Severe Typhoid in Africa Program (SETA): Incidences, methods, preliminary results

Impact of a typhoid conjugate vaccine (THECA): a multicenter study in Ghana and the Democratic Republic of the Congo

Capturing data on Antimicrobial resistance Patterns and Trends in Use in Regions of Asia (Captura)

Florian Marks, MPH, PhD

27 March 2019
Severe Typhoid in Africa Program (SETA)
6 countries
12 study sites
24 healthcare facilities
Standardized with SEAP in Asia
Severe Typhoid Surveillance in Africa (SETA) Program

**Inclusion criteria**
- Objective fever or fever reported >3d days, or
- Blood culture positive for *Salmonella* spp., or
- Gastrointestinal perforation

**Standardized passive surveillance**
- Clinical forms completed
- Study samples collected
  - Blood
  - Urine & stool
  - Swabs
  - Tissue

**12 months follow-up**
- Long-term sequelae assessment
- Cost-of-illness
- Natural immune response
- Identification of carriers

**Health Care Utilization Surveys implemented at each site**
**Crude Incidence**

\[
\text{crude cases} \quad \text{catchment population in PYO} \times 100,000
\]

**Adjusted Incidence**

\[
\frac{\text{crude cases}}{\text{catchment population in PYO}} \times \left( \frac{1}{(A1 \times A2 \times A3 \times A4 \times A5 \times A6)} \right) \times 100,000
\]

**Adjustments**

- **A1**: proportion of individuals who report visiting the SETA healthcare facility in case of fever
- **A2**: proportion of patients meeting inclusion criteria approached by the study
- **A3**: proportion of patients approached by the study consenting to participate
- **A4**: proportion of patients consenting to participate with a blood culture taken
- **A5**: proportion of patients with blood culture NOT contaminated
- **A6**: sensitivity of typhoid culture, 60%

**Parameters**

- PYO: person – years of observation

1 Adjustment applied in adults if the SETA BC contamination is 5% or more AND in children if SETA BC contamination is 15% or more.
THECA - complementing the TyVAC efforts

Additional data needs

- Long-term safety
- Immunogenicity
- Vaccine clinical efficacy, effectiveness, including population-level protection (direct and herd)
- Cost-effectiveness

Ghana
Cluster-randomized TCV trial in children <15 years

DR Congo
TCV mass vaccination campaign in children <15 years, effectiveness study

All THECA countries
- Early adopter countries support for TCV introduction (implementation, GAVI applications)
- Health economic studies

General assembly:

Chaired by
- Florian Marks
- John Clemens
- Kathleen Neuzil
### Design:
A cluster-randomized Phase 3 study of Typbar-TCV®

### Setting:
Asante Akim North, Ghana, characterized by both semi-urban and rural settlements and low population migration

### Population:
The aim is to enroll all eligible, consenting children meeting inclusion criteria within the target age range (9 months to <16 years). Anticipated coverage is 60% (approx. 28,000 children)

### Measurements:
Herd immunity, overall and total effects of vaccination

The trial is designed to mimic the TyVAC-Bangladesh trial. The trial protocols will be harmonized to ensure maximum comparability of data
### Design:
A mass vaccination campaign with nested case-control effectiveness study; cases defined as patients being blood culture-positive for \( S. \) Typhi.

Four controls matched on neighborhood, sex and age will be enrolled for each case.

### Setting:
Kisantu, DR Congo (population 183,750)

### Population:
All children from 9 months to <16 years of age

### Measurements:
Vaccine effectiveness, cost-effectiveness, safety and feasibility
Support regulatory affairs for TCV introduction in African early adopter countries

✓ Three pan-African typhoid conferences will be planned at the beginning, midpoint and end of the study.

    Study objectives, progress and outcomes will be communicated to study partners and stakeholders.

✓ Work within DRC, Ghana, Madagascar, Burkina Faso to support the collection of the necessary data to enable the quick introduction of TCVs

✓ Support THECA countries with the respective GAVI applications
Capturing data on Antimicrobial resistance Patterns and Trends in Use in Regions of Asia (CAPTURA)
The UK Government has established the Fleming Fund to respond to the global threat of antimicrobial resistance (AMR)

- UKAID Development Programme to help build AMR surveillance systems

- Regional Grants round 1; a “call for data”, which aims to expand the volume of historical and current data available on AMR and AMU across regions

- IVI leading an international consortium that has been awarded the grants for South and South East Asia

- Increase the volume of data available to improve spatiotemporal mapping of antimicrobial resistance (AMR) and antimicrobial usage (AMU)

- Undertake analysis of the data and ensure it is disseminated locally and globally
CAPTURA: Organization of regional and in-country work

Data direct impact for typhoid and iNTS disease-related work

Additional data sources for typhoid for future Gavi applications and risk factor-based typhoid occurrence prediction models
Research providing data to understand typhoid fever and iNTS disease burden, severity and antimicrobial resistance in Africa in support of future TCV introduction.

SETA

Ongoing efforts; preliminary data:

• Typhoid fever disease in all countries participating in SETA with higher incidence rates in <15 years old.
• iNTS disease in three countries (DRC, Ghana, Burkina Faso) with higher incidence rates in <2 years old.

THECA

• Recently awarded
• Complementing TyVAC efforts to generate additional data required by WHO, Gavi, other stakeholders supporting TCV introduction in Africa.

CAPTURA

• Currently ongoing; providing additional data on AMR and typhoid fever occurrence
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- **EPI** – Hyon Jin Jeon
- **EPI** – Hye Jin Seo
- **EPI** – Ji Hyun Han
- **EPI** – Marianne Holm
- **EPI** – Ligia Cruz Espinoza
- **EPI** – Nimesh Poudiyal
- **PER** – Vital Mogasale
- **PER** – Enusa Ramani
- **PER** – Monica Moon
- **PER** – Dayoung Sung

**Project teams**
- **BDM** – Yun Chon
- **BDM** – Gi Deok Pak
- **BDM** – Hyeongwon Seo
- **BDM** – Ju Yeon Park
- **BDM** – Geun Hyeog Jang
- **PMU** – Sooyoung Kwon
- **CDR** – Anh Wartel
- **CDR** – Tarun Saluja
- **D&D** - Julia Lynch

**Country collaborators (SETA/TSAP)**
- Mekonnen Terferi (Ethiopia)
- Abraham Aseffa (Ethiopia)
- R. Rakotozaindrindrainy (Madagascar)
- Ellis Owusu-Dabo (Ghana)
- Yaw Adu-Sarkodie (Ghana)
- Michael Owusu (Ghana)
- Octavie Lunguya (DR Congo)
- Marie-France Phoba (DR Congo)
- Lisette Kalonji (DR Congo)
- Abdramane Soura (Burkina Faso)
- Moussa Ouedraogo (Burkina Faso)
- Iruka Okeke (Nigeria)
- Femi Popoola (Nigeria)
- Remi Kehinde (Nigeria)

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- Robert F. Breiman
- Eric Mintz
- Sam Kariuki
- Gbangandepp Kang
- Hope Johnson
- Thomas Cherian
- Jeff Stanaway
- Dennis Chao

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**Other**
- Ken Smith
- Gordon Dougan
- Sophie Palmer
- Simon Hay
- Calman Maclellan
- Karen H. Keddy
- Arvinda Sooka
- Daniel Douek
- Sam Darko
- Jan Jacobs
- Liselotte Hardy
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- Gordon Dougan
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**FRED HUTCH CURES START HERE**
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