Development of *S. Paratyphi* A-Containing Vaccines

Agenda:

1. **Regulatory Science Meeting on bivalent typhoid/paratyphoid vaccines**
2. **PPC and Roadmap**
3. **Update on paratyphoid CHIM**

Annelies Wilder-Smith, WHO

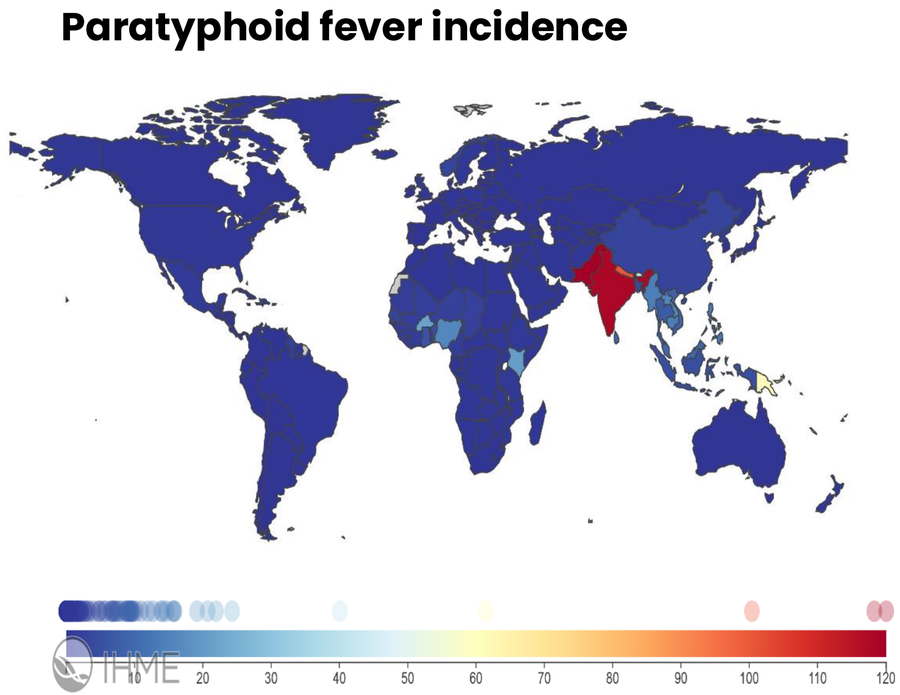
Ana Ibarz-Pavon, WHO

Andrew Pollard, University of Oxford

World Health Organization | IVB

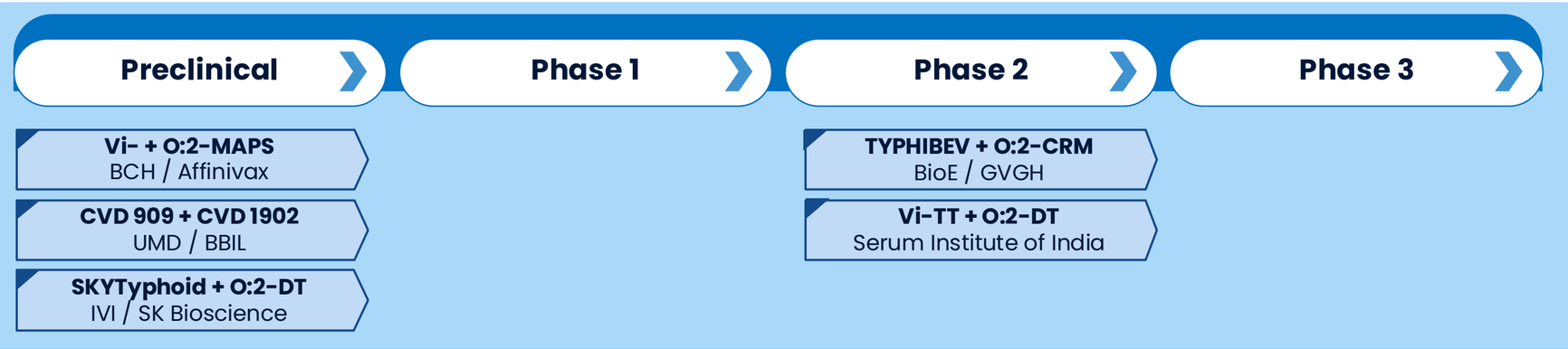
Burden of typhoid versus paratyphoid fever

Disease	Illnesses	Deaths	DALYs
Typhoid fever	7,154,555	93,333	7,087,733
Paratyphoid fever	2,166,063	14,127	1,011,842



https://vizhub.healthdata.org/gbd-results/

Bivalent enteric fever vaccines in development (S.Typhi/S. Paratyphi A)



- BioE/GVGH & Serum Institute are based on licensed/prequalified TCV
- UMD/BBIL vaccine is the only orally-administered vaccine

PDVAC recommendations 2022

PDVAC supported a proposed regulatory pathway for the bivalent conjugate vaccine based on:

1) For the typhoid component, demonstration of immunologic non-inferiority of the typhoid component in comparison to licensed TCVs.

2) For the paratyphoid component, demonstration of protective efficacy in a CHIM study with adults, equivalent immune responses in field immunogenicity trials in children in endemic settings, and commitment from developers to confirm vaccine effectiveness through post-approval studies.

WHO Informal Consultation on the Regulatory Pathway for Bivalent Salmonella Typhi/Paratyphi A vaccines for Use in Endemic Countries July 2024

Conclusions

- Phase 3 efficacy trials are unlikely to be feasible
- For the *S.* Typhi component, immunobridging and demonstration of non-inferiority to current WHO PQ'd TCVs
- Efficacy evaluation through CHIM for the *S.* Paratyphoid A component of the vaccine
- Immunobridging from CHIM (adults) to children
- Durability studies needed
- Safety set of >3000 (children and adults), in endemic or non-endemic country
- Subsequent vaccines can be licensed on the basis of immunobridging, dependent on the strength of the evidence of CoP and the comparability of platform
- Post-introduction Phase 4 studies will be a requirement

Next Steps

- Establishment of correlates of protection
- Standardization of immunoassays
- Development of TRS
- SAGE Working Group

Preferred Product Characteristics

Bivalent *Salmonella* Typhi/Paratyphi A vaccine characteristics

PPC & R&D Roadmap
Development Process

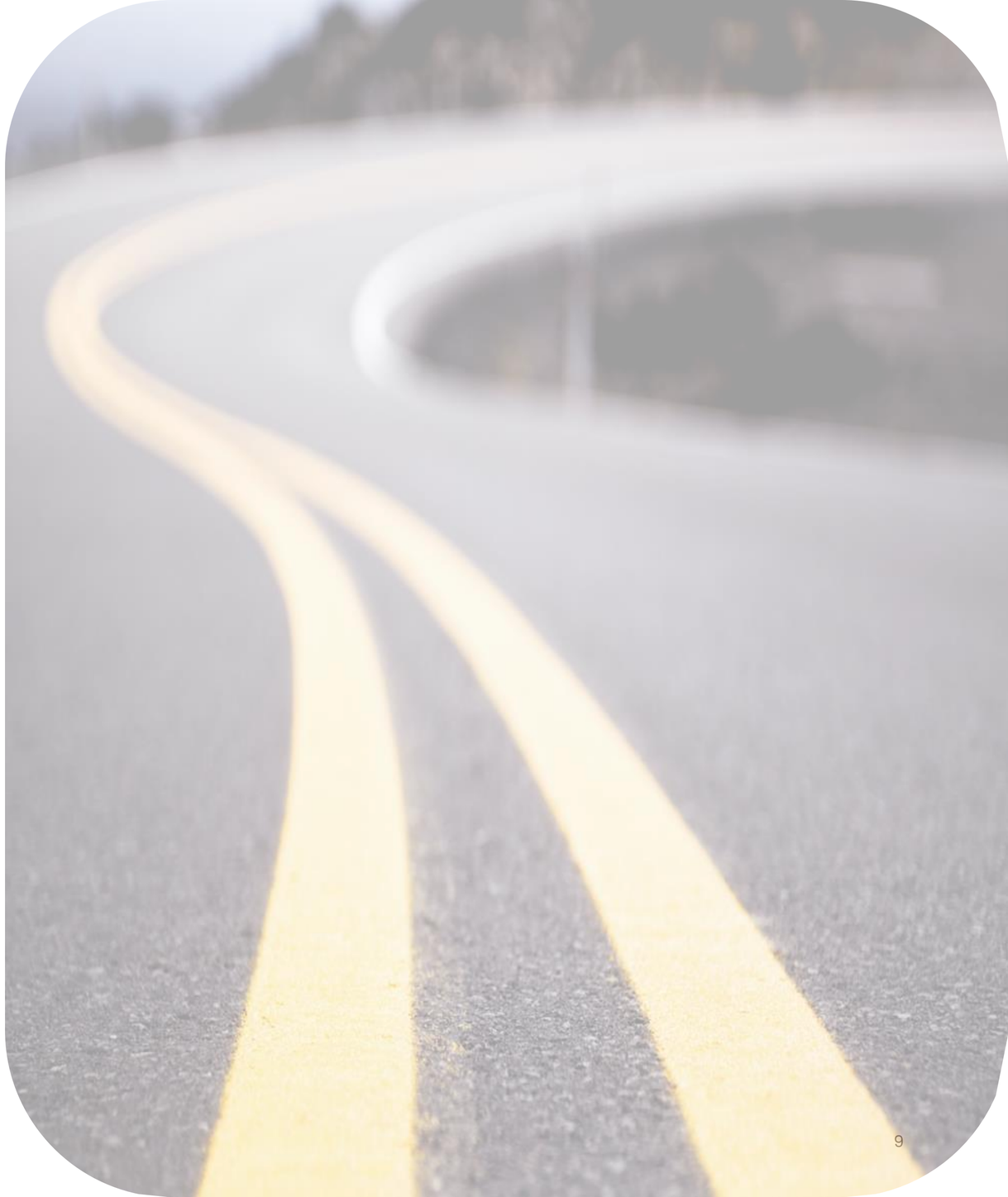
1. Set up the TAG-SV
2. Develop initial documents drafts
3. TAG-SV meetings to inform documents' content
    a. Meeting 1: vaccine development status, target population & market, vaccine efficacy targets, CoP, multivalent *Salmonella* vaccines
    b. Meeting 2: PPC and R&D roadmap draft discussion and refinement
    c. Meeting 3: Manufacturers' update on product development status: products, manufacturers perspectives on upcoming development challenges, market access & sustainability
4. Regulatory science consultation
5. Public consultation ->FINAL DRAFT FOR PDVAC ENDORSEMENT

Preferred product characteristics – bivalent S.Typhi/Paratyphi A vaccine

- **Vaccine type:** conjugate & LAV
- **Indication & coverage:** *Salmonella* Typhi & Paratyphi A
- **Population:** 6 months-65 years (TCV guided)
- **Schedule:** TCV-guided
- **Safety:** no different to TCV & other EPI vaccines
- **Efficacy/Immunogenicity:** non-inferior to TCV & superiority to natural immunity paratyphoid fever
- **Co-administration:** non-interference with EPI antigens

R & D Roadmap

Salmonella Typhi/Paratyphi A Bivalent Vaccine Research and Development Technology Roadmap



Vision

Development of a safe, affordable, and broadly effective vaccine to protect children against invasive disease caused by *Salmonella enterica* for use in low- and middle-income countries

Strategic goals

- Near term: to demonstrate immunogenicity, safety, and efficacy of a candidate bivalent enteric fever vaccine against serovars Typhi and Paratyphi A that protects against *S.* Paratyphi A infection and elicits protection against *S.* Typhi non-inferior to currently licensed monovalent vaccines
- Medium term: Licensure of at least one bivalent enteric fever vaccine to be used in LMICs
- Long term: Programmatic inclusion of vaccine(s) for the prevention of enteric fever in infants and young children to be chosen on the basis of the clinical needs by region

Themes

Addressing evidence gaps

1. Improve epidemiology and burden of disease data, including AMR surveillance
2. Addressing the diagnostic gap
3. Modelling

Accelerating vaccine development

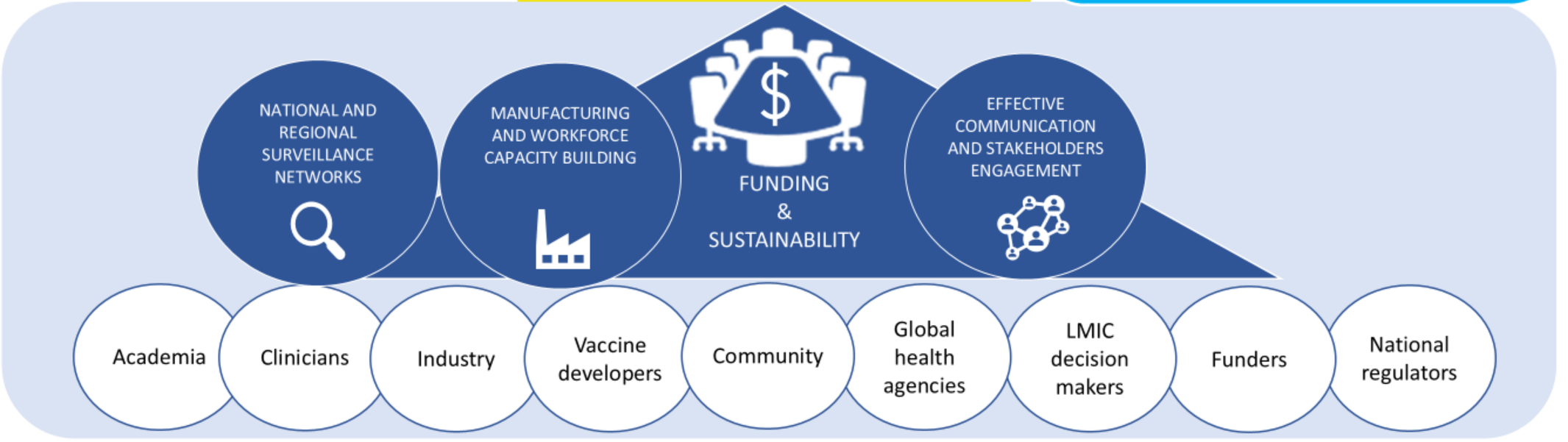
1. Define correlates of protection
2. Define the appropriate trial design and clinical endpoints
3. Immune interference studies for Typhi/Paratyphi A vaccines, and co-administration with existing vaccines
4. Define the regulatory approach and pathway to licensure

Maximizing public health impact

1. Understanding the requirements and needs for vaccine buy-in
2. Demonstrate the cost-benefit value of a bivalent enteric fever vaccine

Actions

Key Capacities



Questions for PDVAC

- Does PDVAC endorse the PPC for bivalent S. Typhi/Paratyphi A vaccines?
- Does PDVAC endorse the R&D Roadmap for bivalent S. Typhi/Paratyphi A vaccines?

Thank you

Comments and Actions

COMMENT	ACTION
Lines 693-8 state: This vaccine platform, known as generalized modules for membrane antigens (GMMA) is currently being used for the development of vaccines against iNTS (183–185), and a bivalent S. Typhi/Paratyphi A vaccine that delivers both: Vi and O:2 antigen proof-of-concept GMMA preparation demonstrated that such vaccine platform can induce the production of functional antibody responses against both antigens without interference (181). But the PPC itself states, under "Vaccine Type Notes": While a GMMA bivalent vaccine could be considered, there are currently not such vaccines in development.	Line 695-699 were rephrased to emphasize the fact the GMMA bivalent *S.* Typhi/Paratyphi A vaccine was a PRROF OF CONCEPT that did not progress further into development : " A, and a bivalent S. Typhi/Paratyphi A vaccine that delivered both: Vi and O:2 antigen was developed as a proof-of-concept GMMA preparation demonstrated that such vaccine platform can induce the production of functional antibody responses against both antigens without interference; however, this vaccine has not progressed further"
Why is the roadmap only restricted to children? Will there be significant differences in the activities for an adult roadmap? **– this could be addressed in a line**	Invasive *Salmonella* disease and enteric fever caused by both:*S.* Typhi and *S.* Paratyphi A affect mostly infants and children, and vaccination with TCV is currently targeting children in the EPI. The Roadmap does not intend to focus research towards a specific age group, but it is true that most of the data gaps and needs that need to be addressed are mostly found in infant population. Rewording throughout to ensure clarity on the fact that adult populations are not excluded.
The executive summary mentions that the strategic goals are categorized into **near-term, medium-term, and long-term objectives** but this is then not mentioned in the document- this could be addressed	The sentence has been re-phrased for clarity. There is one vision and three strategic goals enumerated in the document, not objectives. Goals are classed as near, medium and short-term. "[…] There are three strategic goals outlined in this document, set for the near, medium and long-term. In the near term, the focus is on demonstrating […]"

Technical Advisory Group on *Salmonella* Vaccines – Members

Alejandro Cravioto
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Denise Garrett
Applied epidemiology
Sabin Vaccine Institute

Florian Marks
Epidemiology, public health impact, and development
International Vaccine Institute

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University of Otago

Karen Keddy
Independent Consultant
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University of Maryland

Melita Gordon
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Drugs for Neglected Diseases Initiative (DNDi)
East Africa Regional Office

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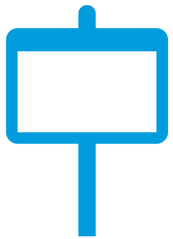
Ana Ibarz
IVB/PDR
WHO

Rob Kaminski (replacing Kate Emary)
IVB/PDR
WHO

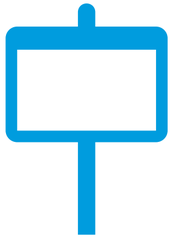
R&D Roadmap Vision & Strategic Goals

- **Overarching vision of a safe, affordable, and broadly effective vaccine to protect children against invasive disease caused by *Salmonella enterica* for use in low and middle-income countries**



Near Term

To **demonstrate safety, immunogenicity, and efficacy** of a candidate bivalent enteric fever vaccine against *Salmonella* serovars Typhi and Paratyphi A that shows **immunological non-inferiority to currently licensed TCVs**, and demonstrates **protection against *S.* Paratyphi A in CHIM** study, which **is confirmed in post-licensure effectiveness studies**



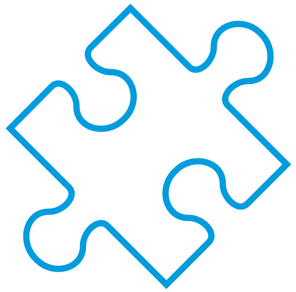
Medium Term

Licensure and WHO prequalification of at least one bivalent enteric fever vaccine to be used in endemic countries

Long Term

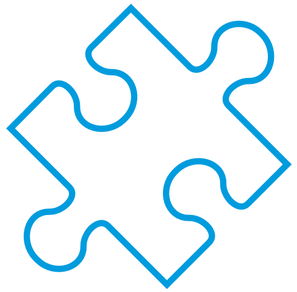
Programmatic inclusion of vaccine(s) for the prevention of enteric fever in infants and young children caused by typhoidal *Salmonella* serovars (which might be **as part of a combination vaccine with additional *Salmonella* serovars and/or with other antigens**) to be chosen on the basis of the **clinical needs by region**

R&D Roadmap Themes



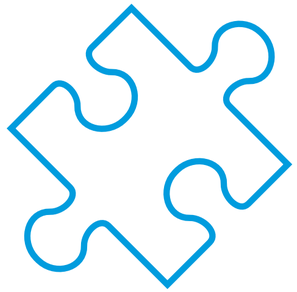
ADDRESSING EVIDENCE GAPS

- Improve surveillance & burden of disease data
- Addressing the diagnostic gap
- Modelling



ACCELERATING VACCINE DEVELOPMENT

- Define appropriate trial design & endpoints
- Define CoPs
- Immune interference studies & co-administration with other antigens
- Reference standards
- Define regulatory approach & pathway to licensure



MAXIMIZING PUBLIC HEALTH IMPACT

- Understanding requirements for vaccine buy-in
- Demonstrate cost-benefit value for a bivalent enteric fever vaccine

R&D Roadmap Key Capacities

Establish manufacturing capacity in LMICs

Workforce capacity building

Establish sustainable financing mechanisms and incentives for vaccine supply

Enhance surveillance capacity

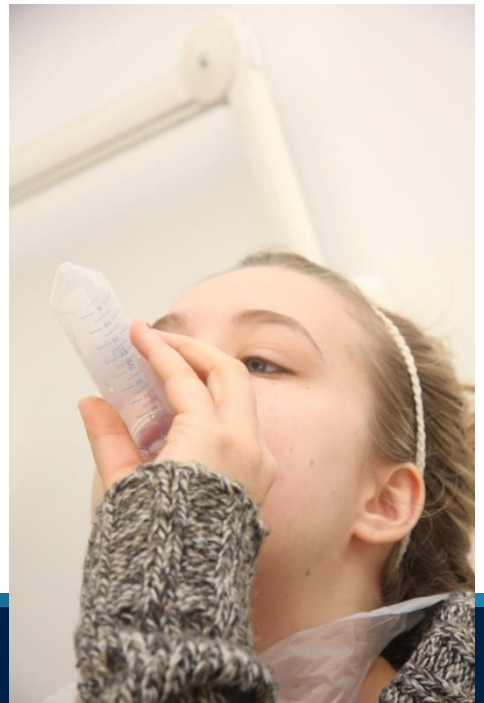
Effective communication and stakeholder engagement

UNIVERSITY OF OXFORD

DEPARTMENT OF PAEDIATRICS

Paratyphoid

Professor Sir Andrew Pollard, Director Oxford Vaccine Group



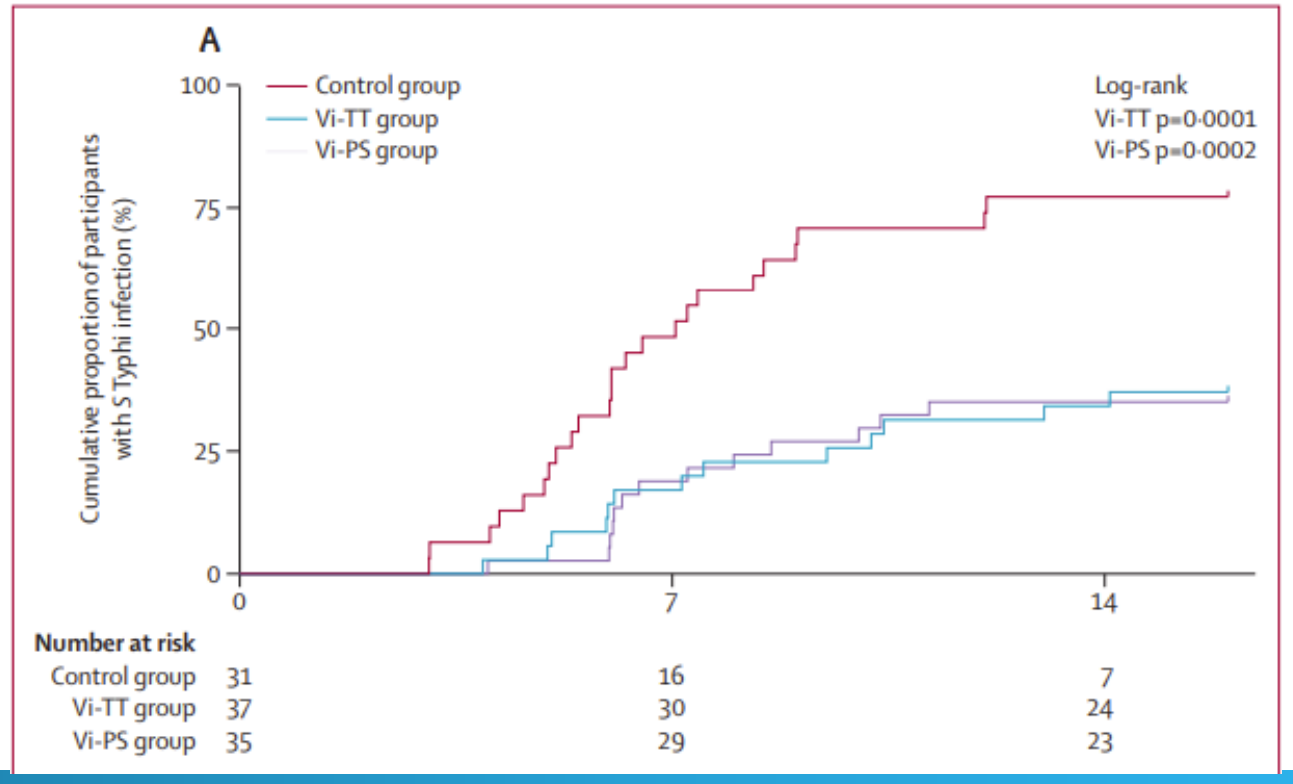
Efficacy and immunogenicity of a Vi-tetanus toxoid conjugate vaccine in the prevention of typhoid fever using a controlled human infection model of *Salmonella* Typhi: a randomised controlled, phase 2b trial

Celina Jin, Malick M Gibani, Maria Moore, Helene B Juel, Elizabeth Jones, James Meiring, Victoria Harris, Jonathan Gardner, Anna Nebykova, Simon A Kerridge, Jennifer Hill, Helena Thomaides-Brears, Christoph J Blohmke, Ly-Mee Yu, Brian Angus, Andrew J Pollard

Lancet 2017; 390: 2472-80
Published Online
September 28, 2017
http://dx.doi.org/10.1016/S0140-6736(17)32149-9
See Comment page 2419

Summary

Background *Salmonella enterica* serovar Typhi (*S* Typhi) is responsible for an estimated 20 million infections and 200 000 deaths each year in resource poor regions of the world. Capsular Vi-polysaccharide-protein conjugate vaccines (Vi-conjugate vaccines) are immunogenic and can be used from infancy but there are no efficacy data for the leading candidate vaccine being considered for widespread use. To address this knowledge gap, we assessed the efficacy of a Vi-tetanus toxoid conjugate vaccine using an established human infection model of *S* Typhi.



Typhoid CHIM supported WHO and Gavi decisions

Typhoid vaccines

WHO SAGE

SAGE noted the continued high burden of typhoid fever and the alarming increase in antimicrobial resistance of *Salmonella* Typhi (*S.* Typhi) in low- and middle-income countries. SAGE re-emphasized the importance of programmatic use of typhoid vaccines for controlling endemic disease. Following review of the available data, SAGE recommended the introduction of typhoid conjugate vaccine(TCV) for infants and children over 6 months of age as a single dose in typhoid endemic countries. Introduction of TCV should first be prioritized to countries with the highest burden of disease or a high burden of antimicrobial resistant *S.* Typhi. SAGE also recommended catch-up vaccination wherever feasible, with priority for catch-up in the youngest age groups (up to 15 years of age), depending on local epidemiology.

Typhoid vaccination is recommended in response to confirmed outbreaks of typhoid fever. Typhoid vaccination may be considered in humanitarian emergencies depending on risk assessment in the local setting.

WHO prequalification

World Health Organization

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Typhoid vaccine prequalified

3 JANUARY 2018 - WHO has prequalified the first conjugate vaccine to prevent typhoid fever called Typbar-TCV® developed by Indian pharmaceutical company Bharat Biotech.

The vaccine has long-lasting immunity, requires only one dose and can be given to children as young as 6 months through routine childhood immunization programmes. Other Typhoid vaccines are recommended for children over 2 years of age.

Prequalification by WHO means that the vaccine meets standards of quality, safety and efficacy, thus making it eligible for procurement by United Nations agencies, such as the United Nations Children's Fund.

A conjugate vaccine is one that is composed of a polysaccharide antigen that is fused to a carrier molecule.

In October 2017, the Strategic Advisory Group of Experts (SAGE) on immunization, which advises WHO, recommended typhoid conjugate vaccine for routine use in children over six months of age in typhoid endemic countries.

Related links

- More information
- See WHO's full list of prequalified vaccines
- Press release pdf, 89kb

Together We Can

Take on Typhoid

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Gavi: Millions of children set to be protected against typhoid

Posted on ***November 30, 2017*** *by* ***admin***

Press Release from Gavi, the Vaccine Alliance: *Gavi Board approves US$ 85 million funding window for 2019-2020 to support the introduction of typhoid conjugate vaccine in developing countries*

Vientiane, 30 November 2017 – Millions of children in the poorest countries could soon be protected against ty fever following the Gavi Board's approval today of a support window for typhoid conjugate vaccines (TCVs).

TOPICS

- Policy & Advocacy
- Global Research
- Drug Resistance
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RELATED POSTS

10 years after typhoid genome sequenced- what is being done to control typhoid fever?

CHIM confirmed by typhoid conjugate vaccine field trials

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 3 Efficacy Analysis of a Typhoid Conjugate Vaccine Trial in Nepal

Mila Shakya, M.P.H., Rachel Colin-Jones, M.A., Katherine Theiss-Nyland, Ph.D., Merryn Voysey, D.Phil., Dikshya Pant, F.C.P.S., Nicola Smith, M.B., B.Chir., Shrijana Shrestha, M.D., Buddha Basnyat, F.R.C.P.E., and Andrew J. Pollard, F.Med.Sci., for the TyVAC Nepal Study Team*

VE 79·0% (95% CI 61·9-88·5; p<0·0001)

N ENGL J MED 381;23 NEJM.ORG DECEMBER 5, 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of a Typhoid Conjugate Vaccine in Malawian Children

Priyanka D. Patel, M.B., B.S., Pratiksha Patel, M.B., B.S., Yuanyuan Liang, Ph.D., James E. Meiring, Ph.D., Theresa Misiri, M.P.H., Felistas Mwakiseghile, M.Sc., J. Kathleen Tracy, Ph.D., Clemens Masesa, M.Sc., Harrison Msuku, B.Sc., Queen Dube, Ph.D., B.S., Matthew B. Laurens, M.D., Ph.D., Melita A. Gordon, M.D., M. Neuzil, M.D., for the TyVAC Malawi Team

VE 80.7% (95% CI, 64.2 to 89.6)

N ENGL J MED 385;12 NEJM.ORG SEPTEMBER 16, 2021

>60 million doses delivered so far

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Health

Typhoid vaccine 'works fantastically well'

By James Gallagher
Health and science correspondent

24 minutes ago Share

A new typhoid vaccine works "fantastically well" and is being used to help stop an almost untreatable strain of the infection, doctors say.

Cases of the bacterial disease fell by more than 80% in trials, published in the New England Journal of Medicine.

Experts said the vaccine was a game-changer and would reduce the "terrible toll wrought by typhoid".

Nine million children are being immunised in Pakistan, where typhoid is now extremely resistant to antibiotics.

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Features

Five 'hot mic' moments that got leaders in trouble

Protection by va… …hildren against typhoid fever with a Vi… …d conjugate vaccine in urban Ba… …luster-randomised trial

…ngga Khanam*, Xinxue Liu*, Katherine Theiss-Nyland, Prasanta Kumar Biswas, Amirul Islam Bhuiyan, Faisal Ahmmed, …ams… …m, Peter O'Reilly, Karin Sofia Scherrer, Virginia E Pitzer, Kathleen M Neuzil, K Zaman, Andrew J Pollard†, John D Clemens†

Vi-TT total protection 85%; 97·5% CI 76 to 91, p<0·0001)

Published online August 9, 2021 https://doi.org/10.1016/S0140-6736(21)01124-7

10-30% of enteric fever caused by Paratyphoid

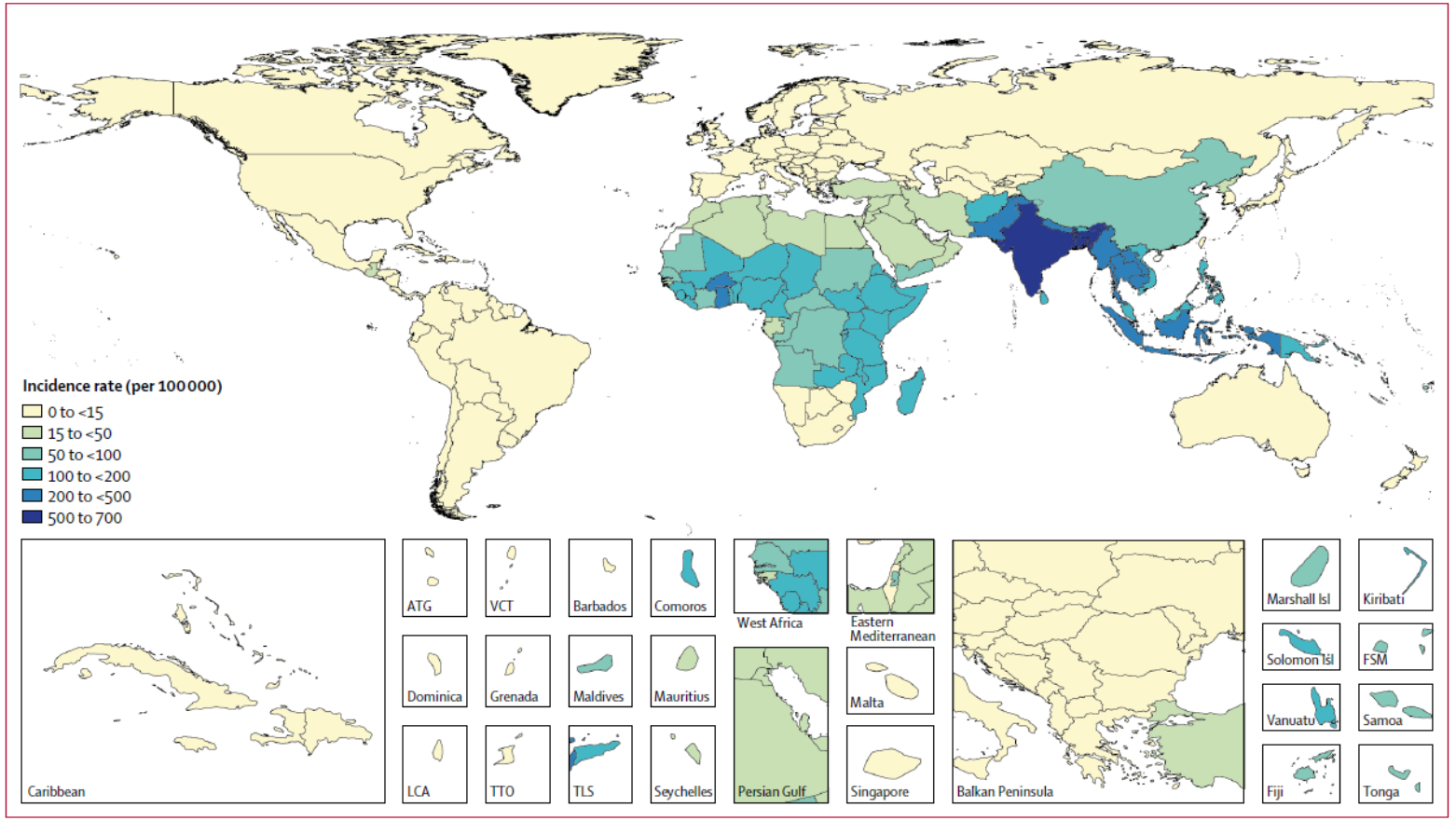
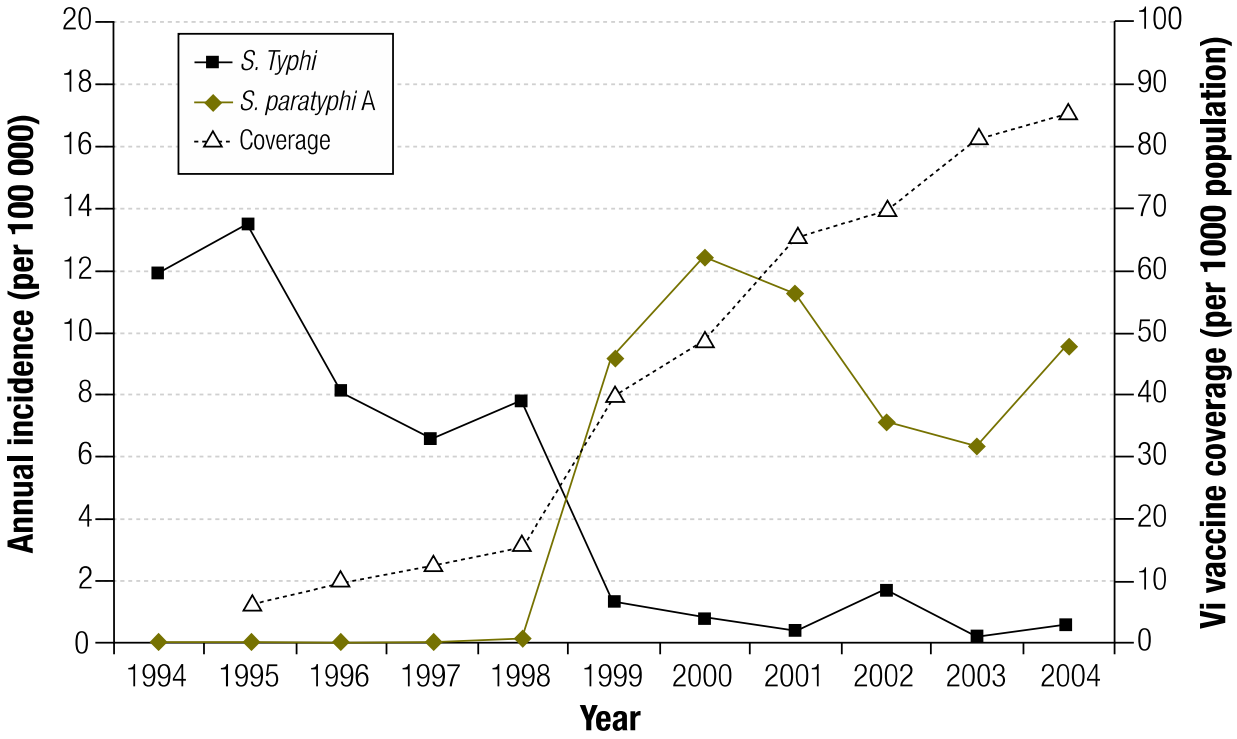


Figure 1: **Incidence rates (per 100 000) of typhoid and paratyphoid fevers, by country, in 2017**
Unfilled locations are those for which GBD does not produce estimates. The inset maps detail smaller locations. ATG=Antigua and Barbuda. FSM=Federated States of Micronesia. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. Isl=Islands. LCA=Saint Lucia. TLS=Timor-Leste. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines.

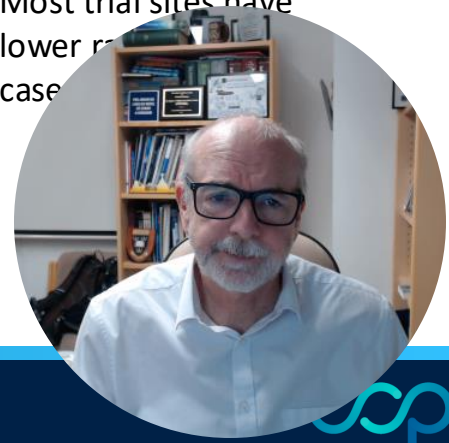
Paratyphoid

Fig. 2. **Estimated *Salmonella typhi* and *Salmonella paratyphi* A incidence with cumulative Vi polysaccharide immunization coverage in Guangxi province, China, 1994–2004**



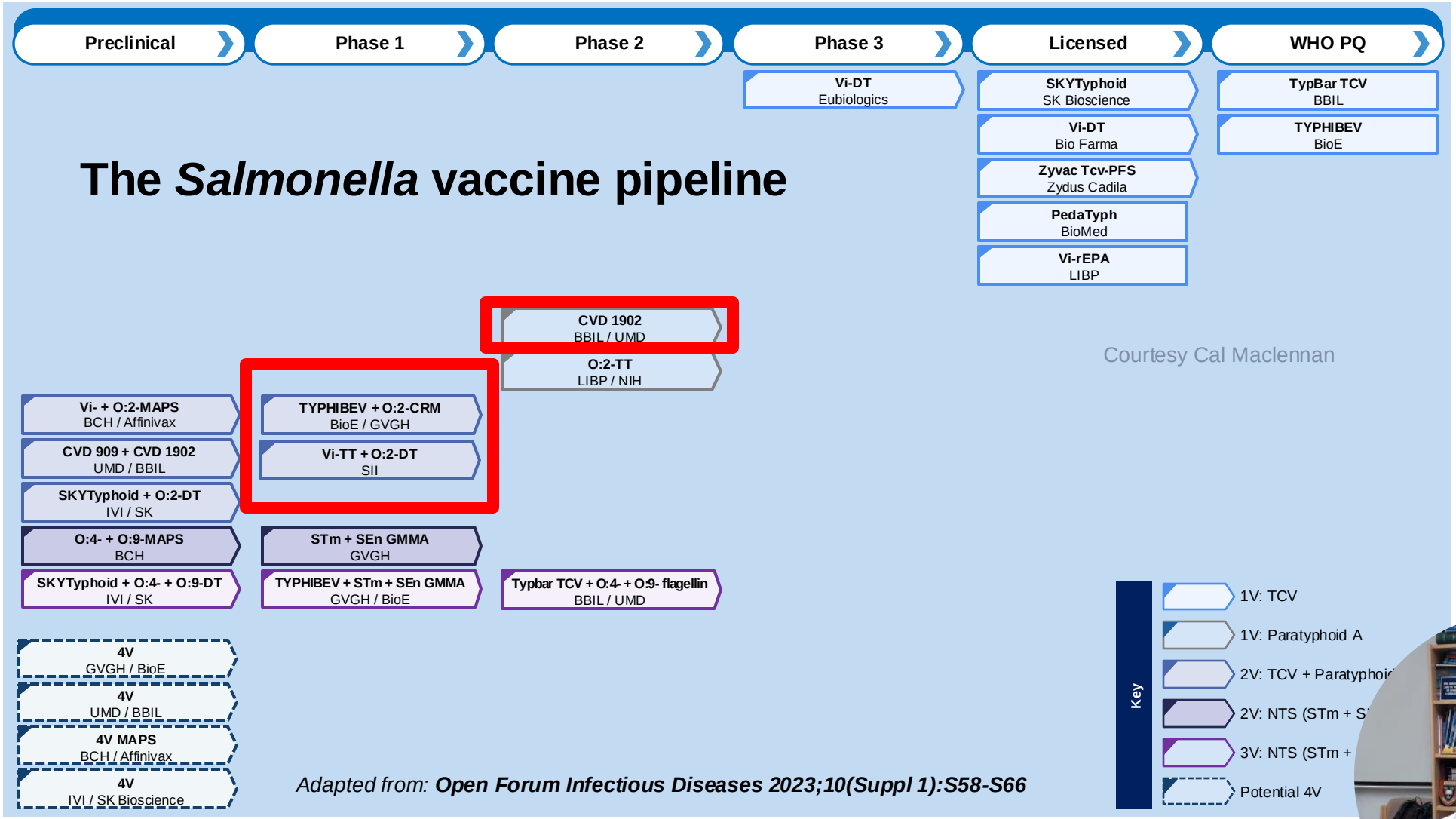
Data from China's Notifiable Infectious Disease Reporting system, laboratory surveillance and outbreak investigation, Guangxi Centers for Disease Control and Prevention, Guangxi, China.

- Up to 50% of enteric fever in returning travelers
- Some areas of Asia, leading cause of enteric fever
- Most trial sites have lower r
case



Dong, B.D et al Bull World Health Organ , 2010 88(9), 689–96

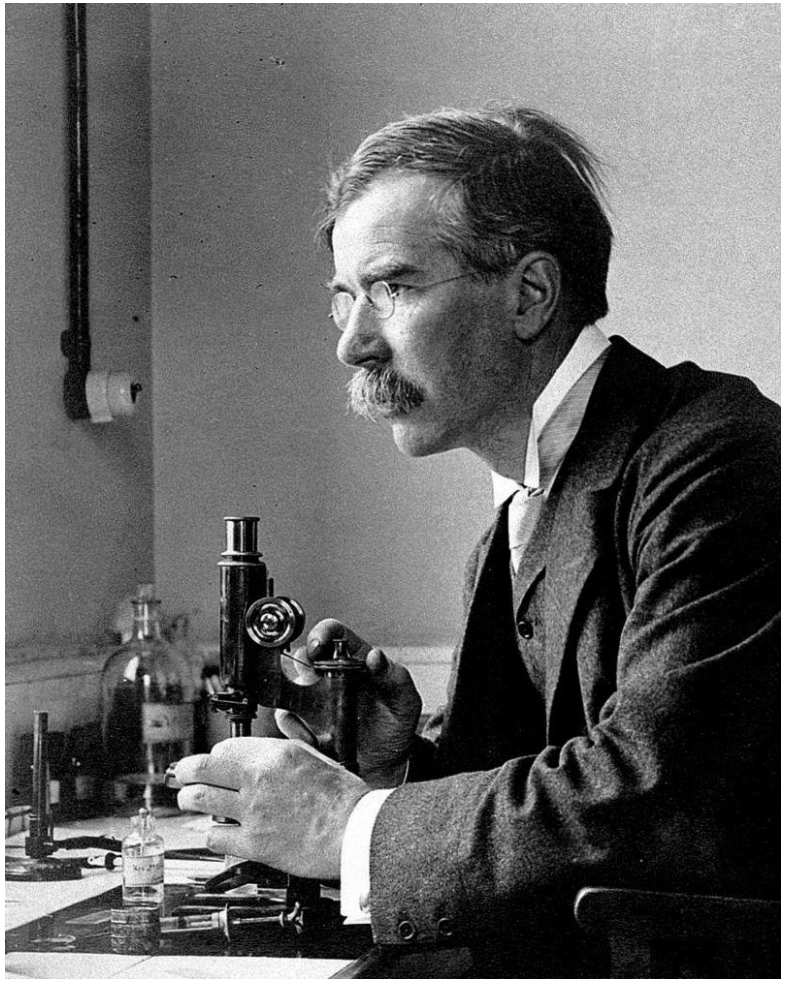
The *Salmonella* vaccine pipeline



Adapted from: ***Open Forum Infectious Diseases 2023;10(Suppl 1):S58-S66***

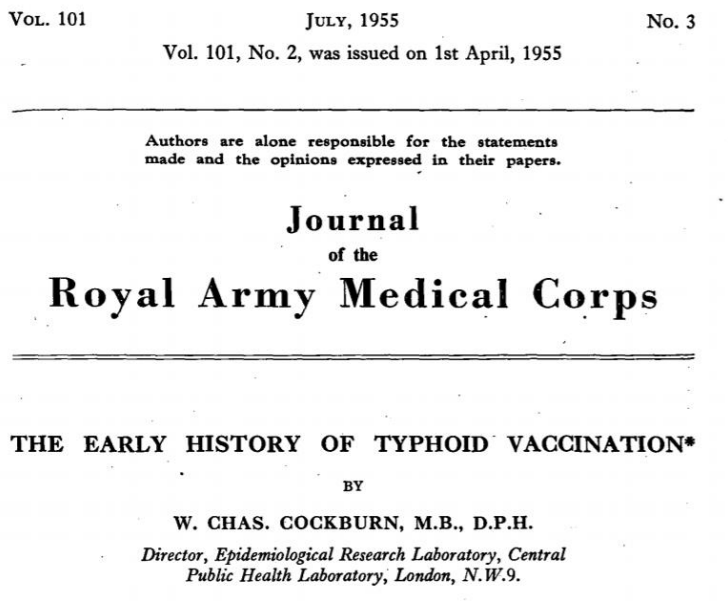
Slide provided by Cal Maclennan

Almroth Wright (1861-1947)



Professor of Pathology at the Royal Army Medical College

Heat Killed S. Typhi vaccine developed in 1896



VOL. 101 JULY, 1955 No. 3

Vol. 101, No. 2, was issued on 1st April, 1955

Authors are alone responsible for the statements made and the opinions expressed in their papers.

Journal of the Royal Army Medical Corps

THE EARLY HISTORY OF TYPHOID VACCINATION*

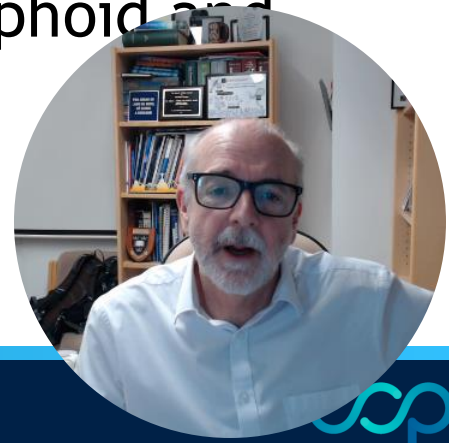
BY

W. CHAS. COCKBURN, M.B., D.P.H.

Director, Epidemiological Research Laboratory, Central Public Health Laboratory, London, N.W.9.

David Harvey

- TAB vaccine
- Developed by David Harvey at RAMC
- Used from circa 1915 during the first World War (90% of troops vaccinated in last 3 years)
- "Covered" typhoid and paratyphoid.

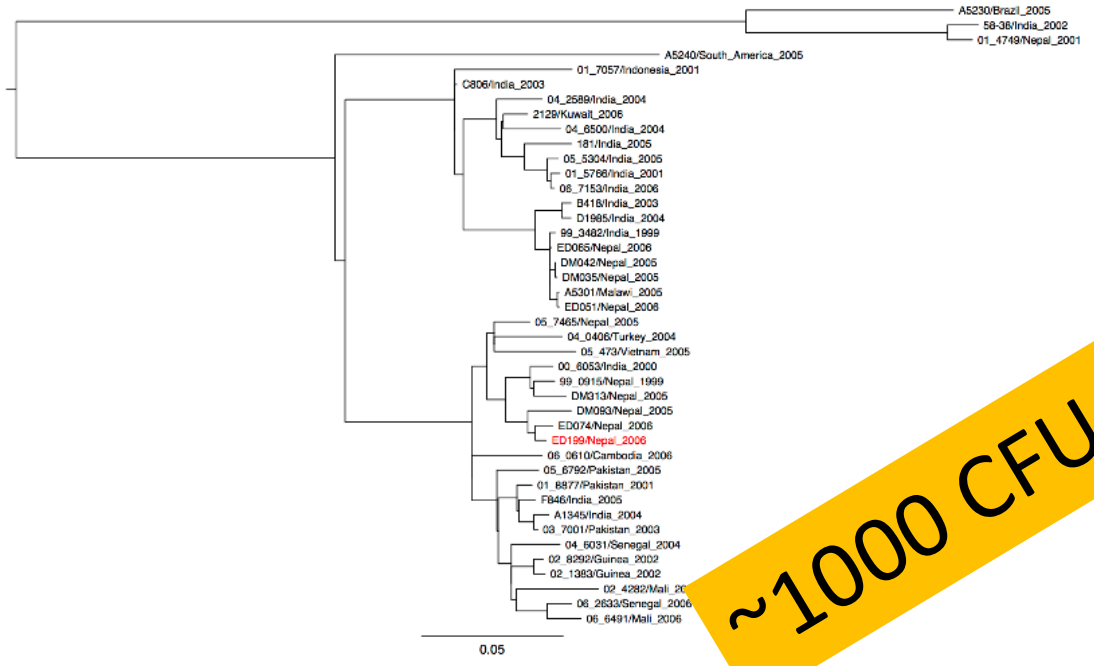


Paratyphoid vaccines

No currently available paratyphoid vaccine

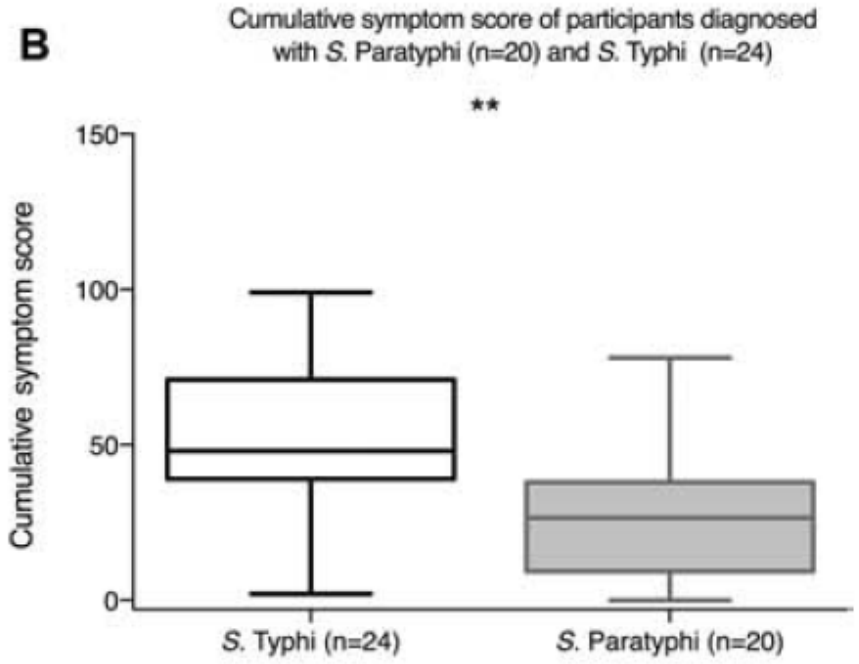
Paratyphoid attack rates in the Controlled Human Infection Model (CHIM)

Strain from Nepal selected



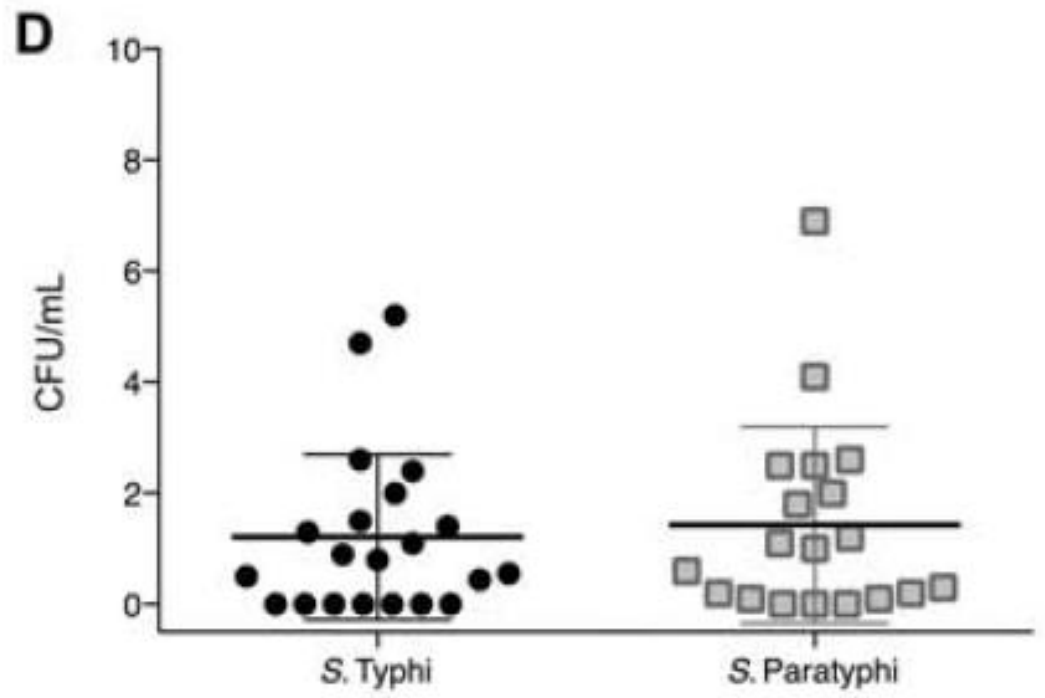
~1000 CFU selected as dose

CHIM volunteers more symptomatic with S. Typhi than S. Paratyphi



Dobinson et

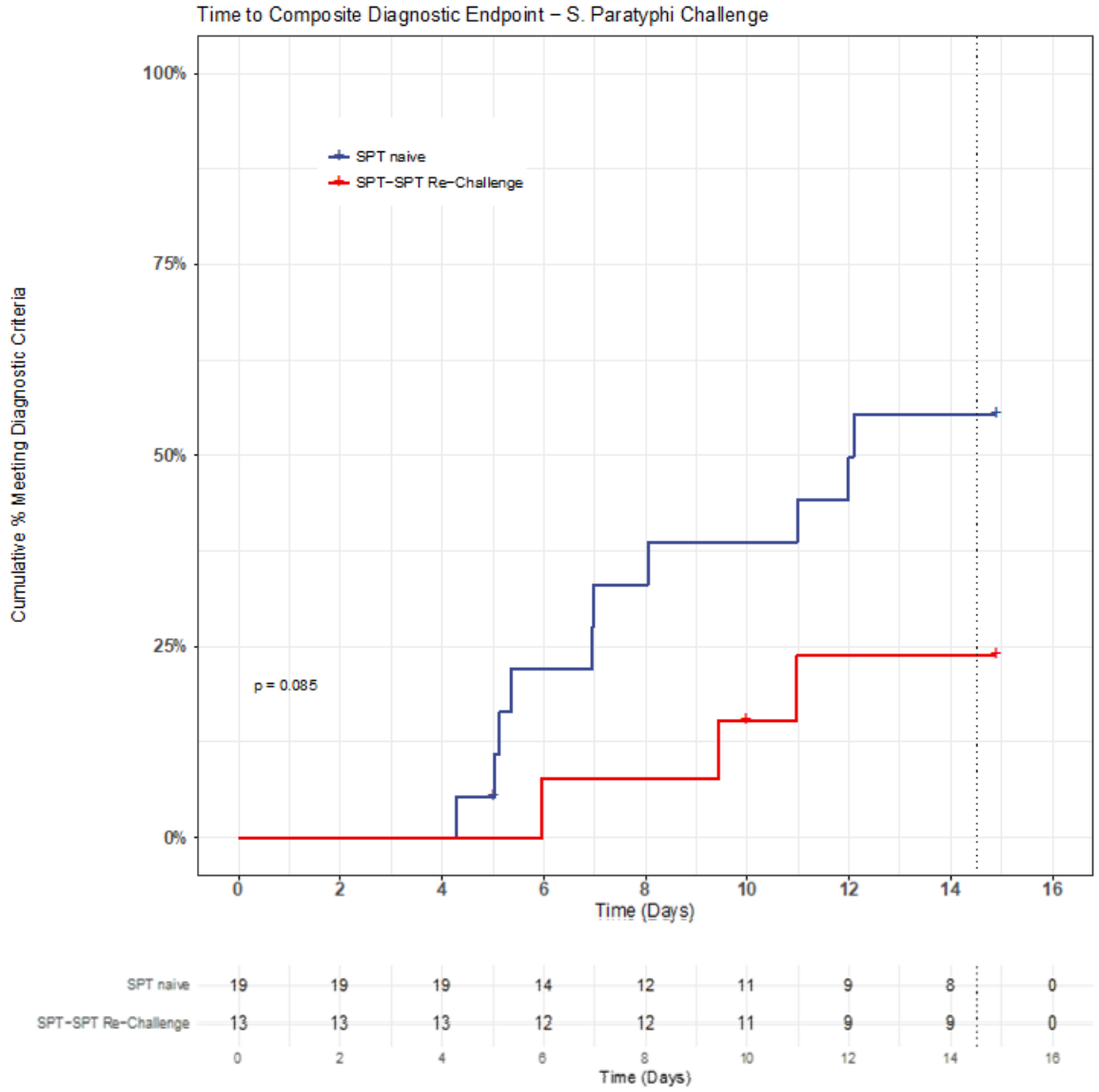
During infection, similar CFU for S Typhi vs S Paratyphi



Dobinson

Prior infection reduces risk of subsequent infection in the paratyphoid CHIM

P vs
PP



PDVAC

PDVAC supported a proposed regulatory pathway for the bivalent conjugate vaccine based on:

- Demonstration of immunologic non-inferiority of the typhoid component in comparison to licensed TCVs.

- For the paratyphoid component,
  - demonstration of protective efficacy in a CHIM study with adults,
  - equivalent immune responses in field immunogenicity trials in children in endemic settings,
  - commitment from developers to confirm vaccine effectiveness through post-approval studies.

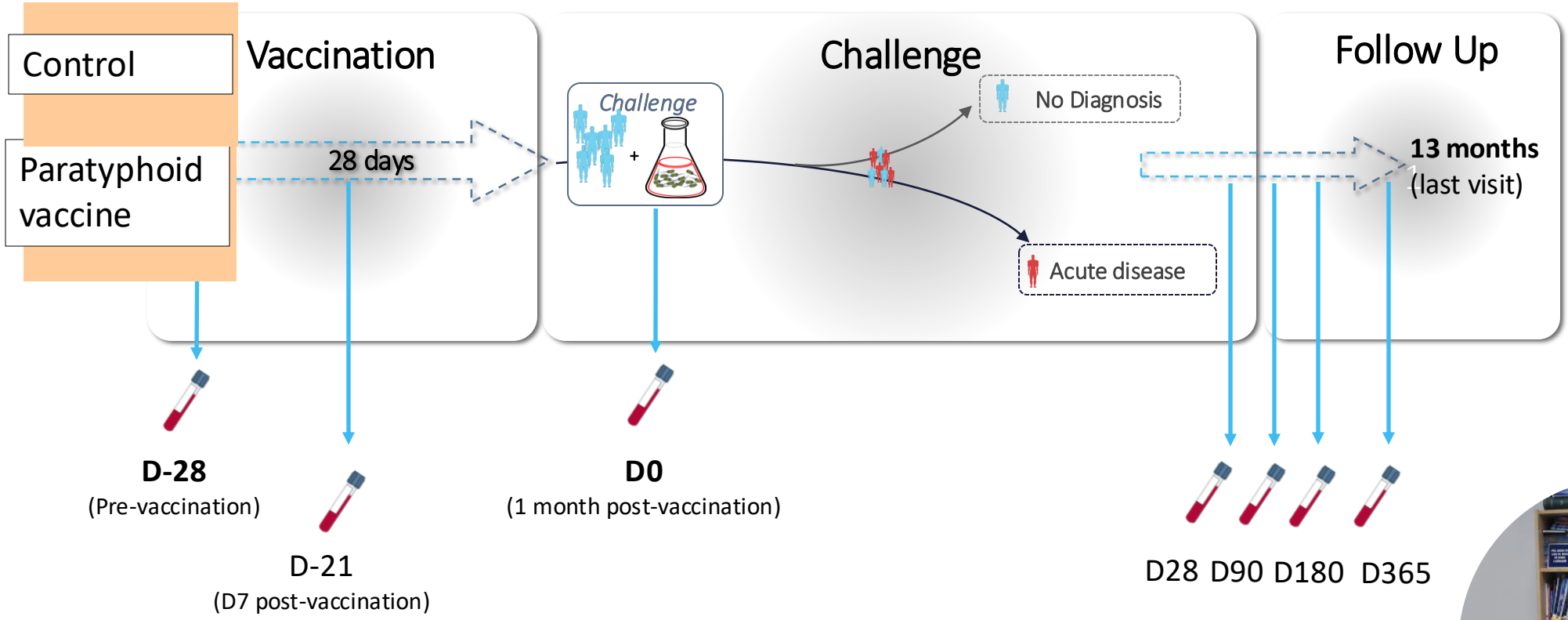
Why CHIM?

- Field trials not feasible (more accurately not affordable)

- License bivalent TCV-PTCV on basis of
  - Non-inferiority of typhoid Vi component against licensed comparator
  - Safety and immunogenicity of paratyphoid O2-conjugate component in field trials
  - Supporting evidence of VE in CHIM

- License live oral on the basis of
  - CHIM data and post-licensure commitment for effectiveness studies

Paratyphoid challenge model



Paratyphoid Diagnosis **defined as fever ≥38°C for >12 hours or positive blood culture**

CVD1902 – Live Attenuated oral vaccine

- Live attenuated oral vaccine – CVD1902
- Deletion of guaBA operon, and clpX gene
- Challenge studies completed in 2024

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Human challenge tests for Oxford paratyphoid vaccine

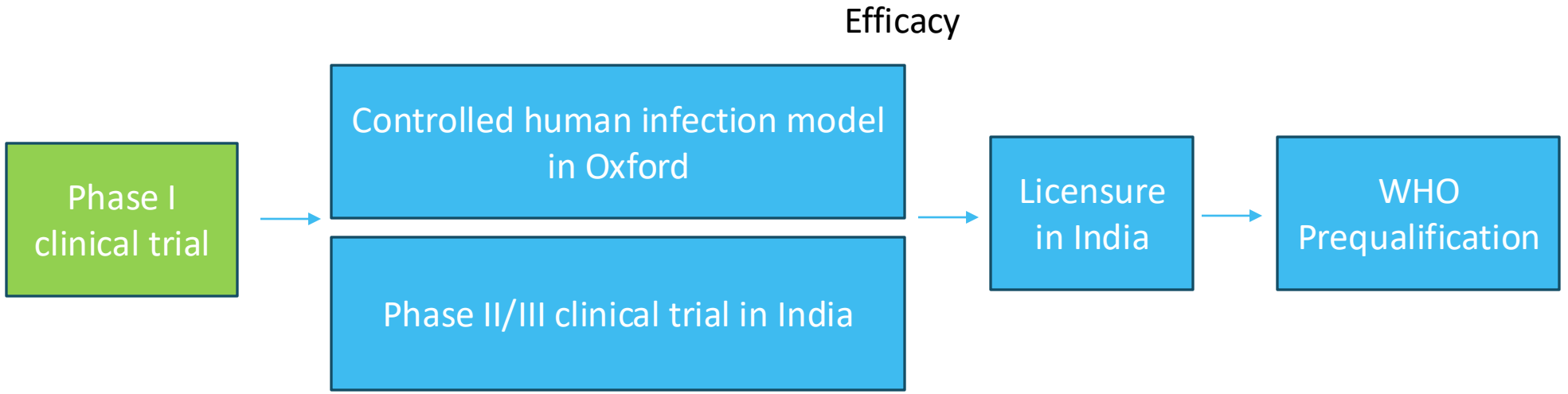
26 April

The first volunteers have received doses of vaccine, or a placebo, in Oxford

Volunteers are set to be infected with a highly contagious bacteria to test a new paratyphoid vaccine.

Bivalent typhoid-paratyphoid conjugate vaccines

CLINICAL DEVELOPMENT PLAN

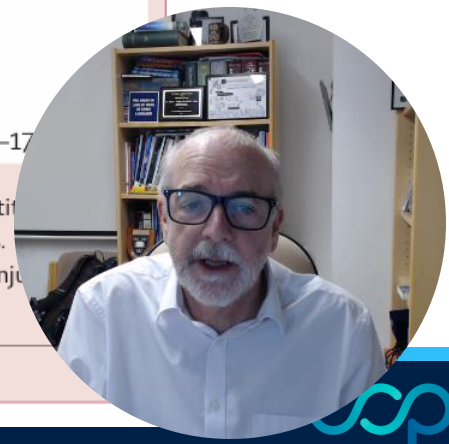


Phase I clinical trial - SII

	Sii-PTCV (n=30)			Typbar-TCV (n=30)		
	GMT (95% CI)	GMFR (95% CI)	Seroconversion, n (%, 95% CI)	GMT (95% CI)	GMFR (95% CI)	Seroconversion, n (%, 95% CI)
Anti-Vi IgG (typhoid)						
Day 1	6·97 (4·75–10·22)	..	..	5·82 (4·13–8·20)	..	..
Day 29	1477·00 (867·80–2513·89)	211·96 (121·69–369·20)	29 (96·7%, 82·8–99·9)	996·38 (676·58–1467·35)	171·25 (103·13–284·38)	30 (100·0%, 88·4–100·0)
Day 181	480·46 (297·94–774·79)	68·95 (43·18–110·10)	29 (96·7%, 82·8–99·9)	482·54 (327·32–711·36)	82·93 (53·25–129·16)	30 (100·0%, 88·4–100·0)
Anti-Vi IgA (typhoid)						
Day 1	1·75 (1·48–2·07)	..	..	1·70 (1·43–2·01)	..	..
Day 29	75·66 (53·25–107·51)	43·27 (28·42–65·87)	28 (93·3%, 77·9–99·2)	85·19 (57·93–125·28)	50·15 (34·82–72·23)	30 (100·0%, 88·4–100·0)
Day 181	27·75 (18·90–40·74)	15·89 (10·51–23·95)	27 (90·0%, 73·5–97·9)	40·59 (27·2–60·59)	23·90 (16·74–34·12)	30 (100·0%, 88·4–100·0)
Anti-LPS (paratyphoid A)						
Day 1	360·46 (237·07–548·07)	..	..	181·04 (126·08–259·96)	..	..
Day 29	28 845·24 (19 679·44–42 280·06)	80·02 (54·93–116·58)	30 (100·0%, 88·4–100·0)	236·81 (169·24–331·37)	1·31 (1·09–1·58)	1 (3·3%, 0·1– 17·2)
Day 181	9535·52 (6281·40– 14 475·46)	26·45 (19·31–36·25)	30 (100·0%, 88·4–100·0)	222·86 (159·58– 311·22)	1·23 (1·05–1·44)	0
SBA (paratyphoid A)						
Day 1	8044·60 (5326·37– 12 150·05)	..	..	6765·70 (4672·43– 9796·85)	..	..
Day 29	155 737·80 (102 803·95–235 927·33)	19·40 (12·61–29·73)	28 (93·3%, 77·9–99·2)	5993·70 (4047·46–8875·91)	0·90 (0·66–1·19)	0 (NC)
Day 181	56 367·40 (33 580·12–94 617·93)	7·00 (3·98–12·32)	20 (66·7%, 47·2–82·7)	1782·30 (520·64–6101·18)	0·30 (0·09–0·81)	1 (3·3%, 0·1–17

GMTs were calculated by taking the anti-log of the arithmetic mean of the log10-transformed titres. GMFR was calculated by taking the arithmetic mean of the difference in the log10-transformed ti difference was post-vaccination $\log_{10}$ titre minus baseline vaccination log10 titre. Seroconversion is defined as four-fold or higher rise in post-vaccination titres compared with pre-vaccination titres. GMFR=geometric mean fold rise from baseline. GMT=geometric mean titre. LPS=lipopolysaccharide. NC=not calculable. SBA=serum bactericidal assay. Sii-PTCV=bivalent paratyphoid A-typhoid conju vaccine. TCV=typhoid conjugate vaccine. Vi=capsular polysaccharide.

Table 3: **Immune response to typhoid and paratyphoid A antigen**



Upcoming studies

- Planning with SII on CHIM for bivalent Vi-O2 conjugate vaccines to start in 2024
- Grant application with Bio-E and GVGH on bivalent Vi-O2 conjugate vaccines

Conclusion

- First oral live attenuated paratyphoid vaccine shown to be protective in CHIM
- Phase I data for two bivalent typhoid-paratyphoid conjugate vaccines positive
- We will know in the next 1-2 years if bivalent vaccines that cover typhoid and paratyphoid will work
- We really need clean water.

Acknowledgements