THE EFFECTIVE STATISTICIAN ACADEMY

Mastering study design and strategy with Simulation

Presenters:

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Agenda Outline

Scene Setting: Challenges and Opportunities for simulation

Simulation: What, Why and When?

Simulation Framework and Plans

Where do you get the data from?

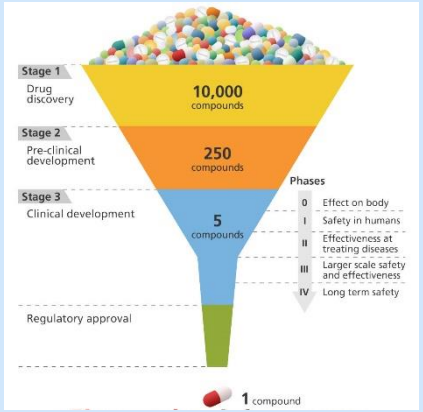
Regulators Viewpoint

Communication of Simulations

Efficient Simulations

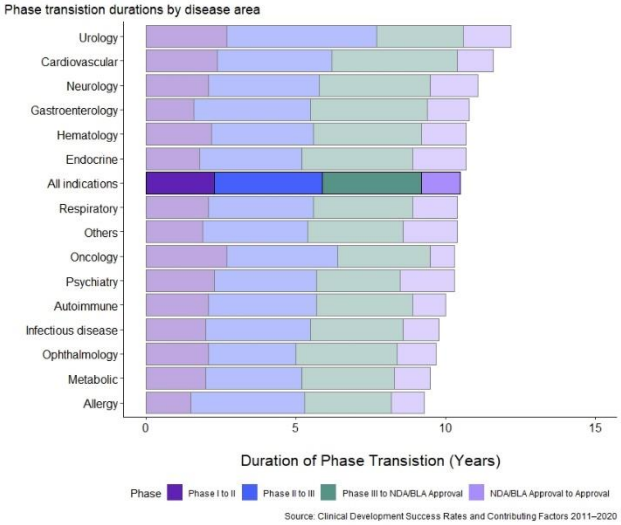
Example

Drug development challenges and the value of simulation in trial design to address them

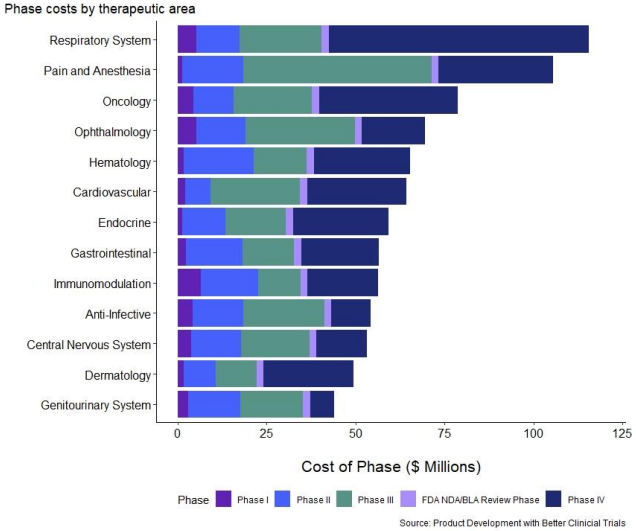


Clinical Development is Hard

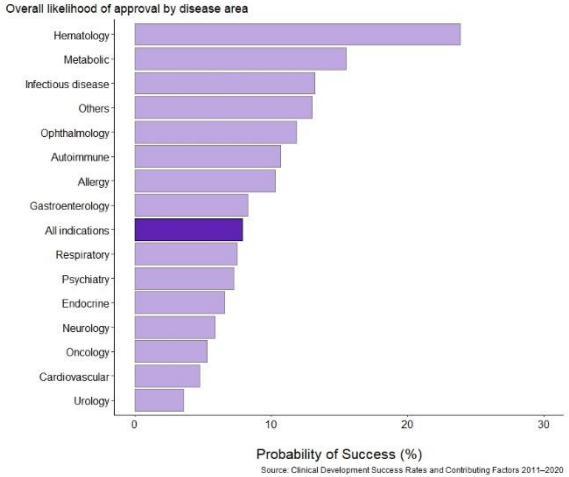
Takes a long time



Costs a lot



Unlikely to succeed



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What are Regulators focusing on?

FDA

2021

Advancing Regulatory Science at FDA:

FOCUS AREAS OF REGULATORY SCIENCE (FARS)

FDA Strategic Initiative	Focus Area of Regulatory Science	Regulated Product Lifecycle			
		Product Characterization, Manufacturing, and Quality	Non-Clinical Pre-market Evaluation	Clinical Pre-market Evaluation	Post-market Activities
Increasing Choice and Competition through Innovation	Individualized Therapies and Precision Medicine	✓	✓	✓	✓
	Complex Innovative Trial Design			✓	
	Microbiome Research	✓	✓	✓	✓
	Novel Foods and Food Ingredients	✓	✓	✓	✓
	Regenerative Medicine	✓	✓	✓	✓
	Advanced Manufacturing	✓			✓
	Increasing Access to Generic Alternatives for Complex Drugs	✓	✓	✓	✓
	Biomarkers	✓	✓	✓	✓
	Novel Technologies to Improve Predictivity of Non-Clinical Studies and Replace, Reduce, and Refine Reliance on Animal Testing	✓	✓		
	Model-Informed Product Development	✓	✓	✓	
Unleashing the Power of Data	Product Safety Surveillance				✓
	Artificial Intelligence	✓	✓	✓	✓
	Digital Health	✓	✓	✓	✓
	Use of Real-World Evidence to Support Medical Product Development and Regulatory Decision-Making			✓	✓

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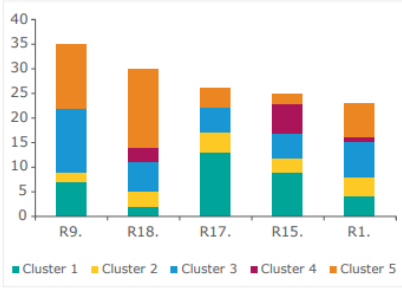
SCIENCE MEDICINES HEALTH

EMA Regulatory Science to 2025

Strategic reflection

Figure 3. Top 5 core recommendations thought to deliver the most significant change - Human



9. Foster innovation in clinical trials

18. Promote use of high-quality real-world data (RWD) in decision making

17. Reinforce patient relevance in evidence generation

15. Contribute to HTA's preparedness and downstream decision making for innovative medicines

1. Support developments in precision medicine, biomarkers and 'omics

Focus Areas of Regulatory Science | FDA; EMA Regulatory Science to 2025 (europa.eu)

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Traditional Statistical Study Support

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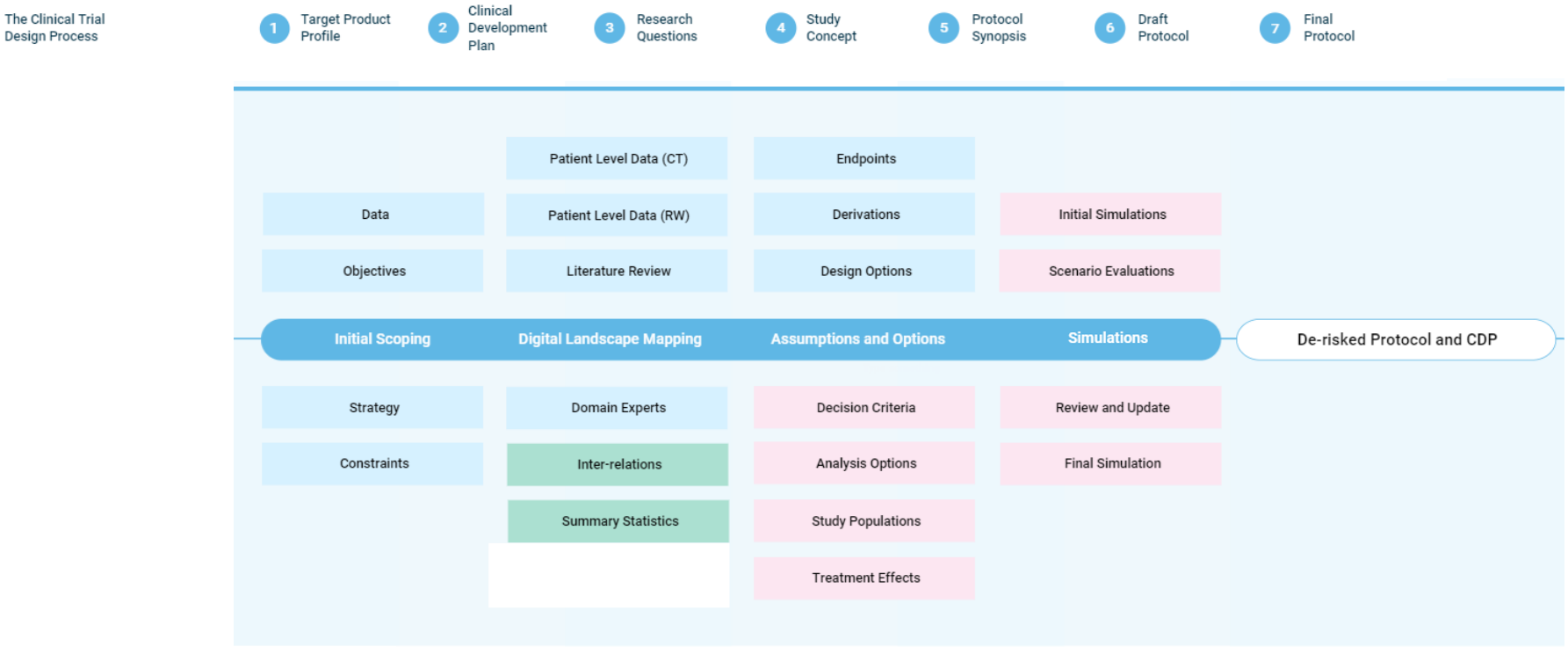
Simulation Based Approach to Study Design



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Pressures on statisticians in clinical trial design and clinical development planning

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How does simulation help statisticians overcome these pressures?

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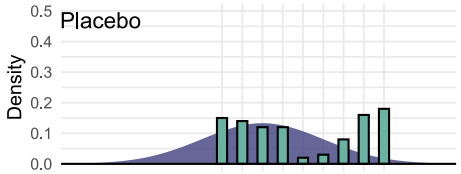
How many times have you ignored the fact you will have…

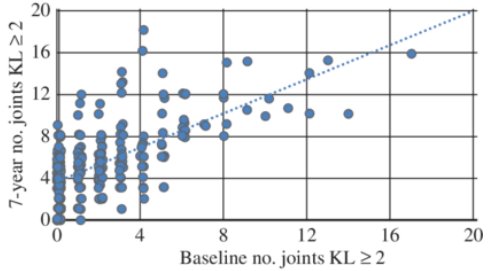
- discrete data?



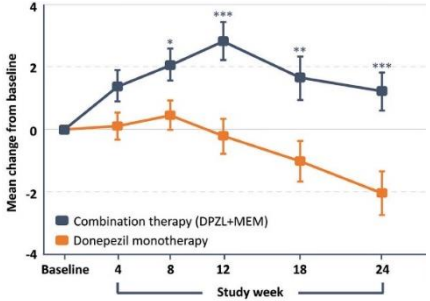
- missing data?

Case Study		
S1	S2	S3
Gender	GLUCOSE	Age
M	?	65
F	120	71
F	99	?
F	140	52
M	88	?
F	85	63
M	170	68
?	153	80
M	115	59
F	103	?

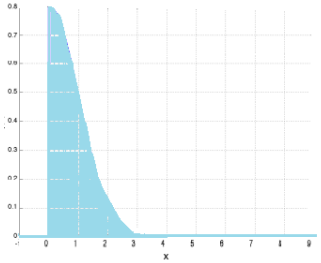
- baseline in your analysis?



- repeated measurements?



- truncated data?



We make simplifying assumptions when designing studies. But how do we know which we can ignore? **Simulation is of value in simple situations!**

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What if we aren't in a simple situation?

Multiple endpoints and correlations	Complex decision criteria	Estimands with intercurrent events	Uncertain setting
Exploration of sub populations	Constrained settings e.g rare diseases	Adaptations and decision rules	Recruitment considerations

Benefits of simulation are huge!

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Summary

- Lots of opportunity for statisticians to influence in drug development to help overcome some of the challenges
- Simulation is a key tool that every statistician should have in their toolbox