Global Leaders Group on Antimicrobial Resistance

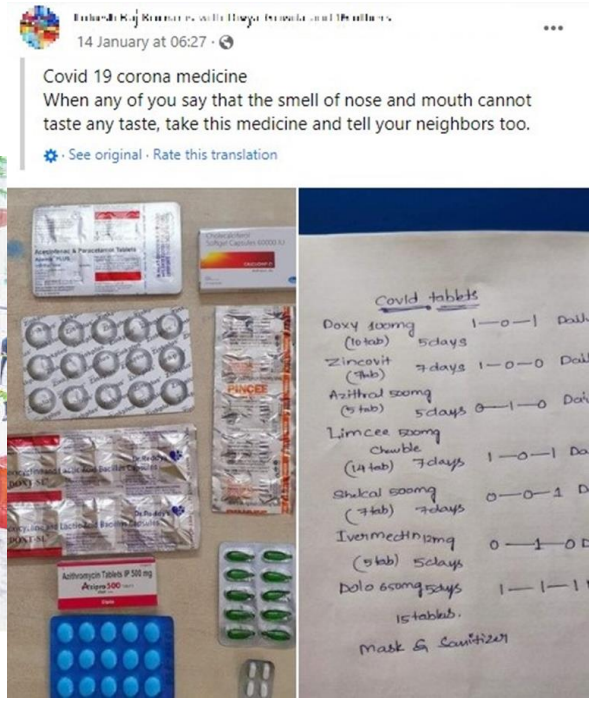
Forging partnerships between science and policy

A view from India

Lessons from COVID-19 in India

Fear drives over-treatment, particularly when drugs are accessible and there are no negative consequences for irrational therapy

- May 2021 Prescription for SPO2 of 96
  - Home care, rest and fluids
  - Tab Ivermectin 12 mg after dinner for 5 days
  - Tab HCQS 400 BD for one week than once daily
  - Tab Fabiflu 1800 mg twice at 12 hr interval followed by 800 mg twice daily after meals for 7 days
  - Tab Doxy 100 mg twice daily after meals for 7 days
  - Tab Placef 200 mg twice daily for 10 days
  - Tab Famotidine 150 mg twice daily before food for 2 weeks
  - Tab Allegra once daily 3 weeks
  - Tab Nucoxia P three times after food ten days
  - Tab Ecosprin 75 once daily after food 6 weeks
  - Cap Zincovit twice daily 2 weeks after breakfast and dinner
  - Cap Limcee twice daily 2 weeks after breakfast and dinner
  - Tab Calpol 650 sos for fever



India's Covid black market

Item	Usual price	Black market price
Oxygen cylinder (50 litres)	$80	$660-1,330
Oxygen concentrator	$330-930	$2,000-2,660
Remdesivir drug (100mg)	$12-53	$330-1,000
Tocilizumab drug (400 mg)	$540	$2,000-4,000
Fabiflu drug (17 tablets)	$15	$66-133

Source: BBC

Overuse of drugs can have unintended consequences

‘Black fungus’ during Covid-19

- Not seen elsewhere in the world
- Different rates in northern/southern India
- In northern India, >30,000 reported cases
- In our hospital
  - 4 cases in hospitalized COVID-19
  - All treated with steroids outside hospital

Forbes

BREAKING • BUSINESS

India Declares ‘Black Fungus’ Epidemic As Infections Rise Among Covid-19 Patients

Siladitya Ray Forbes Staff

Covering breaking news and tech policy stories at Forbes.

May 20, 2021, 09:11am EDT

INDIA TODAY

Home / Coronavirus Outbreak / Black fungus detected in Covid-19 survivors, 8 lose eyesight in Surat

Black fungus detected in Covid-19 survivors, 8 lose eyesight in Surat

At least 40 cases of mucormycosis, also known as black fungus, have been reported from Surat in Gujarat amor infection and who is more vulnerable? Read here.

What does irrational antibiotic use mean for AMR?

The access and excess story

- Infant mortality rate in India has declined from 125 per 1000 live births to <20 per 1000 live births in the state of Tamil Nadu, similar but not as sharp a decline in the rest of India
- Perinatal and neonatal deaths contribute to 40-60% of infant mortality
- Neonatal sepsis is high, driven mostly by Gram negative organisms, with high rates of resistance particularly *Klebsiella pneumoniae*, *Escherichia coli* and increasingly Acinetobacter

- Community based antibiotic use in under 5 children in India
  - 64% of respiratory infections by Day 3
  - 67% fever by Day 3
  - 35% diarrhea by Day 2

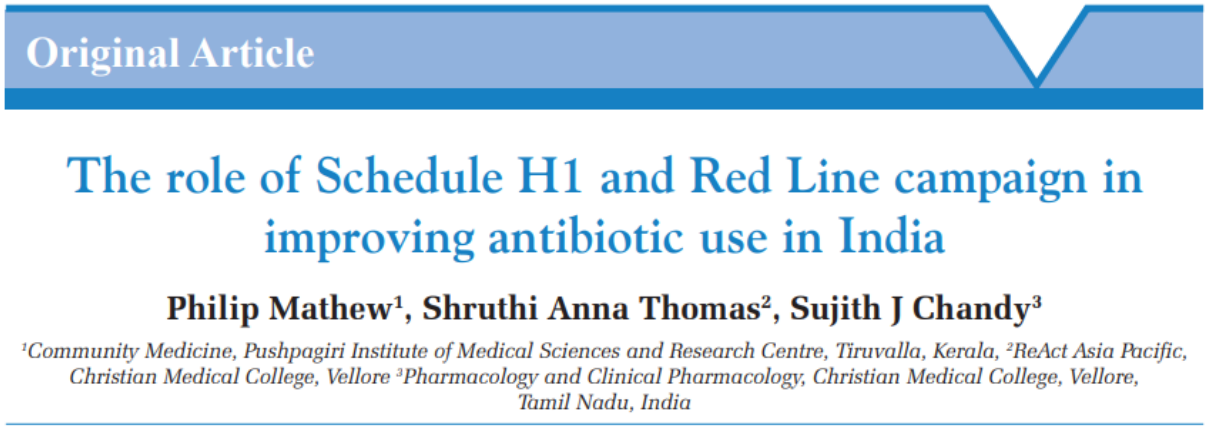
Antibiotics are used everywhere
One Health and AMR

Antibiotic resistance in the food chain

- Animal-human mixing patterns are different between industrialised and low- and middle-income countries
  - Household animals, small-scale backyard poultry and dairy farms and herds, as well as larger scale commercial poultry
- Colistin resistant bacteria reported in India in meat, mutton, fish, fruits and vegetables in 2018
- China exported approximately 100 metric tonnes of colistin-premixed animal feed, supplements and additives per year (2016-2018) to India
  - China reported mcr-1 in 2016 in food samples and banned the use of colistin in food animals
- Prompted a deeper dive into sources
  - Colistin-containing feeds (older brand names Coligro-100, Progrovet, newer unbranded feeds) marketed for treatment and prevention of bacterial infections and as antibiotic growth promoter for better feed conversion and increased weight gain in broilers
  - Colistin banned in 2019
- Complicated picture
  - New genomic studies indicate separation between resistance patterns and mechanisms between animals and humans in India at least in cross-sectional data (V. Balaji, CMC Vellore)
  - But data from other enteric pathogens indicate frequent transmission of bacterial, viral and parasitic species between animal and humans living in close proximity

In this situation, what tools do we have?

- Restriction of antibiotics
- Rational use, including cycling
- Infection prevention and control
- Vaccines



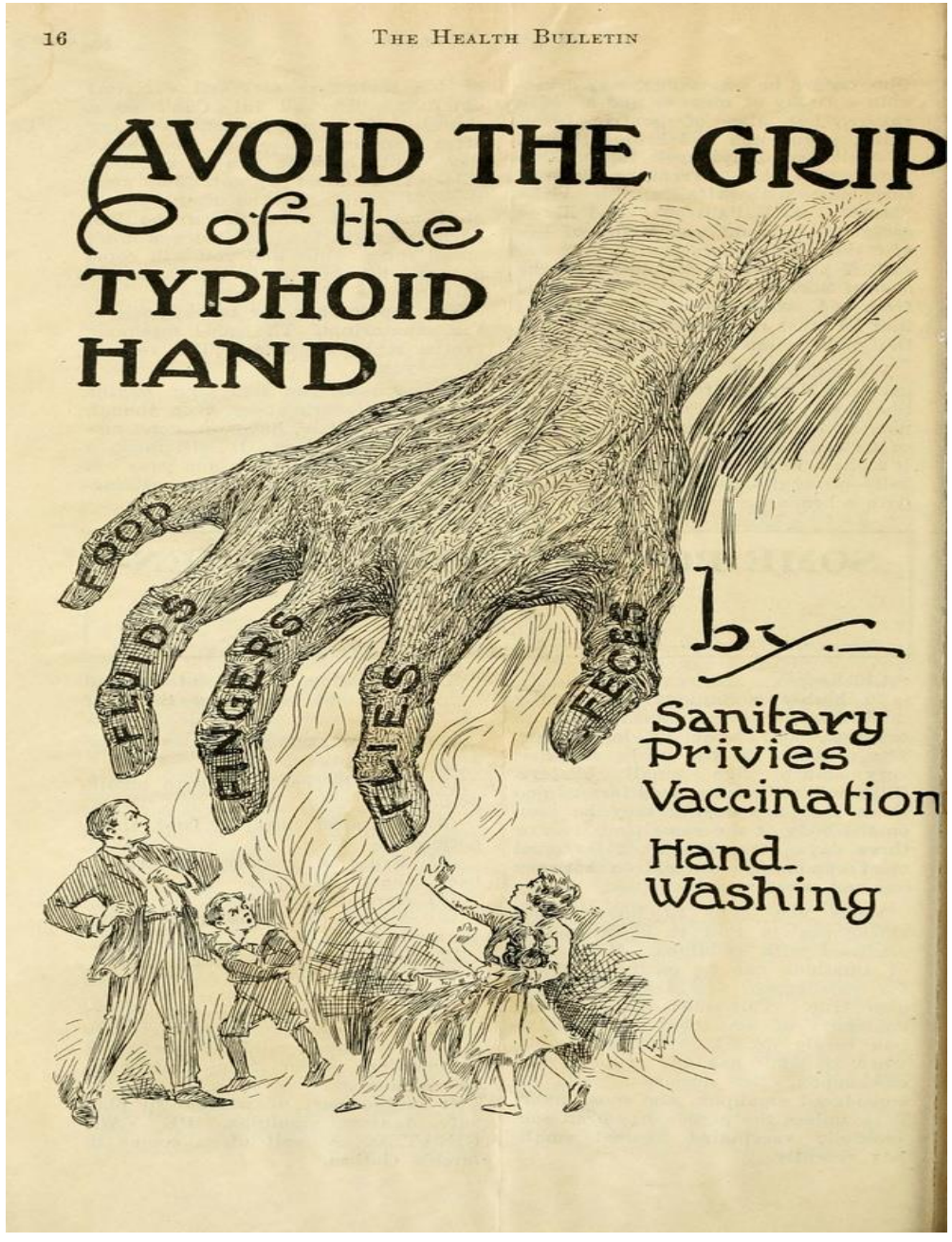
Original Article

The role of Schedule H1 and Red Line campaign in improving antibiotic use in India

Philip Mathew[1], Shruthi Anna Thomas[2], Sujith J Chandy[3]

[1]Community Medicine, Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla, Kerala, [2]ReAct Asia Pacific, Christian Medical College, Vellore [3]Pharmacology and Clinical Pharmacology, Christian Medical College, Vellore, Tamil Nadu, India

Typhoid remains familiar in public perception

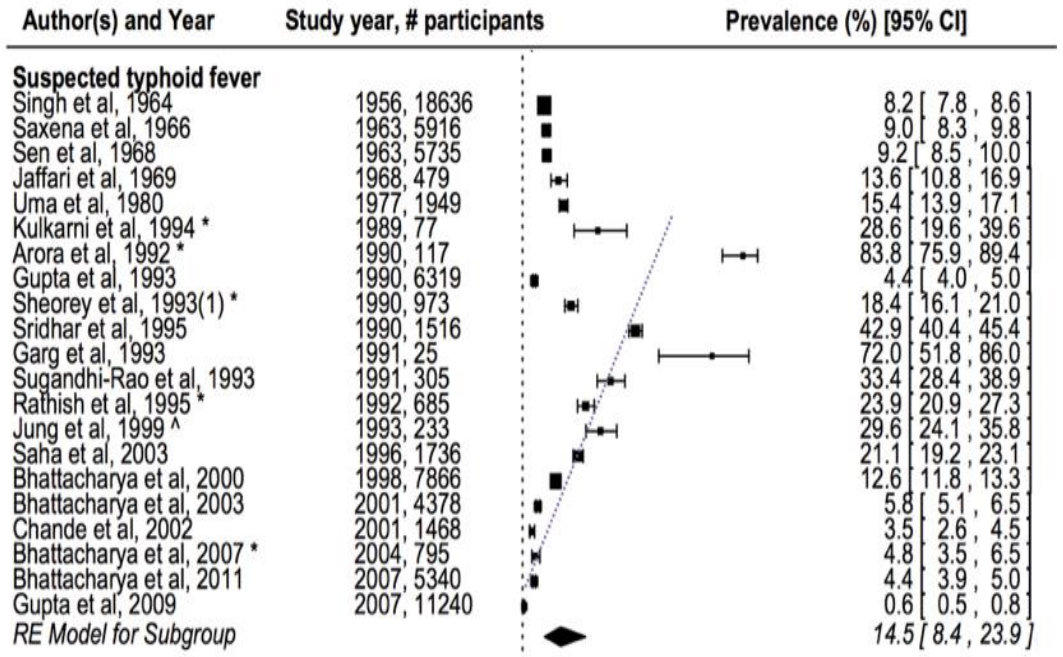


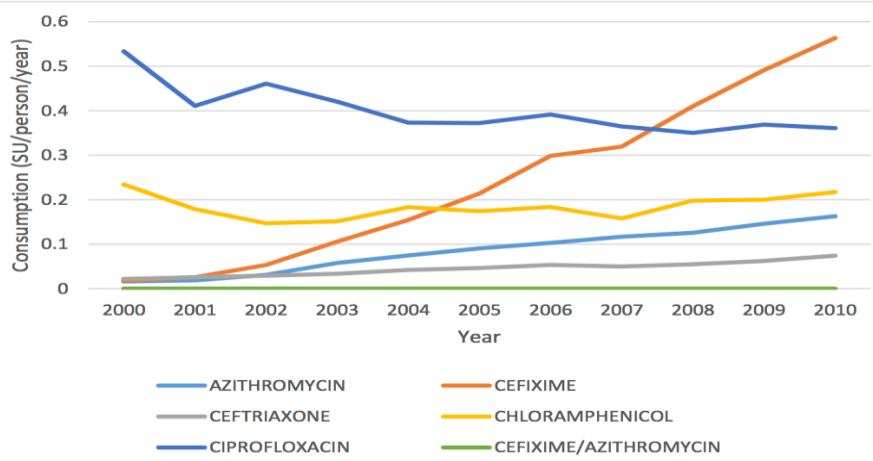
Korean tourists to India stricken with typhoid

2017-08-21 : 13:38

But the medical profession and policy makers think typhoid does not need interventions beyond antibiotics

- Older cohort studies show high incidence of typhoid esp. in young children, no recent studies until 2016
- Decline in *typhoid isolation* at tertiary care facilities





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THE TIMES OF INDIA

Typhoid vaccination programme & doubting doctors

TNN | Nov 20, 2004, 01.52 AM IST

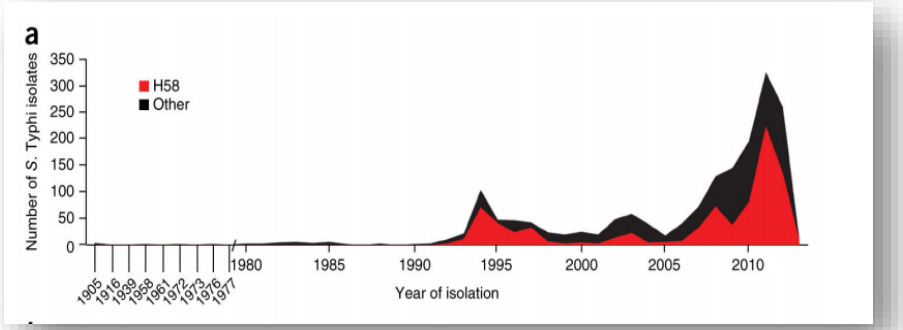
NEW DELHI: The much-hyped typhoid vaccination programme has left the cityâ€™s medical fraternity wondering as to why it was launched at the end of the typhoid "season".

In addition, the injectable vaccine, Typhi-VI, has a "fairly low" efficacy rate of about 60-70% as was proved in the course of clinical trials for the drug. The vaccine provides immunity for a period of two years, but only to typhoid caused by the bacteria Salmonella typhi.

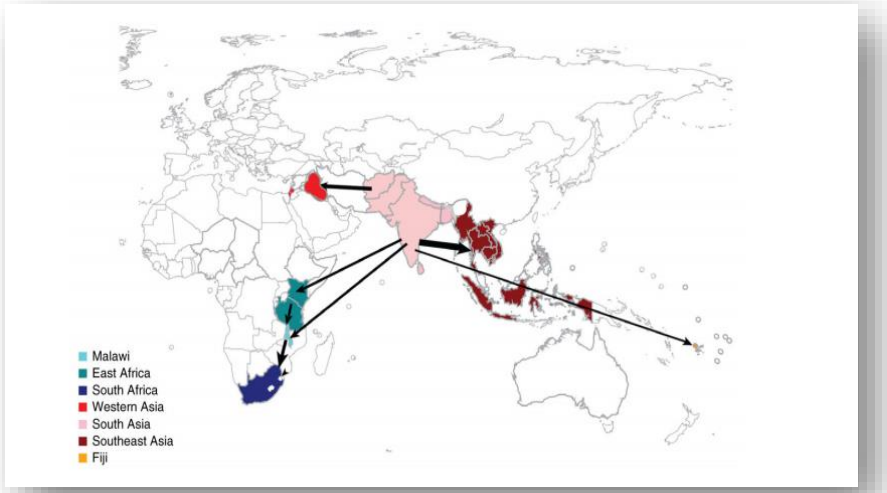
John et al PLosNTDs 2016

Typhoid genomics

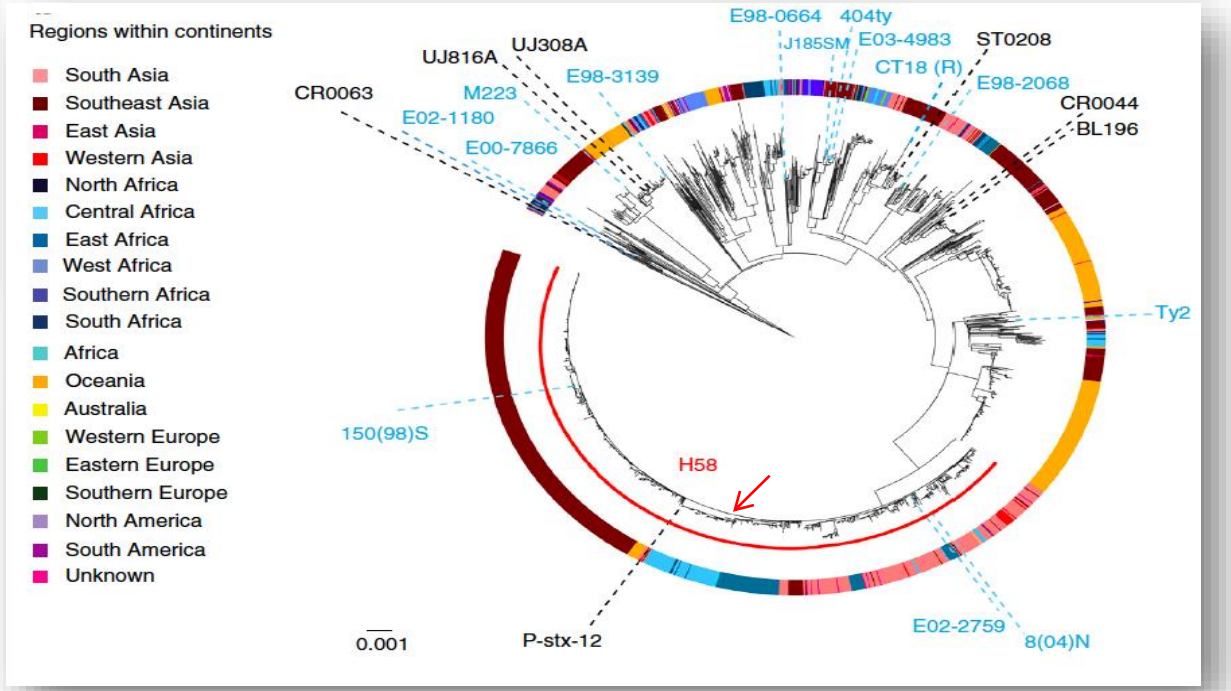
S. Typhi - A single dominant MDR lineage "H58" that has emerged and spread throughout Asia and Africa over the last 30 years



Temporal distribution of S.Typhi Genotypes



Major geographical transfers within the H58 lineage – South Asia (Hub of H58)



Unique lineage of H58 *S. Typhi*

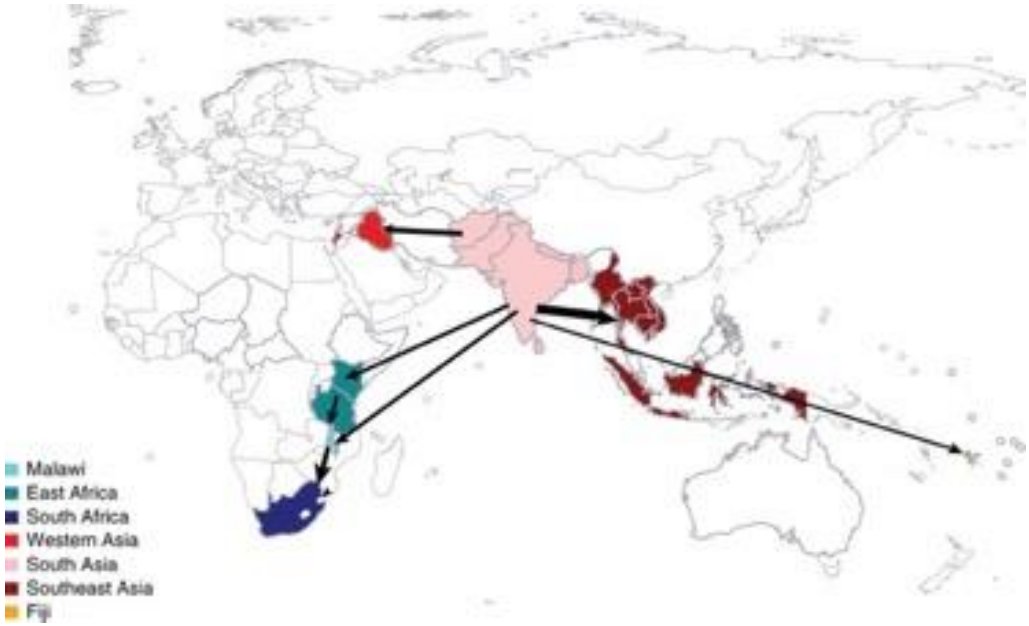
Wong et al., Nat Genet. 2015 June ; 47(6): 632–639

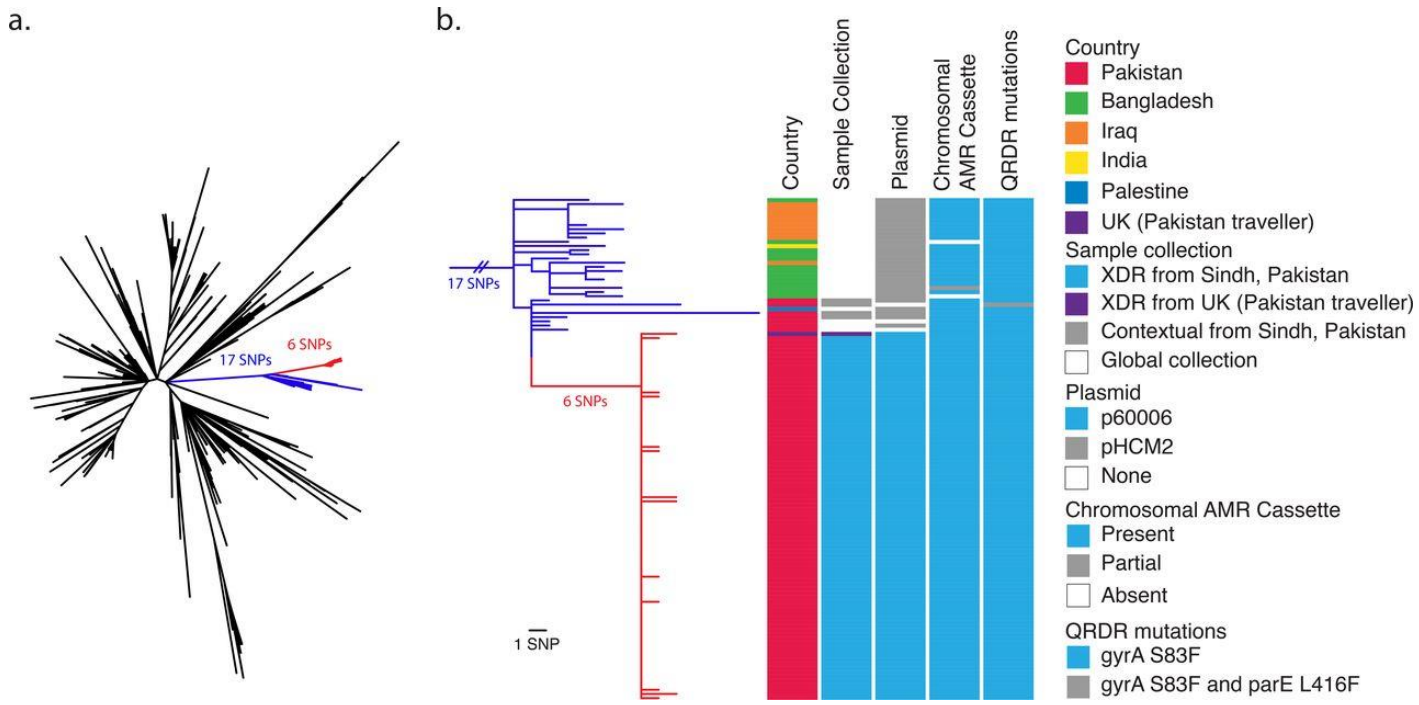
AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

RESEARCH ARTICLE

Emergence of an Extensively Drug-Resistant *Salmonella enterica* Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins

Elizabeth J. Klemm,[a] Sadia Shakoor,[b] Andrew J. Page,[a] Farah Naz Qamar,[b] Kim Judge,[a] Dania K. Saeed,[b] Vanessa K. Wong,[c] Timothy J. Dallman,[d] Satheesh Nair,[d] Stephen Baker,[e,f,g] Ghazala Shaheen,[b] Shahida Qureshi,[b] Mohammad Tahir Yousafzai,[b] Muhammad Khalid Saleem,[b] Zahra Hasan,[b] Gordon Dougan,[a,c] Rumina Hasan[b]





The H58 clade spread from India in the late 1980s

The Pakistan H58 has both plasmid- and chromosomally mediated resistance genes

Surveillanc Fever in India

Incidence in children 1170/100,000 child years of observation

In some locations 80% of children were on antibiotics by Day 3 of fever, whether or not typhoid was proven

Impact of Interventions

Risk o typhoi

Disease

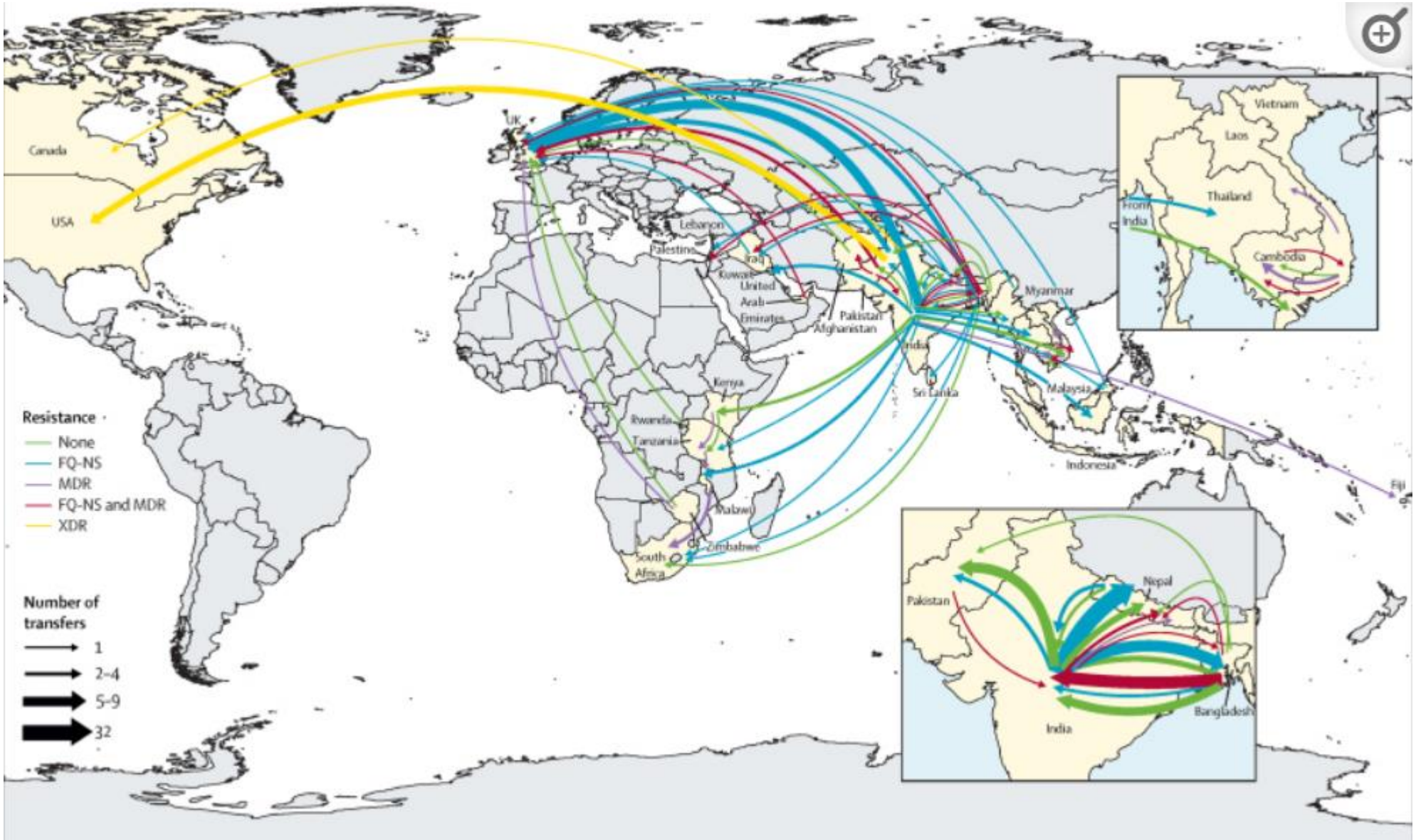
Transmission

Tier 1 surve

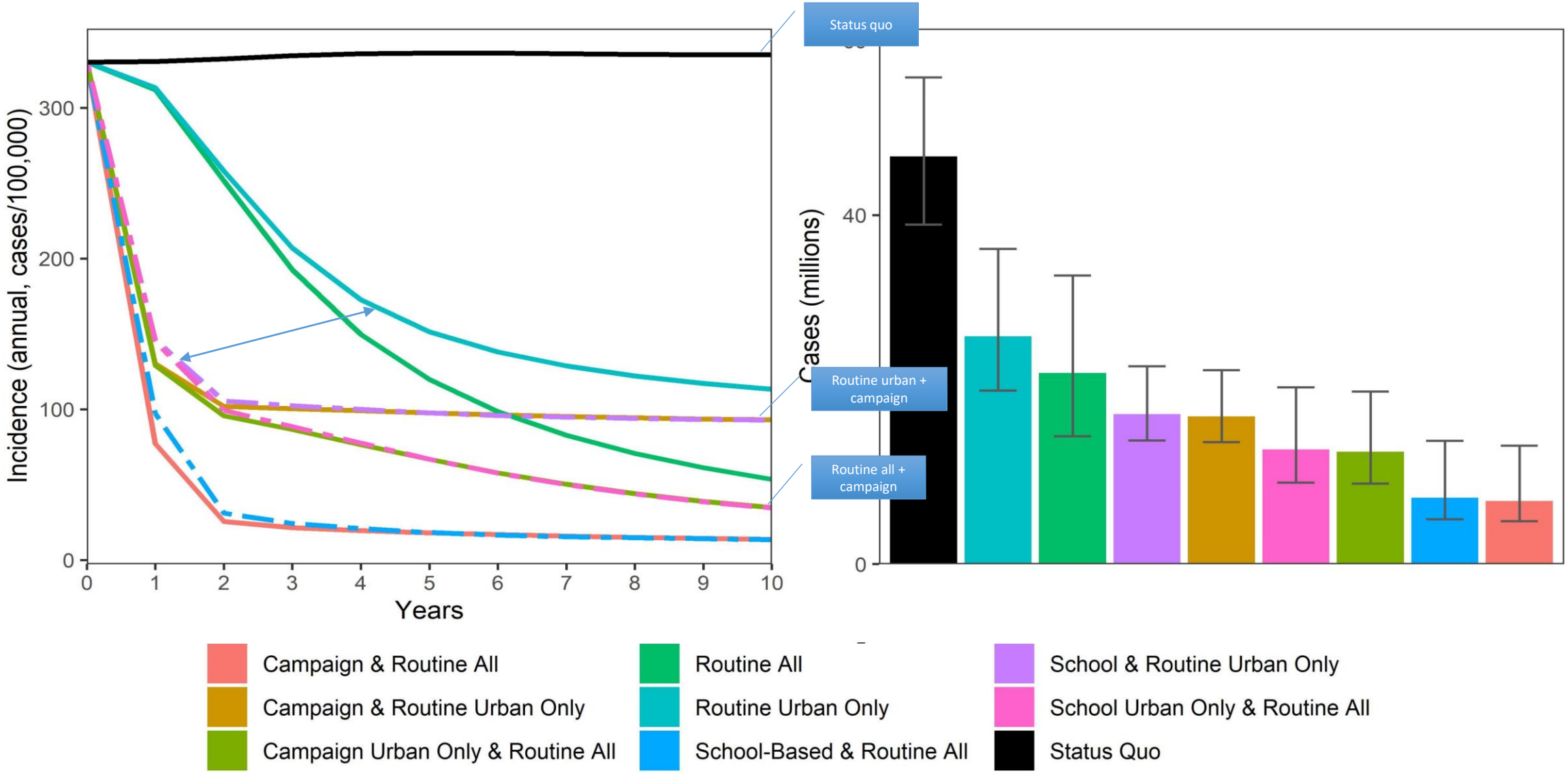
2 surveillance

Tier 3 surveillance

The international and intercontinental spread and expansion of antimicrobial-resistant *Salmonella* Typhi: a genomic epidemiology study. Da Silva et al, Lancet Microbe 2022

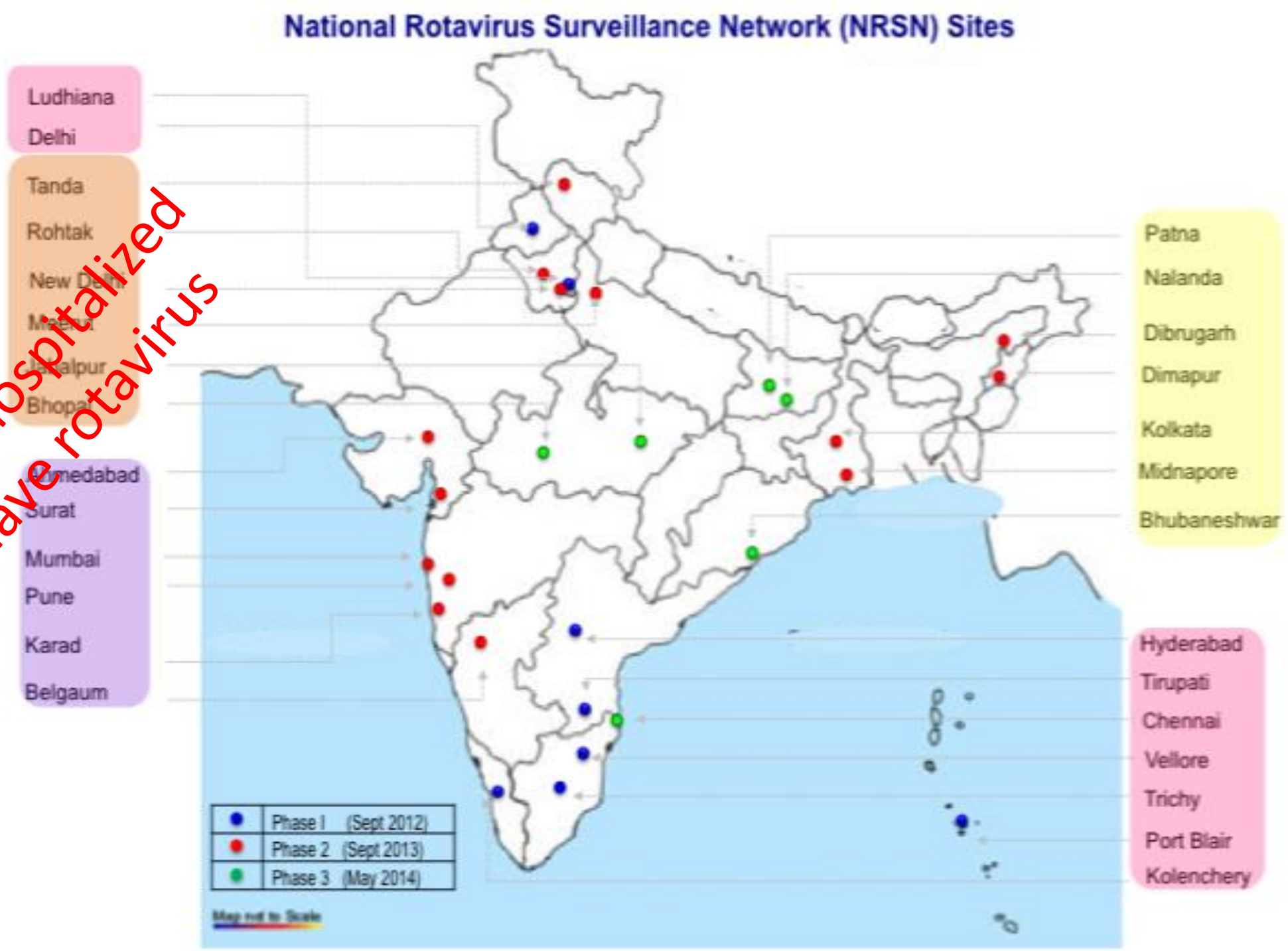


Different vaccination strategies: 10-year incidence projections

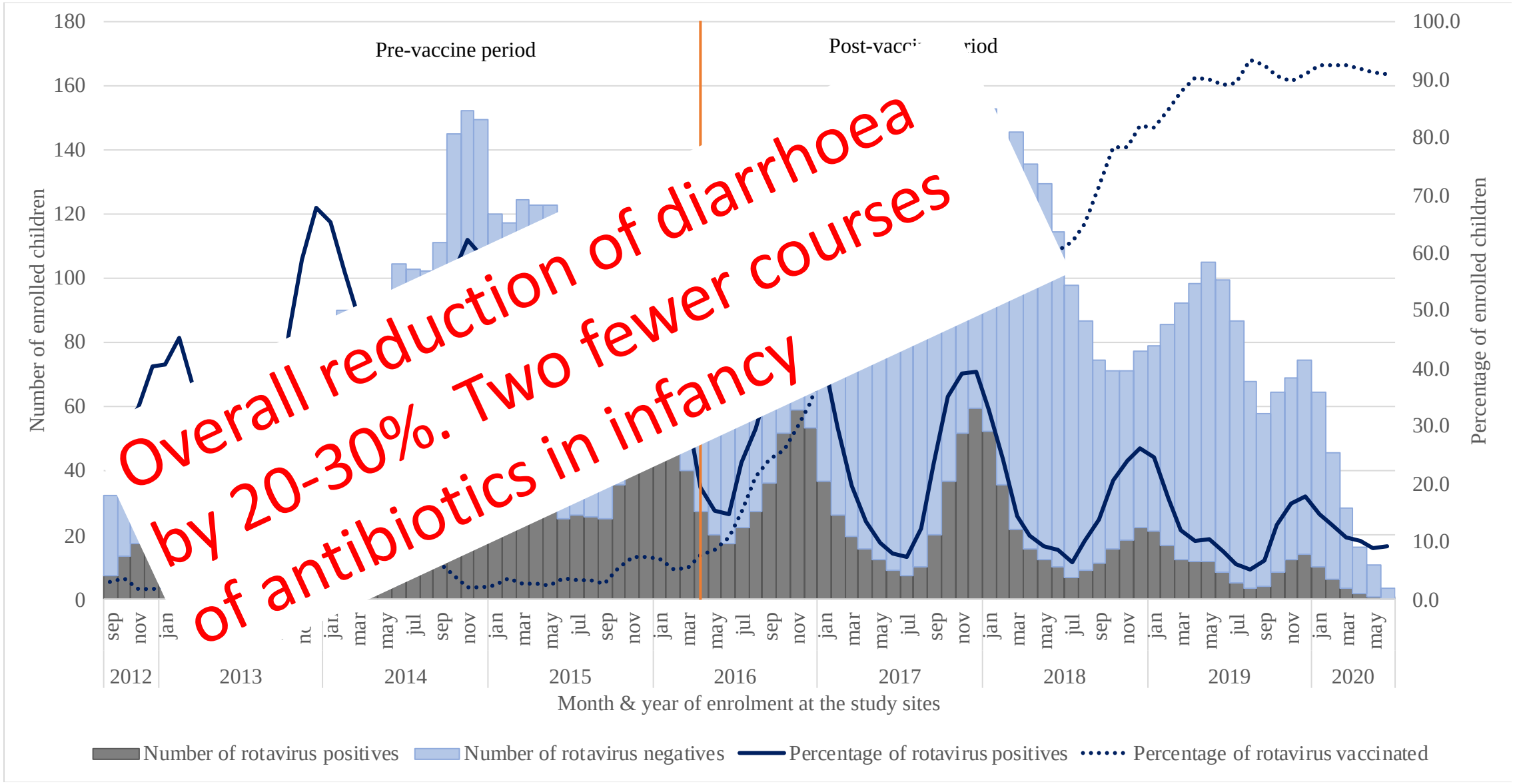


National Rotavirus Surveillance

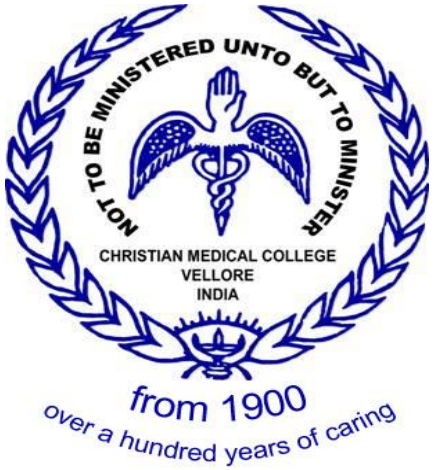
37% of all children hospitalized with diarrhoea have rotavirus



Impact of rotavirus vaccine after introduction into the universal immunization programme in India, pre-vaccine and post-vaccine introduction surveillance comparison



- Science and policy summary
  - Irrational antibiotic use was highlighted during COVID and continues to be a problem in LMICs
  - Solving for both access and excess is necessary (neonatal infections)
  - Some interventions have had effects (ban colistin in food animals, IPC where implemented consistently), not others (other antibiotics in animal feeds, red line)
  - Vaccines hold potential for lowering antibiotic use and hence decreasing AMR



Thank you for your attention