

Accelerating the Fight Against Invasive Salmonella Diseases: Perspectives from WHO



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**World Health
Organization**



Accelerating TCV use/typhoid control

- Updating evidence for SAGE policy
- Leveraging global immunization strategies and initiatives to improve TCV use
- Improving understanding of the role of TCV in preventing AMR
- Expanding application of interventions for control
- Improvements in implementation (immunization delivery)
- Closing surveillance data gaps



Evidence for SAGE policy updates for TCV



Key policy questions/areas for updates include:

Specific policy questions will be defined by a SAGE Working Group when convened

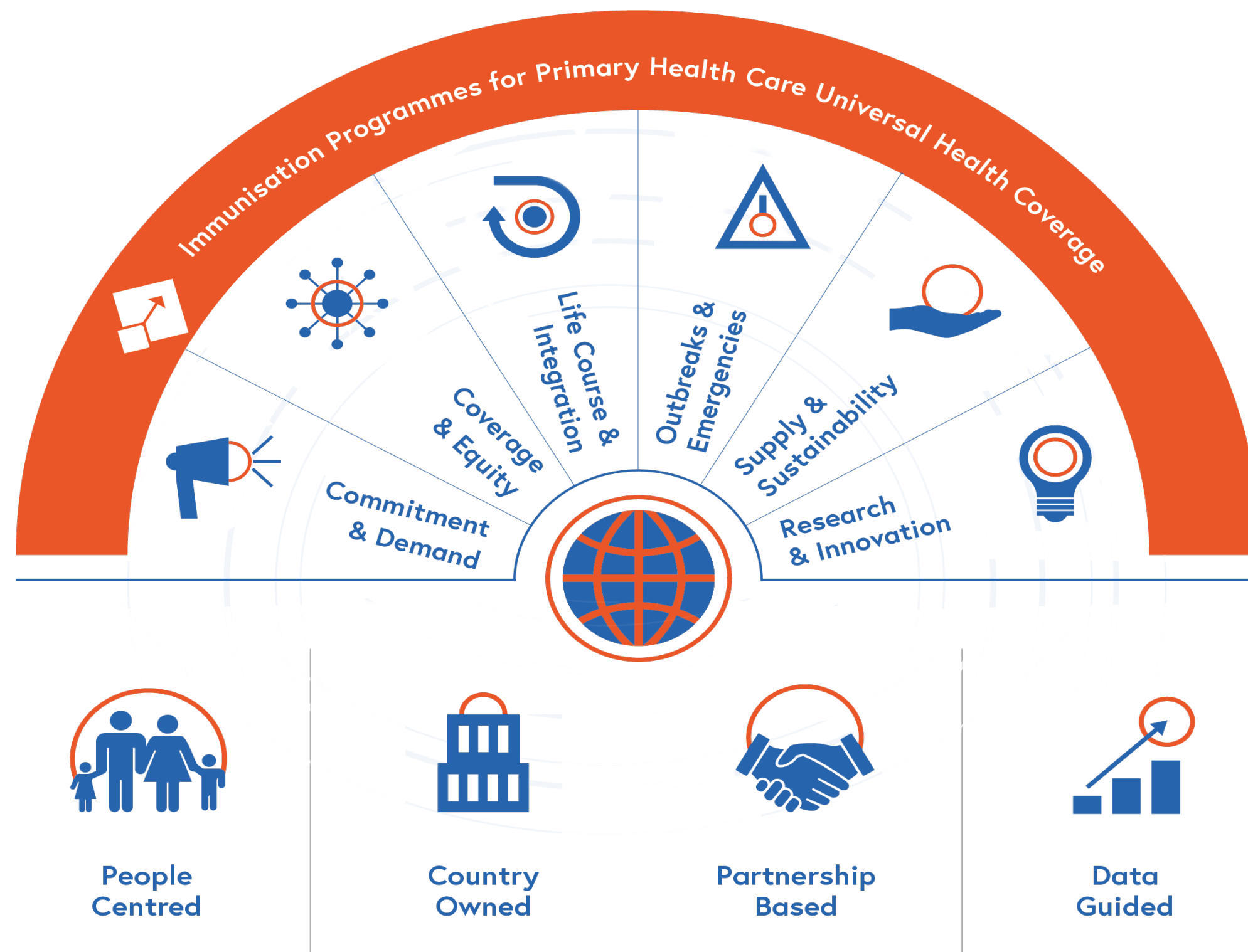
- **Duration of protection and potential need for a booster dose (or booster doses)**
 - impact of age and number of doses at primary vaccination
 - optimal dosing interval
 - relative benefits of heterologous vrs homologous boosting
- Correlates of protection
- Potential effect of natural boosting
- Efficacy or effectiveness of additional WHO PQ'd TCVs (other than Typbar-TCV)
- TCV impact on AMR

Leveraging global immunization strategies and initiatives

Immunization Agenda 2030 (IA2030)

Look for opportunities to leverage all SPs e.g.,

Strategic Priority Area 3: Coverage and Equity



- **Goal:** Everyone is protected by full immunization, regardless of location, age, socioeconomic status or gender-related barriers.
- **Objectives**
 - Extend immunization services to regularly reach “zero dose” and under-immunized children and communities.
 - **Advance and sustain high and equitable immunization coverage nationally and in all districts.**

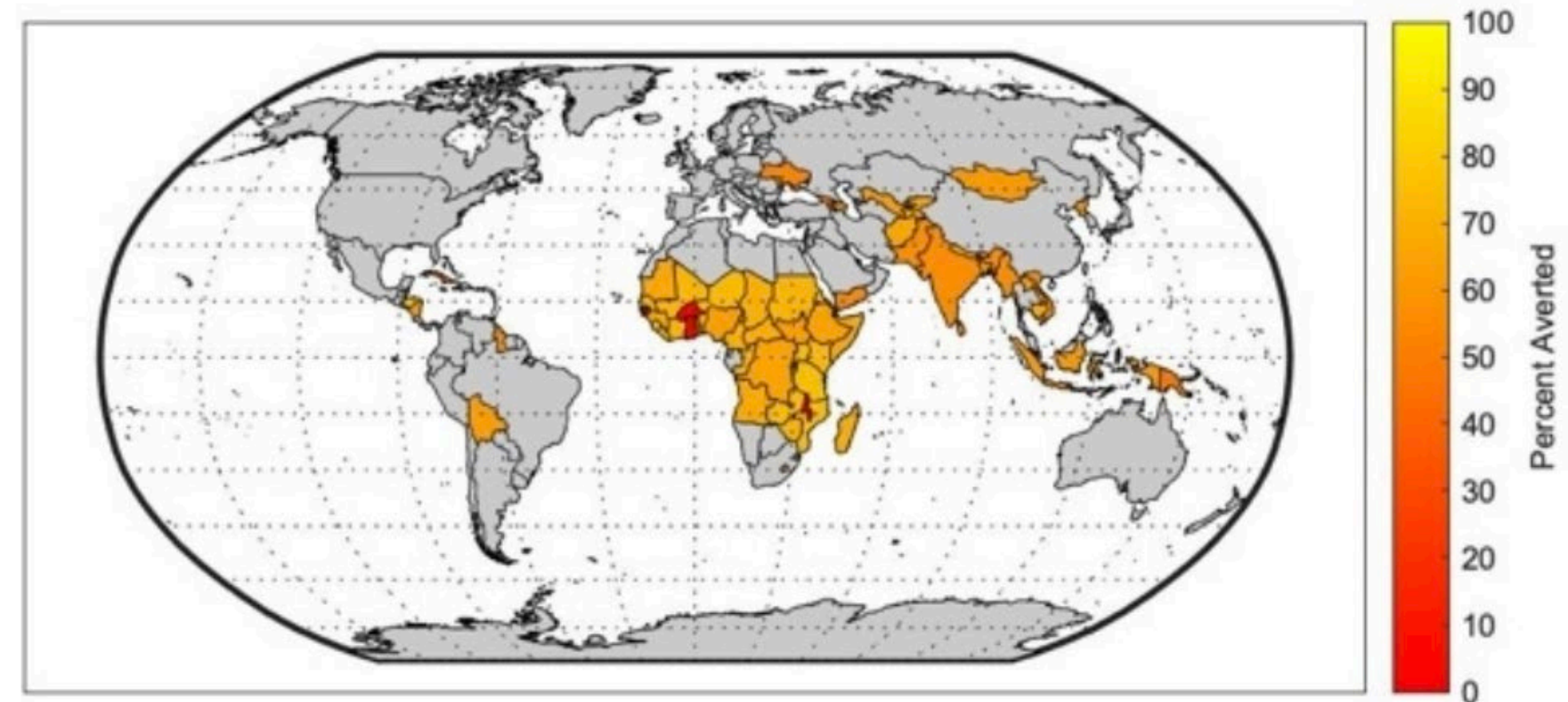
TCV impact on resistant typhoid in Gavi countries: a modelling study

- Routine immunization with typhoid conjugate vaccine at 9 months with catchup campaign to 15 years of age, in Gavi-73 countries, over 10 years, could:
 - Reduce relative prevalence of antimicrobial-resistant typhoid fever by **16% (0-49)**;
 - Avert **42.5 million (95% PI 24.8-62.8 million) cases and 506K (95% PI 187 000-1.9 million) deaths** caused by FQNS typhoid fever;
 - Avert **21.2 million (95% PI 16.4-26.5 million) cases and 342K (95% PI 135 000-1.5 million) deaths** from multidrug resistant typhoid fever.

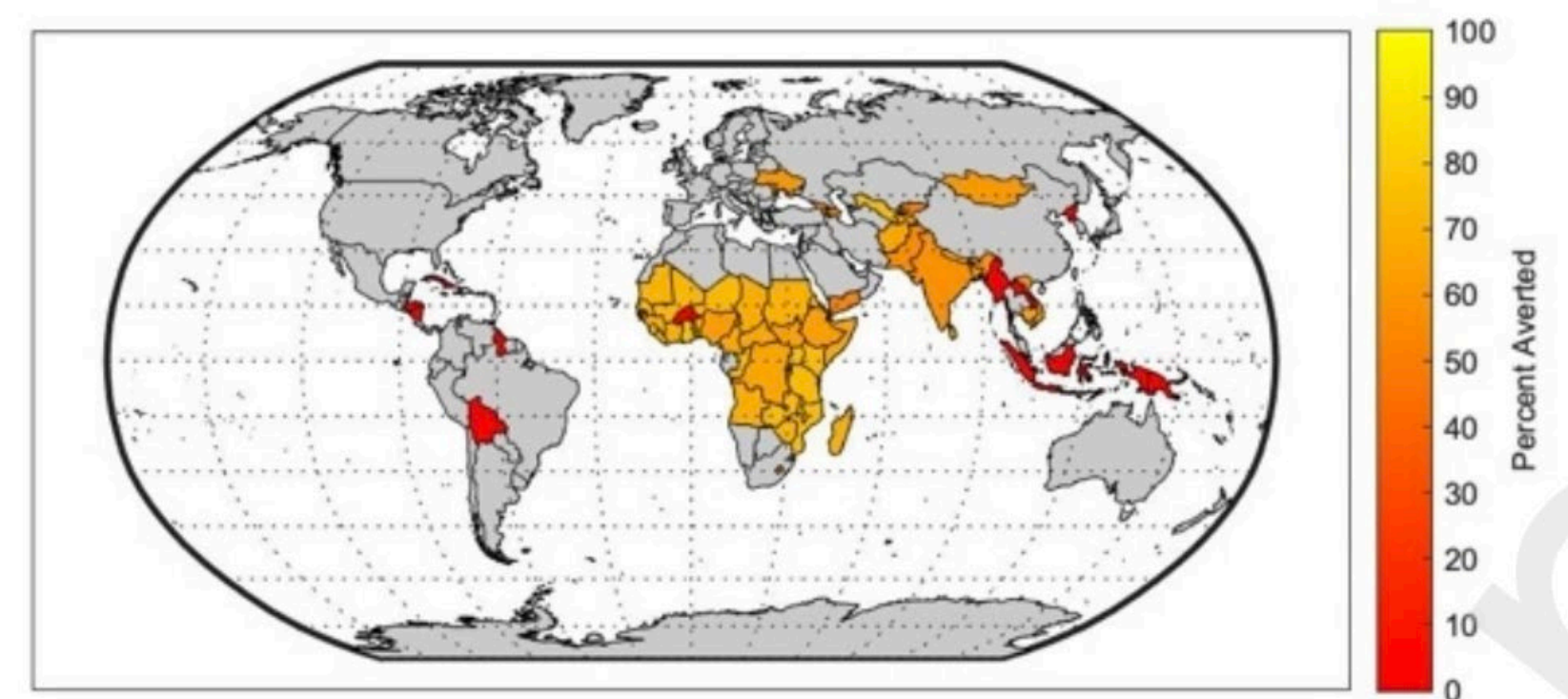
<https://pubmed.ncbi.nlm.nih.gov/35123673/>

Predicted impact of TCV vaccination on the incidence of fluoroquinolone non-susceptible (A) and multidrug resistant (C) cases of typhoid fever

A)



C)



The Action Framework to leverage vaccines against AMR and AMU



Expanding use of licensed vaccines to maximize impact on AMR



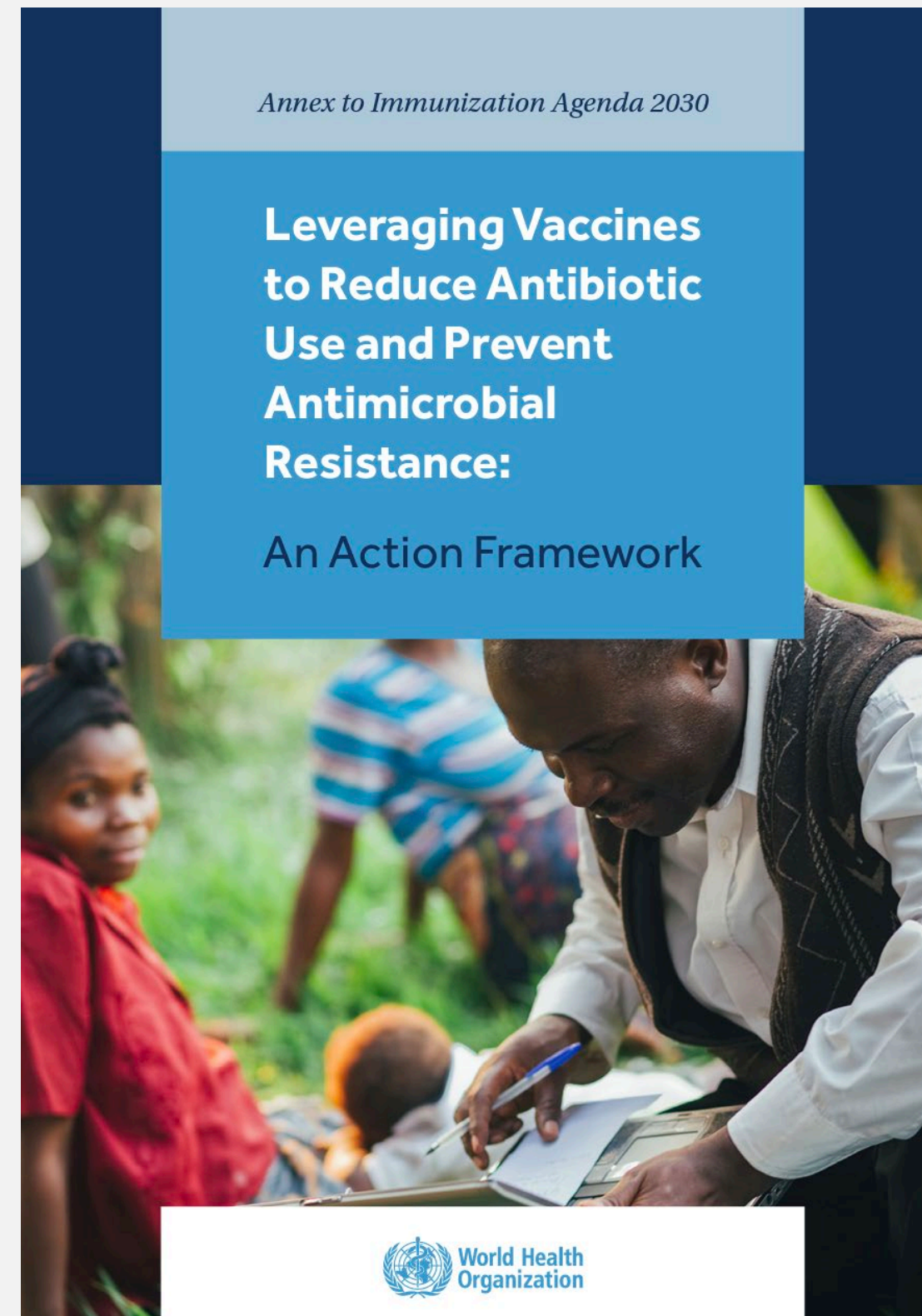
Develop new vaccines that contribute to prevention and control of AMR



Expanding and sharing knowledge of vaccine impact on AMR

<https://www.who.int/publications/m/item/leveraging-vaccines-to-reduce-antibiotic-use-and-prevent-antimicrobial-resistance>

Slide courtesy of WHO programme on Vaccines and AMR

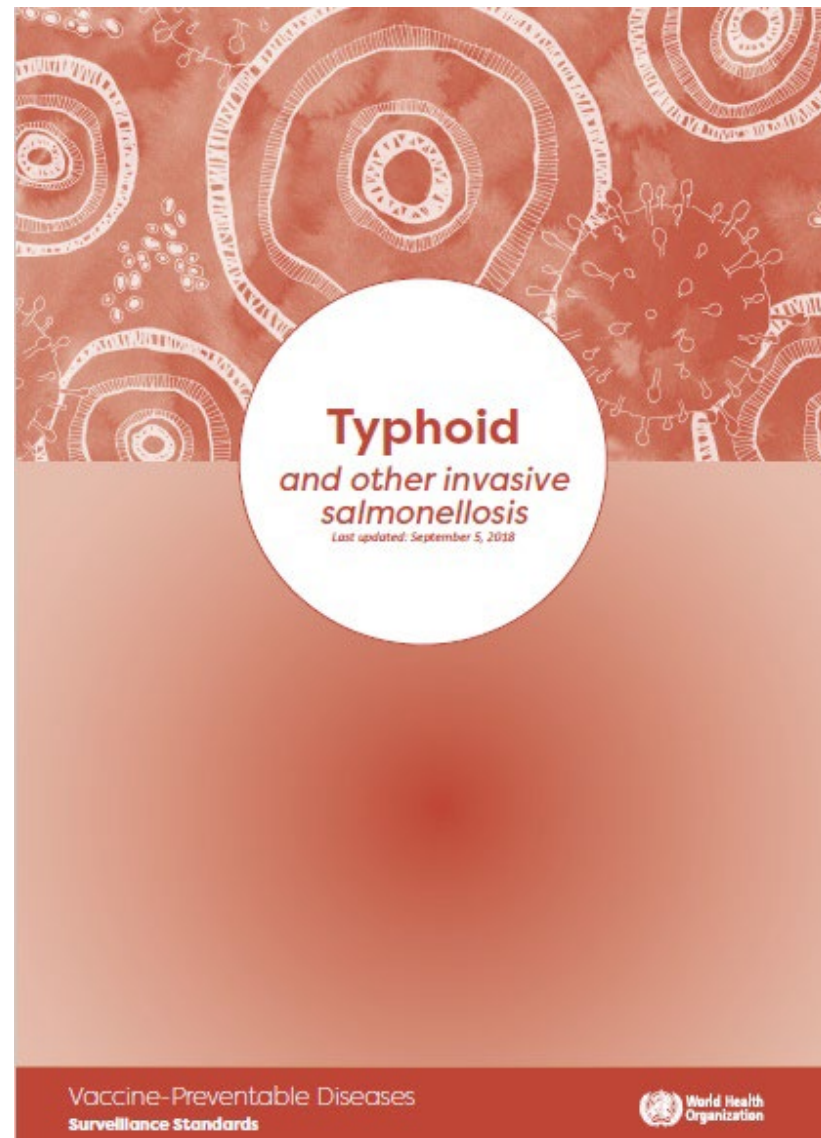


WHO guidance on methodologies to measure TCV impact on AMR in preparation (2024 release)

- Under oversight of Technical Advisory Group on Vaccines and AMR

Expanding application of interventions for control

- **Improved integration with WaSH**
- **Potential role of novel methods and access to diagnostic tests**
 - environmental surveillance
 - improved serodiagnostic tests/serosurveillance
 - improved access to “fit-for-purpose” typhoid diagnostic tests
(Gavi diagnostics grant; role of new WHO Typhoid Diagnostics Reference Panel (TyDRep))
- **Which interventions are most effective/cost-effective?**
 - e.g., What typhoid-specific WaSH interventions?
 - in what setting(s): endemic? epidemic? epidemic on endemic?
- What degree of **integration of strategies** is required? (policy level? service delivery?)



“... there is **not enough evidence to currently recommend environmental sampling of water on a routine basis** to test for *S. Typhi* and *S. Paratyphi*”

“In an outbreak, environmental surveillance may be useful to identify potential environmental sources of infection.”

- *WHO surveillance standards (2018)*

What is the potential role for ES in country decision making on TCV use?

- Correlation between positive ES samples and clinical disease/disease burden?
- Extrapolation of data beyond ES catchment area?
- Policymakers' confidence in ES methodology and data?

Improvements in implementation (immunization delivery)

- Coordinated intersectoral approach (incl. WASH and education sectors)
- community engagement strategies to increase acceptance and demand
- Integrated service delivery (TCV SIA introduction with other SIAs)

Closing surveillance data gaps

- Improve country reporting *S. Typhi*/*S. Paratyphi* and iNTS data through routine channels (JRF) to WHO
- Better understanding and management of the risks of XDR *S. Typhi* including regional and global risks (IHR role?)
- Surveillance data needs population denominators to be comparable across geographies
- More (sustainable) data need to come from national surveillance systems (not limited to research)
- Invasive *Salmonella* landscape in Latin America (other Regions)?
- Good quality diagnostics suitable for LMICs that meet the criteria for WHO prequalification

- **Closing the knowledge gaps for iNTS disease and paratyphoid fever ...**
- **... accelerating development of vaccines against iNTS disease and paratyphoid fever**



«... I knew iNTS was a problem, I didn't know it was this much of a problem.»
 – Denise Garrett, 05 Dec 2023

«Paratyphi has been mostly absent from this conference.»

Gaps in Epidemiology

1. Robust understanding of **NTS reservoirs, sources, and modes of transmission** in high **iNTS** disease incidence.
2. Clear and unbiased data on the **proportion of iNTS disease attributable to key host risk factors** including HIV,

Gaps in Carriage/shedding and Immunology

1. Duration of **NTS shedding after infection and disease**, as both a source for onward transmission and as a potential endpoint for vaccine trials.
2. Does **asymptomatic NTS shedding** following infection or disease have **beneficial/harmful possible outcomes**, either to develop

iNTS
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What is needed to answer key questions?

- Birth cohort study in area(s) of high **iNTS** incidence.
- **Primary outcome**: acquisition of relevant NTS strain in stool.
- **Secondary outcome**: **iNTS** disease.
- **Analyses**:
 - Reservoir- and source-assigned case-control study on **fecal** acquisition
 - Understanding of age at first exposure and patterns of shedding
 - Host risk factors for **iNTS** disease at community level
 - Data on incidence, disability, death at community level
 - Serologic changes with colonisation and disease
 - Immune correlates of protection
 - Site development for vaccine trials

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Slide images credit: Sam Kariuki, KEMRI

We must not tolerate a world in which a child dies from a disease that can be easily prevented with an affordable vaccine.

Dr Tedros Adhanom Ghebreyesus
WHO Director-General

Protected
Together

#VACCINESWORK

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WEEK 2018



Acknowledgements

- **Sam Kariuki**
- **Denise Garrett**

WHO

- **Adidja Amani (AFRO)**
- **Kate Emary**
- **Musa Hindiyyeh**
- **Anna Minta**
- **Ana Ibarz Pavon**
- **Nada Taqi**
- **Carol Tevi Benissan**
- **Jenny Walldorf**