

# Introducing rotavirus vaccine to the Palestinian territories: the role of public–private partnerships

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## ABSTRACT

**Background** Introducing childhood immunization poses challenges in environments of societal fragility. The Palestinian territories (Pt) are considered ‘fragile’ because of their lack of political, economic and territorial sovereignty. Poverty is rife, infant mortality high, and diseases associated with overcrowding widespread. Under these circumstances the Rostropovich Vishneskaya Foundation (RVF) has assembled a network of public and private stakeholders to introduce a country-wide rotavirus immunization program.

**Methods** The incidence of diarrhea was determined for 18 months before and 18 months after the introduction of rotavirus vaccine among all children younger than 5 years presenting to outpatient clinics in Gaza with three or more loose stools per day. Simultaneously the prevalence of rotavirus was established by rotavirus antigen detection in stool samples collected from children younger than 3 years at Caritas Baby Hospital in Bethlehem during the corresponding time periods.

**Results** Within 12 months 97.4% immunization coverage was achieved. The incidence of diarrhea dropped by 32.2%, while the prevalence of rotavirus in stool samples decreased by 64.6% throughout the following year.

**Conclusion** In environments of economic or political instability private–public partnerships for the introduction of comprehensive vaccination programs can work based on close collaboration, shared vision, flexibility and inter-organizational trust.

**Keywords** immunization, management and policy, population-based and preventative services

## Background and introduction

Palestine or the ‘Palestinian territories’ (Pt) of Gaza and the West Bank are considered highly ‘fragile’ under the OECD definition of fragile states.<sup>1</sup> The territories’ fragility comes less from inadequate service provision, but rather from the absence of territorial, economic and political sovereignty.<sup>2</sup> The legitimacy of the Palestinian Authority is challenged both internally and externally making public–private partnerships difficult.<sup>3</sup> Basic health care services are available in the Pt, but the territorial fragmentation and the constraint of travel between the territories make an integration of services and a meaningful referral system difficult, while creating administrative redundancy and cumbersome bureaucracies.<sup>4</sup> Poverty rates remain high, while challenges to water and electricity supply in Gaza, as well as the limitation of

movement of goods and people between the territories inhibit economic development.<sup>5</sup> Infant mortality remains high at 18.9/1000 live births compared to Israel’s of 3.9/1000 and has increased over the last 5 years.<sup>6,7</sup> Basic health services are provided by the Palestinian Authority as well as UNRWA (The United Nations Relief and Works Agency for Palestinian Refugees in the Middle East).

Particularly among the urban poor living in the crowded slums of Gaza diarrhea is very prevalent among children under 5 years of age, reaching 25% among infants younger

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than 6 months, especially for families with poor access to potable water.<sup>8–10</sup> Rotavirus tends to be the most prevalent pathogen accounting for up to 45% of hospitalizations for diarrhea in the region especially among children younger than 3 years of age.<sup>11,12</sup> A study of 150 children presenting with diarrhea to the Central Pediatric Hospital in Gaza documented that 28% suffered from rotavirus infection, 17% from *Entameba histolytica* and other parasites, and 18% from a variety of bacterial pathogens.<sup>13</sup> Infections with rotavirus in the Eastern Mediterranean Region typically follow a seasonal pattern similar to that of other temperate climate regions with peaks in the cooler winter months and lower levels during the summer.<sup>14,15</sup> Lows of 7–10% of rotavirus prevalence in unimmunized children with diarrhea during the midsummer months and highs of up to 75% during the winter have been described throughout the region.<sup>15</sup>

In 2006 two live oral rotavirus vaccines were introduced successfully in the USA and Europe. The vaccines showed excellent efficacy (85–98%) and were associated with a 17–55% decline in hospitalizations for gastroenteritis overall.<sup>16–18</sup> In 2009 the WHO recommended the global use of rotavirus vaccine, and 79 countries had implemented a national vaccine program including rotavirus vaccine by 2015.<sup>16</sup> These countries include Israel and Jordan, but not Lebanon or the oPt.

Immunization coverage for measles, hepatitis B, BCG, diphtheria, pertussis, polio and tetanus is comprehensive

(90.9–98.2%) in the Pt,<sup>19</sup> and a majority of children with diarrhea receive adequate oral rehydration management.<sup>20</sup> In this environment of economic and political fragility on the one side and poverty and disease prevalence on the other, the Rostropovich Vishneskaya Foundation (RVF) has assembled an alliance of key stakeholders including private, public as well as regional and international non-governmental organizations in order to introduce a comprehensive rotavirus immunization program for all children in the Pt.

The RVF negotiated with Glaxo Smith Kline (GSK) to provide the Rotarix<sup>TM</sup> vaccine at a price that can be sustained by the Palestinian Authority Ministry of Health (MoH) on a long term basis, based on recommendations provided by the Global Alliance for Vaccines and Immunization (GAVI). The RVF solicited funding from USAID for the West Bank component and from the Emirates Red Crescent as well as the Arab Fund for Economic and Social Development (Arab Fund) primarily for the Gaza part of the project. The vaccines were purchased and delivered by UNICEF with funding provided by the RVF and distributed to MoH and UNRWA storage facilities. RVF provided MoH and UNRWA staff members with training in vaccine administration, maintenance of cold chains and limitation of wastage, as well as maintenance of supplies and timely delivery of vaccines to storage and immunization sites. Vaccination coverage rates and adverse events following immunization were monitored by the RVF (Fig. 1).

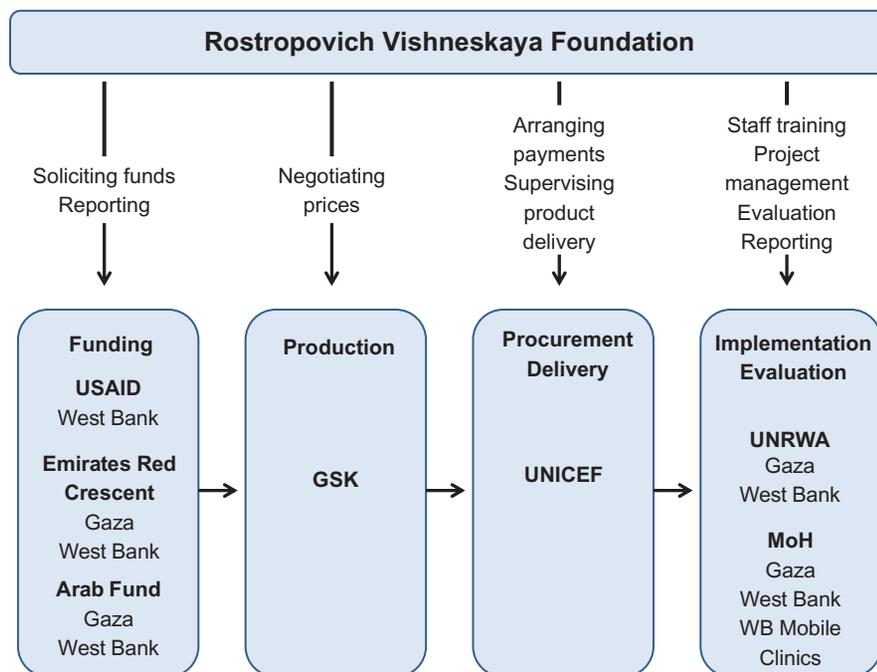


Fig. 1 Organogram of stakeholders in rotavirus vaccination program for the Palestinian territories.

## Methods

Program impact was documented analyzing the incidence of diarrhea in children younger than 5 years of age presenting to all 22 UNRWA and 28 MoH outpatient clinics in Gaza. Diarrhea was defined as three or more liquid or semi-solid stools per day for a duration of up to 14 days.<sup>21</sup> Clinical data is collected routinely by all clinics and reported to the MoH monthly for inclusion in public health data sets made available to the public every 6 months. The incidence of diarrhea for the year before vaccine introduction (2015) was compared with data from the years of (2016) and the year after vaccine introduction (2017) using a *t*-Test format following an ANOVA analysis of variance with the help of GraphPad InStat 3 software (GraphPad Software, Inc, La Jolla, CA, USA).

In addition, the prevalence of rotavirus antigen in stool samples collected from all children younger than 3 years presenting with diarrhea at the inpatient and outpatient services of the Caritas Baby Hospital in Bethlehem in the West Bank was established by Rota Stick One-Step Assay (Novamed, Israel). Mean rates of rotavirus+ stool samples were compared for the year before (2015), and the year after (2017) vaccine introduction in a *t*-Test format.

During the first 12 months of the project 130 773 children were born in the Pt, 58 446 in Gaza and 72 327 in the West Bank. Birth rates were distributed evenly throughout the year. The rotavirus immunization was initiated in May of 2016 in all 14 health districts of the West Bank and in all five health districts in Gaza targeting all babies born 1 March or later. Dosing schedules followed the WHO recommendations with a first dose given between 6 and 14 weeks followed by a second dose between 14 and 24 weeks of age.<sup>22</sup> Between May 2016 and April 2017 129 695 babies received their initial dose (99.2% of the eligible birth cohort). By the end of June 2017 127 396 babies had received a second dose of the vaccine (97.4% of the eligible birth cohort).

## Results

In 2015, 59 567 children under the age of 5 presented to outpatient clinics in Gaza with diarrhea at an average rate of 4964 cases per month (Standard Deviation 466). During 2016 the case load dropped to 50 684 with a monthly average of 4224 (SD 811). While the average monthly incidence of diarrhea remained at the 2015 level for the first 5 months of 2016, a precipitous drop was noted during the remaining 7 months of the year 2016 following the introduction of Rotarix<sup>TM</sup> in May of that year. During 2017 the incidence of

diarrhea remained at the level of the second half of 2016 with a total case load of 40 410 at a monthly average of 3368 (SD 475) (Fig. 2). No children presented to UNRWA or MoH health facilities in Gaza with signs of intussusception within 30 days of vaccine administration during the study period. Equally, no children returned to their clinics within 7 days of vaccination because of fever, irritability or diarrhea.

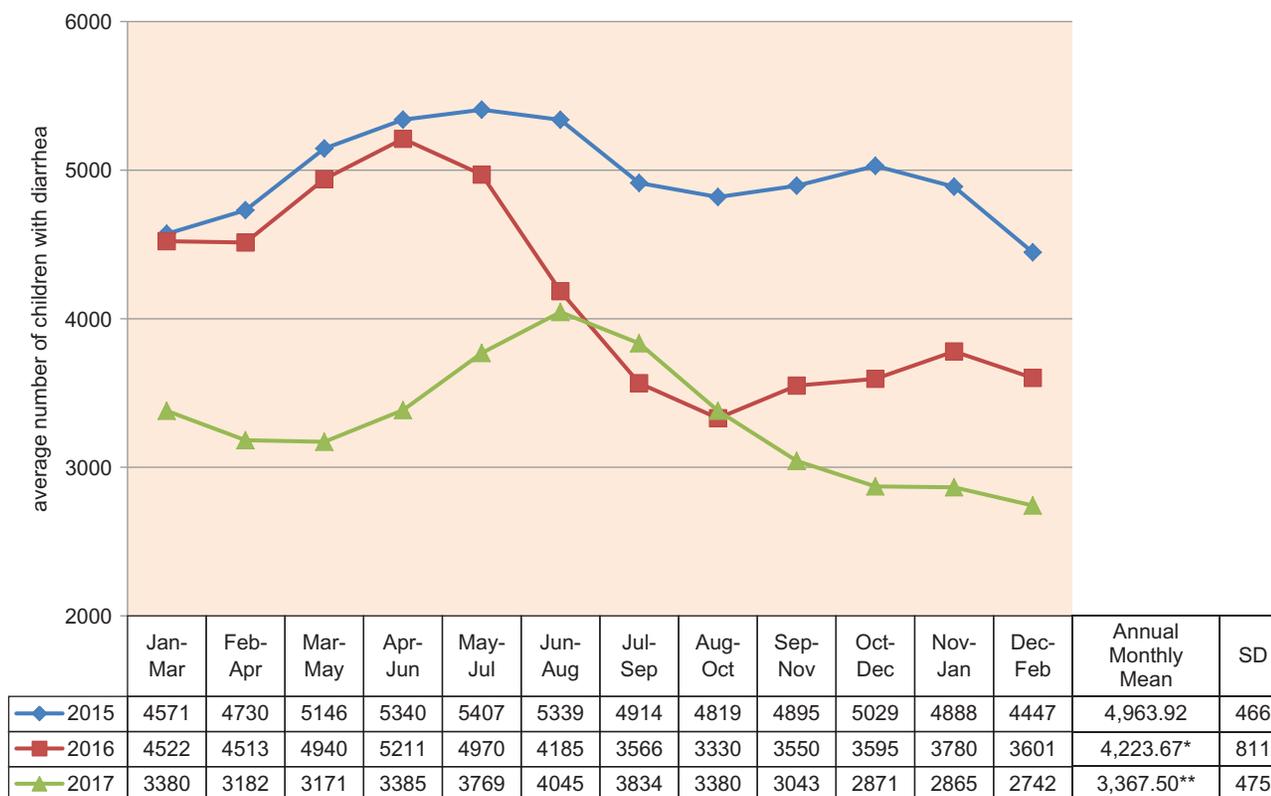
A one-way ANOVA analysis of variance confirmed significant differences of the average monthly case loads between the 3 study years at  $P < 0.001$  for a significance level of 0.05. A student *t*-Test showed a decrease of cases by an average of 740 per month between 2015 and 2016 ( $P = 0.011$ ; 95% CI: 206–1275). Between 2015 and 2017 the decrease of average monthly diarrhea incidence was even more significant at 1 596 cases ( $P < 0.001$ ; 95% CI: 1241–1951) (Fig. 2).

A similar trend could be observed analyzing the prevalence of rotavirus antigen in stool samples of children younger than 3 years of age presenting with diarrhea at the inpatient and outpatient services of the Caritas Baby Hospital in Bethlehem, the main pediatric hospital for the south of the West Bank between January of 2015 and December of 2017. A total of 2217 children presented with diarrhea during 2015, 2180 during 2016 and 1512 during 2017. All patients provided stool samples that were tested at the hospital's laboratory for rotavirus antigen. During the pre-immunization period of the study rotavirus prevalence showed a seasonal pattern with rising levels in December, peaks during March and April and lows from June to November, in line with other countries in the region.<sup>15</sup> The introduction of the rotavirus vaccine provided a significant drop in the rotavirus prevalence, both during high and low prevalence seasons. The overall monthly rotavirus prevalence dropped from an average of 49.8 cases in 2015 to 17.6 cases in 2017 ( $P = 0.005$ ; 95% CI: 11.2–53.3) (Fig. 3).

## Discussion

### Main finding of this study

By assembling and coordinating a network of public, private, local, regional and international stakeholders the RVF was able to foster, direct and monitor the introduction of a country-wide immunization program against rotavirus in the Pt. Within 2 months of program initiation more than 97% of infants throughout the West Bank and Gaza had been immunized, a level that could be sustained throughout the 18 months post-vaccination observation period. During the same time, the number of children presenting with diarrhea at pediatric outpatient facilities in Gaza dropped by a third



**Fig. 2** Three-month rolling averages for acute diarrhea cases among children under age 5 presenting at health centers in Gaza across the years 2015, 2016 and 2017. \*Comparing mean monthly diarrhea case load differences between 2015 and 2016:  $P = 0.011$  (95% CI: 206–1275), \*\*comparing mean monthly diarrhea case load differences between 2015 and 2017:  $P < 0.001$  (95% CI: 1241–1951).

compared to pre-immunization periods, while the prevalence of rotavirus in stool samples investigated at a large pediatric hospital in the West Bank dropped by 65%.

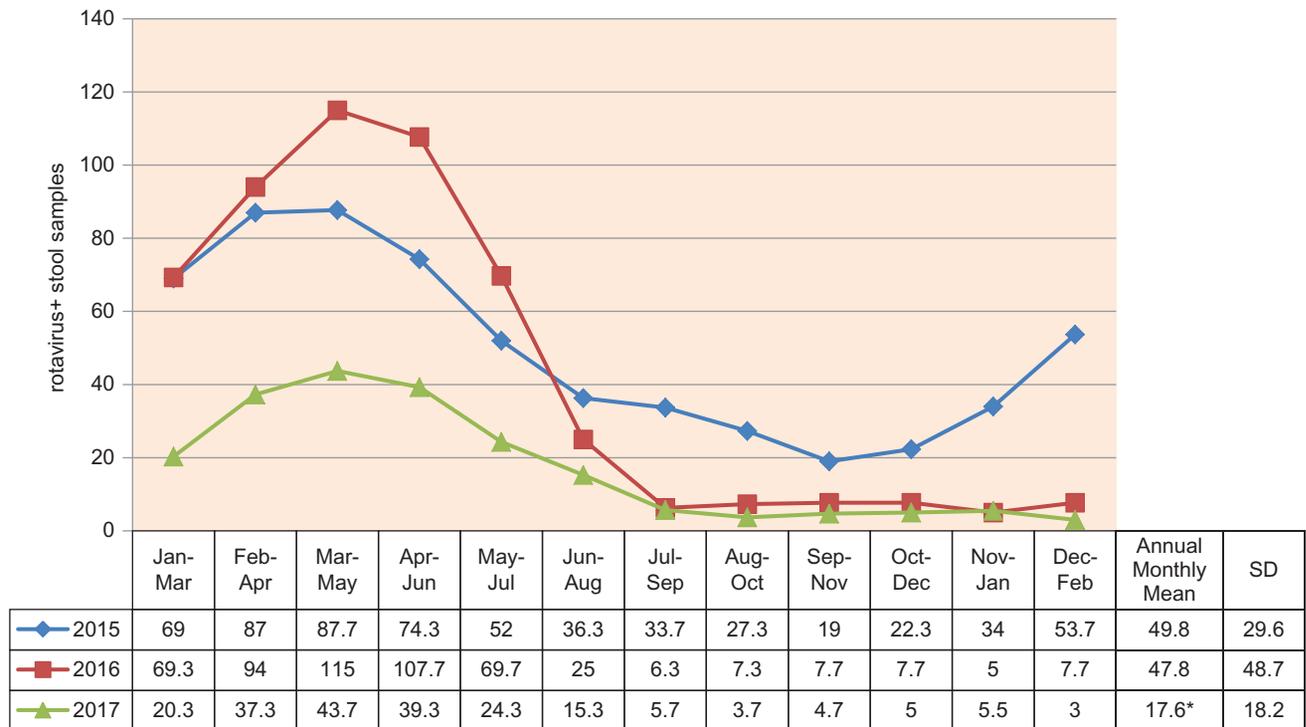
### What is already known on this topic

In countries with newly implemented rotavirus vaccination programs a rapid decline in cases of severe gastroenteritis was observed in young newly immunized infants followed by a progressive decline in hospitalization for older children several years after the introduction of the vaccine.<sup>23,24</sup> In our program we also observed a rapid and sustained decline of cases of gastroenteritis within 2 months of the initiation of the rotavirus immunization program. As the program continues we expect to see a further decrease in gastroenteritis cases among older children as well, as the number of source cases for the spread of rotavirus infection drops. We also noted that the seasonal variations observed with rotavirus infection in unimmunized communities in temperate climates tend to diminish significantly after the introduction of the vaccine—an observation that has been made elsewhere in the region before.<sup>25</sup>

### What this study adds

In many low and middle income countries (LMICs), the private sector plays an important role in health care service delivery. For-profit private providers, non-governmental organizations (NGOs), international donors and traditional practitioners may provide immunization services with or without coordination with local governments.<sup>26</sup> Particularly in ‘fragile’ states NGOs may provide immunization programs on an ad-hoc emergency relief basis.<sup>27</sup> Regulation, contracting, financing, social marketing, training and program coordination are important challenges for private–public collaboration.<sup>28</sup> Particularly the introduction of new vaccines by private service providers may produce obstacles to the public sector, when demands for new vaccines are being created before the public sector is ready to meet them, or when services are provided only to parts of the populations.<sup>29</sup>

The Middle Income Country (MIC) Task Force convened by the WHO in 2015 has identified four areas of unmet needs in countries struggling with the introduction of comprehensive immunization programs: (i) the capacity for evidence-based decision making; (ii) the political commitment to generate and sustain the financing for national



**Fig. 3** Three-month rolling averages of rotavirus+ stool samples in children under the age of 3 presenting with diarrhea at the Caritas Baby Hospital in Bethlehem across the years 2015, 2016 and 2017. \*Comparing mean monthly rotavirus+ stool sample differences between 2015 and 2017:  $P = 0.005$  (95% CI: 11.2–53.3).

immunization programs; (iii) the demand and equitable delivery of immunization services; and (iv) the timely and affordable access to vaccines.<sup>30</sup> While the task force has identified the need for ‘targeted technical assistance’<sup>30</sup> to LMIC countries, it does not offer specific strategies or solutions. In this environment, the RVF has created an organizational network of key stakeholders to provide technical, strategic, managerial and financial assistance to their public partner who in turn is enabled to plan, introduce and sustain a large scale immunization program. The successful public–private partnership is based on inter-organizational trust and information transfer, close cooperation with clearly defined roles and responsibilities, the integration of the program into the local governmental public health agenda, appreciation of and respect for respective organizational limitations and challenges, the fostering of organizational flexibility in the interest of a greater good, and the development of appropriate and measurable performance indicators.<sup>31</sup>

GAVI was willing to align the Pt with countries on the list of nations qualifying for GAVI support. GSK showed flexibility in product pricing. USAID agreed to support the West Bank component of the project while maintaining the US no-contact policy with the regional administration in Gaza at the time. The Emirate Red Crescent and the Arab Fund

picked up the funding for the Gaza component of the project, while UNRWA and the MOH of the Palestinian Authority collaborated in the project implementation on the ground. RVF secured the funding and oversaw the overall program administration, designed and supported the implementation of the project training component, administered a program monitoring and evaluation tool, and maintained data exchange and information transfer between partners.

### Limitations of this study

Most international studies use a 24 months post-vaccination observation period allowing for the establishment of a herd protection effect of the vaccine. The introduction of the rotavirus vaccine in any community will decrease the number of potential source cases for the spread of infection and thereby decrease rotavirus prevalence not only among the vaccinated infant population, but also among their older siblings and contacts.<sup>16</sup> While we observed significant decreases in gastroenteritis case loads for children as well as a substantial decline in rotavirus prevalence during an 18 months period following the introduction of Rotarix<sup>TM</sup> vaccine, we believe that the effect might even be stronger after a longer post-immunization observation period.

## Conclusion

The RVF has succeeded to introduce a national rotavirus immunization program for all children born in the Pt using a network of private, public, regional and international organizations. Cases of gastroenteritis as well as rotavirus prevalence among children with diarrhea dropped significantly within two months of program initiation, indicating a comprehensive protection against rotavirus infection. A further drop in gastroenteritis cases can be expected in the future as source cases for the spread of infection decline with the continuation of the program.

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