



Development of a sustainable and effective vaccine against invasive non-typhoidal salmonellosis in Africa

**Gianluca Breggi, Managing Director
FONDAZIONE ACHILLE SCLAVO
Siena, Italy**

REGIONE
TOSCANA



FAS
Fondo Aree
Sottoutilizzate:
2007-2013



**10th International Conference on
Typhoid & Other Invasive
Salmonellosis
April 4-6, 2017 Kampala, Uganda**



Fondazione Achille Sclavo

- Established in 2011 by private founders: Sclavo Vaccines Association and Dr. Rino Rappuoli on his own right
- Not-for-profit organization (*) carrying out scientific research and training in support of countries in need
- Board of directors:
 - Chairman. Prof. Dr. A. Riccaboni, Chair of UN SDSN Assembly and SDSN-MED
 - Deputy, Dr. R. Rappuoli, world leading vaccinologist and Head of external R&D, GSK
 - Dr. S. Malvolti, former GAVI and PATH officer
- Mission:
Reduce infant mortality in low-income countries by accelerating availability of new, affordable life-saving vaccines against neglected infectious diseases and training local doctors, thereby reducing poverty

(*) U.S. 501(c) Public Charity equivalent certified (Feb 2017)

REGIONE
TOSCANA

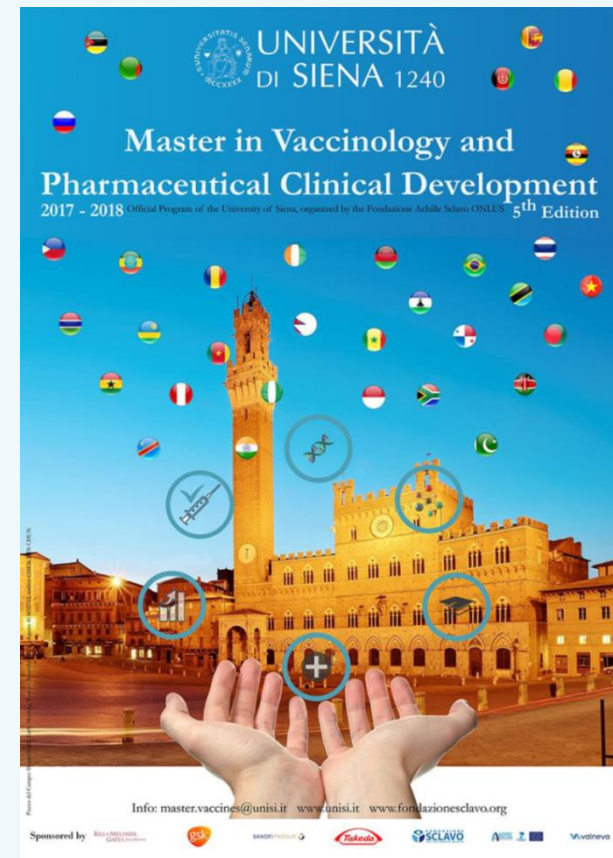


Training: Master in Vaccinology and Pharmaceutical Clinical Development

The Fondazione Sclavo is coordinating from this year the 5th edition of the Master in Vaccinology and Pharmaceutical Clinical Development, offered by the University of Siena, Italy, to MDs operating in LMICs. Supported by:

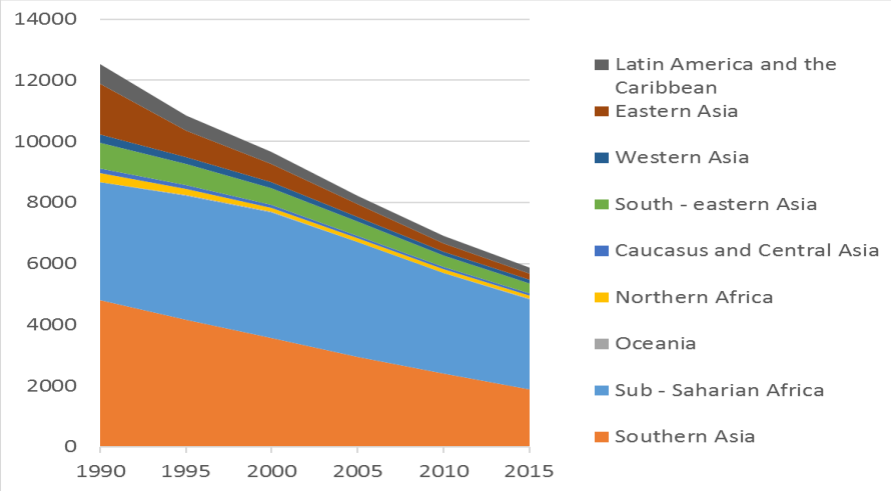
- Bill & Melinda Gates Foundation
- European Commission
- Curevac
- GSK Vaccines
- Sanofi-Pasteur
- Takeda Vaccines
- Valneva

One of the Alumni is in the audience

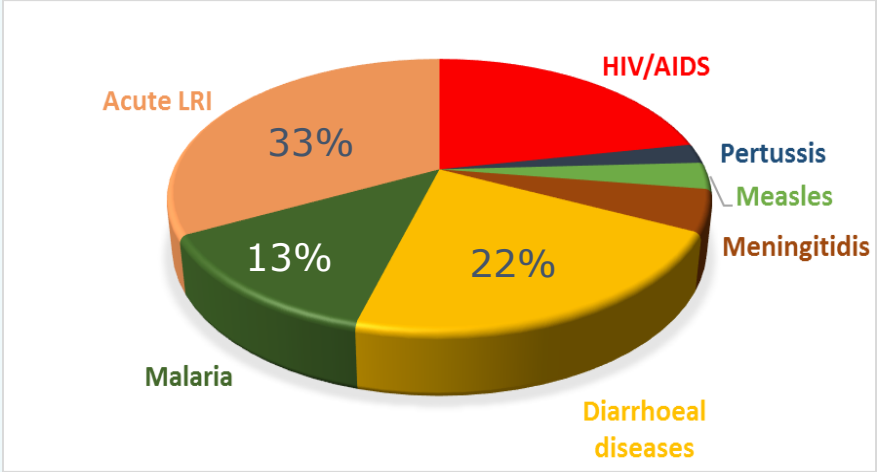


Accelerating availability of sustainable vaccines against enteric diseases

Global under 5 year mortality ('000)



Mortality Causes: Infectious Diseases



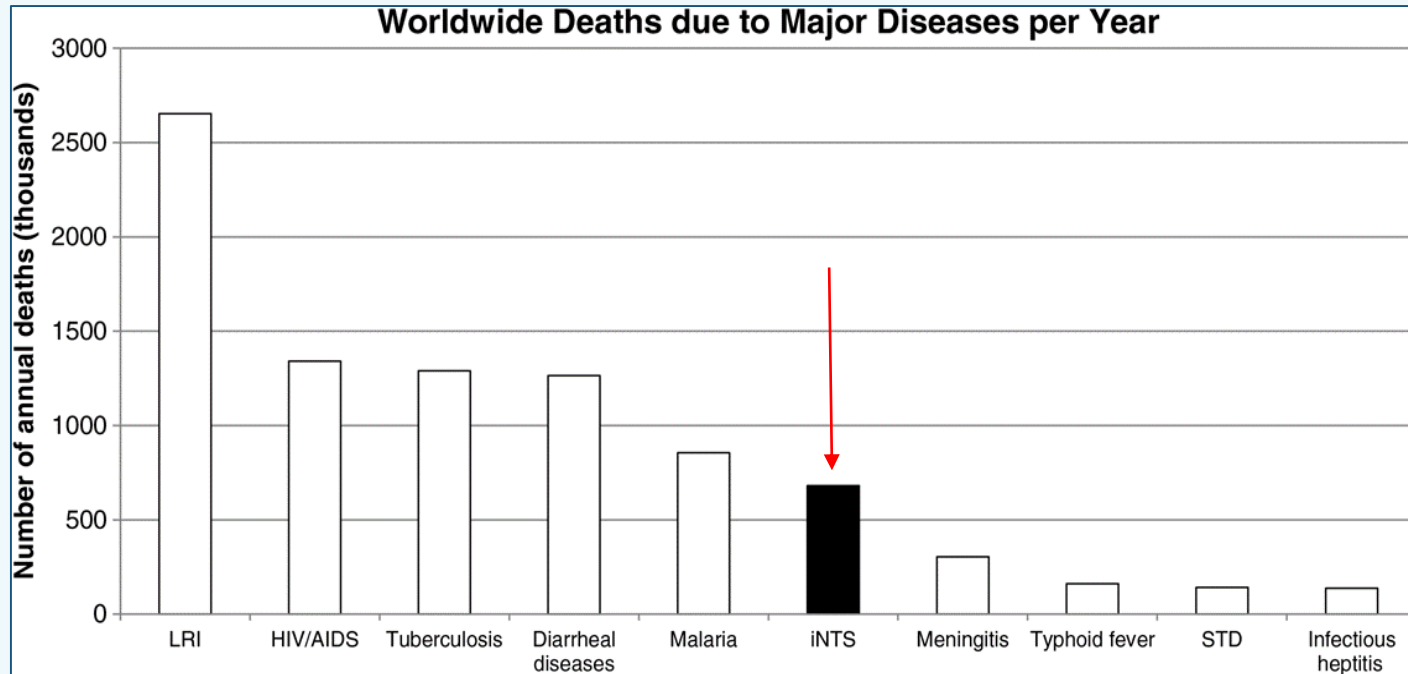
Elaboration from WHO 2015

We can reduce deaths caused by EDD by facilitating development and uptake of the most needed vaccines, technically feasible but unfunded

- Using vaccine development/delivery expertise to identify needed vaccines that can also be developed at a sustainable cost using existing technology,
- Attracting funds needed for development, anticipating impact on children’s mortality where is highest → successfully used for TCV ... now iNTS



A dramatic confirmation of iNTS B.o.D.



Khan IM *et al* (*)

REGIONE
TOSCANA



(*)Khan IM *et al*. Clin Infect Dis (2015) 61 (suppl_4): S380-S385, elaboration from GBD 2013 death, 1990 to 2013: a systematic analysis for the global burden of disease study 2013, Lancet 2015; 385 :117–71 and Ao TT *et al* Global Burden of Invasive Nontyphoidal Salmonella Disease, 2010. E.I.D. Vol21, No.6, June 2015

iNTS Disease burden

- Estimated WW at 3.4MM illnesses and up to 681,000 fatalities/year
- Majority of m&m in Africa:1.9MM illnesses [1.3-2.9]; CFR: 19-20%
- Leading cause of sepsis in Africa (up to 39%)
- Major cause of <5 mortality (68.3%) and in fragile categories
- More prevalent among HIV-infected individuals, infants and young children with malaria, anemia and malnutrition
- Increase in persisting AMR has been observed
- Difficult to diagnose and with uncertain transmission mechanisms

See  poster presented by Valentine I. Uche

Ao TT, Feasey NA, Gordon MA, Keddy KH, Angulo FJ, Crump JA, Global Burden of Invasive Nontyphoidal *Salmonella* Disease, 2010. E.I.D. Vol21, No.6, June 2015

A Systematic Review of the Incidence, Risk Factors and Case Fatality Rates of Invasive Nontyphoidal Salmonella (iNTS) Disease in Africa (1966 to 2014), IV Uche et al. PLoS Negl Trop Dis 11 (1), e0005118. 2017 Jan 05.



iNTS disease: treatment & prevention

- Public hygiene interventions (sanitization, water purification & increased hygiene) are crucial
- They cannot eliminate the disease and are only effective long-term
- Prevention: vaccination has been indicated as a high priority, also considering uncertainties about disease reservoirs and transmission
- Vaccine developments are ongoing with different technologies
- BUT no licensed vaccines are available or close to licensing
- Funding an issue: 3 applications turned down for BoD underreporting



S-AFRIVAC Project

Initiative to attract funding and attention on this neglected disease of disadvantaged groups and populations

- Approved, co-financed by the Tuscany Regional Government, Italy
- Two-year grant >€1M, started September 2016
- Partnership:
 - Two not-for-profit beneficiaries/co-funders:
 - Fondazione Achille Sclavo
 - University of Siena (UNISI)
 - Two private partner companies, fully funding their work:
 - GSK Vaccine Institute for Global Health (GVGH) → Vaccine
 - VisMederi → Assays

The collaborative network against iNTS in Siena, Italy

REGIONE
TOSCANA



The Goal of S-AFRIVAC

Accelerate development and availability
of an effective GMMA-based vaccine
against a deadly neglected disease
endemic in Africa
at risk for increasing AMR

GMMA: Generalized Modules for Membrane Antigens → next presentation

REGIONE
TOSCANA



S-AFRIVAC project objectives

1. Epidemiological and disease modeling for iNTS disease in Africa (Sclavo/UNISI)
2. Pharmaco-economic study for sustainable vaccine deployment (UNISI-Economics/Sclavo)
3. Support preclinical activities accelerating Phase I (GVGH/Sclavo)
4. Profiling vaccine's mucosal and cellular immunological response in preclinical infection models (UNISI-Biological labs/GVGH)
5. Qualification and validation of immuno-assays (VisMederi)



S-AFRIVAC:

Main activities carried out by Fondazione Sclavo

- Scientific Coordination: Dr. Rino Rappuoli, Ph.D
- Dissemination of results and disease awareness
- Support pre-clinical activities to be Phase I -ready
- Co-funding
- B.o.D. model for pharmacoeconomic and sustainability modeling
- Project Management: Dr. Diletta Magini Ph.D.
- Literature and publication monitoring: Dr. Tiziana Spadafina, Ph.D.



Integrated Public Health Approach

REGIONE
TOSCANA



Epidemiological and B.o.D. models for pharmaco-economic evaluations

Objective: build updated disease models for immunization forecasting and sustainability in Africa

- Literature update to 2017 through *PubMed & Embase, ongoing*
- Modeling iNTS B.o.D. in Africa (SCLAVO/UNISI, *ongoing*)
- Modeling of scenarios for vaccine development and delivery costs for sustainable immunization strategies
- Cost-effectiveness and broader benefits of vaccination modeling
- Outstanding problems:
 1. Lack of peer-reviewed data for many countries
 2. Incomplete or duplicate information
 3. Difficulty in making correct diagnosis

We appreciate any information we can share on these points!



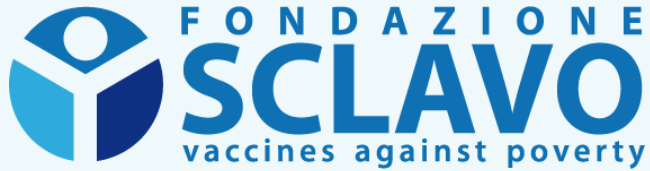
Summary/Conclusions on iNTS

- The major cause of bloodstream infections in Sub-Saharan Africa
- Major burden for disadvantaged groups and populations: CFR 19-20%
- Transmission routes are unclear and AMR increasing
- More effective prevention measures needed, but no vaccine available yet
- S-AFRIVAC will help bring a sustainable vaccine to be Phase 1-ready and model its introduction in Africa to fight the disease

We are searching for support to continue the work we're doing on the vaccine and the BoD and economic analyses



Acknowledgments



Rino Rappuoli
Angelo Riccaboni
Stefano Malvoti
Gianluca Breggi

Diletta Magini
Tiziana Spadafina



Our Partners:



Donata Medaglini
Nicola Dimitri
Maria Pia Maraghini
Fabio Fiorino



Oliver Koeberling
Ifeanyi Valentine Uche
Allan James Saul
Laura Bartle Martin



Emanuele Montomoli



THANK YOU FOR YOUR ATTENTION

Gianluca Breggi, M.B.A.
Managing Director
FONDAZIONE ACHILLE SCLAVO ONLUS

breggi@sclavo.org
Tel. + 39 0577 539 444
www.fondazione-sclavo.org