Clinical Infectious Diseases

SUPPLEMENT ARTICLE

Decision Making and Implementation of the First Public Sector Introduction of Typhoid Conjugate Vaccine—Navi Mumbai, India, 2018

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Background. Typhoid fever prevention and control efforts are critical in an era of rising antimicrobial resistance among typhoid pathogens. India remains one of the highest typhoid disease burden countries, although a highly efficacious typhoid conjugate vaccine (TCV), prequalified by the World Health Organization in 2017, has been available since 2013. In 2018, the Navi Mumbai Municipal Corporation (NMMC) introduced TCV into its immunization program, targeting children aged 9 months to 14 years in 11 of 22 areas (Phase 1 campaign). We describe the decision making, implementation, and delivery costing to inform TCV use in other settings.

Methods. We collected information on the decision making and campaign implementation in addition to administrative coverage from NMMC and partners. We then used a microcosting approach from the local government (NMMC) perspective, using a new Microsoft Excel–based tool to estimate the financial and economic vaccination campaign costs.

Results. The planning and implementation of the campaign were led by NMMC with support from multiple partners. A fixed-post campaign was conducted during weekends and public holidays in July–August 2018 which achieved an administrative vaccination coverage of 71% (ranging from 46% in high-income to 92% in low-income areas). Not including vaccine and vaccination supplies, the average financial cost and economic cost per dose of TCV delivery were $0.45 and $1.42, respectively.

Conclusion. The first public sector TCV campaign was successfully implemented by NMMC, with high administrative coverage in slums and low-income areas. Delivery cost estimates provide important inputs to evaluate the cost-effectiveness and affordability of TCV vaccination through public sector preventive campaigns.

Keywords. typhoid; typhoid conjugate vaccine; vaccine introduction; *Salmonella* Typhi.

Each year, typhoid fever accounts for an estimated 11 million illnesses and 116 800 deaths globally [1]. It is the major form of enteric fever, caused by the bacterium *Salmonella enterica* serotype Typhi. It manifests primarily as an acute systemic febrile illness and is transmitted via the fecal-oral route from people who are acutely infected, convalescent, or chronic carriers. Most illnesses and deaths occur in populations that lack access to potable water and adequate sanitation and hygiene. Southern Asia and sub-Saharan Africa have the highest incidence, especially among children [1–3].

Supportive management with appropriate antibiotics is required for typhoid fever treatment; however, increasing resistance to antimicrobial agents among Typhi isolates is limiting treatment options [4–6]. Reviews in recent years show an increasing trend in antimicrobial resistance in the form of plasmid-mediated multidrug resistance to chloramphenicol, ampicillin, and cotrimoxazole, in addition to resistance to fluoroquinolones, such as ciprofloxacin, used in many parts of the world [5, 7, 8]. Recently, resistance to more potent, broader spectrum antibiotics such as third-generation cephalosporins, including extensively drug resistant (XDR) strains and azithromycin resistance have been reported [9, 10]. Systemic complications of typhoid range from intestinal perforation to neurologic manifestations, especially because of inadequate treatment. These complications contribute to disease severity and mortality, as effective treatment options become limited [6].

Safe water, adequate sanitation and hygiene, and vaccination constitute important prevention and control measures [11]. While improvements in water and sanitation infrastructure are being made in some parts of the world, rapid urbanization and population growth pose enormous challenges for the

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construction of new systems and the maintenance and upgrades of existing ones [12]. Typhoid vaccination is, therefore, an important complementary tool recommended by the World Health Organization (WHO) for endemic and epidemic disease control [11]. Safe and effective typhoid vaccines—an oral live, attenuated vaccine (Ty21a) and an injectable Vi capsular polysaccharide—have been available since the early 1990s [11]. However, these vaccines are not licensed for young children <2 years old and need to be readministered every 3–5 years, making them less suitable from a programmatic perspective.

In December 2017, WHO prequalified the first typhoid conjugate vaccine (TCV), Typbar-TCV (Bharat Biotech International) [13] and recommended that TCV use be prioritized for countries with the highest burden of the disease or a high burden of antimicrobial resistance [11]. TCVs have several advantages compared with the other typhoid vaccines, including robust immune response in young children and longer duration of protection [11]. In 2017, Gavi, the Vaccine Alliance, endorsed funding support for TCV introduction in Gavi-eligible countries [14]. Modeling studies have shown that TCVs have the potential for a substantial impact in reducing typhoid disease burden, while longer-term water and sanitation systems are put in place [15, 16].

India, the world's second most populous country, has consistently had one of the highest estimated burdens of typhoid disease in the world, with >8.3 million cases and >72 400 deaths per year—the majority among children <15 years old [1]. A systematic review demonstrated a high typhoid burden in India, especially among young children, and several hospital-based studies have shown that shown that *Salmonella* Typhi is one of the most frequently isolated bacteria from blood cultures taken from febrile patients [17–19]. Available data from tertiary care hospitals show that typhoid ileal perforations are a common occurrence [20, 21]. India remains one of the countries with the highest usage of antibiotics [22], and antimicrobial resistance among typhoid fever isolates is increasingly noted [18]. Typhoid vaccines have been widely available and used in the private sector in India. In 2013, Typbar-TCV was licensed in India and recommended for use by the Indian Academy of Pediatrics (IAP) [23]; it is reported that this vaccine is also being used widely in the private sector (personal communication, Bharat Biotech).

Navi Mumbai, an urban township on the west coast of India, has an active local chapter of the IAP, and pediatricians report typhoid as an important illness among children (personal communication, IAP). In 2008–2009, a study conducted in 2 hospitals in Navi Mumbai demonstrated a high burden of disease among pediatric patients. Over a 16-month period, 98 blood culture–confirmed cases were detected, with most isolates exhibiting multidrug resistance and nalidixic acid resistance [24]. Data from one private laboratory showed a consistent disease burden with >750 blood culture–confirmed clinical cases from 2014 to 2016, with worsening antimicrobial resistance profiles (personal communication, Joshi Laboratory).

The Navi Mumbai Municipal Corporation (NMMC), the local government body, provides healthcare and immunization services to the citizens of Navi Mumbai within its jurisdiction. In 2014, NMMC introduced measles-mumps-rubella vaccine to provide additional protection against mumps and rubella for children living within its jurisdiction—in addition to the national schedule for measles vaccine [25]. In 2018, it made a notable decision to introduce TCV into the public sector immunization program. Multiple national and international organizations have partnered to conduct monitoring and evaluation activities. In this paper, we describe the decision-making process, campaign implementation, administrative coverage, and delivery costing of TCV introduction in Navi Mumbai, India.

METHODS

Setting

Navi Mumbai is an extension of the suburbs of Mumbai, one of the largest metropolitan cities and the financial capital of India [26]. Developed as a planned township by the City and Industrial Development Corporation in the 1970s [26] and has been home primarily to a low- to upper-middle-class population. However, high migration rates in recent years have increased slum settlements [26]. Navi Mumbai comprises 14 administrative areas (nodes), of which 8 are within NMMC jurisdiction. According to the 2011 census, the estimated population of the NMMC-governed Navi Mumbai area is about 1.12 million persons, with an estimated 129 500 children 0–6 years old [27].

In 2018, for the purpose of health services provision (including immunization), these 8 nodes were subdivided into 22 urban health posts (UHP) areas, of which 9 UHPs designated as "high risk" by NMMC based on the proportion of the population living in slum areas (>70%) (personal communication, NMMC). However, there are some UHPs with high-income structures and no slums, where most people seek health services (including vaccination) from private providers. NMMC reports >95% administrative coverage for measles in the routine immunization program and for polio during vaccination campaigns (personal communication, WHO India Country Office). A phased TCV campaign was planned for all children aged 9 months to 14 years, targeting 11 UHPs in 2018 (phase 1) and the remaining UHPs in 2019–2020 (phase 2) (Supplementary Figure 1).

Data Collection and Methods of Analysis

We collected information regarding the decision making, planning, and implementation of the first phase of the campaign from stakeholders, including NMMC officials, the National Technical Advisory Group on Immunization and other key partners. Data on administrative vaccine coverage (defined as number of doses administered to the target population), vaccine

vials usage and reported adverse events following immunization (AEFIs) were obtained from NMMC officials. We also compiled information on the rapid convenience monitoring of the campaign from WHO, and state and local officials. Vaccine wastage rate was calculated, using the following formula: (100 − [doses administered/doses issued × 100]) [28].

We used a microcosting approach from the local government (NMMC) perspective, using a new Microsoft Excel–based tool specifically developed for TCV delivery costing purposes. We collected information on both financial costs (direct expenditures) and economic costs (financial costs, plus the monetized value of the additional donated or existing items) of the campaign that were incremental to the existing immunization and public health program. The cost items used during the vaccination campaign activities and their respective prices and quantities were collected under predefined programmatic activity categories (ie, planning and preparation, sensitization, training, microplanning, social mobilization, service delivery, AEFI management, supervision, and monitoring) from NMMC and WHO financial and programmatic records, by consultation with NMMC and WHO personnel involved in these activities and purchase decisions, and by interviews with the medical officers of 3 UHPs. Of the 11 UHPs involved in phase 1, 3 UHPs were sampled to represent the 3 residence types in the municipality: a high-rise area (sector 48), a slum area (Indiranagar), and a mixed area (Ghansoli).

Total costs were estimated by multiplying resource quantities by their unit prices per financial and economic cost, activity type, and level of activity (NMMC and UHPs), which were then summed across these dimensions. At each level (NMMC and UHP), per-dose costs were calculated by dividing total costs by the number of doses administered. Total weighted average costs across both levels were estimated by multiplying the cost per dose from each of the 3 sampled UHPs by the number of doses administered at UHPs of the same type (1 high-rise, 7 mixed, and 3 slum UHPs) and then summing with NMMC-level costs and dividing the sum by the total number of doses administered during the campaign across all 11 UHPs. Costs were collected in 2018 Indian rupees and converted to 2018 US dollars at the rate of $1 = ₹68.31.

The overall project was reviewed and approved by the institutional review committees of the World Health Organization, Centers for Disease Control and Prevention, Indian Council of Medical Research, Stanford University and evaluation sites.

RESULTS

Decision Making

In 2017, after a review of available data on blood culture–confirmed typhoid fever in Navi Mumbai and a stakeholder meeting (December 2016), NMMC leadership made an initial decision to introduce TCV, using its own funds for vaccine purchase and operational costs, with support from partners who pledged additional funding for monitoring and evaluation of the introduction.

In keeping with WHO TCV recommendations for age targets, all children aged 9 months–14 years old were targeted for vaccination. Since there was no prior experience with a public-sector TCV roll-out, NMMC decided to conduct the campaign in two phases at least one year apart for the following reasons, (1) to manage logistics including personnel availability; (2) to conduct a rigorous evaluation of the campaign including vaccine impact; and (3) apply lessons learned during the first phase to the second phase, and to improve future campaigns in the Navi Mumbai area. NMMC's 22 UHPs were grouped into 3 strata based on the percentage of the population residing in slum areas (stratum 1, <10%; stratum 2, 10%–70%, and stratum 3, >70%). Of those 11 UHPs (six in Stratum 1, three in Stratum 2, and two in Stratum 3) were selected for Phase 1 TCV introduction in 2018. The remaining 11 UHPs were designated for vaccine roll-out during phase 2. The manufacturer, Bharat Biotech International Limited, offered a cost subsidy for public sector use.

NMMC received technical approval from the state of Maharashtra and the central government for vaccine use not currently in the country's Expanded Program on Immunization schedule. In February 2018, the overall proposal was approved by the NMMC General Body and the financial committees for a phased campaign.

Campaign Planning and Preparations

Campaign planning and implementation were led by NMMC with support from multiple partners and stakeholders at the local, national and international levels. Partners included WHO-India, the Centers for Disease Control and Prevention, the Ministry of Health and Family Welfare—Government of India, Government of Maharashtra, the IAP–Navi Mumbai chapter, and the private sector (leading pediatricians, general practitioners, clinics, and hospitals). To avoid disruption of routine immunization services and other health services at the UHPs, the campaign was planned during weekends and public holidays from 14 July to 25 August 2018 (with catch-up during weekdays at UHP health centers).

Planning and advocacy meetings were conducted with (1) NMMC staff at headquarters and UHP health centers and (2) IAP–Navi Mumbai chapter, other private pediatricians, and other private physicians. Focus group discussions were conducted with immunization campaign workers, pediatricians, and caregivers in high-, middle- and low-income communities, with support from Centers for Disease Control and Prevention and WHO communications specialists. The information gathered from these discussions was used to inform campaign messaging, social mobilization, and crisis communication planning with support from a local communications agency.

In preparation for the campaign, multiple training sessions were conducted for NMMC pediatricians, UHP medical

officers, and auxiliary nurse midwives. The topics included microplanning, campaign logistics, injection techniques, and the management of AEFIs, in accordance with TCV introduction plans that were adapted from the national measles-rubella campaign guidelines. Field workers were trained on headcount surveys and social mobilization activities. Detailed microplanning activities were conducted by the NMMC officer in charge along with other NMMC officials and UHP medical officers, using the latest polio microplans and headcount surveys. Each of the 11 targeted UHPs was paired with a nearby phase 2 UHP for additional personnel and logistical support.

One vaccination session was planned for every 150 children targeted for a total of 1200 sessions over a 6-week period; session sites included health posts, immunization clinics, residential society offices, and community centers; each vaccination session booth included 1 vaccinator, 1 technician and 2 social mobilizers. A total of 50 000 vaccine doses were donated by the manufacturer, and injection supplies were obtained from the Government of India. Special AEFI kits were prepared by NMMC, and local AEFI committees were formed at the UHP level. Other preparations, such as biomedical waste management and forms for reporting of administrative coverage, were developed according to the measles-rubella vaccine campaign guidelines.

Social mobilization activities were conducted by field workers who distributed information booklets through house-to-house visits starting 1 week before the campaign in each subarea and during the campaign. Banners were posted in selected locations, and a media briefing was held by the NMMC mayor and commissioner 1 week before the launch of the campaign. No other mass media social mobilization activities were conducted, to avoid raising expectations among communities who would not be receiving vaccine in the first year.

Campaign Implementation

Vaccines were received in 5-dose vials and maintained in cold chain per manufacturer and WHO guidelines. The campaign was implemented as a fixed-post campaign from 14 July to 25 August 2018 in 11 of the 22 UHPs of Navi Mumbai, per the campaign microplan. Approximately, 113 420 children were reported to have received the vaccine, resulting in administrative coverage = 71%. Administrative coverage was high in low-income UHPs (e.g., 92% in Chinchpada) and it was lowest in high income UHPs (e.g., 46% in Sector 48).

A total of 222 vaccine recipients reported ≥1 AEFI, as defined in the national AEFI guidelines; 211 events (95%) were classified as mild AEFI (pain, fever, and swelling), 2 (1%) were considered serious, and 9 (4%) were considered severe; most people reported resolution within 7 days. No deaths were reported. Details of AEFIs and additional safety evaluation findings are described elsewhere (in press).

Overall, 495 vaccination sessions were selected (convenience sampling) for rapid convenience monitoring using independent campaign monitors across 11 UHPs to evaluate the quality of immunization sessions. Quality indicators ranged from 89%–100% for all selected sessions (including sessions with mobilizers per the microplan=89%, sessions with vaccinators per microplan=95%, session sites visited by supervisors=97%, sessions held per microplan=99%, session sites having functional hub cutter=99%, session sites with date and time of vial opening noted on vial label=99% and session sites with an AEFI management kit available=100%). A total of 328 subareas were selected for household monitoring and vaccination status was verified for 6560 children (86% were found to be vaccinated); 48 subareas were recommended for mop-up activities. The reported vaccine wastage was 3% (3505 of 116 925 doses issued).

Campaign Delivery Costing

Excluding the costs of vaccine, syringes, and safety boxes, the average financial cost of TCV delivery per dose was $0.45 (range, $0.44–$0.60), and the average economic costs per dose was $1.42 ($1.30–$3.93) (Table 1). The high-rise areas with the lowest vaccination coverage had the highest delivery costs per dose.

DISCUSSION

To our knowledge, the NMMC introduction is the first public sector TCV introduction in the world. This successful first phase of the NMMC TCV introduction suggests that it is practical to implement TCV in a catch-up campaign in a large metropolitan area. This success mirrors earlier state and local government initiatives for vaccine introduction in India. In 2004, the state of Delhi in India introduced the typhoid polysaccharide vaccine into its routine immunization program for children 2–5 years old [29] and the states of Punjab and Sikkim introduced human papillomavirus vaccine in 2017 and 2018 respectively [30]; however, data on implementation and impact of these programs remain limited.

Based on locally available typhoid fever disease burden data at the time and increasing concerns with antimicrobial resistance, NMMC made a notable decision to introduce TCV into the immunization program, using its own infrastructure and resources. They demonstrated a high level of technical and administrative acumen in obtaining approvals and technical support at multiple levels of the local, state and central governments and partner support for evaluation of the program. NMMC conducted meticulous planning, preparations, attention to detail and leveraged partnerships (especially with the WHO-India polio program). NMMC conducted rigorous monitoring of the campaign, not only to inform its planning for the second phase of the campaign, but also partnered with multiple local, national, and international organizations for additional evaluations of the different components, including vaccine safety, coverage, effectiveness, and impact, which

Table 1. Typhoid Conjugate Vaccine Campaign Costs in 2018 Prices, Phase 1 Campaign, Navi Mumbai, India

		UHP-Level Costs						
		Majority-slum UHP (Indiranagar)		Mixed-residence UHP (Ghansoli)		High-rise UHP (Sector 48)		
	NMMC-Level Costs	Alone	+ NMMC	Alone	+ NMMC	Alone	+ NMMC	Total Weighted Average (NMMC + UHP)[a]
Vaccine coverage, %		76.1		70.9		46.5		71.0
Doses administered, no.		6832		19 528		2673		113 420
Total delivery cost per dose, 2018 US$[b]								
Including vaccine, syringes, and safety boxes								
Financial	2.31	1.99	4.30	2.00	4.31	2.15	4.46	4.31
Economic	3.88	3.73	7.61	3.52	7.40	6.15	10.03	7.52
Excluding vaccine, syringes, and safety boxes								
Financial	0.38	0.06	0.44	0.07	0.45	0.22	0.60	0.45
Economic	0.83	0.68	1.51	0.47	1.30	3.10	3.93	1.42

Abbreviations: NMMC, Navi Mumbai Municipal Corporation; UHP, urban health post.

[a]For a total of 11 UHPs.

[b]Financial costs included direct expenditures; economic costs, financial costs plus the monetized value of the additional donated or existing items.

are ongoing. The overall administrative coverage achieved was comparable with that of a typhoid polysaccharide vaccine campaign in India [31], but reported coverage was low in high-income areas, which is not surprising, given the preference for private healthcare among high-income populations in these settings.

The vaccine implementation strategy had several strengths. Vaccination campaigns are generally considered to have an adverse effect on routine immunization services [32]. To avoid disruption of routine services, NMMC planned the campaign over weekends and public holidays during a 6-week period, and the vaccine was offered to children who missed receiving it during campaign days at the 11 UHP clinics on weekdays during routine immunization sessions. Vaccine wastage was low and well within the acceptable range for supplementary immunization activities. In addition, each of the 11 UHPs was paired with a nearby UHP (to be vaccinated in the subsequent phase) for resource sharing during both phases, which reduced the need to hire additional campaign personnel and leveraged the existing health infrastructure. Partnerships with the private sector and establishment of local UHP committees was instrumental in crisis communication planning in the event of an AEFI, which were successfully reported using the national AEFI guidelines. The TCV introduction also provided an opportunity for additional AEFI trainings and AEFI surveillance strengthening efforts. These efforts also contributed to a successful subsequent measles-rubella vaccination campaign in Navi Mumbai (personal communication, NMMC).

There were also several difficulties encountered. There were numerous administrative delays with multiple levels of approvals within and outside NMMC that had to be sought. In addition, the NMMC administration changed twice during decision making and implementation of the TCV campaign. Owing to the delays, the campaign was conducted during the peak rainy season, which added logistical difficulties including session site selection (avoiding areas with potential waterlogging), difficulties with transportation, and potential beneficiary attendance. The rainy season also coincides with the peak typhoid season in India; hence, the campaign missed protecting the population from the peak season in Navi Mumbai. Based on the recently published clinical efficacy data for TCV at 82% [33], the campaign might have been more effective had it been conducted before the peak season.

The delivery costing represents the first estimation of TCV delivery costs through a public sector campaign. The financial cost of TCV delivery from the local government perspective was low and comparable with an oral cholera vaccine campaign (not including cost of vaccine and vaccination supplies) conducted in Odisha, India, where the per-dose cost was $0.49 in 2011 prices [34], or $0.44 in 2018 prices [35, 36]. As more countries introduce TCV, more TCV delivery costing studies are needed to better understand cost variations and factors that affect delivery costs for budgeting and planning purposes, since Gavi, the Vaccine Alliance, has made financing available for TCV introduction.

Nevertheless, NMMC's public sector introduction of TCV and related evaluations provide data on TCV implementation for other similar settings. In December 2016, the National Technical Advisory Group on Immunizations in India recommended that studies be conducted to better determine disease burden in India and learn from TCV introductions to inform a national recommendation [37]. A large typhoid surveillance study has been launched in India to better define typhoid disease burden, which, combined with data from the Navi Mumbai introduction may help facilitate nationwide TCV introduction decisions [38].

In addition, lessons learned from Navi Mumbai have been shared with other countries using TCV. An emergency TCV campaign was conducted in Zimbabwe in 2018 [39], and Pakistan introduced the vaccine into its routine immunization system with a Gavi-supported introduction in November 2019 [40]. The second phase of the campaign in Navi Mumbai is planned for 2021 (Originally planned for 2019 and moved to 2020 – timelines may be impacted by the current Covid-19 pandemic) and will provide additional information on a phased approach as well as overall vaccine impact. TCVs represent an important public health tool especially in the current extensively drug-resistant–typhoid situation, and documentation of campaign implementation strategies will help better understand acceptability, costs, and impact.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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References

1. GBD 2017 Typhoid and Paratyphoid Collaborators. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis **2019**; 19:369–81.
2. Mogasale V, Maskery B, Ochiai RL, et al. Burden of typhoid fever in low-income and middle-income countries: a systematic, literature-based update with risk-factor adjustment. Lancet Glob Health **2014**; 2:e570–80.
3. Marks F, von Kalckreuth V, Aaby P, et al. Incidence of invasive *Salmonella* disease in sub-Saharan Africa: a multicentre population-based surveillance study. Lancet Glob Health **2017**; 5:e310–23.
4. Hooda Y, Sajib MSI, Rahman H, et al. Molecular mechanism of azithromycin resistance among typhoidal *Salmonella* strains in Bangladesh identified through passive pediatric surveillance. PLoS Negl Trop Dis **2019**; 13:e0007868.
5. Kariuki S, Gordon MA, Feasey N, Parry CM. Antimicrobial resistance and management of invasive *Salmonella* disease. Vaccine **2015**; 33(suppl 3):C21–9.
6. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL. Typhoid fever. Lancet **2015**; 385:1136–45.
7. Dyson ZA, Klemm EJ, Palmer S, Dougan G. Antibiotic resistance and typhoid. Clin Infect Dis **2019**; 68:165–70.
8. Park SE, Pham DT, Boinett C, et al. The phylogeography and incidence of multi-drug resistant typhoid fever in sub-Saharan Africa. Nat Commun **2018**; 9:5094.
9. Klemm EJ, Shakoor S, Page AJ, et al. Emergence of an extensively drug-resistant *Salmonella enterica* serovar Typhi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. mBio **2018**; 9:e00105-18.
10. Levine MM, Simon R. The gathering storm: is untreatable typhoid fever on the way? mBio **2018**; 9:e00482-18.
11. Typhoid vaccines: WHO position paper. Wkly Epidemiol Rec **2008**; 83:49–59. e00105-18
12. Steele AD, Hay Burgess DC, Diaz Z, Carey ME, Zaidi AK. Challenges and opportunities for typhoid fever control: a call for coordinated action. Clin Infect Dis **2016**; 62(suppl 1):S4–8.
13. Bentsi-Enchill AD, Hombach J. Revised global typhoid vaccination policy. Clin Infect Dis **2019**; 68:31–3.
14. Gavi the Vaccine Alliance. Gavi new vaccine support—typhoid conjugate vaccine. https://www.gavi.org/types-support/vaccine-support/typhoid. Accessed 12 December 2019.
15. Bilcke J, Antillón M, Pieters Z, et al. Cost-effectiveness of routine and campaign use of typhoid Vi-conjugate vaccine in Gavi-eligible countries: a modelling study. Lancet Infect Dis **2019**; 19:728–39.
16. Pitzer VE, Bowles CC, Baker S, et al. Predicting the impact of vaccination on the transmission dynamics of typhoid in South Asia: a mathematical modeling study. PLoS Negl Trop Dis **2014**; 8:e2642.
17. Abhilash KP, Jeevan JA, Mitra S, et al. Acute undifferentiated febrile illness in patients presenting to a tertiary care hospital in South India: clinical spectrum and outcome. J Glob Infect Dis **2016**; 8:147–54.
18. Das S, Samajpati S, Ray U, Roy I, Dutta S. Antimicrobial resistance and molecular subtypes of *Salmonella enterica* serovar Typhi isolates from Kolkata, India over a 15 years period 1998–2012. Int J Med Microbiol **2017**; 307:28–36.
19. Ganesh R, Janakiraman L, Vasanthi T, Sathiyasekeran M. Profile of typhoid fever in children from a tertiary care hospital in Chennai-South India. Indian J Pediatr **2010**; 77:1089–92.
20. Verma H, Pandey S, Sheoran KD, Marwah S. Surgical audit of patients with ileal perforations requiring ileostomy in a tertiary care hospital in India. Surg Res Pract **2015**; 2015:351548.
21. Sur D, Barkume C, Mukhopadhyay B, Date K, Ganguly NK, Garrett D. A retrospective review of hospital-based data on enteric fever in India, 2014–2015. J Infect Dis **2018**; 218(suppl 4): S206–s213.
22. Farooqui HH, Selvaraj S, Mehta A, Heymann DL. Community level antibiotic utilization in India and its comparison vis-à-vis European countries: evidence from pharmaceutical sales data. PLoS One **2018**; 13:e0204805.
23. Balasubramanian S, Shah A, Pemde HK, et al; IAP Advisory Committee on Vaccines and Immunization Practices, 2018-19. Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices (ACVIP) recommended immunization schedule (2018-19) and update on immunization for children aged 0 through 18 years. Indian Pediatr **2018**; 55:1066–74.
24. Gavhane J, Yewale V, Weekey P, Dhanya D, Warrior D. Enteric fever in children from Navi Mumbai—clinical profile, hematological features, sensitivity patterns and response to antimicrobials. Pediatr Infect Dis **2010**; 2:5–9.
25. DNA India. NMMC starts MMR vaccination to stop deformity among newborn babies. https://www.dnaindia.com/mumbai/report-nmmc-starts-mmr-vaccination-to-stop-deformity-among-newborn-babies-1966086. Accessed .
26. NMMC. About Navi Mumbai. https://www.nmmc.gov.in/navimumbai/history1540201195. Accessed .
27. India COo. Navi Mumbai city census 2011 data. https://www.census2011.co.in/census/city/368-navi-mumbai.html. Accessed .
28. USAID. Immunization essentials—a practical field guide, **2003**.
29. Sharma P, Taneja DK. Typhoid vaccine: a case for inclusion in national program. Indian J Public Health **2011**; 55:267–71.

30. Sankaranarayanan R, Basu P, Kaur P, et al. Current status of human papillomavirus vaccination in India's cervical cancer prevention efforts. Lancet Oncol **2019**; 20:e637–44.
31. Sur D, Ochiai RL, Bhattacharya SK, et al. A cluster-randomized effectiveness trial of Vi typhoid vaccine in India. N Engl J Med **2009**; 361:335–44.
32. Chakrabarti A, Grépin KA, Helleringer S. The impact of supplementary immunization activities on routine vaccination coverage: an instrumental variable analysis in five low-income countries. PLoS One **2019**; 14:e0212049.
33. Shakya M, Colin-Jones R, Theiss-Nyland K, et al; TyVAC Nepal Study Team. Phase 3 efficacy analysis of a typhoid conjugate vaccine trial in Nepal. N Engl J Med **2019**; 381:2209–18.
34. Kar SK, Sah B, Patnaik B, et al. Mass vaccination with a new, less expensive oral cholera vaccine using public health infrastructure in India: the Odisha model. PLoS Negl Trop Dis **2014**; 8:e2629.
35. World Bank. Inflation, GDP deflator (annual %), World Bank national accounts data and OECD National Accounts data files. https://data.worldbank.org/indicator/NY.GDP.DEFL.KD.ZG. Accessed.
36. World Bank. Official exchange rate (LCU per US$, period average). International Monetary Fund, International Financial Statistics. https://data.worldbank.org/indicator/PA.NUS.FCRF. Accessed.
37. National Technical Advisory Group on Immunization. Minutes of the meeting of the National Technical Advisory Group on Immunization (NTAGI), **2016**.
38. John J, Bavdekar A, Rongsen-Chandola T, Dutta S, Kang G. Estimating the incidence of enteric fever in children in India: a multi-site, active fever surveillance of pediatric cohorts. BMC public health **2018**; 18(1): 594.
39. World Health Organization. Africa's first-ever mass typhoid fever vaccination campaign ends in Zimbabwe. 4 March 2019. https://www.afro.who.int/news/africas-first-ever-mass-typhoid-fever-vaccination-campaign-ends-zimbabwe. Accessed.
40. Gavi the Vaccine Alliance. Pakistan becomes first country to introduce new typhoid vaccine into routine immunisation program. https://www.gavi.org/news/media-room/pakistan-becomes-first-country-introduce-new-typhoid-vaccine-routine-immunisation. Accessed.