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Cost-effectiveness of typhoid vaccine strategies: evidence gaps and recommended methods

Ginny Pitzer

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Yale SCHOOL OF PUBLIC HEALTH

STRATAA
STRATEGIC TYPHOID ALLIANCE ACROSS AFRICA & ASIA

TyVAC Typhoid Vaccine Acceleration Consortium

What is the question?

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- What are the types of questions that can be addressed through economic evaluations?
  - Is it cost-effective to implement typhoid vaccination in conjunction with existing public health interventions?
  - Is it more cost-effective to introduce routine vaccination with TCV alone or in combination with a one-time catch-up campaign?
  - Is targeted or universal typhoid vaccination more cost-effective?

Components of economic evaluations

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- Clearly define question and target audience (e.g. MoH vs Gavi)
- Type of evaluation
  - **cost-utility analysis** ($ per DALY averted) vs **cost-benefit analysis** (compare monetary investment vs costs averted)
- Target population
  - e.g. specific age group or geographic area
- Define comparators:
  - type of vaccine (e.g. TCV vs Vi-PS)
  - delivery strategy (routine EPI vs catch-up campaign) and coverage
  - “current practice” should be baseline comparator
- Perspective of analysis:
  - healthcare provider vs societal (ideally)
- Analytical horizon:
  - should be long enough to capture all impacts from the vaccine (*at least* 10 years for TCV)

Cost components of economic evaluations

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Vaccine costs	• Include wastage rate and uptake of vaccination
Administration associated costs	• Depends on the vaccine delivery strategy selected
Costs of strategies to increase uptake of typhoid vaccination	• The uptake of typhoid vaccination affects both costs and outcome of the program
Costs for patients and family	• Inclusion of indirect costs in societal perspective or patients out of pocket expense when patient perspective is selected, but report separately
Typhoid fever treatment costs	• Inclusion of medical costs related to typhoid treatment, possibly accounting for AMR

- ***Which costs components to be included depends primarily on the perspective of the analysis***

Assessing the impact of vaccination

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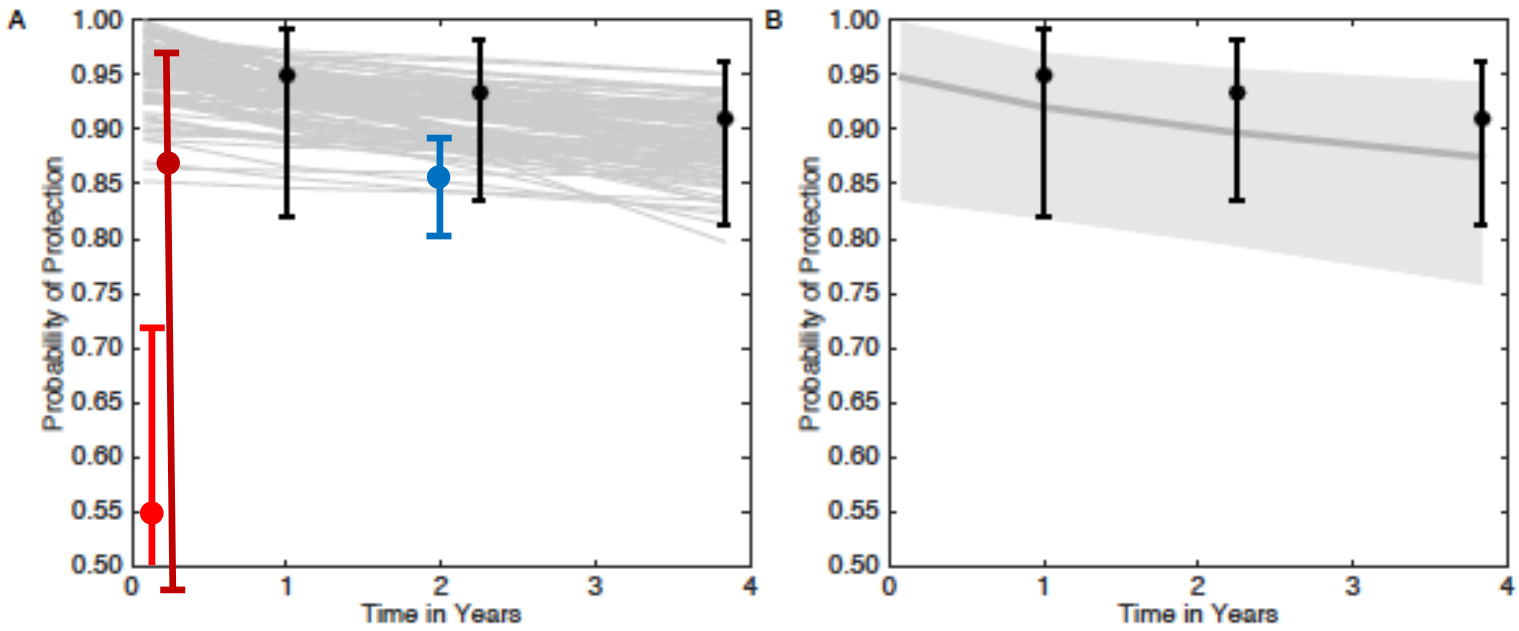
- Should be based upon the best available evidence of vaccine effectiveness
  - including duration of protection
  - rate of vaccine uptake



Vi-rEPA Vi-TT (challenge) Vi-TT (seroefficacy)

Lin F et al (2001) NEJM; Lahn MN et al (2003) NEJM; Jin et al (2017) NEJM; Voysey & Pollard

Assessing the impact of vaccination

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- Incorporation of herd effects
  - **Dynamic transmission models** needed to estimate the overall impact across different levels of coverage
  - **Chronic carriers** are expected to affect the level of indirect protection: the more carriers, the lower the level of indirect protection expected
  - Indirect effects could lead to an **increase in age of infection** by decreasing transmission and the rate at which immunity from natural infection is acquired among unvaccinated
  - Incorporating indirect effects in **static models** should be done in sensitivity analysis **only**

Presenting results of economic evaluations

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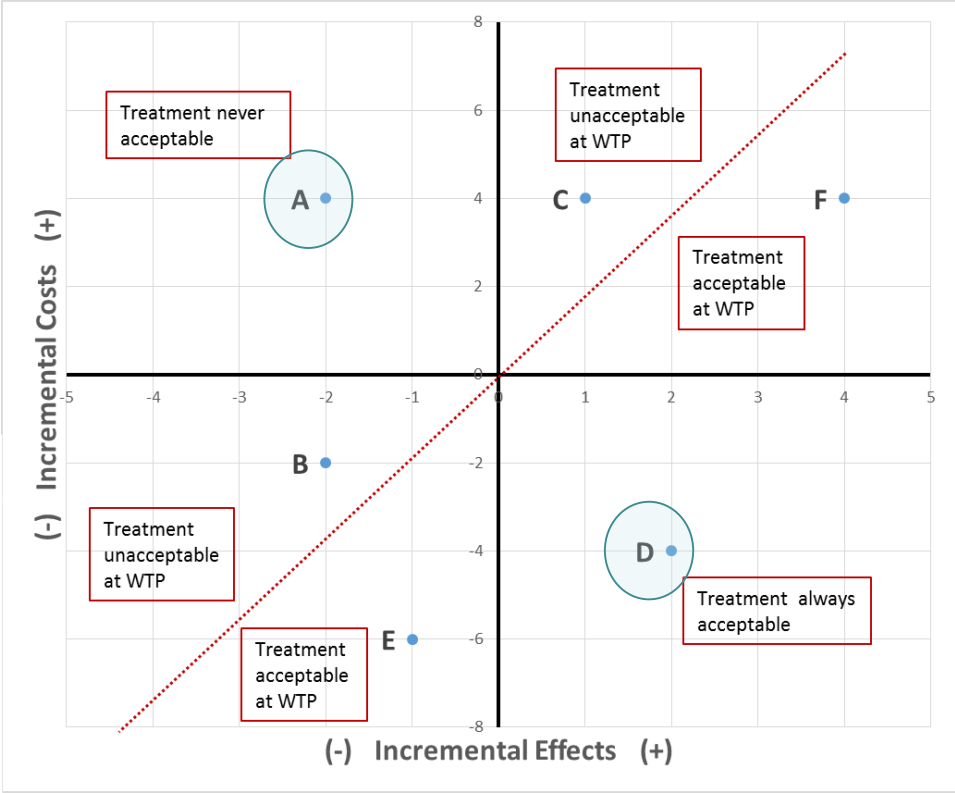
- Incremental Cost-Effectiveness Ratio (ICER) should be calculated and presented with a range of willingness-to-pay thresholds

$$\frac{\Delta Costs}{DALYs\ averted}$$

Program	D	A
Incremental Cost	-4	4
Incremental Benefit	2	-2
Preference	Dominant	Dominated
ICER	***-2***	***-2***



Presenting results of economic evaluations

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Sensitivity analyses

- Some parameters are uncertain or unknown especially for newly-developed TCVs
- Uncertainty can be explored using **probabilistic sensitivity analysis**, with results presented using cost-effectiveness acceptability curve (CEAC)
- Uncertain parameters:
  - costs of illness
  - vaccine price and delivery costs
  - vaccine effectiveness
  - hospitalization rate
  - case fatality rate
  - incidence of typhoid
- **Value of information analysis** (estimating EVPPI) is also recommended

Example: Cost-effectiveness of TCV strategies

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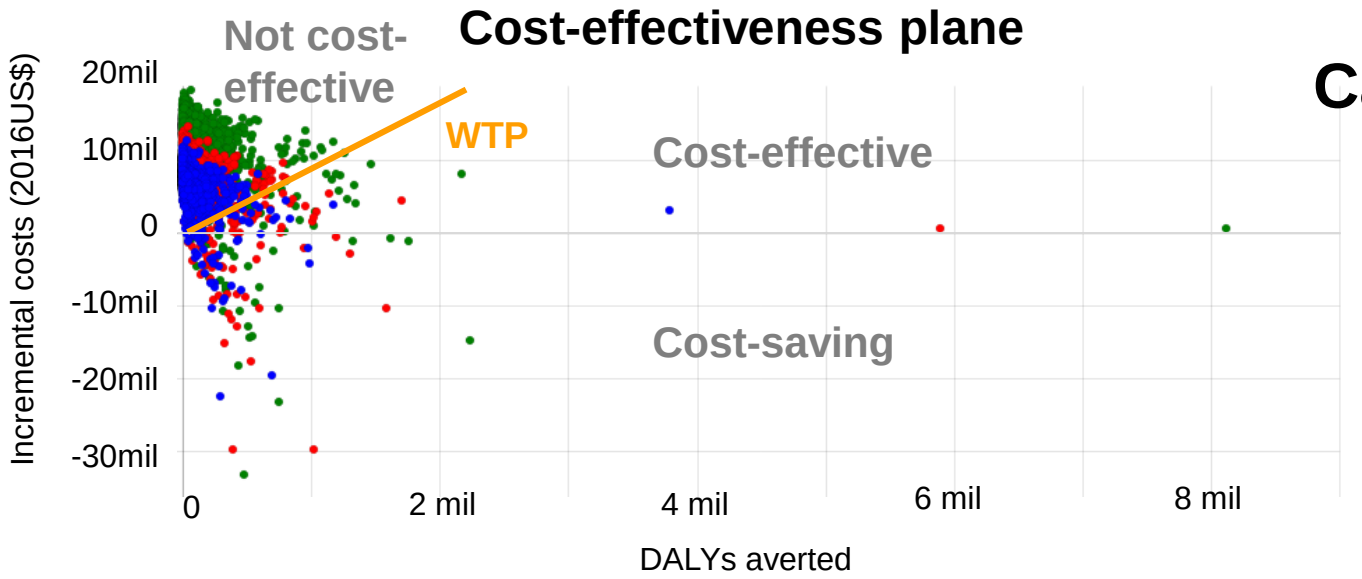

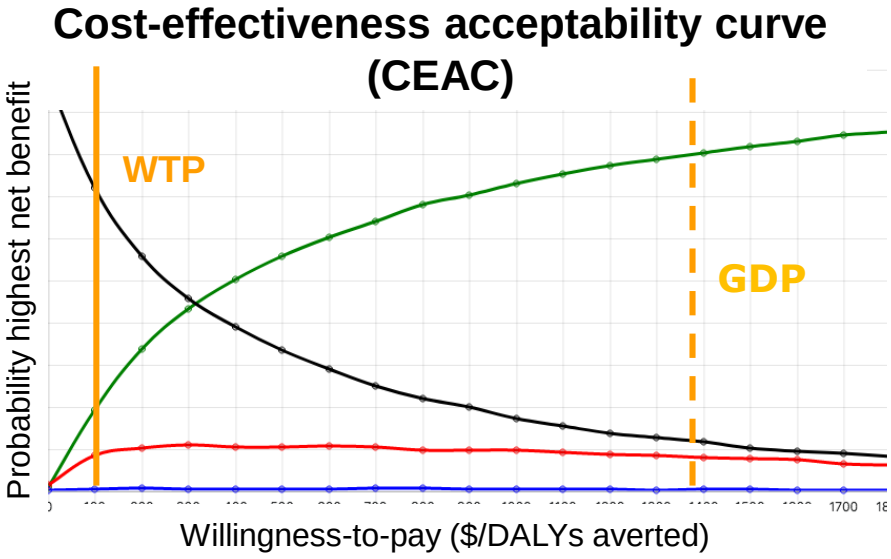

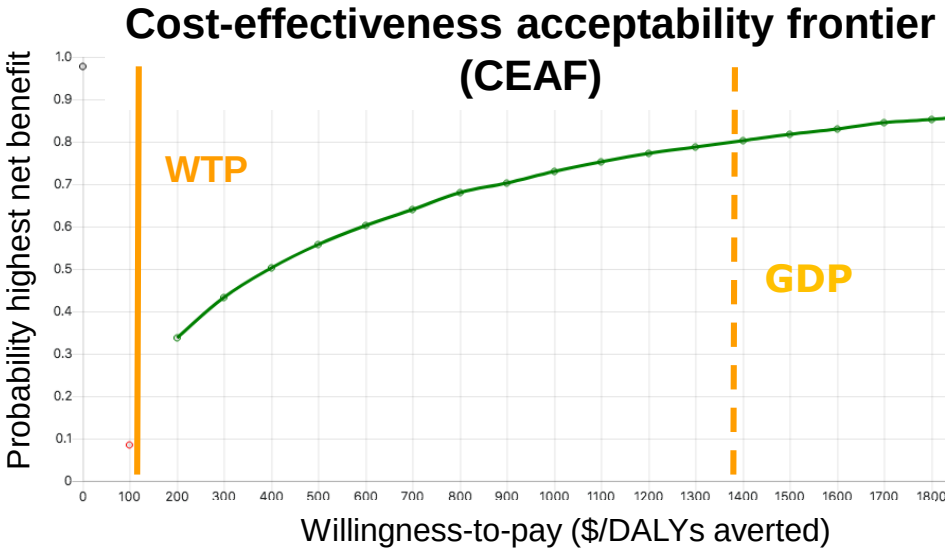

routine | routine + campaign up to 5 years | routine + campaign up to 15 years

Example: Cost-effectiveness of TCV strategies

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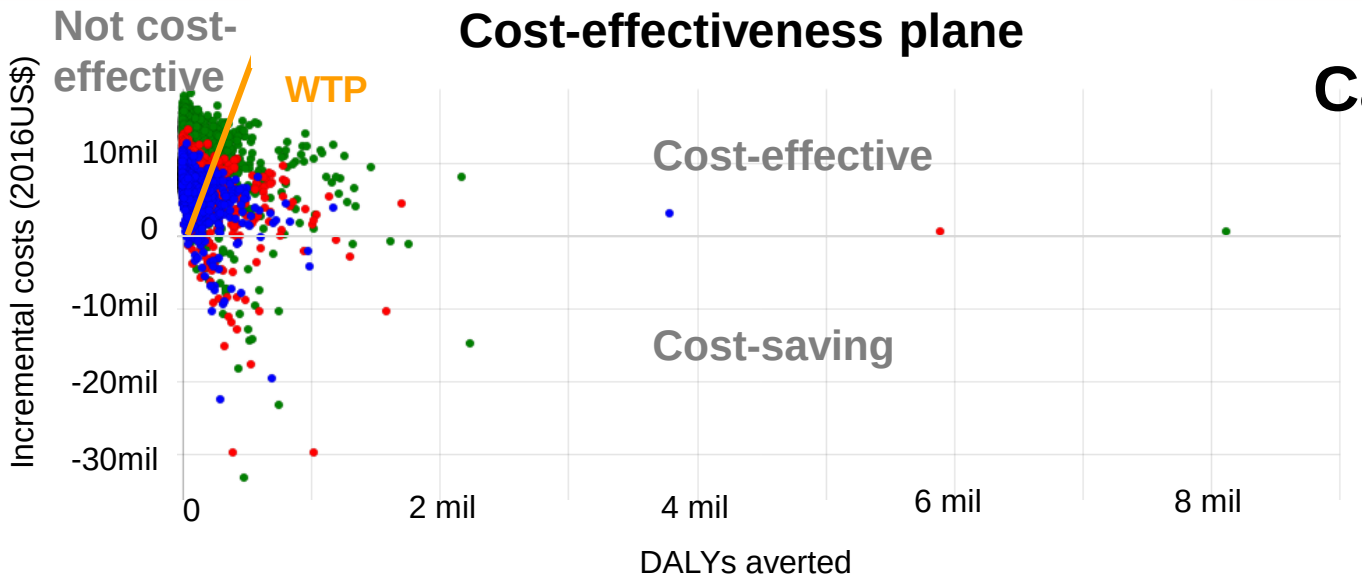

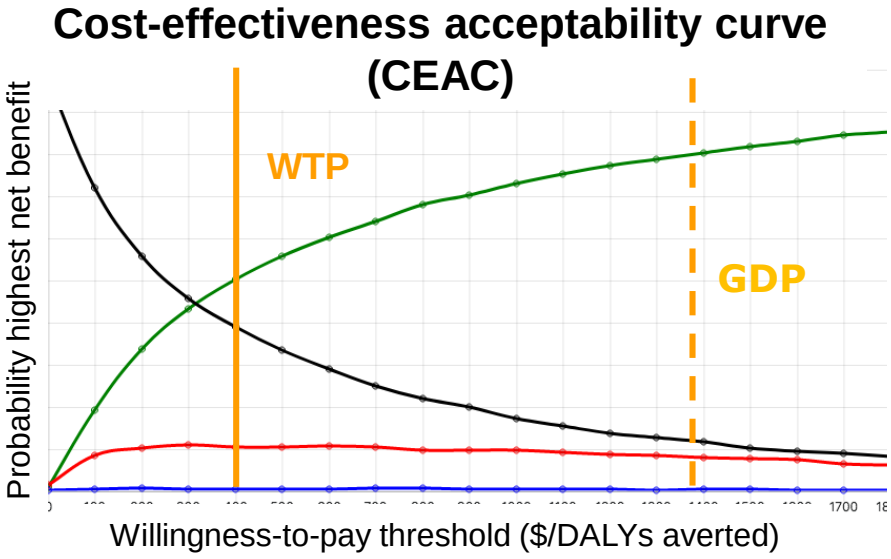

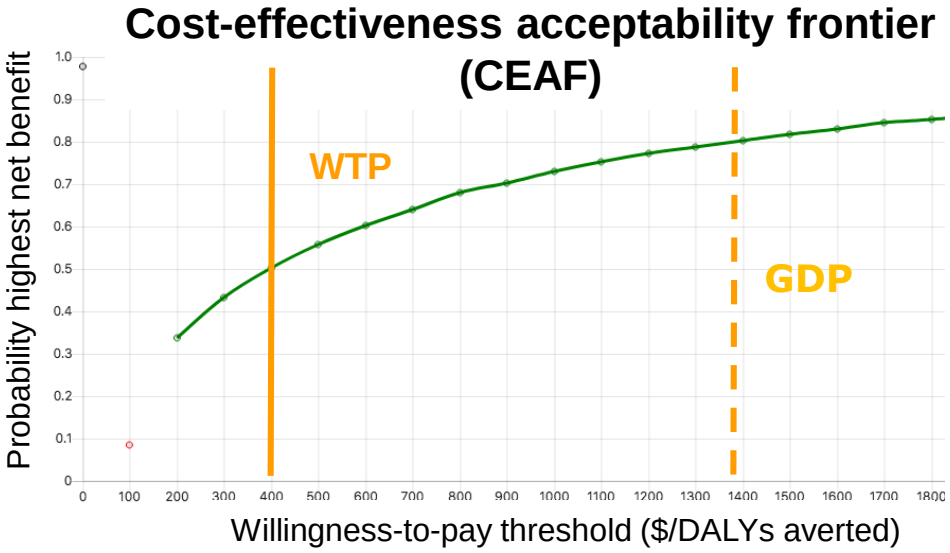

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Value of information analysis

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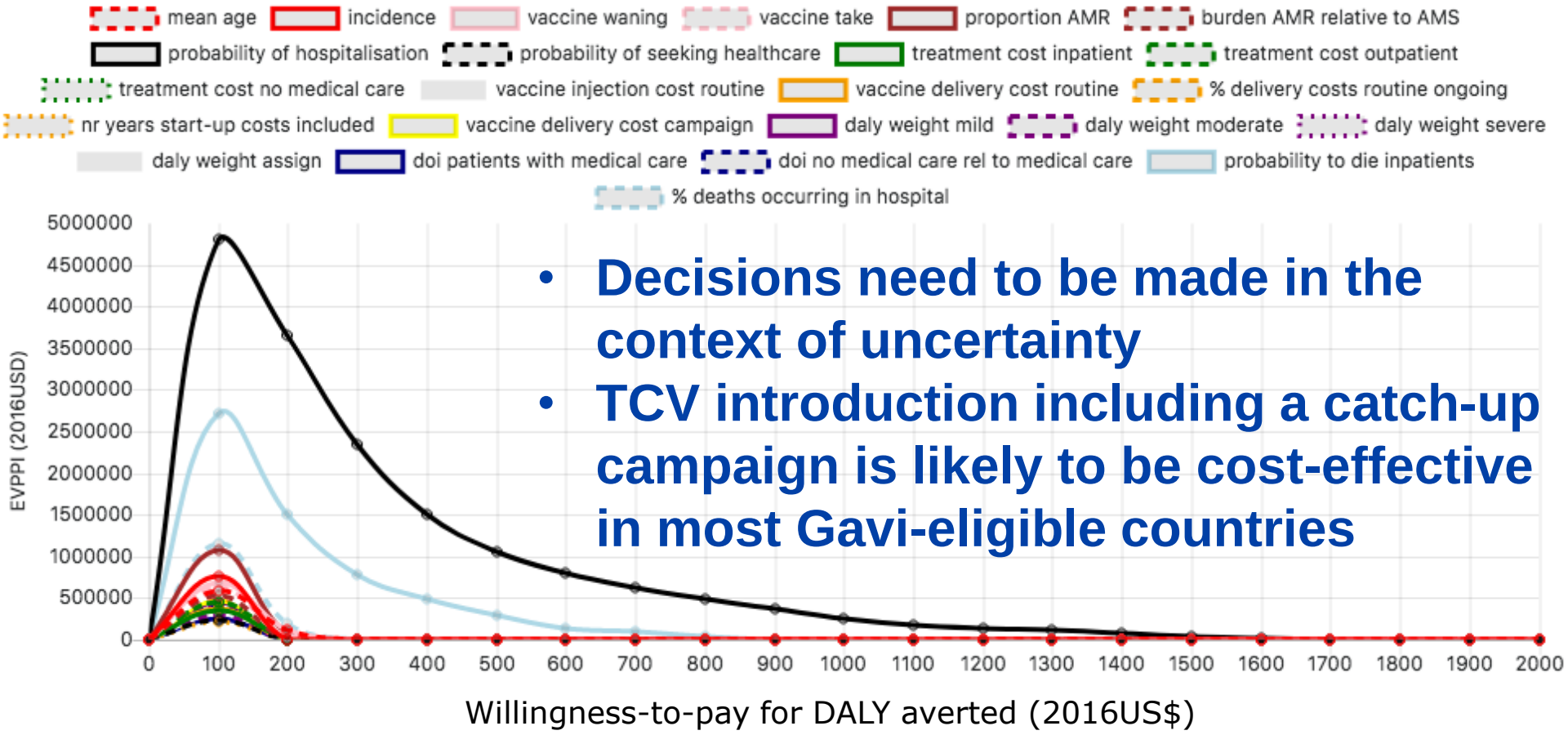

- **Decisions need to be made in the context of uncertainty**
- **TCV introduction including a catch-up campaign is likely to be cost-effective in most Gavi-eligible countries**

- **Probability of hospitalization**, **case fatality rate**, and **typhoid incidence rate** were the primary sources of uncertainty in most settings

Bilcke et al, Lancet Infect Dis (in press)

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https://ceatyphoid.uantwerpen.be/home/

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