A quantitative framework for balancing ethical tradeoffs in vaccine study design

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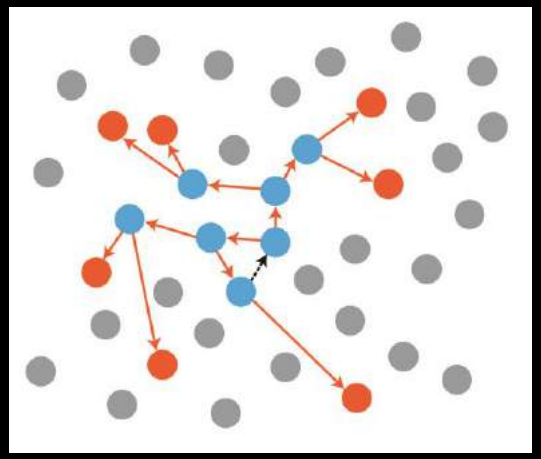
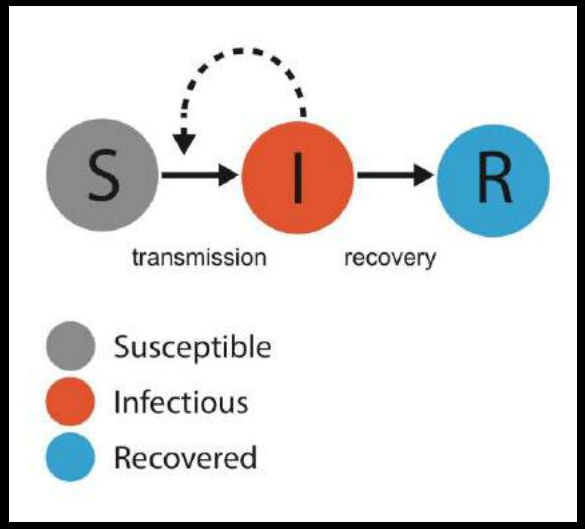
DAIDD 2017

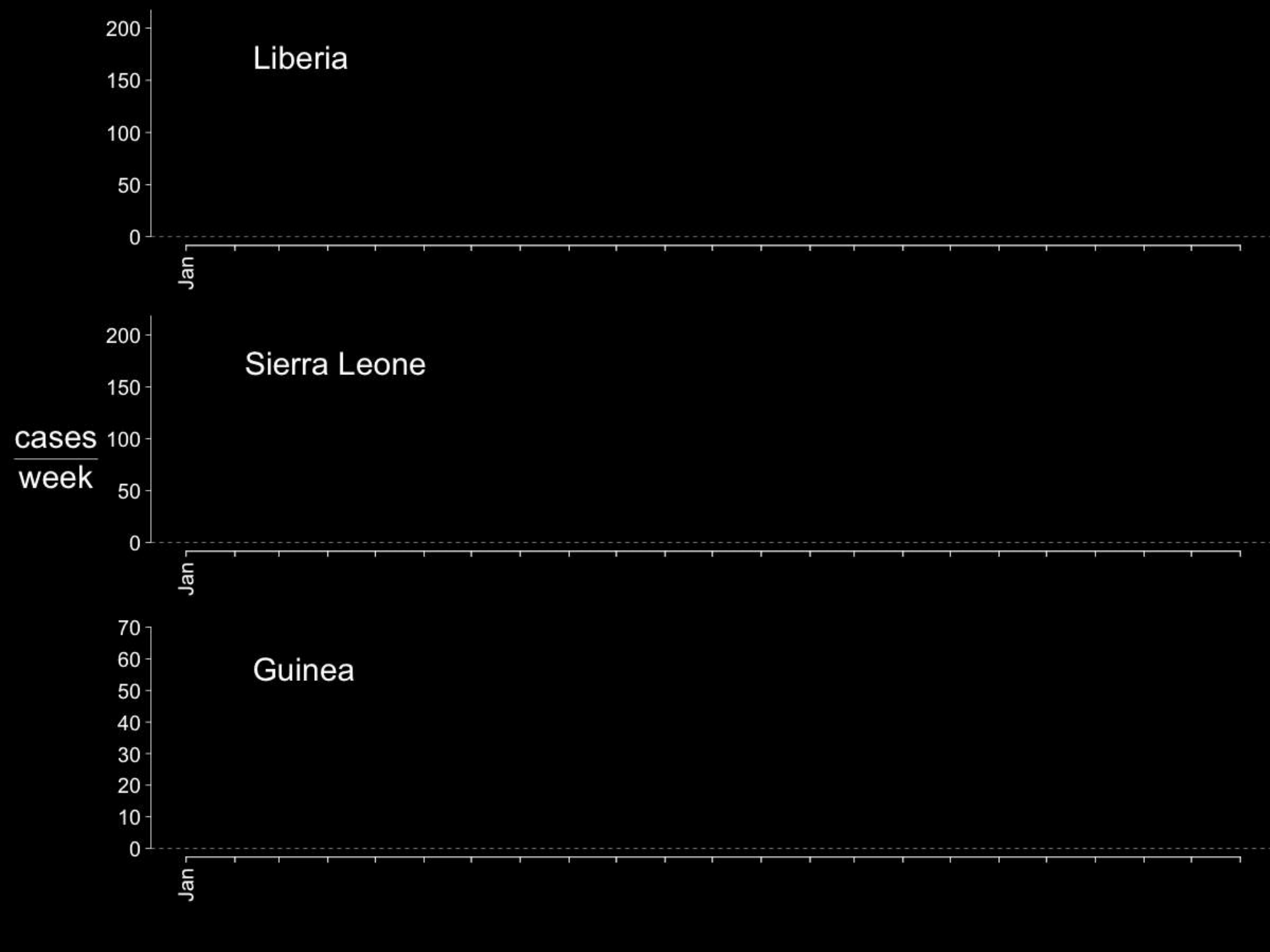
Transmission Modeling

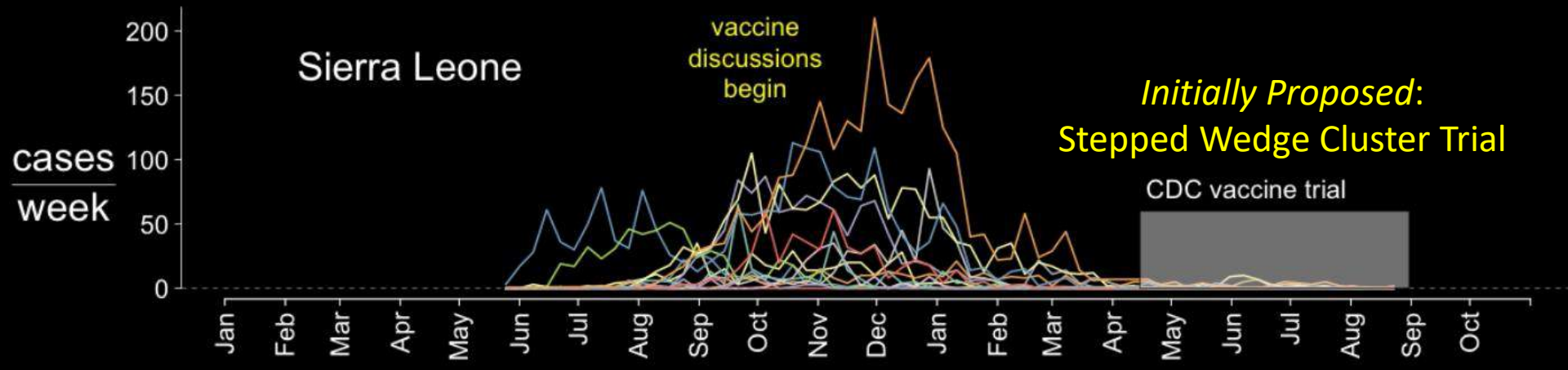
individual processes ➔ population patterns





Explore study design
of epidemic processes through
simulation

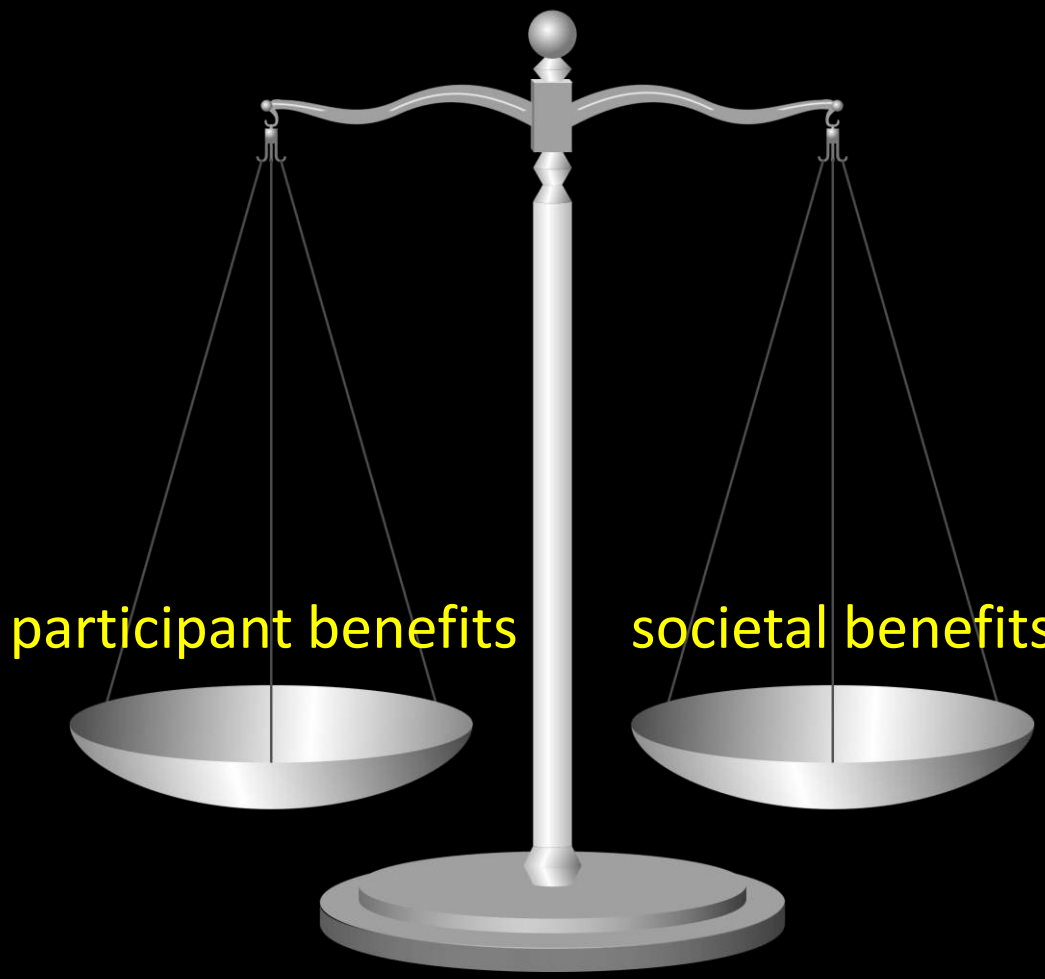

Liberia
200
150
100
50
0
Jan
Sierra Leone
cases
week
200
150
100
50
0
Jan
Guinea
70
60
50
40
30
20
10
0
Jan

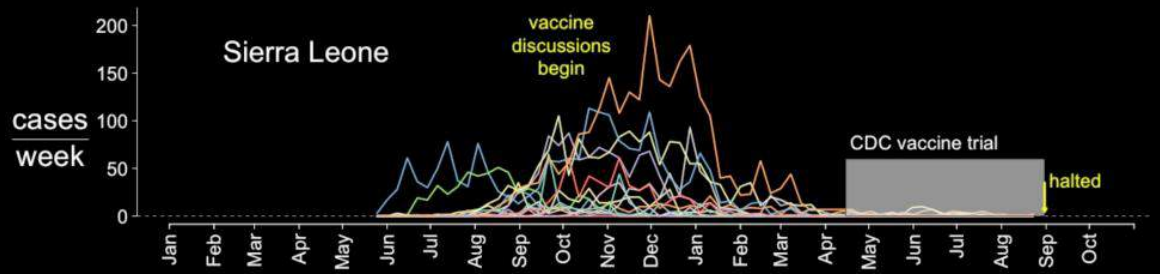


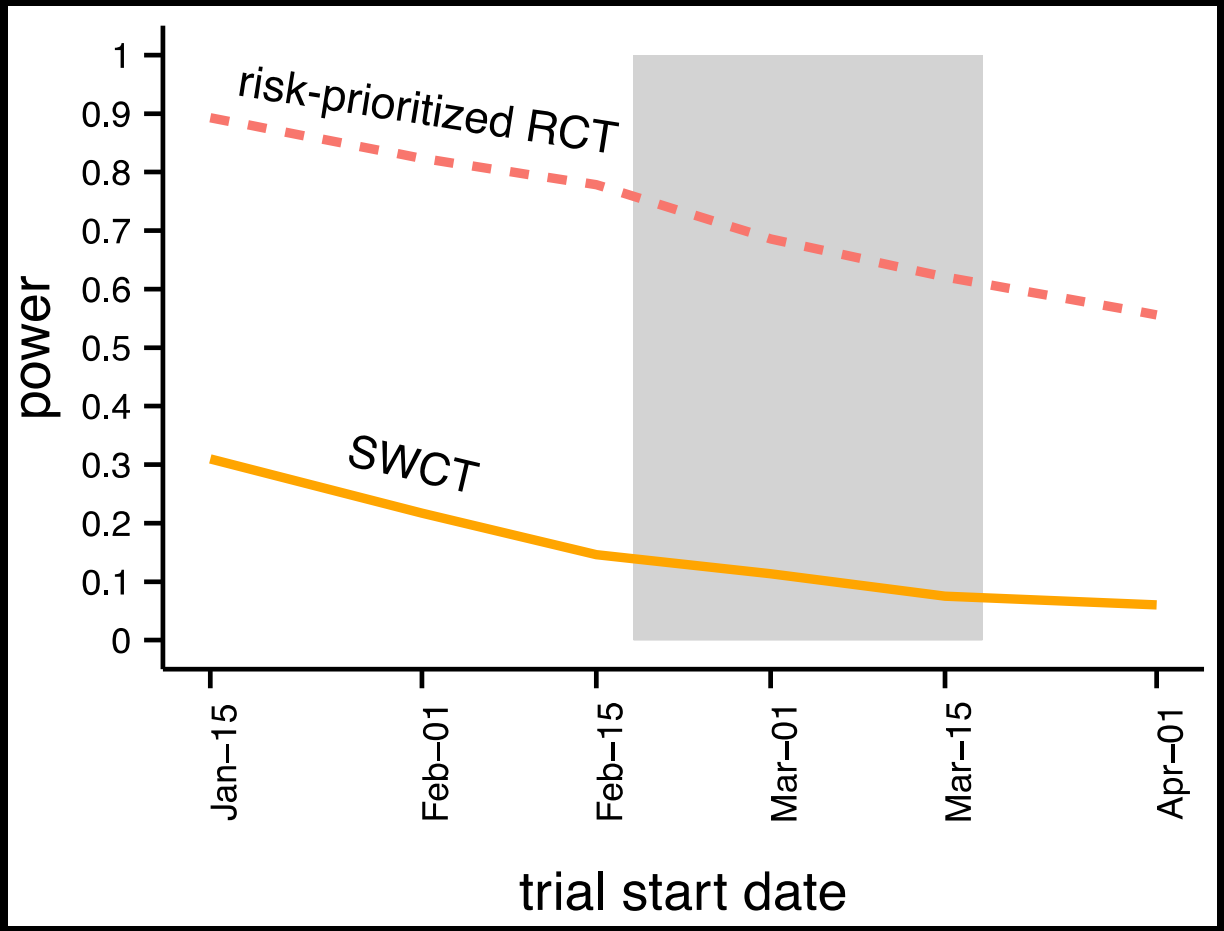
Dual goals

Evaluate & Roll Out

Balancing Rollout and Evaluation







Bellan et al. 2015. *Lancet Infectious Diseases.*

But experimental interventions are unproven…

Therapeutic Misconception
or
Probabilistic Benefit

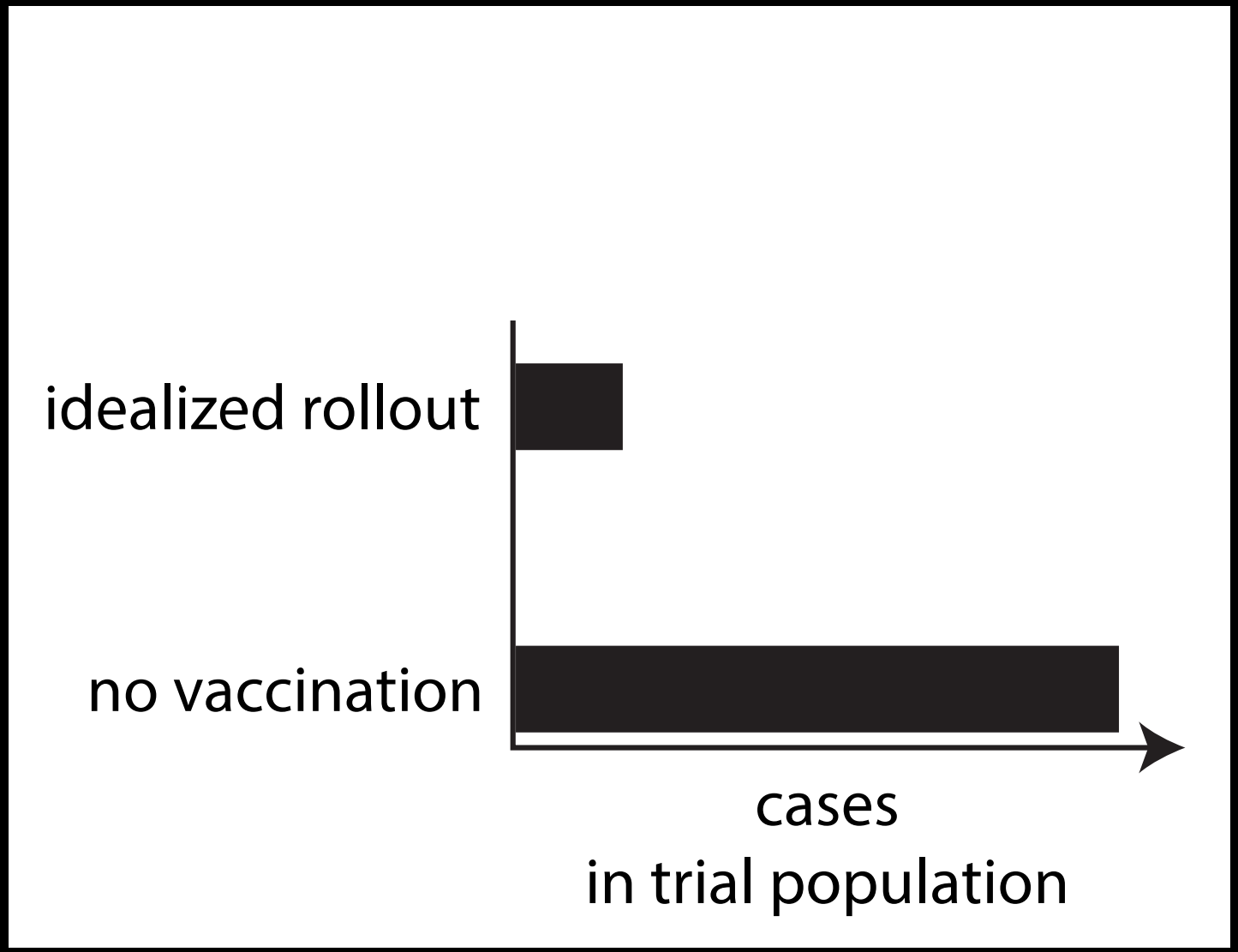
Bellan et al. 2015. *BMJ*; Bellan et al. 2017. *biorXiv.*

Relaxing the dichotomy of clinical equipoise

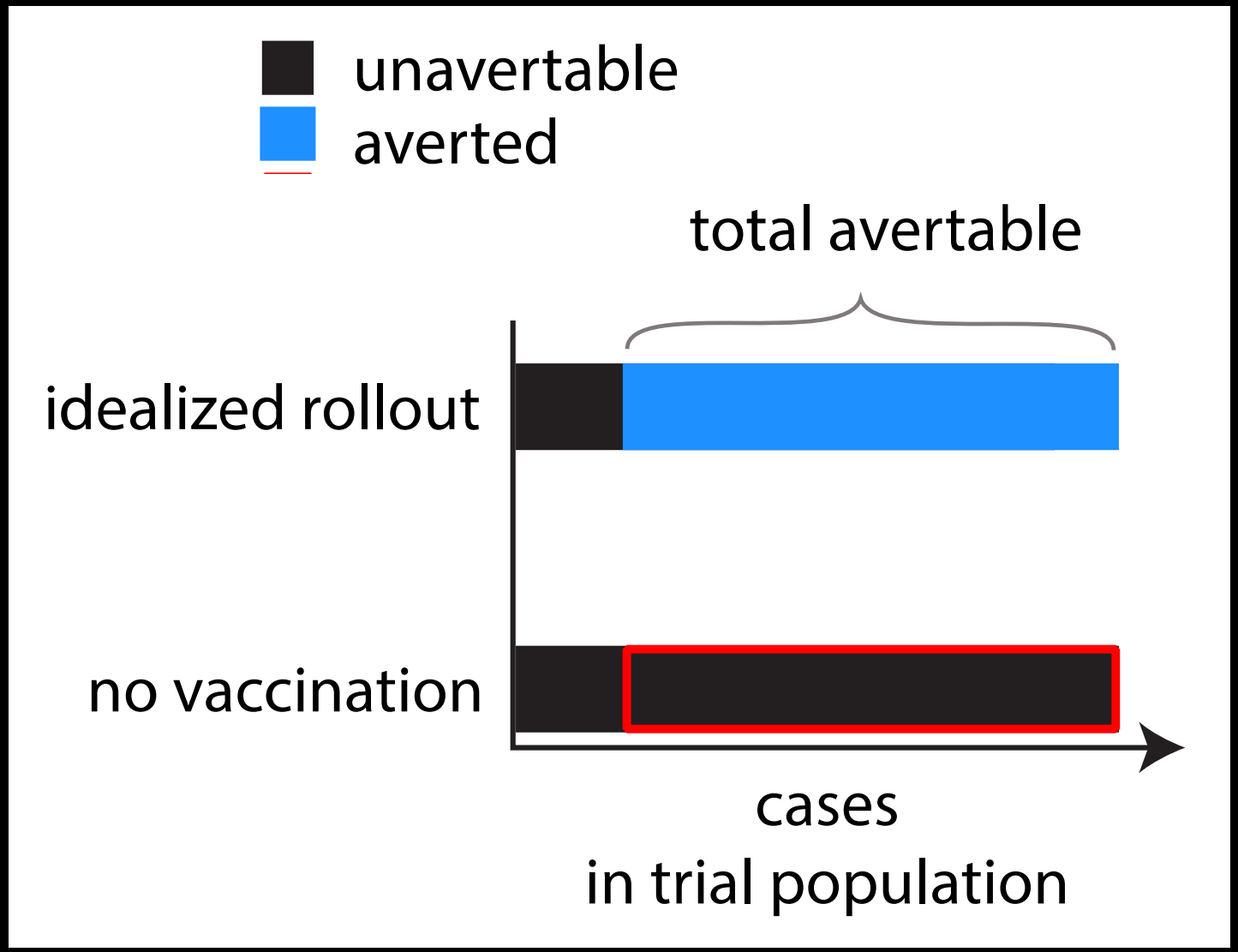
explore quantitative tradeoffs via simulation

power, speed, bias VS risk spent

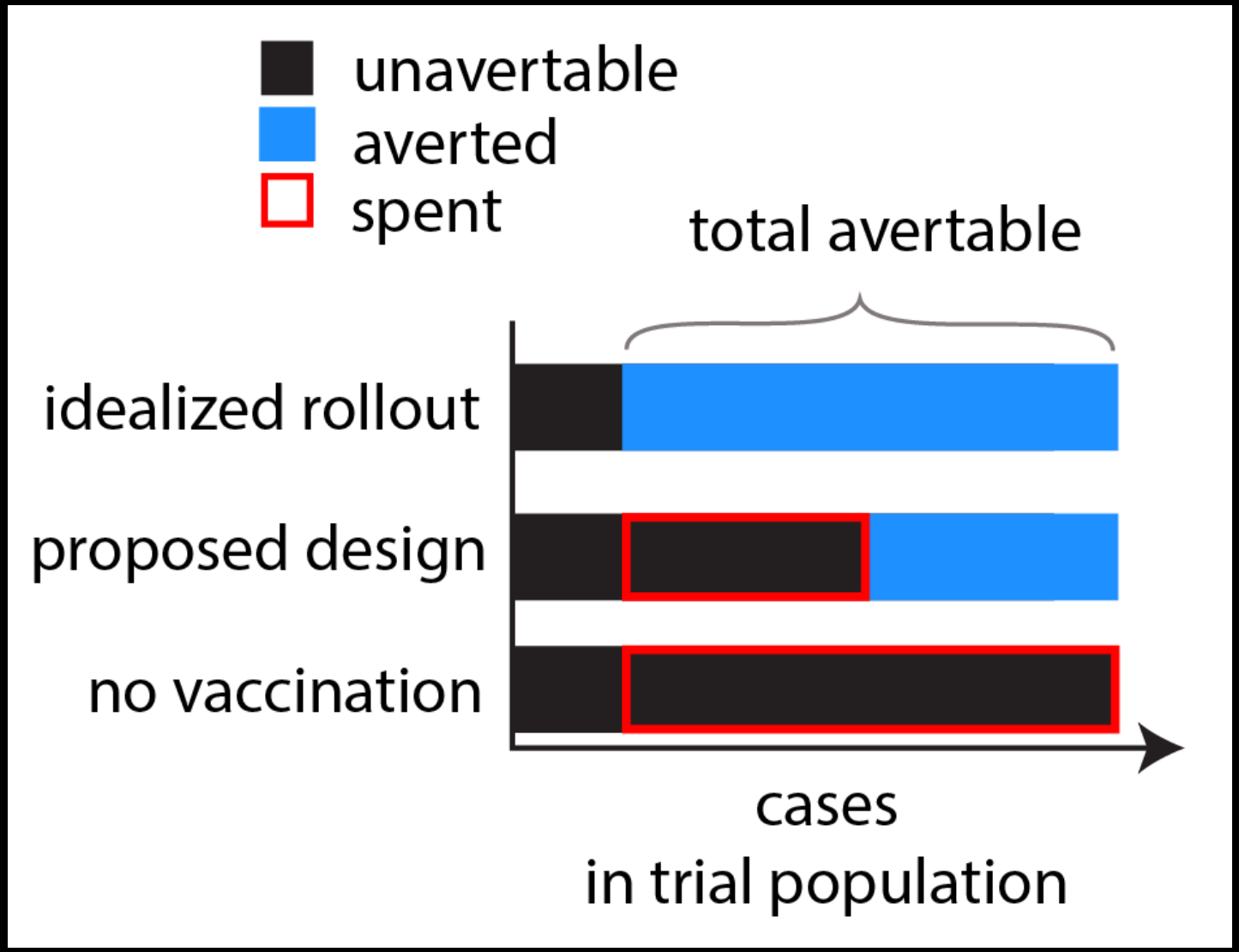
Counterfactual Risk Partitioning



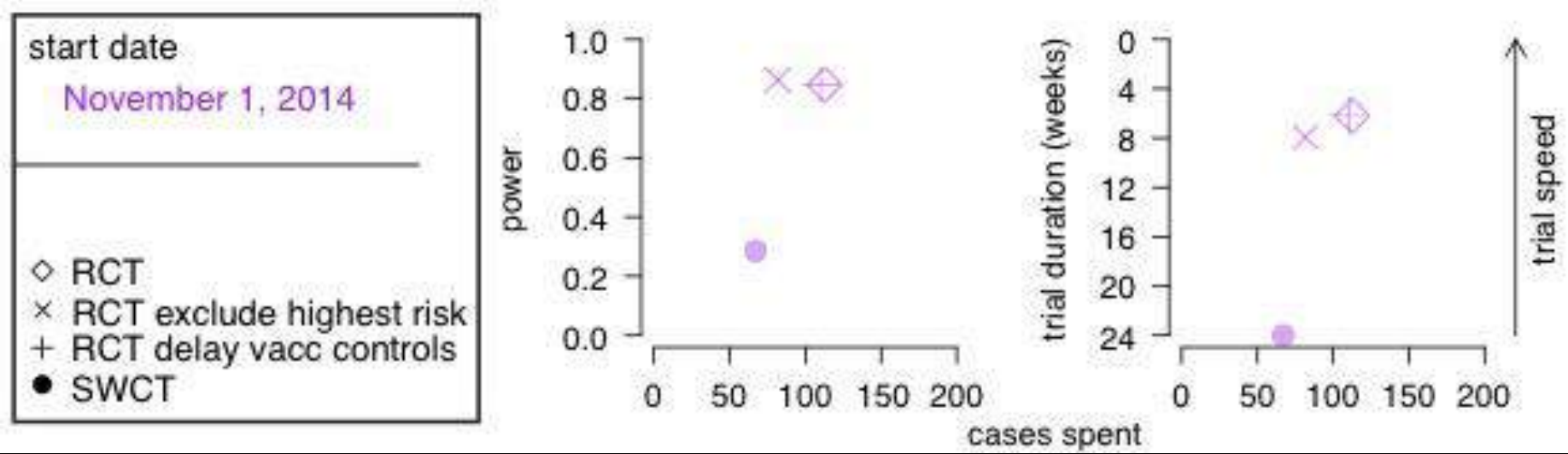
Counterfactual Risk Partitioning



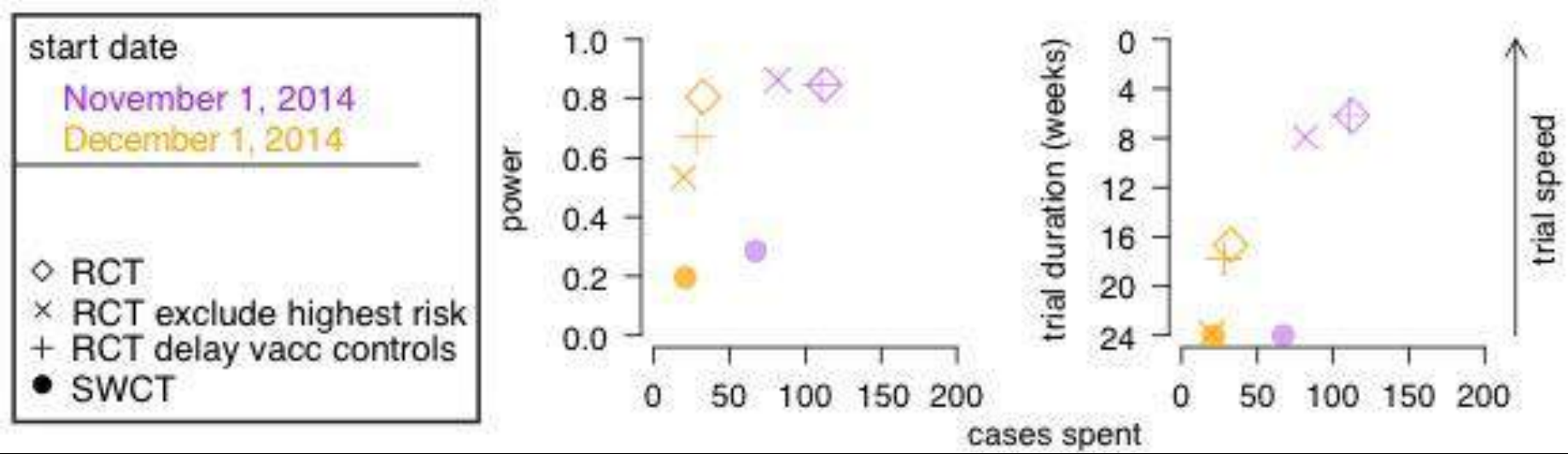
Counterfactual Risk Partitioning



Information versus Risk Spent



Information versus Risk Spent



Cold Spring Harbor Laboratory

bioRχiv beta

THE PREPRINT SERVER FOR BIOLOGY

New Results

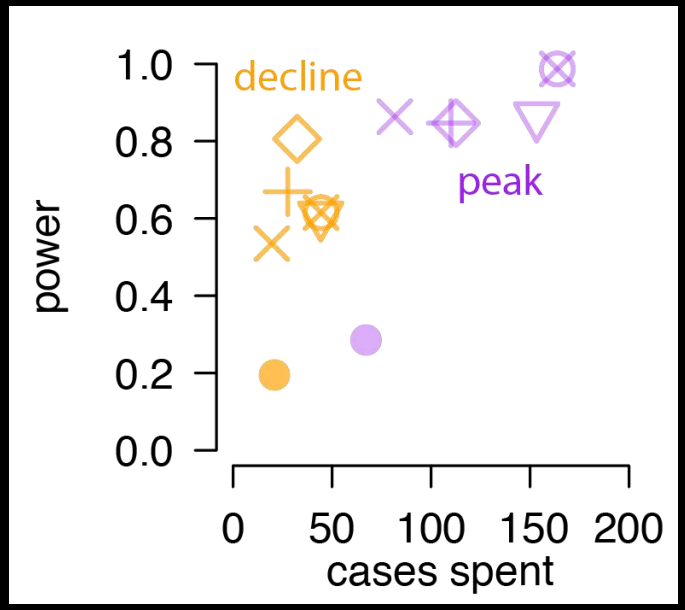
Quantifying ethical tradeoffs for vaccine efficacy trials during severe epidemics

Steven E. Bellan, Juliet R. C. Pulliam, Rieke van der Graaf, Spencer J. Fox, Jonathan Dushoff, Lauren Ancel Meyers

doi: https://doi.org/10.1101/193649

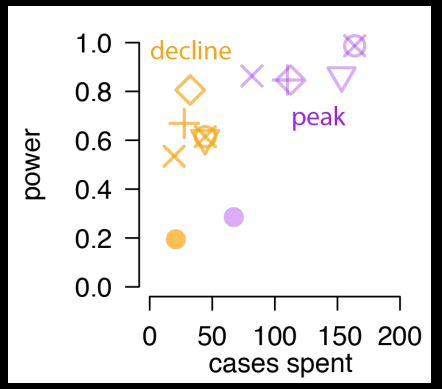
Reducing Risk Spent

- *Indirect*:
  - Faster trial
- *Direct*:
  - Delayed vaccination
  - Presumptive vaccination of high infection risk individuals

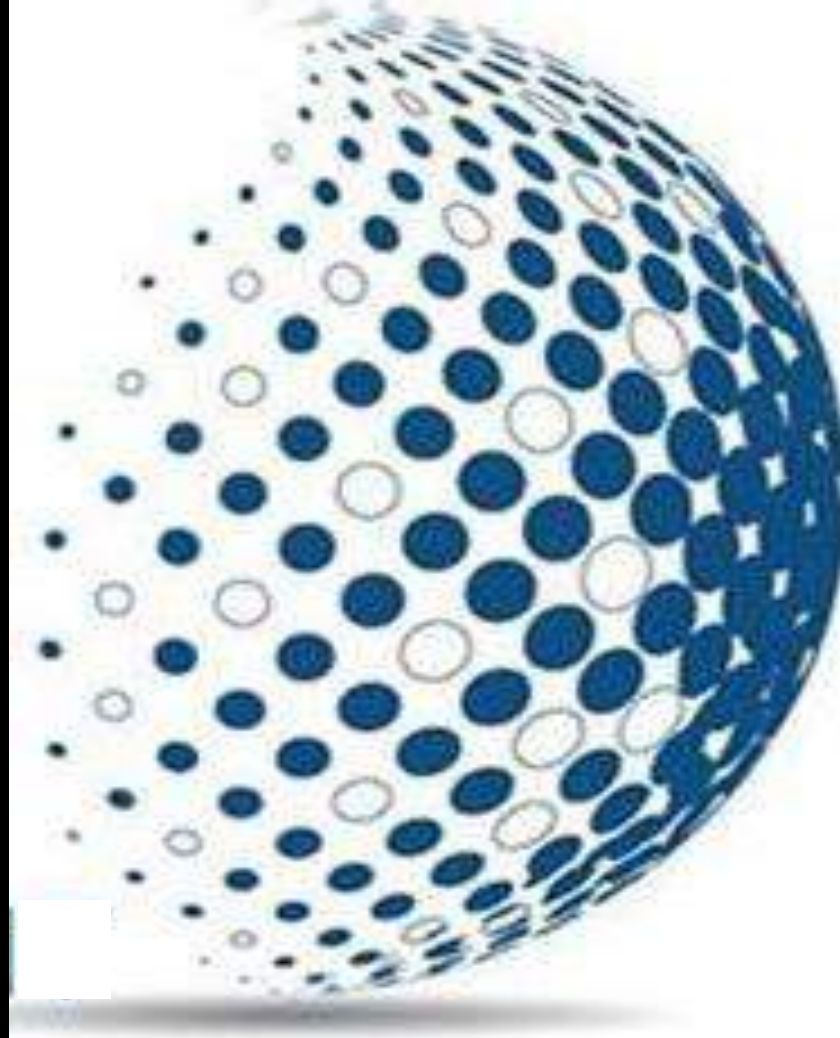


Model Taxonomy

	Continuous treatment of individuals (averages, proportions, or population densities)	Discrete treatment of individuals
Deterministic	Continuous time Discrete time	
Stochastic	Continuous time Discrete time	Continuous time Discrete time



The Blueprint **aims to reduce the time** between the PHEIC of international concern and the availability of effective tests, vaccines and medicines



R&D BLUEPRINT

World Health Organization

A Blueprint - Workplan on Efficacy Trials during PHE

March 2016 : 1st Consultation in Chamonix, *France*

→ Workplan: 4 Action Points

G1 – Grid of major study designs / *Prof. Longini*

- ***Comprehensive methodological discussion paper on vaccine trial designs***

G2 – Decision Tree / *Dr Bellan*

- ***A guide for experts and stakeholders during trial design***

G3 – Trial Simulator / *Prof. Brisson*

- ***Facilitate assessment of trial feasibility using realistic outbreak scenarios***

G4 – Generic Protocols / *Dr Henao Restrepo*

- ***Annotated pathogen-specific generic protocols for various study designs***

vaxeval.com

(work in progress)

Collaborators & Acknowledgements

Ethics

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WHO R&D Blueprint InterVax Tool

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