseline NTx at 336 hours

population variability and parameter uncertainty

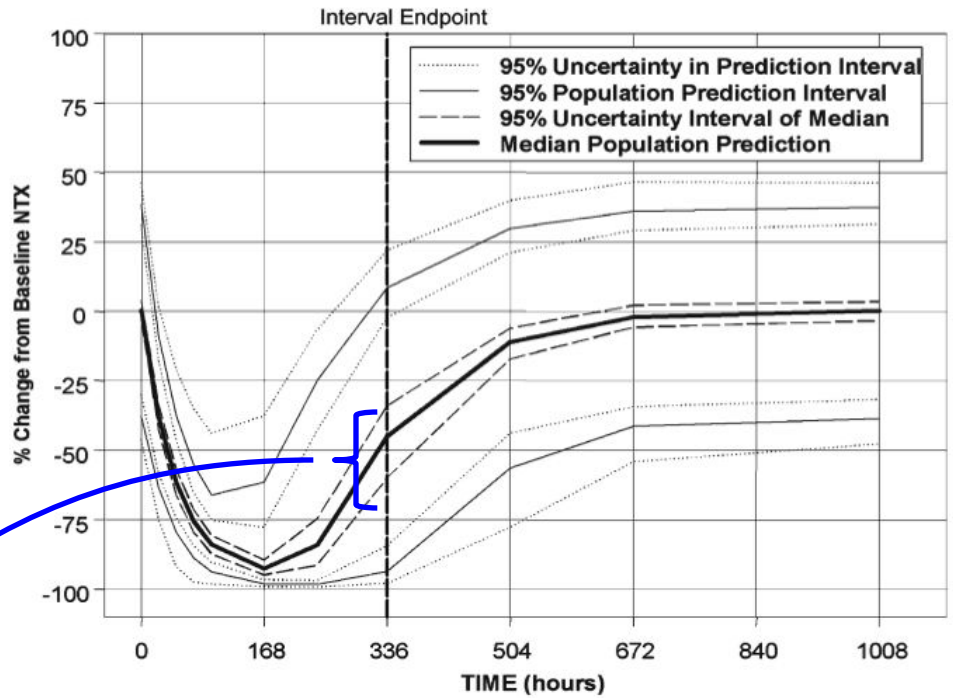
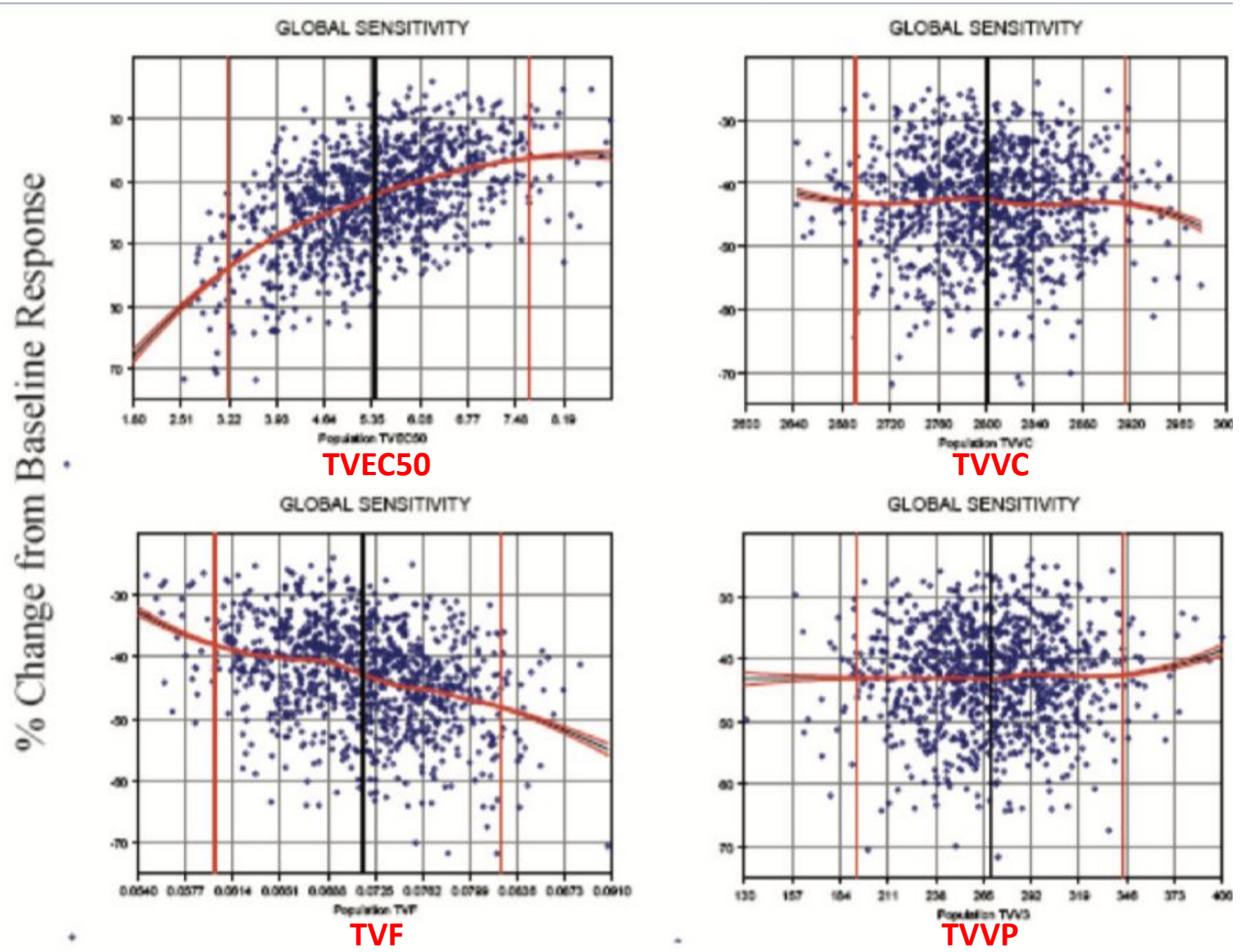


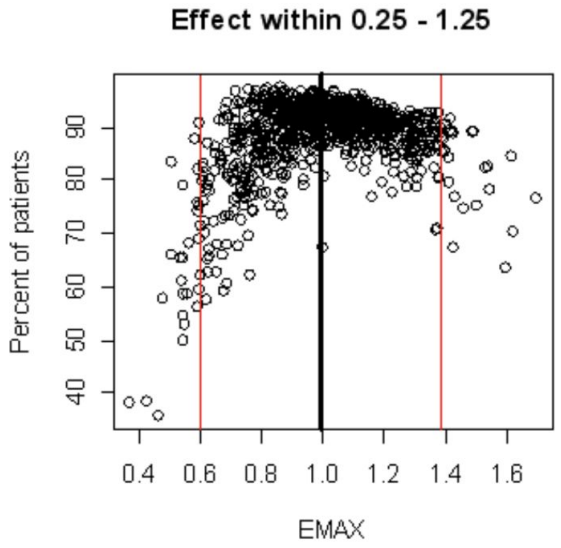
Fig. 7 Simulation of 200 replicate trials, each with 200 subjects, based on a single SC dose of 3 mg/kg, reflecting cohort 4 dosing in the original data set (body mass was assumed to be 70 kg for all subjects). The thick solid line represents the median value of all median NTX percent changes from baseline (across the 200 simulated trials; one median value is obtained from each simulated trial). The dashed lines delimit the 95% uncertainty interval for the population median value. The thin solid lines show the median values of all 95% population variability prediction intervals (across the 200 simulated trials). The dotted lines show the 95% uncertainty interval in the population 95% prediction intervals. The vertical dashed line intersects the computed profiles at 2 weeks after drug administration, and it helps to gauge visually how effective a biweekly dosing regimen might be. See text for further details

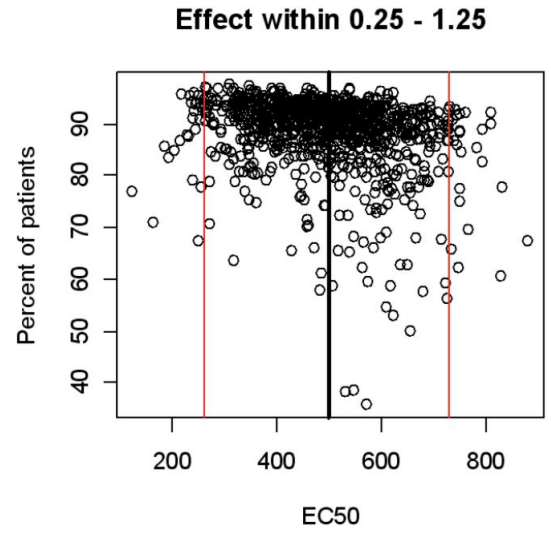
Zierhut et al. *J Pharmacokinet Pharmacodyn. 2008 Aug;35(4):379-99. Epub 2008 Jul 17.*

Global Sensitivity Analysis



Uncertainty in PD Parameters & Sensitivity Analysis





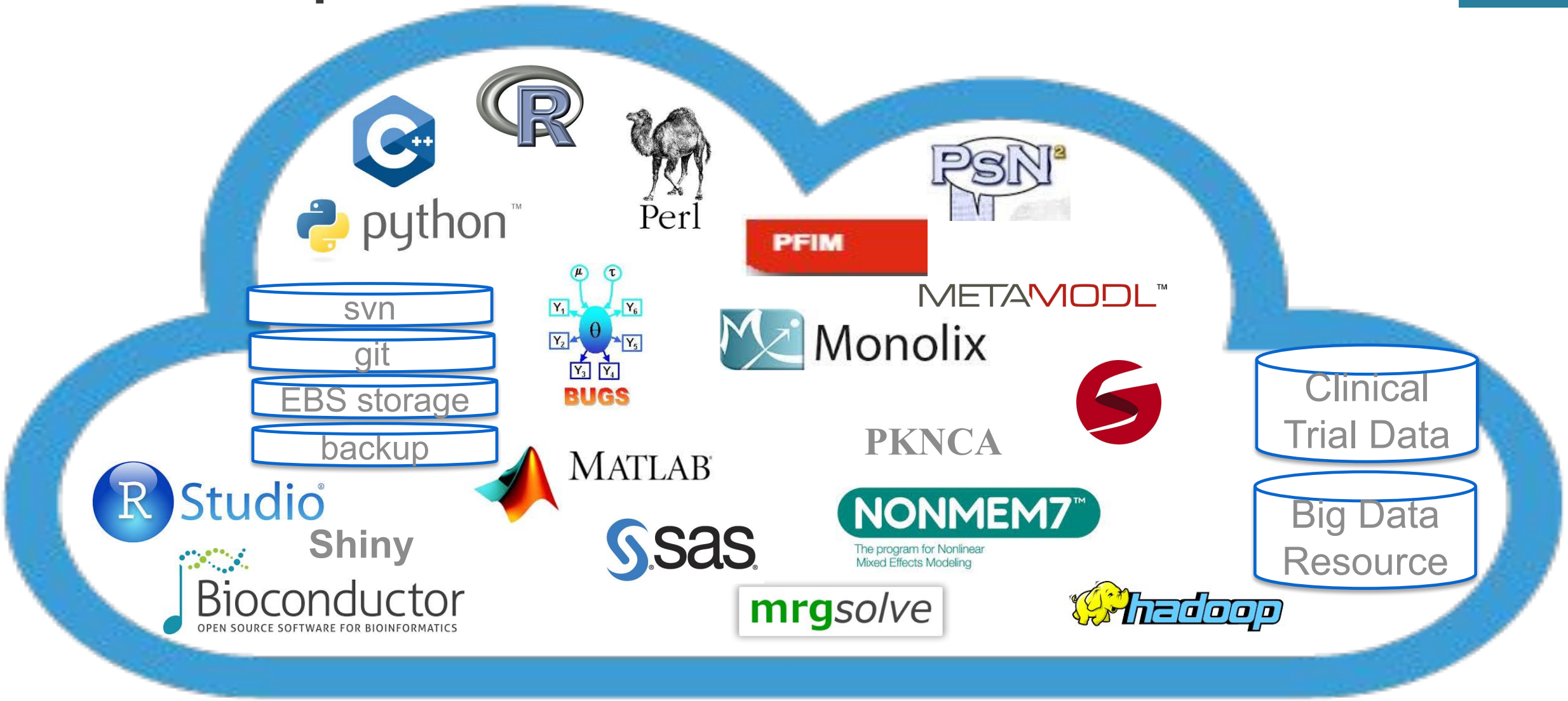
Criterion: 80% of patients within target effect range

- Conclusions depend on the value of EMAX.
- Precise knowledge of EMAX is very important to answer this question.
- Uncertainty in EC50 is less important than uncertainty in EMAX

Black: median

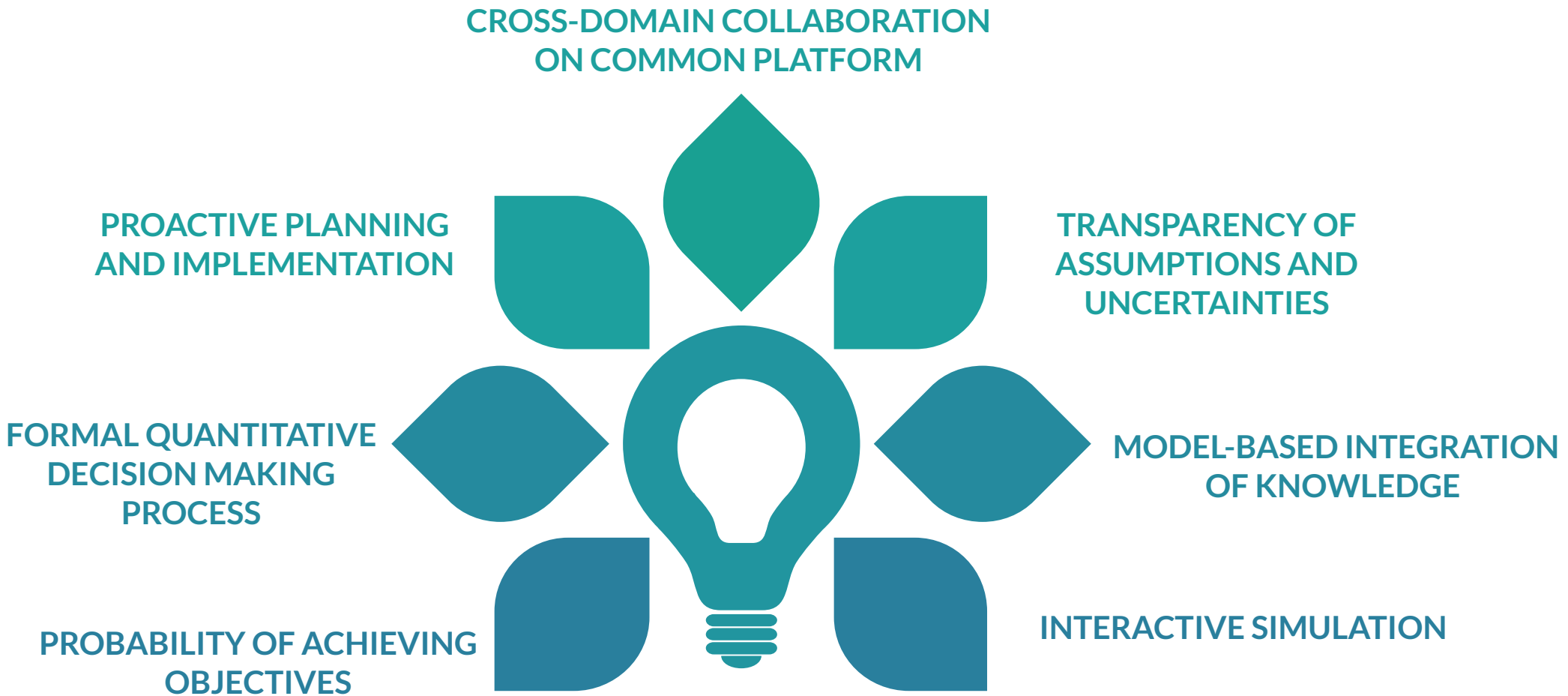
Red: 95% CI

Cross-Discipline Decision Informatics Platform



Computational & Systems Biology, Pharmacology | Pharmacometrics | Statistics, Data Science | HEOR | RWE

Opportunities for Model Based Decision-Making



Thank You

References (1)

"Decision Making in Your Organization: Cutting through the Clutter." n.d. Accessed March 10, 2019. https://www.mckinsey.com/business-functions/organization/our-insights/decision-making-in-your-organization-cutting-through-the-clutter.

Kahneman, Daniel, and Patrick Egan. 2011. Thinking, Fast and Slow. Vol. 1. Farrar, Straus and Giroux New York.

Kahneman, Daniel, Dan Lovallo, and Olivier Sibony. n.d. "A Structured Approach to Strategic Decisions | MIT Sloan Management Review." MIT Sloan Management Review. Accessed March 9, 2019. https://sloanreview.mit.edu/article/a-structured-approach-to-strategic-decisions/.

Luoma, Jukka. 2016. "Model-Based Organizational Decision Making: A Behavioral Lens." European Journal of Operational Research 249 (3): 816–26.

McGregor, Jena. 2019. "Analysis." The Washington Post, March 4, 2019. https://www.washingtonpost.com/business/2019/03/04/nobel-prize-winning-psychologist-ceos-dont-be-so-quick-go-with-your-gut/.

References (2)

Nathan Matias, J. 2017. “Bias and Noise: Daniel Kahneman on Errors in Decision-Making.” Medium. Medium. October 17, 2017. https://medium.com/@natematias/bias-and-noise-daniel-kahneman-onerrors-in-decision-making-6bc844ff5194.

Newell, Ben R., David A. Lagnado, and David R. Shanks. 2015. Straight Choices: The Psychology of Decision Making. Psychology Press.

Pettigrew, Andrew M. 2014. The Politics of Organizational Decision-Making. Routledge.

Teirlinck, Peter. 2017. “Configurations of Strategic R&D Decisions and Financial Performance in Small-Sized and Medium-Sized Firms.” Journal of Business Research 74 (May): 55–65.

Tenney, Elizabeth R., Nathan Meikle, and David Hunsaker. 2018. “Research: When Overconfidence Is an Asset, and When It’s a Liability.” Harvard Business Review, December 11, 2018. https://hbr.org/2018/12/research-when-overconfidence-is-an-asset-and-when-its-a-liability.