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Building the case for wider use of typhoid vaccines

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Abstract

Efficacious typhoid fever vaccines have been available for decades. Typhoid fever burden of disease estimates indicate a substantial burden of illness and death in low-resource areas. The World Health Organization has recommended that countries consider the use of typhoid vaccines for high-risk groups and populations, and for outbreak control. Despite this, typhoid vaccines are not widely used in endemic areas. By examining strategies to improve burden of disease data, use of transmission dynamic models, economic evaluations, vaccine strategies, and experiences with typhoid vaccine pilot projects, the papers in this supplement help to plot the path toward rational and wider use of typhoid vaccines.

Keywords

Developing countries; Typhoid fever; Vaccines

Salmonella enterica serovar Typhi, the cause of typhoid fever, is a human host restricted pathogen transmitted by food or water contaminated with human feces. It may cause endemic disease across a range of incidence levels and is associated with outbreaks that can be large. Access to safe water and improved sanitation facilities are effective control strategies. However, progress with improvements in water and sanitation coverage has been slow in many areas. Typhoid fever vaccines represent a complementary means of preventing disease. Typhoid vaccines have been used for more than a century. Clinical trials, some conducted decades ago, have demonstrated efficacy of a range of typhoid vaccines including whole cell inactivated vaccines [1], Vi capsular polysaccharide vaccines [2], live attenuated vaccines [3,4], and more recently Vi conjugate vaccines [5]. The World Health Organization has recommended that countries consider the use of typhoid vaccines for high risk groups and populations, and for outbreak control [6]. Despite this, typhoid vaccines have not been widely applied in typhoid endemic areas or are they often used in outbreaks. The papers in this supplement address some of the barriers to and pathways for wider use of typhoid vaccines.

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Conflicts of interest statement: JAC serves as a Resource Advisor, Invasive *Salmonella* infections, World Health Organization Foodborne Diseases Burden Epidemiology Reference Group; an Expert, Institute for Health Metrics and Evaluation, Global Burden of Disease 2013 project; and a Reviewer, Coalition against Typhoid (CaT) typhoid vaccine investment case.

Reliable estimates of burden of disease are essential to build the investment case for disease control efforts. Indeed, an understanding of typhoid epidemiology at the national and sub-national level is needed for countries to adopt current WHO recommendations on use of typhoid vaccines [6]. Burden of disease estimates for typhoid fever have grown in sophistication since the 1980s [7-11]. Today, there is considerable convergence between recent estimates from groups at the International Vaccine Institute [12]; the Institute of Health Metrics and Evaluation [13]; and the World Health Organization Foodborne Diseases Epidemiology Reference Group [14]. This convergence might provide reassurance about the accuracy of the estimates or may simply reflect use of similar sets of quite limited input data following broadly similar natural history models. In their paper, Luby and others review approaches to typhoid fever surveillance [15]. They advocate for affordable systems that combine sentinel laboratory facilities with community-based surveillance of health care facility use in order to provide reliable data from many sites to both improve global burden and to inform country-level policies. Andrews and others outline the challenges inherent to improving diagnostics for typhoid fever, an area where advances would not only help to extend surveillance efforts but also improve patient management and outcomes [16].

Strengthening the quality and representativeness of typhoid fever incidence data has proven challenging, but securing reliable estimates of complications and deaths is even more difficult [17]. The lack of robust data on disability and deaths is of concern, since these metrics are key elements for decision making on investments in typhoid fever control against competing health conditions. Naz and others describe approaches to sure up estimates of typhoid fever deaths, including by improved tracking of health records from large healthcare facilities in endemic areas [18]. Since effective and timely antimicrobial therapy is lifesaving in typhoid fever, the emergence and expansion of antimicrobial resistant *Salmonella* Typhi threatens to fuel complicated and fatal infection. Kariuki and others describe the current sobering situation with antimicrobial resistance in *S. enterica* [19]. The growing challenge of effectively treating invasive *Salmonella* infections sharpens focus on prevention, including with vaccines.

Vaccine probe studies have proven useful for better defining burden of illness for other vaccine-preventable illnesses including those caused by *Haemophilus influenzae* type b, *Streptococcus pneumoniae*, and rotavirus. Accounting for vaccine efficacy, the difference in disease incidence between vaccinated and unvaccinated persons represents the vaccine preventable disease incidence, a valuable input for disease burden estimation [20]. Gessner and others develop the case for a typhoid vaccine probe study and examine the design and required scale of such a study [21]. Besides providing improved burden of disease data, vaccine probe studies make typhoid vaccine available to large populations thereby serving as a bridge between burden of disease research and implementation.

Overviews of the status of typhoid vaccines and vaccine development efforts have been described elsewhere [22]. In this supplement Tennant and others provide an update on the situation with live attenuated vaccines for *S. enterica* [23]. They highlight the need to develop multivalent vaccines protective against both typhoidal and non-typhoidal serovars of *S. enterica*.

Typhoid transmission dynamic models are key to exploring the potential impact of various typhoid vaccines under a range of epidemiologic conditions and vaccine strategies. Extending burden data and transmission models to include economic evaluation builds the investment case for support of vaccine interventions. Progress has been made in all of these areas for typhoid fever in recent years. In this supplement Watson and others review available transmission models and economic analyses, highlighting gaps in data required to inform models, summarizing their key findings, and identifying areas of priorities for future work [24].

Further underscoring the importance of robust, local epidemiologic data on typhoid fever, Date and others examine strategies for using available typhoid fever vaccines for endemic and epidemic typhoid fever, both in community-based and school-based programs [25]. Khan and colleagues detail their experience with school-based Vi polysaccharide vaccination pilot programs in two districts in Kathmandu, Nepal, and two towns in Karachi, Pakistan [26].

Despite the availability of a range of efficacious vaccines [2-5], typhoid fever continues to exact a substantial toll of illness and death worldwide each year [12,13]. Taken together, the papers in this supplement help to plot the path toward rational and wider use of typhoid vaccines in populations at greatest risk.

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