INDUSTRIAL CONSIDERATIONS FOR STATISTICAL TOOL USED TO SUPPORT SUBMISSIONS

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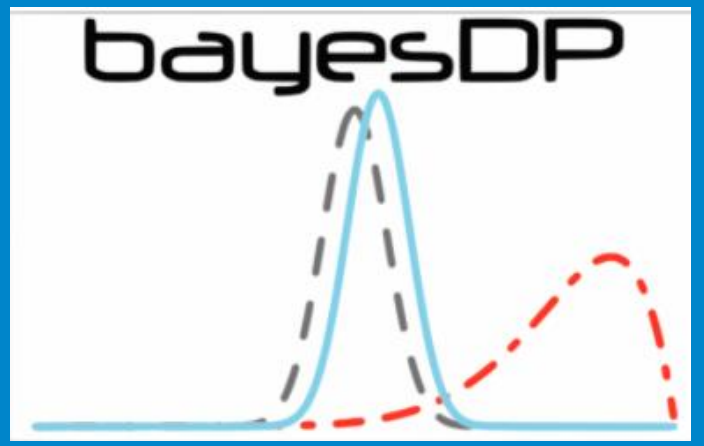

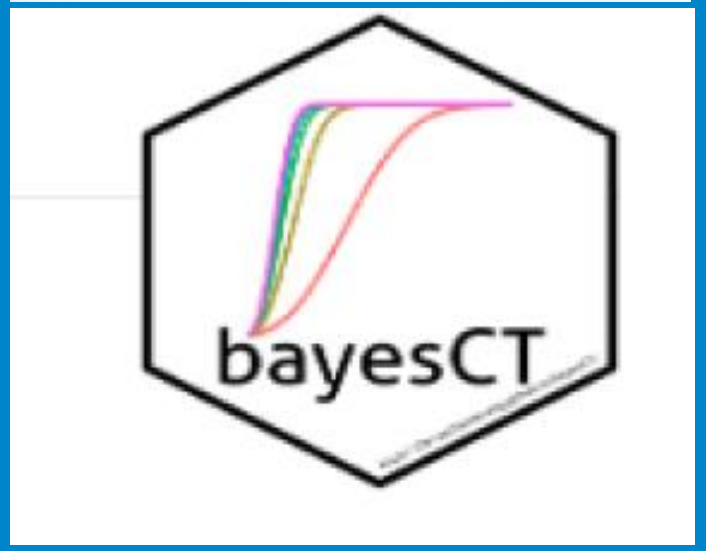

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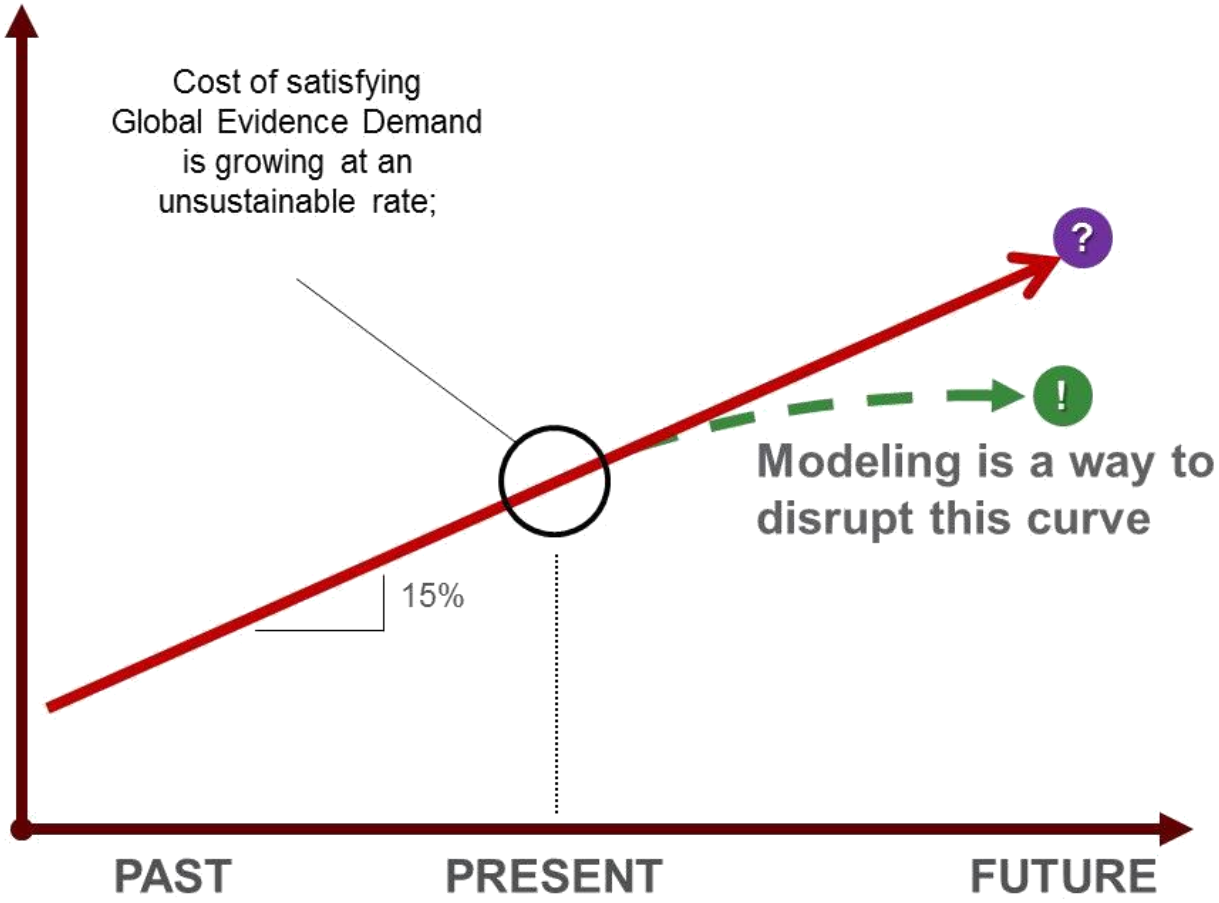
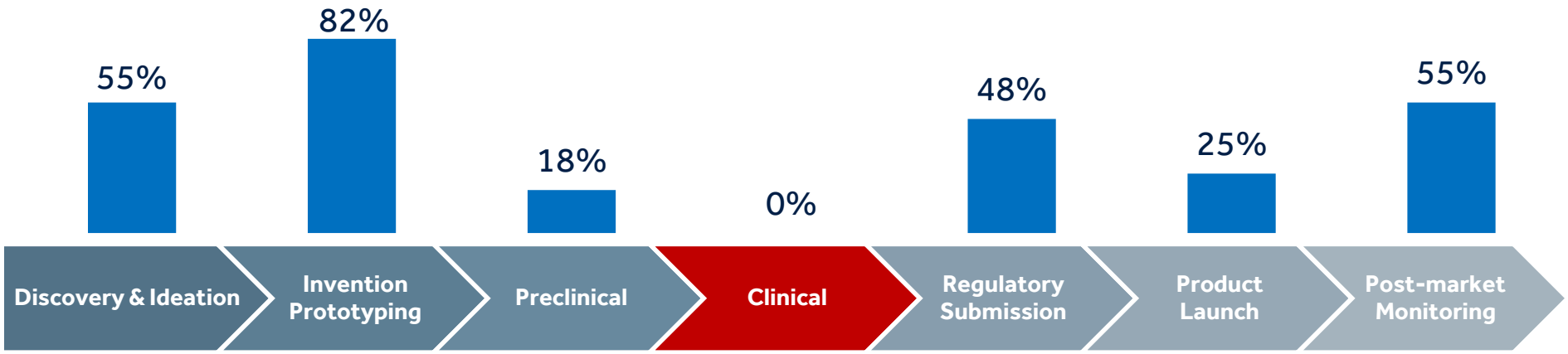
TRENDS TRANSFORMING CLINICAL RESEARCH

<u>Demands:</u>
↑ Evidence
↑ Stakeholders
↑ Geographies
↑ Value

<u>Rapid rise in costs due to:</u>
↑ Complexity
↑ Number of outcome variables
↑ Follow-up time
↑ Post-market data

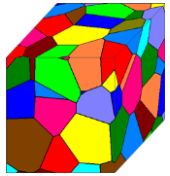
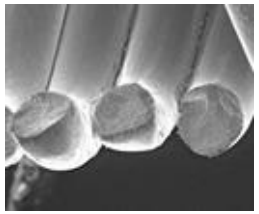
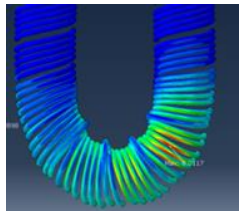
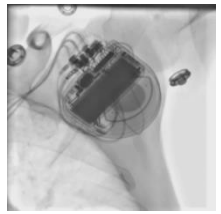
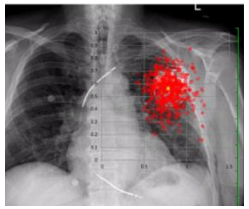
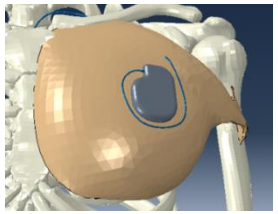


USE OF MODELING ACROSS LIFECYCLE



- Animal studies
- Use conditions
- Virtual prototyping
- Material characterization

- Device structure & function
- Systems interaction
- Design optimization
- Failure analysis

* Results from 2014 MDIC survey of 35 participating medical device companies

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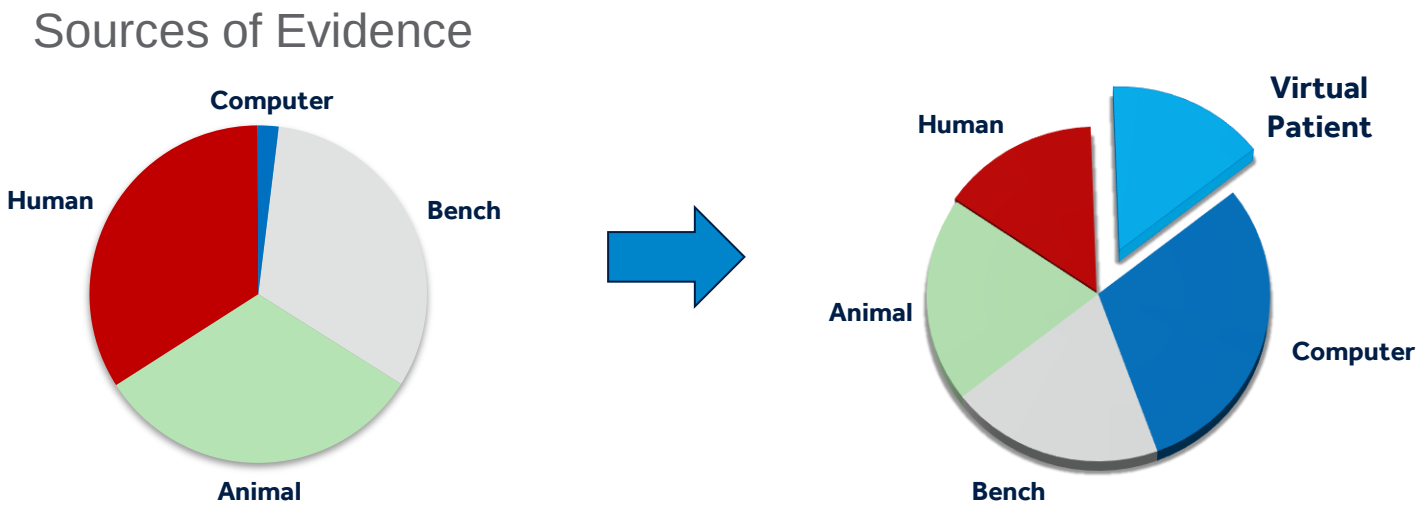
DISRUPTING CLINICAL TRIAL DESIGN WITH VIRTUAL PATIENTS

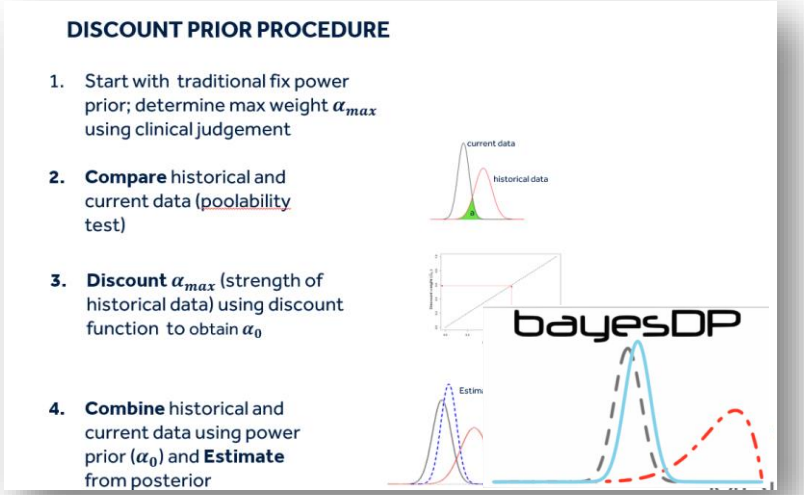


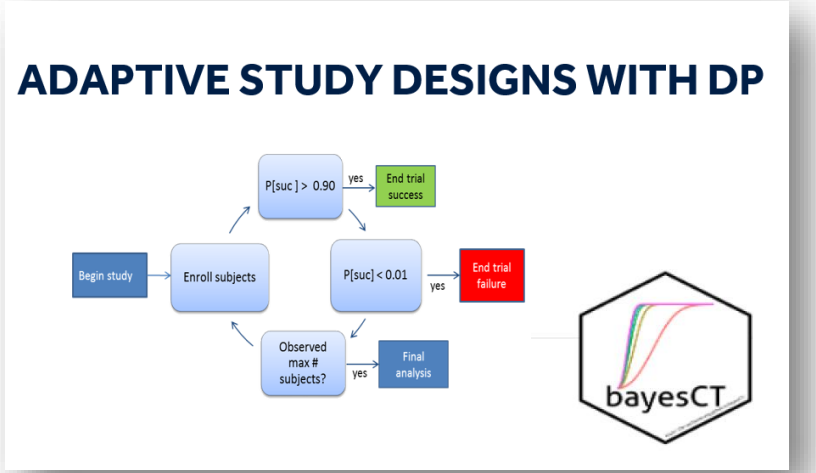
- Combine physical and probabilistic models to simulate clinically relevant outcomes in virtual patients
- Use Bayesian methods to integrate virtual patients into clinical trial
- Maintain clinical endpoints with reduced sample size

INCORPORATION OF VIRTUAL PATIENTS IN ADAPTIVE BAYESIAN CLINICAL TRIALS USING INFORMATIVE PRIOR

TWO R PACKAGE

- Some statisticians were uncomfortable with non-standard methods and with coding it up
- Regulatory: more work to read custom code
- Code that are simple to understand (Think SAS Proc mixed)
  - Universal language used for describing Bayesian adaptive trials.
  - Ease of developing an entire adaptive trial using these packages.
- Fast implementation: days and weeks →hours and min
- Employable for multiple trials with most common data types.
- Ability for a smaller company with a single statistician to be able to develop an entire adaptive clinical trial code





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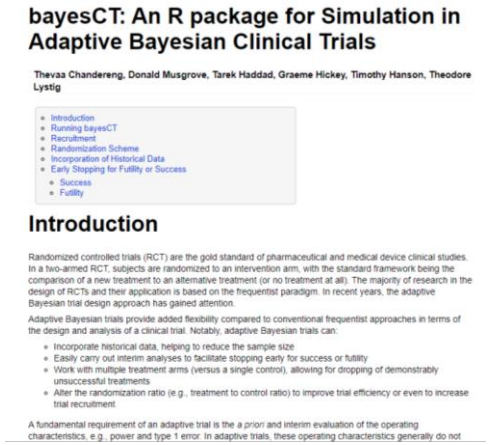
PACKAGE DEVELOPMENT

- Fast implementation
- Copied standard input & outputs (lm)
- dplyr bayesCT
- Meeting R's requirements for packages

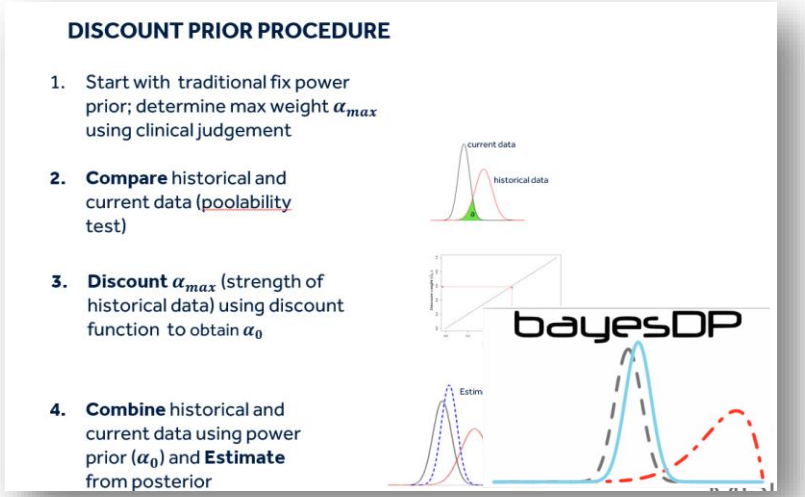
- Documentation
  - Lots of documentation→ Vignettes!!

- Credibility
  - Method credibility→ Publications & conferences
  - Regulatory workshops
  - Validation →External validation (re-coding)



CONSIDERATIONS

- Package Management:
  - Not necessarily a software organization → management of the package
  - Package owner vs Package developer
  - Continued package maintenance
  - Implementation errors
    - Modifications on the Fly
    - Data preprocessing → Centering the data
    - Protocol modifications



Thank you
Questions?