Impact of Typhoid Conjugate Vaccine Use on Global Disease Burden

ASTMH symposium 126 - Typhoid Fever: the accelerated agenda to deliver conjugate vaccines

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- NVGH, in partnership with Biological E Ltd (Hyderabad, India), is developing a typhoid conjugate vaccine, Vi-CRM_{197}
- Concepts presented do not necessarily represent the official position of Novartis Vaccines Institute for Global Health nor Biological E Ltd

Typhoid disease burden

Current global distribution estimates

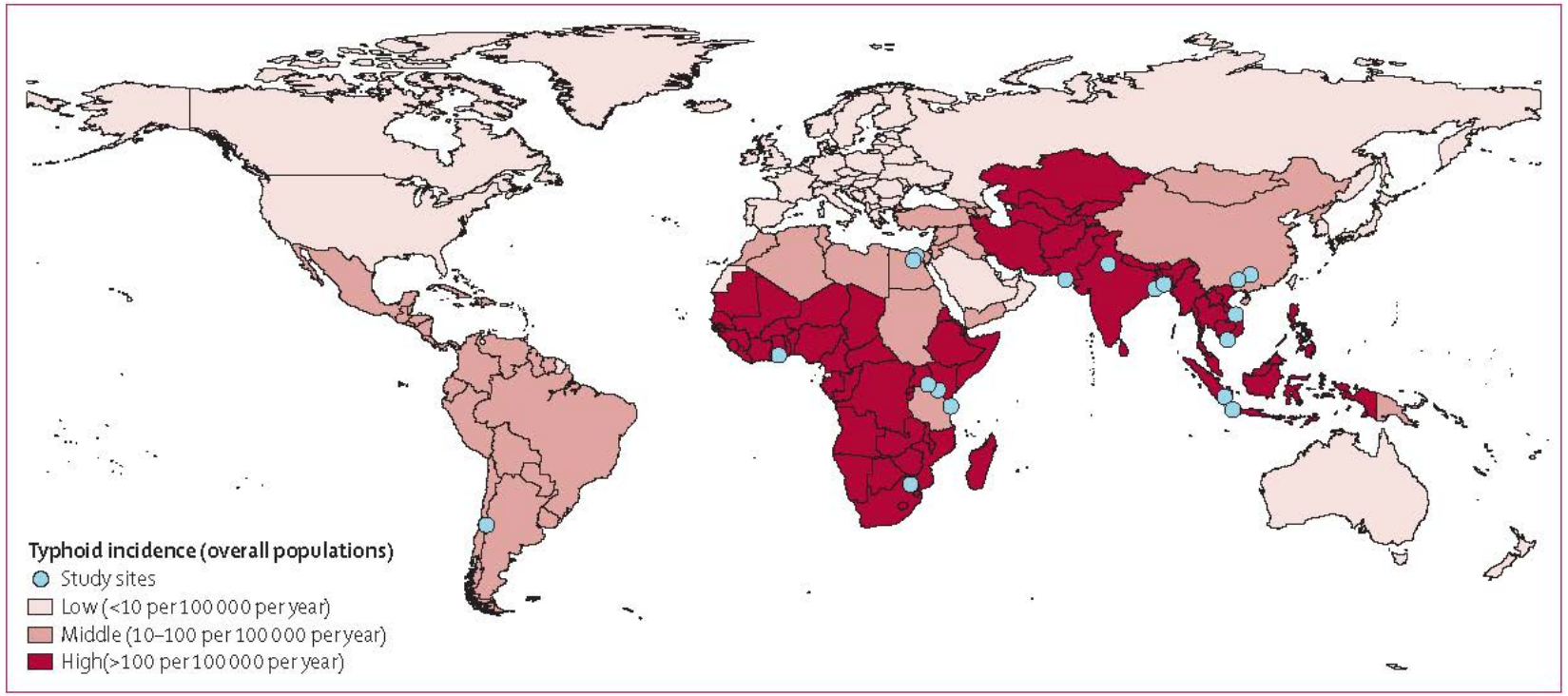

Figure 3: Typhoid incidence in low-income and middle-income countries (risk-adjusted and corrected for blood culture sensitivity)

From Mogasale, Lancet 2014

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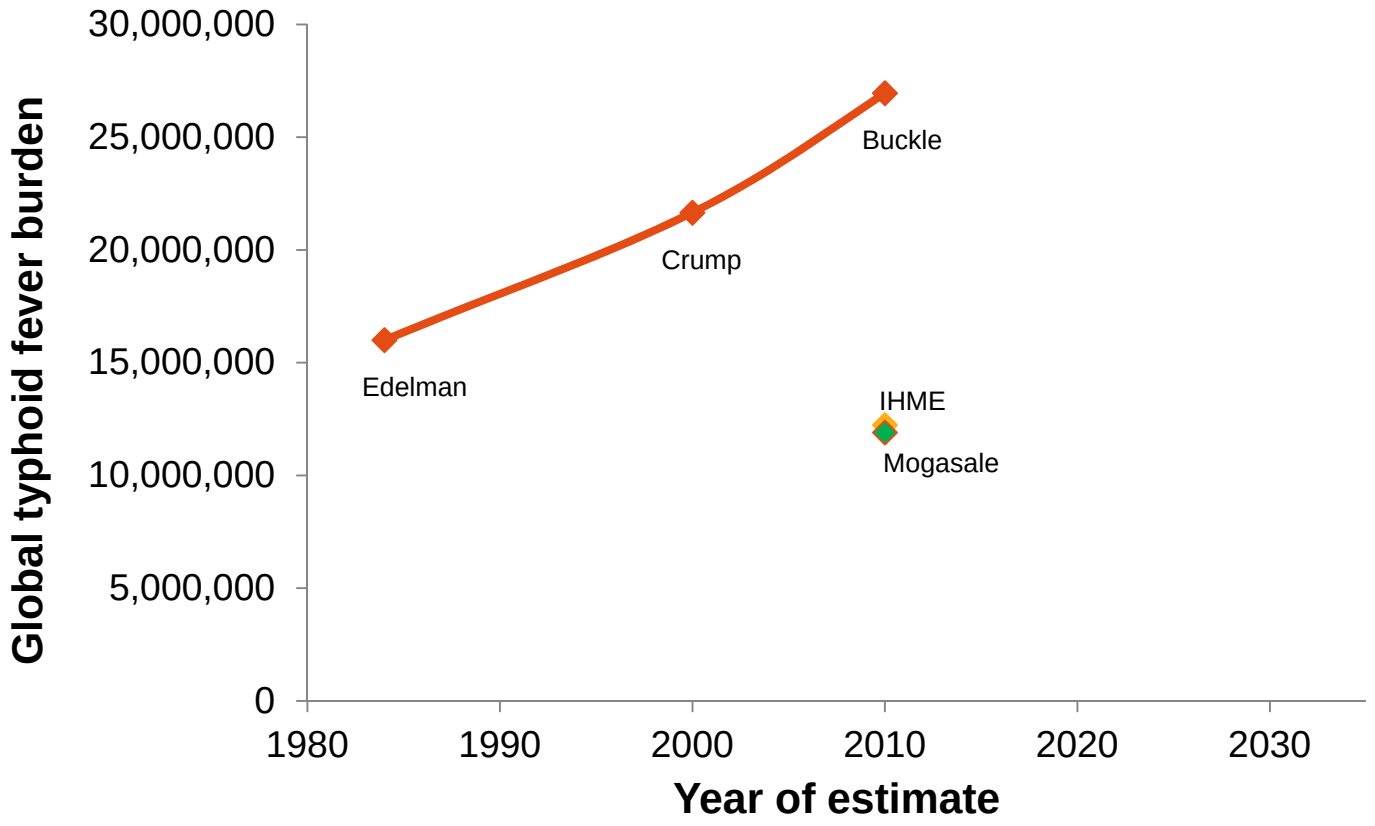
Typhoid disease burden

Trends in global estimates; numbers increase with population



Compiled from Edelman, Rev Infect Dis 1986
Crump, Bull WHO 2004
Buckle, J Global Health 2012
IHME, GBD database
Mogasale, Lancet 2014

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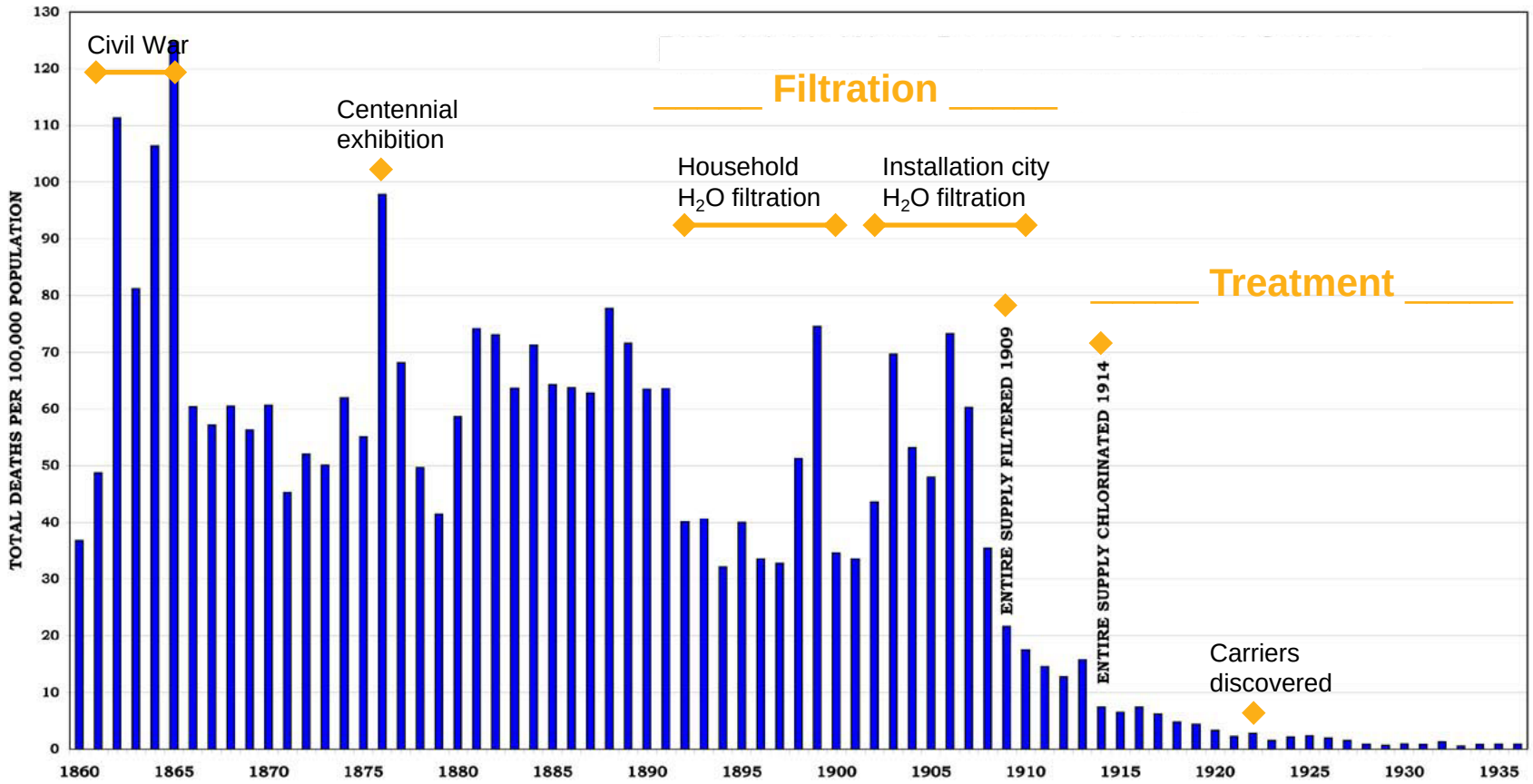
Typhoid disease burden

Estimations are not easy

- Data gaps in epidemiology and surveillance
- Incidence differs by
  - region, country and municipality
  - degree of industrialization
  - population and age
- Prevention in long & short term via
  - Safe water & sanitation
  - Food safety
  - Health education
  - Vaccination

Impact of improved water supply

On typhoid disease burden (Philadelphia 1860-1936)



Modified from www.phillyh2o.org

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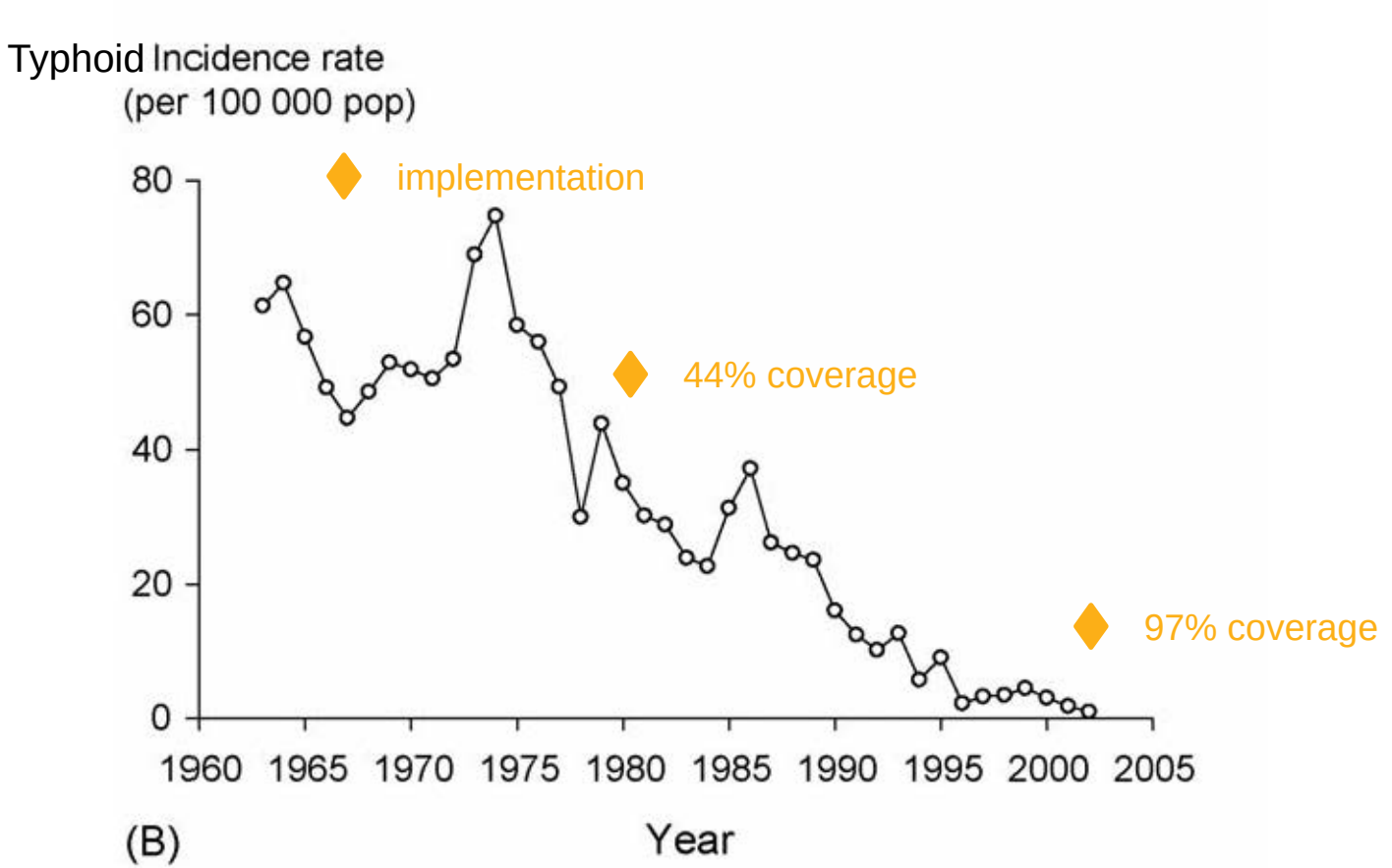
Impact of simple water systems & latrine use

On typhoid disease burden (Sarawak, Malaysia 1963-2002)



Modified from Liew, Trans Roy Soc Trop Med Hyg 2006

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Impact of inactivated whole-cell vaccine

On typhoid disease burden (in US Navy admissions)

Modified from Cook, Am J Public Health 1934

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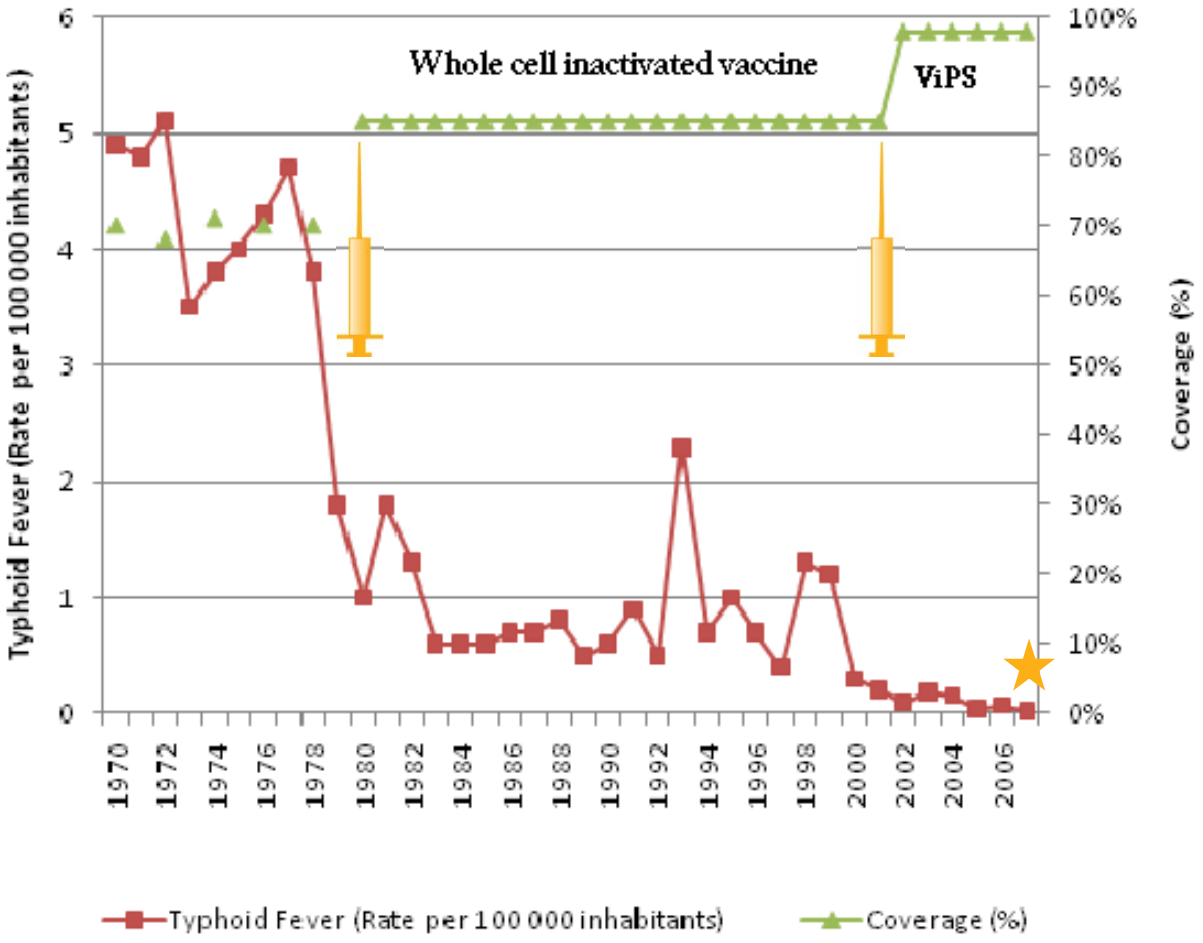
Impact of inactivated whole-cell & Vi PS vaccines

On typhoid disease burden (Cuba 1980-2007)



Population: 10-13-16 yr
Schedule: one dose Vi PS

Modified from mediccreview.medicc.org/articles/mr_56.pdf

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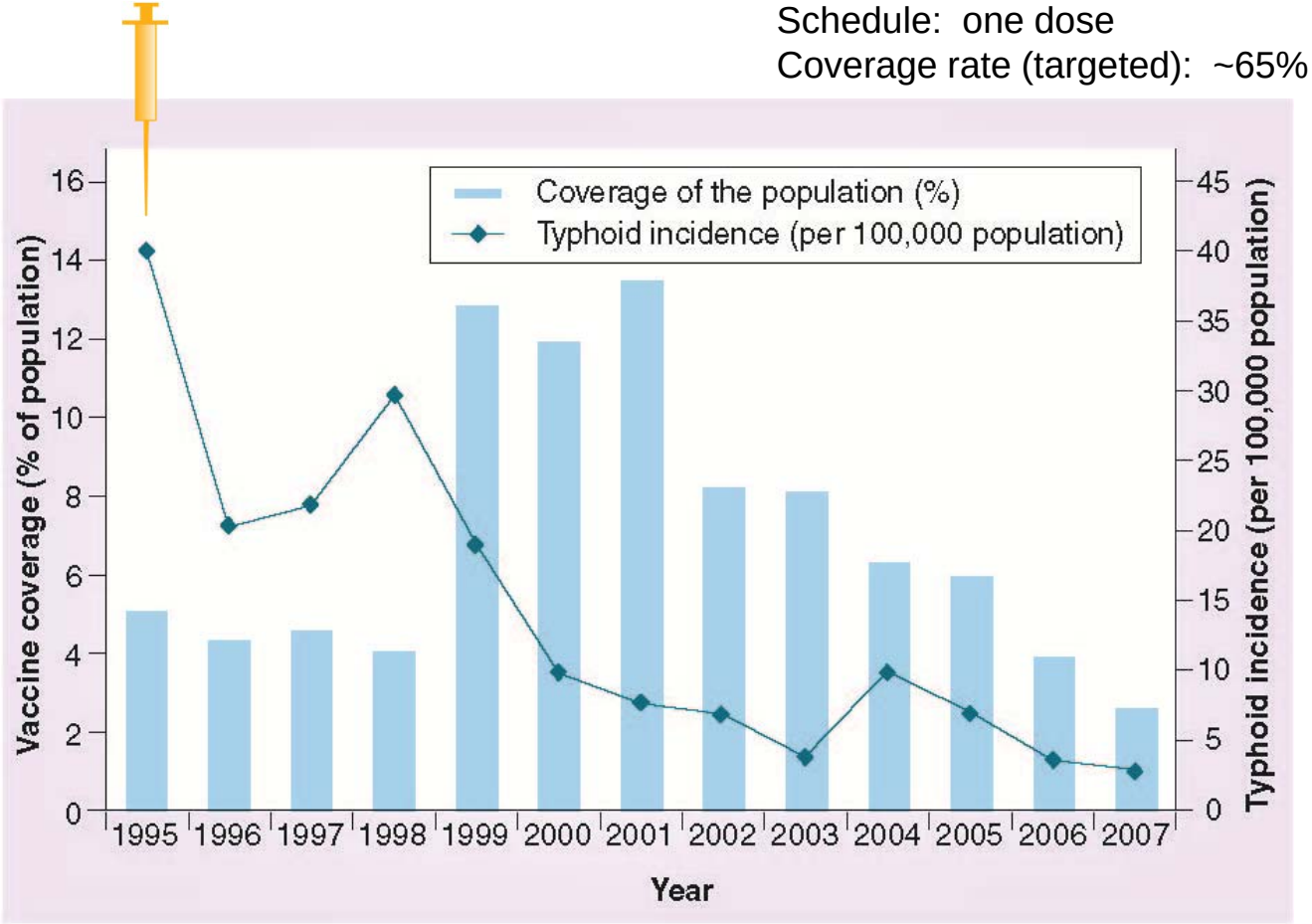
Impact of Vi polysaccharide vaccine (1)

On typhoid disease burden (Southwest China, Guilin Guangxi Province)

Population: school aged kids & high risk
Schedule: one dose
Coverage rate (targeted): ~65% & ~82%



From Khan, Expert Rev Vaccines 2010

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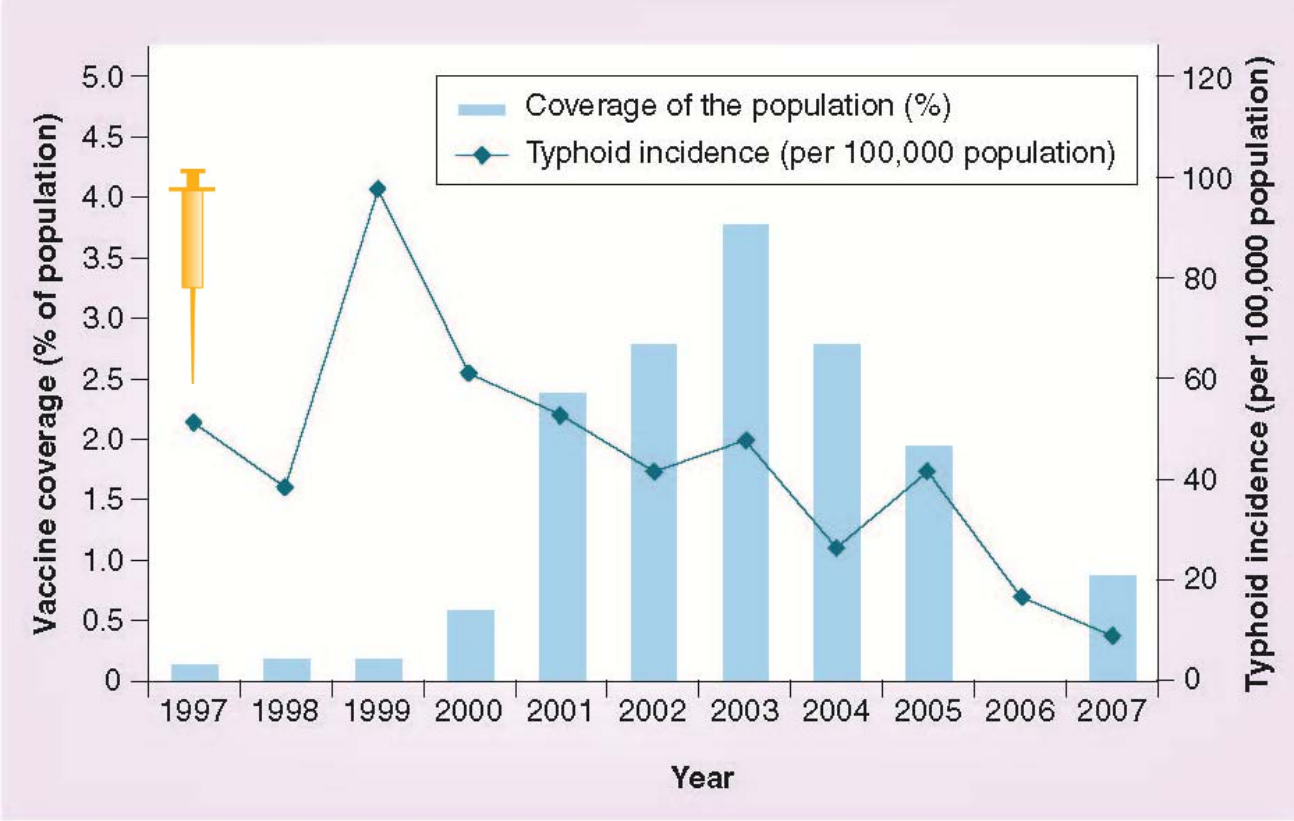
Impact of Vi polysaccharide vaccine (2)

On typhoid disease burden (Northwest Vietnam)

Population: kids 3-10 yr
Schedule: one dose
Coverage rate (targeted): 70 - 90%



From Khan, Expert Rev Vaccines 2010

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Estimating impact of Vi conjugate vaccines

Role for mathematical modelling

- Models validated against Vi polysaccharide vaccine data
- Vaccine impact relative to vaccine characteristics

Vi polysaccharide reality	Vi conjugate vaccine expectation
Licensed for > 2 years of age	Delivery with EPI from 9 months
Seroconversion 85-95%	Seroconversion 85-95% including infants
Efficacy ~65%	Efficacy >85%
Duration of protection ~3 years	Duration of protection ~10 years
Antibody response not boostable with possible immune tolerance	Boostable antibody response

- (type of immunity, carriers, herd immunity, typhoid endemicity, population coverage, other interventions, etc)

Estimating impact of Vi conjugate vaccines

Some key vaccine parameters used as input in the models

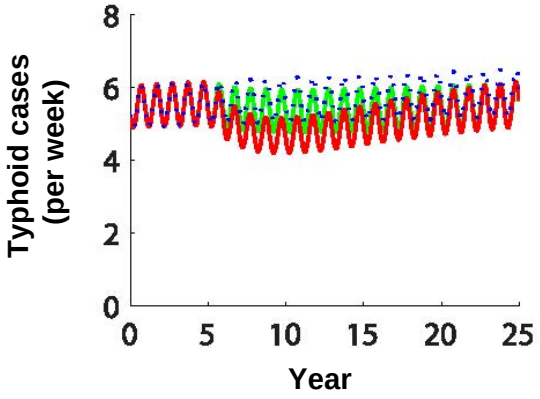
Parameter	Yale model	NVGH model
Vi PS vaccine efficacy	80% (68% over 1st year)	72%
Vi PS protection	36 months (exponential decay)	34 months (truncated normal distribution)
Vi conjugate vaccine efficacy	95.6%	96%
Vi conjugate protection	230 months (exponential decay)	85 months (truncated normal distribution)
Population	Vellore, India	Kolkata, India Dhaka, Bangladesh
Duration natural immunity	104 weeks	160 months clinical 800 months sterile

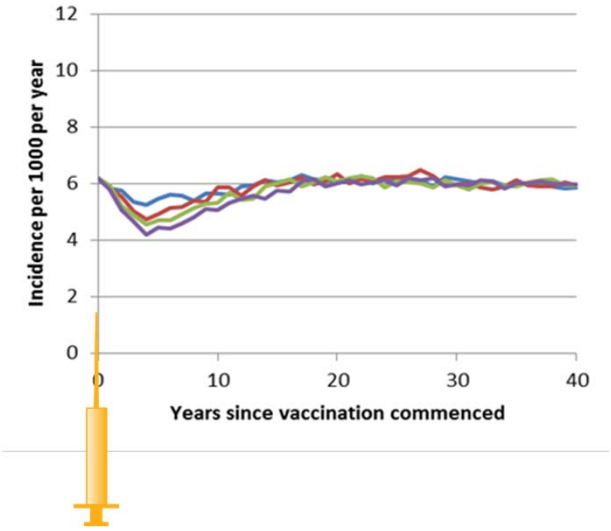
- Vaccination scenarios: which, who, when, where

Modeling the “which” – vaccination at 6 years

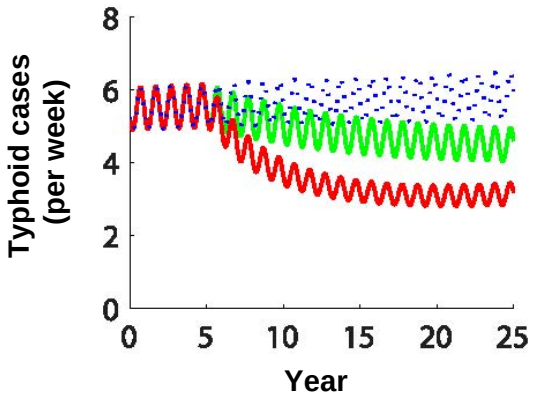
Longer duration vaccine gives bigger impact

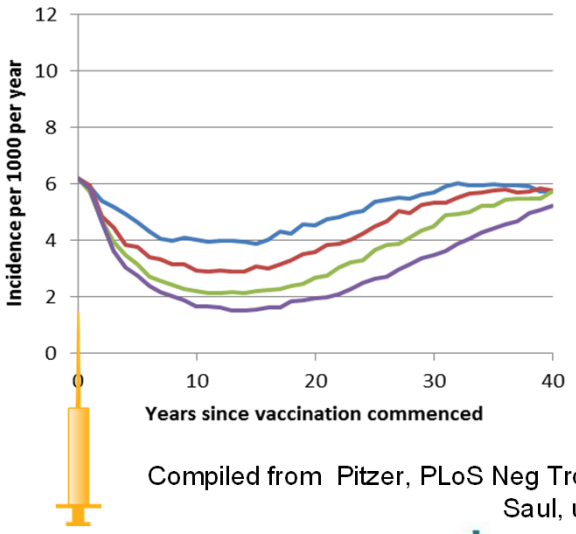
Vi polysaccharide





Vi conjugate





No vaccination

Population direct effect

Overall effect

Compiled from Pitzer, PLoS Neg Trop Dis 2014
Saul, unpublished

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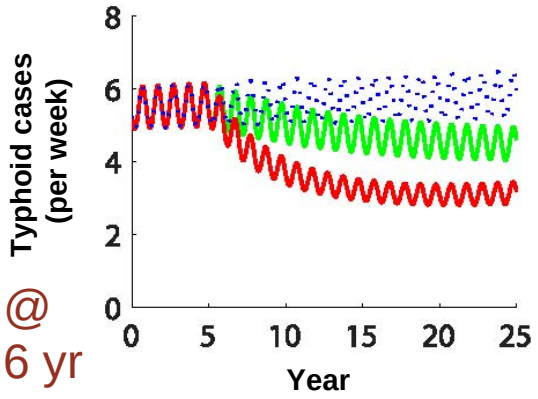
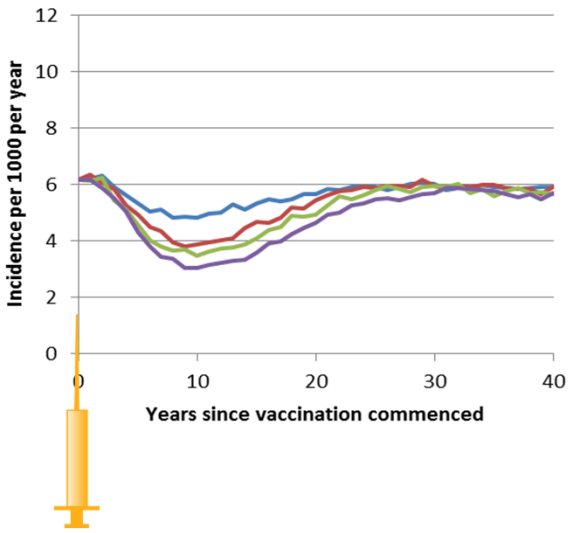
Modeling the "who" – routine vs campaign only

Campaign gives rapid & big reduction, but also pronounced rebound

Routine

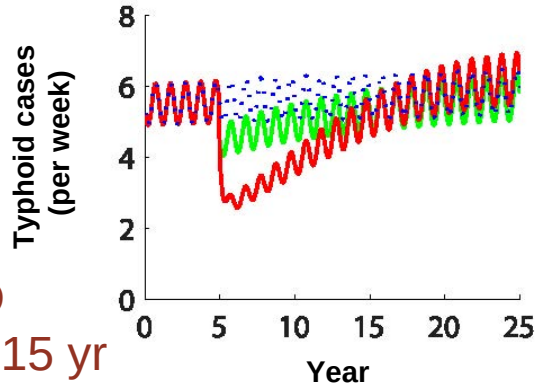


@ 6 yr

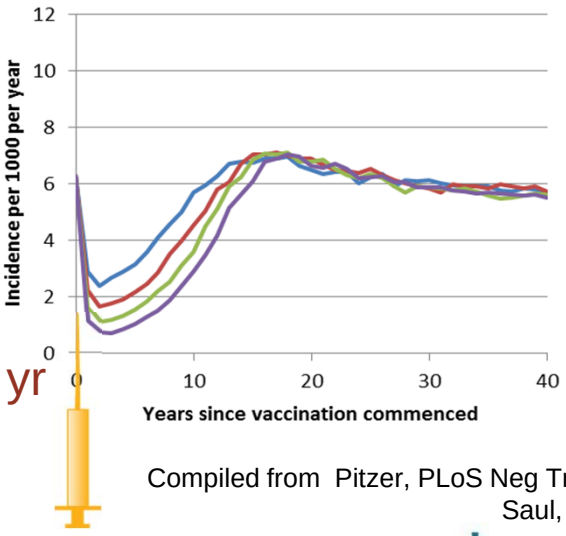


@ 9 mo

Campaign



@ 6-15 yr



@ 9 mo-15 yr

No vaccination
Population direct effect
Overall effect

Compiled from Pitzer, PLoS Neg Trop Dis 2014
Saul, unpublished

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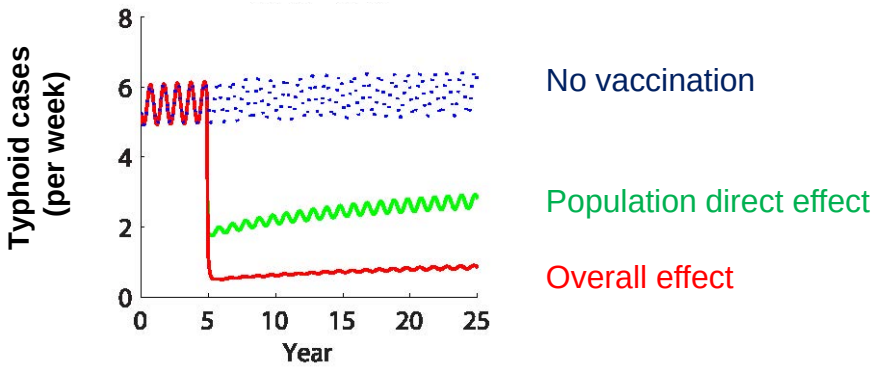
Modeling the "when" – 9 mo + booster

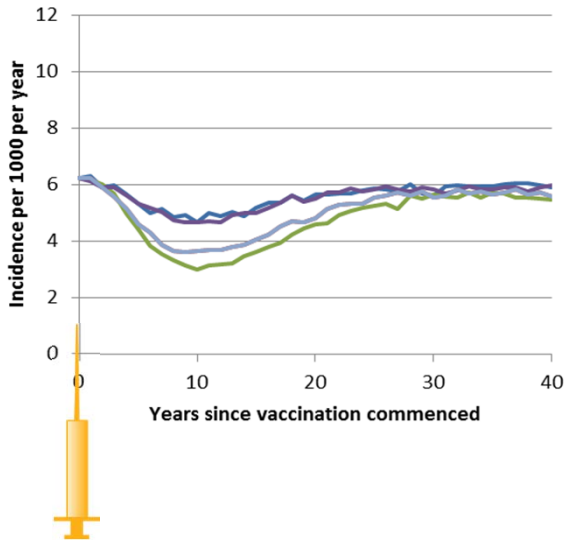
Booster can give sustained effectiveness

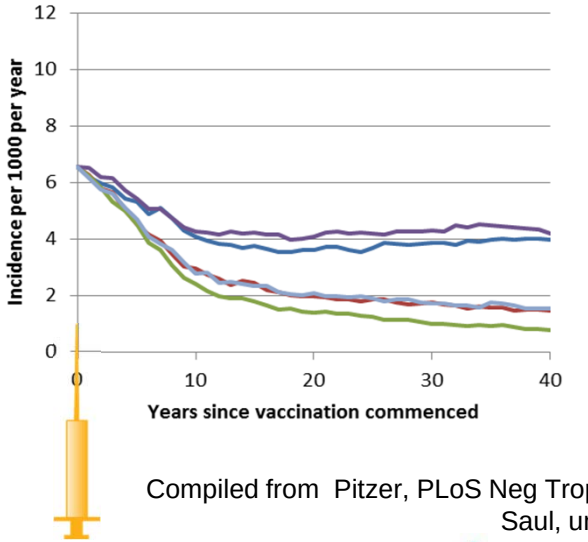
9 months only

Model output not published

9 month + booster @ 6-7 yr







Compiled from Pitzer, PLoS Neg Trop Dis 2014
Saul, unpublished

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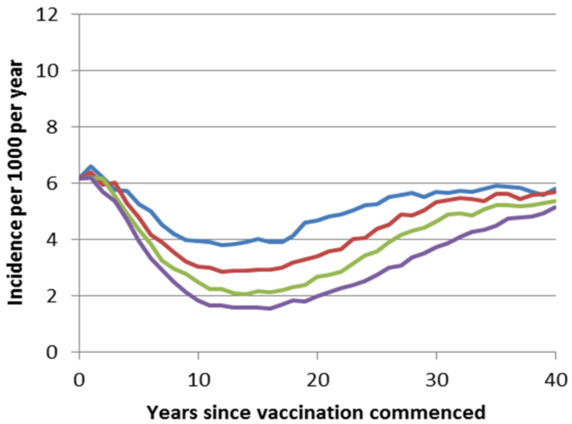
Modeling the “where” – Kolkata vs Dhaka

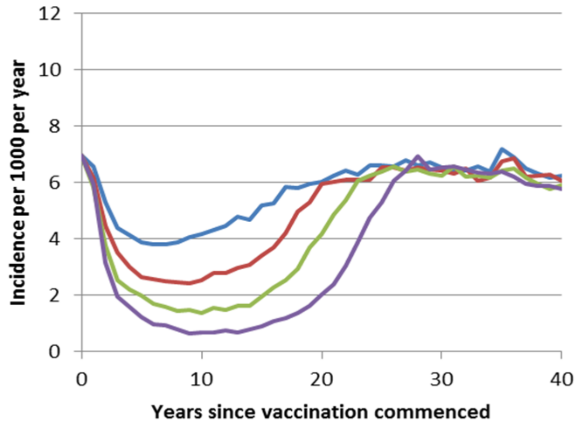
Endemicity matters for vaccine impact

Kolkata, India

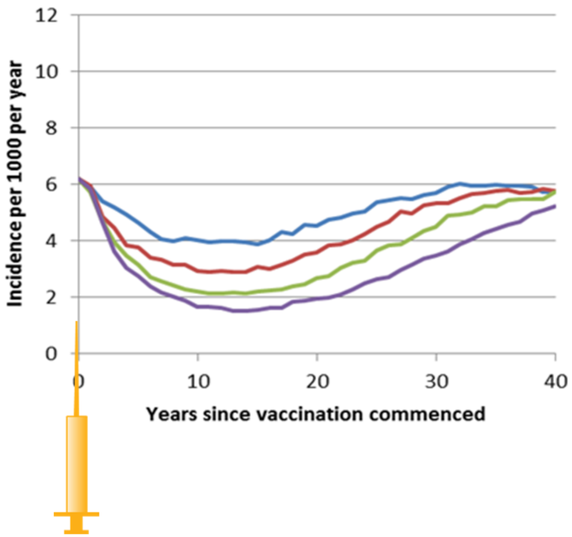
Dhaka, Bangladesh

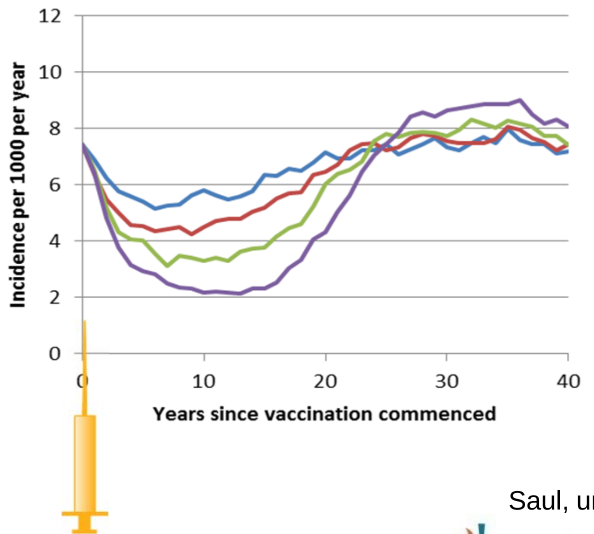
@
9 mo





@
6 yr





Saul, unpublished

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Outcomes of mathematical modeling

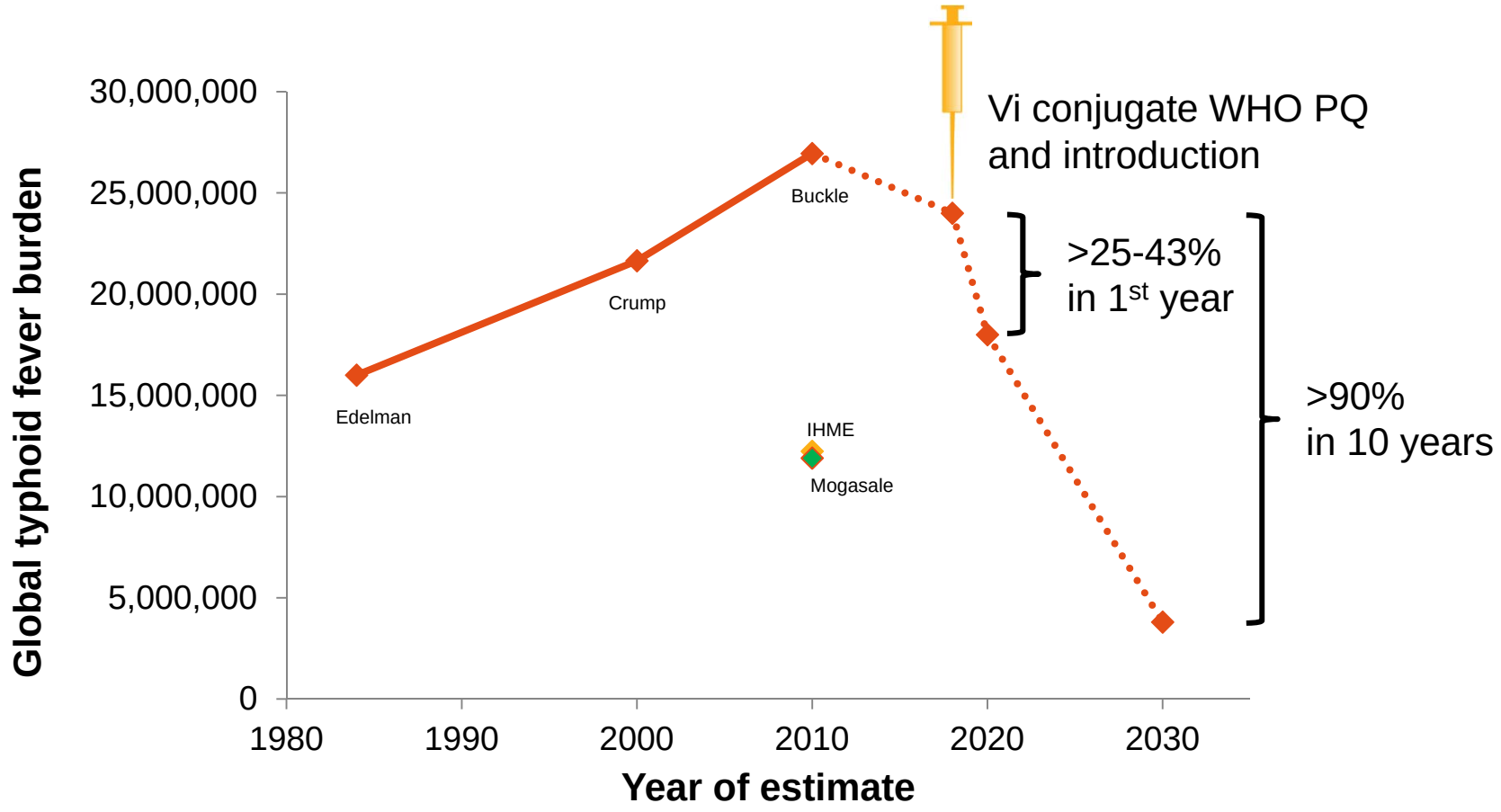
Positive outlook on typhoid disease burden

- Vi conjugate vaccines give bigger impact than Vi polysaccharide
- Vaccine campaigns give rapid and big reduction in cases but, with rebound
- Routine + booster vaccination give best sustained effectiveness
- Age of vaccination may impact disease reduction, especially when disease is present in youngest age groups, and should match risk
- Vaccine impact will vary dependent on disease heterogeneity

Vi conjugate vaccine implementation reduces transmission but on its own will not eliminate typhoid !

Vi conjugate impact on typhoid disease burden

Extrapolating from Vi polysaccharide in Thailand, China and Vietnam



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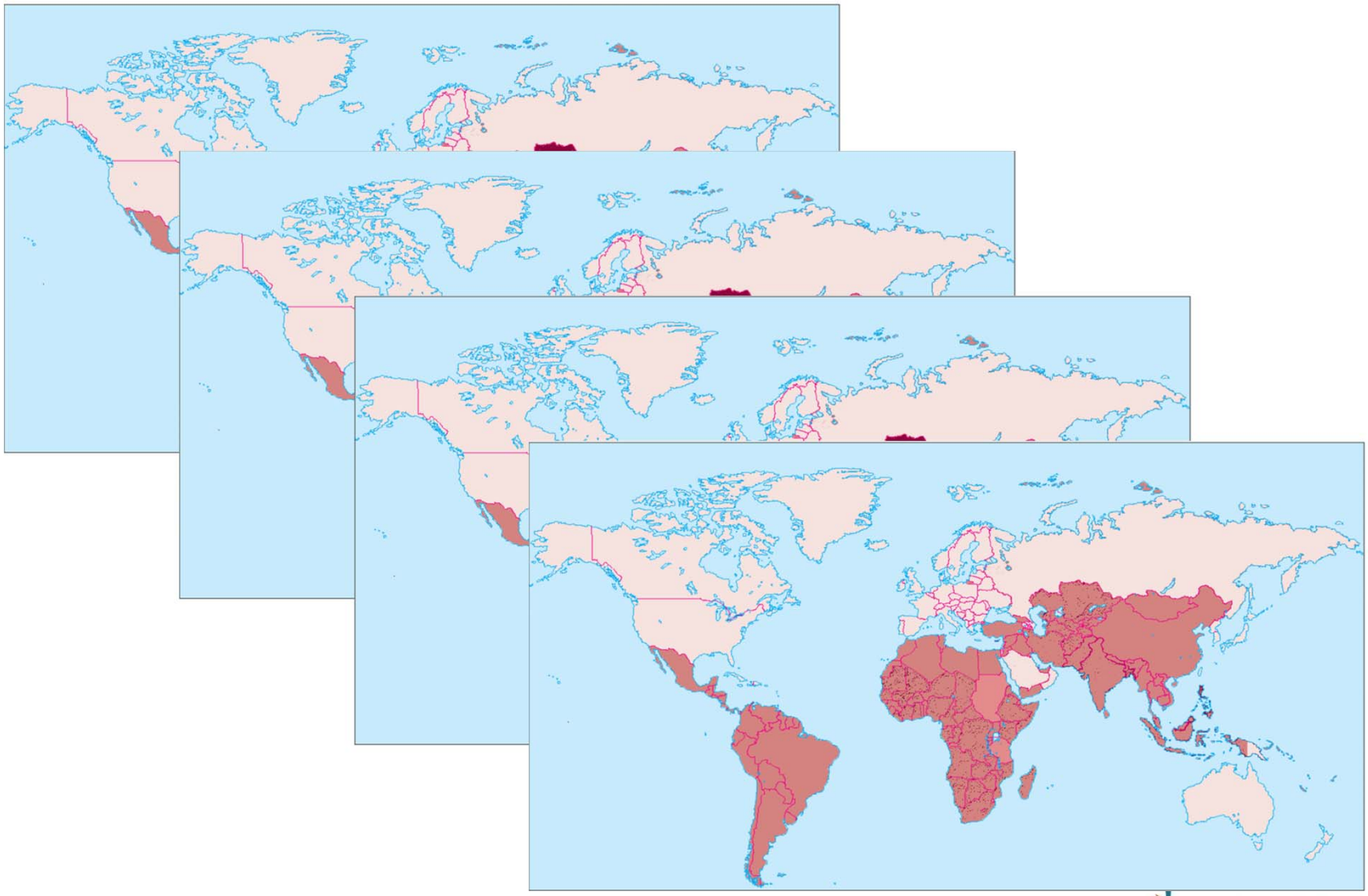
Vi conjugate impact on typhoid disease burden

Towards elimination



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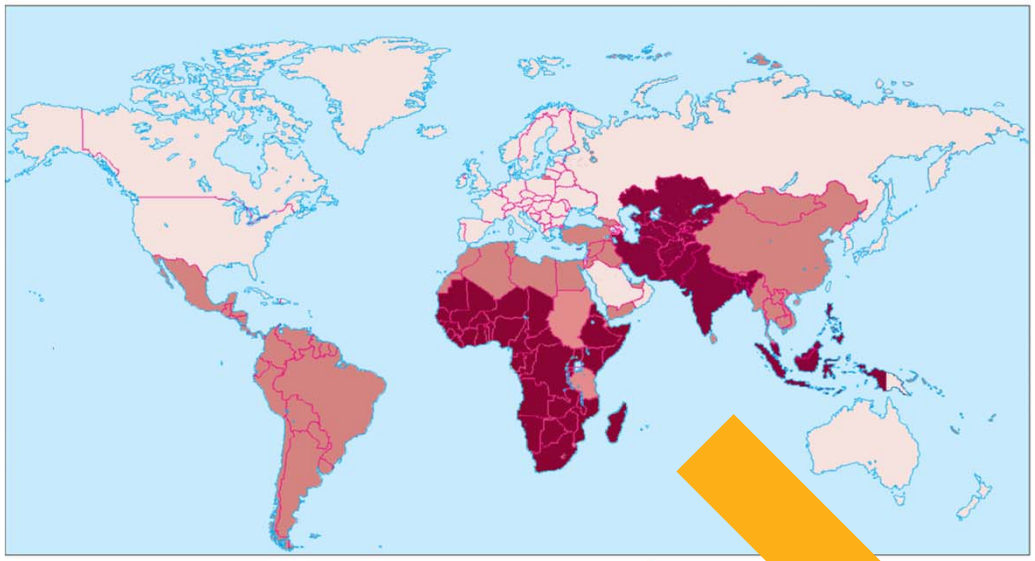
Vi conjugate impact on typhoid disease burden

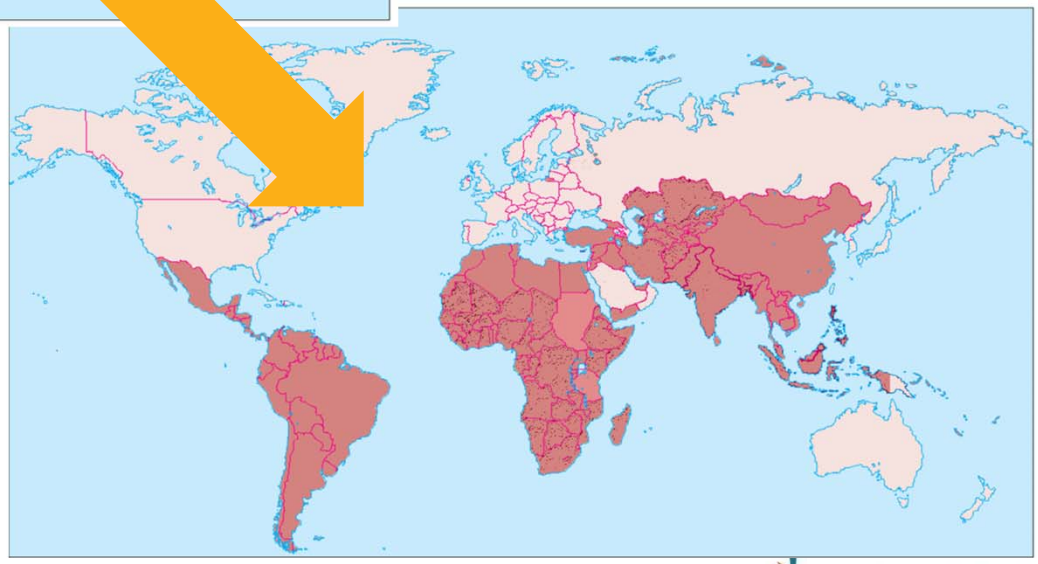
Towards elimination



- Attention to
  - Carriers
  - Rebound effect of vaccination
  - Co-infections (ie, paratyphoid)
- Improved WASH

- Better epidemiology

  especially in Africa
- Vi conjugate vaccine
  - Field data
  - Sufficient supply
  - Appropriate policy
  - Adequate coverage



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