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Using surveillance and economic data to make informed decisions about rotavirus vaccine introduction

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Abstract

While rotavirus vaccines are available, safe, and effective, many countries are not yet widely using these vaccines. Surveillance for rotavirus disease and potential vaccine adverse events is critical for country decision making about rotavirus vaccine. This special issue shares rotavirus and intussusception disease surveillance data and rotavirus vaccine cost-effectiveness analyses from countries that have yet to introduce rotavirus vaccines into their routine infant immunization programs. The studies highlight the substantial burden of rotavirus disease and the cost-effectiveness of rotavirus vaccine in a broad set of countries without rotavirus vaccine in their routine immunization programs.

Keywords

Rotavirus; Vaccine; Surveillance; Economic analyses; Vaccine safety; Intussusception

Diarrhea remains a leading cause of death and disease in children worldwide and confers substantial morbidity and long-term health consequences [1]. Rotavirus is the leading cause of pediatric diarrhea, and available rotavirus vaccines are safe and effective in reducing rotavirus-specific and all-cause diarrhea mortality in a wide variety of settings [2,3]. The World Health Organization (WHO) recommends that countries prioritize the inclusion of rotavirus vaccine in their national immunization programs, especially countries with a high burden of mortality due to rotavirus gastroenteritis, such as those in south and south-eastern Asia and sub-Saharan Africa [3]. However, rotavirus vaccines are used in the routine immunization program of less than half of WHO member states and are not commonly used in Asia where rotavirus disease burden is high (Fig. 1). Rotavirus vaccine coverage lags behind all other childhood vaccines recommended by WHO and only reaches a quarter of the world's children [4].

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Surveillance for rotavirus and potential vaccine adverse events is key to generate local data for decision making regarding vaccine introduction. Thus, the focus of this special issue is to share country-level data from regions with slower rotavirus vaccine uptake. This supplement contains three types of articles from countries that have yet to introduce rotavirus vaccine into their routine infant immunization programs: (1) analyses of the epidemiology and clinical characteristics of children enrolled in rotavirus surveillance programs, (2) descriptive analyses from surveillance of intussusception, a bowel obstruction caused by many factors that has been identified as an adverse event linked with rotavirus vaccination, and (3) projected cost-effectiveness analyses for rotavirus vaccination programs (Table 1). WHO coordinates the Global Rotavirus Surveillance Network (GRSN), a network of more than 130 sentinel hospitals in more than 50 primarily low- and middle-income countries that conduct surveillance for rotavirus in children hospitalized with acute watery diarrhea [5,6]. Most of the analyses in this special issue come from countries that have conducted surveillance as part of GRSN with support from WHO, the Gavi Alliance, and other partners.

One could ask why it is necessary to continue surveillance for rotavirus and intussusception considering the vast and growing published data on rotavirus disease and the impact of rotavirus vaccination [2]. First, rotavirus surveillance helps document burden of disease and circulating genotypes before vaccine is introduced (Fig. 2). Although rotavirus diarrhea occurs in all countries globally and local rotavirus disease burden should not be a prerequisite for countries to decide to introduce rotavirus vaccine [3], there is a wide range of morbidity related to rotavirus infections [6,7], and local data can be useful to inform country-specific vaccine policy decisions. Baseline burden from routine surveillance systems has been used by many countries to justify rotavirus vaccine introduction in Gavi vaccine introduction grant applications [8]. Among the 16 countries from 5 WHO Regions with rotavirus disease surveillance manuscripts in this special issue, the annual prevalence of rotavirus among children hospitalized with acute watery diarrhea ranged from 13% in Azerbaijan [9] to 64% in Bangladesh [10], with all but two reporting a prevalence of at least 30%. Rotavirus surveillance also contributes to rotavirus vaccine cost-effectiveness analyses which have been used by many countries to make or support decisions to introduce rotavirus vaccine [11]. All three cost-effectiveness analyses in this special issue found that rotavirus vaccination was a cost-effective intervention.

Since a previously available rotavirus vaccine was associated with an increased risk of intussusception [12], monitoring the safety of the current rotavirus vaccines is needed [13,14]. As is done in the six intussusception surveillance manuscripts in this special issue, describing the epidemiology of intussusception is important before rotavirus vaccine introduction [3], and establishing standardized intussusception surveillance prior to vaccine introduction can act as a platform to evaluate the risk once vaccine has been introduced [15]. Surveillance for intussusception is often conducted in conjunction with rotavirus disease surveillance and often in the same hospitals.

Pediatric diarrhea surveillance systems also have other benefits beyond the initial decision to introduce rotavirus vaccines. The surveillance systems provide a platform for documenting short- and long-term vaccine impact and effectiveness. Sentinel hospital-based surveillance

for rotavirus can be used to document vaccine effectiveness through test-negative case-control study designs [16]. Although not the focus of the papers included in this special issue, ongoing surveillance is needed to monitor vaccination programs and determine the impact of vaccine on the burden of disease, the ultimate goal of any vaccination program. This topic is covered in manuscripts from a separate concurrent special issue in *Vaccine* and a recent supplement in *Clinical Infectious Diseases* that both focused on rotavirus vaccine impact in early-adopting lower income countries [17,18]. In addition, new rotavirus vaccines currently under development or prequalified (i.e., approved for procurement and use) by WHO will need to be monitored with ongoing surveillance [19,20].

These surveillance systems also allow for investigation of other causes of pediatric diarrhea in the post-rotavirus vaccine era. Rotavirus remains a leading cause of diarrhea in children even after rotavirus vaccine is introduced, but other causes of diarrhea with vaccines in the development pipeline, such as Shigella, enterotoxigenic *Escherichia coli* (ETEC), and norovirus, are now causing a larger proportion of pediatric diarrhea [21]. In 2017, approximately 30 countries in GRSN were leveraged to conduct Global Pediatric Diarrheal Surveillance which continues to monitor the impact of rotavirus vaccine while also testing for other etiologies of severe pediatric diarrhea in the post-rotavirus vaccine era [6].

The use of these valuable surveillance data both before and after vaccine introduction highlight the need to maintain high quality global rotavirus and pediatric diarrhea surveillance. Sentinel surveillance for pediatric diarrhea with laboratory-confirmation of rotavirus in one or more sites per country as recommended by WHO is sufficient to meet these objectives and make policy decisions at a country and global level [22,23]. Surveillance should ideally be maintained long-term and for at least 2–5 years after vaccine introduction to continue monitoring the impact of the vaccine on disease and circulating genotypes and to maintain laboratory capacity for testing rotavirus. Updated rotavirus surveillance standards will be available from WHO in 2018 (http://www.who.int/immunization/monitoring_surveillance/burden/vpd/standards/en/).

The studies in this special issue reinforce the substantial burden of rotavirus disease and the cost-effectiveness of rotavirus vaccine in countries that have not yet introduced rotavirus vaccine into their national immunization programs and should facilitate decision making regarding rotavirus vaccine introduction. Publishing papers such as these make comparable data available for decision makers and their partners in all countries. It is critical that countries remain vigilant in monitoring rotavirus disease, other causes of diarrhea in children, and intussusception after rotavirus vaccine is introduced.

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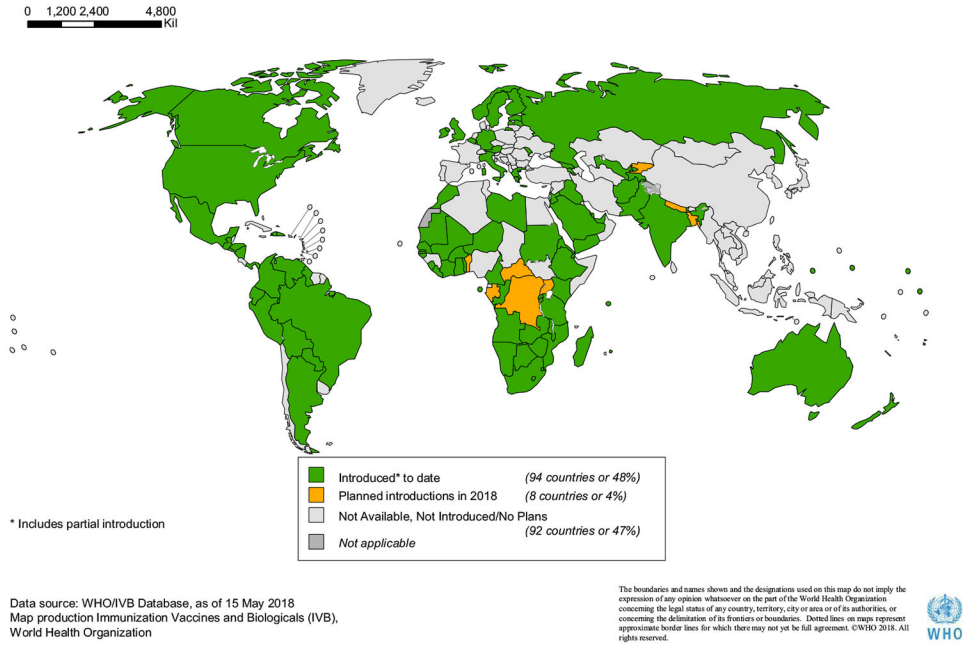

Fig. 1.

Countries with rotavirus vaccine in the national immunization programme and planned introductions in 2018.

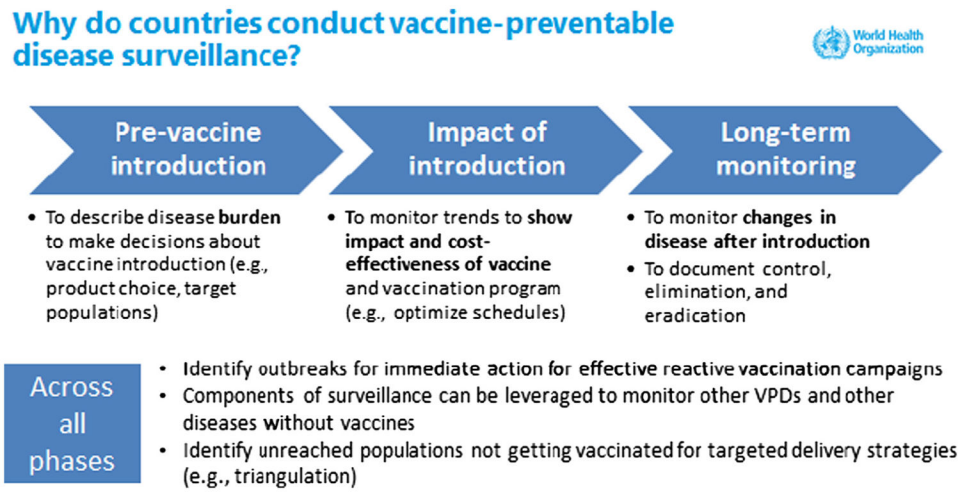

Fig. 2.
Why do countries conduct vaccine-preventable disease surveillance?

Table 1

Manuscripts included in this special issue.

Rotavirus disease surveillance	Intussusception surveillance	Projected rotavirus vaccine cost-effectiveness
African Region	Eastern Mediterranean Region	Eastern Mediterranean Region
• Nigeria	• Pakistan	• Afghanistan
Eastern Mediterranean Region	South-East Asian Region	• Pakistan
• Afghanistan	• Bangladesh	Western Pacific Region
European Region	• India	• Lao People's Democratic Republic
• Azerbaijan	• Nepal	
• Tajikistan	Western Pacific Region	
• Ukraine	• China	
South-East Asian Region	• Vietnam	
• Bangladesh		
• India		
• Indonesia		
• Myanmar		
• Nepal		
• Sri Lanka		
• Regional		
Western Pacific Region		
• Cambodia		
• Lao People's Democratic Republic		
• Mongolia		
• Philippines		
• Vietnam		